Abstracts and Case Studies From the College of American Pathologists 2009 Annual Meeting (CAP ‘09)

Abstract and case study poster sessions will be conducted during the College of American Pathologists Annual Meeting (CAP ‘09), which is scheduled for October 11 to October 14, 2009. The meeting will take place at the Gaylord National Resort, National Harbor, Maryland. The poster sessions will occur in the Connection Café and Exhibits Hall. Specific dates and times for each poster session are listed below. Also shown below each poster session listing are the subject areas that will be presented during that session.

POSTER SESSION 100: SUNDAY, OCTOBER 11, 2009, 9:00 AM–11:30 AM

Gastrointestinal and Liver Pathology

Blue Nevus of the Colorectal Mucosa
(Poster No. 1)

Zvika J. Schreiber, MD (zschreiber@notes.cc.sunysb.edu); Timothy R. Pal, MD; Sonya Hwang, MD. Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

The blue nevus is a benign melanocytic proliferation that generally occurs on the skin. Infrequently, blue nevi are found on mucosal surfaces. The most common location for mucosal blue nevi is the oral mucosa, with reported cases in the sinonasal mucosa, genital tract, and other locations. To our knowledge, blue nevi of the anorectal mucosa have not been reported. We report the case of an asymptomatic 60-year-old woman who presented for a high-risk screening colonoscopy after being diagnosed with 2 tubular adenomas during the previous year. The study revealed a pigmented lesion in the colorectal region, adjacent to the anal transition zone. Histologic sections revealed otherwise unremarkable colonic and transitional mucosa with pigmented cells in the lamina propria. The pigmented cells consisted predominantly of long dendritic melanocytes with scant cytoplasm and abundant fine melanin granules. The nuclei were round to ovoid with a uniform chromatin pattern and inconspicuous nucleoli. No cytologic atypia or mitotic figures were identified. Scattered melanophages were also present. All of the previously mentioned features are consistent with the diagnosis of blue nevus (Figure 1). As with any pigmented lesion, the possibility of melanoma should be considered. Although mucosal melanomas are rare, 24% arise in the anorectal region. These patients commonly present with pain, rectal bleeding, and a polyloid mass. There are also rare reports of malignant transformation of cutaneous blue nevi. Pigmented lesions, including blue nevi, of the anorectal region are rare and sampling is indicated to rule out malignancy.

Evaluation of Mast Cells and Their Association to Eosinophils in the Gastrointestinal Tract of the Pediatric Population
(Poster No. 2)

Yasi Saffari, MD1; Kristen Thomas, MD; Kerry Zabriskie, NP2; Joseph Levy, MD; M. Alba Greco, MD1. Departments of 1Pediatric Pathology and 2Pediatrics, New York University, New York.

Context: Intestinal mast cells have been known to be related to food allergy and immediate hypersensitivity and are implicated as a Th2-mediated regulator in eosinophilic gastritis. In this study, numbers of mast cells and eosinophils were investigated in biopsies from the upper gastrointestinal tract of children (n = 30; mean age, 14 years) with histopathologically confirmed eosinophilic enteropathy (n = 7), inflammatory bowel disease (n = 10), nonspecific chronic inflammation (n = 6), and no pathologic changes (n = 7).

Design: Formalin-fixed samples from stomach and duodenum were stained using toluidine blue to highlight the mast cells. Quantitative evaluation of mast cells and eosinophils was performed counting their number per 10 high-power fields.

Results: In the histopathologically defined groups, clear correlation between mast cell and eosinophil numbers was detected in patients with eosinophilic enteropathy (stomach, P = .02; duodenum, P = .03) and inflammatory bowel disease (stomach, P = .04; duodenum, P = .02). Overall, the mean number of mast cells was higher in stomach than in duodenum in all groups aside from their pathologic diagnosis (11.6 ± 1.3 stomach vs 8.1 ± 1.9 duodenum, mean ± standard error of the mean, P = .004).

Conclusions: Our results demonstrate the participation of mucosal mast cells in stomach and duodenum in disease process with more eosinophils and in inflammatory bowel disease. In these cases, increased numbers of mucosal mast cells along with eosinophils may indicate a role of mast cells as a regulatory mediator of visceral hypersensitivity due to either dietary antigens or inflammatory stimulator. Further studies will help in understanding the role and distribution of mast cells particularly in the gastrointestinal tract of children.

A Case of Systemic Mastocytosis and Anal Squamous Carcinoma
(Poster No. 3)

Michele K. McElroy, MD; Lance L. Stein, MD; Bard Cosman, MD; Samuel B. Ho, MD; Jessica Wang-Rodriguez, MD. Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

A Case of Systemic Mastocytosis and Anal Squamous Carcinoma.
Acinar Cell Carcinoma With a Prominent Intraductal Growth Pattern
(Poster No. 4)
Adam D. Toll, MD (adam.toll@jeffersonhospital.org); Agnieszka K. Witkiewicz, MD. Department of Pathology, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

Acinar cell carcinoma of the pancreas is rare, accounting for less than 1% of pancreatic cancer. Patients are typically between the fifth and seventh decade of life and show a 2:1 male predominance. Symptoms tend to be nonspecific, and approximately 50% of patients have metastasis at time of presentation. There have been recent case reports of acinar cell carcinoma showing both intraductal and/or papillary patterns of growth that could potentially be mistaken for intraductal neoplasia. The cases reported to date have presented as solitary nodules. We describe the first case of acinar cell carcinoma with intraductal and tubuloglandular growth diffusely involving the pancreas. The patient is a 31-year-old woman who had suffered from multiple attacks of pancreatitis beginning in March 2007 requiring several hospitalizations. Imaging studies showed chronic obstructive pancreatitis and diffuse duct dilatation. The patient underwent distal pancreatectomy and splenectomy. Microscopic examination revealed acinar cell carcinoma with an intraductal growth pattern diffusely involving the pancreas (Figure 2) and extending to the proximal margin. Histologic findings in the completion pancreatectomy specimen revealed multiple foci of tumor with similar histologic findings to those seen in the distal pancreatectomy. Despite chemotherapy, the patient developed liver metastasis 6 months following her second surgery. We present a case of acinar cell carcinoma with a rare, diagnostically challenging histologic appearance. It is important to correlate clinical, histologic, and immunohistochemical findings to differentiate this lesion from a more benign intraductal neoplasm, notably intraductal papillary mucinous neoplasm.

Acute Fulminant Hepatic Necrosis in First 12 Hours of Amiodarone Administration
(Poster No. 5)
Vladislav Zakharov, MD (vladislav-zakharov@ouhsc.edu); Lewis A. Hassell, MD. Department of Pathology, University of Oklahoma, Health Sciences Center, Oklahoma City.

Amiodarone is a commonly used antiarrhythmic with well-known common side effects with prolonged therapy. We present a case of fulminant hepatic necrosis proven by liver biopsy following intravenous administration of amiodarone within the first 12 hours of infusion. A 60-year-old man with a history of congestive heart failure, chronic renal insufficiency, and positive serology for hepatitis C antibody was admitted to the hospital with complaints of gradually increasing shortness of breath and dyspnea on exertion. The results of initial liver function tests showed values within the reference range. An electrocardiogram on admission revealed atrial flutter with a variable rate and the patient was administered intravenous amiodarone. Within the first 12 hours of infusion repeat liver function testing showed extremely high hepatic parameters: aspartate aminotransferase 3491 U/L, alanine aminotransferase 2029 U/L, and bilirubin 3.77 mg/dL. Infusion of amiodarone was stopped. The patient developed symptoms of acute abdomen and an exploratory laparotomy was performed with a concern of ischemic bowel. However, other than an acutely edematous liver, there was no evidence of acute pathology, and wedge liver biopsy was taken. Microscopic examination of the liver sample revealed acute hepatic necrosis with minimal steatosis and mild chronic inflammation. The findings were consistent with acute fulminant hepatic necrosis secondary to intravenous amiodarone administration. Electron microscopy showed hepatocytes with phospholipid inclusions with occasional foci suggestive of amiodarone-type inclusions, with areas of cholestasis and steatosis. Although acute amiodarone hepatic toxicity is rare, pathologists should be aware of this possibility and associated histologic findings.

Assessment for Residual Intestinal Metaplasia and Dysplasia in Postablative Barrett Esophagus Using Deeper Jumbo Biopsies
(Poster No. 6)
Ajay J. Patel, MD (ajpatel1@gmail.com); Dawn Bradley, MD; Maria McIntyre, MD; Deborah Giusto, MD; Shriram Jakate, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Recent therapeutic trends for Barrett esophagus (BE) with high-grade dysplasia (HGD) are evolving toward local ablative therapies. Such therapy resolves both the dysplastic area and metaplastic bed. However, this poses new challenges in follow-up as residual and recurrent metaplastic or dysplastic foci become endoscopically invisible, buried under regenerative neoesophagus. This study documents our surveillance of postablative BE with deeper jumbo biopsies, ensuring recovery of buried glands.

Design: Review of our records from 2004 to 2008 identified 8 patients with BE who underwent ablation and follow-up surveillance with jumbo biopsies. The following characteristics were reviewed: indication, follow-up duration, presence of residual or recurrent metaplasia, dysplasia, and/or carcinoma.

Results: All 8 patients (6 men, 2 women; 62–83 years; mean age, 69 years) had ablation for metaplasia and HGD with margins free of dysplasia. Their follow-up ranged from 1 month to 5.4 years with a median of 1 year. Protocol surveillance jumbo biopsies included mucosa and superficial submucosa. At follow-up, 3 of 8 (37.5%) had no metaplasia or dysplasia, 3 of 8 had residual metaplasia without dysplasia, and 2 of 8 (25%) had metaplasia and focal HGD beneath neoesophageal mucosa.

Conclusions: Ablative therapy for BE with HGD produces prolonged dysplasia-free states in 75% of cases and metaplasia-free states in 37% of cases. When residual or recurrent metaplasia or dysplasia occurs, it is likely to be buried under a regenerated squamous lining. Although the endoscopic distinctiveness of the BE segment is lost through neoeosphagealized squamous mucosa, protocol surveillance using jumbo forceps is essential in ensuring assessment of submerged glands.

Morphoproteomics Defines the Cell Cycle Biology of Fibrolamellar Hepatocellular Carcinoma
(Poster No. 7)
Sadhna Dhingra, MD1 (Sadhna.Dhingra@uth.tmc.edu); Wei Li, MD; Dongfeng Tan, MD; Robert E. Brown, MD.1 Department of Pathology and Laboratory Medicine, University of Texas Health Sciences Center-
Medical School, Houston; and Department of Pathology, MD Anderson Cancer Center, Houston, Texas.

Context: Fibroblast growth factor receptor 1 (FGFR1) signaling is a frequent driver of colorectal cancer. However, the role of FGFR1 in primary or second primary colorectal cancers and its clinical significance is not well understood. We sought to investigate the FGFR1 signaling profile in primary and second primary colorectal cancers.

Design: This is a retrospective study of patients diagnosed with colorectal cancer from 2004 to 2018 at MD Anderson Cancer Center. We identified patients with a second primary colorectal cancer. FGFR1 expression was assessed by immunohistochemistry on formalin-fixed paraffin-embedded sections.

Results: Of the 26 patients with a second primary colorectal cancer, 24 cases had sufficient tissue available for analysis. The mean age at diagnosis of the second primary was 76.6 years. FGFR1 expression was positive in 17 cases (70.8%). Patients with FGFR1-positive tumors had a mean age at diagnosis of 77.3 years, while patients with FGFR1-negative tumors had a mean age of 76.2 years. There was no significant difference in the incidence of metastasis between the two groups (P = 0.12).

Conclusions: FGFR1 expression is common in second primary colorectal cancers. Future studies are needed to determine if FGFR1 expression has a clinical impact on patient outcomes.


dation of the tonsils revealed noncaseating epithelioid granulomas, along with reactive follicular hyperplasia, but no active inflammation. Acid-fast, Gomori methenamine silver, and Gram stains were performed to exclude tuberculous infection, fungi, and bacteria, respectively, and were read as negative. Considering the patient's history, the findings were consistent with the involvement of tonsils by Crohn disease. This is a rare manifestation of Crohn disease. Repeated episodes of tonsillitis in such a clinical setting related to its relatively indolent nature and chemoresponsiveness.

Design: Morphometric and protein analytes indicating cell cycle progression and inhibition were assessed in 7 cases of FLHCC. These included Ki-67 (G1, S, G2, M phases), S-phase kinase-associated protein (Skp) 2, and mitotic index. Inhibitors of G0, S phase included p27Kip1 and p16INK4a. The percentage of Ki-67–positive nuclei was determined by an automated cellular imaging system. Immunoreactivity of other markers was assessed for subcellular localization by bright-field microscopy.

Results: The mean percentage of Ki-67 nuclear positivity in neoplastic hepatocytes ranged from 1.0% to 29.7% in the 7 cases. Nuclear Skp2 immunoreactivity was negative and the mitotic index was very low (0–1 per 10 high-power fields). Correspondingly, all showed p16INK4a nuclear positivity. The adjacent nonneoplastic hepatocytes were negative for p16INK4a expression. Immunoreactivity for p27Kip1 was negative in 6 of 7 cases.

Conclusions: Morphoproteomic analysis reveals cell cycle arrest in the G0/G1, phase associated with overexpression of the cell cycle inhibitor p16INK4a in the nuclei of tumoral cells vis-a`-vis the nonneoplastic hepatocytes. In conjunction with our previous demonstration of a constitutively activated NFkB pathway in FLHCC, cell cycle arrest helps explain the biology of its indolent nature and also its relative chemoresistance.

A Rare Finding in a Patient With Crohn Disease

Sanda Alexandrescu, MD (sanda@erdani.com); Robert E. Brown, MD. Department of Pathology, University of Texas–Houston.

Crohn disease can occur anywhere in the gastrointestinal tract, with ileum and colon being the most affected parts. Rarely, it can occur in other places like the upper digestive tract, peritoneum, or tonsils. We report a case of involvement of the palatine tonsils, manifested as chronic tonsillitis. A 23-year-old African American woman with a history of ileum and colon being the most affected parts. Rarely, it can occur in other places like the upper digestive tract, peritoneum, or tonsils. We report a case of involvement of the palatine tonsils, manifested as chronic tonsillitis. A 23-year-old African American woman with a history of Crohn disease that was managed with immunosuppressive therapy presented with an episode of tonsillitis. A year prior she had experienced a sore throat and a peritonsillar abscess, which was treated with incision, drainage, and antibiotics. Considering the recurrent nature of the tonsillitis, it was decided to proceed with a tonsillectomy. Microscopic examination of the tonsils revealed noncaseating epithelioid granulomas, along with reactive follicular hyperplasia, but no active inflammation. Acid-fast, Gomori methenamine silver, and Gram stains were performed to exclude tuberculous infection, fungi, and bacteria, respectively, and were read as negative. Considering the patient's history, the findings were consistent with the involvement of tonsils by Crohn disease. This is a rare manifestation of Crohn disease. Repeated episodes of tonsillitis in such a clinical setting should always raise the suspicion for granulomatous tonsillitis to proceed with the best management for the patient.

Second Primary Colon Cancers Associated With First Primary Colon Cancers: A Population-Based Study

Noa Sagy, MPH (Noasagy@gmail.com); Donald E. Henson, MD; Heather Young, PhD; Steven Patierno, PhD. Department of Epidemiology, George Washington University School of Public Health and Health Services, Washington, DC; and Department of Pathology and The Molecular and Cellular Oncology Program, George Washington University Cancer Institute, Washington, DC.

Context: Patients diagnosed with a primary colorectal cancer are at increased risk of developing a second primary colorectal cancer. We studied second primary colon cancers in a population.

Design: Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) registry for 1973 to 2005. Data included the first and second primary invasive colorectal carcinoma. According to SEER, a tumor is considered a second primary if diagnosed more than 2 months after the first primary. The SEER Multiple Primary-Standardized Incidence Ratio tool was used to calculate the incidence of second primary cancers (observed/expected [O/E]).

Results: Of 574,726 cases with a first primary cancer in the colorectum, 7,137 developed a second primary in the colorectum (O/E, 1.45). Mean age at first primary was 67.9 years and for the second primary was 73.5 years. When stratified by race, African Americans had higher incidence of second primary tumors than whites (O/E, 1.83 vs 1.43), as well as a higher age-adjusted rate of first primary tumors. First and second primaries occurred at an earlier age in African Americans than in whites. All anatomical divisions of the colon showed a decrease in O/E with age. When analyzed by surface area, the mucosal surface of the colorectum was equally susceptible to second primary cancers in all anatomic divisions.

Conclusions: Persons with a first primary colorectal cancer are more susceptible to second primary cancers, specifically in the colon. First and second primary cancers in the colorectum show racial variations. No anatomic division of the colon appears to be more susceptible than any other to a second primary.

Cystic Lesions of the Pancreas: A Review of Cases in a 4-Year Period

Carlos E. Parra-Herrain, MD (cparraherrain@med.miami.edu); Monica T. Garcia, MD; Loren P. Herrera, MD; Pablo A. Bejarano, MD. Department of Pathology, University of Miami-Jackson Memorial Hospital, Miami, Florida.

Context: Cystic lesions of the pancreas represent a significant proportion of pancreatic cancers. The characterization and classification of these has evolved in recent years and will continue changing according to the increasing number of biopsies and resection performed.

Design: Pancreatectomy specimens collected during a 4-year period that had diagnosis of pancreatic cyst(s) were reviewed. The demographic and pathologic features were recorded.

Results: Of 361 pancreatic lesions, 97 cysts corresponding to 95 patients were studied. Overall, 61% occurred in women and the mean age was 60 years. Among the 97 cysts, 8% were nonneoplastic (pseudocysts, enterogenous, congenital, oncocytic, and squamous cysts) and 92% were neoplastic (58% benign, 10% borderline, 24% malignant) (Table). Intraductal papillary mucinous neoplasm (IPMN) was the most common diagnosis (48%). Benign and borderline neoplasms were mostly seen in the head (42% and 70%, respectively), whereas nonneoplastic and malignant cysts were more common in the tail (37% and 42%, respectively). Excluding patients with solid and cystic pseudopapillary tumor (SCPT) who were significantly younger (23 years; range, 16–38 years; P = .001), patients with borderline and malignant neoplasms were older (mean, 65.6 and 65.1 years, respectively) than patients with nonneoplastic cysts and benign neoplasms (mean, 61.6 and 61.1 years, respectively). Malignant cysts were significantly larger and borderline lesions (mean, 4.7 cm; P = .05).

Conclusions: In our series, most cystic lesions were neoplastic, mostly benign mucinous and malignant tumors. Location is not useful in differentiating malignant from nonneoplastic cysts. Malignancy in cystic neoplasms was associated with older age (when excluding SCPT) and larger size.

Distribution of Pancreatic Cystic Lesions

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign nonneoplastic (n = 8; 8.2%)</td>
<td></td>
</tr>
<tr>
<td>Pseudocyst</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>Enterogenous cyst</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>Congenital cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Oncocytic cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Squamous cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Benign neoplastic (n = 56; 57.7%)</td>
<td></td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>11 (11.3)</td>
</tr>
<tr>
<td>Oligocystic serous cystadenoma</td>
<td>11 (11.3)</td>
</tr>
<tr>
<td>Microcystic serous cystadenoma</td>
<td>11 (11.3)</td>
</tr>
<tr>
<td>IPMN benign</td>
<td>22 (22.6)</td>
</tr>
<tr>
<td>Cystic schwannoma</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Borderline neoplasms (n = 10; 10.3%)</td>
<td></td>
</tr>
<tr>
<td>Borderline mucinous neoplasm</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Borderline IPMN</td>
<td>9 (9.2)</td>
</tr>
<tr>
<td>Malignant neoplasms (n = 23; 23.7%)</td>
<td></td>
</tr>
<tr>
<td>IPMN malignant noninvasive</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>IPMN malignant invasive</td>
<td>11 (11.4)</td>
</tr>
<tr>
<td>Neuroendocrine cyst</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>SCPT</td>
<td>6 (6.1)</td>
</tr>
</tbody>
</table>
Discriminating Between Benign and Malignant Gastrointestinal Stromal Tumors Using CD10 Immunohistochemistry
(Poster No. 11)
Sharif Ali, MD (sali2@hfhs.org); Hwajeong Lee, MD; Adrian Ormsby, MD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan.

Context: Prediction of gastrointestinal stromal tumor (GIST) behavior has been studied for many years. The problem is that proposed tumor risk indices do not correlate closely with the malignant potential. Researchers are developing targeted anti-CD10 monoclonal antibody therapy, which may impact the future management of CD10 immunoreactive tumors. Our study aims to assess the utility of CD10 immunostaining in GIST and whether it can be a useful adjunct to define malignant tumors.

Design: Seventeen cases occurring since 2000 with at least 3 years of clinical follow-up were retrieved. Tumor locations included stomach (10 cases), small intestine (3), and colon (4). Two microarray blocks were created using a 3-mm needle, 2 cores from each case and the 5 metastatic sites.

Results: Cases were divided into benign (10 cases; no metastasis, local invasion, high-risk morphology, or recurrence) and malignant (7 cases; 6 exhibited distant metastases, 1 was locally invading the fallopian tube [Table]). Histologically only the malignant cases exhibited variable cytologic atypia, high mitotic rate (>6–10 per high-power fields), areas of necrosis, and large tumor size. All benign tumors showed no reactivity with CD10 (0 of 6). In contrast, 3 of 6 (50%) malignant metastatic cases were strongly CD10-positive (3+). One case (1 of 6) showed weak (1+) staining in the corresponding metastatic liver tissue. The locally invasive case was negative.

Conclusions: CD10 immunoreactivity may be helpful in identifying cases of GIST with metastatic potential (50% of cases are positive). Also CD10-positive cases may be of clinical interest with the new therapy.

<table>
<thead>
<tr>
<th>Location</th>
<th>Size, cm</th>
<th>Metastatic Sites</th>
<th>c-Kit and CD34 Staining</th>
<th>CD10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach (6 cases)</td>
<td>1.2–7.0</td>
<td>None</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Small intestine (2 cases)</td>
<td>7.5 and 18</td>
<td>None</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Colon (2 cases)</td>
<td>3.5 and 5</td>
<td>None</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Stomach (2 cases)</td>
<td>4 and 12</td>
<td>Splenic, liver, and lymph node</td>
<td>c-Kit +</td>
<td>Negative</td>
</tr>
<tr>
<td>Colon (2 cases)</td>
<td>11 and 27</td>
<td>Mesentry, uterus, small bowel nodules, and local invading fallopian tube</td>
<td>Both +</td>
<td>Negative</td>
</tr>
<tr>
<td>Small intestine</td>
<td>3.5</td>
<td>Omentum</td>
<td>Both +</td>
<td>+ (strong)</td>
</tr>
<tr>
<td>Stomach</td>
<td>15</td>
<td>Anterior abdominal wall</td>
<td>Both +</td>
<td>+ (strong)</td>
</tr>
<tr>
<td>Stomach</td>
<td>8.5</td>
<td>Liver, omentum, peritoneum</td>
<td>Both +</td>
<td>+3 (strong); (weakly staining +1 of metastatic liver site)</td>
</tr>
</tbody>
</table>

Angiosarcoma of the Sigmoid Colon Complicated by Disseminated Intravascular Coagulation: A Case Report and Literature Review
(Poster No. 12)
Christopher N. Thompson, MD (cthompson@swmail.sw.org); Debby Rampisela, MD; Ludvik R. Donner, MD, PhD. Department of Pathology, Scott and White Hospital, Temple, Texas.

We report a case of angiosarcoma of the sigmoid colon in an elderly man. Multiple metastases to the liver were identified during sigmoid colon resection. The tumor cells were strongly and diffusely positive for endothelial markers CD31, CD34, Fli-1, and von Willebrand factor. The patient later developed disseminated intravascular coagulation and expired 4 months after surgery. A review of the literature was performed. Eighteen cases of colonic angiosarcoma, including our case, are known. A slight majority (55%) of the patients were female. The patient ages ranged from 16 to 77 years with a mean age of 55 years. Most patients presented with rectal bleeding. Nine cases involved the sigmoid colon, 4 cases the cecum, 3 cases the rectum, 1 case the descending colon, and 1 case involved the cecum, transverse colon, and rectum. Six of 7 patients with colonic angiosarcoma less than 5 cm were alive at last follow-up (13–48 months postoperatively), whereas only 2 of 8 patients with tumor size greater than 5 cm were alive at last follow-up. Five of 6 patients younger than 50 years were alive at last follow-up, whereas 8 of 12 patients older than 50 years had rapid progression of their disease leading to death. The longest survival without evidence of recurrence was 3 years and occurred in a 16-year-old girl.

Positive Immunoreactivity of Thyroid Transcription Factor 1 in Colorectal Carcinoma: A Tissue Microarray Study of 104 Cases
(Poster No. 13)
Bo Xu, MD, PhD (bxu@buffalo.edu); Tyuyen Thong, MD; Dongfeng Tan, MD; Thaer Khouyri, MD. Department of Pathology, State University of New York at Buffalo; Department of Pathology, MD Anderson Cancer Center, Houston, Texas; and Department of Pathology, Roswell Park Cancer Institute and State University of New York at Buffalo.

Context: Thyroid transcription factor 1 (TTF-1) is a member of homeodomain transcription family expressed in epithelial cells of thyroid and lung. Although TTF-1 nuclear expression is generally considered a specific marker for lung and thyroid neoplasms, nuclear immunoreactivity was reported in other types of tumor. Few studies examined TTF-1 expression in colorectal carcinoma (CRC) with inconsistent results. The purpose of this study is to investigate TTF-1 expression in CRC.

Design: During metastatic adenocarcinoma workup for patients who have history of CRC, we identified 4 of 14 cases that had TTF-1 expression using a more specific antibody clone (clone 8G7G3/1). Therefore, we sought to retrospectively investigate the expression of TTF-1 in 90 CRC cases constructed in tissue microarray (TMA) blocks as well as whole tissue sections of the 4 primary tumors corresponding to the 4 positive metastases.

Results: In TMA studies, although all 90 cases had negative nuclear expression of TTF-1, cytoplasmic expression was seen in 1 case (1%). Four of 14 cases of metastatic CRC displayed positive nuclear staining of TTF-1. Three of the 4 corresponding primary carcinomas were also positive for TTF-1 in the whole tissue sections.

Conclusions: Our results suggest that during immunohistochemical workup, especially when the differential diagnosis includes lung and CRC, TTF-1 results should be interpreted with caution as a small subset of CRC expresses this marker. Positive TTF-1 nuclear expression in a metastatic carcinoma cannot rule out colorectal primary. Clinico-pathologic correlation combined with a panel of immunohistochemical markers is essential to render correct diagnosis.

Correlation of Histologic and Endoscopic Scores for Evaluation of Crohn Disease Recurrence After Ileal Resection and Infliximab Therapy
(Poster No. 14)
Miguel F. Palma Diaz, MD; Miguel Regueiro, MD; Wolfgang Schraut, MD; Leonard Baidoo, MD; Marilyn Pesci, MD; Janet Harrison, MD; Kevin E. Kip, PhD, FAHA; Scott E. Pley, MD; Antonia R. Sepulveda, MD PhD (asepulveda@med.upenn.edu). Department of Pathology & Laboratory Medicine, University of Pennsylvania, Philadelphia; Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania; College of Nursing Research Center, University of South Florida, Tampa; and Department of Medicine, University of North Carolina, Chapel Hill.

Context: Evaluation of Crohn disease recurrence after ileal resection requires assessment of endoscopy with biopsy. Studies evaluating the cor-
Correlation between histologic and endoscopic grading for follow-up of disease activity and response to infliximab are lacking.

**Design:** Twenty-four adult Crohn disease patients who underwent ileocolonic resection were assigned to receive either intravenous infliximab 5 mg/kg or placebo for 1 year in a randomized 2-armed double-blind placebo-controlled trial. Follow-up endoscopy with neontemal ileal biopsy at 1 year was performed in all patients. Endoscopic grading ranged from 0 to 4. Biopsy samples stained with hematoxylin-eosin were scored with a modified scheme for epithelial damage, crypt architectural changes, mononuclear or neutrophils in the lamina propria or epithelium, erosion or ulcer, and granulomas and pyloric metaplasia.

**Results:** The overall Pearson correlation coefficient between histologic activity score and endoscopy grade was 0.75 ($P < 0.001$). Among individual histologic criteria, endoscopy grades correlated with neutrophils ($R^2 = 0.74$, $P < 0.001$), presence of erosion or ulcer ($R^2 = 0.60$, $P = 0.004$), epithelial damage ($R^2 = 0.76$, $P < 0.001$), and crypt architecture changes ($R^2 = 0.61$, $P = 0.003$). Agreement between endoscopy grades and histologic scores was significant for the presence of neutrophils, erosion or ulcer, and crypt architectural changes with $\kappa$ values of 0.82, 0.58, and 0.75, respectively.

**Conclusions:** Application of a well-defined histologic scoring system for evaluation of Crohn disease activity in the neonatal ileum of patients randomized to receive placebo or infliximab therapy correlated well with endoscopic activity grades. The single most significant histopathologic change correlating with endoscopic evaluation of Crohn disease activity was the presence or absence of neutrophils in biopsy specimens.

**Primary Rectal Kaposi Sarcoma: Presentation of a Case in a 23-Year-Old Human Immunodeficiency Virus–Positive Male** (Poster No. 15)

Renuka Kulkarni, MBBS (rkulkarni@mcg.edu); Ningli Cheng, MD; Scott Drury, MD; Michelle Reid-Nicholson, MBBS. Department of Pathology, Medical College of Georgia, Augusta.

A 23-year-old homosexual male with HIV and full-blown acquired immunodeficiency syndrome presented with rectal bleeding and constipation. He was diagnosed with HIV at 14, used illicit drugs, was noncompliant with antiretroviral treatment, and had slowly decreasing CD4 counts with quadrupling viral titers in the previous months. Rectal examination revealed a mass involving 80% of the rectal circumference. Rectal biopsy revealed CD31- and CD34-positive spindled cells, slitlike vascular channels, extravasated red blood cells, and hyaline globules, consistent with Kaposi sarcoma (KS). Because of the absence of concomitant skin lesions the tumor was classified as primary rectal KS. Abdominal and chest computerized tomography (CT) scan revealed a circumferential submucosal 15 × 12 × 12-cm rectal mass with extensive muscularis propria invasion. CT also showed a single 5-mm lung nodule and several subcentimeter liver nodules. The patient opted for local radiation. One month later he presented to the emergency room with acute dyspnea and chest pain. CT revealed multiple “too numerous to count” bilateral lung and liver lesions that had not been seen on the earlier CT scan. Chemotherapy was then initiated and the patient remains alive 2 months postdiagnosis. This case is notable because of the unusual primary location of KS in the rectum, the patient's extremely young age, and his extensive local and metastatic disease. The tumor's rapid progression was likely the result of the patient's long-standing, untreated HIV, high viral load, and the tumor's propulsion by human herpes virus type 8.

**Medullary Carcinoma Also Occurs in the Ampulla of Vater: Report of a Case and Its Association With Microsatellite Instability** (Poster No. 16)

Haitham Nasser, MD (haitham.nasser@stjohn.org); Paul Kowalski, MD; N. Volkan Adsay, MD. Department of Pathology, St John Hospital and Medical Center, Detroit, Michigan; and Department of Pathology, Emory University Hospital, Atlanta, Georgia.

Medullary carcinoma of the gastrointestinal tract is a distinct tumor type that has been shown to have strong association with microsatellite instability and, in some cases, with hereditary nonpolyposis colorectal carcinoma. We report a 22-year-old woman with family history of colon cancer who presented with a tumor arising in the ampullary region causing obstructive jaundice. Grossly, it appeared solid, homogenous, and tan fleshy. Histologically, it revealed a poorly differentiated carcinoma without any precursor lesions in the ampulla, duodenum, or pancreas. The tumor showed characteristic “medullary” morphology, displaying syncytial growth pattern, pushing-border-like infiltration, and prominent lymphoplasmacytic infiltrates. Tumor cells were positive only for pankeratin (AE1/AE3). Among microsatellite instability markers analyzed immunohistochemically, msh1 and msh6 were retained, but there was a loss of msh2. Studies have shown that medullary carcinomas are different not only morphologically but also biologically and prognostically from the conventional adenocarcinomas of the respective sites. In fact, the experience in lower gastrointestinal tract has shown that microsatellite instability–related cancers including medullary carcinomas should receive a different chemotherapeutic protocol than ordinary carcinomas. The case presented here is, to our knowledge, the first pure medullary carcinoma to be reported in the ampulla. The young age of the patient and family history, combined with the morphology and loss of msh2, suggests that this tumor is most likely genetically driven. As more cases accumulate, it will be possible to determine whether the ampullary examples of this entity also have the same prognostic and therapeutic implications of their kindreds in the lower gastrointestinal tract.

**Pseudopolyposis of the Stomach Presenting in a Bariatric Patient With Atrophic Gastritis** (Poster No. 17)

James E Shikle, MD (JESHIKLE@yahoo.com); Bradley C. Bandera, MD. Departments of Pathology and Surgery, Eisenhower Army Medical Center, Fort Gordon, Georgia.

A 60-year-old woman with morbid obesity underwent a laparoscopic sleeve gastrectomy with removal of the gastric remnant and the specimen was submitted for pathologic examination. Gross examination revealed numerous (greater than 50) polypoid lesions measuring from 0.3 cm to 2.6 cm (Figure 3). Microscopic analysis of the nonpolypoid mucosa showed histologic features of atrophic gastritis with intestinal metaplasia. Histologically the polypoid lesions consisted of preserved oxyntic mucosa without evidence of atrophy consistent with pseudopolyposis. No dysplasia was present in either the pseudopolypos or the background atrophic gastric mucosa. Pseudopolyposis is a rarely observed finding in patients with atrophic gastritis. The gross differential diagnosis is broad and includes fundic gland polyposis, hyperplastic polyps, and lymphoma among others. This unusual case of pseudopolyposis with lesions measuring up to 2.6 cm in the setting of morbid obesity in a surgical specimen highlights the need to sample the background gastric mucosa in these cases to demonstrate the underlying atrophic gastritis, which explains the etiology of the pseudopolyposis.

**Morphologic Assessment of Intestinal Metaplasia at the Gastroesophageal Junction and Association with Helicobacter pylori Status as Detected by Multiplex Polymerase Chain Reaction** (Poster No. 18)

Benjamin L. Witt, MD (b-witt@northwestern.edu); Tat K. Tsang, MD; Marc Scheer, MD; Xiangwen Meng, MD; William G. Watkin, MD. Departments of Pathology, Gastroenterology, and Medicine, Evanston Hospital, NorthShore University HealthSystem, Evanston, Illinois; and Department of Pathology, NorthShore University HealthSystem, Research Institute, Evanston, Illinois.
Context: Gastroesophageal reflux disease–associated Barrett esophagus (BE) and Helicobacter pylori–associated carditis with intestinal metaplasia (CIM) differ in their risk of malignancy and implications for patient management but are difficult to distinguish in biopsies of the gastroesophageal junction (GEJ). We used a polymerase chain reaction (PCR) assay for *H pylori* in a series of GEJ biopsies to establish the prevalence of *H pylori* in groups diagnosed as BE and CIM on the basis of established histologic criteria.

**Design:** Ninety patients with reflux-induced esophageal disease who underwent upper endoscopy and had GEJ biopsies were the study subjects. Biopsies with intestinal metaplasia (IM) were divided into BE and CIM using established histologic criteria. *Helicobacter pylori* status was determined by multiplex PCR performed on concomitant esophageal biopsies.

**Results:** Twenty-seven (30%) patients demonstrated IM at the GEJ. Of these, 13 of 27 (48%) were classified as BE (4 or more BE histologic features) and 14 of 27 (52%) as CIM (fewer than 4 BE histologic features). The incidence of *H pylori* infection determined by PCR is shown in the Table. The infection rate at the distal esophagus did not significantly differ among those with IM versus those without, or in relation to the number of BE features among those demonstrating IM.

**Conclusions:** As determined by PCR, there is a high prevalence of esophageal *H pylori* infection in patients with reflux-induced esophageal disease, irrespective of their histologic categorization. The role of PCR for *H pylori* in stratifying the risk of development of neoplasia in gastroesophageal reflux disease requires further study.

### Incidence of *Helicobacter pylori* (HP) Infection in Distal Esophagus Biopsies

<table>
<thead>
<tr>
<th>HP Positive</th>
<th>No.</th>
<th>HP Negative</th>
<th>No.</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>No IM at GEJ</td>
<td>44</td>
<td>19</td>
<td>69.8</td>
<td></td>
</tr>
<tr>
<td>IM with 4 or more BE features</td>
<td>9</td>
<td>4</td>
<td>69.2</td>
<td></td>
</tr>
<tr>
<td>IM with fewer than 4 BE features (CIM)</td>
<td>11</td>
<td>3</td>
<td>78.5</td>
<td></td>
</tr>
</tbody>
</table>

**The Role of JAK3/STAT3 Pathway in Colorectal Carcinogenesis and Colorectal Carcinoma Progression in Egyptian Patients:**

**An Immunohistochemical Study**

**Poster No. 19**

Mohamed M. Shareef, MD, PhD; Maha M. Shamroulou, MD, PhD; Asem A. Elfert, MD, PhD; Mohamed I. El-sawaf, MD, PhD; Hanan H. Soliman, MD, PhD; Departments of Pathology, Tropical Medicine, and Surgery, Faculty of Medicine, Tanta University, Tanta, Egypt.

**Context:** The JAK3/STAT3 pathway is involved in the genesis of several cancers and proposed as a molecular target in such malignancies as colorectal carcinoma (CRC) in Western patients. The unique clinicopathologic and molecular characteristics of CRC in Egyptian patients has stimulated us to investigate the JAK3/STAT3 pathway in CRC and its precursors in Egyptian patients.

**Design:** Tissue sections from 10 samples of normal colonic mucosa, 10 colonic adenomas, 15 cases with ulcerative colitis, and 45 cases with primary CRC were evaluated immunohistochemically for JAK3 and STAT3 expression and their phosphorylated forms (p-JAK3 and p-STAT3).

**Results:** Frequency of p-JAK3 expression was positively correlated with degree of dysplasia in adenomas (*P* = .01). The frequency of p-STAT3 expression increased significantly with the degree of dysplasia in cases with ulcerative colitis (*P* = .003). The frequency of expression of all the JAK3/STAT3 pathway proteins was significantly higher in CRC than in precancerous lesions (*P* = .01, .03, .04, and .002 for JAK3, p-JAK3, STAT3, and p-STAT3, respectively). In CRC cases, p-STAT3 expression showed significant correlation with grading (*P* = .002) and nodal status (*P* = .04).

**Conclusions:** Increased expression of the components of JAK3/STAT3 pathway with increasing grades of dysplasia and malignant transformation points to their potential role in colorectal carcinogenesis. The significant correlation of the JAK3/STAT3 pathway components with anaplasia and invasion suggests a definitive role in progression of CRC, making this pathway a promising target for therapy in Egyptian patients.

**Histopathologic Characterization of 350 Consecutive Pancreatic Resections: The University of Miami/Jackson Memorial Hospital Experience**

**Poster No. 20**

Loren P. Herrera, MD (lherrera@med.miami.edu); Monica T. Garcia, MD; Pablo A. Bejarano, MD; Department of Pathology, Jackson Memorial Hospital, Miami, Florida; and Department of Pathology, University of Miami, Miami, Florida.

**Context:** Pancreatectomies are performed for many benign and malignant conditions. The histopathologic findings of pancreatic resections performed in a high-volume center are described.

**Design:**Slides from 350 pancreatic specimens (361 lesions) collected during a 4-year period were reviewed. Histopathologic findings were analyzed.

**Results:** Neoplastic conditions comprised most cases (91%) (Table). Pancreatic adenocarcinomas represented 66%, whereas ampullary were 20%. Moderate differentiation was seen in 56% of cases and poor differentiation in 33%. Stage III was more prevalent (63%), followed by stage II (23%). Lymphovascular invasion (LVI) was found in 68%, perineural invasion (PNI) in 60%, and lymph node metastasis in 52% of adenocarcinomas. The number of benign and malignant neuroendocrine tumors (NETs) was identical (20%). Among the malignant NETs, 40% were low grade, 55% intermediate, and 5% high grade. Necrosis, LVI, PNI, and node metastasis were seen in 15%, 55%, 22%, and 80% of malignant NETs, respectively. Among intraductal papillary mucinous neoplasms, 35% were adenomas, 15% were borderline, and 50% harbored in situ or invasive carcinoma or were associated with ductal adenocarcinoma. Cystadenomas represented 64% of the mucinous cystic neoplasms, whereas 21% were borderline tumors, 14% noninvasive carcinomas, and 1% cystadenocarcinomas. Metastasis from kidney (40%), lung (20%), colon (20%), choriocarcinoma (10%), and melanoma (10%) were observed.

**Conclusions:** This is one of the largest single institution series of pancreatic resections. Carcinomas of the pancreatic head and ampulla of Vater were the most common neoplasms. These lesions often present at advanced stage, with aggressive histologic features as demonstrated by a high incidence of LVI, PNI, and regional node metastasis.

<table>
<thead>
<tr>
<th>Lesions</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>180 (50)</td>
</tr>
<tr>
<td>Intraductal papillary mucinous neoplasm</td>
<td>41 (11)</td>
</tr>
<tr>
<td>NET</td>
<td>40 (11)</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>32 (9)</td>
</tr>
<tr>
<td>Cystic lesions (serous and mucinous)</td>
<td>33 (9)</td>
</tr>
<tr>
<td>Tubulovillous lesions</td>
<td>11 (3)</td>
</tr>
<tr>
<td>Others (solid pseudopapillary tumor, gastrointestinal stromal tumor, acinar carcinoma, schwannoma)</td>
<td>15 (4)</td>
</tr>
<tr>
<td>Metastasis</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Total</td>
<td>361 (100)</td>
</tr>
</tbody>
</table>

**A Unique Simultaneous Presence of Adenocarcinoma, Carcinoid Tumor, and Gastrointestinal Stromal Tumor in the Stomach**

**Poster No. 21**

Shouying Du, MD, PhD (sdu@ucsd.edu); Farnaz Hasteh, MD; Noel Weidner, MD; Ahmed Shabaik, MD; Department of Pathology, University of California, San Diego Medical Center, San Diego.

<table>
<thead>
<tr>
<th>Details</th>
<th>Number and Percentage of Positive Cases for Each Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>JAK3</td>
<td>p-JAK3, No. (%)</td>
</tr>
<tr>
<td>Normal mucosa</td>
<td>(n = 10)</td>
</tr>
<tr>
<td>Adenoma</td>
<td>(n = 10)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>(n = 15)</td>
</tr>
<tr>
<td>CRC</td>
<td>(n = 45)</td>
</tr>
</tbody>
</table>

### Distribution of the Histopathologic Findings in Pancreatectomy Specimens

<table>
<thead>
<tr>
<th>Lesions</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>Adenocarcinoma</td>
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<td>Chronic pancreatitis</td>
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<td>Metastasis</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Total</td>
<td>361 (100)</td>
</tr>
</tbody>
</table>
We report a unique synchronous presence of an adenocarcinoma, carcinoid tumor, and gastrointestinal stromal tumor in a near-total gastrectomy specimen from a 75-year-old woman with a long-standing history of pernicious anemia (Figure 4). A pedunculated polypoid mass (6.2 × 4.1 × 3.0 cm) was identified in the middle third of the gastric body with the stalk base attaching to the lesser curvature. Microscopic examination of the polyp revealed a moderately differentiated adenocarcinoma invading the lamina propria of the stalk. In the polyp stalk, a carcinoid tumor of 0.6 cm in greatest dimension was noted consisting of monotonous cells with granular cytoplasm and centrally located nuclei, which are strongly and diffusely positive for both chromogranin and synaptophysin, confirming their neuroendocrine origin. Approximately 11.2 cm away, in the subserosa of the greater curvature, one 0.8 × 0.8-cm firm nodule with a tan cut surface was incidentally identified consisting of spindle cells with high nuclear to cytoplasmic ratio, displaying a fascicular or storiform growth pattern, and with a diffuse and strong positive immunoreaction for CD117. It was negative for smooth muscle actin and desmin, consistent with gastrointestinal stromal tumor. The adenocarcinoma and carcinoid components in our case were entirely separated into adjacent but distinct areas, with no transition or intermixing between these 2 different tumors, indicating a collision pattern. To the best of our knowledge, this is the first case of such a triple entity occurring simultaneously in the stomach.

### α-Methylacyl Coenzyme A Racemase Expression in Barrett Esophagus, Low- and High-Grade Dysplasia, and Carcinoma

Anupama Gupta, MD; Wooin Yu, MD (wy2121@columbia.edu); Fabrizio Remotti, MD; Helen Remotti, MD. Department of Pathology, Columbia University, New York, New York.

**Context:** Surveillance biopsies in patients with Barrett esophagus (BE) are done for morphologic detection of preneoplastic/neoplastic lesions to determine future therapy. It is often a challenge to histologically distinguish reactive changes from preneoplastic/neoplastic changes in this location. Some authors have proposed the use of α-methylacyl coenzyme A racemase (AMACR) in such situations. This study was performed to evaluate utility of AMACR expression in detecting low-grade dysplasia (LGD), high-grade dysplasia (HGD), and carcinoma (CA) in patients with BE.

**Design:** Twenty-three esophageal resection and 5 endoscopic mucosal resection (EMR) specimens with histologically confirmed dysplasia and/or CA in BE were obtained from the archival files of the Department of Pathology, Columbia University. Immunohistochemical staining for AMACR (Dako, rabbit anti-human P504S, Clone 13H4) was performed on all cases. The percentage of lesionals cells staining with AMACR was noted and the intensity of staining was graded from 1+ (faint) to 4+ (strong). Less than 1% of lesionals cells staining was considered negative. BE, LGD, HGD, and CA were evaluated and graded separately on each case.

**Results:** AMACR positivity was seen in 0% (0 of 19) of BE, 0% (0 of 6) of LGD, 20% (3 of 15) of HGD, and 32% (7 of 22) of CA. When positive, the percentage of immunoreactive lesionals cells ranged from 1% to 40% in HGD and 5% to 80% in CA (Table).

**Conclusions:** AMACR staining when positive is helpful; however, negative staining does not rule out HGD or CA. Low sensitivity and variability in extent of staining limits the diagnostic utility of AMACR immunostaining for detection of preneoplastic/neoplastic lesions in BE, especially in small surveillance biopsies.

### α-Methylacyl Coenzyme A Racemase–Positive Cases

<table>
<thead>
<tr>
<th>Type of Lesion</th>
<th>% of Cells Staining</th>
<th>Intensity of Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGD-1</td>
<td>40</td>
<td>2+</td>
</tr>
<tr>
<td>HGD-2</td>
<td>5</td>
<td>2+</td>
</tr>
<tr>
<td>HGD-3</td>
<td>80</td>
<td>2+</td>
</tr>
<tr>
<td>CA-1</td>
<td>5</td>
<td>1+</td>
</tr>
<tr>
<td>CA-2</td>
<td>20</td>
<td>3+</td>
</tr>
<tr>
<td>CA-3</td>
<td>30</td>
<td>3+</td>
</tr>
<tr>
<td>CA-4</td>
<td>70</td>
<td>3+</td>
</tr>
<tr>
<td>CA-6</td>
<td>10</td>
<td>3+</td>
</tr>
</tbody>
</table>

### Serrated Lesions of the Appendix: Morphologic and Immunohistochemical Appraisal

Jonathan Rock, MD (Jonathan.Rock@osumc.edu); Andrew M. Bellizzi, MD; William L. Marsh, MD; Wendy L. Frankel, MD. Department of Pathology, The Ohio State University Medical Center, Columbus.

**Context:** There is increasing interest in serrated colorectal polyps. Less is known regarding morphologically similar appendiceal lesions. We performed a morphologic and immunohistochemical assessment, appropriating diagnostic terminology and immunohistochemical markers shown useful in differentiating serrated polyps of the colon.

**Design:** Fifty-three noninvasive epithelial appendiceal lesions were classified hyperplastic polyp (HP), sessile serrated adenoma (SSA), mucinous cystadenoma (MCA), MCA with serrated features (MCAS), or conventional adenoma (CAD). Cytokeratin (CK) 20, Ki-67, and β-catenin staining was performed. CK20 was normal (NI, surface staining), expanded (Ex, beyond surface), expanded/irregular (Ex/L, expanded with random expression in deep crypts), diffusely, or no pattern. Ki-67 was NI (base), Ex (beyond base), Ex/L (expanded with asymmetry), or no pattern. MUC6 was positive or negative. β-Catenin was NI (membranous) or abnormal (nuclear/ decreased membranous).

**Results:** Diagnoses of HP (6), SSA (12), indeterminate (3), MCA (14), MCAS (16), and CAD (2) were rendered. All HPs showed Ex CK20 expression and Ex (3/6) or NI (3/6) Ki-67 expression; MUC6 was positive in 1. Most SSAs and MCASs showed Ex or Ex/L CK20 expression, and Ex or Ex/L or NI Ki-67 expression. MUC6 was positive in all SSAs and 8 of 16 MCASs. Flat architecture of MCAs made CK20 and Ki-67 difficult to interpret; MUC6 was negative. CAD expressed CK20 and Ki-67 Ex/L and MUC6 negative; abnormal β-catenin was noted in one.

**Conclusions:** Serrated appendiceal lesions can be categorized using terminology from the colon. MUC6 is most associated with SSA morphology. Similar patterns of MUC6, CK20, and Ki-67 reactivity in SSA and MCAS suggest a link between these lesions.

### A Rare Case of Gastric Leiomyosarcoma in a Young Hispanic Man

Nisrin Motiwala, MD1 (nmotiwal@mcm.edu); Jeffrey Lee, MD; Nidia Messias, MD; Suash Sharma, MD; Asha Nayak-Kapoor, MD.1 Department of Pathology and 2Hematology, Medical College of Georgia, Augusta; and 3Department of Pathology, Charlie Norwood Veterans Affairs Medical Center, Medical College of Georgia, Augusta.

Leiomyosarcomas of the stomach are vanishingly rare neoplasms. In fact according to the World Health Organization, classification of tumors as true gastric leiomyomas and leiomyosarcomas are so infrequent that there are no significant data on demographic, clinical, or gross features. In the few cases found in literature, patients presented at older age (median age, 60 years). Most of the tumors historically designated as leiomyosarcoma are now classified as gastrointestinal stromal tumor (GIST), hence the older literature on gastric leiomyosarcomas largely pertain to malignant GISTs. This is a case of a 26-year-old Hispanic man who initially presented with gastrointestinal bleeding. Gross examination revealed a circumscribed, exophytic proximal gastric mass measuring 7.0 cm in maximum dimension, located within the submucosa, and arising from the muscularis mucosa. Microscopic findings were that of a highly cellular pleomorphic tumor with eosinophilic cytoplasm and abundant
mitoses (>20 per 10 high-power fields) with atypical mitotic figures. Immunohistochemistry was diffusely positive for desmin and smooth muscle actin and negative for CD117 and CD34. Molecular studies were negative for c-KIT and PDGFR-α mutations, thus confirming the diagnosis of leiomyosarcoma and not GIST, which is one of the most important differential diagnoses. GIST accounts for 2.2% of malignant gastric tumors in the SEER data. It is extremely important to differentiate leiomyosarcoma from GIST, as they require radically different courses of treatment. Most GISTs (80%) are responsive to the tyrosine kinase inhibitor imatinib, whereas leiomyosarcomas are treated with chemotherapy.

Cladtréudium difficile Colitis Presenting as Collagenous Colitis on Biopsy: Case Report and Review of Literature (Poster No. 25)

Saryn V. Stramecki Doucette, MD1; Alan Epstein, MD,2 Departments of1Pathology and 2Gastroenterology, Roger Williams Medical Center, Providence, Rhode Island.

Rare reports describe the development of collagenous colitis after prolonged Cladtréudium difficile infection. We describe C difficile colitis presenting as collagenous colitis on initial biopsies. A 49-year-old man with a history of bipolar disorder and polysubstance abuse in remission presented with a 1-month history of acute-onset watery diarrhea. His medications included celecoxib, methadone, and quetiapine fumarate. Colonoscopy was suggestive of ulcerative colitis and showed pancolitis, scattered ulcerations, and a normal terminal ileum and rectum. Multiple biopsies throughout the colon and rectum showed increased subepithelial collagen deposition (trichrome verified), increased lamina propria chronic inflammation, and minimal neutrophilic infiltrates without crypt architectural abnormalities (Figure 5). Biopsy of the terminal ileum showed normal villous architecture and increased intraepithelial lymphocytes. Results of stool cultures, C difficile assay, and celiac serologies were negative. Treatment with metronidazole and 5-aminosalicylic acid mildly improved the diarrhea. However, because of continuing diarrhea 4 weeks later, colonoscopy was repeated and showed pancolitis with rectal involvement and ulcerations. Subsequent biopsies showed less collagen deposition and more active inflammation. A repeated C difficile toxin assay was positive and vancomycin was given with prompt resolution of diarrhea. Our case is an unusual histologic presentation of C difficile colitis. We wish to emphasize that a histologic diagnosis of collagenous colitis with endoscopically evident colitis should prompt rigorous workup for a cause. Expansion of the subepithelial collagen layer may be a protective/reactive response to enterotoxins produced by C difficile. Although the exact etiology of idiopathic collagenous colitis is unknown, luminal antigens/otoxins are believed to be triggers.

Granulomatous Inflammation Presenting as an Ileocecal Mass With Involvement of the Bladder and Abdominal Wall (Poster No. 26)

Yuanming Zhang, MD1; Roberto Bergamaschi, MD, PhD; Philip Kane, MD2; Meenakshi Singh, MD3 (meenakshi.singh@stonybrook.edu). 1Department of Pathology and 2Division of Colorectal Surgery, State University of New York at Stony Brook University Medical Center, Stony Brook.

A 34-year-old man presented with signs and symptoms of subacute intestinal obstruction. Radiology revealed a mass involving the ileocecum, bladder, and abdominal wall. There were no prior biopsies. The ileocecal resection specimen consisted of distorted adherent bowel with a 5.5 cm firm, tan-yellow mass that extended transmurally. Frozen and permanent sections revealed transmural granulomatous inflammation and marked fibrinopurulent infiltrate extending to margins. The bladder “mass” and pelvic/abdominal wall “mass” also showed granulomatous inflammation. No neoplasm or features of Crohn disease were identified. Special stains did not show acid-fast bacilli. The granulomatous inflammation had abundant foreign body–type giant cells, some of which contained polarizable foreign material, including vegetable matter. This is consistent with a phlegmon, secondary to long-standing bowel perforation. This case emphasizes that the history may not be particularly helpful in arriving at an accurate diagnosis and the etiology may not be evident at frozen section analysis. Cultures should be submitted to rule out an infectious agent. Crohn disease and tuberculosis are certainly more common causes of granulomatous inflammation of the bowel and tuberculosis may produce a mass effect. Gross and histologic examination with adequate sampling, negative cultures, and special stains for organisms can help exclude this diagnosis. A careful look at the giant cells and a polarized light examination can help identify the foreign body nature of the granulomatous inflammation. Food material in the wall of the bowel serves as “foreign matter.” An exuberant response to it can lead to a mass effect and mimic a neoplasm.

Adenomyoma of the Jejunum: Report of an Unusual Case (Poster No. 27)

Xin Qing, MD, PhD (dqingx@yahoo.com); Samuel French, MD. Department of Pathology, Harbor-UCLA Medical Center, Torrance, California.

Adenomyoma of the small intestine is an extremely rare benign non-neoplastic lesion. The rarity of this entity may be attributed to underreporting or nonrecognition by both surgeons and pathologists. Although it has been theorized that this lesion may represent incomplete heterotopic pancreas, its pathogenesis is not clearly understood. We describe an unusual case of adenomyoma in the jejunum with new pathologic and immunohistochemical features. The patient was a 61-year-old woman with cancer of the sigmoid colon and multiple liver cysts who underwent exploratory laparotomy and sigmoidectomy for cancer. At surgery, a polypoid lesion was incidentally found in the lower jejunum, which was resected. On histologic examination, the lesion was located in the submucosa and composed of an admixture of different types of glandular structures and surrounding smooth muscle. The large glands lined by columnar/cuboidal epithelium with occasional goblet cells. The surrounding small glands were morphologically similar to, but immunohistochemically different from, Brunner glands. There were foci of connection between the epithelial component of the lesion and the overlying small intestine mucosal epithelium. No pancreatic tissue was identified. The immunohistochemical features are summarized in the Table. In conclusion, these novel findings suggest that adenomyoma of the small intestine is a form of intestinal epithelial hamartoma with altered differentiation, instead of incomplete heterotopic pancreas. Increased vigilance in watching for this entity and a better pathologic knowledge of it may result in an increase in its diagnosis and spare the patient unnecessary surgery.

<table>
<thead>
<tr>
<th>Immunohistochemistry of Epithelial Cells in Adenomyoma, Small Intestine, and Brunner Gland</th>
<th>Adenomyoma (Large Gland)</th>
<th>Adenomyoma (Small Gland)</th>
<th>Small Intestine Mucosa</th>
<th>Brunner Gland</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK7</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CK20</td>
<td>–</td>
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</tr>
<tr>
<td>CA 19-9</td>
<td>+</td>
<td>–</td>
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</tr>
<tr>
<td>CDX-2</td>
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<td>+</td>
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<td>+</td>
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<td>HMW</td>
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<tr>
<td>(34BE12)</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>AE1/AE3</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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Mesenteric Fibromatosis Mimicking a Gastrointestinal Stromal Tumor: Case Report and Review of Literature (Poster No. 28)

Kilik Kesha, MD (kilik.kesha@danhs.org); Ramapriya Vidhun, MD. Department of Pathology, Danbury Hospital, Danbury, Connecticut.
The differentiation of mesenteric fibromatosis (MF) from a gastrointestinal stromal tumor (GIST) involves careful analysis of specific pathologic features. We report a case of MF initially diagnosed as a GIST. A 33-year-old man presented to the emergency department with a history of nausea and vomiting. Computerized tomography (CT) scan showed a partial small bowel obstruction. On resection, a diagnosis of GIST was made. Two years later the patient was diagnosed by CT scan with a mass in the mesentery. The patient underwent a second resection for a well-circumscribed, tan white, firm nodule measuring 2.5 cm in greatest dimension. Histologic sections showed fascicles of monotonous spindle and stellate cells. These cells had abundant eosinophilic cytoplasm and bland basophilic nuclear features. The cells were strongly positive for c-Kit and were negative for CD34, actin, desmin, and S100. These morphologic and immunohistochesmial features are consistent with a MF. On retrospective review of the slides from the prior resection 2 years prior, it was noted that the morphologic and immunohistochemical features are similar and consistent with a fibromatosis. Historically, even though there is an overlap in their immunohistochemical profiles, these entities can be distinguished primarily by their light microscopic and ultrastructural features. Recent studies have shown that β-catenin can be used to distinguish between these entities (90% positive staining in fibromatoses; 0% in GIST) (Table). We recommend that multiple diagnostic features including CD34 and β-catenin expression be used in conjunction with c-Kit to accurately differentiate GIST from MF.

**Key Features Between Mesenteric Fibromatosis and Gastrointestinal Stromal Tumor**

<table>
<thead>
<tr>
<th>Mesenteric Fibromatosis</th>
<th>GIST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td></td>
</tr>
<tr>
<td>Mesentery or retroperitoneum</td>
<td>60%–70% stomach</td>
</tr>
<tr>
<td>May extend into small bowel</td>
<td>20%–30% small bowel</td>
</tr>
<tr>
<td><strong>Immunohistologic staining</strong></td>
<td></td>
</tr>
<tr>
<td>Positive C-kit/CD117 (0%–75%)</td>
<td>Positive C-kit/CD117 (95%)</td>
</tr>
<tr>
<td>Negative CD34</td>
<td>Positive CD34 (60%–70%)</td>
</tr>
<tr>
<td>Positive β-catenin (&gt;90%)</td>
<td>Negative β-catenin</td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
<td></td>
</tr>
<tr>
<td>Uniform spindle cells</td>
<td>Spindle-shaped fascicles</td>
</tr>
<tr>
<td>Microscopic infiltrative borders</td>
<td>High mitotic count/atypia</td>
</tr>
<tr>
<td>Keloidlike collagen</td>
<td>Foci of necrosis</td>
</tr>
<tr>
<td>Small arteries/dilated vein</td>
<td>Hyalinized vessel walls</td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td></td>
</tr>
<tr>
<td>Associated with FAP, Gardner syndrome, and surgical trauma</td>
<td>Prognosis related to size and mitotic index</td>
</tr>
<tr>
<td>No metastatic potential</td>
<td>Low metastatic potential</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Resection</td>
<td>Resection with or without imatinib mesylate</td>
</tr>
</tbody>
</table>

**Russell Body Gastritis: A Unique Association With Gastric MALToma and Gastric Ulcer** (Poster No. 29)

Sreelakshmi Ravula, MD (sree.lrus@yahoo.com); Jacek Polski, MD. Department of Pathology, University of South Alabama Medical Center, Mobile.

Russell body gastritis is a recently recognized lesion of the gastric mucosa associated with inflammatory conditions like Helicobacter pylori, human immunodeficiency virus, and fungal infections. We report a case of Russell body gastritis in an elderly patient. A 90-year-old male patient was admitted to our emergency department with bleeding gastric ulcer. The patient underwent a second resection for a well-circumscribed, tan white, firm nodule measuring 2.5 cm in greatest dimension. Histologic sections showed fascicles of monotonous spindle and stellate cells. These cells had abundant eosinophilic cytoplasm and bland basophilic nuclear features. The cells were strongly positive for c-Kit and were negative for CD34, actin, desmin, and S100. These morphologic and immunohistochemical features are consistent with a MF. On retrospective review of the slides from the prior resection 2 years prior, it was noted that the morphologic and immunohistochemical features are similar and consistent with a fibromatosis. Historically, even though there is an overlap in their immunohistochemical profiles, these entities can be distinguished primarily by their light microscopic and ultrastructural features. Recent studies have shown that β-catenin can be used to distinguish between these entities (90% positive staining in fibromatoses; 0% in GIST) (Table). We recommend that multiple diagnostic features including CD34 and β-catenin expression be used in conjunction with c-Kit to accurately differentiate GIST from MF.

**Signet Ring Cell Change in Pseudomembranous Colitis: An Underrecognized Gastrointestinal Phenomenon?** (Poster No. 30)

Paula A. Navarro, MD (pnavarro@tuftsmedicalcenter.org); Tee U. Lang, MD; Jennifer J. O’Brien, MD, PhD; Joseph Alroy, DVM; Maria L. Garcia-Moliner, MD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

**Context:** Signet ring cells are characteristic of high-grade adenocarcinoma, particularly of the gastrointestinal tract. Signet ring cell change (SCC) has also been reported in benign gastrointestinal processes, such as pseudomembranous colitis (PMC), tubular adenomas, and inflammatory bowel disease. The purpose of our study is to determine the incidence of SCC in cases of PMC because this phenomenon can represent a diagnostic challenge to pathologists, especially in small biopsies.

**Design:** Archival hematoxylin-eosin–stained slides from 21 resected colonic specimens with the diagnosis of PMC accessioned at Tufts Medical Center between 1994 and 2008 were reviewed for the presence of SCC and their pattern of distribution in the colon.

**Results:** Of these 21 cases, 18 (86%) demonstrated SCC within the crypts and within overlying exudate. Interestingly, one case showed signet ring–like cells in the lamina propria. The remaining 3 cases show the classic histologic changes of PMC but no SCC.

**Conclusions:** Our study highlights that SCC is a common finding in colon specimens with PMC. These changes may be focal and, hence, go unrecognized. When more extensive or, as in one of our cases, when the crypts are disrupted with spillage of signet ring–like cells into the lamina propria, there may be diagnostic confusion with adenocarcinoma. The mechanism for the production of this change is unclear but may represent a degenerative change. Pathologists must become aware that SCC is a phenomenon present in a variety of nonneoplastic gastrointestinal processes. Overdiagnosis of this pathologic change as signet ring cell adenocarcinoma may have serious consequences.

**Polarity Rather Than Count of Eosinophils Better Discriminates Between Eosinophilic and Reflux Esophagitis** (Poster No. 31)

Dawn Brady, MD (dawn.brady@rush.edu); Ajay Patel, MD; Maria McIntire, MD; Deborah Giusto, MD; Shriram Jakate, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

**Context:** Eosinophilic esophagitis (EE) and gastroesophageal reflux disease (GERD) often have overlapping histologic features, particularly eosinophilia. Previous attempts to differentiate based on the quantity of intraepithelial eosinophils have shown conflicting results. We sought to...
DLEC. All GERD-EE cases demonstrated bottom heavy eosinophils. Twenty patients had pure EE, 20 patients had pure GERD, 5 patients had primary EE with histologically overlapping GERD (EE-GERD), and 5 patients had primary GERD with histologically overlapping EE (GERD-EE). Hematoxylin-eosin preparations were evaluated. The epithelial polarity of distribution of eosinophils was noted nearest the surface (“top heavy”) or nearest the basal layer (“bottom heavy”). Additionally, the presence of discrete luminal eosinophilic colonies (DLECs) was assessed.

Results: There were 2 to 35 eosinophils per high-power field for all cases. Fifteen of 20 (75%) EE cases showed DLEC and top heavy eosinophilia. Eighteen of 20 (90%) GERD cases demonstrated bottom heavy eosinophils, and none showed DLEC. EE-GERD showed 2 of 5 (40%) top heavy cases, 3 of 5 (60%) cases were bottom heavy, and none showed DLEC. All GERD-EE cases demonstrated bottom heavy eosinophils.

Conclusions: DLEC is most encountered in EE. DLEC is missing in GERD, EE-GERD, and GERD-EE. Bottom heavy eosinophilia appears strongly supportive of GERD or GERD-EE. This polarity pattern recognition is a more practical, easily reproducible, and adaptable method of differentiation between these 2 closely related but separately treated entities.

Collagenous Sprue: Case Study and Review of Literature (Poster No. 32)

Xiangrong Zhao, MD, PhD (xzhao@bhs1.org); Rebecca Johnson, MD, Department of Pathology and Laboratory Medicine, Berkshire Medical Center, Pittsfield, Massachusetts.

Collagenous sprue is a rare, severe malabsorptive disorder. There are only 49 cases reported to date in the English medical literature worldwide, including cases reported under different terms in early records, for example it was first described as idiopathic malabsorption in 1947. We report a case of collagenous sprue in a 69-year-old Caucasian woman who presented with severe watery diarrhea. She was seronegative for classic celiac disease. History, physical examination, and laboratory tests excluded other etiologies for diarrhea. Endoscopy revealed diffuse tiny white mucosal papillae, especially prominent in the distal jejunum. Biopsies showed severe small intestinal villous blunting with crypt atrophy, in contrast to the crypt hyperplasia seen in classic celiac disease. Characteristic for collagenous sprue, there were diffuse subepithelial collagen deposits (thicker than 12 μm) entrapping small capillaries and lamina propria cellular elements, as shown in hematoxylin-eosin (Figure 7) and trichrome (inset A) stains of biopsies from duodenum, jejunum, and ileum. There were aberrant intraepithelial and lamina propria CD3-positive (inset B), CD8-negative (inset C) T lymphocytes. Due to the rarity of collagenous sprue, its exact relationship with classic celiac disease and other refractory sprue-like intestinal disorders remains controversial. Our report represents the 50th collagenous sprue case described to date, with relevant literature reviewed and the histologic phenotype characterized with special and immunohistochemical stains.

Intestinal Necrosis Following Oral Administration of Sodium Polystyrene Sulfonate (Kayexalate) in Sorbitol: A Report of 5 Cases (Poster No. 34)

Bryan L. Jansen, MD (BLJansen@mhs.org); Hema Khurana, MD; Ashok Balsaver, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Sodium polystyrene sulfonate (Kayexalate) in sorbitol, a cation exchange resin used to treat hyperkalemia in uremic patients, has been well implicated in cases of intestinal necrosis. The incidence of this complication, however, is not known and the literature for many years has represented this as something of a rare entity. We report here a series of 5 patients at our institution in whom, during a 1-year period, Kayexalate crystals were observed on either endoscopic biopsy (n = 1) or surgical resection specimens (n = 4) demonstrating intestinal necrosis. All of the patients had documented oral administration of Kayexalate on admission to the hospital and clinical history of renal insufficiency with 3 of the 5 patients receiving hemodialysis. Currently, the available literature reports only sporadic cases and the largest case study (n = 15) spans a 10-year period. We propose that Kayexalate-induced intestinal damage continues to be an underrecognized and underreported entity. The purpose of this study is to further highlight the clinical and pathologic features of Kayexalate-associated intestinal necrosis.

The Use of IgG4 to Distinguish Autoimmune Hepatitis From Hepatic Cholangiopathic Diseases (Poster No. 35)

Sherry M. Thompson, MD1 (smthompson78@hotmail.com); Pablo A. Bejarano, MD2; Monica T. Garcia, MD; Chakradhar Reddy, MD. Departments of Pathology and Gastroenterology, University of Miami Hospital/Jackson Memorial Hospital, Miami, Florida.

Context: Primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH), and the so-called overlap syndrome (OS) share clinical and histologic characteristics, making them difficult to distinguish from each other. Immunoglobulin (Ig) G4–positive plasma cells detected by immunohistochemistry have been identified in patients with autoimmune hepatitis.
with extrahepatic autoimmune disorders. However, the role of IgG4 in distinguishing various liver diseases has not been fully investigated.

Design: Eighty-one patients with needle biopsies showing features consistent with PBC, AIH, OS, or ductopenia were selected and stained for IgG4. Quantitation of IgG4-positive plasma cells and portal tracts (PTs), done blinded to the clinical diagnosis, and the ratio of IgG4:PTs, was obtained for each biopsy. Findings were then correlated to the patient’s final clinical diagnosis.

Results: Portal tracts with IgG4-positive plasma cells showed strong cytoplasmatic staining. Of the 81 patients, 64 had the following clinical diagnoses: 24 AIH, 14 PBC, 10 OS, 3 PSC, 1 ductopenia of adulthood, 1 Alagille syndrome, and 11 non-AIH, noncholangiopathic (NANC) diagnoses. The mean ratio of IgG4-positive plasma cells to PTs was 1.80 for AIH, 0.22 for PBC, 0.19 for OS, 0.54 for PSC, and 0.39 for NANC. The P value of IgG4 separating AIH from PBC was 0.02, and was 0.03 , and 0.06 for OS, NANC, and PSC, respectively.

Conclusions: IgG4-positive cells are more predominated in AIH compared with other hepatic diseases with cholangiopathic features. Staining plasma cells with IgG4 may elucidate disease processes among various hepatic entities. Although the numbers of PSC cases were few, PSC may also be driven by an association with IgG4.

Histoplasma capsulatum Granulomatous Hepatitis: Clinicalopathologic Analysis of 6 Cases (Poster No. 36)

Kirtree Raparia, MD (kirtreeraparia@gmail.com); Mary R. Schwartz, MD; Alberto G. Ayala, MD; Steven S. Shen, MD; Jae Y. Ro, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Context: The increased rate of Histoplasma capsulatum infection is an emerging issue among immunocompromised individuals. The differential diagnosis of granulomatous inflammation in the liver is important for the accurate identification of the etiology and appropriate treatment.

Design: We report 6 cases of H capsulatum granulomatous hepatitis seen at our institution from 1999 to 2008, three of them in 2008. Comorbidities included silver (GMS) and acid-fast bacilli stains were performed in all cases.

Results: There were 4 women and 2 men ranging from 42 to 73 years. All patients had underlying diseases: 2 patients had rheumatoid arthritis, 1 had systemic lupus erythematosus, 1 patient was infected with human immunodeficiency virus, and 2 patients had received neoadjuvant chemotherapy for colon/rectal carcinoma. Two patients with rheumatoid arthritis were on Remicade medication. A urine histoplasma antigen test was performed in 3 of the 6 cases and all showed moderate elevation (4.73–5.56 ng/mL). A liver biopsy showed multiple noncaseating granulomatous disease in the lobular parenchyma in 4 of 6 cases. Hyalinized and calcified granuloma were present in the remaining 2 cases. The organisms were generally few in number and were both intracellular and extracellular. The organisms were highlighted by the GMS stain but were generally smaller, not well visualized with periodic acid-Schiff with diastase stain.

Conclusions: Infection by H capsulatum should be considered in the differential diagnosis of granulomatous hepatitis in immunocompromised patients. Urine Histoplasma antigen assay, liver tissue culture, and identification of the fungal organisms by GMS stain can be critical in identifying this infection.

IMP3, S100P, and XIAP Are Valuable Biomarkers in the Distinction Between Chronic Pancreatitis and Pancreatic Ductal Adenocarcinoma (Poster No. 37)

Ognjen Kosarac, MD1 (okosarac@tmhs.org); Qihui Zhai, MD; Hidehiro Takei, MD; Dina R. Mody, MD; Mary R. Schwartz, MD; Philip T. Cagle, MD.1 1Department of Pathology, The Methodist Hospital, Houston, Texas; and 2Department of Pathology, The Methodist Hospital and Weill Cornell Medical College, Houston, Texas.

Context: The differential of pancreatic ductal adenocarcinoma (PDA) versus chronic pancreatitis is a challenge in daily practice with significant therapeutic implications. The aim of our study was to evaluate a panel of biomarkers in this setting.

Design: Following a search of our database for PDA from 2003 to 2008, 14 pancreatic resections of PDA were selected with paired chronic pancreatitis from 10 men and 4 women with mean age of 66.2 years (range, 48–82 years). Immunostains for IMP3, S100P, and XIAP were performed on formalin-fixed, paraffin-embedded sections. Staining intensity (0, no staining; 1+, weak; 2+, moderate; 3+, strong) and proportion of positive cells (<10%, negative; 1+, 10%–25%; 2+, 25%–75%; 3+, >75%) were assessed. Positive stains were defined as >10% cells with at least 1+ intensity.

Results: The sensitivity of S100P, IMP3, and XIAP immunoreactivity for a diagnosis of PDA was 100%, 85.7%, and 100.0%, respectively. All 3 immunostains were negative in all tested nonneoplastic pancreatic tissue (Table). Eleven OS, or ductopenia PDAs had positive staining for all 3 biomarkers. Additionally, S100P (85%) and IMP3 (75%) showed more consistent moderate to strong staining than XIAP in most cases.

<table>
<thead>
<tr>
<th>Immunostain</th>
<th>PDA, No. (%)</th>
<th>NPT, No. (%)</th>
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<tbody>
<tr>
<td>S100P</td>
<td>14/14 (100.0)</td>
<td>0/14 (0)</td>
</tr>
<tr>
<td>IMP3</td>
<td>12/14 (85.7)</td>
<td>0/14 (0)</td>
</tr>
<tr>
<td>XIAP</td>
<td>14/14 (100.0)</td>
<td>0/14 (0)</td>
</tr>
</tbody>
</table>

*Nonneoplastic pancreatic tissue including chronic pancreatitis.

Conclusions: These novel biomarkers have high sensitivity and specificity in the diagnosis of PDA, especially when used as a panel. We recommend using at least 2 of these biomarkers in difficult cases of well-differentiated PDA versus chronic pancreatitis. Studies of additional cases are needed to confirm the sensitivity and specificity of these antibodies for this differential diagnosis.

Spectrum of Hepatic Dysgenesis and Associated Disorders in Explanted Polycystic Liver Disease (Poster No. 38)

Marlene Gallegos, MD (marlene.gallegos@rush.edu); Shirram M. Jadeate, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Polycystic liver disease (PCLD) belongs to a family of hepatic ductal plate malformations, with variable presence of other components of biliary dysgenesis and cysts in other organs. PCLD may be associated with intracranial aneurysms and inguinal hernias, and its complications include infected liver cysts and cholangiocarcinoma. Our study addresses the spectrum of dysgenesis and associated conditions in 4 PCLD patients.

Design: We searched our databases for PCLD and found 3 cases in 1200 OLs between the years 1996 to 2008 (0.3%) and 1 autopsy case. The patients’ clinical data, imaging studies, and pathology findings were reviewed. A search was performed for cysts in other organs, associated clinical features, spectrum of biliary dysgenesis, and complications of PCLD.

Results: All 4 patients were women (34–61 years; mean, 48.5 years) and had hepatic PCLD and renal cysts. One third of the patients with OL had concomitant renal transplant, while 1 of 4 had inguinal hernia. All 4 patients had enlarged livers (average, 2800 g) with diffuse cysts and admitted von Meyenberg complexes (VMCs). Three cases had infected cysts and the autopsy case had cholangiocarcinoma with VMCs, partial concomitant hepatic fibrosis, extensive biliary dysplasia, and widespread metastasis.

Conclusions: PCLD is quite rare and is seen predominantly in middle-aged women. There is a strong concomitance of renal cysts, but cysts in other organs and other associated conditions are uncommon. PCLD is always admixed with VMcs and sometimes with congenital hepatic fibrosis. Explanted native livers frequently show infected cysts and when cholangiocarcinoma occurs, it tends to be multifocal with extensive biliary dysplasia and poor prognosis.

Colorectal Mucinous Adenocarcinoma: A Clinicopathologic Study of 74 Cases (Poster No. 39)

Xiaoxian Li, MD PhD (xli@tmhs.org); Jae Y. Ro, MD PhD; Mary R. Schwartz, MD; Steven S. Shen, MD, PhD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Context: Mucinous adenocarcinoma is defined as adenocarcinoma with significant extracellular mucin. Some studies have suggested that colorectal mucinous adenocarcinoma has unique clinical presentations and is associated with more advanced stage and worse prognosis. However, these results have not been corroborated by others. In this study, we present our experience with 74 colorectal mucinous adenocarcinomas.

Design: Slides and reports of 521 invasive colorectal adenocarcinomas were reviewed. Only cases of mucinous and mucinous adenocarcinomas (≥50% extracellular mucin) were included. Carcinomas associated with inflammatory bowel disease or familial polyposis syndromes were
associated with adenomatous change than conventional adenocarcinoma.

Results: Seventy-four of the 521 cases were identified as mucinous adenocarcinoma. The average tumor size of mucinous adenocarcinoma was slightly larger than that of conventional adenocarcinoma (4.9 vs 3.8 cm, \( P < .001 \)). Mucinous adenocarcinoma tended to present at more locally advanced stage (81.1% vs 61.5%, \( P = .001 \)) and was more likely to be associated with adenomatous change than conventional adenocarcinoma (45.9% vs 22.8%, \( P < .001 \)). In addition, mucinous adenocarcinoma was more likely to be located in the right colon (48.6% vs 31.8%, \( P < .001 \)). No significant difference was found in age, total number of lymph nodes recovered, incidence of positive lymph nodes, or grade distribution between mucinous and conventional adenocarcinoma.

Conclusions: Compared with conventional adenocarcinoma, mucinous adenocarcinoma tends to be in the right colon, present with larger tumor size and more advanced stage, and is more commonly associated with adenomatous changes. Our results suggest that mucinous adenocarcinoma has distinctive clinicopathologic features and may warrant special attention.

Duodenal Inflammatory Pseudotumor: An Additional Extrapancreatic Manifestation of Autoimmune Pancreatitis

(Poster No. 40)

Jane L. Bernstein, BA (janeila@mail.med.upenn.edu); Rachel H. Gormley, BS; Emma E. Furth, MD. Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia.

Autoimmune pancreatitis may present as a localized sclerosing process; however, it is now recognized that this inflammatory process is part of a wider, systemic IgG4-associated sclerosing disorder. We report the first case of a duodenal inflammatory pseudotumor with concomitant autoimmune pancreatitis, in which the duodenal polyp exhibits a similar lymphoplasmacytic sclerosing process with infiltration of IgG4-positive plasma cells as seen in the pancreas. A 71-year-old man presented to his clinician with a 30-lb weight loss during the preceding 6 months. A computed tomography scan of the abdomen revealed a 5.7-cm mass in the head of the pancreas. Because of the clinical suspicion of pancreatic carcinoma, the patient underwent a pancreaticoduodenectomy. Intraoperative gross examination revealed a diffusely firm, white pancreas and multiple white nodules studding the liver. Histologic evaluation of the pancreas revealed a histologic pattern similar to that seen in both the liver and pancreas. The case adds to the broadening collection of extrapancreatic lesions associated with autoimmune pancreatitis.

The Demographics and Clinical Course of Carcinoid Tumors and Small Cell Carcinomas of the Gallbladder and Extrahepatic Bile Ducts

(Poster No. 41)

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Context: Neuroendocrine tumors of the gallbladder (GB) and extrahepatic bile ducts (EHBD) include carcinoid tumors (CTs) and small cell carcinomas (SCCs). They are uncommon and little is known about their demographics and clinical course.

Design: Using data from National Cancer Institute’s SEER Program (1973–2005), demographics and 10-year survival rates of patients with CTs and SCCs of the GB and EHBD were analyzed. Logarithmic transformation plots of age-adjusted incidence were analyzed.

Results: Among GB cancers, 119 cases (0.85%) were CTs and 54 (0.39%) were SCCs. Within EHBD, 31 cases (0.34%) were CTs and 17 (0.19%) were SCCs. The female to male ratios of CTs in the GB and EHBD were 2.7 and 1.6, respectively. The ratios for SCC in the GB and EHBD were 2.2 and 1.1, respectively. In the GB the mean age of diagnosis for CT and SCC were 64.5 and 67.5 years, respectively. In the EHBD the mean ages for CT and SCC were 58.2 and 68.4 years, respectively. The 10-year relative survival rate of CTs of the GB and EHBD were respectively 36% and 79%. For SCC, there were no survivors in either site at 10 years. Transformation plots identified CT and SCC as separate carcinogenic pathways.

Conclusions: CT and SCC of the extrahepatic biliary tree are more common in women, more frequent in the GB, and show differences in biologic behavior. Therefore, these tumors should be separately classified and not designated with the single generic term ‘neuroendocrine carcinoma’ without further specification. CTs and SCCs, though possibly similar in histogenetic origin, have distinct carcinogenic pathways.

Persistent Gastrocutaneous Fistulas: A Histopathologic Analysis of Antral and Oxyntic Mucosa Containing Fistulas in the Pediatric Population

(Poster No. 42)

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Context: Percutaneous endoscopic gastrostomy (PEG) is the preferred method of tube feeding gastrostomy in pediatric patients. PEG placement typically occurs above the incisura angularis, along the greater curvature, corresponding to the region of oxyntic gland mucosa. It has been reported that up to 24% of cases develop a persistent gastrocutaneous fistula (GF) following PEG removal. Previous research links the duration of tube placement, fibrosis of tract, and obesity as significant factors involved in GF formation. Published data are lacking regarding the type of gastric mucosa found in this population.

Design: Archived hematoxylin–eosin–stained slides limited to GF cases following PEG placement from the past 5 years at a single large pediatric institution were retrieved for review. Two pathologists, blinded to the mucosa type, reviewed the slides. Mucosa type was placed into one of three categories: oxyntic mucosa only, antral mucosa only, or both types.

Results: A total of 161 cases were reviewed. Eighty-two cases (51%) showed only antral mucosa, 35 cases (22%) showed only oxyntic mucosa, and 43 cases (27%) showed features of both. Statistical analysis between these groups revealed the \( P \) value for the source of variation between these groups to be \( P < .001 \).

Conclusions: A statistically significant difference was detected when comparing GF mucosa types among pediatric patients at our institution. Although the oxyntic mucosa region of the stomach is the typical target for PEG tube insertion, GF with antral gland mucosa was the predominant finding in our study. This finding raises questions regarding the pathophysiology of antral mucosa in GF formation.
A Case of Esophageal Lymphangioma Clinically Susicious for a Gastrointestinal Stromal Tumor
(Poster No. 43)

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We present the case of a 62-year-old Hispanic man with a long-standing history of dysphagia who was found to have a 1.0 cm esophageal ulcer and a large hiatal hernia on endoscopic examination. Six months later a routine follow-up endoscopic exam revealed resolution of the previous ulcerative esophagitis; however, a new 1.5-cm submucosal mass on the posterior wall of the distal esophagus was identified, which was suspicious for a gastrointestinal stromal tumor. Endoscopic ultrasound evaluation showed the mass to have a heterogenous, cystic, multisepated, well-circumscribed appearance. Fine-needle aspiration was inconclusive and suggested the possibility of a mucosal lymphoid aggregate. Owing to the clinical suspicion of a malignancy, the nodule was removed by banding with endoscopic mucosal resection. The tumor histologically consisted of variably sized cystic spaces lined by lymphatic endothelial cells with occasional intramural reactive lymphoid follicles. Further, the endothelial cells were positive for D2-40 staining, a marker specific for lymphatic endothelial cells. Taken together, the diagnosis of lymphangioma was rendered. Lymphangiomas most commonly occur in the head and neck and are exceedingly rare lesions of the esophagus with only 14 cases reported.

Mucosal Hyperplasia of the Appendix:
A Retrospective Review of 33 Cases
(Poster No. 44)

Robert Willim, BS (robert.willim@hsc.stonybrook.edu); Sui Y. Zee, MD. Department of Pathology, Stony Brook University Hospital, Stony Brook, New York.

Context: The term “mucosal hyperplasia” (MH) of the appendix has been used to describe nondysplastic serrated hyperplastic lesions of the mucosa. Recent attempts were made to reclassify some of these lesions as sessile serrated adenoma (SSA). This entity is similar to its colonic counterpart. An association between MH and colorectal carcinoma has been reported. We evaluated cases with a diagnosis of MH to determine its incidence in our patient population, to see if this association exists in our cohort, and to better classify the epithelial proliferations.

Design: We identified 33 appendices diagnosed with MH. Each appendiceal epithelial proliferation (AEP) was categorized as reactive hyperplasia (RH), hyperplastic polyp (HP), SSA, serrated adenoma (SA), or mixed lesion (ML).

Results: Of the 33 cases, 16 were reclassified SSA, 10 as HP, 4 as ML, 2 as RH, and 1 as SA. Four patients (3 HP and 1 SSA) had colorectal carcinoma (12%). Fifteen patients (8 SSA, 3 HP, 3 ML, and 1 RH) had gynecologic neoplasms (46%). Eleven patients (5 SSA, 3 HP, 1 RH, 1 ML, and 1 SA) presented with acute appendicitis (33%). Three patients (2 SSA and 1 HP) had other pathologies (9%) (Table).

Conclusions: Many of the AEPs were reclassified as SSAs. In our study, a lower percentage of patients had AEP with concurrent or past history of colorectal carcinoma. In addition, we identified an unexpectedly large number of patients with AEP and concurrent gynecologic neoplasia. Further studies are needed to determine the significance of this finding.

Epithelial Proliferations of the Appendix

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%)</th>
<th>Type of Mucosal Epithelial Proliferation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal carcinoma</td>
<td>4 (12)</td>
<td>3 HP, 1 SSA</td>
</tr>
<tr>
<td>Gynecologic neoplasm</td>
<td>15 (46)</td>
<td>1 RH, 3 HP, 8 SSA, 3 ML</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>11 (33)</td>
<td>1 RH, 3 HP, 5 SSA, 1 SA, 1 ML</td>
</tr>
<tr>
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</tr>
</tbody>
</table>

Appendiceal Mucinous Neoplasms:
The Mayo Clinic Experience
(Poster No. 45)

David A. Barrett, MD (barrett.david@mayo.edu); Tsung-Teh Wu, MD, PhD; Thomas Smyrk, MD. Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.

Context: There has been a debate in the literature as to the terminology applied to appendiceal neoplasms. This is especially true when peritoneal mucin is discovered. Various terms have been used to describe these neoplasms including low-grade appendiceal mucinous neoplasm (LAMN), mucinous neoplasm of low malignant potential, disseminated peritoneal adenomucinosis, peritoneal mucinous carcinomatosis, and mucinous adenocarcinoma. In this study we looked at 52 patients with mucinous appendiceal neoplasms (not including typical mucinous cystadenomas) to determine the correlation between histologic features and clinical outcomes.

Design: The slides were then reviewed by 2 pathologists and divided into 5 groups: group 1, low-grade morphology with mucin/epithelium confined to periappendiceal tissue; group 2, high-grade morphology with mucin/epithelium confined to periappendiceal tissue; group 3, low-grade morphology with intraabdominal mucin (no epithelium); group 4, low-grade morphology with intraabdominal mucin and mucinous epithelium; and group 5, high-grade morphology with intraabdominal mucin and mucinous epithelium. These patients had a follow-up period ranging from 6 to 151 months (mean, 43.2 months).

Results: The outcomes by group are shown in the Table.

Abbreviations: AWD, alive with disease; DOD, died of disease; NEOD, no evidence of disease.

Cholecdochal Cyst With Associated Signet Ring Cell Carcinoma of the Ampulla
(Poster No. 46)

Timothy R. Pal, MD (tpal@notes.cc.sunysb.edu); Kevin Watkins, MD; Sui Y. Zee, MD. Departments of Pathology and Surgery, Stony Brook University Medical Center, Stony Brook, New York.

A cholecdochal cyst is a dilation of the biliary system with a well-established increased risk of carcinoma. Although many of the neoplasms arise within the cyst wall, some have been described in the gallbladder, the pancreas, and nondilated portions of the biliary system. We report the first case of a type I cholecdochal cyst with a concurrent ampullary signet ring cell carcinoma. A 48-year-old woman presented with right upper quadrant abdominal pain, elevated liver enzymes, and jaundice. Computed tomography and magnetic resonance imaging revealed a type 1 cholecdochal cyst. The patient underwent excision of the cholecdochal cyst. The gallbladder was received with an attached cystic duct and an 8-cm cholecdochal cyst. Following the excision of the cyst, palpation of the duodenum revealed a 1.5-cm mass in the ampulla of Vater. The ampullary mass was excised and on frozen section showed signet ring cell carcinoma. A subsequent pancreaticoduodenectomy was performed. Histologic examination of the cyst showed mucosal ulceration, marked acute and chronic inflammation, and fibrosis. The ampulla was infiltrated by signet ring cell carcinoma involving the duodenal wall (Figure 10). Lymphovascular invasion was present, but the lymph nodes were uninvolved. To our knowledge, this is the first case of ampullary signet ring cell carcinoma seen in conjunction with a type 1 cholecdochal cyst.
Signet Ring Cell Change of the Gallbladder: Case Report and Review of the Literature  
(Poster No. 47)  
Amanda C. Mullins, MD1 (amullins@utmem.edu); Thomas R. Callihan, MD2 (Department of Pathology, University of Tennessee-Memphis; and 3Department of Pathology, Trumbull Laboratories, LLC, German- town, Tennessee.  
The presence of signet ring cells in gastrointestinal specimens typically indicates malignancy. Rarely, however, they can be found in benign specimens as a degenerative feature. We present the case of a 65-year-old woman who presented with symptoms of cholecystitis. A cholecystectomy was performed and the gallbladder submitted to pathology. Gross examination showed numerous gallstones. Microscopic examination of hematoxylin-eosin slides revealed acute, subacute, and chronic cholecystitis. Scattered throughout from the cystic duct margin to the fundus were multiple aggregates of signet ring cells on the mucosal surface and within gland lumens. Mitotic activity was not noted and nuclei were bland. The signet ring cells were positive for mucin, for cytokeratin (CK) 7, for E-cadherin, and variably for CK20. They were predominantly negative for carcinoembryonic antigen and for Ki-67. These features are consistent with benign signet ring cell change. Awareness of this rare degenerative finding can prevent mistaken diagnoses of signet ring cell carcinoma.

Is the Diagnosis of Flat Low-Grade Dysplasia on Surveillance Biopsy for Inflammatory Bowel Disease an Indication for Colectomy?: The Hartford Hospital Experience  
(Poster No. 48)  
Christopher J. Nero, MD (cjnero@gmail.com); Saverio Ligato, MD. Department of Pathology & Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.  
Context: In patients with chronic inflammatory bowel disease (IBD) the presence of flat high-grade dysplasia (FHGD) is a major risk factor for the development of adenocarcinoma and is an indication for colectomy. However, there is controversy regarding the appropriate management of patients with flat low-grade dysplasia (fLGD). The goal of our study is to assess whether the discovery of fLGD during surveillance colonoscopy for IBD may represent an indication for colectomy.  
Design: We reviewed 175 colectomies performed for IBD at Hartford Hospital (1998–2009). All patients had at least one surveillance colonoscopy within a year prior to colectomy. All diagnoses of dysplasia were independently reviewed by the authors.  
Results: Dysplasia was identified in 8 (6 fLGD and 2 FHGD) of 138 (5.8%) colectomies performed for IBD without a prior diagnosis of dysplasia. fLGD was identified in 2 of 7 (29%) colectomies with a prior diagnosis (within 4.5 months after surveillance biopsy) of fLGD. Invasive carcinoma was found in 6 of 13 (46%) colectomies with a prior diagnosis of FHGD.  
Conclusions: In our IBD population, the failure rate of surveillance colonoscopy and biopsy to identify dysplasia was 5.8%. We confirmed that FHGD is associated with a high rate (46%) of adenocarcinoma. The finding of fLGD is associated with a significant risk (29%) of concurrent advanced dysplasia and in our opinion justifies serious consideration for a colectomy in these patients.

Preexisting Villous Adenoma in Colorectal Adenocarcinoma Predicts the Status of KRAS Mutation in Targeted Therapy  
(Poster No. 49)  
Hui Chen, MD, PhD (hui.chen@hitchcock.org); Joel A. Lefferts, PhD; Gregory J. Tsongalis, PhD; Ariell A. Surianiwnata, MD. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.  
Context: Cetuximab is an epidermal growth factor receptor inhibitor effective in treating advanced colorectal adenocarcinoma (CA); however, patients with downstream mutations, such as KRAS mutants at codon 12 or 13, respond poorly to cetuximab. Although KRAS mutations had been previously reported to associate with isolated villous adenoma (16%–40%), the correlation of KRAS mutation with a histologic subset of CA is still lacking.  
Design: Recent surgical resection specimens of CA (n = 27) were collected. The histopathologic features of these CAs were thoroughly reviewed, including tumor types, differentiation, and the presence of persistent preexisting adenomatous polyp. DNA was extracted from formalin-fixed paraffin-embedded sections. These DNA samples were amplified by polymerase chain reaction, using a pair of primers flanking the first coding exon of the KRAS, sequenced using the CEQ 8000 platform (Beckman Coulter), and analyzed for mutations in codons 12 and 13.  
Results: KRAS mutation was found in 4 cases (15%) and was undetectable in the remaining 23 cases (85%). The mutations (G12D, G12V, G12C, and G13D) were consistent with previously identified mutations that predict poor response to cetuximab treatment. Interestingly, all 4 cases with KRAS mutation had gross and histologic features of CA with a persistent preexisting adenomatous polyp with villous architecture (4 of 4; 100%). None of the cases without KRAS mutation showed this feature. Furthermore, other histologic features are not associated with KRAS mutation.  
Conclusions: KRAS mutations have a strong association with CA with persistent preexisting villous adenoma. Patients with a large villous adenoma that progresses to invasive adenocarcinoma may not respond to cetuximab.

An Unusual Coexistence and Impending Collision of a Malignant Gastrointestinal Stromal Tumor and Ovarian Cystadenocarcinomas  
(Poster No. 50)  
Roy E. Lee, MD (rlee@tuftsmedicalcenter.org); Rolf Pfannl, MD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.  
Malignant gastrointestinal stromal tumors (GISTs) are infrequent neoplasms that are usually solitary and are rarely associated with other malignant neoplasms. We present a case of coexisting malignant GIST of the colon and bilateral ovarian cystadenocarcinomas. A 59-year-old woman was admitted for deep venous thrombosis, pulmonary embolism, upper gastrointestinal bleed, renal failure, and a large abdominal mass. Exploratory laparotomy revealed a large intraperitoneal mass wrapping around a segment of colon and bilateral ovarian masses. The ovarian tumors were cystadenocarcinomas with serous and endometrioid differentiation. There were multiple invasive metastatic tumor nodules in the pericolic fat that were composed of pure adenocarcinoma. The colon and peritoneum had multiple, necrotic, friable tumor nodules with transmural tumor extension into colonic mucosa. These tumors were composed of spindle cells with varying degree of nuclear pleomorphism, large areas of necrosis, and more than 50 mitoses per 50 high-power fields. Additionally, some of these spindle cell tumors were admixed with areas of metastatic ovarian cystadenocarcinoma. The spindle cell tumors stained positive for C-Kit, smooth muscle actin (SMA), desmin, and myoglobin and were negative for cytokeratin (CK) 20, CD34, S100, estrogen receptor, and progesterone receptor. These findings were consistent with the diagnosis of malignant GIST. Both the ovarian cystadenocarcinomas and the glands admixed with the GIST were positive for pancytokeratin, CK7, CAM 5.2, and progesterone receptor, and negative for desmin, c-Kit, SMA, and CK20. Neither carcinosarcoma nor sarcomatous differentiation was identified in the ovarian tumors. This case represents an unusual coexistence and impending collision of a malignant colon GIST and ovarian cystadenocarcinomas.

Retrorperitoneal Margin Involvement in Whipple Procedure Correlates with Tumor Characteristics  
(Poster No. 51)  
Hayma Al-Ghawi, MD; Olayomi Asojo, MD1 (asojooa@umail.uc.edu); Ninad Patil, MD; Laura James, MS2; Syed Ahmad, MD1. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.  
Context: The presence of signet ring cells in gastrointestinal specimens typically indicates malignancy. Rarely, however, they can be found in benign specimens as a degenerative feature. We present the case of a 65-year-old woman who presented with symptoms of cholecystitis. A cholecystectomy was performed and the gallbladder submitted to pathology. Gross examination showed numerous gallstones. Microscopic examination of hematoxylin-eosin slides revealed acute, subacute, and chronic cholecystitis. Scattered throughout from the cystic duct margin to the fundus were multiple aggregates of signet ring cells on the mucosal surface and within gland lumens. Mitotic activity was not noted and nuclei were bland. The signet ring cells were positive for mucin, for cytokeratin (CK) 7, for E-cadherin, and variably for CK20. They were predominantly negative for carcinoembryonic antigen and for Ki-67. These features are consistent with benign signet ring cell change. Awareness of this rare degenerative finding can prevent mistaken diagnoses of signet ring cell carcinoma.

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Christopher J. Nero, MD (cjnero@gmail.com); Saverio Ligato, MD. Department of Pathology & Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.  
Context: In patients with chronic inflammatory bowel disease (IBD) the presence of flat high-grade dysplasia (FHGD) is a major risk factor for the development of adenocarcinoma and is an indication for colectomy. However, there is controversy regarding the appropriate management of patients with flat low-grade dysplasia (fLGD). The goal of our study is to assess whether the discovery of fLGD during surveillance colonoscopy for IBD may represent an indication for colectomy.  
Design: We reviewed 175 colectomies performed for IBD at Hartford Hospital (1998–2009). All patients had at least one surveillance colonoscopy within a year prior to colectomy. All diagnoses of dysplasia were independently reviewed by the authors.  
Results: Dysplasia was identified in 8 (6 fLGD and 2 FHGD) of 138 (5.8%) colectomies performed for IBD without a prior diagnosis of dysplasia. fLGD was identified in 2 of 7 (29%) colectomies with a prior diagnosis (within 4.5 months after surveillance biopsy) of fLGD. Invasive carcinoma was found in 6 of 13 (46%) colectomies with a prior diagnosis of FHGD.  
Conclusions: In our IBD population, the failure rate of surveillance colonoscopy and biopsy to identify dysplasia was 5.8%. We confirmed that FHGD is associated with a high rate (46%) of adenocarcinoma. The finding of fLGD is associated with a significant risk (29%) of concurrent advanced dysplasia and in our opinion justifies serious consideration for a colectomy in these patients.
ments of Pathology and Laboratory Medicine, Surgery, and Surgery, Division of Surgical Oncology, University of Cincinnati, Cincinnati, Ohio.

**Context:** Pancreatic cancer is a malignant tumor with extremely poor prognosis. The status of the retroperitoneal resection margin (RPM) in Whipple procedure is an independent prognostic factor in predicting survival. We attempt to evaluate if certain tumor characteristics are associated with positive RPM.

**Design:** Seventy cases of Whipple procedure performed to treat pancreatic ductal adenocarcinoma were retrospectively studied to assess the relation between the status of RPM and certain tumor characteristics. These include site, size, histologic grade, lymph nodes metastasis, vascular perineural microscopic involvement, and extrapancreatic extension.

**Results:** The pancreatic head was the primary site of tumor in 93% of cases. The RPM was microscopically involved by tumor in 14 cases and the superior mesenteric artery was grossly and microscopically involved in only one case. Positive RPM was significantly associated with tumor size (t = −2.27, P = .02). The mean size was 3.67 cm in the positive RPM group and 2.84 cm in the negative group. Microscopic vascular involvement correlated with positive RPM (χ² = 5.03, P = .02) with 71.4% in the positive RPM group versus 33.9% in the negative group. Histologic grade, perineural involvement, lymph nodes invades, and extrapancreatic extension did not correlate with positive RPM (P values .19, .47, .66, and .20, respectively).

**Conclusions:** The retroperitoneal margin in Whipple procedure tends to be involved by tumor in cases of larger tumor size and intratumoral vascular involvement.

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**Enteritis Cystica Profunda Mimicking Invasive Adenocarcinoma in an Adolescent Patient with Peutz-Jeghers Syndrome**

(Poster No. 52)

Susan L. Haley, MD (slahaley@utmb.edu); Mary R. Schwartz, MD; Garth P. Davis, MD; Qihui “Jim” Zhai, MD. 1 Department of Pathology, The University of Texas Medical Branch, Galveston; 2 Department of Pathology, The Methodist Hospital/Baylor College of Medicine, Houston, Texas; 3 Department of Surgery, The Methodist Hospital, Houston, Texas; and 4 Department of Pathology, The Methodist Hospital/Weill Cornell Medical College, Houston, Texas.

Enteritis cystica profunda is a rare benign intestinal lesion associated with Peutz-Jeghers syndrome and other conditions, including Crohn disease. It mimics adenocarcinoma radiographically, grossly, and histologically and, thus, may pose a difficult diagnostic challenge. We describe the case of a 16-year-old boy with Peutz-Jeghers syndrome who presented with intussusception. At exploratory laparotomy, there was a hemorrhagic mass emerging from a previous staple line, and a segment of small bowel was resected. Extending through the intestinal wall and onto the serosal surface was a Peutz-Jeghers polyp whose stalk displayed features suggestive of infiltrative adenocarcinoma, including dilated glands, mucin pools, and transmural misplaced epithelium. However, the lack of significant cytologic atypia and desmoplasia, as well as the lamina propria associated with the misplaced epithelium, supported a benign lesion. Immunohistochemical staining for biomarkers that are frequently overexpressed in malignancy, specifically p53, IMP3, and XIP, was similar to that of adjacent normal mucosal tissue. Patients with Peutz-Jeghers syndrome develop hamartomatous polyposis throughout the gastrointestinal tract, though few develop epithelial misplacement. Additionally, “pseudo-intussusception" has been infrequently described in children, in adolescents, or in the small intestine. Because of the increased incidence of malignancy in individuals with Peutz-Jeghers syndrome, atypical findings such as enteritis cystica profunda may be misinterpreted and overlooked as adenocarcinoma. Differentiation between the two is paramount for appropriate patient management, especially in younger patients, who are particularly vulnerable to long-term complications of unnecessary intervention. Careful assessment of all histologic details and selected immunohistochemical studies is necessary for an accurate diagnosis.

**The Overexpression of RNA-Binding Protein IMP3 in Human Gastric Adenocarcinoma**

(Poster No. 53)

Wei Feng, MD (fengpossible@gmail.com); Camtu D. Truong, MD; Qihui Zhai, MD; Dongfeng Tan, MD. 1 Department of Pathology, MD Anderson Cancer Center Houston, Texas; and 2 Department of Pathology, The Methodist Hospital, Houston, Texas.

**Context:** Insulin-like growth factor II mRNA-binding protein 3 (IMP3) is an oncofetal protein highly expressed in fetal tissue and malignant tumors such as endometrial carcinomas, renal cell carcinomas, and melanoma but only rarely within adult benign tissues. In this study, we evaluated the expression of IMP3 in gastric adenocarcinoma (GAC).

**Design:** Samples from 207 cases of GAC and 25 cases of nonneoplastic gastric mucosa (NNGM) within formalin-fixed paraffin-embedded tissue microarray blocks were examined. Cases with preoperative treatment were excluded. Tissue microarrays were stained with mouse monoclonal anti-IMP3 antibody (180; Dako). The percent (0%-100%) and intensity (1–3+) of positive cytoplasmic and/or membranous IMP3 staining cells were determined. IMP3 expression was also correlated with American Joint Committee on Cancer (AJCC) stage grouping and Lauren classification.

**Results:** A portion of GAC cases (70 of 207; 34%) showed positive cytoplasmic and/or membranous IMP3 staining (1+ in 42 [20%]; 2+ to 3+ in 28 [14%]). On the other hand, only 1 of 25 (4%) NNGM controls showed focal IMP3 staining. Two samples of intestinal metaplasia were negative for IMP3. AJCC stage grouping 3 and 4 cases showed statistically significant higher IMP3 expression compared with AJCC stage grouping 1 and 2 cases (P < .05). Intestinal type GAC showed statistically significant higher IMP3 expression compared with diffuse type GAC (P = .007).

**Conclusions:** IMP3 is overexpressed in a subset of GAC and is usually not overexpressed in NNGM. Higher level of IMP3 overexpression is seen in intestinal type GAC than in diffuse type GAC. Furthermore, higher level of IMP3 expression is associated with higher tumor stage.

**Downregulation of Bax-Interacting Factor 1 in Pancreatic Ductal Adenocarcinoma**

(Poster No. 54)

Domenico Coppola, MD (domenico.coppola@moffitt.org); Leslie M. Turner, MD; James Helm, MD; Mo Malafa, MD; Hong-Gang Wang, PhD. 1 Department of Pathology, 2 Department of Surgery, 3 University Medical Center, Columbus; and 4 Drug Discovery Program, Moffitt Cancer Center, Tampa, Florida.

**Context:** Bax-interacting factor 1 (Bif-1) protein is a member of the endoplasmic reticulum that plays a critical role in apoptosis, autophagy, and mitochondrial morphology. Loss of Bif-1 suppresses programmed cell death and promotes tumorgenesis. To date the role of Bif-1 in pancreatic carcinogenesis has not been studied.

**Design:** To determine Bif-1 expression in human pancreatic ductal adenocarcinoma (PDA), we performed immunohistochemistry (IHC) using pancreatic cancer tissue microarrays containing 82 PDAs and 82 samples of nonneoplastic pancreatic ductal epithelium (NMP). Both PDA and NMP from the same patient were stained in 75 cases. In an additional 7 patients only PDA samples were stained. In an additional 7 patients only NMP samples were stained. Formalin-fixed, paraffin-embedded core sections on the tissue array were immunostained using the avidin-biotin-peroxidase method and the anti–Bif-1 murine monoclonal antibody (dilution 1:2500; Imgenex, San Diego,California). The Bif-1 stain was scored by 2 independent observers.

**Results:** High Bif-1 expression (IHC score 6–9) was identified in 55% (45 of 82) of PDAs but 77% (63 of 82) of NMPs. This difference was statistically significant (P = .003; RR 0.58). Low Bif-1 staining (IHC score 0–4) was present in 45% (37 of 82) of PDAs but only 23% (19 of 82) of NMPs. This difference was also statistically significant.

**Conclusions:** We report the downregulation of Bif-1 during the transition from NMP to PDA in a subset of PDAs. This is a novel finding in agreement with the tumor suppressor function of Bif-1.

**Activation of Mammalian Target of Rapamycin (mTOR) in Gastrointestinal Stromal Tumors**

(Poster No. 55)

James W. Horvath, MD (james.horvath@osumc.edu); Wendy L. Frankel, MD; Andrew M. Bellizzi, MD; Mark Bloomston, MD; Obituaju H. Iwenofu, MD. 1 Departments of Pathology and Surgery, The Ohio State University Medical Center, Columbus.

**Context:** Recent data suggest that alteration of P38/Akt could be a crucial survival pathway in gastrointestinal stromal tumors (GISTs). Mammalian target of rapamycin (mTOR) is a serine/threonine kinase of the P38/Akt signaling pathway known to play an important role in tumor growth as well as a therapeutic target in cancer therapy. Phosphorosorbon S6 protein (p-S6) is a downstream molecule and a surrogate marker of mTOR activation. We examined the reactivity of 61 GISTs for p-S65 expression.

**Design:** Tissue microarrays were built from 61 cases of GIST. Cases included high-risk (n = 18), intermediate-risk (n = 22), and low-risk (n = 21) tumors. Outcome data on the response to imatinib, stratified into complete response, partial response, stable disease, and progressive disease, were available in 15 of 61 patients. Sections were stained with the
antibody to p-S6rp (cell signaling) and cytoplasmic staining was scored 0 to 3+. **Results:** There is a high frequency of p-S6rp expression indicating activation of the mTOR pathway in GIST. Overall, 41 of 61 cases were positive (67%) and 20 were negative (33%). Twenty-four were 1+ (39%), 11 were 2+ (18%), and 6 were 3+ (10%). Approximately a third of the cases showed intermediate to high expression. Response to imatinib did not correlate with expression of p-S6rp.

**Conclusions:** Our data show a high frequency of activation of mTOR (a third with intermediate to high-level expression), suggesting a possible role for mTOR inhibitor therapy in addition to conventional treatment. Testing a large cohort in a prospective fashion is needed to confirm clinical utility.

**Primary Small Bowel Mucosal Melanoma in a Patient With a Previous History of Lentigo Maligna**

**(Poster No. 56)**

**Laura L. Nelsen, MD** (laura.nelsen@usd.edu); **Ali D. Jassim, MD, PhD.** Department of Pathology, Sanford School of Medicine of the University of South Dakota, Sioux Falls.

Although metastatic melanoma can commonly spread to the small bowel, it rarely is the primary presentation and usually involves the serosa; mucosal melanoma is a rare condition. A completely excised lentigo maligna also rarely progresses to metastatic melanoma. Five years after complete excision of a lentigo maligna on his left temple, a 65-year-old man presented to our hospital for gastrointestinal bleeding. The patient had a history of lentigo maligna; however, a repeat examination failed to show any sign of a previous lesion. Physical examination showed no signs of chronicity. Upper endoscopy revealed a complex left upper quadrant lesion with both solid and cystic components. Imaging showed a complex left upper quadrant lesion with both solid and cystic components. Exploratory laparotomy revealed a mesenteric mass with extensive adhesions affecting the small bowel. A portion of small bowel with the associated mesenteric mass was received for frozen section. Microscopically, the mass demonstrated elements of chronic inflammation, fat necrosis, and significant areas of characteristic fibrosis, indicating a diagnosis of sclerosing mesenteritis. The nomenclature attached to this process has been less rigid in the past, with terms such as “mesenteric lipodystrophy,” “mesenteric panniculitis,” and “sclerosing mesenteritis” commonly used in conjunction with the relative proportions of the 3 most common histopathologic findings: fat necrosis, chronic inflammation, and collagen deposition. It has been suggested that the term sclerosing mesenteritis is adequate when there is some degree of characteristic fibrosis. This case underscores the importance of recognizing sclerosing mesenteritis, especially in the absence of clinical suspicion, in the differential of nonspecific mesenteric lesions and supports the contention that sclerosing mesenteritis can be confidently diagnosed intraoperatively.

**Improved Identification of Dysplastic Lesions in Barrett Esophagus**

**(Poster No. 58)**

**Tanya Varma, MD** (tvarma@lsuhsc.edu); **Mary L. Nordberg, PhD.** Department of Pathology, Louisiana Health Sciences Center, Shreveport; and **Department of Pathology, Feist-Weiller Cancer Center, Shreveport, Louisiana.**

**Context:** Detection of certain biomarkers is useful in identifying cases of Barrett esophagus with dysplasia (high and low grade). The detection of low-grade dysplasia remains the grey zone as many dysplastic lesions are missed using light microscopy alone.

**Design:** Eleven cases of Barrett esophagus with no dysplasia and low-grade dysplasia on light microscopy were studied. Immunohistochemistry (IHC) for Ki-67 (Ventana Medical Systems, Inc, Tucson, Arizona), p53 (Ventana), and α-methylacyl coenzyme A racemase (AMACR) (Abcam, Cambridge, Massachusetts) was performed. The cases that showed increased expression by IHC were analyzed by fluorescence in situ hybridization (FISH) for loss of heterozygosity (LOH) at 17p13.1 (p53 gene) and abnormal copy numbers of chromosome 17 using centomeric enumeration probe (CEP17).

**Results:** The IHC results for Ki-67, p53, AMACR, and FISH are shown in the Table.

**Table: Immunohistochemistry Results**

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**Abbreviation:** TBD, to be done.

**Conclusions:** The p53 stain by IHC was normal in all but 3 cases; therefore, its expression is usually unaltered in low-grade dysplasia. FISH analysis showed trisomy of chromosome 17 but no LOH at 17p13.1(p53). Ki-67 is a proliferation marker; hence its expression would be increased in regeneration or repair. The efficacy of this marker is not reliable in the 5 biopsies with increased expression but with significant inflammation. AMACR proved to be a sensitive marker to detect dysplasia. The cases with increased staining with AMACR also showed trisomy of chromosome. Studies to include more cases of high-grade dysplasia are ongoing.

**Sclerosing Mesenteritis: Intraoperative Evaluation of a Clinically Nonspecific Mesenteric Lesion**

**(Poster No. 57)**

**Daniel S. Atherton, MD** (daniel.atherton@bhsala.com). Department of Pathology, Baptist Health System, Birmingham, Alabama.

Sclerosing mesenteritis is a rare disease characterized by an expansile tumorlike process that can affect both the small and large bowel mesenteries. Because it is not a common diagnosis, along with the fact that its presentation can be identical to more common abdominal disorders, sclerosing mesenteritis is often only first suspected and diagnosed intraoperatively. A 48-year-old woman presented to our institution with progressive symptoms of upper abdominal pain along with sporadic episodes of nausea and occasional vomiting. Imaging showed a complex left upper quadrant lesion with both solid and cystic components. Exploratory laparotomy revealed a mesenteric mass with extensive adhesions affecting the small bowel. A portion of small bowel with the associated mesenteric mass was received for frozen section. Microscopically, the mass demonstrated elements of chronic inflammation, fat necrosis, and significant areas of characteristic fibrosis, indicating a diagnosis of sclerosing mesenteritis. The nomenclature attached to this process has been less rigid in the past, with terms such as “mesenteric lipodystrophy,” “mesenteric panniculitis,” and “sclerosing mesenteritis” commonly used in conjunction with the relative proportions of the 3 most common histopathologic findings: fat necrosis, chronic inflammation, and collagen deposition. It has been suggested that the term sclerosing mesenteritis is adequate when there is some degree of characteristic fibrosis. This case underscores the importance of recognizing sclerosing mesenteritis, especially in the absence of clinical suspicion, in the differential of nonspecific mesenteric lesions and supports the contention that sclerosing mesenteritis can be confidently diagnosed intraoperatively.

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**Abstracts**

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Assessment and Follow-Up of Explanted Livers in α1-Antitrypsin Deficiency (Homozygous ZZ Genotype) (Poster No. 59)

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Context: Accumulation of defective α1-antitrypsin (A1AT) in the liver may lead to hepatocellular injury and cirrhosis. Diastase-resistant periodic acid-Schiff (d-PAS)–positive A1AT globules are currently the only significant pathologic finding. We aim to evaluate pathologic findings in explanted livers, coexistent pulmonary disease, and posttransplantation follow-up.

Design: From January 1993 to May 2008, patients with ZZ genotype (PiZZ) who underwent orthotopic liver transplantation were selected at our institution among 1200 transplants. The explants were reviewed for gross and histologic findings, concomitant liver disease, pulmonary disease, and follow-up hepatic graft biopsies.

Results: A total of 3 patients were identified (0.2% of total transplants). All patients were men (age range, 56–58 years). All showed mixed macronodular and micronodular cirrhosis and abundant d-PAS–positive large hepatocytic cytoplasmic globules. One case showed incidentally increased iron. Another case showed severe macrovesicular steatosis consistent with incidental coexistent NASH. None had a dysplastic nodule or carcinoma. There was no symptomatic pulmonary dysfunction, but 2 cases exhibited mildly emphysematous changes on computed tomography scan and chest x-ray. One case required retransplantation due to bile cast syndrome within 1 year. Follow-up biopsies of the grafts for up to 5 years showed no reaccumulation of d-PAS–positive globules.

Conclusions: A1AT deficiency is an extremely rare indication for hepatic transplantation. Other than d-PAS–positive globules and incidental findings such as NASH and increased iron, there are no distinctive pathologic findings. No A1AT globule reaccumulation is seen in the graft. There is no coexistent pulmonary dysfunction, and only mild pulmonary emphysema is detected radiologically.

Diagnostic Utility of von Hippel-Lindau Gene Product (pVHL) and S100P in Adenocarcinoma and Dysplasia of the Gallbladder (Poster No. 60)

Fan Lin, MD, PhD1 (flin1@geisinger.edu); Haiyan Liu, MD, PhD; Jianhui Shi, MD, PhD; Yiran Xu, BS; Jun Zhang, MD, MD; Hanlin L. Wang, MD, PhD.1 1Department of Laboratory Medicine, Geisinger Health System, Danville, Pennsylvania; 2Department of Pathology, Mayo Clinic, Rochester, Minnesota; and 3Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California.

Context: Our recent study demonstrated the nearly perfect inverse correlation of upregulation of S100P and downregulation of von Hippel-Lindau gene product (pVHL) in pancreatic intraepithelial neoplasias and ductal adenocarcinoma of the pancreas (Lin et al. AJSP. 2008;32:78–91). This study investigates the utility of these 2 markers in the diagnosis of adenocarcinoma and dysplasia of the gallbladder.

Design: Immunohistochemical stains for S100P and pVHL were performed on 65 gallbladder specimens, including adenocarcinoma (n = 25, 8 cases also containing glandular dysplasia), reactive glandular atypia (n = 20), and normal gallbladder (n = 20). The staining intensity was graded as weak or strong. The distribution was recorded as negative, 1+, 2+, 3+, and 4+.

Results: The results demonstrated a nuclear and cytoplasmic staining pattern of S100P in 19 of 25 (76%) adenocarcinoma cases and 8 of 8 (100%) cases with glandular dysplasia. In contrast, none of the 40 reactive/normal gallbladder cases was positive for S100P. Glandular epithelia in all normal and reactive cases were diffusely (3+ and 4+) positive for pVHL with membranous/cytoplasmic staining. In contrast, all cases of adenocarcinoma and dysplasia were negative for pVHL, whereas the adjacent normal ductal/glandular epithelia were positive for pVHL.

Conclusions: Our data suggest that (1) the findings of upregulation of S100P and downregulation of pVHL in adenocarcinoma and dysplasia are similar to that of pancreatic intraepithelial neoplasia and pancreatic ductal adenocarcinoma, indicating a possible role of these 2 proteins in tumorigenesis; and (2) the expression patterns of pVHL and S100P can be used as a pair of diagnostic markers to confirm the diagnosis of adenocarcinoma and dysplasia of the gallbladder.

Unusual Presentations of Cecal Carcinomas (Poster No. 61)

Katherine J. Downey, MD (katherine.downey@bmc.org); Marier Hernandez, MD; Bethany J. Tierno, MD; Sandra Cerda, MD. Department of Mallory Institute of Pathology, Boston Medical Center, Boston, Massachusetts.

With the exception of the rectum and sigmoid, the cecum is the most common site of carcinoma of the large intestine and carries a poorer prognosis than other colon cancers (overall 5-year survival rate, 57%) because of long-standing obscure symptoms including intermittent diffuse abdominal pain (70%), intestinal obstruction (60%), and palpable mass (10%). We report 2 cases of cecal carcinomas with unusual clinical presentations. The first case involves a 68-year-old man with a past medical history of diverticulosis, hypertension, and hyperlipidemia who presented to the emergency room complaining of a 1-week history of intermittent symptoms including severe epigastric abdominal pain exacerbated by movement, decreased appetite, and change in bowel movements. He denied fever or prior abdominal surgeries. Laboratory results showed leukocytosis (15,000/µL, reference range 4000–11,000/µL). Computed tomography imaging showed appendicitis without perforation. Emergent appendectomy was scheduled and a frozen section of the appendix during surgery showed adenocarcinoma at the appendiceal orifice. Final pathology showed low-grade adenocarcinoma with positive nodal metastases (AJCC Stage IIIA [pT2, pN1, pMx]) and acute appendicitis. Our second case involved an 88-year-old woman with past medical history of hypertension and diabetes mellitus who presented to the emergency room complaining of severe abdominal pain. Computed tomography imaging showed perforated bowel. An emergent hemicolectomy was scheduled. Pathology showed low-grade adenocarcinoma (AJCC Stage II [pT2, pN0, pMx]). Cecal carcinomas can have unusual clinical presentations thereby causing a significant delay in diagnosis. These delays are due to a lack of suspicion, and thus cecal carcinomas should always be in the differential.

Possible Histopathologic Changes in Contaminated Heparin (Poster No. 62)

Cesar V. Reyes, MD (creyes@morrishospital.org). Department of Pathology, Morris Hospital, Morris, Illinois.

Contaminated heparin with oversulfated chondroitin sulfate has recently been suggested as the cause of severe anaphylactoid reactions after intravenous heparin. It has also been postulated that the supposed contaminant directly activates the kinin-kinin system in human plasma, which leads to the generation of bradykinin, along with C3a and C5a, also potent anaphylatoxins. Activation of these pathways is linked and dependent on fluid-phase activation of factor XII. The resulting histopathologic changes, however, have not been documented. This case involves a 27-year-old woman who underwent laparoscopy-assisted vaginal hysterectomy 2 days prior to presenting with acute abdomen due to pelvic hemorrhage. On laparoscopy, large blood clots were found in the lower abdomen and pelvis. Clot removal and lysis were supplemented with heparin washing of the lower abdominal and pelvic cavities and was tolerated well. Ten days later, there was recurrence of acute abdomen, associated with small intestinal obstruction. Laparoscopic reevaluation of the pelvis and lower abdomen revealed a peritoneal/pelvic severe exu-
Sessile Serrated Adenoma of the Colon: A Case Report and Review of the Literature (Poster No. 63)

Danisha L. Allen, MD1 (danisha@gwu.edu); Anupamjit K. Mehrrota, MD2; Wen Chen, MD; Suman S. Chauhan, MD.1 Department of Pathology, The George Washington University Medical Center, Washington, DC; 2Department of Hepatic and Gastrointestinal Pathology, Armed Forces Institute of Pathology, Washington, DC; and 3Department of Pathology and Laboratory Medicine Services, Veterans Affairs Medical Center, Washington, DC.

Sessile serrated adenomas, a recently described entity of colonic polyps, display features similar to hyperplastic polyps such as sessated architectural growth and lack of cytologic dysplasia. These lesions commonly arise in the proximal colon and appendix. Grossly, the polyps are flat or slightly raised in relation to the adjacent mucosa. Microscopic features include basal dilation and flask-shaped crypts, often oriented parallel to the muscularis mucosae conferring an inverted T- or L-shaped appearance to the crypts. Cells lining the crypts are cytologically bland and serration is often present at the surface and bases of the crypts (Figure 13, B through D). Patients are generally treated and followed the same as those with traditional adenomatous polyps. We present a case of a 54-year-old male smoker who underwent a colonoscopy for hematochezia, notable for an 8-mm sessile polyp in the cecum and a 15-mm polyp in the proximal colon. Macroscopically the polyloid masses were pale tan, brown, and finely granular. Microscopic examination of both polyps demonstrated the aforementioned characteristic features, consistent with sessile serrated adenomas. Reports have shown that sessile polyps progress to adenocarcinoma via methylation of CpG islands of the promoter regions of suppressor and mutator genes. The adenocarcinomas demonstrate a defect in DNA mismatch repair, with subsequent metastasis of hepatocellular carcinoma (HCC). Antiangiogenic agents like bevacizumab and sorafenib, targeting vascular endothelial growth factor (VGEF-A) and the VEGF receptor (VEGFR), respectively, have become a standard of care for conventional HCC. Because VEGF-A and VEGFR activate the extracellular signal-regulated kinase (ERK) 1/2 pathway, we analyzed the relative expressions of VEGF-A and activated (phosphorylated) ERK 1/2 in this study of fibrolamellar hepatocellular carcinoma (FLHCC).

Design: Morphoproteomic analysis was performed in 7 cases of FLHCC using immunostaining for the detection of VEGF-A and a phosphospecific probe at the putative sites of activation, threonine 202 tyrosine 204 on ERK 1/2. Subcellular immunolocalization of the chromogenic signal was determined and signal intensity was graded on a scale of 0 to 3+ by bright-field microscopy.

Results: All 7 of 7 cases showed strong (3+) PRRK 1/2 nuclear expression in endothelial cells of intratumoral vessels and fibroblasts. This overexpression was most prominent at the interface of the neoplastic polyp with the adjacent mucosa. VEGF-A expression was observed in the cytoplasm of neoplastic hepatocytes in all 7 cases. The signal intensity was variable (1–3+). Focal cytoplasmic positivity for VEGF-A was also seen in fibroblasts.

Conclusions: ERK pathway is constitutively activated and contributes to angiogenesis and fibroplasia in FLHCC. Targeting this pathway by therapeutic agents may be beneficial in FLHCC. The molecular mechanism(s) of ERK pathway in FLHCC progression merits further investigation.

Expression of Claudin-3 and Claudin-4 Proteins in Gastric Adenocarcinoma (Poster No. 65)

Reenu Malhotra, MD; Amanda L. Peterson, MD (amanda.l.peterson@uth.tmc.edu); Wei Li, MD. Department of Pathology, University of Texas Health Science Center-Houston.

Context: Claudins comprise a family of integral membrane proteins, which play a major role in tight junction formation and function. Alterations in expression of Claudins have been described in various malignancies and have been suggested as possible biomarkers and targets for cancer therapy. The aim of this study was to determine the expression pattern of claudin-3 and claudin-4 in gastric adenocarcinoma and correlate expression with clinicopathologic variables.

Design: Paraffin-embedded tissue from 21 cases of gastric adenocarcinoma (11 intestinal, 10 diffuse/mixed subtypes) were analyzed for expression of claudin-3 and claudin-4 protein by immunohistochemistry. Additionally, expression of these proteins in 20 gastric biopsies with chronic active gastritis and intestinal metaplasia were evaluated for comparison. The protein expression was categorized into 3 grades: 1+ (weak), 2+ (moderate), or 3+ (strong) based on staining intensity.

Results: Moderate to strong staining of claudin-3 and claudin-4 was detected in 90.1% and 72.7%, respectively, of the intestinal type and 90% and 80%, respectively, of the diffuse subtypes of adenocarcinoma. In comparison, weak to moderate staining of claudin-3 was observed in chronic active gastritis and intestinal metaplasia (P = .007). Significant statistical difference in claudin-4 protein expression was observed between carcinoma and chronic active gastritis and intestinal metaplasia (P < .001).

Conclusions: Claudin-3 and claudin-4 are strongly expressed in intestinal and diffuse subtypes of gastric adenocarcinoma. The upregulation of claudin expression suggests their possible role in gastric carcinogenesis, their potential utility as diagnostic biomarkers, and possible targets for innovative therapy.

A Pancreatic Mass in a 56-Year-Old Woman (Poster No. 66)

Fernando Antelo, MD1 (antelo@ucla.edu); Bruce E. Stabile, MD; Samuel W. French, MD. Departments of Pathology and Surgery, Harbor-UCLA Medical Center, Torrance, California.

We report a rare case of pancreatic cystic tumor with features of both serious microcystic adenoma and mucinous cystic adenoma. Our patient is a 56-year-old woman evaluated for epigastric pain, with identification of a 9-cm mass in the pancreas on computed tomography (arrow, Figure 14, A). A distal pancreatectomy with splenectomy was performed. On gross examination, the pancreatic tumor was composed largely of innumerable small, thin-walled cysts, ranging in size from less than 0.1 to 0.5 cm (Figure 14, B). Light microscopy revealed that these cysts were lined by a single layer of clear cuboidal epithelial cells (Figure 14, C); staining Constitutive Activation of ERK Pathway Is Associated With Tumoral Angiogenesis and Fibroplasia in Fibrolamellar Hepatocellular Carcinoma (Poster No. 64)

Sadhna Dhingra, MD2 (Sadhna.Dhingra@uth.tmc.edu); Wei Li, MD; Dongfeng Tan, MD; Robert E. Brown, MD1.1 Department of Pathology and Laboratory Medicine, University of Texas Health Sciences Center—Medical School, Houston; and 2Department of Pathology, MD Anderson Cancer Center, Houston, Texas.

Context: Angiogenesis is the propelling force for tumor growth and metastasis of hepatocellular carcinoma (HCC). Antiangiogenic agents like bevacizumab and sorafenib, targeting vascular endothelial growth factor (VEGF-A) and the VEGF receptor (VEGFR), respectively, have become a standard of care for conventional HCC. Because VEGF-A and VEGFR activate the extracellular signal-regulated kinase (ERK) 1/2 pathway, we analyzed the relative expressions of VEGF-A and ERK 1/2 in this study of fibrolamellar hepatocellular carcinoma (FLHCC).

Design: Morphoproteomic analysis was performed in 7 cases of FLHCC using immunostaining for the detection of VEGF-A and a phosphospecific probe at the putative sites of activation, threonine 202 tyrosine 204 on ERK 1/2. Subcellular immunolocalization of the chromogenic signal was determined and signal intensity was graded on a scale of 0 to 3+ by bright-field microscopy.

Results: All 7 of 7 cases showed strong (3+) PRRK 1/2 nuclear expression in endothelial cells of intratumoral vessels and fibroblasts. This overexpression was most prominent at the interface of the neoplastic polyp with the adjacent mucosa. VEGF-A expression was observed in the cytoplasm of neoplastic hepatocytes in all 7 cases. The signal intensity was variable (1–3+). Focal cytoplasmic positivity for VEGF-A was also seen in fibroblasts.

Conclusions: ERK pathway is constitutively activated and contributes to angiogenesis and fibroplasia in FLHCC. Targeting this pathway by therapeutic agents may be beneficial in FLHCC. The molecular mechanism(s) of ERK pathway in FLHCC progression merits further investigation.
with periodic acid–Schiff for glycogen and anti-inhibin antibodies was consistent with serous microcystic adenoma. The tumor also contained a focus of cystic spaces lined by a single layer of tall columnar cells with apical vacuoles (Figure 14, D); staining of the epithelium with Alcian blue/periodic acid–Schiff for mucin and of the stroma with anti–smooth muscle actin antibody was diagnostic of mucinous cystadenoma. Three cases have been previously described in Japan (Abe et al. *Pancreas*. 2005; 31:98–100). To our knowledge, this is the first case of mixed serous and mucinous cystic tumor of the pancreas in the United States.

is generally believed that GPs arise from endodermal/neuroectodermal complexes and represent a pancreatic-type hamartoma. However, reports of GP metastases to locations away from the duodenum, including lungs, mediastinum, esophagus, nasopharynx, and ovary are consistent with the idea that these tumors represent true neoplasms. To our knowledge, this is the first report of a case of primary rectal GP and supports the hypothesis that these lesions arise from neuroendocrine tumors/paragangliomas with ganglionic/neuroectodermal differentiation.

### Intraductal Papillary Mucinous Neoplasm of the Pancreas: Histopathologic Characterization of 46 Consecutive Cases

(Monica T Garcia, MD; Loren P Herrera, MD; Pablo A Bejarano, MD; Department of Pathology, University of Miami Miller School of Medicine, Miami, Florida; and Department of Pathology, Jackson Memorial Hospital, Miami, Florida.)

**Context:** Intraductal papillary mucinous neoplasms (IPMNs) of pancreas are intraductal mucin-producing cystic tumors showing variable degree of atypia ranging from adenoma to invasive carcinoma. We investigated the incidence and histopathologic characteristics of IPMNs in a single tertiary center.

**Design:** We reviewed 350 consecutive pancreaticoduodenectomies performed during a 4-year period. The IPMNs were assessed for size, location, malignant features, perineural invasion (PNI) or lymphovascular invasion (LVI) and TNM when applicable.

**Results:** Of 243 pancreatic neoplasms, 18.3% were IPMNs. The mean age of patients was 66.9 years and tumor size was 3.3 cm. Sixty-seven percent of IPMNs were located in the head, 15% in the body, 15% in the tail, and 2% in heterotopic pancreas. Forty-eight percent were adenomas, 15% were borderline, 4.3% showed in situ carcinoma, and 32.6% showed invasive carcinoma. Five cases of IPMN-adenoma were associated with ducal carcinoma. Three cases showed IPMN with serous cystadenoma, endocrine microadenoma, and ampullary adenocarcinoma. Most ducal carcinomas with associated IPMN-adenoma were pT3 (83%) or N1 (80%), whereas 53% of the invasive-IPMN were pT3 and 22% were N1. LVI was observed in 33% of the invasive-IPMN and 67% of ducal carcinomas with associated IPMN-adenoma. PNI was observed in 53% of invasive-IPMN and 100% of ducal carcinomas with associated IPMN-adenoma (Table). **Conclusions:** In this series, IPMNs represent 18% of all pancreatic tumors. IPMNs without the presence of invasive carcinoma were more common. Patients with invasive-IPMN showed lower TNM stage and less LVI and PNI compared with patients whose pancreas contained both conventional duclal carcinoma and IPMN-adenoma (P < .001).

### Estimated Frequency and Clinicopathologic Characteristics of Intraductal Papillary Mucinous Neoplasm (IPMN)

<table>
<thead>
<tr>
<th>Estimated Frequency and Clinicopathologic Characteristics of Intraductal Papillary Mucinous Neoplasm (IPMN)</th>
<th>Mean Age, y/ Size, cm</th>
<th>LVI, %/ PNI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma</td>
<td>66.1/2.9</td>
<td>N/A</td>
</tr>
<tr>
<td>Borderline</td>
<td>67.3/3.1</td>
<td>N/A</td>
</tr>
<tr>
<td>In situ IPMN</td>
<td>59.6/1.8</td>
<td>N/A</td>
</tr>
<tr>
<td>Invasive IPMN</td>
<td>66.8/4.4</td>
<td>53% T3/ 33/53</td>
</tr>
<tr>
<td>Adenoma associated with ducal carcinoma</td>
<td>71.3/2.0</td>
<td>83% T3/ 67/100</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

### First Report of a Massive Hepatocellular Carcinoma of the Liver in a Pediatric Patient, as a Sequela of Therapy for a High-Grade Glioma

(Sree Lakshmi Ravula, MD; Jeffrey Soonsowski, MD, PhD; Elizabeth Manci, MD; Department of Pathology, University of South Alabama Medical Center, Mobile; and Department of Pediatric Pathology, University of South Alabama Children’s and Women’s Hospital, Mobile.)

Hepatocellular carcinoma (HCC) of the liver is one of the common malignant tumors in children. We present an unusual case of HCC of the liver in a pediatric patient with high-grade glioma. This is the first re-
Donor-Derived Small Cell Neuroendocrine Carcinoma of Pulmonary Origin in a Liver Transplant Recipient

(Poster No. 71)

Adeel Ahmad, MD (ahmad@tuftsmedicalcenter.org); Faisal A. Kho- kar, MD; Janet Cowan, PhD; Jeffrey Cooper, MD; Monica Pilichowska, MD, PhD. Departments of Pathology and Transplant Surgery, Tufts Medical Center, Boston, Massachusetts.

Donor-derived malignancies in transplant recipients are rare and found in 0.02% to 0.2% of allograft recipients. We report a case of donor-derived small cell neuroendocrine carcinoma in a liver transplant recipient. To the best of our knowledge such a case has not been previously reported. A 44-year-old man with end-stage liver disease secondary to hepatitis C and hepatocellular carcinoma received a cadaveric liver transplant from a 58-year-old female donor. The donor was an active smoker (2 packs per day) for several years with chronic obstructive pulmonary disease but without history of cancer. Donor screening included chest radiograph, which had normal results. Recipient’s clinical course was unremarkable until 8 months posttransplant when he presented with abdominal pain and multiple liver nodules. Computed tomography–guided fine-needle aspiration and core biopsy of the liver revealed sheets and clusters of small cells with high N/C ratio, round nuclei, fine chromatin, and indistinct nucleoli. Tumor cells were positive for pankeratin, cytokeratin 7, thyroid transcription factor 1, and chromogranin and negative for CD45, CDX-2, Hep Par 1, α-fetoprotein, serotonin, somatostatin, vasoactive intestinal peptide, calcitonin, bombesin, and gastrin. The diagnosis of small cell neuroendocrine carcinoma consistent with pulmonary derivation was made. Subsequent workup revealed no primary tumor in the recipient. Fluorescent in situ hybridization analysis of tumor cells revealed a 46,XX chromosome complement consistent with donor origin (Figure 17). The risk of transplant-related tumor xenograft is very low. However, donor-derived small cell carcinoma can occur. A donor’s smoking history could be of interest, and expanded smoking screening of donors might be warranted.

Cutaneous Manifestations in a Patient With Juvenile Polyposis Syndrome:
A Case Report and Review of the Literature

(Poster No. 72)

Luigi K. Rao, MD (LuigiRao@alumni.nd.edu); Joel T. Moncur, MD, PhD. Department of Pathology and Laboratory Services, Walter Reed Army Medical Center, Washington, DC.

Juvenile polyposis syndrome (JPS), associated with SMAD4 and BMPR1A gene mutations, is defined clinically by at least 6 juvenile colon polyps, multiple gastrointestinal tract juvenile polyps, or any number of juvenile polyps along with a family history of juvenile polyps. Many familial polyposes, including Cowden, Gardner, and Muir-Torre syndromes, have been recognized to have distinct cutaneous manifestations. We present a patient with skin lesions believed to represent cutaneous manifestations of JPS, a phenomenon never previously reported based on our review of the literature. The patient presented at 6 months with rectal bleeding and a lesion protruding from the anus. Subsequent colonoscopy revealed innumerable polyps carpeting the colon with multiple biopsies showing juvenile polyps, and a diagnosis of JPS was rendered. No mutations in SMAD4 or BMPR1A were detected during genetic workup. Continued surveillance discovered multiple gastric and small bowel juvenile polyps. Furthermore, several perianal verrucous polyoid lesions were biopsied on 4 separate occasions beginning at age 2. These polyps ranged in size from 0.5 to 1.5 cm. They exhibited a papillomatous architecture and were lined by an epidermis with varying degrees of acute inflammation with overlying hyperkeratosis and parakeratosis. The dermis dis-
played gaping vessels with prominent lymphocyte and plasma cell–rich chronic inflammation. Parakeratotic spires, keratohyalin granules, or viral cytopathic effect were not identified. In situ hybridization for human papillomavirus was negative. We believe the architecture of these inflamed verruciform fibroepithelial polyps, their recurrent nature, and their proximity to the gastrointestinal tract support the notion that these lesions represent cutaneous manifestations of JPS.

POSTER SESSION 200: SUNDAY, OCTOBER 11, 2009, 1:00 PM–3:30 PM

Clinical Chemistry; Clinical Immunology; Breast Pathology; Gynecologic and Placental Pathology; Pulmonary and Mediastinal Pathology

Serum Protein-Bound Thyroxine Induced Biases in Antibody-Based Single-Phase Assays for Free Thyroxine (Poster No. 1)

Yvette C. Tanhecho, MD, PhD; Octavia M. Palmer, PhD; Linda S. Derrick, MT; Jorge L. Sepulveda, MD, PhD; Harry C. Blair, MD; Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia; and Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania.

Context: Thyroid function is assessed by measuring free thyroxine (T<sub>f</sub>) when thyroid-stimulating hormone (TSH) is inconclusive. Interference in single-phase antibody-based assays for free T<sub>f</sub> is a major problem. Accurate measurement of free T<sub>f</sub> is important when thyroid-binding globulins might vary (eg, during pregnancy). We evaluated the ability of several assays in excluding signal from protein-bound T<sub>f</sub>. Design: We examined TSH and free T<sub>f</sub> in a mostly female population (50% were pregnant) at Magee-Women’s Hospital. Protein-bound T<sub>f</sub> bias was assessed by dialyzing samples and assaying retentate with increasing amounts of dialysate being added. TSH was measured for all samples. Results: Assays of free T<sub>f</sub> using the Vitros ECi platform (Ortho-Clinical Diagnostics, Rochester, New York) were essentially independent from several assays in excluding signal from protein-bound T<sub>f</sub>. The ECi assay was largely insensitive to protein-bound T<sub>f</sub>. The DxI assay was largely insensitive to protein-bound T<sub>f</sub>. The Cenia assay was largely insensitive to protein-bound T<sub>f</sub>. The LX20 assay was largely insensitive to protein-bound T<sub>f</sub>. The Beckman assay was largely insensitive to protein-bound T<sub>f</sub>. The Olympus assay was largely insensitive to protein-bound T<sub>f</sub>. Conclusions: Some single-phase, direct, free T<sub>f</sub> immunoassays have important interference from protein-bound T<sub>f</sub>. The DxI assay was largely unaffected by serum protein. In a mostly female and 50% pregnant population, correlation of TSH to free T<sub>f</sub> was poor for all tested assays.

A New Study of Intraosseous Blood for Laboratory Analysis (Poster No. 2)

Larry J. Miller, MD; Thomas E. Philbeck, PhD; Diana F. Monteze, RN, BSN; Cathy J. Spadaccini, MD; Department of Science & Clinical, Vidacare Corporation, San Antonio, Texas; and Department of Pathology, Ameerpath South Texas, San Antonio.

Context: Improved devices that enable providers to deliver critically needed drugs as quickly as central lines have ignited a resurgence in the use of IO space, including drawing IO blood for laboratory analysis. Despite previously favorable studies, some laboratory staff have concerns about the reliability of IO-derived blood for use in laboratory tests. This study validates earlier studies and addresses concerns raised by laboratory staff regarding the use of IO-derived blood. Design: We obtained institutional review board approval. Ten adult volunteers consented to participate, and blood samples were obtained from peripheral veins in the forearm. Within 5 minutes, an IO catheter was placed in the proximal humerus, and 2 sets of IO blood samples were obtained from each participant, one set following 2 mL of marrows/blood waste and one set following 6 mL of waste. At a reference laboratory, all sample sets were analyzed for complete blood count and chemistry profile. Means were compared for each blood value of the drawn samples (intraosseous, IO-1, and IO-2), with intraosseous blood values serving as controls for IO blood values.

Results: IO and intravenous values were clinically similar, except in the case of white blood count and carbon dioxide (Table). Conclusions: We found that IO space is a reliable source of blood for laboratory analysis when conducting tests commonly performed in emergency medicine, such as complete blood count and chemistry profile. Results, however, may be moderately reliable for carbon dioxide and unreliable for white blood count.

<table>
<thead>
<tr>
<th>Value</th>
<th>IV</th>
<th>IO-1</th>
<th>IO-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC, 1000/μL</td>
<td>7.6 ± 1.6</td>
<td>15.0 ± 7.1</td>
<td>10.4 ± 4.0</td>
</tr>
<tr>
<td>RBC, million/μL</td>
<td>4.8 ± 0.4</td>
<td>4.7 ± 0.4</td>
<td>4.3 ± 0.2</td>
</tr>
<tr>
<td>Hgb, g/dL</td>
<td>14.3 ± 0.9</td>
<td>13.9 ± 1.6</td>
<td>13.7 ± 0.8</td>
</tr>
<tr>
<td>Hct, %</td>
<td>42.5 ± 2.8</td>
<td>40.6 ± 2.9</td>
<td>39.9 ± 1.7</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>106.8 ± 14.1</td>
<td>110.0 ± 16.3</td>
<td>108.9 ± 15.9</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>13.9 ± 2.5</td>
<td>13.9 ± 2.4</td>
<td>13.9 ± 2.4</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.0 ± 0.2</td>
<td>0.8 ± 0.2</td>
<td>1.0 ± 0.2</td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>140.3 ± 3.7</td>
<td>136.4 ± 1.7</td>
<td>136.4 ± 1.5</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.6 ± 0.5</td>
<td>5.4 ± 1.0</td>
<td>5.0 ± 1.0</td>
</tr>
<tr>
<td>Chloride, mmol/L</td>
<td>104.8 ± 1.7</td>
<td>105.2 ± 1.4</td>
<td>105.4 ± 2.0</td>
</tr>
<tr>
<td>CO&lt;sub&gt;2&lt;/sub&gt;, mmol/L</td>
<td>22.7 ± 3.2</td>
<td>17.4 ± 2.5</td>
<td>17.3 ± 2.1</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.9 ± 0.5</td>
<td>9.2 ± 0.3</td>
<td>9.2 ± 0.3</td>
</tr>
<tr>
<td>Total protein, g/dL</td>
<td>3.7 ± 1.0</td>
<td>7.0 ± 0.4</td>
<td>7.3 ± 0.4</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.5 ± 0.2</td>
<td>4.4 ± 0.2</td>
<td>4.4 ± 0.3</td>
</tr>
</tbody>
</table>

Abbreviations: BUN, blood urea nitrogen; Hct, hematocrit; Hgb, hemoglobin; RBC, red blood cell; WBC, white blood cell.

Variation of Analytic Method for High-Density Lipoprotein Cholesterol Determination Is Clinically Significant (Poster No. 3)

Stanley J. Podlasek, MD (spodlas2@jhu.edu). Department of Pathology, Johns Hopkins University, Baltimore, Maryland.

Context: High-density lipoprotein cholesterol (HDL-C) is lower in hospitalized patients; this has been attributed to stress or dietary changes related to hospitalization. Because outpatients are tested in commercial laboratories while inpatients are tested in hospital laboratories, we hypothesized that different analytic methods might explain the difference in HDL-C values.

Design: We sent 50 random patient samples from physicians’ offices to a commercial laboratory where they were simultaneously assayed on the AU2700 chemistry analyzer (Olympus, Melville, New York) and the LX20 chemistry analyzer (Beckman-Coulter, Fullerton, California) on the day of collection. Design: The EP Evaluator (David G. Rhoads Associates, Kennett Square, Pennsylvania) was used to calculate means and bias to perform regression analysis.

Results: The Olympus method (mean HDL-C, 59.2 mg/dL) had a positive bias of 13.4 mg/dL compared with the Beckman method (mean HDL-C, 45.8 mg/dL). Olympus-based HDL-C equals 1.271 × (Beckman-based HDL-C) + 1 mg/dL.

Conclusions: Patients who go from a laboratory that uses the Olympus analyzer to one that uses the Beckman analyzer experience a significant method-dependent decrease in the level of HDL-C, which may change treatment. Manufacturers and laboratories should note the standardization program for HDL-C sponsored by the Centers for Disease Control and Prevention in which the reference range is specified by the National Cholesterol Education Program and not by a population study. Comparing the frequency of race- and sex-matched individuals with low HDL-C values from a particular laboratory with those published for like segments of the US population by the Centers for Disease Control and Prevention would be of value.

Assessment of Fetal Maternal Fetal: Concordance Between TDx-FLM II Values and Lecithin to Sphingomyelin Ratios (Poster No. 4)

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Context: Respiratory distress syndrome represents a significant disease entity in newborns. Assessment of fetal lung maturity (FLM) is essential when clinicians are determining whether to delay delivery. Several measurements exist to elucidate FLM, including the traditional gold standard ratio of lecithin to sphingomyelin (L/S) and the newer TDx-FLM II assay (Abbott Laboratories, Abbott Park, Illinois). We evaluated concordance be-
Primary Sternal Cryptococcoma With Dissemination in a Human Immunodeficiency Virus–Negative Patient With Selective Idiopathic CD4-Positive T-Cell Lymphocytopenia  
(Poster No. 6)

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This case study highlights the importance of considering idiopathic CD4-positive lymphocytopenia in nonimmunosuppressed, human immunodeficiency virus–negative patients who present with atypical fungal infections. Medical history was noncontributory for causes of immunosuppression. Findings included a cavitary sternal lesion. Chest x-ray was unremarkable. 

Biopsy of sternum showed granulation tissue with teardrop-shaped, budding yeasts. Culture confirmed Cryptococcus neoformans. Flow cytometry demonstrated selective CD4-positive lymphocytopenia with CD8-positive lymphocytes in the normal range. The patient was diagnosed with idiopathic primary sternal cryptococcoma within a background of CD4-positive lymphocytopenia. Treatment included amphotericin B lipid complex followed by oral fluconazole. Follow-up at 6 months showed persistent CD4-positive lymphocytopenia. The sternal lesion was also persistent. A second cryptococcal hip lesion was identified by computed tomography and was biopsied; results suggested chronic disseminated cryptococcosis with CD4-positive lymphopenia. The patient died from CD4-positive lymphopenia. The patient remained less than 60 cells per micrometer for 6 months. Newer treatments may include interleukin 2 to restore T4 levels; prophylaxis for opportunistic infections remains the central treatment. The differential diagnosis may be complicated by false-negative serology in 60% of patients with local cryptococcal infection and by 80% cross-reactivity among blastomycosis, histoplasma, and cryptococcal antigens. CD4-positive lymphocytopenia in human immunodeficiency virus–negative patients with no other explanation for immunosuppression has been associated with opportunistic fungal infections. We believe this is the first reported case of primary sternal cryptococcoma in a patient with idiopathic CD4-positive lymphocytopenia. Idiopathic CD4-positive lymphocytopenia is likely underdiagnosed and should be considered in otherwise healthy patients with atypical fungal infections.

A Systemic Lupus Erythematosus Case With a Wide Spectrum of Autoantibodies and t(1;6)(q25;q23) Translocation  
(Poster No. 8)

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Systemic lupus erythematosus is well known for being difficult to diagnose; diagnosis requires extensive clinical laboratory studies for evidence of autoimmune markers and organ damage. Genetic etiology of this disease also remains elusive. We report a case of a 49-year-old woman who presented with fatigue, shortness of breath for 1 month, and years of menorrhagia. After thorough workup, systemic lupus erythematosus was diagnosed. We detected a wide spectrum of autoantibodies, including...

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antineuclear antibody, anti-double-strand DNA antibody, anti-Smith antibody, antineutrophil cytoplasmic antibody (pANCA and cANCA), antithyroid peroxidase antibody, anti-smooth muscle antibody, and serum warm antibody. These findings parallel the patient’s condition, including damage to multiple organs, and highlight her body’s loss of tolerance toward its own antigens. Blood cells are negative for JAK2 mutations.

Cytogenetic analysis on bone marrow and phytohemagglutinin-stimulated blood cells both revealed a 46 XX, t(1;5)(q25;p23) translocation, which has been considered a hallmark of leukemia. This translocation is poorly described in systemic lupus erythematosus. Our case is the second report of systemic lupus erythematosus associated with a chromosome translocation.

A Comparison of HLA Crossmatching Methodologies

(Poster No. 9)
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Context: The crossmatch is a vital test performed by the transplant or HLA laboratory. Basic/modified microcytotoxicity, anti-human globulin, and flow-based bead/microparticle assay/enzyme immunoassay crossmatching methods are the major techniques used.

Design: Using data collected from the College of American Pathologists’ Proficiency Testing Surveys, we evaluated the relative sensitivities of these 3 major crossmatching methods, changes in sensitivities for each method during a 5-year period, and positive and negative predictive values for each method.

Results: We reviewed 11 College of American Pathologists’ Proficiency Testing Surveys (MX1 and MX2 surveys for 2003 and 2008) and analyzed 7959 major histocompatibility complex I crossmatches and 2203 major histocompatibility complex II crossmatches. The flow/enzyme method was the most sensitive method in the MX1 and MX2 surveys in both 2003 and 2008 (Table) and showed improved sensitivity during the 5-year period (MX1, P < .001; MX2, P < .001). The other methods showed no improvement or decreased sensitivity during the same period. The flow/enzyme method had higher positive predictive values (87%–94%) than the other methods.

Conclusions: These results strongly suggest that laboratories and their transplant programs that rely on microcytotoxicity (direct, modified, or anti-human globulin–augmented) crossmatches may be missing a significant number of clinically significant HLA antibodies. Those laboratories and programs should consider more sensitive methods of antibody detection and crossmatching, such as flow-based bead/microparticle assay/enzyme immunoassay crossmatching methods.
accurate determination of prognosis and management. In addition to the potential for missing lymphatic invasion, another problem occurs when Medical Branch, Galveston.

Results: LCIS variants represented 0.34% (30 of 8712) of all CBs. Average age was 55 years (range, 41–78 years). Seven (23%) patients had a family history, and 8 (31% of LCIS-P and 18% of LCIS-N) had a personal history of BC. Six LCIS-P and 1 LCIS-N were associated with a mass; the remainder were associated with calcifications. Forty percent (12 of 30) of variant LCIS had associated invasive lobular carcinoma (ILC) in either CB or SE, with 58% (7 of 12) staged as T1mic. Twenty-five percent of LCIS variants detected in CB were upstaged in SE: 14% (2 of 14) of LCIS-P and 40% (4 of 10) of LCIS-N.

Conclusions: LCIS variants are often associated with ILC, suggesting they act as direct precursors to BC. LCIS-P can exhibit an unfavorable biomarker profile (high Ki-67, ER negative, p53 positive, and HER2/neu positive), a feature not present in LCIS-N. As 25% of LCIS variants diagnosed in CB are upstaged in SE, complete excision of these lesions is mandatory.

D2-40 Increases Detection of Lymphatic Invasion in Breast Carcinoma (Poster No. 13)

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Context: Detection of lymphatic invasion is an important component of complete histopathologic evaluation of primary breast carcinoma for accurate determination of prognosis and management. In addition to the potential for missing lymphatic invasion, another problem occurs when artificial tissue retraction around tumor (false lumen) is confused with true lymphatic invasion. We hypothesized that using D2-40 antibody, a sensitive marker for lymphatic endothelium, can increase the sensitivity of detecting true lymphatic invasion in breast carcinoma, thus helping to identify patients at higher risk for metastatic disease.

Design: Sixteen cases of lymph node–positive invasive breast carcinoma (14 ductal and 2 lobular) from 2003 to 2007 were retrospectively collected from our institutional archives. In the original pathology reports, all cases were negative for lymphovascular invasion within hematoxylin-eosin–stained tissue sections. Original slides from the cases were reviewed to confirm the study’s inclusion criteria were met, and tissue blocks were selected for D2-40 immunostaining. The original hematoxylin-eosin–stained and D2-40–stained slides were reviewed independently by 2 pathologists. Only cases with unequivocal tumor emboli within positively stained, endothelial-lined, lymphatic vessels were counted as positive.

Results: Four of 16 (25%) cases showed definitive lymphatic invasion within tissue sections that were previously unidentified by hematoxylin-eosin–stained slides alone.

Conclusions: Using D2-40 immunostain on selective tumor sections may increase the diagnostic sensitivity of lymphatic invasion detection in cases of primary breast carcinoma. This study demonstrates the usefulness of D2-40 immunostain as a tool to confirm or reject suspected foci of lymphatic invasion that are questionable in hematoxylin-eosin–stained tissue sections. Original slides from the cases were reviewed including Ki-67, estrogen receptor, progesterone receptor, and HER2/neu data. Immunohistochemical stains were performed following the vendor’s protocols. The Ki-67 positivity cutoff groups were <10%, 10% to 20%, >20%, and <10%, 10% to 29%, and >30%.

Results: Fifty-three percent of tumors in the low proliferative Ki-67 group of <10% were grade 1 tumors. Fifty-two percent of tumors with Ki-67 values of 10% to 20% were grade 2 tumors, and 55% of cases with values >20% were grade 3 tumors. At a cutoff value of >30%, 27% of grade 2 and 28% of grade 1 tumors were excluded from the high proliferative group. All grade 3 tumors were in this high proliferative group.

Conclusions: Our study suggests that Ki-67 cutoff values of <10%, 10% to 29%, and >30% are more closely associated with histologic grade and, therefore, may be more representative of low, intermediate, and high proliferative activity. Ki-67 positivity is not associated with estrogen receptor, progesterone receptor, or HER2/neu status. Further studies with a larger number of cases and correlation of Ki-67 positivity with prognosis are required.

The Role of Fibrinolytic Proteins in Angiogenesis and Tumor Progression (Poster No. 15)

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Context: Angiogenesis, an essential component of tumor progression, has been studied by various methods. One method is to look for the proteases and protease inhibitors produced in the growth and elongation of existing vessels; another is to look for endothelial cell markers. We used both methodologies to prove that angiogenesis was occurring and to identify the specific sites of angiogenesis in and around mammary carcinoma.

Design: Clinical history, histopathology, and immunohistochemistry results were obtained for 11 women (range, 41–87 years) with breast cancer who were diagnosed and treated at Hahnemann University Hospital (Philadelphia, Pennsylvania).

Results: Tissue plasminogen activator and annexin II staining were present in both tumor and proximal surrounding tissue, confirming the presence of protease and fibrinolytic/anti-fibrinolytic protein receptor–regulated steps that are specific to angiogenesis. Additionally, CD105 (endoglin) antibody selectively stained the endothelial cells of angiogenic blood vessels within and adjacent to tumors (Figure 18). Tissue uninvolved by tumor did not show positive staining, thereby serving as an internal control.

Conclusions: Invasive mammary carcinoma and adjacent desmoplastic tissue showed an increased concentration of fibrinolytic proteins and an upregulation of the binding site for proteases and antiproteases. This area of increased fibrinolysis coincides with the area containing blood vessels that stained for CD105, a marker of endothelial cells undergoing angiogenesis. These findings make a strong argument for the existence of the fibrinolytic/anti-fibrinolytic mechanism of tumor-induced angiogenesis.
Of interest, the finding of CD105-positive blood vessels in desmoplastic stroma suggests that the tumor is priming the blood vessels beyond its periphery for local expansion.

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A Rare Case of Bilateral Multinodular Pseudoangiomatous Stromal Hyperplasia in a Patient With Gigantomastia

(Poster No. 16)

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Pseudoangiomatous stromal hyperplasia (PASH) is a benign breast lesion composed of dense collagenous stroma with complex, anastomosing, empty, slitlike pseudovascular spaces that are either aecellular or lined by spindle stromal cells. Its appearance mimics a vascular lesion, including angiosarcoma. PASH is usually seen as incidental microscopic foci in normal breast tissue or in association with various benign and malignant breast lesions. Occasionally, it can present as a distinct lesion, either in a diffuse pattern or as a unilateral discrete nodule (nodular PASH). Grossly, the nodule is indistinguishable from fibroadenoma, ranging from 1 to 17 cm. Reports of nodular PASH are rarely present in the literature, and even fewer cases of bilateral nodular PASH are described. We report a case of bilateral multinodular PASH in a 42-year-old woman who has a long history of gigantomastia with progressive enlargement and who has elected to undergo bilateral reduction mammoplasty.

CD1A Expression in Poorly Differentiated Estrogen Receptor- and Progesterone Receptor-Negative Invasive Ductal Carcinoma of the Female Breast

(Poster No. 17)

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Context: Recent studies suggest that primary invasive female breast carcinomas with positive estrogen receptor (ER) and progesterone receptor (PR) have greater dendritic cell infiltration; these patients may also have a better prognosis.

Design: Our study population consisted of patients diagnosed with ER- and PR-negative poorly differentiated invasive ductal carcinoma at Rush University Medical Center between 1975 and 1988. Two distinct groups of patients were compared: group 1 consisted of 16 women who were alive and free of disease for an average of 14 years. Group 2 consisted of 20 women who died of disease within 3 years of diagnosis. The 2 groups were matched for clinical stage and ER/PR receptor status. The following breast cancer marker profile was obtained for all patients: ER (Dako), PR (Dako), and CD1A (Dako).

Results: The average age of group 1 patients was 52.4 years (range, 31–74 years). The average age of group 2 patients was 52.6 years (range, 34–80 years). Evaluation of CD1A did not show a difference between the 2 groups: (group 1, 1 of 16; 6%) versus (group 2, 2 of 20; 10%). CD1A expression was observed in dendritic and tumor cells.

Conclusions: Similar expression of CD1A-positive cells was seen in patients with short- and long-term survival. Strong correlation was found between no expression and/or low expression of CD1A-positive cells and ER- and PR-negative tumors. Tumor cells also expressed CD1A, suggesting a possible costimulatory effect by this molecule on the functional immune response. In patients with ER- and PR-negative invasive breast carcinoma, lack of expression or low expression of CD1A does not appear to predict survival.

Tissue-Specific Expression of Estrogen Receptor-β Wild Type and Isoforms

(Poster No. 18)

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Context: Estrogen receptor-β (ER-β) has been mostly studied in breast and some prostate cancers and has been shown to be associated with progression. We tested ER-β wild type (wt) and its isoforms in different tissues to further elucidate tissue- and cell-specific expression of ER-β.

Design: Tissue microarray slides of 130 normal and 260 malignant tissues from 13 different organs were tested for ER-Bwt (Biogenex, San Ramon, California), 2 clones of ER-B1 (Dako, Carpenteria, California and AbD Serotec, Raleigh, North Carolina), ER-B2 (AbD Serotec), ER-BCT (Upstate, Lake Placid, New York), ER-B NT (Millipore, Billerica, Massachusetts), and ER-A (Dako) using immunohistochemistry procedures. Nuclear staining less than 5% was considered negative.

Results: ER-Bwt and isoforms were detected in nuclei and/or cytoplasm. In normal tissues, ER-Bwt was expressed in 93% (12 of 13) of the organs in the range of 60% to 90% in breast, stomach, kidney, thyroid, endometrium, bladder, pancreas, prostate, brain, and ovary and less than 10% in lung and colon. Hepatocytes showed only cytoplasmic reaction. ER-B1 and ER-B2 isoforms were expressed heterogeneously in only (5 of 13) of the organs. In neoplastic tissues, expression of ER-Bwt, ER-B1, and ER-B2 was decreased in colon, kidney, endometrium, brain, and pancreas and increased in stomach, lung, and ovary. ER-B and ER-A were coexpressed in 30% of normal and malignant endometrium, brain, and ovary tissues.

Conclusions: ER-B is expressed in many normal tissues but variably in neoplastic tissues. ER-B may play a stimulatory or suppressive role in tumorigenesis. Testing ER-B in different tissues may provide further insights on ER-B in tumorigenesis.

Lupus Mastitis: An Unusual and Underrecognized Entity

(Poster No. 19)

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Lupus panniculitis is an infrequent manifestation of systemic lupus erythematosus, occurring in approximately 2% to 3% of patients. Up to 70% of patients with lupus panniculitis have discoid lesions. Lupus mastitis (LM) is a rare manifestation of lupus panniculitis involving the breast, and it clinically and radio logically mimics carcinoma. Approximately 20 cases have been reported in the literature. We added 2 cases with clinical and radiologic findings suspicious for malignancy. The first patient is a 58-year-old African American woman who was diagnosed with systemic lupus erythematosus in 1995. In July 2005, a firm, palpable mass was discovered in the right upper breast. Mammo graphy showed a 2.6-cm, hazy, ill-defined, soft tissue density that was suspicious for malignancy. An excisional biopsy showed a nodular, angiogenic, and angioinvasive lymphoid infiltrate involving fat lobules with associated hyaline fat necrosis and was diagnostic of lupus panniculitis. The patient was treated on Plaquenil and showed improvement in the palpable mass. However, in November 2006, a new firm, palpable mass was discovered in her left breast. An excisional biopsy again showed LM. The second patient is a 52-year-old African American woman with a diagnosis of discoid lupus. Mam mography and ultrasound in November 2008 revealed 2 suspicious left breast masses with associated microcalcifications and an enlarged axillary lymph node. The masses were excised and showed changes diagnostic of LM. LM has characteristic histologic findings but clinically mimics malignancy and, therefore, necessitates tissue biopsy. LM should be considered in the differential diagnosis of breast masses in patients with lupus.

Low-Grade Adenosquamous Carcinoma of the Male Breast

(Poster No. 20)

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Low-grade adenosquamous carcinoma of breast is an uncommon neoplasm in women and is exceedingly rare in men. In the literature, we found only one reported case of low-grade adenosquamous carcinoma in a man. This tumor is known for local recurrence after incomplete excision but also has low metastatic potential. Histologically, the tumor is composed of syringoma-like glandular structures with variable amounts of squamous differentiation in a background of bland spindle cell stroma. Due to its characteristically bland histopathology, this tumor is often confused with infiltrating syringoma of the nipple and tubular carcinoma of breast. We report a case of a 73-year-old man who presented with a 2-cm subareolar left breast hard nodule with increased size and tenderness. Biopsy of the mass revealed the tumor, which was made up of multiple irregular ducts, many of which were curved, convoluted, and irregularly dilated (Figure 19). They were lined by 2 rows of epithelium and squamous cells. The epithelial cells showed bland nuclear morphology. Ductal structures and squamous cell nests were seen infiltrating the muscle bundles of nipple and underlying breast and fibroadipose tissue. Following radical debulking, axillary lymph nodes were negative for metastatic carcinoma. The tumor was positive for HER2/neu and negative for p53. This study reports a rare example of low-grade adenosquamous...
carcinoma arising in a male breast. The histopathology of the present tumor is similar to that seen in low-grade adenosquamous carcinoma occurring in the female breast.

The Expression of Leptin, Polo-like Kinase-1, and HMG-CoA Reductase in Human Carcinomas and Sarcomas

(Poster No. 21)

Ashish Barman, MD1 (abarman@mcvh-vcu.edu); Tina Ipe, BA2; Katherine Kimmelshue, MD3; Michael Idowu, MD4 (1Department of Pathology and 2School of Medicine, Virginia Commonwealth University, Richmond. 3Context: Leptin (Lep/Ob), polo-like kinase-1 (PLK1), and HMG-CoA reductase inhibitors (statins; HMGCR inhibitors) have been reported as possible risk factors for cancer incidence, cancer aggressiveness, and cancer lowering effects, respectively, according to studies using cell lines and epidemiologic studies. There is limited information regarding the expression of these proteins in clinical specimens. This study evaluates the differential expression of these proteins in clinical specimens using immunohistochemistry.

Design: Immunohistochemical stains were performed on 41 randomly selected cases of invasive breast carcinoma with adjacent benign breast and 10 cases of sarcoma using paraffin-embedded tissue with antibodies to Ob, PLK1, and HMG-CoA reductase inhibitors (statins; HMGCR inhibitors) (Santa Cruz Biotechnology, Inc, California). Two pathologists evaluated the stains for intensity and cell staining percentage. Cases exhibiting moderate to intense staining with at least 10% positivity were interpreted as positive.

Results: There was no significant difference between breast versus breast carcinoma with Ob (10% vs 24%; P = .88), HMGCR (54% vs 63%; P = .57), and PLK1 (7% vs 12%; P = .46). There was no differential expression between breast carcinoma and sarcoma with Ob (24% vs 40%; P = .32) and HMGCR (63% vs 80%; P = .32); there was differential expression with PLK1 (12% vs 50%; P = .007) (Fisher exact test).

Conclusions: The lack of differential expression of Ob, PLK1, and HMGCR in benign breast and carcinoma suggests that these proteins may not be clinically useful for diagnostic purposes. The apparent differential expression of PLK1 between carcinoma and sarcoma may benefit from further studies.

Intraoperative Frozen Section on Sentinel Lymph Nodes Is Not Indicated in Patients With Ductal Carcinoma In Situ of the Breast or in Those Undergoing Prophylactic Mastectomy

(Poster No. 22)

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Context: The appropriateness and cost-effectiveness of routine intraoperative sentinel lymph node (SLN) assessment remains to be defined. We aim to determine whether routine intraoperative frozen section (FS) examination of SLNs is worthwhile in all patients undergoing surgery for breast cancer.

Design: We conducted a retrospective study, reviewing 184 consecutive cases of SLN biopsy performed by a single experienced breast surgeon in 2007 with attention to variations by histologic subtype and tumor size. This number included 91 invasive ductal carcinomas, 22 invasive carcinomas with mixed lobular-ductal features, 19 invasive lobular carcinomas, 18 ductal carcinomas in situ, and 34 prophylastic mastectomies. All patients underwent SLN biopsy with intraoperative FS evaluation. The nodes negative on FS were further subjected to an enhanced histopathologic evaluation protocol with 3 levels of routine hematoxylin-eosin–stained sections and 3 levels of immunocytochemical-stained sections using pancytokeratin antibody (AE1/AE3).

Results: The overall sensitivity of intraoperative FS of SLNs was 66%. The intraoperative FS of SLNs was negative for all cases of ductal carcinoma in situ and prophylactic mastectomies. Of 46 cases with invasive breast cancer smaller than 1.0 cm, only 2 (4.3%) cases were found to be positive on intraoperative FS.

Conclusions: Intraoperative FS of SLNs is not worthwhile for patients with ductal carcinoma in situ or for those undergoing prophylactic mastectomy. Whether intraoperative FS of SLNs should be performed on patients with early (smaller than 1.0 cm) invasive tumors will be discussed. An effort to expand the study by increasing the number of cases is currently underway.

Laboratory Compliance With the American Society of Clinical Oncology and College of American Pathologists’ Guidelines for HER2 Testing: A College of American Pathologists Survey of 757 Laboratories

(Poster No. 23)

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Context: To ensure quality HER2 testing in breast cancer, the ASCO/CAP introduced guidelines with the intent of compliance by 2008. We conducted this survey to assess the effect of these guidelines on pathology laboratories and their ability to address key components.

Design: In late 2008, the survey was distributed with the HER2 immunohistochemistry (IHC) proficiency testing program. It included questions regarding institutional and pathology practice characteristics, assay validation using fluorescence in situ hybridization (FISH) or another IHC laboratory test, and pathologist HER2 scoring competency assessment.

Results: We received 757 of 907 surveys. The median laboratory accessioned 15 000 cases and annually performed 190 HER2 tests. Quantitative computer image analysis was used by 33% of laboratories. In-house FISH was performed in 23% of laboratories. Sixty percent of laboratories addressed the 6- to 48-hour tissue fixation requirement by embedding tissue on the weekend. HER2 testing was performed on the initial biopsy in 40% of laboratories; on the resection specimen in 6%; and either in 54%. Forty-seven percent of laboratories validated with FISH only, 10% with another IHC test only, 13% with both; 12% had not validated; 15% chose “not applicable.” Ninety percent concordance rate with FISH results was achieved in 88% IHC-negative and 81% IHC-positive cases. Ninety percent concordance rate with another IHC test was achieved in 80% negative and 75% positive cases. Ninety-one percent of laboratories had a pathologist competency assessment program.

Conclusions: This survey demonstrates the extent and characteristics of HER2 testing. Although some ASCO/CAP guidelines have been implemented, gaps remain in validation of HER2 IHC testing.

Intraoperative Axillary Sentinel Lymph Node Evaluation: False-Negative Rate in Neoadjuvant Versus Nonneoadjuvant Cases

(Poster No. 24)

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Context: The false-negative (FN) intraoperative interpretation for sentinel lymph nodes may increase the health care cost due to delayed completion axillary dissection. This study evaluates the rates of FN, true positive, true negative, and false positive in patients with and without prior

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neoadjuvant treatment and compares the differences in the rates for cases evaluated using tumor imprint cytology (TIC) versus TIC and/or frozen section.

**Design:** We reviewed 174 consecutive cases with intraoperative evaluation of axillary sentinel lymph nodes using both TIC and/or frozen section. The rates of FN, true positive, true negative, and false positive were determined by correlation with permanent hematoxylin-eosin sections. Completion axillary dissection, if performed, was also reviewed.

**Results:** Thirty-one (17.8%) had neoadjuvant treatment, while 82.2% did not have neoadjuvant treatment (Table). One hundred thirty-three (76.4%) cases were evaluated by TIC only, while 23.6% were evaluated by TIC and/or frozen section (4 cases were evaluated by FS only). There was no false-negative intraoperative diagnosis. Of the 22 total FN, 40.9% had metastasis on permanent hematoxylin-eosin sections larger than 2 mm, while 59.1% had isolated tumor cells (13.6%) and micrometastasis (45.5%). For cases with completion axillary dissection, only 7.1% of the FN intraoperative diagnosis had additional positive lymph nodes, compared with 64% in patients with a true-positive intraoperative diagnosis.

**Conclusions:** The relatively higher rate of FN in patients with prior neoadjuvant treatment may be due to treatment-induced fibrosis. There appears to be a low chance of additional positive lymph nodes on completion axillary dissection with an FN intraoperative diagnosis.

**Discordance Between the Immunohistochemical (Estrogen Receptor, Progesterone Receptor and HER2/new) Characteristics in Primary Breast Cancer Versus Axillary Lymph Node Metastases: Should Lymph Node Metastases Be Retested?**

(Poster No. 25)

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**Context:** Patients with stage III breast carcinoma and similar hormone receptor and HER2 gene product status by immunohistochemistry may respond differently to similar therapeutic regimens. The therapy is generally based on the immunohistochemical features of the primary breast tumor, and the metastatic axillary lymph nodes are never tested. We hypothesize that discordance in the immunohistochemical features between the primary tumor and the axillary lymph node metastases might explain different clinical responses to hormonal treatment and/or chemotherapy. In previously published studies, the discordance varied from 0% to 14.9%.

**Results:** Discordance was found for all 3 immunohistochemical markers; the highest was for estrogen receptor (13.8%). Prospective studies with larger sample sizes are needed to establish statistical significance and the possible need to test both the primary and metastatic tumor prior to making treatment decisions.

**Protein Manifestations of Amyloidosis of the Breast in Core and Mammothome Biopsy Specimens**

(Poster No. 26)

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**Context:** Core and mammothome breast biopsy (C/M Bx) are the primary techniques for initial sampling of most mass lesions and suspicious calcifications. Prior studies of breast amyloidosis (BA) involved primarily excisional specimens. We report our experience with the manifestations of BA within C/M Bx.

**Design:** An 11-year retrospective search of our pathology archives was conducted for cases with BA identified in C/M Bx. Cases were evaluated with hematoxylin-eosin, Congo red stain, and electron microscopy (1 case). We analyzed clinical findings and subsequent follow-up.

**Results:** We identified 4 patients with BA in C/M Bx, representing 0.05% of 8170 patients with C/M Bx reviewed during this 11-year period. All patients were women with a mean age of 60 years (range, 49–73 years). BA was unilateral in 2 patients and bilateral in 2 patients. Amyloid distribution was as follows: stromal, perivascular, and/or periductal/perilobular. In 2 patients, BA was associated with infiltrating and/or in situ ductal carcinoma; one case had subsequent documentation of systemic amyloidosis (primary AL type). One patient had a benign amylod tumor and serum IgG λ electrophoretic band. The remaining patient had BA associated with a giant cell histiocytic reaction and microcalcifications.

**Conclusions:** BA may present as a mass lesion, nodus for suspicious calcifications, or in association with infiltrating and/or in situ carcinoma. Its presence within C/M Bx is rare (less than 0.1% of all cases). In limited core material, BA may be misinterpreted as fibrosis or elastosis. Recognition in C/M Bx is critical due to the potential for systemic involvement and/or sinister autoimmune or lymphoproliferative disorders.

**MRE11, RAD50, and NBS1 Gene Expression in Breast Cancer Progression**

(Poster No. 27)

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**Context:** MRE11, RAD50, and NBS1 comprise the MRN protein complex involved in DNA double-strand break repair and are reportedly downregulated in invasive breast carcinoma. We compare MRN levels in benign breast tissue, carcinoma in situ, and invasive carcinoma.

**Design:** Western blot analysis was performed on HMF-3522 cell lines (benign S1, preinvasive S3-C, invasive T4-2 cells) grown in 2- and 3-dimensional cultures. Forty-seven randomly selected cases of invasive breast carcinoma with adjacent in situ tumor and benign epithelium were immunohistochemically stained with antibodies to MRE11, RAD50, and NBS1 (BD Biosciences, San Jose, California). Two pathologists independently scored nuclear staining, using a 0 to 3 scale (negative to strongly positive). Cohort analysis was performed to compare staining between tissue types using a linear model with the tissue type and pathologist as explanatory variables. Variance component due to tissue type was tested using F-distribution (SAS Software; Cary, North Carolina). A P value of .01 or less was considered significant.

**Results:** Western blot analysis showed MRN protein levels decreasing progressively between S1, S3-C, and T4-2 cells (Figure 20). There were
Reevaluation of Diagnostic Value of p120 Catenin in Differentiating Lobular Carcinoma From Low-Grade Ductal Carcinoma of the Breast
(Poster No. 28)

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Context: The confirmation of lobular carcinoma is usually based on negative E-cadherin staining. A recent study reports that p120 catenin is a sensitive and specific positive marker for lobular carcinoma, with strong and diffuse cytoplasmic staining. To our knowledge, there are few follow-up published studies.

Design: Forty-four cases of invasive lobular carcinoma (ILC) and 26 cases of low-grade invasive ductal carcinoma (IDC) were included in this study. Eighteen of 44 ILC cases also contained lobular carcinoma in situ. All IDC cases were negative for E-cadherin, and all IDC cases were positive for E-cadherin. Most cases (n = 65) also contained normal breast tissue. Immunohistochemical staining was performed with monoclonal antibody to p120 catenin (clone 98; 1:200 dilution; BD Biosciences, San Jose, California). The staining intensity was graded as weak, moderate, or strong. The distribution was recorded as negative, 1+, 2+, 3+, and 4+. Results: All IDC cases were positive for p120 catenin, with strong and diffuse cytoplasmic staining (greater than 3+) in 34 of 44 (77%) cases and moderate to weak staining in 10 (23%) cases. All IDC cases were positive for p120 catenin, with strong and diffuse membranous staining (greater than 3+) in 22 of 26 cases. Four IDC cases showed focal (1+ or 2+) and weak membranous staining.

Conclusions: Our data show that p120 catenin is useful in differentiating ILC from IDC. However, caution should be taken: Twenty-three percent of ILCs showed moderate to weak cytoplasmic and membranous staining, and a small portion of IDCs showed only focal and weak membranous staining.

Detection of Chromosomal Anomalies in Uterine Endometrial Carcinoma Using Fluorescence In Situ Hybridization (UteroFISH)
(Poster No. 30)

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Context: Endometrial cancer is the most common pelvic gynecologic malignancy. The diagnosis of well-differentiated endometrial adenocarcinoma, atypical hyperplasia, and marked hyperplasia is often challenging. We investigated the utility of chromosomal anomalies for the detection of endometrial carcinoma using multitarget fluorescence in situ hybridization (FISH).

Design: Samples were collected by endometrial brush and processed by liquid-based thin-layer cytologic preparation protocol. We collected samples from consecutive cases to include 50 benign, 50 hyperplasia without atypia, 50 atypical hyperplasia, and 50 endometrial carcinomas. Each was hybridized using fluorescence labeled DNA probes to chromosomes 1, 8, and 10 (UteroFISH). FISH signals were enumerated in 100 cells per case, and the chromosomal anomalies were correlated with pathological findings, including histologic diagnoses on endometrial tissue samples.

Results: Numeric chromosomal anomalies were found in 0% (0 of 50) of benign, 20% (10 of 50) of hyperplasia, 76% (38 of 50) of atypical hyperplasia, and 86% (43 of 50) of carcinoma specimens. The mean percentage of cells with chromosomal changes was 54% in cancer specimens, which was significantly higher than in nonatypical hyperplasia (15%, P < .001) and atypical hyperplasia (34%, P < .001). The most frequent chromosomal anomaly was gain of chromosome 1. FISH anomalies had an overall sensitivity of 81% and specificity of 90% for the detection of atypical hyperplasia and/or endometrial carcinoma. There was no association with grade of endometrial carcinoma.

Conclusions: Multitarget UteroFISH appeared to be useful for the differential diagnosis of reactive hyperplasia, atypical hyperplasia, and endometrial adenocarcinoma, showing a high level of sensitivity and specificity. Endometrial hyperplasia with chromosomal anomalies may require close follow-up.

Malignant Mixed Mullerian Tumor of the Cervix: Case Report and Review of Literature
(Poster No. 31)

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Malignant mixed mullerian tumors (MMMTs) of the female reproductive system represent an uncommon, aggressive, and complex set of tumors with histologic features of both carcinomas and sarcomas. Cervical MMMTs are particularly rare, presenting mostly after menopause. We report a rare case of a MMMT of the cervix in a 38-year-old Hispanic woman who had a history of abnormal uterine bleeding for 1 month. Her mother had uterine cancer at age 48. She underwent an exploratory laparotomy with total abdominal hysterectomy and bilateral salpingo-oophorectomy. Grossly, there was a circumferential mass measuring 3.3 cm in greatest dimension located within the endocervix and partially replacing its wall. The tumor extended into the lower uterine segment and infiltrated the endometrium and myometrium. The serosa and parametrial soft tissues were involved by tumor. Three of 10 pelvic and paraaortic...
lymph nodes were involved by metastatic disease. Histologically, the carcinomatous component was composed of high-grade endometrioid adenocarcinoma, focal clear cell carcinoma, and areas of keratinizing squamous cell carcinoma. A high-grade homologous sarcomatous component was sharply demarcated from the carcinomatous elements. No heterologous sarcomatous component and no lymphatic or vascular invasion were identified. Radiologic imaging included a chest computed tomography scan, which showed multiple pulmonary nodules suspicious for metastatic disease and involving both lungs. Given the complexity and extreme rarity of these tumors and the absence of a large volume of clinical data regarding cervical MMMTs, it is important that all cases be documented as thoroughly as possible to ensure appropriate disease treatment and prognosis.

**Twins Reversed Arterial Perfusion Sequence: A Review of 9 Cases With an Emphasis on the Cord Insertion**

**Poster No. 32**

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**Context:** The etiology of twins reversed arterial perfusion sequence has not been clearly defined, even though it remains one of the most severe consequences of monzygotic twinning. All theories include one main point: intraplacental vascular communication supporting growth of acardiac fetus.

**Design:** We retrospectively reviewed the acardiac acephalus twin gestations during a 19-year period (1990–2008). Nine cases were identified, and the placentas and obstetrical histories were reviewed.

**Results:** Seven of 9 were monoamniotic-monochorionic and 2 of 9 were diamicnt-monochorionic twin placentas. Vascular communications were identified in 7 cases. The other 2 cases were macerated and inappropriate for vascular communication assessment. Five of 9 demonstrated velamentous umbilical cord insertions; 3 cords were marginal and 1 was eccentrically inserted. Five cords supplying the acardiac fetus had a single umbilical artery; 2 cords had 3 vessels, and 2 cords were severely macerated, meaning the number of vessels could not be accurately assessed.

**Conclusions:** Velamentous cord insertions occur in approximately 1% of placentas and more frequently in multiple gestations. The most serious consequence of velamentous insertions is rupture of unprotected vessels resulting in fetal morbidity and mortality. Twin transfusion syndrome is also associated with velamentous cord insertion. We believe a special type of velamentous cord insertion at the dividing membrane may lead to unidirectional shifting of blood flow from the pump twin to the acardiac cotwin. Characterization of umbilical cord insertion is important in understanding this entity, as there is a need to better assess factors that influence the hemodynamics of vascular communication in the placentas and fetal maldevelopment.

**Cutaneous Heterotropia of Cervix: Use of Molecular Tissue Identity Genotyping to Support Diagnosis**

**Poster No. 33**

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Cutaneous derivatives in cervix is a rare type of cervical heterotropia (CH). Diagnostic certainty depends on definitively excluding preanalytical contamination. We used a molecular tissue identity genotyping method to exclude preanalytical contamination. A 56-year-old postmenopausal woman with negative Papanicolaou tests was referred to the gynecology clinic for evaluation of a small polyplike lesion on the cervix. We biopsied this lesion, which was at the 9-o’clock position. It contained 2 distinct tissue fragments. The first fragment was unremarkable ectocervix. The second fragment showed squamous epithelium with multiple underlying hair follicle–like structures and surrounding inflammatory infiltrate suggestive of p63 and negative for p16. Malignant transformation occurs in less than 2% of ovarian cystic teratomas and is most commonly SCC. In locally advanced tumors, transmural extension into the adjacent colon occurs. This case illustrates a rare example of malignant transformation of cystic teratoma that was first diagnosed by colonic biopsy.

**CD10 Immunoreactivity in Metaplastic and Neoplastic Squamous Lesions of the Endometrium and Cervix and Its Potential Diagnostic Applications**

**Poster No. 35**

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**Context:** The utility of CD10 immunohistochemistry in the differential diagnosis of metaplastic squamous lesions of the endometrium and cervix remains controversial. CD10 is a calcium channel regulator that is not expressed in most squamous lesions but is expressed in metaplastic squamous lesions and some cervical carcinomas.

**Potential Diagnostic Applications:** We assessed CD10 immunoreactivity in cases of squamous lesions of the endometrium and cervix. The majority of squamous carcinomas (82%) were CD10 negative, while most metaplastic squamous lesions were CD10 positive. CD10 immunoreactivity in metaplastic squamous lesions can be used to distinguish them from squamous carcinomas and other squamous lesions.
diagnosis of endometrial stromal lesions and mesonephric glands is established. However, there are limited data available regarding CD10 expression in metastatic and neoplastic squamous epithelial lesions of the female genital tract.

**Design:** We examined the expression of CD10 in a series of 278 cervical lesions (99 invasive squamous cell carcinoma, 14 invasive adenocarcinoma, 118 squamous dysplasia, 12 adenocarcinoma in situ, and 35 squamous metaplasia) and 151 endometrial lesions (104 endometrial carcinoma, 42 complex hyperplasia, and 5 atypical polypoid adenomyoma). CD10 immunoreactivity was analyzed on a 4-tier scale and was correlated with clinicopathologic features, the presence and type of squamous differentiation, and patient outcome.

**Results:** Benign tissues showed no CD10 immunoreactivity. CD10 reactivity was seen in 48 of 118 (41%) squamous dysplasias and in 34 of 99 (34%) invasive squamous cell carcinomas of the cervix; it was also associated with improved recurrence-free survival (\(P < 0.03\)). In contrast, invasive and in situ cervical adenocarcinomas showed no CD10 expression. No CD10 activity was observed in glandular components of endometrial lesions, including adenocarcinomas with keratinizing squamous differentiation. However, strong, diffuse CD10 staining was seen in nonkeratinizing squamous metaplasia present in these lesions.

**Conclusions:** In contrast to squamous metaplasia, CD10 immunoreactivity is present in dysplastic and neoplastic cervical squamous lesions and may be a useful marker in predicting patient outcome. Strong CD10 immunoreactivity in nonkeratinizing squamous metaplasia in endometrial lesions may be a useful marker in their differentiation from solid glandular growth of adenocarcinomas and may aid in tumor grading in difficult cases.

**Adenoid Basal Carcinoma of the Cervix:**

**Two Cases of a Rare Pathologic Entity With Distinctive Ages of Presentation**

(Poster No. 36)

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Adenoid basal carcinoma is a very rare neoplasm of the cervix, classically presenting in postmenopausal women (median age 65) in association with high-grade squamous dysplasia of the cervix. The relative rarity of this lesion has kept it an enigma in regard to its precise biologic evolution, but the lesion has been associated with high-risk human papillomavirus type 16 DNA. The first case of adenoid basal carcinoma encountered at our institution (2004) was an asymptomatic lesion in a 25-year-old woman that was diagnosed on cervical conization subsequent to a previous biopsy demonstrating high-grade squamous dysplasia (CIN III). Smooth irregular nests of bland glandular and mildly atypical squamous cells surrounded by basal epithelium were noted. A p16 stain was focally positive in the tumor. A Ki-67 stain subsequently demonstrated a low proliferation index. The second case of adenoid basal carcinoma (2008) was diagnosed in a 63-year-old woman on cervical conization for severe squamous dysplasia (CIN III). A p16 stain demonstrated strong diffuse positivity within the overlying high-grade epithelial dysplasia and within the deeper well-differentiated adenoid basal carcinoma component. Ki-67 showed a low proliferation index with markedly decreased staining compared with the overlying dysplastic epithelium. Adenoid basal carcinoma is a rare neoplasm of the cervix that usually occurs in association with overlying squamous dysplasia. Although adenoid basal carcinoma appears to be associated with high-risk human papillomavirus, this neoplasm has a low proliferation index and excellent prognosis and may present as an incidental finding in women of any age.

**An Increase in Uterine Natural Killer Cells in First Trimester Miscarriages With Karyotypic Abnormalities: A Flow Cytometry/Cytogenetic Correlation**

(Poster No. 37)

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**Context:** It has been reported that uterine natural killer cells (uNKCs) may play a role in first trimester miscarriages. The function of these cells in human pregnancy is not completely known; however, they are thought to support placental growth through angiogenesis and immune modulation at the maternal-fetal interface. The most common etiology of miscarriage is karyotypic abnormalities. Therefore, in an effort to understand the relationship of these cells to miscarriage, we determined the percent of uNKCs and compared that with the presence or absence of karyotypic abnormality.

**Design:** Twenty products of conception specimens from women who miscarried in their first trimester (6–12 weeks) were submitted for cytogenetic analyses and were prospectively studied for CD56+ uNKCs via flow cytometry.

**Results:** Fifteen patients had an abnormal karyotype; findings included both numerical and structural abnormalities. In 5 specimens, the karyotype was normal. The mean uNK percent for cases with karyotypic abnormality was 8.76% (range, 0.18%–38.67%), and the mean uNK percent for cases with no karyotypic abnormality was 0.84% (range, 0%–1.83%; \(P = 0.02\)).

**Conclusions:** The percent of uNKCs found in samples with karyotypic abnormality is significantly statistically higher than in samples with normal karyotypes. To our knowledge, this is the first study that correlates the 2 parameters. This finding may be of benefit, possibly indicating a surrogate marker for early detection of karyotypic abnormalities. Additionally, continued study of uNKs in human products of conception by flow cytometry may help to elucidate the role these cells play in miscarriage.

**Primary Peritoneal Carcinosarcoma in Conjunction With Tubal Intraepithelial Dysplasia**

(Poster No. 38)

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A 62-year-old woman (gravida 2, para 2) presented with abdominal pain. The abdominal imaging showed bilateral adrenal masses without a definite connection to the uterus. An exploratory laparotomy was performed to establish a diagnosis. The tumor extensively involved the uterine serosa and parametrial tissue as well as 2 foci on the sigmoid colon serosa. Histologically, the tumor was composed of high-grade, pleomorphic, solid nests of epithelial cells with intervening hyaline cartilage. No involvement of the endometrium was seen. The left fallopian tube had diffuse serous tubal intraepithelial carcinoma, while the right fallopian tube had focal serous tubal intraepithelial carcinoma. Immunohistochemical stains Pax-2 and WT-1 were positive in the epithelial portion of the carcinosarcoma. The left fallopian tube showed overexpression of p53 and MIB-1. The right fallopian tube showed focal overexpression of p53. Primary carcinosarcoma of the peritoneum (malignancy mixed Mullerian tumor) is a rare, aggressive entity. Presumably, the tumor arises from cells of the “secondary Mullerian system,” which is the peritoneum mesothelium and adjacent mesenchyme of the pelvis and lower abdomen. Although previously considered to be a collision tumor, carcinosarcomas are now thought to be metastatic carcinoma with monoclonal epithelial and mesenchymal components. To our knowledge this is the first case of carcinosarcoma with concurrent serous tubal intraepithelial carcinoma, a precursor to pelvic serous carcinoma. Although coincidental concurrence is possible, this case represents a possible link between carcinosarcoma and serous carcinoma, or at least a possible common precursor lesion.

**Comparison of Polymerase Chain Reaction and In Situ Hybridization Methods for Detection of Cervical Human Papillomavirus Infection: Cases That May Not Be Identified by Polymerase Chain Reaction But That May Be Detected by In Situ Hybridization**

(Poster No. 39)

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**Context:** Detection of epithelial cell abnormalities by cervicovaginal cytology screening necessitates human papillomavirus (HPV) testing. Although polymerase chain reaction (PCR) is a very sensitive method for detecting HPV, it still results in some cases being undiagnosed.

**Abstracts**

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Design: Results from 108 cervicovaginal liquid-based cytology samples analyzed for the presence of HPV DNA by PCR were compared with the results of in situ hybridization (ISH) on 108 cervical biopsies obtained from the same patients using commercial HPV probes and primers.

Results: Positive ISH signals for high-risk, low-risk, and both high- and low-risk HPV types were observed in 70 of 108 (64.8%), 9 of 108 (8.3%), and 5 of 108 (4.6%) cases, respectively, whereas negative signals were found in 24 of 108 (22.2%) cases. By PCR, 52 of 108 (48.2%), 7 of 108 (6.5%), and 5 of 108 (4.6%) cases were positive for the respective HPV risk types. Eight (7.4%) patients were positive for unknown HPV risk types, and in 36 (33.3%) patients, PCR was negative. The degree of concordance between PCR and ISH was 69.4% (75 of 108) for all samples (Table). Interestingly, 16 of 108 (14.8%) cases were negative for HPV by PCR but positive by ISH in cervical biopsies.

Conclusions: A higher number of positive results were detected by ISH in tissue biopsies (84 of 108; 77.8%) than by PCR in liquid-based cytologic specimens (73 of 108; 67.6%). In our series, ISH was an adequate method for detecting HPV in high-grade lesions with similar efficacy to PCR. Patients with abnormal cervicovaginal cytology and undetectable HPV on testing with PCR could be tested by ISH on biopsy specimens.

| Comparison of Detection of Different Risk Types of HPV DNA Using PCR and ISH |
|----------------------------------------|-----------------|-----------------|-----------------|-----------------|
| High-Risk Type HPV DNA (PCR), No. (%) | Low-Risk Type HPV DNA (PCR), No. (%) | High- and Low-Risk Type HPV DNA (PCR), No. (%) | Negative (PCR), No. (%) |
| High-risk type HPV DNA (ISH), No (%) | 47 (43.5) | 3 (2.8) | 0 (0) | 13 (12) |
| Low-risk type HPV DNA (ISH), No (%) | 2 (1.9) | 4 (3.7) | 1 (0.9) | 2 (1.9) |
| Low- and high-risk type HPV DNA (ISH), No (%) | 0 (0) | 0 (0) | 4 (3.7) | 1 (0.9) |
| Negative (ISH), No (%) | 3 (2.8) | 0 (0) | 0 (0) | 20 (18.5) |
| Cyologic diagnosis for 16 patients with negative PCR and positive ISH | Atypical squamous cells of undetermined significance | Low-grade squamous intraepithelial lesion | High-grade squamous intraepithelial lesion | |
| No (%) | 7 (43.75) | 6 (37.5) | 3 (18.75) | |

PAX8: An Immunohistochemical Marker for Endometriosis (Poster No. 40)
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Context: Endometriosis is defined as the presence of endometrial tissue outside of the uterine cavity. Although most often confined to the peritoneal cavity, endometriosis may occur in unusual sites, including skin, lung, and brain. Histologic diagnosis of endometriosis is sometimes difficult, especially when the lesion occurs in atypical sites. Variability in the appearance of glands due to cyclic hormonal changes may also confound diagnosis. Characterization of molecular markers of endometriosis enables pathologists to circumvent these diagnostic challenges. In this study, we investigated the transcription factor PAX8 as an immunohistochemical marker of endometriosis.

Design: Twenty-two cases of endometriosis and 1 sample each of endocervical tissue, endometrium, and fallopian tube were retrieved from archived material. PAX8, estrogen receptor, and progesterone receptor immunohistochemical staining was performed using the avidin-biotin peroxidase method after antigen retrieval. Distinct and strong nuclear staining was required for PAX8 positivity.

Results: The 22 endometriosis cases were from women ranging in age from 19 to 70 years. The sites included abdominal wall, appendix, hernia sac, ureter, pelvic wall, and colon. Strong PAX8 nuclear staining was detected in all 22 (100%) cases, as well as in benign endocervical and endometrial glands, fallopian tube epithelium, and lymphocytes. No PAX8 staining was identified in adjacent colonic or appendiceal tissue or in the urothelium.

Conclusions: We observed PAX8 expression in all 22 cases of endometriosis and in 1 sample each of endocervical, endometrial, and fallopian tube epithelium. These findings suggest that PAX8 is a marker for the Mullerian system and that PAX8 immunohistochemistry may be a sensitive method for diagnosing endometriosis.

Invasive Paget Disease of the Vulva With Concurrent Basal Cell Carcinoma (Poster No. 41)
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We report a case of an 81-year-old woman who had a granular, red-tan vulvar lesion that she had noticed for more than a year. The vulvectomy specimen showed invasive vulvar Paget disease with concurrent basal cell carcinoma (BCC). This is the first reported case of BCC associated with invasive vulvar Paget disease and the second reported case of concurrent vulvar Paget disease and BCC. The epithelium of the specimen showed nests of cells with abundant clear cytoplasm, large pleomorphic nuclei with vesicular chromatin, and conspicuous nucleoli. These malignant cells were also seen infiltrating the dermis in direct continuity with the intraepidermal component. The overlying and adjacent epidermis showed extensive pseudoepitheliomatous hyperplasia and several foci of BCC arising immediately adjacent to Paget disease. The intraepidermal nested malignant cells showed immunoreactivity for cytokeratin (CK) 7 and were negative for CK20, S100 protein, Melan-A, and HMB-45. The infiltrating component showed the same immunoprofile. The diagnosis of invasive Paget disease was based on cytologic similarities and intimate association of the intraepidermal and invasive components as well as their shared immunoprofile. The overlying squamous epithelium and pseudoepitheliomatous hyperplasia were positive for high-molecular-weight cytokeratin and negative for CK7. The BCC was weakly positive for CK7. Because the BCC in this case arose in an ulcerated reactive epidermis with pseudoepitheliomatous hyperplasia, it is possible that Paget disease was the predisposing factor for the development of BCC. However, we cannot rule out the possibility that the 2 lesions developed independently.

Severe Dysplasia and Adenocarcinoma In Situ Within an Endocervical Polyp (Poster No. 42)
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Endocervical polyps, the most common benign neoplasia of the uterine cervix, are frequently seen in multigravid women during the fourth to sixth decades of life. The polyps can present with vaginal discharge or bleeding. In situ and invasive carcinoma arising in endocervical polyps is extremely rare. The incidence of squamous dysplasia in polyps is estimated between 0.5% and 2%. The association between adenocarcinoma in situ and squamous dysplasia of the cervix is well known; however, the coexistence of squamous dysplasia and adenocarcinoma in situ within an endocervical polyp has not been previously described. We present a case of an endocervical polyp with severe dysplasia and associated adenocarcinoma in situ. We searched Tufts Medical Center’s archival files from 1998 to 2008 (1004 cases) for the diagnosis of dysplasia and adenocarcinoma in situ arising in cervical polyps. We found 9 (0.89%) cases with
squamous dysplasia, including CIN 1 (0.39%), CIN 2 (0.09%), and CIN 3 (0.39%). No other cases of severe dysplasia with adenocarcinoma in situ were found. A 58-year-old woman presented with episodic postmenopausal spotting. Pelvic examination revealed atrophic changes in the external genitalia and vagina and a 1.5-cm reddish polyp at the cervical os. Histologic findings showed an endocervical polyp with focal severe squamous dysplasia (CIN 3) (Figure 22, A) and focal adenocarcinoma in situ (Figure 22, B). Carcinoma arising in endocervical polyps is very uncommon and carries an excellent prognosis if limited to the polyp. A subsequent hysterectomy revealed no residual tumor or dysplasia.

**Thyroid Transcription Factor–Positive Primary Endocervical Adenocarcinoma**

(Ster No. 45)

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**Context:** Thyroid transcription factor 1 (TTF-1) is considered a reliable marker in distinguishing primary and metastatic adenocarcinomas of the lung from metastatic tumors of other origin. A challenging case of TTF-1–positive primary endocervical adenocarcinoma metastatic to the mediastinum in a 63-year-old patient interested us, leading us to conduct a study exploring the expression of TTF-1 in primary endocervical adenocarcinoma cases diagnosed at our institution.

**Design:** Twenty cases of primary endocervical adenocarcinoma with no previously known history of any cancer were retrieved from our archived data and matched against 20 negative control cases of benign endocervical biopsies/excisions. Cases were matched using age and date of exploration as criteria. TTF-1 staining was performed on the 40 cases. TTF-1 positivity was defined by a nuclear pattern (scored from 0 to 3+).

**Results:** Of 20 cases of primary endocervical adenocarcinoma, 1 (5%) case was TTF-1 strongly positive (nuclear score 3+). Of 20 cases of negative controls, 0 (0%) cases were TTF-1 positive. The TTF-1–positive case was a primary noninvasive endocervical adenocarcinoma in a 37-year-old patient with no history of malignancy.

**Conclusions:** In our study, 1 of 20 (5%) of the selected primary endocervical adenocarcinomas were TTF-1 positive, whereas none of the benign cervical tissues were positive. The mechanism behind TTF-1 positivity in tumors of other origin than lung or thyroid is not well understood. While waiting for larger studies exploring TTF-1 in different kinds of tumors, we should be overly cautious when dealing with a TTF-1–positive metastasis, especially in the absence of clinical pulmonary and thyroid history.

**Morphoproteomic Evidence of a Constitutively Activated and Overexpressed Signal Transducer and Activator of Transcription-3 Pathway With Interleukin 8 Coexpression in Cervical Cancer and High-Grade Dysplasia**

(Poster No. 46)

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**Context:** Interleukin 6 (IL-6) is known to be associated with cervical cancer, promoting tumor growth via activation of the signal transducer and activator of transcription 3 (STAT3) pathway. Recent literature also describes increased levels of IL-6 transfection by human papillomavirus type 16, E6 and E7 genes. Both IL-6 and IL-8 levels are increased in cervicovaginal secretions of patients with cervical cancer. IL-8 is a target gene of STAT3. In this study, we apply morphoproteomics to investigate the STAT3 pathway in cervical cancer and dysplasia.

**Design:** A tissue microarray comprised of benign cervical tissue, high-grade dysplasia, and invasive squamous cell carcinoma was assembled. Immunohistochemical probes using monoclonal antibodies to STAT3 phosphorylated (p-STAT3) on tyrosine 705 and to IL-8 were applied. Results were graded according to intensity of staining (0–3+ scale) and percentage of cells stained (0%–100%).

**Results:** Our data showed no immunoreactivity for IL-8 and only rare nuclear expression of p-STAT3 in basal cells of the benign squamous epithelium. Ninety-five percent of cancer and dysplasia cases showed strong positivity (2+–3+) for nuclear p-STAT3. Additionally, all cases of carcinoma and dysplasia were strongly positive for IL-8. There was no difference in the intensity or quantity of staining between high-grade dysplasia and invasive squamous carcinoma for these protein analytes.

**Conclusions:** Morphoproteomic analysis showed constitutive activation and overexpression of the STAT3 pathway in invasive squamous cell carcinoma and high-grade dysplasia versus nonneoplastic cervical mucosa by virtue of p-STAT3 (Tyr 705) nuclear expression and correlative expression of IL-8.
Carcinosarcoma of the vulva is a very rare neoplasm. Only 2 vulvar carcinosarcomas in which the carcinomatous component was squamous carcinoma have been reported. The sarcomatous component in one case was endometrial adenocarcinoma, and in the other case, it was leiomyosarcoma. We present the first case of a primary vulvar adenocarcinomatous carcinosarcoma with homologous leiomyosarcomatous and heterologous osteosarcomatous differentiation. A 51-year-old African American woman presented with a labial mass. She underwent right radical vulvectomy, received whole pelvic radiation therapy, and has been without evidence of disease for 6 months. The multicentric cystic tumor, measuring 7.5 × 6.5 × 3.1 cm, contained papillary excrescences and necrosis, and invaded underlying soft tissue. Microscopically, the carcinosarcomatous component was positive for cytokeratin AE1/AE3 and epithelial membrane antigen; the sarcomatous component contained osteosarcoma and pleomorphic poorly differentiated cells that expressed CD10 and smooth muscle actin. Some of the poorly differentiated sarcomatous cells were also positive for cytokeratin AE1/AE3, which may support the hypothesis that the carcinomatous and sarcomatous components of carcinosarcoma are clonally related; however, further investigation of this tumor is needed. Carcinosarcomas in the female genital tract are usually highly aggressive malignancies with poor clinical prognosis. Therefore, in our case, even though no lymph nodes were available for evaluation and the surgical margins were free of tumor, the patient still underwent whole pelvic radiation therapy postoperatively. Additionally, due to the different histopathologic characteristics, continuous patient follow-up is warranted to monitor clinical outcome for anything unusual and for clinical management.

Endometrial Adenocarcinoma: Intratumor Variability in Estrogen Receptor and Progesterone Receptor Immunostain Results

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Context: Estrogen receptor (ER) status and progesterone receptor (PR) status are used as prognostic and treatment indicators for endometrial adenocarcinomas. Many studies have reported variable results regarding correlation among prognosis, clinical stage, and histologic grade. Intratumoral differences in receptor status have not been well characterized; this was the purpose of our study.

Design: Twenty-five cases of endometrioid adenocarcinoma with noninvasive and invasive areas were used, with a range of International Federation of Gynecology and Obstetrics grades (10 grade 1, 12 grade 2, and 3 grade 3) and depths of invasion (17 cases ≤50% invasion, 8 cases >50% invasion). Immunostains for ER and PR were performed using an optimized biotin-free, polymer-based immunoperoxidase methodology. The stains were scored as positive (>10% staining) or negative (<10% staining). In a subset of cases, percentage of tumor and staining intensity (weak, moderate, strong) were evaluated (Table).

Results: In 21 (84%) cases, ER and PR were positive in both noninvasive and invasive areas. In these cases, morphology was similar in the noninvasive and invasive areas. Four cases showed quantitative and qualitative staining differences in areas of different morphologies; these were analyzed in more detail (Table).

Conclusions: We found no intratumoral differences in ER and PR status in invasive versus noninvasive areas when morphology was the same. However, we did see intratumoral differences in ER and PR immunostains, depending on tumor differentiation. Because ER and PR status may indicate prognosis and treatment, we feel immunostains should be done on the least differentiated areas of tumors to provide the most accurate analysis.

**Intratumoral Differences in ER/PR Immunostains**

<table>
<thead>
<tr>
<th>Case</th>
<th>ER WD</th>
<th>ER PD</th>
<th>PR WD</th>
<th>PR PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>90% SI</td>
<td>50% MI</td>
<td>90% SI</td>
<td>10% MI</td>
</tr>
<tr>
<td>G</td>
<td>90% SI</td>
<td>0%</td>
<td>80% M-SI</td>
<td>0%</td>
</tr>
<tr>
<td>N</td>
<td>No difference</td>
<td>No difference</td>
<td>80% SI</td>
<td>5% MI*</td>
</tr>
<tr>
<td>P</td>
<td>No difference</td>
<td>No difference</td>
<td>60% SI</td>
<td>0%</td>
</tr>
</tbody>
</table>

Abbreviations: MI, moderate intensity; PD, poorly differentiated (solid areas); SI, strong intensity; WD, well differentiated (gland-forming areas).

*PD area was noninvasive.
Expression of Thyroid Transcription Factor 1 and Loss of Expression of Estrogen Receptors in Endometrial Adenocarcinoma

(Poster No. 51)

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Context: Thyroid transcription factor 1 (TTF-1) is a relatively sensitive and specific marker for carcinomas of lung and thyroid. In recent studies, TTF-1 expression was observed in tumors other than lung and thyroid, such as small cell carcinoma of the bladder and endometrial and endocervical adenocarcinomas. We investigate the expression of TTF-1 and estrogen receptor in endometrioid adenocarcinomas.

Design: We immunohistochemically evaluated the expression of TTF-1 on conventional tissue sections in 80 cases of endometrioid adenocarcinoma, including 25 cases of grade 1, 35 cases of grade II, and 20 cases of grade III tumors. Two TTF-1 monoclonal antibodies were used (1:25, SCG3/1, Cell Marque Corporation, Rocklin, California and 1:50, sc-56606, Santa Cruz Biotechnology, Santa Cruz, California). We recorded staining intensity (weak or strong) and distribution (negative, 1+, 2+, 3+, and 4+).

Results: Strong and diffuse (4+) nuclear staining for TTF-1 was demonstrated in 2 of 80 (2.5%) cases, with identical patterns for both antibodies. Both cases were grade II endometrioid adenocarcinomas, with a positive cytokeratin 7 and negative estrogen receptor profile. In 1 of the 2 cases, a lung metastasis developed 4 years after a hysterectomy.

Conclusions: Our data confirm previous findings with 2 different antibodies against TTF-1; however, the positive percentage is significantly lower than in a previous study (2.5% vs 19%). Caution should be taken when working on an unknown primary because a small portion of endometrioid adenocarcinomas may carry an immunophenotype of cytokeratin 7 positive, TTF-1 positive, and estrogen receptor negative, which is similar to the immunophenotype of a primary adenocarcinoma of lung.

Primary Small Cell Carcinoma of the Endometrium: Case of a Rare and Aggressive Tumor

(Poster No. 52)

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Primary small cell carcinomas of the female genital tract constitute less than 2% of all gynecologic malignancies. Small cell carcinomas of the endometrium are very rare. Most patients present with vaginal bleeding. Macroscopically, the lesions are large, occupying most of the uterus and often showing evidence of an intraabdominal spread. Microscopy shows nests and sheets of small cells with scant cytoplasm, evenly dispersed chromatin, and inconspicuous nuclei. Immunohistochemical stains demonstrate positivity for one or more neuroendocrine markers. Electron microscopy can be used to demonstrate neurosecretory granules. The patient is a 60-year-old postmenopausal woman who presented with vaginal spotting. Endometrial biopsy was diagnostic of a small cell carcinoma. Gross examination showed an enlarged uterus (770 g) that was almost entirely occupied by a soft, red to brown, ill-defined mass. Microscopy demonstrated an infiltrative lesion composed of small blue cells with scant cytoplasm and a high nuclear to cytoplasmic ratio. Vascular invasion was frequent. Immunohistochemical stains for synaptophysin and chromogranin were positive. Microscopic examination of right fallopian tube and ovarian, appendix, portions of large bowel, and mesentery also showed extensive involvement by the tumor and associated necrosis. The patient was surgically staged IV (International Federation of Gynecology and Obstetrics system). Small cell carcinomas of the endometrium are very rare and aggressive neoplasms. They are notorious for rapid systemic spread and poor prognosis. Early and aggressive therapy may improve survival in these patients.

Histologic Type, Stage of Disease, and Tumor Grade Are Unrelated Racial Disparity Among Blacks and Whites for Endometrial Cancer

(Poster No. 53)

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Context: It is well known that endometrial cancer varies by race; however, the reason for this disparity remains unclear. Adjusting for clinical pathologic factors may clarify endometrial cancer racial disparities.

Design: Endometrial cancer data were obtained from Surveillance, Epidemiology and End Results registry data (1990-2005). Invasive cancers in blacks and whites were stratified by histologic type and adjusted for stage and grade. Descriptive techniques included age-adjusted temporal trends, age-specific incidence rates, incidence rate ratios, Kaplan-Meier plots, and hazard rates for endometrial cancer-specific deaths. Statistical significance was assessed (α = .05).

Results: There were 81,620 endometrial cancer cases, including 93.0% white individuals and 7.0% black individuals. Age-adjusted incidence rates were higher for whites (incidence rate ratio white to black, 1.38; 95% confidence interval: 1.34, 1.42) and have decreased during the past 15 years, whereas incidence rates for blacks have increased. Despite decreasing rates in mortality, mortality rates for blacks remain significantly higher than for whites (P < .001). Compared with whites, blacks have significantly higher incidence rates of more aggressive histologic types, such as serous carcinoma, clear cell carcinoma, and carcinosarcoma, and higher rates of late-stage and high-grade cancers. Kaplan-Meier plots and hazard rates showed survival was worse for blacks than whites, even after stratifying for histologic type and adjusting for stage and grade.

Conclusions: Endometrial cancer survival rates were worse for blacks than whites, and racial survival disparities persisted even after adjustment for clinical pathologic factors. Histologic type, stage, and tumor grade are not the only determinants that contribute to the disparity seen in endometrial cancer among blacks and whites.

Clinical and Histopathologic Features Differentiating Benign and Malignant Solitary Fibrous Tumors of the Thorax

(Poster No. 54)

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Context: Solitary fibrous tumor of the thorax (SFT) is a rare tumor that may occur benign or malignant. SFTs have a variety of histologic patterns, including patternless pattern and hemangiopericytoma-like and cellular patterns. We investigated the clinicopathologic features differentiating benign SFT from malignant SFT in a series of SFTs excised during a 14-year period at 2 hospitals.

Design: We searched surgical pathology databases (1994-2008) of 2 hospitals, identifying 24 patients with SFT. The surgical pathology reports were reviewed, and the following demographic and histologic features were analyzed: age, gender, location, size, histologic patterns, mitosis, necrosis, nuclear pleomorphism, and immunohistochemistry.

Results: The group consisted of 17 (71%) patients with benign SFT and 7 (29%) patients with malignant SFT. The average age of patients with benign SFT was 48.5 years (range, 20-77 years), whereas the average age of patients with malignant SFT was 69 years (range, 62-76 years). Female to male ratio was 11:6 for benign SFT and 2:5 for malignant SFT. Average tumor size was 4.5 cm for benign SFT and 11.5 cm for malignant SFT. Histologic patterns in benign SFT were 71% patternless pattern, 23% hemangiopericytoma-like pattern, and 6% cellular pattern. Histologic patterns in malignant SFT were 0% patternless pattern, 72% hemangiopericytoma-like pattern, and 28% cellular pattern.

Conclusions: In our series, malignant SFT occurred in patients older than 60 years, tended to have a large tumor size, and had a predominantly hemangiopericytoma-like pattern. Benign SFT occurred in a wide age range (20-76 years), with a slightly female predominance and a predominantly patternless pattern.

Solitary Fibrous Tumor of Pleura: A Rare Macrocytotic Form

(Poster No. 55)

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A 75-year-old woman presented with shortness of breath for 2 months. Respiratory system findings were suggestive of a mass lesion in the left hemithorax. Thorax computed tomography scan showed a soft tissue mass with several macrocysts in the left pleural cavity that was compressing the left lower lobe. Posteriorolateral thoracotomy was done for exploration. The tumor was attached to the visceral pleura of lung by a pedicle. Grossly, the surface was smooth and had a shiny, tan-red multilobular appearance. Sectioning revealed a large lobulated tumor (20 × 15 × 15 cm).
cm) with tan-pink, soft parenchyma with a multinodular cystic appearance. The biggest cyst measured 5 cm in diameter. Histologically, the tumor consisted of bland looking spindle cells alternating with numerous bundles of small collagen fibers, resulting in an interlaced appearance characteristic of solitary fibrous tumor of pleura. Immunohistochemical stain showed some of the spindle cells were positive for CD34. The clinical presentation of solitary fibrous tumor of pleura varies according to size and intrathoracic localization. The treatment of choice is surgical removal, which is curative in 90% of cases. Cystic degeneration may be seen in addition to the classic presentation of a pleural-based solid mass. Macroscopic degeneration of solitary fibrous tumor of pleura is a rare variant that should be considered in the differential diagnosis of intrathoracic tumors.

Primary Adenoid Cystic Carcinoma of the Bronchus: A Case Report and Review of the Literature
(Poster No. 56)

Maximo K. Laludes, MD (laludes@gmail.com); Steven Sieber, MD; Michael Walker, MD; Hani El-Fanek, MD. Department of Pathology, Danbury Hospital, Danbury, Connecticut.

Primary salivary gland-like lung cancers are rare neoplasms, constituting less than 0.3% of all respiratory malignancies in the United States. In particular, adenoid cystic carcinoma has been described in the trachea and more rarely in the mainstem bronchus. This carcinoma usually presents clinically as an endobronchial mass lesion, causing obstructive symptoms and pneumonia. We present a rare case of an 82-year-old man who was previously diagnosed with bladder and renal pelvis urothelial carcinoma. The patient was admitted, and a left mainstem bronchus biopsy and subsequent subtotal resection of the mass showed antibody recognizing podoplanin, and it is selective for lymphatic endothelia. Several studies have confirmed the reliability of D2-40 in the diagnosis of pleural MM, but the evaluation of this antibody in other pleural neoplasms is limited. This study aims to determine the diagnostic value of D2-40 in the segregation of MM from other pleural neoplasms.

Design: D2-40 immunohistochemical staining was performed on 36 pleural MMs, 15 solitary fibrous tumors (SFTs), 13 pleomorphic carcinomas, and 3 synovial sarcomas. A tumor was considered positive if more than 10% of tumor cells stained with D2-40 antibody. The staining intensity was graded as weak, moderate, or strong. A P value less than .05 was considered statistically significant.

Results: Twenty-five of 36 (69%) MMs (21 epithelioid and 4 biphasic) and 2 of 15 (13%) SFTs were positive for D2-40. No D2-40 positivity was detected in pleomorphic carcinomas (n = 13) or synovial sarcomas (n = 3). The difference of D2-40 positivity between MMs and SFTs was significant (P < .001).

Conclusions: D2-40 was highly positive in MM, but it was also positive in a small percentage of SFTs. These findings indicate that D2-40 is a useful marker for MM, but caution should be taken in diagnosing small biopsy specimens of D2-40-positive pleural spindle cell neoplasms, especially in rendering the differential diagnosis between SFT and MM.

An Unusual Presentation of Pulmonary Talcosis in a 55-Year-Old Woman
(Poster No. 58)

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Repetitive inhalational exposure to talc can lead to chronic pulmonary disease. This condition has been reported in millers, miners, and drug abusers but has rarely been associated with exposure to cosmetic talc-containing products. A 55-year-old woman presented with a 3- to 4-month history of progressive dyspnea and cough. She had a history of alcohol and cocaine abuse, which was discontinued approximately 10 years ago. There was no known exposure to occupational dusts, pets, or travel. Chest computed tomography scan revealed evidence of interstitial lung disease. Based on this presentation, differential diagnosis included bronchiolitis obliterans-organizing pneumonia, sarcoidosis, and hypersensitivity pneumonitis. A transbronchial biopsy of the right middle and lower lobes was performed. On microscopic examination, biopsy revealed fragments of lung parenchyma with alveolar septal expansion by non-necrotizing, foreign body-type granulomas. There were scattered multinucleated giant cells, many of which contained polarizable, birefringent, platelike and needle-shaped talc particles. The granulomas and talc particles were not identified in association with blood vessels, ruling out exposure related to intravenous drug abuse. Questioning of the patient revealed no known exposure to talc-containing products, and she admitted to using a cornstarch-based powder, which she routinely applied to her body after showering. Given her remote history of cocaine abuse, the possibility of talc exposure via inhalation of crushed talc-containing pills was considered. We report a rare case of inhalational pulmonary talcosis with an unclear source of exposure in a 55-year-old woman. This chronic pulmonary disease can progress to interstitial fibrosis, emphysema, and chronic respiratory failure (Figure 24).

Diagnostic Utility of D2-40 in Pleural Neoplasms
(Poster No. 57)

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Context: Accurate diagnosis of malignant mesothelioma (MM) is crucial. Identification of a biomarker to assist in differential diagnosis between MM and other neoplasms is desirable. D2-40 is a new monoclonal antibody recognizing podoplanin, and it is selective for lymphatic endothelia. Several studies have confirmed the reliability of D2-40 in the diagnosis of pleural MM, but the evaluation of this antibody in other pleural neoplasms is limited. This study aims to determine the diagnostic value of D2-40 in the segregation of MM from other pleural neoplasms.

Conclusions: D2-40 immunohistochemical staining was performed on 36 pleural MMs, 15 solitary fibrous tumors (SFTs), 13 pleomorphic carcinomas, and 3 synovial sarcomas. A tumor was considered positive if more than 10% of tumor cells stained with D2-40 antibody. The staining intensity was graded as weak, moderate, or strong. A P value less than .05 was considered statistically significant.

Results: Twenty-five of 36 (69%) MMs (21 epithelioid and 4 biphasic) and 2 of 15 (13%) SFTs were positive for D2-40. No D2-40 positivity was detected in pleomorphic carcinomas (n = 13) or synovial sarcomas (n = 3). The difference of D2-40 positivity between MMs and SFTs was significant (P < .001).

Conclusions: D2-40 was highly positive in MM, but it was also positive in a small percentage of SFTs. These findings indicate that D2-40 is a useful marker for MM, but caution should be taken in diagnosing small biopsy specimens of D2-40-positive pleural spindle cell neoplasms, especially in rendering the differential diagnosis between SFT and MM.

Extranodal Natural Killer Cells/T-Cell Lymphoma: A Case of Pulmonary Presentation With Unique Alveolar-Tropic Infiltration Resembling Organoid Pattern Seen in Carcinoid or Other Neuroendocrine Tumors
(Poster No. 59)

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A 31-year-old woman presented with cough, shortness of breath, and abdominal pain. Imaging studies revealed a right middle lobe perihilar-

chial lung mass and duodenal wall thickening. Lung biopsy revealed a monotonous population of small- to medium-sized round cells in an intravascular distribution showing an organoid pattern at low magnification (Figure 25, original magnification ×100; inset, original magnification ×600). Flow cytometric analysis and immunohistochemical staining demonstrated expression of CD45, CD7, cytoplasmic CD3, CD2, TIA1, granzyme B, CD56, and CD57. There was no expression of surface CD3, CD5, CD4, CD8, CD10, Tdt, and CD34. Additionally, there was no expression of B-cell and myeloid-specific antigens. A T-cell receptor gene rearrangement study detected no clonally rearranged product. These findings support a diagnosis of extranodal natural killer/T-cell lymphoma. Duodenal wall biopsy demonstrated involvement by a similar monotonous lymphoid population. After high-dose chemotherapy, the patient underwent matched unrelated donor stem cell transplant and has continued in clinical remission. Extranodal natural killer/T-cell lymphoma is a rare, clinically aggressive neoplasm with frequent involvement of upper aerodigestive tract. Other extranodal sites, such as gastrointestinal tract and skin, can also be preferentially involved; however, primary pulmonary presentation is extremely rare. Although natural killer/T-cell lymphoma usually shows angiocentric/angiodestructive morphology, the alveolar-tropic lung infiltration in our case is unique and has never been reported in English literature to the best of our knowledge. Because of this unusual presentation, potential misdiagnoses include carcinoid tumor in particular, small cell carcinoma, and other tumors of neuroendocrine origin. A panel of immunohistochemical studies, including CD45, is recommended for initial identification.

Squamous Cell Carcinoma of the Lung Secreting Human Chorionic Gonadotropin and β-Human Chorionic Gonadotropin in a Young Female Smoker

(Paper No. 60)

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A 43-year-old woman presented with dysfunctional uterine bleeding for approximately 1 year. She had a human chorionic gonadotropin level of 14,000 mIU/mL (normal upper limit, 0.7 mIU/mL) and a β-human chorionic gonadotropin level of 20,132 mIU/mL (normal upper limit, 0.5 mIU/mL). Pelvic examination and ultrasonography showed no abnormal findings and no signs of pregnancy. At that time, the patient developed pain in the left upper quadrant, which was aggravated by deep breathing. She also reported weakness, intermittent night sweats, and an unintentional 12-lb weight loss during the past year. She denied shortness of breath or cough. A computed tomography scan of the thorax showed a 7-cm right lower lobe lung mass and a 1.2-cm left apex nodule contiguous with pleura. A positron emission tomographic scan showed potential metastatic lesions throughout the right and left lobes of the liver, spleen, and left kidney and a left frontal brain lesion. A fine-needle aspirate of a liver mass and bronchoscopy with a Wang needle biopsy of the right lower lung mass were performed. The pathology showed metastatic squamous cell carcinoma with immunohistochemical staining as follows: positive for human chorionic gonadotropin, AE1/AE3, cytokeratin 7, and p63 and negative for cytokeratin 20, thyroid transcription factor 1, and carcinoembryonic antigen. The patient died 4 months after diagnosis. Although pulmonary squamous cell carcinoma secreting human chorionic gonadotropin is rare (only 2 cases have been reported in the literature), it should be considered in any case in which a woman has elevated human chorionic gonadotropin and no evidence of pregnancy.

Expression of Excision Repair Cross-Complementation Group 1 in Tissue Microarray of 222 Non–Small Cell Lung Cancers: Correlation With Patient Survival

(Poster No. 61)

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Context: Patients with non–small cell lung cancers (NSCLCs) have a poor prognosis, with half of patients with stage I and II cancers dying of their disease despite tumor resection. Excision repair cross-complementation group 1 (ERCC1) is 1 of 16 genes that encode the proteins of the nucleotide excision repair complex. We examined the correlation between ERCC1 expression and long-term survival of patients with resected NSCLC prior to current adjuvant therapy protocols to determine its potential status as an independent prognostic biomarker for survival.

Design: We included 222 cases with pathologically confirmed NSCLC (stages I-II) from the 1970s to early 1990s. Immunohistochemistry was used to measure the expression of ERCC1 in tissue microarray sections with 3 punches from each case. Immunopositivity in tumor cells was graded on a scale from 0 to 3 and was averaged for the 3 punches from each tumor. ERCC1 expression was compared with 5-year survival using Kaplan-Meier analyses, including by cell type and tumor stage.

Results: Negative/weak ERCC1 expression was observed in 157 of 222 (71%) of NSCLC (47% of adenocarcinomas, 20% of squamous cell carcinomas, 18% of large cell carcinomas). In patients with stage I and II disease, absent or weak ERCC1 expression was associated with a strong trend toward shorter survival (P = .06).

Conclusions: ERCC1 expression is absent or weak in more than two thirds of NSCLC patients. Negative or weak expression is associated with a strong trend toward decrease in 5-year survival. ERCC1 expression may serve as a biomarker of prognosis for patients with NSCLC.

Giant Cell Tumor Primary in the Lung

(Poster No. 62)

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Giant cell tumors (GCTs) are primarily regarded as tumors of the bone. Despite their potential to metastasize to the lung and other organs, GCTs are commonly benign. Although cases of GCT have been reported in the pancreas, thyroid, skin, lung, and soft tissue, few GCT primary in organs other than bone are included in the literature. We report a case of primary GCT of the lung in a patient without bone involvement. A 75-year-old man presented with a history of heavy smoking, chronic obstructive pulmonary disease, hypertension, hyperlipidemia, glaucoma, and cerebrovascular disease. He had a chronic unreconstructive cough and was found to have a solitary 1.7-cm right lower lobe lung mass. A transbronchial biopsy of the mass showed a tumor composed of sheets of round to oval cells with a delicate connective tissue stroma. Admixed with the tumor cells were multinucleated giant cells without atypia. An occasional mitotic figure was identified. Cytokeratins were negative in tumor cells. The patient underwent resection of the right lower lobe and has been without evidence of disease for the past 1.5 years. Microscopically, this tumor resembled a GCT of the bone. This is the 11th case reported in the literature to date of a primary GCT of the lung. Pathologists should be aware that GCT may occur as a primary neoplasm in the lung.

CD34 and α-Smooth Muscle Actin Distinguish Idiopathic Cryptogenic Organizing Pneumonia From Secondary Bronchiolitis Obliterans With Organizing Pneumonia

(Poster No. 63)

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Context: Secondary bronchiolitis obliterans with organizing pneumonia (BOOP) is a reaction to injury, forming granulation tissue within airspaces. Idiopathic cryptogenic organizing pneumonia (COP) and secondary BOOP are histologically similar. COP has been reported to show increased collagen in the granulation plugs and fewer myofibroblasts and capillaries. Using CD34 for capillaries and α-smooth muscle actin for myofibroblasts, we assessed these stains to differentiate COP from secondary BOOP.

Results: From the α-smooth muscle actin and CD34 staining, 6 of 21 cases were diagnosed as COP. The clinical records revealed a cause in 1 of 6 cases. Thus, 5 of 6 cases were correctly classified as COP. We diagnosed 15 of 21 cases as secondary BOOP. A cause was determined in 9 of 6 cases. Thus, 5 of 6 cases were correctly classified as COP. We diagnosed 15 of 21 cases as COP. The clinical records revealed a cause in 1 of the remaining 6 cases; therefore, no cause was found.

Conclusions: Fourteen of 21 cases were correctly classified histologically as COP or secondary BOOP. One case was inappropriately classified; the remaining 6 were classified as secondary BOOP without an apparent clinical etiology. The data suggest that CD34 and α-smooth muscle actin are useful in distinguishing COP from secondary BOOP.

Sclerosing Mediastinitis Presenting as Superior Vena Cava Syndrome in a Patient With History of Coccioidoites Pneumonia

(Poster No. 64)

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Sclerosing mediastinitis is an extremely rare fibrotic reaction involving the mediastinum and is associated with fungal and mycobacterial infections. In the United States, sclerosing mediastinitis is most commonly associated with Histoplasma capsulatum and often presents as superior vena cava syndrome. A 27-year-old man presented with a 3-week history of dry cough and night sweats. Chest x-ray revealed consolidation of the right upper lobe with lymphadenopathy in the right hilum and mediastinum. Needle biopsy revealed a granulomatous reaction with fibrosis, chronic inflammation, and increased eosinophils. Periodic acid–Schiff, Gomori methenamine silver, and acid-fast bacillus stains were negative for fungal and bacterial forms. However, Coccioidoites immitis titer was positive, and the patient was started on fluconazole. Three years later, he presented with complaints of shortness of breath and head pressure. He reported his face turning purple whenever he ran or played basketball. These episodes were associated with dizziness and visual changes. Physical examination revealed prominent veins and swelling in the right anterior chest and shoulder. Radiologic studies revealed a 4-cm mass encasing the superior vena cava with 90% stenosis; all findings were consistent with superior vena cava syndrome. A needle-core biopsy of the mediastinal mass revealed fibrotic scar tissue with chronic inflammation (Figure 26), and periodic acid–Schiff stain showed absence of fungal elements; these findings are most consistent with the diagnosis of fibrosing mediastinitis. The patient was effectively treated with stent placement. We present this rare case of Coccioidoites associated with sclerosing mediastinitis and the classic presentation of superior vena cava syndrome.

Invasive Ductal Carcinoma of the Breast With Metastasis to Primary Adenocarcinoma of the Lung

(Poster No. 65)

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Breast cancer most commonly metastasizes to the brain, liver, lungs, and bone. Solitary pulmonary nodules in women with breast cancer are most likely primary lung cancer. We present a 58-year-old woman diagnosed with invasive ductal carcinoma of the right breast (Nottingham grade 3 of 3) and associated ductal comedocarcinoma in situ. The tumor was positive for hormone receptors. After the patient underwent right modified radical mastectomy, imaging studies showed a 1-cm right upper lobe nodule. Given the patient’s extensive smoking history, we were concerned that this represented a primary lung cancer; accordingly, the patient underwent right thoracotomy with right upper lobectomy. The lung was remarkable for a 1.9-cm moderately differentiated primary lung adenocarcinoma, papillary variant. Approximately 1 year after her diagnosis of breast cancer and concurrent lung cancer, we performed a punch biopsy on a chest wall nodule. Within the dermis, there were both clusters and single malignant epithelial cells. The immunoprofile favored a breast primary. Based on the finding of metastatic breast cancer in the skin, the lung lesion was reexamined and showed a small focus of solid tumor in the papillary adenoecarcinoma of the lung. This focus was BRST2 positive and thyroid transcription factor 1 negative. The lung primary had the opposite staining pattern. The presence of 2 tumors is not uncommon; however, increased awareness regarding the metastasis of one tumor to another is needed because this information can potentially impact tumor stage at an earlier time. In addition, further molecular study is needed to understand how one tumor to another.

Atypical Proteinosis: A Pathologic Disorder Mimicking Pulmonary Alveolar Proteinosis

(Poster No. 66)

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Context: Pulmonary alveolar proteinosis (PAP) is a rare condition in which macrophages fail to clear surfactant from the lungs, resulting in the alveolar accumulation of lipoproteinaceous debris. The histopathology of PAP is typified by the diffuse filling of alveoli with periodic acid–Schiff–positive acellular material. However, the significance of cases of proteinosis that vary from the classic morphology of PAP is uncertain.

Conclusions: Clinical histories, radiographic findings, and pathologic features of pulmonary wedge biopsies from patients diagnosed with PAP at the Massachusetts General Hospital between 2006 and 2008 were reviewed.

Results: Three patients with respiratory distress showed histopathologic changes in the lungs that were most consistent with mild PAP; there was no other discernible pathology. The pathologic features of these cases were distinct from “usual” PAP and on ultrastructural examination showed abundant degenerating histiocyes, weak periodic acid–Schiff staining of the intraalveolar lipoproteinaceous material, and few well-formed lamellated bodies. On computed tomography, only one of the cases showed the “crazy-paving” pattern typical of PAP, and bronchoalveolar lavage did not yield the opalescent fluid emblematic of PAP. Of importance in one case, whole-lung lavage appeared to exacerbate the patient’s respiratory distress. All 3 patients showed at least a partial response to high-dose steroid therapy.

Conclusions: The diagnostic distinction between PAP and “atypical proteinosis” may be clinically significant. Despite the diffuse accumulation of lipoproteinaceous material in alveoli in the latter, the presence of abundant degenerating histiocyes and atypical histochemical, ultrastructural, and radiographic features suggests a steroid-responsive form of atypical proteinosis that may not be amenable to whole-lung lavage.
Diffuse Thymic Fibrosis Mimicking Neoplasia: Report of 4 Cases
(Poster No. 67)

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Context: Extensive thymic fibrosis in the absence of a primary thymic lesion (neoplasm or cyst) is unusual. We describe 4 cases of diffuse thymic fibrosis presenting as mass lesions.

Design: We identified 4 cases of diffuse thymic fibrosis referred to our consultation service between 2001 and 2004. Clinical features, gross reports, and histologic slides were reviewed. Immunohistochemical studies were performed using commercial antibodies to pancytokeratin, CD3, CD1a, and IgG4 (Dako, Carpinteria, California).

Results: The 4 cases included 2 men and 2 women ranging in age from 28 to 62 years (mean, 48 years). Both women had myasthenia gravis; 1 man presented with fever and dyspnea; the mass was discovered incidentally in 1 man. The masses measured 5.5 to 16.5 cm (mean, 9.75 cm) in greatest dimension. The lesions were confined to the thymus/anterior mediastinum by imaging or as determined from intraoperative notes. They were well demarcated and lobulated. There were 3 to 15 (mean, 11) hematoxylin-eosin–stained sections available for review on each case. Microscopically, the fibrosis was diffuse and dense and resembled the fibrosis of fibrosing mediastinitis. No granulomas were identified. There were small residual islands of involuted thymic tissue with paucity of lymphocytes in all cases. One case showed increased IgG4-positive plasma cells.

Conclusions: To the best of our knowledge, the observed diffuse thymic fibrosis is unique and not previously documented in the literature. Although the etiology of the fibrosis is undetermined, the history of myasthenia gravis and the history resembling fibrosing mediastinitis raise the possibility of autoimmune or infectious causes. Alternatively, the lesions may be idiopathic in nature.

Clinicopathologic Correlation of Pulmonary Dirofilariasis
(Poster No. 68)

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Human pulmonary dirofilariasis (HPD) is a rare vector-born parasitic infection that is a clinical simulator of malignant lung neoplasm. Dogs and cats are the usual natural hosts of Dirofilaria immitis. Transmission to humans occurs through mosquito bites. Humans are a dead-end host and nonnatural hosts of Dimmittis. As a result, the larvae cannot develop into adult form. HPD develops when the larva dies in circulation, embolizes to the lung, lodges in a small pulmonary artery branch, and releases antigens. These antigens lead to an inflammatory response, with development of a parasitic granuloma containing a parasitic worm characteristic of D immitis (Figure 27). The preoperative diagnosis of HPD is difficult because of a lack of characteristic clinical symptoms, laboratory results, and roentgenographic findings. The probability of definitely diagnosing HPD on either biopsy or fine-needle aspiration biopsy is low. Extensive sampling of necrotic granulomas, with attention specifically directed toward detection and examination of a central supplying artery, is recommended.

Hematopathology; Kidney and Genitourinary Pathology
Composite Classic Hodgkin Lymphoma and Langerhans Cell Histiocytosis Arising in the Mediastinum of a Pediatric Patient
(Poster No. 1)

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Langerhans cell histiocytosis (LCH) is a neoplastic process defined by a proliferation of Langerhans cells. Rarely, LCH is found to occur asynchronously and synchronously with classic Hodgkin lymphoma (CHL) and other neoplasms. Synchronous occurrences of LCH and CHL have been reported in different anatomic locations (eg, CHL in a lymph node and LCH in the bone) and as composite tumors (eg, CHL and LCH occurring in the same lymph node). Most cases of composite CHL and LCH involve adults and are found in peripheral lymph nodes. We describe a case of a previously healthy 15-year-old adolescent boy who presented to the emergency department with a 2- to 3-week history of progressive superior vena cava syndrome symptoms. A computed tomography scan demonstrated a 22 × 14 × 8-cm heterogeneous mediastinal mass with associated mediastinal and right cervical lymphadenopathy. Core biopsies of the mediastinal mass revealed a composite CHL and LCH. By immunohistochemistry, the CHL component was positive for CD30, CD15, and Pax-5 and negative for CD1a, CD20, and S100 protein. The LCH component was positive for CD1a and S100 protein and negative for CD30, CD15, CD20, and Pax-5. While composite CHL and LCH has been described in the literature, this is the youngest patient reported so far to have a composite LCH and CHL and the first case reported to arise in the mediastinum.

Signet Ring Follicular Lymphoma Presenting as a Soft Tissue Mass
(Poster No. 2)

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Signet ring follicular lymphoma is a rare morphologic variant of follicular lymphoma. It has been reported in lymph nodes, bone marrow, and various extranodal sites. We report a case of a 54-year-old woman who presented with a popliteal mass. Magnetic resonance imaging performed on the patient's knee showed an oval mass in the posterior subcutaneous tissue that measured 2.8 cm in greatest dimension with no other evidence of disease. Microscopically, the lymphoma showed signet ring features. The tumor was grade 3/3 with areas of diffuse large B-cell lymphoma (Figure 28). By immunohistochemistry, the tumor was positive for CD20, CD10, Bcl-2, and Bcl-6 and negative for CD5, CD23, CD43, Bcl-1, IgG, IgA, IgM, IgD, κ, and λ. Fluorescence in situ hybridization (FISH) demonstrated a translocation with the BCL-2 gene on chromosome 18q21 and IgH gene on chromosome 14q32. Gene rearrangement by polymerase chain reaction showed that the tumor was positive for clonal Ig heavy chain and Ig light chain rearrangements. To our knowledge, this is the first reported case of a signet ring follicular lymphoma with a documented presence of t(14;18) by FISH and with a presentation of a soft tissue mass clinically mimicking a sarcoma. This case serves to illustrate that follicular lymphoma may morphologically mimic a soft tissue neoplasm and the diagnosis should be considered when other studies do not support a sarcoma or carcinoma.
Primary Cardiac Lymphoma Should Be Included in the Differential Diagnosis of a Right Atrial Mass
(Poster No. 3)

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A 63-year-old woman with no significant past medical history presented to the emergency room in October 2008 complaining of dyspnea on exertion and chest pain of 3 weeks' duration. Echocardiogram showed a large right atrial mass that extended and prolapsed into the right ventricle. The mass was attached to the interatrial septum with right ventricular inflow obstruction. Preoperative cardiac catheterization showed mild coronary artery disease and a 60% left ventricular ejection fraction. Presumptive diagnosis of large blood clot versus atrial myxoma was made and the patient underwent open chest exploration. Needle core biopsies of the mass were obtained and a frozen section was requested that showed atypical lymphoid infiltrate suggestive of lymphoma. The mass was not resected. Permanent section evaluation displayed diffuse infiltrates of large atypical lymphocytes with moderate mitotic activity. Fresh tissue sent for cell surface analysis by flow cytometry revealed the presence of monoclonal B-cell population with Ki-67 staining, was very high and estimated at 90%. These findings were indicative of diffuse large B-cell lymphoma. The right atrium and right ventricle are the 2 most frequently involved sites in primary cardiac lymphoma, the majority (plasmablastic lymphoma, lymphoblastic leukemia/lymphoma, adult T-cell leukemia/lymphoma, peripheral T-cell lymphoma, NOS, and NK/T cell lymphoma, nasal type) showed diffuse or interstitial pattern of infiltration; anaplastic large cell and hepatosplenic lymphomas were characterized by sinusoidal infiltration. In B-cell lymphomas, the majority (plasmablastic lymphoma, lymphoblastic leukemia/lymphoma, hairy cell leukemia, and marginal zone cell lymphoma) showed interstitial infiltration, sometimes admixed with sinusoidal infiltration; small lymphocytic lymphoma/chronic lymphocytic leukemia presented as nodular or diffuse patterns; and Burkitt lymphoma demonstrated diffused pattern. Immunophenotyping by IHC or flow cytometry can assist classification and recognize some infiltration patterns, such as interstitial and sinusoidal infiltrations.

Bone Marrow Infiltration of Non-Hodgkin Lymphoma
(Poster No. 5)

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Context: The pattern of bone marrow (BM) involvement and combination of immunophenotypic are important in BM biopsy specimens to establish diagnosis of lymphoma or to determine the extent of disease dissemination for staging purposes.

Design: We retrospectively reviewed 231 BM biopsy specimens obtained from January 2006 to December 2008 in Kings County Hospital Center and investigated the histologic patterns of non-Hodgkin lymphoma (NHL) according to World Health Organization 2008 classification. BM involvement patterns are divided into categories of paratrabeicular, diffuse, nodular, interstitial, sinusoidal, and mixed. Immunohistochemistry (IHC) and flow cytometry data were also analyzed.

Results: Of the 231 BM biopsy specimens, 23 cases (10%) with NHL involvement were identified; 11 cases were T-cell lymphomas and 12 cases were B-cell lymphomas. In T-cell lymphomas, the majority (lymphoblastic leukemia/lymphoma, adult T-cell leukemia/lymphoma, peripheral T-cell lymphoma, NOS, and NK/T cell lymphoma, nasal type) showed diffuse or interstitial pattern of infiltration; anaplastic large cell and hepatosplenic lymphomas were characterized by sinusoidal infiltration. In B-cell lymphomas, the majority (plasmablastic lymphoma, lymphoblastic leukemia/lymphoma, hairy cell leukemia, and marginal zone cell lymphoma) showed interstitial infiltration, sometimes admixed with sinusoidal infiltration; small lymphocytic lymphoma/chronic lymphocytic leukemia presented as nodular or diffuse patterns; and Burkitt lymphoma demonstrated diffused pattern. Immunophenotyping by IHC or flow cytometry can assist classification and recognize some infiltration patterns, such as interstitial and sinusoidal infiltrations.

Conclusions: Recognition of infiltration pattern is important in the diagnosis and staging of patients with NHL. The combination of histology, IHC, and/or flow cytometry aid the diagnosis and subtyping of NHL BM infiltration.

Subdural Hematoma and Associated Accelerated Phase of BCRABL1-Positive Chronic Myelogenous Leukemia Occurring in the Setting of Long-Standing JAK-2V617F-Positive Polycythemia Vera
(Poster No. 6)

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A 74-year-old male patient with a long-standing history of polycythemia vera, pulmonary hypertension, congestive heart failure, and left ventricular thrombus presented with marked shortness of breath and left-sided weakness at the emergency room. A head computerized tomography examination revealed an acute and chronic right subdural hematoma. The complete blood count showed white blood cell count of 51.1 × 10^9/L; absolute neutrophil count of 36.3 × 10^9/L; signs of monocytosis 2.6 × 10^9/L; eosinophilia of 1.5 × 10^9/L, and slight basophilia of 0.5 × 10^9/L; mean corpuscular volume 89.7 μm^3; hemoglobin 6.5 g/dL; and platelets 10 × 10^12/L. A leukoerythroblastic picture was noted on the peripheral blood smear, with circulating dysplastic neutrophils. The hypercellular bone marrow had increased trilineage hematopoiesis, dysmegakaryopoiesis, dyserythropoiesis, increased reticulin deposition, and absent iron stores. By immunohistochemistry, there were 5%–6% CD34 and approximately 20% CD117+ nucleated bone marrow cells. While a 46.XY karyotype was noted, molecular studies detected the BCR/ABL translocation in both the peripheral blood and the bone marrow aspirate. The bone marrow was positive for the JAK2-V617F mutation. The findings were in keeping with an accelerated phase of chronic myelogenous leukemia, BCR/ABL positive, which evolved in a background of long-standing polycythemia vera. The unusual occurrence of chronic myelogenous leukemia in the setting of polycythemia vera has been rarely reported in the medical literature and should be of consideration in the differential diagnosis of so-called myeloid metaphasia in patients with long-standing polycythemia vera. Whether these findings represent disease evolution or just a random association remains to be discovered.

### A Rare Case of Moyamoya Disease with Sickle Cell Trait

**Poster No. 7**

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Moyamoya disease is a rare, idiopathic cerebrovascular disorder primarily affecting children. It features bilateral narrowing occlusion of the distal internal carotid arteries and presence of a fine network of collateral channels at the base of the brain (moyamoya means "puff of smoke" in Japanese and describes the angiographic appearance). It can be fatal because of intracerebral hemorrhage. We report a rare case of an adult with moyamoya disease and sickle cell trait (HbAS). A 44-year-old East Indian man presented with left-sided weakness. A magnetic resonance angiogram revealed moyamoya disease (Figure 30). Pneumosurgery workup found normal white blood cells (9.6 × 10^9/L); red blood cells (RBC) (4.70 × 10^12/μL); hemoglobin (13.5 g/dL); hematocrit (38.8%); mean corpuscular volume (82.6 fl); mean corpuscular hemoglobin (28.6 g/dL); platelet count (299 × 10^9/μL); high red cell distribution width (15.6%); normal iron (79 μg/dL); transferrin (381 μg/dL); transferrin saturation (21%); and high ferritin (394 ng/mL). The differential count and RBC morphology were normal. Solubility test result for sickling was positive and hemoglobin electrophoresis by high-performance liquid chromatography showed 40% HbS, <1% HbF (remaining being HBa and HbA2), confirming a diagnosis of sickle cell trait. He had no family history of sickle cell disorder and is doing well postoperatively. Although HBSS, HBSC, HbS-thalassemia, HBSO (Arab), HBF/f-thalassemia have all been reported in children with moyamoya disease, the association is distinctly rare in adults and in "hematologically benign" conditions like sickle cell trait (HBASE). The possible pathogenesis of cerebrovascular disorder in such a case remains unclear.

### Simultaneous Chronic Lymphocytic Leukemia and Chronic Myeloid Leukemia: Identification of Two Distinct Clones by Fluorescence In Situ Hybridization

**Poster No. 8**

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Chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) are the most common chronic lymphoid and myeloid leukemias, respectively. However, their simultaneous occurrence is rare. We present a case of simultaneous CLL and CML in which fluorescence in situ hybridization (FISH) was used to determine whether the 2 leukemias derive from 1 common clone or 2 distinct clones. A 76-year-old man without significant history presented with leukocytosis. Physical examination was unremarkable. Peripheral blood examination revealed a hemoglobin of 17.0 g/dL, white cell count of 37.5 × 10^9/L (70% neutrophils, 1% eosinophils, 1% basophils, 2% monocytes, and 26% lymphocytes), and platelet count of 288 × 10^9/L. Bone marrow examination revealed a markedly hypercellular marrow with myeloid predominance and scattered nonparatrabecular lymphoid aggregates. Flow cytometric characterization of the peripheral blood and bone marrow showed a monoclonal B-cell population expressing CD5, CD11c, CD19, CD20, and CD23, and e-light chain restriction, consistent with CLL. Karyotyping done on the bone marrow revealed 46,XY,t(9;22)(q34;q11). FISH done on the bone marrow confirmed the presence of a BCR/ABL rearrangement and additionally showed 13q14 deletion (the most common cytogenetic abnormality in CML). To ascertain the presence of 1 common or 2 distinct clones, the bone marrow was hybridized with 3 separate probes in a single cocktail: BCR/ABL, 13q14 (D13S319), and 17q21 (D17S189). The FISH results confirmed one clone (66%) with only a BCR/ABL rearrangement, and the other (27%) with only 13q14 deletion, indicating the presence of 2 distinct clones in this rare case of simultaneous CLL and CML.

### Utility of Bone Marrow Examination in Systemic Lupus Erythematosus

**Poster No. 9**

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**Context:** Autoimmune-mediated cell destruction has been considered the most frequent cause of cytopenias in systemic lupus erythematosus (SLE). Both central and peripheral mechanisms may contribute to peripheral cytopenia in most cases of SLE. Since bone marrow examination is not routinely performed for patients with SLE, reported data on the subject are scarce. Design: The frequency and features of bone marrow abnormalities were studied in 18 patients with systemic lupus erythematosus. Bone marrow aspiration and biopsy were performed to assess the hematopoietic activity, and to rule out infectious and infiltrative disorders. Peripheral blood findings showed pancytopenia in most (10/18) of the cases.

**Results:** Quantitative hematopoietic abnormalities were common including hypopcellular marrow in 8 patients and hyperplasia of erythroid or myeloid lineage in each of 4 patients. Stromal changes included cellular depletion, edema, and infiltration by lymphocytes, plasma cells, and macrophages in 10 cases. Focal increase in reticulin fibers was seen in 3 cases. One case showed presence of lymphoid aggregates and epithelioid cell granuloma without demonstrable microorganisms. In one case extensive bone marrow necrosis was present; test results for the patient were found to be negative for anti-phospholipid antibody. In this brief series, we observed hemophagocytic syndrome or overt myelodysplastic changes.

**Conclusions:** All these features provide persuasive evidence that the...
bone marrow is a common target organ affected in SLE. Hematopoietic alterations and bone marrow stromal changes may both contribute to peripheral cytopenia in most cases of SLE.

An Unusual Human Herpesvirus-8–Negative Primary Effusion Lymphoma-like Lymphoma With Biphenotypic Features: A Case Report and Review

(Poster No. 10)

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Primary effusion lymphoma (PEL), as defined by the World Health Organization, is a B-cell neoplasm universally associated with human herpesvirus-8 (HHV-8) and most often occurs in the setting of immunodeficiency. We present a case of a primary effusion lymphoma (PEL)-like large cell lymphoma of undetermined lineage in the ascitic fluid of a 74-year-old man with human immunodeficiency virus (HIV)–negative status, hepatitis C virus (HCV) cirrhosis, and no lymphadenopathy or lymphomatous masses by physical examination or computed tomography scan. From 1997 to 2004 there have been 5 reported cases of HIV-negative patients with chronic HCV infection who had primary lymphomatous effusions involving the abdominal cavity and who were HHV-8 and Epstein-Barr virus (EBV) negative. Unlike the 5 previously reported cases, our case is also negative for HHV-8 and EBV. Like the 5 previously reported cases, our case is not morphologically or immunophenotypically consistent with this disease. The Table shows the few reported cases of T-PEL-like lymphoma. The case reported herein is different and appears to be an unusual biphenotypic lymphoma, that is, a CD7−, CD3− T-cell lymphoma with a cMYC-IGH gene rearrangement. The largest percentage of cases with negative to weak staining occurred in lymphoblastic lymphoma (33%) followed by T-ALCL (20%) and DLBCL (15%). These findings are especially important in small-needle core biopsies of undifferentiated tumors, as NHL may be falsely excluded when only a minority of cells show CD45 expression and are missed with sampling. Although CD45 can be used as a screening marker for NHL in most cases, a negative CD45 stain result should not be considered as sole evidence for a nonhematopoietic tumor. Additional B- and T-cell lineage specific markers should be routinely performed in undifferentiated tumors when the CD45 immunostain result is negative.

**Conclusions:** The largest percentage of cases with negative to weak staining occurred in lymphoblastic lymphoma (33%) followed by T-ALCL (20%) and DLBCL (15%). These findings are especially important in small-needle core biopsies of undifferentiated tumors, as NHL may be falsely excluded when only a minority of cells show CD45 expression and are missed with sampling. Although CD45 can be used as a screening marker for NHL in most cases, a negative CD45 stain result should not be considered as sole evidence for a nonhematopoietic tumor. Additional B- and T-cell lineage specific markers should be routinely performed in undifferentiated tumors when the CD45 immunostain result is negative.

**Cutaneous Marginal Zone B-Cell Lymphoma Six Years After Initial Presentation with IgM Monoclonal Gammopathy**

(Poster No. 12)

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Marginal zone B-cell lymphoma may be associated with monoclonal gammopathy. However, cases with significant IgM paraprotein years before the emergence of marginal zone B-cell lymphoma are rarely reported in the literature. A 65-year-old man presented with a 2-year history notable for IgM A monoclonal protein (2.3 g). He had no evidence of lymphadenopathy and a bone marrow biopsy result was negative. A diagnosis of Waldenström macroglobulinemia was clinically rendered. The patient received 1 course of rituximab and the paraprotein amount decreased to 0.5 g. Several months later, the patient experienced lower extremity palpable purpura and an increase of paraprotein to 2.6 g. A biopsy revealed leukocytoclastic vasculitis. Rituximab therapy was repeated, resulting in a decrease of paraprotein that remained stable at 0.5 g. Four years later, he presented with multiple subcutaneous nodules measuring up to 3 cm located on the lower back and upper chest. These nodules were hypermetabolic on positron emission tomography scan. Biopsy of a lower back nodule showed subcutaneous tissue with a diffuse lymphoid infiltrate of heterogeneous small to medium lymphocytes including centrocytes, mono-

**Results**

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<th>Grade, No. (%)</th>
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<tr>
<td>0</td>
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<tr>
<td>DLBCL</td>
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<tr>
<td>T-ALCL</td>
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<tr>
<td>B-ALCL</td>
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**Abstracts**

**Is CD45 a Reliable Marker to Rule Out Aggressive Non-Hodgkin Lymphomas?**

(Poster No. 11)

Joanna J. Xie, MD (joanna.xie@cslns.org); Randa Alsaheb, MD. Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California.

**Context:** Aggressive lymphomas can mimic other neoplastic processes and are considered in the evaluation of undifferentiated malignancies. For example, anaplastic large cell lymphoma (ALCL), CD45 is thought to be consistently expressed in most non-Hodgkin lymphomas (NHLs), and therefore a negative immunostain result is thought to exclude this diagnosis. The aim of this study is to evaluate expression of CD45 in a large number of aggressive lymphomas.

**Design:** One hundred forty-six cases of aggressive lymphomas were stained with CD45 antibody (1:100 Dako) by using the Dako Autostainer. Cases included 124 diffuse large B-cell lymphomas (DLBCLs), 6 lymphoblastic lymphomas (LBLs), 5 anaplastic T-cell lymphomas (T-ALCLs), and 11 anaplastic B-cell lymphomas (B-ALCLs). The intensity of CD45 staining for each case was evaluated by 2 pathologists. Grades of 0 (negative), 1 (weak), 2 (moderate), and 3 (strong) corresponded to <5%, 5%–25%, 26%–50%, and >50% positivity, respectively.

**Results:** See the Table.

**Abbreviations:** N, negative; P, positive; TCR, T-cell receptor rearrangement.
Extranodal marginal zone lymphomas primary to the central nervous system are extremely rare, and are typically dural based, and are known to mimic meningiomas. They typically present with single or multiple extra-axial masses that enhance diffusely with additional contrast material and can be easily confused with a meningioma. MALT lymphomas comprise 7%–8% of all B-cell lymphomas and up to 50% of primary gastrointesti- nal lymphomas. A 52-year-old woman presented with a complaint of a severe headache that was not responsive to medication. Magnetic resonance imaging demonstrated a 1.1 × 4.7 × 2.3-cm extra-axial enhancing mass through the interhemispheric falx, near the vertex just right of the midline in the right parafalcine region. The mass was considered a meningioma in the right parafalcine aspect. Frozen section biopsy results were positive for a lymphocytic infiltrate in a fibrous background, possibly dural. Microscopic examination of hematoxylin-eosin–stained sections revealed dural tissue with focal psammomatosus calcification and a nodular infiltrate composed of a mixture of monocytoid lymphocytes and plasma cells. Immunohistochemical staining shows strong reactivity of CD20 and bcl-2 by the infiltrating cells. CD3 and CD5 highlighted reactive T lymphocytes in the background. A reported k light chain restriction was detected in the plasma cell population; there was no expression of epithelial membrane antigen. A diagnosis of extranodal marginal zone lymphoma was made. This case demonstrates that one must be wary because the classic radiologic findings of meningioma can be seen with extranodal marginal zone lymphoma arising in the dura.

**Dural Extranodal Marginal Zone Lymphoma Mimicking a Meningioma**

(Poster No. 14)

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Nonsecretory, Nonproducing Plasma Cell Myeloma Presenting with Clinical Features of Hairy Cell Leukemia

(Poster No. 15)

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Plasma cell myeloma is not an uncommon diagnosis and 97% of cases demonstrate the presence of an M-spike on immunofixation electrophoresis. Of the 3% of cases that fail to do so, 85% demonstrate clonal light chains in the cytoplasm of the neoplastic cells by immunohistochemistry and are therefore termed nonsecretory. Of the nonsecretory cases, 15% do not have cytoplasmic immunoglobulin synthesis and are termed nonpro- ducing. Consequently, nonsecretory, nonproducing plasma cell myeloma constitutes less than 0.5% of cases. The presence of this entity as a mimic of hairy cell leukemia has yet to be reported. In our case, a 69-year-old man presented with diarrhea, anorexia, and weight loss. Peripheral blood showed numerous lymphoid cells with oval nuclei and pale blue cytoplasm with circumferential projections best characterized as classic hairy cells. Peripheral blood flow cytometry showed an immunophenotype of CD19, dim CD45, dim CD33, CD4, CD38, and CD56 positive cells. This was inconsistent with a diagnosis of hairy cell leukemia. Immunofixation electrophoresis showed hypogammaglobulinemia and no M-spike. The bone marrow showed an abnormal population of cells, 92% of which were positive for CD4, CD38, CD13, and CD26. Cytogenetic analysis demonstrated multiple abnormalities including (11;14), k/λ light chains by in situ hybridization showed a clonal k population of cells. In conclusion, nonsecretory, nonproducing plasma cell myeloma is rare and can mimic hairy cell leukemia: therefore it constitutes a unique entity that warrants increased awareness.

**Systemic Mastocytosis Presenting With Chronic Monocytosis and Osteoblastic Lesions in a Patient With History of Breast Cancer**

(Poster No. 16)

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We present an interesting case of an 80-year-old woman with a remote history of breast cancer who presented to an outside hospital with weakness, weight loss, fatigue, loss of appetite, dyspnea, and loss of muscle tone. Imaging showed sclerotic lesions in the abdomen, pelvis, and thorax that were suggestive of metastases. An extensive workup yielded negative results for bone marrow biopsy, JAK-2 mutation, and BCR/ABL fluorescence in situ hybridization) and normal cytogenetics. The patient was seen...
at our institution 2 months later. Peripheral blood showed leukocytosis (13.4 K/µL) and absolute monocytosis (2.4 K/µL). A differential diagnosis of myeloproliferative/myelodysplastic disorders was initially considered. A bone marrow biopsy showed alternating areas of hypercellular marrow with hypocellular spindled cells intermixed with increased reticulin fibrosis amidst markedly thickened bony trabeculae. The fibrosis and osteosclerotic bone, in light of the patient’s history of breast cancer, warranted the consideration of a myeloproliferative disorder and/or radiation-induced fibrosis with osteosclerosis. However, the typical morphology of paratrabecular infiltrates of spindled cells resulted in an unexpected diagnosis of systemic mastocytosis (Figure 33). This was confirmed by tryptase immunostaining and elevated serum tryptase levels (505 µg/L). Systemic mastocytosis is a rare disease and diagnosis requires a high degree of suspicion. Our case is unusual in its presentation with chronic mononcytosis, vague constitutional symptoms, and absence of clear clinical symptoms of mast cell degranulation in the context of remote breast cancer. This case also emphasizes the importance of a meticulous bone marrow examination before resorting to more extensive diagnostic testing.

A Retrospective Review of Pathologic Diagnosis of Bone Marrow Biopsy in Hospitalized Patients

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Context: Bone marrow biopsy is indicated in the evaluation of a broad variety of diseases including both hematologic lesions and nonhematologic lesions with bone marrow involvement. Many hospitalized patients with abnormal complete blood count (CBC) findings undergo bone marrow evaluation. This study evaluates the necessity of the bone marrow biopsy in hospitalized patients by reviewing the bone marrow biopsy reports and related clinical information.

Design: During 2007 a total of 138 bone marrow samples were collected from 133 hospitalized patients. The pathologic reports were retrospectively reviewed. Patient’s information, including age, sex, clinical diagnosis for hospitalization, and the clinical indication for bone marrow biopsy were recorded.

Results: The patients consisted of 65 males and 68 females (mean age, 64 years). Hematologic diseases were detected in 64 patients (48.1%). Three patients (2.2%) showed nonhematologic diseases. Another 66 patients (49.6%) showed nonspecific histologic findings without specific pathologic diagnosis. Among these patients, 61 were hospitalized because of nonhematologic diseases, mainly respiratory failure, cardiovascular diseases, and diabetes; 5 because of lymphoma/plasma cell neoplasm without bone marrow involvement. The most frequent abnormal CBC findings are anemia, pancytopenia, bicytopenia, and thrombocytopenia.

Conclusions: In this retrospective study, nearly half (49.6%) of the bone marrow biopsy samples collected from the hospitalized patients showed nonspecific histologic findings without specific pathologic diagnosis. Although the nonspecific or negative bone marrow findings can be important information for patient care during hospitalization, in some patients, the bone marrow biopsy may be performed at an outpatient clinic after discharge for the evaluation of abnormal CBC parameters.

Aberrant Expression of T-Cell Antigens in Diffuse Large B-Cell Lymphoma of the Testis

(Poster No. 18)

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The aberrant expression of T-cell antigens in B-cell non-Hodgkin lymphoma occurs rarely. We report the case of a 78-year-old man with a history of diffuse large B-cell lymphoma (DLBCL) in the left testicle that was diagnosed in 1995. He was treated with unilateral orchietomy plus multiagent chemotherapy and radiation therapy and achieved complete remission. Recently, however, he presented with a contralateral testicular mass. Hematoxylin-eosin-stained sections showed displacement of residual testicular tissue by sheets of atypical lymphoid cells, consistent with recurrence of DLBCL. On further immunohistochemical characterization by 5-color flow cytometry, a monoclonal B-cell population was identified that expressed dim λ light chains, CD19, CD20, and the T-cell antigens CD5 and CD7 without CD3, CD10, CD22, CD30, CD45, FMC-7, or any additional T-cell markers. Immunohistochemical staining for the proliferation marker MIB-1 was performed and showed positivity in approximately 50% of the neoplastic cells. The patient went on to receive multiple cycles of chemotherapy and achieved a complete clinical remission. The occurrence of T-cell markers in DLBCL is unusual and appears to be primarily of diagnostic relevance. No unusual or aggressive clinical behavior was observed in this case. B-cell non-Hodgkin lymphoma may express 1 or more T-cell antigens. One or more pan-B-cell antigens, such as CD22 in this case, may be absent. Awareness of these possibilities is necessary to avoid diagnostic errors.

Nasopharyngeal Hodgkin Lymphoma With Necrosis and Fungal Proliferation: A Challenging Diagnosis

(Poster No. 19)

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Classic Hodgkin lymphoma (CHL) is a lymphoid neoplasm with at least some B-cell differentiation, typically arising in lymph nodes. Extranodal presentation is unusual; when it occurs, spleen or bone marrow is commonly affected. We report the case of a 41-year-old woman with primary nasal CHL. She presented with a progressive ulcerative nasal septal lesion. Hematoxylin-eosin–stained slides of nasal biopsies revealed extensive surface necrosis with fungal hyphae. Beneath the necrosis was acute and chronic inflammation with lymphohistiocytic proliferation. Large cells with polylobulated nuclei and macronucleoli were also noted. Immunohistochemical staining revealed that the large cells were variably positive for CD20, CD79a, Ki67, and Bcl-2 and negative for CD3, CD5, CD10, and CD45. The occurrence of the neoplastic cells was at least some B-cell differentiation, typically arising in lymph nodes. Hematoxylin-eosin–stained sections showed extensive surface necrosis. Beneath the necrosis was acute and chronic inflammation with lymphohistiocytic proliferation. Large cells with polylobulated nuclei and macronucleoli were also noted. Immunohistochemical staining revealed that the large cells were variably positive for CD20, CD79a, Ki67, and Bcl-2 and negative for CD3, CD5, CD10, and Bcl-6. B-cell lymphoma was first considered. Additional staining showed that the cells were CD30+ and CD45+. They were also positive for EBER. A diagnosis of CHL, stage IIe, was made. Because of the necrosis and fungal hyphae, it was initially unclear whether this was reactive or neoplastic, confounding the correct diagnosis. However, as necrosis often accompanies CHL, CHL should be included in the differential diagnosis whenever marked necrosis is noted and (2) primary CHL in the nasal septum, while rare, does occur and should be included in the differential diagnosis of nasal lesions.

Histiocytic Necrotizing Splenitis: Kikuchi-Fujimoto-like Splenic Findings in Patients With Chronic Autoimmune Disorders

(Poster No. 20)

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Autoimmune diseases are associated with enlarged lymph nodes and
Splenomegaly in many cases. The histologic findings in these lymph nodes have been described as follicular hyperplasia, with similar findings in the splenic white pulp being described less commonly. Histiocytic necrotizing lymphadenopathy has also been reported in autoimmune diseases, but a similar counterpart in the spleen has not been documented. We report 2 cases of histiocytic necrotizing splenitis (Kikuchi-Fujimoto-like) findings in spleens from patients with chronic autoimmune disorders. The patients' medical histories were significant for systemic lupus erythematosus. Splenectomy was performed secondary to thrombocytopenia in one case and to rule out a lymphoproliferative disorder in the other. Both exhibited features characteristic of histiocytic necrosis without acute inflammation similar to Kikuchi-Fujimoto disease described in lymph node specimens. Splenic involvement was extensive and diffuse and centered predominantly in the red pulp or nonwhite pulp areas. Fibrinoid necrosis was present in all cases (Figure 34). The most striking features of the cases were the marked extracellular and intracellular karyorrhectic nuclear debris (apoptotic debris) that was present without an associated neutrophilic or eosinophilic response. Surrounding these necrotic areas were benign histiocytes, immunoblasts, and plasmacytoid mononuclear cells. Plasma cells (a normal splenic constituent) were present in all cases and hematoxylin bodies were not identified. Staining results for infectious organisms were negative in all cases. Splenomegaly in autoimmune disease is rarely studied and is assumed to be hyperplastic in most cases, but we present rare cases of histiocytic necrotizing splenitis, which calls into question that assumption.

**Primary Amyloidosis of the Glans Penis: A Painful k-Positive Lesion**

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Primary amyloidosis is uncommon and extremely rare when localized to the glans penis. We report a case of a 53-year-old uncircumcised man with a history of diabetes and hypertension presenting with a broad-based flat lesion of the glans penis. The patient had complaints of penile pain for 1 month. The penile biopsy under microscopic examination revealed a pink homogenous subepithelium stroma with thickened blood vessel walls. Congo red-stained section showed apple-green birefringent Congo red crystals localized to the glans penis. Rare cases of localized amyloidosis of the penis present as a painless lesion composed of light chains, which have a particular “amyloidogenicity.” Here we illustrate the first case reported in the literature that was painful and positive for light chains.

**Bilateral Synchronous Testicular Involvement in Multiple Myeloma**

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Testicular plasmacytomas are rare tumors and make up 2% of plasma cell neoplasms. In the current report we present the case of a 49-year-old man with bilateral synchronous testicular plasmacytoma. The patient had a 2-year history of multiple myeloma with bone metastasis and presented with bilateral testicular enlargement. He underwent bilateral orchietomy, which revealed a well-defined, 3-cm, pink mass in the right testis and 2 masses, 1.5 and 1.2 cm, in the left testis (Figure 36). Histologically, the tumor showed an infiltration of plasma cells with round-shaped nuclei, some with prominent nucleoli, clumped chromatin, basophilic cytoplasm, and Golgi apparatus. Immunohistochemical studies showed strong cytoplasmic staining for IgG anti-κ antisera, weak staining for LCA, and negativity for IgG anti-λ antisera, supporting the diagnosis of plasmacytoma. Since the first reported case in 1939, approximately 60 cases of testicular plasmacytoma have been reported so far. Most cases reported thus far have been unilateral, or bilateral but with asynchronous testicular involvement. To our knowledge, only 4 cases of synchronous bilateral testicular involvement with plasmacytoma have been reported in the literature.

**A Nodal Marginal Zone Lymphoma With Bright CD10 Expression Mimicking Follicular Lymphoma**

*Dava S. West, MD (dava.west@duke.edu); Endi Wang, MD, PhD. Department of Pathology, Duke University Medical Center, Durham, North Carolina.*

Nodal marginal zone lymphoma (NMZL) is a small B-cell neoplasm...
that lacks a unique immunophenotype. It is thus, in part, a diagnosis of exclusion that must be differentiated from other small B-cell lymphomas, including follicular lymphoma (FL). Previous studies have demonstrated a high specificity for CD10 expression in FL in comparison to other small B-cell neoplasms. Here, we report a CD10+/NMZL in a 62-year-old man who presented with weight loss, night sweats, and anemia. Imaging revealed widespread lymphadenopathy without splenomegaly. Histologic sections of inguinal lymph node showed a nodular lymphoid proliferation with an interfollicular infiltrate of small/medium-sized lymphocytes with a “monocytoid” appearance. Flow cytometry detected a monoclonal B-cell population with bright CD10 expression. Immunohistochemical staining confirmed CD20 and CD10 positivity in both follicle center and interfollicular lymphocytes, with brighter CD10 staining in neoplastic interfollicular areas (Figure 37). Bcl-2 immunohistochemical staining highlighted a marginal zone growth pattern. Interphase fluorescence in situ hybridization for t(14;18)(IGH/BCL2), a genetic hallmark for FL, was performed on paraffin-embedded tissue. No fusion signal was observed. Rare cases of MZL with weak CD10 expression have been described in the literature. However, to our knowledge, this is the first case of a strongly CD10+/NMZL in which FL was definitely excluded by molecular studies. The case underscores the importance of recognizing architectural and cytomorphologic features of NMZL even when CD10 expression suggests FL. Immunohistochemical analysis for B-cell markers and Bcl-2 can be used to highlight NMZL morphologic pattern. Molecular studies can then be used for definitive diagnosis.

Conclusions: Our results indicate that CD58 is significantly and consistently overexpressed in B-ALL patients with active disease when compared to its expression in B-ALL patients lacking evidence of ongoing leukemia. The expression of CD58 on leukemic lymphoblasts appears to be a useful biomarker for detecting minimum residual or recurrent disease because it remains elevated in positive cases and is decreased in absence of active leukemia.

CD3+ Primary Mediastinal Large B-Cell Lymphoma in a 42-Year-Old Woman
(Poster No. 25)

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Primary mediastinal large B-cell lymphoma (PMBCL), a subtype of diffuse large B-cell lymphoma (DLBCL), arises in the anterior mediastinum, presumably from thymic B cells. Whereas aberrant expression of antigens of other lineages is frequently observed in lymphomas, DLBCL with aberrant expression of CD3, a T-cell specific antigen, is rare. We report the case of a 42-year-old woman with chest pain radiating to the left arm that developed during a 2-month period. Radiographs showed a 9.9-cm, anterior mediastial mass, which was fluoroscopically biopsied. Hematoxylin-eosin–stained sections demonstrated a diffuse proliferation of mixed small and large lymphocytes in a background of fibrosis. The large cells formed cohesive clusters with few intermingled small lymphocytes. Immunohistochemical stains demonstrated homogeneous positive staining in large cells for CD45, CD20, CD79a, Pax-5, bcl-2, bcl-6, and MUM-1. Many large cells had weak-moderate membranous staining with CD3 and CD4. Other T-cell–associated antigens, CD5, CD2, CD7, CD4, and CD8, were negative in large cells. CD20 was positive in a subset of large cells (15%–20%), but CD15 was essentially negative. Polymerase chain reaction–based immunoglobulin (Ig) gene and T-cell receptor (TCR) gene rearrangement studies were performed on paraffin-fixed tissue that revealed a clonally rearranged Ig κ light chain gene without clonal rearrangement of TCR. While rare cases of conventional DLBCL with aberrant CD3 have been recently described, aberrant expression of CD3 in PMBCL has never been reported, to the best of our knowledge. We emphasize application of immunohistochemical antibody panels and the value of molecular tests for definitive diagnosis of uncommon lymphomas with ambiguous phenotype.

Recurrence Classic Hodgkin Lymphoma--Type Posttransplant Lymphoproliferative Disorder
(Poster No. 26)

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The least common subtype of posttransplant lymphoproliferative disorder (PTLD) is classic Hodgkin lymphoma type (cHL), an entity most often described in renal transplant patients. We present a case of a 17-year-old cardiac transplant recipient with cervical lymphadenopathy 11 years after transplant. Lymph node biopsy revealed complete effacement of nodal architecture by large, atypical Hodgkin/Reed-Sternberg (HRS) cells against a background of small lymphocytes. The HRS cells expressed Epstein-Barr virus on in situ hybridization and CD30, CD15, Pax-5 weakly, but not CD20 or CD45. The diagnosis of cHL-PTLD was made. Complete remission was achieved following immunosuppression withdrawal. Six years later, the patient died following unrelated multiorgan failure. Autopsy revealed cHL-PTLD in the mediastinal lymph nodes and liver, identical morphologically and immunohistochemically to the lymph node biopsy 4 years earlier. The main differential diagnosis for cHL-PTLD is Hodgkin-like PTLD. Until recently, both were considered the same entity because of their similar morphology. They can be distinguished as follows: HRS cells in cHL-PTLD express CD30, CD15, and Epstein-Barr virus but not CD45 and/or CD20, while HRS-like cells in Hodgkin-like PTLD express CD45, CD20, and/or CD30 but not CD15. Hodgkin-like PTLD also shows expression of Epstein-Barr virus in both HRS-like cells and bystander small lymphocytes and demonstrate Ig gene rearrangement. It is important to distinguish between these 2 entities because cHL-PTLD responds to chemotherapies targeted for Hodgkin lymphoma, while Hodgkin-like PTLD responds to non-Hodgkin lymphoma therapies. To the best of our knowledge, recurrent cHL-PTLD is extremely rare in pediatric cardiac transplant patients. An accurate diagnosis is vital for optimal management.
A Case of Primary Omental Peripheral T-Cell Lymphoma Presenting With Marked Hypereosinophilia, Omental Caking, a Tubo-Ovarian Mass, Ascites, and Elevated CA125: An Illustration of Anchoring Bias in Clinical Decision-Making

(Poster No. 27)

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A 53-year-old Asian woman with peripheral blood eosinophilia (126,300/µL) presented with left-upper-quadrant pain and lghery. Stool examination for parasites was negative. Bone marrow with molecular and cytogenetic analysis along with flow cytometry was negative for chronic eosinophilic leukemia, chronic myelogenous leukemia, acute leukemia, malignant lymphoma, and other malignancies. Computerized tomography did not show lymphadenopathy but showed a large omental cake, a small amount of ascites, and a small left tubo-ovarian mass. Serum levels of CA125 were elevated (368 U/mL). A clinical diagnosis of metastatic ovarian carcinoma was made. Hysterecetomy with bilateral salpingo-oophorectomy, omentectomy, and bilateral iliac lymphadenectomy were done without a preoperative or intraoperative biopsy. Malignant lymphoma was suspected from the postsurgery frozen section done to select tissue for chemotherapeutic sensitivity testing. Flow cytometric analysis of omental tissue showed only CD7+/CD11c+ cells. Hematoxycin-eosin sections showed medium to large lymphoid cells with brisk mitotic activity, angiocentricity, intense eosinophil infiltrate (Figure 38), and focal necrosis in the removed tissue, mass-forming only in omentum. The neoplastic infiltrate was seen only in the serosa and subserosa of bilateral adnexa and uterus. Iliac lymph nodes were negative for lymphoma. Paraffin in-mandhistochemistry was positive for CD3, CD7, CD43, granzyme, TIA-1, perforin, TCRβ, and Ki-67 (about 80%). Results for CD56, CD57, EBV-LMP1, and EBER were negative. Polymerase chain reaction for T-cell receptor gene rearrangement yielded positive results. Primary omental peripheral T-cell lymphoma, not otherwise specified, was diagnosed because of a large mass in omentum and lack of any other mass. This represents a good example of anchoring bias in clinical decision-making.

LMP1 expression in MEGs has not been previously reported. CD79a expression has been previously recognized, but has not been extensively studied. We compared these markers to better-known MEG markers.

Design: Forty cases were examined: 29 bone marrow (5 myeloproliferative disease [MPD]), 3 myeloproliferative disease/myelodysplastic syndrome (MPD/MDS), 21 various diagnoses, and 11 EMH (8 spleen, 3 lymph node). Tests with CD61, LMP1, Factor VIII, and CD79a were performed on paraffin-embedded sections (Table). In situ detection of EBV-encoded RNA was performed in 5 cases that were immunoreactive for LMP1 to exclude Epstein-Barr virus infection. Each stained slide was graded for the percentage of MEGs stained, intensity, and background. Each parameter was given a numerical score from 0–3. The average scores are reported.

Results: LMP1 staining was observed in 39 of 40 cases and the overall staining profile for the 3 characteristics was 2.8/3.0/2.08. CD79a staining was observed in 35 of 38 cases (2.84/2.58/0.89). Factor VIII staining in 39 of 39 cases (3.0/2.92/2.08); and CD61 staining in 39 of 40 cases (2.90/2.50/1.75). The presence of EBV-encoded RNA was negative in all cases.

Conclusions: LMP1 staining was not as intense but was consistently positive with a cleaner background. CD79a performed comparably, except in extramedullary tissues because of background. LMP1 and CD79 were expressed in dysmorphic MEGs of MPD and MDS. The mechanism for expression of CD79a and LMP1 is unknown. Use of CD79a and LMP1 increases the repertoire of immunohistochemical stains available for megakaryocytes; in addition, recognition of their expression is helpful in excluding hematopoietic disease and misidentification.

Streck Cell Preservative Reagent Stabilizes Bone Marrow Cells and Their Antigen Expression Profiles for Extended Analysis by Flow Cytometry

(Poster No. 29)

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Context: Streck Cell Preservative (SCP, formerly Cyto-Chex Reagent) is a cell and tissue preservative used to stabilize samples for analysis by flow cytometry. Current flow cytometry protocols require analysis of bone marrow samples within 24 hours of collection.

Design: The goal of this study was to determine whether bone marrow is preserved beyond 24 hours by using SCP, thus avoiding the rejection of samples delayed during shipping and eliminating the need for weekend staffing.

Results: We report that SCP can preserve bone marrow samples for flow cytometric analysis for 72 hours. Bone marrow samples drawn from patients were mixed 1:1 with SCP and evaluated by flow cytometry at 6 hours and 72 hours after isolation. We reported on the stabilization of bone marrow samples from 13 patients. Now we report on a total of 23 patient samples that were stabilized by diluting into SCP and tested for CD marker expression by using standard leukemia and lymphoma panels. The SCP-diluted bone marrow sample results were compared to bone marrow samples collected in K2EDTA tubes. We have tested samples with a presumptive clinical diagnosis of myelodysplastic syndrome, chronic lymphocytic leukemia, or acute myeloid leukemia. Results indicate that regardless of the leukemia and lymphoma panel type, the samples diluted in SCP and tested at 6 hours and 72 hours yielded results phenotypically comparable to samples collected in K2EDTA tubes and tested at 6 hours.

Conclusions: We conclude that bone marrow samples diluted in Streck Cell Preservative are stable for immunophenotyping analysis for up to 72 hours.
Flow Cytometry in Predicting Morphologic Patterns of Lymphoma
(Poster No. 30)

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Context: Flow cytometry (FC) is generally considered a reliable supplement to tissue diagnosis of lymphomas. However, its use as a standalone diagnostic tool for predicting morphologic patterns has been cautiously considered.

Design: FC cases performed in our institution (2003–2008) were reviewed by 4- and 6-color methods. Lymph nodes (LN) or solid tissue biopsies with corresponding definitive tissue diagnosis was selected. Cases were reviewed by FC in blinded fashion to the final diagnosis and findings were then correlated by using tissue diagnosis as the gold standard.

Results: Three hundred and twelve cases were included. Reactive cases (147/147) and small B-cell lymphomas (61/68) approached 100% diagnostic accuracy. Diffuse large B-cell lymphomas and T-cell lymphomas (TCLs) demonstrated an accuracy of 83% (29/35) and 60% (6/10), respectively. All 4 TCLs missed by FC were anaplastic large cell lymphomas. One hundred percent (3/3) of Burkitt lymphomas were predicted by FC. Ninety-four percent (16/17) of nonhematolymphoid (non-H) lesions were ruled out. Thirty cases were nondiagnostic for Hodgkin lymphoma (HL); however, 75% (3/4) of cases of nodular lymphocyte predominant (NLP-HL) were suspected by FC. The diagnostic accuracy of all cases (excluding HL) was 93% (263/282).

Conclusions: FC pattern can reliably predict reactive or non-H lesions and can be used to morphologically subtype B-cell non-Hodgkin lymphomas. Although the use of FC has limitations in HLs, the pattern can predict certain subtypes such as NLP-HL. The application of multiparametric FC may be of greater value in predicting morphologic lesions than previously thought.

Blastic Plasmacytoid Dendritic Cell Neoplasm:
Report of 2 Cases with Review of Literature
(Poster No. 31)

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Blastic plasmacytoid dendritic cell neoplasm is a rare and aggressive hematodermic tumor with distinct clinical, pathologic, and immunophenotypic features. Patients usually present with a cutaneous lesion followed by dissemination to involvement of bone marrow, blood, and lymph nodes and the central nervous system. Clinical course is aggressive with median survival of 14 months. The history of this entity dates back to 1994 when Adachi et al reported the first case. Since then, approximately 150 cases have been reported in literature by using a gamut of names such as blastic NK cell lymphoma, CD4-CD56+ hematodermic neoplasm, and aggressive granular NK cell leukemia. For many years, it was believed to be derived from NK cells because of its unique B, T, and myeloid lineage–negative CD4-CD8, and partial CD7, and myeloid lineage–negative CD4+/CD56+/CD123+/HLA-DR+ immunophenotype. Recent recognition of expression of antigens CD123, blood dendritic cell antigen (BDCA-2), and myxovirus A by tumor cells provided strong evidence that the precursor of the plasmacytoid dendritic cell may be the cell of origin for this rare neoplasm. Incorporation of these data lead to the renaming of this entity as blastic plasmacytoid dendritic cell neoplasm in the revised WHO (2008) classification for hematopoietic and lymphoid neoplasms. We present here 2 cases of blastic plasmacytoid dendritic cell neoplasm recently diagnosed at our institution (Table), along with a review of the literature highlighting its unique clinical, histopathologic, and immunophenotypic features. Awareness and recognition of this rare entity by pathologists is vital for early diagnosis and aggressive treatment of this lethal neoplasm.

Table: Summary of 2 Cases

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, y/ Sex</th>
<th>Extracutaneous Sites Involved</th>
<th>Flow Cytometry</th>
<th>IHC</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>68/M Central nervous system</td>
<td>Blast population 40% of all cells; positive for dim CD45, HLA-DR, CD4, CD56, partial CD33, and partial CD7; negative for CD3, CD5, CD8, CD19, CD20, CD13, CD34 and CD117</td>
<td>Positive for CD123, CD4, CD56, CD43, CD68, LCA, Bcl2, CD33, CD79a, and TdT</td>
<td>Negative for CD3, CD5, CD10, CD20, CD30, CD34, CD117, MPO, lysozyme, MUM-1, Bcl1, and Bcl6</td>
</tr>
<tr>
<td>2</td>
<td>59/M Bone marrow</td>
<td>Blast population 83% of all cells; positive for HLA-DR, TdT, CD4, CD56, CD2, CD7, CD33, CD38; negative for CD5, CD10, CD19, CD20, CD13, CD34, and CD117</td>
<td></td>
<td>Negative for CD3, CD7, CD20, and MPO</td>
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Abbreviation: IHC, immunohistochemistry.

Primary Pulmonary Adult T-Cell Lymphoma Presenting With Recurrent Spontaneous Pneumothorax
(Poster No. 32)

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Primary pulmonary lymphoma is a very rare condition in adults, accounting for less than 0.5% of all primary lung malignancies. Most of these lymphomas are B-cell type and the incidence of other non-B-cell type of pulmonary lymphomas is unknown. Human T-cell lymphotropic virus types 1 and 2 (HTLV-1 and HTLV-2), and human immunodeficiency virus-1 (HIV-1) have been associated with pulmonary lymphomas. Herein, we present a case of a 36-year-old man who presented with recurrent spontaneous pneumothorax with bullae formation and a history of HTLV-1 seropositivity. A diagnosis of lymphocytic interstitial pneumonitis (LIP) was considered initially. However, pathologic examination of a pleural biopsy and a bilateral bullectomy specimen showed a cytologically atypical...
ical small T-cell lymphocytic population immunoreactive to CD3 and CD5 antibodies (Figure 39). Gene rearrangement studies performed on the paraffin-embedded tissue demonstrated rearrangement of the T-cell receptor. These findings, in addition to the HTLV-1 seropositivity, pointed to a diagnosis of a primary pulmonary adult T-cell lymphoma. Infection with HTLV-1 has been associated with other pulmonary conditions such as lymphoid interstitial pneumonitis (LIP) and diffuse panbronchiolitis (DBP). In our case it is unclear whether LIP or DBP existed as a prema-

lignant condition that predisposed to the development of the lymphoma or if the macroscopic pulmonary changes were secondary to the presence of pulmonary lymphoma.

An Unusual Case of Near-Tetraploid Early B-Precur
or Acute Lymphoblastic Leukemia With Multiple Chromosomal Abnormalities

(Poster No. 33)

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In childhood acute lymphoblastic leukemia, gene rearrangement, blast cell DNA content, and ploidy have important prognostic implications. Approximately 1% are near-tetraploid clonal populations. Of these, the median number of chromosomes is 55 with ~65 chromosomes being of rare occurrence. ETV6/RUNXI [TEL/AML1] gene rearrangement is a known favorable prognostic factor. We describe the case of a 15-year-old adoles-
cent female who presented with a 1-month history of fatigue, shortness of breath, and headache. Her initial white blood cell count was 4800/mm3, with 25% blast count and hemoglobin level of 4.7g/dL. The blast cells were markedly enlarged with unusual nuclear configuration. Bone marrow examination revealed increased cellularity with almost complete replace-
ment of the normal marrow elements by the blast cells. These blast cells expressed CD19, TdT, and aberrant coexpression of CD13. DNA ploi-
dy revealed a near-tetraploid population with a DNA index of 1.87. Chromosomal analysis (Figure 40) revealed multiple chromosomal abnormalities and confirmed the near-tetraploid karyotype (67 chromosomes) with loss of chromosomes X, 7, 8, and 14; gain of chromosome 22; and structural rearrangement of 1p, 5q, 12p, 15q, 20p, and 22q. Fluorescence in situ hybridization (Figure) analysis showed ETV6/RUNXI [TEL/AML1] gene rearrangement. The patient began chemotherapy and the day 8 bone mar-
row contained 15%–20% blasts, but by day 15 there was no residual dis-
ease. She subsequently had good clinical outcome despite multiple che-
motherapeutic complications. We will review literature on whether the presence of near-tetraploid population, and subsequently several copies of ETV6/RUNXI [TEL/AML1] gene, would have had an influence on a patient's clinical outcome.

Concomitant Chronic Lymphocytic Leukemia and Acute Lymphoblastic Leukemia at Initial Presentation:
Report of 2 Cases

(Poster No. 34)

Shilpa Jain, MD (drjainsh@gmail.com); Suqing Xie, MD, PhD; Hu-
mayun K. Islam, MD, PhD. Department of Pathology, Westchester Medical Center/New York Medical College, Valhalla, New York.

Chronic lymphocytic leukemia (CLL) has been reported as concurrently presenting with other hematopoietic and nonhematopoietic malignancies, including acute myeloid leukemia, multiple myeloma, systemic mastocy-
tosis, large granular lymphocytic leukemia, and renal cell carcinoma. However, it has never been reported with acute lymphoblastic leukemia (ALL). We describe 2 unique cases of CLL concurrently presenting with ALL and discuss their clinical, immunophenotypic, cytogenetic, and bio-
logic features. Case 1 was that of a 63-year-old man who presented with pancytopenia, while case 2 was that of a 74-year-old man with bicyto-
penia. Complete hematologic workup was done in both cases, including flow cytometry of peripheral blood (PB) and bone marrow (BM). Both cases had relative lymphocytosis and increased blast counts in PB. BMs were hypercellular in both and essentially packed with blasts. Immunophenotypic analysis by flow cytometry and/or immunohistochemistry re-
vealed that the blasts were precursor B cells expressing CD19, CD22, CD10, and TdT. In addition, the Cytometry of peripheral blood showed a ulation of mature CD5+ B cells expressing CD19, CD20, CD22, and CD23. The latter also focally involved the BM in the second case. Cytogenetics showed normal karyotype in both cases. True incidence of concurrent CLL and ALL might be underestimated and may be increasingly detected with simultaneous immunophenotypic analysis of PB and BM. Synchron-
ous CLL and ALL represents either a clonal evolution of the initial asymtomatic CLL clone or simultaneous presence of 2 separate clones, a distinction which remains to be confirmed in future studies.

Unusual Presentation of a Hepatosplenic T-Cell Lymphoma

(Poster No. 36)

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A 42-year-old man presented with 4 months of weight loss, night sweats, pruritic skin rash, and arthralgia for which he was taking large amounts of acetaminophen. Initial clinical examination identified an extensive contiguous skin rash, fever, and hepatosplenomegaly. No peripheral adenopathy was detected. Laboratory data showed the following: white blood cell count, 1.7 × 10^3/mm3; hemoglobin, 12.7 g/dL; platelets, 17 × 10^3/mm3; lactate dehydrogenase, 1349 U/L (reference range, 63–200 U/L); alanine transaminase, 1158 U/L (reference range, 0–30 U/L); as-
partate transaminase, 1270 U/L (reference range, 10–32 U/L); alkaline phosphatase, 262 U/L (reference range, 30–120 U/L); and normal levels of creatinine. Computed tomographic scans showed no lymphadenopathy but confirmed the splenomegaly. Results of viral hepatitis and human immunodeficiency virus screen were negative; skin biopsy was nondiagnostic. A bone marrow aspirate showed a predominant population of in-
termediate to large-sized cells with blastic morphology. The bone marrow biopsy showed infiltration by lymphoid cells located in the sinusoidal and interstitial spaces. Flow cytometry showed the infiltrate was predominately T cells, with virtually all expressing TCR γ-δ and most with loss of CD7. The immunohistochemistry showed the abnormal cells were positive for CD45, CD3, CD8, CD56, and Ki-67 (50%) and negative for CD5, CD20, ALK-1, CD30, and CD15. A diagnosis of hepatosplenic γ-δ T-cell lympho-
ma with blastic morphology was rendered. The confounding factor of toxic hepatitis due to chronic acetaminophen abuse, which could have been responsible for hepatomegaly, might obscure the diagnosis.

**Idiopathic Neutropenia in a Cocaine User: A Case Report and Review of the Literature**

(Poster No. 37)

Tahmeena Ahmed, MD (tahmed@notes.cc.sunysb.edu), Department of Pathology, Stonybrook University Medical Center, Stonybrook, New York.  

Idiopathic neutropenia is a rare benign disorder of granulopoiesis characterized by an unexplained reduction in the absolute neutrophil count below the lower limit of the reference range for a prolonged period. Laboratory testing for anti-neutrophil antibodies is technically challenging and not widely available. Neutropenia associated with levamisole contamination of cocaine is becoming a public health hazard. A young male with a history of cocaine use and neutropenia presented with fever, skin lesions, and lymphadenopathy in 2007. The bone marrow was evaluated and showed arrested granulopoiesis at the myelocyte stage and dysplastic megakaryocytes (Figure 41). Anti-neutrophil antibody testing was positive. The patient has been followed up for 2 years and has demonstrated continued cocaine use. The bone marrow morphology is suggestive of chronic idiopathic neutropenia, but the case illustrates the need for adequate history and communication between pathologist and hematologist. This case presents a diagnostic challenge and emphasizes the need for clinicopathologic correlation.

**Diagnostic Pitfalls of Chronic Myelogenous Leukemia**

(Poster No. 38)

Kun Ru, MD, PhD (kru@wpahs.org); John Pawloski, MD, PhD; Patrick Storto, PhD; Donald Halinka, MBA, BS. Departments of Pathology and Hematology/Oncology, Allegheny General Hospital, Pittsburgh, Pennsylvania; Department of Medical Genetics, The West Pennsylvania Hospital, Pittsburgh.

As a prototype of myeloproliferative neoplasms, chronic myelogenous leukemia (CML) is constantly associated with the BCR-ABL1 translocation, and often presents with typical morphologic findings. We report 2 cases with unusual morphologic features that were not recognized as CML before the cytogenetic results were available. The first case is that of a 64-year-old woman with history of hypertension and hypercholesterolemia. She presented with an increased blast count in her peripheral blood. The bone marrow biopsy demonstrated a hypercellular marrow with increased numbers of myeloblasts (10%–15%), myeloid and erythroid hyperplasia, multilineage dysplasia, and reticulin fibrosis. The presence of blasts was confirmed by flow cytometry and immunohistochemistry. These findings were interpreted as refractory anemia with excess blasts. However, the cytogenetic results revealed the BCR-ABL1 translocation in 95% of cells, in addition to other abnormalities: t(6;18) and trisomy 19. The second case is that of a 52-year-old man presenting with thrombocytopenia (502,000 /μL). He had a history of adenocarcinoma of lung (T2N0M1X) and was treated with surgery and Tarceva 1 year ago. The bone marrow biopsy showed a hypercellular marrow with myeloid hyperplasia and micromegakaryocytes. No obvious eosinophilia or basophilia was noted. This case was described as “reactive changes” before cytogenetic results revealed that the BCR-ABL1 translocation in all cells was the sole abnormality. A diagnosis of CML was finally made in both cases. The patients were treated with Gleevec and were hematologically asymptomatic. Although the definitive diagnosis relies on the cytogenetic or fluorescence in situ hybridization results, CML must be considered in the differential diagnosis when hypercellularity or myeloid hyperplasia is present, even with atypical morphology.

**Sex Cord/Gonadal Stromal Tumor, Incompletely Differentiated, Low Malignant Potential**

(Poster No. 40)

Vighnesh Walavalkar, MD (vwalaval@uci.edu); Fritz Lin, MD; Jane Elaine Tongson-Ignacio, MD. Department of Pathology and Laboratory Medicine, University of California at Irvine, Orange.

Sex cord–stromal tumors of the testis are rare, comprising approximately 5% of all testicular tumors. Based on World Health Organization classification, these are classified into 4 forms: pure, incompletely differentiated, mixed forms, and malignant. The incompletely differentiated sex cord/gonadal stromal tumors are extremely rare neoplasms composed predominantly of undifferentiated spindle cells admixed with foci of abortive tubules arrested in different stages of maturation. A 25-year-old white man presented with a painless, slow-growing mass in his right testicle. Ultrasound showed a hypoechoic, heterogeneous solid mass with internal flow that measured 3.6 × 3.3 × 2.6 cm and was consistent with...
Is Digital Planimetry Preferable to Visual Estimate in Routine Evaluation of Prostate Carcinoma? (Poster No. 41)

Maheshwari Ramineni, MD (mramine1@hfhs.org); Daniel Schultz, MD; Zhaoli Lane, MD. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.

Context: Tumor volume (TV) is an important determinant of clinical outcome after radical prostatectomy. Recently, various studies have discussed the digitized methods for estimating TV. We sought to measure TV by digital planimetry (DP) and compare the values with visual estimate (VE).

Design: TV was determined from whole-mount hematoxylin-eosin slides by using VE as well as DP from 70 consecutive patients with prostate carcinoma, Gleason score 8-10. MacroPATH Imaging System was used for digital planimetry. Additionally, correlation of TV by both methods with various parameters such as Gleason grade, margin positivity, extraprostatic extension, seminal vesicle invasion, and angiolympathic invasion were assessed by Pearson correlation.

Results: TV by DP is statistically significantly correlated to that by VE ($r^2 = 0.64, P < .001$). Mean TV by VE differs significantly between extraprostatic extension negative (16.7) and extraprostatic extension positive (37.3) cases ($P = .02$) and in angiolympathic invasion negative (33.2) versus angiolympathic invasion positive (45) cases ($P = .05$) (Figure 44). Gleason grade, margin positivity, and seminal vesicle invasion does not show statistically significant association with TV by both methods.

Conclusions: Our findings differ from the previous studies in that we found that both methods (digital planimetry and visual estimate) had positive correlation in estimating tumor volume. Visual estimate can serve as a reliable, inexpensive prognostic indicator in predicting extraprostatic extension and angiolympathic invasion. Digital planimetry, which is potentially expensive, time consuming, and labor-intensive, may not yield much additional benefit.
Demonstration of Lower Expression of BRMS1 in Primary Prostatic Adenocarcinoma Than in Normal Prostatic Glandular Tissue
(Poster No. 44)

Erin J. Morris, MD1 (emorris@tuftsmedicalcenter.org); Pushkar A. Phadke, MD, PhD; Harty Ashby-Richardson, DO; Annette Shepard-Barry, HT(ASCP); Stephen F. Naber, MD, PhD; Danny R. Welch, PhD1. Department of Pathology, Tufts Medical Center, Boston, Massachusetts; Department of Pathology, University of Alabama at Birmingham.

Context: Breast cancer metastasis suppressor 1 (BRMS1) has been implicated as an important gene in preventing multiple steps of the metastatic cascade from occurring in various tumor xenograft models, notably in breast, melanoma, and ovarian models. Evaluation of the expression of BRMS1 in prostatic adenocarcinoma has not been performed. Our purpose was to determine expression of BRMS1 in the evolution of prostatic adenocarcinoma from normal gland to metastatic adenocarcinoma.

Design: A tissue microarray (Biomas, Rockville, Maryland) containing formalin-fixed, paraffin-embedded prostatic tissue was stained with a monoclonal antibody (Clone 3a1.21). Fifteen cores of normal prostatic tissue, 5 cores of prostatic adenocarcinoma, and 4 cores of high-grade prostatic intraepithelial neoplasia (PIN) were evaluated for BRMS1 protein expression. Some cores with absent cellularity were excluded from the study. The intensity of nuclear BRMS1 staining was graded on a scale of 0-3.

Results: BRMS1 was strongly expressed in all cases of normal prostate tissue, with an average staining intensity of 2.73±0.1. Staining was diffuse, intense, and nuclear. There was no statistical difference observed between staining intensity of PIN lesions (2.75±0.25) and normal prostatic tissue. The prostatic adenocarcinoma group demonstrated a significant decrease in staining intensity (2.04±0.1) compared to that in normal and PIN lesions (P = .003).

Conclusions: The staining results are consistent with a decrease in expression of BRMS1 in prostatic adenocarcinoma as compared to that in normal prostate tissue and high-grade PIN lesions, which suggests a role for BRMS1 in prostate tumor progression. Further study of the role of BRMS1 in the regulation of tumor progression is necessary.
and polyuria, and cystoscopy demonstrated a bladder mass. Biopsy of the mass revealed sheets of discohesive malignant cells with abundant, eosinophilic cytoplasm and eccentrically placed large nuclei infiltrating the muscularis. Immunohistochemical staining in both cases was positive for AE1/3, Cam5.2, CK7, CD10, CD138, and VS38c and negative for CK20, CD79a, and CD45, confirming the diagnosis of plasmacytoid urothelial carcinoma. Figure 47 shows a hematoxylin-eosin photomicrograph at ×40 magnification (a), as well as immunohistochemical staining for AE1/3 (b), CD138 (c), and VS38c (d).

Renal Oncocytic Neoplasms: Molecular and Immunohistochemical Analysis With an Emphasis on the Birt-Hogg-Dube´ Gene and Mammalian Target of Rapamycin-Related Proteins
(Poster No. 47)

Stephen M. Rohan, MD (rohan@mskcc.org); Maria E. Dudas, MD; Samson W. Fine, MD; Anuradha Gopalan, MD; Victor E. Reuter, MD; Satish K. Tickoo, MD. Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, New York.

Context: Patients with Birt-Hogg-Dube´ (BHD) syndrome develop renal tumors, wherein renal oncocytic neoplasms (RONs) are overrepresented. Alterations of the BHD gene on chromosome 17 (ch17) have been documented in sporadic renal tumors. The protein product of the BHD gene interacts with the mammalian target of rapamycin (mTOR) pathway. We evaluated the mutational status of the BHD gene, ch17 copy number by fluorescence in situ hybridization (FISH), and immunohistochemistry (IHC) expression of mTOR pathway activation markers (p-S6, p-4EBP1) in sporadic RONs.

Design: Fifty-four RONs from oncocytomas (RONs), 26 chromophobe carcinomas (CHRs), and 19 renal cell carcinomas, unclassified, oncocytic type (URCCs) were examined. The unclassified category included oncocytic tumors with features that precluded their inclusion among RO or CHR. IHC for CK7, CD117, TFE3, p-S6, and p-4EBP1 was performed. Staining was graded as absent/weak (0 or 1−), 0%−25% cells positive) or strong (2+ or 3+, 25%−100%) on the BHD gene was sequenced and mutational analysis was performed. FISH was done using a ch17 centromeric probe.

Results:

<table>
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<th>Marker</th>
<th>CHR, No. (%)</th>
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<tr>
<td></td>
<td>(n = 26)</td>
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<td>CD117</td>
<td>22 (85)</td>
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<td>15 (79)</td>
</tr>
<tr>
<td>CK7</td>
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Most tumors expressed CD117. CK7 was expressed in most CHRs, but in none of the ROs or URCCs. No mutations of the BHD gene were detected. Most (15/25, 60%) CHRs showed loss of ch17. Ch17 loss was seen in 1 URCC. No ROs showed ch17 loss. There was no correlation between ch17 copy number and mTOR marker expression.

Conclusions: Our data suggest that URCCs are more closely related to ROs than CHRs. Mutations of the BHD gene and mTOR marker expression appear to be infrequent in sporadic RON.

p63 Is Not Expressed in Most Micropapillary Urothelial Carcinomas
(Poster No. 48)

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Context: Carcinomas with micropapillary features have been described in urinary bladder, ovary, breast, lung, and salivary gland. They are characterized by small papillary clusters of cells located within a lacuna and associated with high pathologic stage with early vascular invasion, metastasis, and high mortality. Micropapillary urothelial carcinoma (MPUC) represents approximately 1% of all bladder urothelial carcinomas. Because of its aggressive behavior, metastasis may be the initial presentation. p63, a member of the p53 family, is expressed in the nucleus of squamous and urothelial cells in their carcinomas. However, loss of expression of p63 occurs in a subset of high-grade urothelial carcinomas. The objective was to identify the expression of p63 immunohistochemistry in MPUC and its potential role in distinguishing MPUC from other carcinomas with micropapillary morphology.

Design: Six cases of MPUC were identified in a period of 10 years (1998–2008). Four cases corresponded to transurethral resection of bladder tumor, 1 case to a radical cystectomy, and 1 case to a nephrectomy/ureterectomy. Immunohistochemical analysis for p63 (1:50; M7247, Dako) was performed in all cases by using the LSAB method.

Results: p63 positivity was defined as strong nuclear staining. All cases but one were negative for p63.

Conclusions: p63 is not expressed in most MPUCs. Lack of expression of p63 in MPUC can be associated with a possible glandular differentiation or to a loss of expression of p63 due to the tumor’s higher grade. p63 immunostain is not useful in differentiating MPUC from other micropapillary carcinomas of nonurothelial origin when metastasis is the initial presentation.

Use of Image Analysis for Interpretation of PIN-4 Immunohistochemical Staining in Prostate Needle Biopsies
(Poster No. 49)

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Context: Immunohistochemistry markers routinely used in the interpretation of prostate biopsies include P504S, p63, and high-molecular-weight cytokeratins. The combination of these in the PIN-4 cocktail can be useful in the distinction between adenocarcinoma, high-grade prostatic intraepithelial neoplasia, and benign glands, particularly in cases with limited tissue. However, interpretation of multiple markers staining different subcellular compartments of different cell types can be challenging. An image analysis algorithm was therefore developed to assist in the interpretation of PIN-4–stained tissue.

Design: Fifty prostate needle biopsy cases, each consisting of corresponding hematoxylin-eosin– and PIN4–stained slides, were selected. Slides were scanned at ×20 magnification on the BioImagene iScan Scanner. Manual interpretation was performed on a computer monitor that permitted the viewing of whole slide images at magnifications from ×1 to ×40. After a 2-week wash-out period, the same cases were reviewed by using image analysis for selected regions of interest in the PIN-4 study. For both manual and automated scoring, cases were categorized as adenocarcinoma or benign (includes PIN).

Results: A high degree of concordance (>95%) was observed between manual and automated interpretation of benign and malignant biopsies. The automated algorithm accurately distinguished benign from malignant glands based on PIN-4 staining in almost all cases. PIN was more frequently diagnosed by image analysis than by manual review.

Conclusions: Image analysis can accurately distinguish between benign and malignant prostate glands in PIN-stained tissue, without assistance from the pathologist. To our knowledge, this is the first example of image analysis of multicolor immunohistochemistry for interpretation of prostate biopsies.
Obstructive Uropathy Secondary to Familial Mediterranean Fever-Related Amyloidosis
(Poster No. 50)

Erin Morris, MD (emorris@tuftsmedicalcenter.org); Pushkar A. Phadke, MD, PhD; Monika E. Pilichowska, MD, PhD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

Familial Mediterranean fever (FMF) is a rare hereditary autosomal disorder characterized by recurrent paroxysmal febrile episodes and serosal inflammation. Secondary amyloidosis, most commonly involving the kidney, is a well-known long-term complication and significant source of morbidity and mortality in FMF. We report a case of a 76-year-old male renal transplant recipient who underwent renal biopsy for increased creatinine 3 years posttransplantation. The biopsy revealed tubular epithelial cell injury suggestive of calcineurin inhibitor toxicity and vascular mural eosinophilic deposits positive for amyloid by Congo red staining and apple green birefringence under polarized light. There was no evidence of cellular or antibody-mediated rejection. Direct immunofluorescence did not reveal light chain restriction. Immunohistochemical studies for AA amyloid revealed deposition in blood vessel walls and interstitium. These findings were diagnostic of renal allograft involvement by AA amyloidosis. Detailed history revealed that the end-stage renal disease was due to obstructive uropathy secondary to prostatic hypertrophy. Retrospective immunohistochemical examination of the prostate resection specimen revealed prominent interstitial deposits of AA amyloid. Additionally, the patient and his brother had suffered from episodes of chronic episodic diarrhea. Based on the history and clinical findings, a diagnosis of FMF was made. The patient’s presentation in this case is unusual because renal failure was caused by obstructive uropathy secondary to amyloid-related prostatic hypertrophy, as opposed to primary renal involvement, which is the usual case in FMF. Furthermore, this case highlights that AA amyloidosis can recur in a kidney allograft, thereby complicating the clinical course.

Adult Testicular Granulosa Cell Tumor:
A Case Report and Review of the Literature
(Poster No. 51)

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Adult testicular granulosa cell tumors are rare sex cord–stromal tumors of which only 28 have been reported. As compared to their ovarian counterparts, these tumors follow a more aggressive course and the proportion of malignant cases is higher. To date, there are no features that definitively predict malignancy. We present the 29th case of an adult testicular granulosa cell tumor and review the literature in an attempt to identify features that may predict its malignant potential. Our patient is a 21-year-old man who was referred to his urologist for a painless left testicular mass. Orchiectomy revealed a 1.0-cm, well-circumscribed mass abutting the tunica albuginea. Histologic sections showed a solid to focally trabecular pattern of medium-sized cells with grooved ovoid nuclei and scant cytoplasm. The cells displayed mild pleomorphism and showed distinct nuclear molding. The mitotic count was 15/10 high-power fields. There was no hemorrhage, necrosis, or lymphovascular invasion. Immunohistochemistry was strongly positive for inhibin, and focally positive for calretinin. At 16 months follow-up, the patient was free of disease.

Abstracts

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Abbreviation: NS, not significant.

Bladder Urothelial Carcinoma Metastatic to the Testicle
(Poster No. 52)

Matthew D. Geller, DO (mgeller327@yahoo.com); Nicole M. Durie, MD; Robert D’Esposito, MD; Andrea Fleder, MD. Departments of Pathology and Urology, Winthrop University Hospital, Mineola, New York.

Most testicular neoplasms are primary in nature; however, an estimated 3.6% are metastatic from distant sites. Numerous cases of neoplasms metastatic to the testicles have been reported. Of these, the most common organs of origin are prostate, lung, kidney, stomach, skin (melanoma), and colon. There have been few reports of bladder urothelial carcinoma metastasizing to the testis. We add to the small repertoire of published reports of this rare occurrence. Our patient is an 87-year-old man with a history of infiltrating, poorly differentiated bladder urothelial carcinoma who presented with a hard right testicle. His testicular tumor was found to be histomorphologically identical to his prior bladder tumor. In addition, his primary and metastatic tumors both showed squamous differentiation, a finding that, to our knowledge, has not been reported.

Collision Angiomyolipoma and Renal Cell Carcinoma in an Elderly Woman:
A Case Report and Review of the Literature
(Poster No. 53)

Anna T. Vischio, MD, MPH (annavischio@gmail.com); Jeet Sandhu, MD; Hani El-Fanek, MD. Departments of Pathology and Laboratory Medicine and Radiology, Danbury Hospital, Danbury, Connecticut.

The coexistence of a renal cell carcinoma and an angiomyolipoma is quite rare, with only 31 cases cited in the literature. Renal angiomyolipoma is a relatively benign retroperitoneal tumor. Histologically, it is a choriostoma composed of an intimate admixture of fat, smooth muscle, and vessels. Despite the lack of cellular anaplasia, angiomyolipomas represent a significant aberration in normal development that cause hematuria, flank pain, renal failure, or even spontaneous hemorrhage and shock, if symptomatic. Angiomyolipomas are highly associated with the hereditary disease tuberous sclerosis; therefore, all patients with renal angiomyolipomas should be evaluated. We present the case of an 80-year-old woman who initially presented with painless hematuria in 2005. An abdominal computed tomography (CT) showed a 2.8-cm left renal mass containing fatty elements and soft tissue suggestive of an angiomyolipoma. In 2008 the patient re-presented with recurrent painless hematuria. A heterogeneously enhancing 4.4 × 4.4 × 3.6-cm mass in the upper pole of the left kidney was seen on CT. An ultrasound-guided core needle biopsy was performed. Histologic examination of the core needle biopsy of the renal mass demonstrated a collision tumor of a well-differentiated renal cell carcinoma, clear cell type, and an associated angiomyolipoma (Figure 48). The angiomyolipoma was composed mainly of smooth muscle fibers without the adipose tissue component. Immunoperoxidase stains demonstrated strong positivity for desmin, actin, and melan-A, and weak positivity for HMB-45. The patient is scheduled for a radical nephrectomy. These tumors are rare and usually have a good prognosis if detected and excised early.
Context: Deficiency of copper is unusual, but occasionally occurs in infants or adults fed a copper deficient enteral formula. In these subjects, the blood displays leukopenia with myelodysplastic changes. Recently, there have been reports of sporadic copper deficiency manifested by neuropsychologic symptoms. Clinical laboratories serving hemodialysis patients receive occasional specimens showing leukopenia resembling that described in copper deficiency. We thought it possible that copper might be lost in the hemodialysis process and tested these specimens for copper deficiency. Previous studies had shown that peritoneal dialysis does not remove copper from the blood. There are no hemodialysis studies.

Design: Plasma copper was measured by inductively coupled plasma emission spectroscopy. Three studies were done. Copper was measured from 27 volunteers, from 29 dialysis patients with normal white blood cell counts, and from 39 dialysis patients who had white blood cell counts of 2000/μL or lower.

Results: Copper levels in normal subjects ranged from 67–247 μg/dL, with a mean of 105 μg/dL and a standard deviation of 38 μg/dL. Copper levels in dialysis patients with normal white counts ranged from 67–152 μg/dL with standard deviation of 23 μg/dL. Copper levels in leukopenic dialysis patients ranged from 44–139 μg/dL, with a mean of 86 μg/dL and standard deviation of 23 μg/dL.

Conclusions: Patients described in the literature with a dysplastic leukopenia due to hypocupremia have copper values in the range of 0–9 μg/dL. No leukopenic patient approached these levels, so that hypocupremia is not an explanation for their dysplastic leukopenia. Hemodialysis does not remove copper from blood.

Primary Renal Carcinoid: A Case Report and Review of the Literature
(Poster No. 56)

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Primary renal carcinoid is a rare tumor, mostly reported as isolated cases in the literature. We report the case of a 52-year-old man who presented with abdominal pain and an abdominal mass at clinical examination. At computed tomography, a solid enhancing mass was seen in the right renal pelvis, which prompted right nephrectomy. At gross pathologic examination, the renal hilum contained a well-circumscribed, 5.0 × 3.5 × 3.0-cm, yellow-tan tumor that compressed the neighboring renal parenchyma into a pseudocapsule. At microscopy (Figure 50), the tumor contained monotonous small cells with “salt-and-pepper” chromatin, arranged in anastomosing trabecular cords, and some solid sheets. Extensive lymphovascular involvement was present. The working differential diagnoses included carcinoid tumor, small cell neuroendocrine carcinoma, primitive neuroectodermal tumor, paraganglioma, Wilms tumor, and neuroblastoma. Cellular monomorphism with typical architectural arrangements, immunoreactivity with neuron-specific enolase, chromogranin, synaptophysin, and CD56, as well as no other site evidence for carcinoid tumor, clinched the diagnosis of primary renal carcinoid in this case. Tumor cells also did not immunoreact with EMA, TTF-1, WT-1, CD99 and PS045. Carcinoid tumors are distinct entities within the 2004 World Health Organization classification scheme of renal tumors, with similar features to carcinoid tumors found elsewhere. Awareness for primary renal carcinoid is likely to lead to an accurate diagnosis.
Combined Neoplasm of the Urinary Bladder: Case Report With Review of Literature (Poster No. 57)

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Small cell carcinoma of the urinary bladder is a rare tumor known to have a dismal prognosis. This neoplasm often coexists with high-grade invasive transitional cell carcinoma and, in up to 40% of cases, with transitional cell carcinoma in situ. Currently, only a few cases of large cell neuroendocrine tumor of the urinary bladder have been reported in the literature. In our case report, we describe the coexistence of small cell carcinoma of the urinary bladder with large cell neuroendocrine tumor, as well as an invasive transitional cell carcinoma with an in situ component in a 79-year-old male patient. We also show the tumor's immunohistochemical profile. Simultaneous presence of the multiple lines of differentiation in 1 neoplasm raises significant questions about the molecular events of this neoplastic process.

Pathologic Correlation of Radiologically Detected Prostate Cancer Lesions by a Novel Technique (Poster No. 58)

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Context: Whole mount sections of prostates allow pathologic-radiologic correlations and tumor volume determination, factors that are important in patient management. However, whole mount sectioning often results in gland distortion and an inability to achieve these aims.

Design: To alleviate the problems of specimen distortion and for precise sectioning of prostatectomy specimens, we used a novel technique. Eight consecutive patients with biopsy-proven prostate cancer were accrued. Based on preoperative magnetic resonance imaging (MRI), a 3-D prostate model was generated to create a customized mold for each patient. Prostatectomy specimens were demasked and sectioned in their respective molds at 6 mm intervals (to facilitate comparison with the 3-mm-interval MRIs). Tumor foci were mapped on whole mount hematoxylin-eosin–stained sections and correlated with MRI findings.

Results: Sectioning in the mold yielded uniform slices, without distortion, and excellent quality histologic results. There were 2 to 5 (mean 2.8) foci of tumor per specimen with tumor volumes up to 11.9 cc. One case showed focal extraprostatic extension. Preoperative imaging had overall detection sensitivity of 69% and specificity of 61%; the sensitivity improved to 90% when central gland tumors and tumors less than 0.125 cc were excluded from analysis. Imaging detected both gland-rich and infiltrating foci of tumors but overestimated extraprostatic extension.

Conclusions: This novel technique of sectioning prevents specimen distortion and allows precise measurement and mapping of prostate cancer. The high correlation of preoperative imaging with histopathology suggests that this technique will aid in directed tissue procurement for research to better understand pathology of prostate cancer.

Lymphovascular Invasion in Micropapillary Urothelial Carcinoma (Poster No. 59)

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Context: Micropapillary urothelial carcinoma (MPCU) is characterized by clusters of tumor cells floating in lacunar spaces that are conventionally understood to represent retraction artifact. This morphology is associated with high frequency of lymph node metastasis and low survival; reasons for this aggressiveness remain unclear. We hypothesize that some lacunae are lymphovascular channels and that invasion of lymphovascular channels may explain MPCU’s aggressive behavior.

Design: Twenty-five cases of MPCU were studied retrospectively. Clinical information was gathered by chart review. Consecutive tissue sections were immunostained with D2-40 and CD34 for comparison with routine hematoxylin-eosin–stained sections.

Results: Of 25 patients, 22 were men with a median age of 70 (range, 56–85 years). All cases were associated with high-grade urothelial carcinoma (transitional cell carcinoma grade 3/3). Stage grouping was available in 9 cases; 7 of these (78%) presented with stage III disease and greater. Tissue was available for immunostaining in 22 cases. Lacunar spaces were almost uniformly negative for D2-40 and CD34. However, lymphovascular invasion was present in 21/22 cases (95%), a rate significantly higher than for conventional urothelial carcinoma (28% in previous work at our institution).

Conclusions: Our results confirm that most lacunar spaces are not lymphovascular channels. However, nearly all MPCU tumors (95% in this series) show evidence of lymphovascular invasion. The high incidence of lymphovascular channels in MPCU tumors partially explains MPCU’s tendency to present with higher rates of lymph node metastasis than conventional urothelial carcinoma. Our data support the use of MPCU as a morphologic marker for aggressive disease.

Epithelioid Angiomyolipoma of the Kidney With a Unique t(6;11)(q13;p15) Chromosome Translocation (Poster No. 60)

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Epithelioid angiomyolipoma is a potentially malignant, rare variant of renal angiomyolipoma, characterized by proliferation of predominantly or exclusively of epithelioid cells. It often presents as a part of a tuberous sclerosis complex. Peculiar pattern of immunoreactivity includes expression of melanocytic differentiation markers such as human melanoma black–45, Mart1/Melanin-A, and microphthalmia transcription factor and variable expression of smooth muscle markers. Expression of epithelial markers is always negative. Histologic characteristic of epithelioid angiomyolipoma with cells having enlarged nuclei and prominent nucleoli may lead to misdiagnosis of high-grade carcinoma especially renal cell carcinoma. Perivascular cellular arrangement, focal features of otherwise classic angiomyolipoma, and characteristic immunoprofile are clues to the correct diagnosis. Cytogenetic abnormalities include allelic loss of chromosomal arm 16p in classic, epithelioid, and sarcomatoid areas and TP53 mutation mostly detected in epithelioid areas. We report the case of a 76-year-old man with history of left renal mass who subsequently developed local recurrence and distant metastasis to the liver. Histologically, all of the lesions appeared similar and characterized by proliferation of large, bizarre, epithelioid cells with abundant clear to deep eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli. Multinucleated giant cells, coagulative tumor necrosis, mitosis, and atypical mitotic figures are easily discernable. Immunohistochemical staining revealed positivity of neoplastic cells for human melanoma black–45 and melan A and negative staining for S100, pancytokeratin, vimentin, and CD10. Genotypic analysis, with standard G TG2 banding technique, revealed a unique, previously unreported t(6;11)(q13;p15) chromosome translocation. In conclusion, we present this case because of its rarity and detection of a new, unique chromosome translocation.

Interobserver Agreement for Extracapsular Extension of Prostatic Adenocarcinoma (Poster No. 61)

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Context: Extracapsular extension (EPE) of adenocarcinoma beyond the prostatic capsule is a common occurrence and an important factor determining tumor stage but may be difficult to interpret even by experienced urologic pathologists. We measured expert interobserver agreement (multirater κ) from responses to 6 questions that pathologists face when evaluating EPE.

Design: Routinely processed, hematoxylin-eosin–stained slides (n = 46) of prostatectomy were reviewed by 9 pathologists. EPE was defined as separate viable tumor located outside of the prostatic capsule and was present if it (1) was present in the prostatectomy specimen, (2) was present with EPE present; (3) is the tumor stage pT3; (4) is the capsule identified; (5) is extraprostatic fat present; and (6) are deeper levels necessary.
Results: See Table.

Conclusions: Our results demonstrate moderate agreement between expert urologic pathologists on the presence of prostatic adenocarcinoma with EPE and the assignment of tumor stage pT3. As expected, there was only slight agreement when characterizing the capsule and periprostatic soft tissue, with diversity between pathologists regarding the necessity of deeper levels to complete the diagnostic workup. These findings reflect the subjectivity inherent in evaluating adenocarcinoma with EPE and suggesting a need for consensus definitions and guidelines to improve agreement, the clinical significance of which has yet to be prospectively determined.

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Morphometric and Ultrastructure Study of Peritubular Capillaries in Renal Biopsies of Childhood Idiopathic Nephrotic Syndrome

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Context: Peritubular capillary (PTC) loss is present in tubulointerstitial damage in adult glomerulonephritis. PTC rarefaction correlates with decreased renal function in kidney transplants. PTC status is not known in childhood idiopathic nephrotic syndrome (CINS).

Design: We performed (1) quantification of PTCs in kidney biopsies of CINS; (2) correlation of PTC number with tubular atrophy, interstitial fibrosis, and renal function; and (3) transmission electron microscopic study of PTCs. Kidney needle biopsies of 30 cases and 7 controls (autopsy) were studied with immunohistochemistry for CD34 (IgG1, mouse monoclonal, Dako), Masson trichrome, and transmission electron microscopy. PTC number and interstitial fibrosis were calculated by Image-Pro Plus (Media Cybernetics, USA) image analysis software. Glomerular filtration rate was calculated by Schwartz formula.

Results: Mean PTC number/mm² was as follows: control (n = 7), 604 ± 16 (Figure 51); minimal change disease (n = 13), 540 ± 55 (P = .02); focal segmental glomerulosclerosis (n = 10), 461 ± 54 (P = .001); and mesangiotioproliferative glomerulonephritis (n = 7), 564 ± 55 (P = .06). For interstitial fibrosis, the results were as follows: control, 5.24 ± 0.93; minimal change disease, 7.25 ± 2.3 (P = .04); focal segmental glomerulosclerosis, 16.63 ± 6.0 (P = .005); mesangiotioproliferative glomerulonephritis, 7.73 ± 3.7, (P = .08). There was a significant positive correlation between PTC number and glomerular filtration rate (P = .04, r² = 0.15). Transmission electron microscopy showed widening, splitting, and multilayering of endothelial basal lamina in 3/10 cases of focal segmental glomerulosclerosis.

Conclusions: PTC loss is present in CINS. PTC loss is significant in minimal change disease and focal segmental glomerulosclerosis. PTC loss correlates positively with interstitial fibrosis and negatively with renal function. Basal lamina splitting and multilayering consistent with PTC damage was present in focal segmental glomerulosclerosis.

Seminoma With Rete Testis Hyperplasia Mimicking Mixed Germ Cell Tumor: An Entity Every Pathologist Should Be Aware of

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Lesions of the intratesticular excretory ducts are rare and include adenocarcinoma, adenoma, adenofibroma, cystic dysplasia, and nodular proliferation of connective tissue involving the rete testis. A more frequently encountered scenario is that of infiltration of the rete testis by adjacent infiltrating testicular tumors, particularly seminoma. We present a case of seminoma with extension into the rete testis in which secondary hyperplasia and secretory change of the rete testis were identified. Microscopic examination revealed a proliferation of arborizing glandular structures with bland nuclear features infiltrating between the seminomatous lesion. The glandular structures were filled with eosinophilic colloidlike material, simulating a yolk sac tumor. We performed tests with a panel of immunohistochemical stains to help differentiate rete testis hyperplasia from yolk sac tumor and from stroma ovarii. Immunohistochemical results revealed vimentin and cytokeratin positivity with lack of staining for alpha fetoprotein, TTF-1, and thyroglobulin, supporting the diagnosis of rete testis hyperplasia. Rete testis hyperplasia is a rarely seen lesion and is usually detected as an incidental microscopic finding. It is hypothesized to be a pseudoneoplastic reaction to secondary invasion of the rete testis by tumor. The histologic features of this lesion mimic the well-recognized features of yolk sac tumors. Because of the difference in treatment protocols between seminomatous and nonseminomatous germ cell tumors, it is important to avoid misdiagnosis of this lesion as a mixed germ cell tumor with seminomatous and yolk sac components from a pure seminoma.

Utility of Immunohistochemical Markers to Confirm the Presence of Vas Deferens in Vasectomy Specimens

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Context: Vasectomy-related cases are one of the most frequent types of malpractice claims filed against urologists. As such, many urologists routinely send vas deferens (VD) for histologic confirmation. However, in certain cases histology is indeterminate for the presence of VD because of innate properties of the specimen or processing errors. CD10 has recently been described as a marker that can distinguish wolffian duct derivatives from Mullerian remnants but has yet to be tested in vasectomy specimens.

Design: We determined whether CD10, as well as nonspecific epithelial marker pankeratin (PK), could corroborate the presence of VD. One hundred three consecutive vasectomy specimens were subjected to immunohistochemical analysis for CD10, PK, and CD31. Luminal and basal layer cells were semiquantitatively analyzed.

Results: In all cases with optimal epithelial histology (92/103), CD10 demonstrated intense apical membranous expression in all VD and weak basal cytoplasmic staining in 98% of cases. PK demonstrated cytoplasmatic and membranous expression in both apical and basal layers in 99% of VD. CD31 did not show apical or basal reactivity in any VD. In cases with suboptimal epithelial histology (11/103), the detection of epithelia was 100% for CD10 and PK. Similar CD10 and PK expression was seen in the glandular epithelium of prostate, vas deferens, seminal vesicle, and ejaculatory ducts of radical prostatectomy samples.

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Conclusions: CD10 and CD31 are useful markers to highlight the epithelium of VD and these markers can be used to confirm the presence of VD in vasectomy specimens in which the epithelial histology is suboptimal.

Bilateral Synchronous Testicular Tumors in a 31-Year-Old Man
(Poster No. 65)

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Simultaneous bilateral germ cell tumors of the testis are a relatively rare finding, having an incidence of approximately 1%–2%. In most cases the histology is classic seminoma. Seminomas are largely found in an older group of men (mean, 40 years), whereas nonseminomatous germ cell tumors are found in a younger group (mean, 25 years). We present a case of seminoma and embryonal carcinoma occurring simultaneously in the bilateral testes of a 31-year-old man. The patient complained of right testicular enlargement and left testicular pain. The serum a-fetoprotein level was 34.3 ng/mL (reference range, 0–8 ng/mL), serum b-human chorionic gonadotropin level was 2780 mIU/mL (reference range, 0–6 mIU/mL), and serum lactate dehydrogenase level was 512 IU/L (reference range, 98–192 IU/L). Ultrasoundography showed echogenic masses in both testes. The patient had bilateral congenital undescended testes, of which one later descended and the other was surgically corrected. The patient subsequently underwent bilateral orchidectomy. Gross examination of the right testis revealed a 3.5 × 2.5 × 2.4-cm, poorly demarcated yellow mass with areas of hemorrhage and necrosis on cut surface. Microscopic and immunohistochemical staining pattern was consistent with embryonal carcinoma (Figure 52, left). The left testis revealed a 1.5 × 1.0 × 1.0-cm, well-demarcated white mass with a 0.5 × 0.5 × 0.5-cm cystic area on cut surface. The microscopic and immunohistochemical staining pattern was consistent with classical seminoma (Figure, right). Our case represents the third reported in the English literature of bilateral synchronous testicular tumors of seminoma and embryonal carcinoma histology.

Isolated Testicular Relapse of Acute Myeloid Leukemia 7 Years After Initial Diagnosis
(Poster No. 66)

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Isolated testicular relapse in acute myeloid leukemia (AML) is a rare event in children. We report a case of an 18-year-old man who had an isolated testicular relapse 86 months after the initial diagnosis and 81 months after finishing chemotherapy. He was originally diagnosed with AML with minimal differentiation at age 11. He was treated with cytarabine-based chemotherapy and did well until age 18 when he presented with a left testicular mass. He had no other signs or symptoms and the results of his hematologic workup were unremarkable. An inguinal or- thochorion was performed and he was diagnosed with a myeloid sarcoma. There was no evidence of bone marrow involvement by morphology, immunohistochemistry, flow cytometry, or cytogenetics. The cerebrospinal fluid and a positron emission tomography–computed tomography scan were also negative for disease. The original AML and the myeloid sarcoma were immunophenotypically (CD34+, CD117+, CD33+, myeloperoxidase negative, terminal deoxynucleotidyl transferase negative) and cyogenetically (trisomy 8) identical except for loss of CD15 expression in the myeloid sarcoma. To our knowledge, this is the longest reported inter- terval between remission and an isolated testicular relapse in AML. This case also demonstrates the use of immunophenotyping and cytogenetic studies to differentiate AML relapse from a secondary AML or a de novo myeloid sarcoma.

The Nonneoplastic Kidney in Tumor Resections: Tumor-Related Alterations and Their Clinical Significances
(Poster No. 67)

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Context: The nonneoplastic changes of kidney are often not reported in tumor nephrectomies. There are 2 published studies on nonneoplastic changes in nephrectomies that focused on glomerular and arterial lesions. Significant diabetic glomerulopathy and arterial sclerosis were common and predicted renal failure. This study investigated peritumoral alterations and their clinical significances in nephrectomies for renal cell carcinoma (RCC).

Design: Nephrectomy specimens from 75 patients with RCC, 60 cases of clear cell RCC, and 15 cases of papillary RCC were reviewed. Tumor-related alterations in the peritumoral cortex were identified and correlated with clinical information.

Results: Sixty-nine of 75 tumors formed a 0.5–5.5-mm pseudocapsule. Six papillary RCCs lacked a pseudocapsule. Within the pseudocapsule were atrophic tubules, sclerotic glomeruli, and compressed arteries with marked fibrointimal thickening. These changes appeared unrelated to tumor size or stage and occurred in clear cell and papillary RCC. The pseudocapsule was inflamed and associated with lymphangiogenesis in a pri- or study. In 14/22 cases with follow-up, the creatinine level was elevated (mean, 0.34). Two cases showed postnephrectomy creatinine level >3 mg/dL. The change in creatinine level after nephrectomy did not correlate with peritumoral changes of the kidney.

Conclusions: Tumor-related alterations in renal cell carcinoma include a peritumoral pseudocapsule representing nephron atrophy and fibrosis, likely a consequence of tubular and vascular obstruction. Peritumoral inflammation is invariably present and associated with lymphangiogenesis. These tumor-related alterations did not correlate with size or staging of the tumor and do not predict deterioration of renal function after nephrectomy.

Atypical Glomus Tumor of Uncertain Malignant Potential in the Urinary Bladder: Case Report and Literature Review
(Poster No. 68)

Lindsay L. Waters, MD1 (llwaters@tmhs.org); Qihui “Jim” Zhai, MD2; Scott Buie, MD; John A. Pumphrey, MD; Sang Wu, MD. 1Department of Pathology, The Methodist Hospital, Houston, Texas; 2Department of Pathology, ProPath Associates, Dallas, Texas; 3Department of Urology, Associates of Urology, Fort Worth, Texas.

We present a case of atypical glomus tumor of uncertain malignant potential arising in the urinary bladder of an 84-year-old woman with recurrent low-grade noninvasive papillary urothelial carcinoma of the bladder, which was previously resected in June 2006. Glomus tumors are mesenchymal neoplasms characterized by small size, benign nature, and location often in the dermis or subcutis of extremities. Histologic features include uniformly round cells with pale eosinophilic cytoplasm and cen- tral round to oval nuclei. Immunostaining demonstrates muscle-specific actin and desmin positivity and usually CD34 negativity. Specifically, atypical glomus tumors of uncertain malignant potential are defined by lack of criteria for malignant glomus tumor and the following: high mitotic count (>5/50 HPF) and superficial location or large size only or deep location only. Microscopically, this case has an abnormal proliferation of ovoid cells in the lamina propria, uniform ovoid nuclei with indistinct eosinophilic cytoplasm, sheet-like growth pattern with a prominent capillary network, mild nuclear atypia, and high mitotic rate (2/HFF). This case showed smooth muscle actin and smooth muscle myosin positivity and CD34 negativity. A PubMed search revealed 1 reported case of a malignant glomus tumor and no cases of atypical glomus tumors in the urinary bladder. A recent follow-up, 6 months after the initial diagnosis, did not show recurrences of this lesion. This unique case of atypical glomus tumor of uncertain malignant potential represents a challenging, rare neoplasm occurring in an unusual location. Distinction of this entity from the adjacent noninvasive papillary urothelial carcinoma is important.
A Case of a Collision of Renal Cell Carcinoma and Transitional Cell Carcinoma (Poster No. 69)

Monica I. Ruiz, MD (miruzi@bcm.edu); Linh M. Dang, MD; Chris J. Finch, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Renal cell carcinoma accounts for up to 90%-95% of all neoplasms of the kidney, while transitional cell carcinoma is the most common tumor of the renal pelvis, accounting for more than 90% of renal pelvis tumors. A collision of renal cell carcinoma and transitional cell carcinoma is very rare. There are only 26 cases reported in the English literature. We report an unusual case of a collision of transitional cell carcinoma and renal cell carcinoma in the kidney. The patient was a 57-year-old woman who initially presented with flank pain. Upon imaging studies, a left upper pole renal mass and a left necrotic hilar mass with a staghorn calculus was found. Subsequently, the patient underwent a total left nephrectomy and splenectomy. Grossly, the mass in the upper pole of the kidney was golden-yellow with areas of hemorrhage. The upper pole mass and the hilar mass appeared to merge together into a single tumor measuring 8 cm in greatest dimension. Microscopically, the upper pole mass showed a high-grade unclassified renal cell carcinoma and the adjacent pelvic mass showed a grade 2 papillary transitional cell carcinoma. Cases of renal cell carcinoma and transitional cell carcinoma found in the same kidney are extremely rare. This case illustrates the importance of a thorough gross examination and careful study of surgical specimens to ensure the correct diagnoses and treatment of combined renal malignancies.

The Unproportional Number of Reports on Coexisting Adenocarcinoma and Carcinoid Tumor in the Urinary Bladder (Poster No. 70)

Jiong Zhang, MD, PhD (pathdoc.zhang@gmail.com); Vivekanand Datla, MD, PhD. Department of Pathology, The University of Tennessee Health Science Center at Memphis.

We encountered a rare case of 2 neoplastic processes coexisting in the urinary bladder. These neoplastic processes consist of adenocarcinoma and carcinoid tumors. The mucinous adenocarcinoma is positive for cytokeratin-20 and carcinoembryonic antigen and negative for cytokeratin-7, neuron-specific enolase, prostate-specific antigen, synaptophysin, CDX-2, and chromogranin A. The carcinoid lesion is positive for cytokeratin-7, carciinoembryonic antigen, neuron-specific enolase, synaptophysin, and chromogranin and negative for cytokeratin-20, prostate-specific antigen, and CDX-2. This is the fifth reported case of carcinoid tumors coexisting with another carcinoma in the urinary bladder. Among urinary bladder carcinomas, urothelial carcinomas are more than 10 times more frequent than adenocarcinoma. Therefore, we would normally expect that if another malignancy co-occurs with carcinoid tumor in the urinary bladder, it would most often be urothelial carcinoma by chance alone. Interestingly, only 1 of 15 of these reported mixed tumor cases involved urothelial carcinoma. Four of them involved adenocarcinomas, as in our case. This prompts us to suspect that the co-occurrence of these 2 different tumors in the bladder may have 1 underlying pathogenesis pathway, such as a novel tumor syndrome.

Mucinous Cystadenocarcinoma of the Testis (Poster No. 71)

Alina C. Iuga, MD (aiuga@chpnet.org); Jason Mull, MD; William Miller, MD. Department of Pathology, St.Luke's Roosevelt Hospital Center, New York, New York.

Ovarian-type surface epithelial carcinomas of the testis are a rare primary testicular malignancy, and most of the previously reported cases are of the serous variety. We present a case of unilateral invasive intratesticular cystadenocarcinoma with mucinous differentiation. Extensive literature review revealed only 3 similar reported cases. The patient is a 71-year-old man with a history of melanoma who presented with a left testicular hydrocele secondary to a mass. Imaging studies and colonoscopy revealed no other suspicious lesion. Gross examination of the orchietomy specimen revealed a 3.5-cm, white, soft, glistening, well-delineated mass with a 0.1-cm yellow undulating border, completely replacing the testicular parenchyma. Microscopically, the mass was a well-differentiated cystic neoplasm with elongated fine pseudopapillary structures lined by columnar epithelium with alternating goblet and ciliated cells. Mitotic activity was rare. Foci of neoplastic epithelial lining overlying fibrous stroma in the testicular mediastium were identified as a possible in situ component. The tumor invaded into but not through the fibrous capsule. The cyst wall showed extensive inflammatory and xanthogranulomatous reaction, dystrophic calcification, and thrombus formation. No involvement of the tunica albuginea, rete, or appendages was noted. The patient underwent a total left nephrectomy and splenectomy. Subsequently, the patient underwent a total left nephrectomy and splenectomy. Grossly, the mass in the upper pole of the kidney was golden-yellow with areas of hemorrhage. The upper pole mass and the hilar mass appeared to merge together into a single tumor measuring 8 cm in greatest dimension. Microscopically, the upper pole mass showed a high-grade unclassified renal cell carcinoma and the adjacent pelvic mass showed a grade 2 papillary transitional cell carcinoma. Cases of renal cell carcinoma and transitional cell carcinoma found in the same kidney are extremely rare. This case illustrates the importance of a thorough gross examination and careful study of surgical specimens to ensure the correct diagnoses and treatment of combined renal malignancies.

Discrepancy in Cancer Localization Between Prostate Biopsy and Radical Prostatectomy Specimens in Patients With Unilateral Positive Biopsy Cores: Implications for Focal Ablative Therapy (Poster No. 72)

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Context: Ablative treatment has gained acceptance as treatment strategy for patients with prostate cancer (PCA) who are not candidates for prostatectomy (RP). The success of unilateral ablative strategy depends on the reliable prediction of unilateral PCA by biopsy.

Design: A total of 1326 men had PCA on 12-needle biopsy (12Bx). In 435 (32.8%), PCA was detected only in 1 side. RP was available for 183 patients. All specimens were reviewed by a pathologist who mapped the tumor outline, determined the number of PCA, their volume (TV), zone of origin, Gleason score (GS), and stage.

Results: Mean age, preoperative prostate-specific antigen (PSA) level, and prostate weight were 59 years, 6.1 ng/mL, and 53 g, respectively. In 50 men, 12Bx findings correlated with RP findings (unilateral PCA). In the remaining 133 patients (72.7%), 1–5 PCA foci/RP were detected in the contralateral side. In 110/133 patients, 173 significant PCAs (>5 mm² and GS ≥ 6) were missed. The contralateral PCAs were GS6 (72%), GS7 (26%), and GS7 with pattern 5 (2%); their TV ranged from 6 to 274 mm². Stage was T3 (n = 3), T2+ (n = 2), and T2 (n = 161). PCA location was distributed as follows: apex (14.4%), mid (46.2%), base (4%), apical-mid (26%), apical-base (5.2%), and mid-base (4%). Thirty percent of PCAs involved transitional/anterior and 70% involved peripheral zone.

Conclusions: Most men with unilateral positive biopsy have pathologically proven bilateral PCA and focal treatment is unlikely to be curative. Additional biopsies of the mid/apical-mid prostate could be suggested before considering focal ablative therapy.
highlights the importance of being aware of this emerging entity as a potential cause of respiratory distress.

A Fatal Case of Diffuse Pulmonary Lymphangiomatosis in a Postpartum Patient (Poster No. 2)

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Diffuse pulmonary lymphangiomatosis is a rare, debilitating disease that is characterized by abnormal lymphatic vessel proliferation and most often presents in the first 2 decades of life. We present an autopsy case of a 32-year-old woman who was incidentally diagnosed with lymphangiomatosis after a motor vehicle accident 4 years before autopsy. On initial diagnosis, the disease involved the right upper lung lobe, mediastinum, and pleural surfaces with retractional bilateral chyloous effusions. Subsequent treatments included lung wedge resection, pleurocentesis, bilateral pleurectomies, and pleurodesis. Her baseline symptoms included cough and decreased exercise tolerance. Three weeks before her demise, she gave birth to a 29-week-old male newborn delivered by cesarean delivery secondary to exacerbation of maternal disease symptoms, including chylothoraces, respiratory compromise, and failure to thrive. After delivery, she developed respiratory failure and a persistent pericardial effusion requiring intubation and pericardial sac drainage. She died soon after. At autopsy, the right lung had a 10-cm infiltrative proliferation of lymphatic vessels that extended onto the visceral pleura and adjacent mediastinal soft tissue. The left lung had a similar 13-cm lesion. Histologic findings demonstrated ectatic lymphatic spaces (CD34-positive), capillary vessels that extended onto the visceral pleura and adjacent mediastinal fibrous tissue. The lack of HMB-45 staining distinguished the lesion from lymphangioleiomyomatosis, a rare entity more commonly associated with women of reproductive age. This is an unusual initial presentation of diffuse pulmonary lymphangiomatosis that was fatal 4 years after diagnosis because of disease progression and increased respiratory complications related to pregnancy.

A Case of Idiopathic Sclerosing Polyserositis With Multiorgan Failure (Poster No. 3)

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Sclerosing encapsulating peritonitis, also known as “abdominal cooon,” is a rare entity. We describe a case of generalized idiopathic sclerosing polyserositis affecting not only peritoneum but also pericardium and pleura. Besides anecdotal reports of prolonged β-blocker therapy–associated idiopathic sclerosing polyserositis, we did not find any cases in the literature. A 66-year-old man was followed up for 9 years for presumptive alcohol-induced liver cirrhosis with low serum albumin, recurrent ascites, pleural effusions requiring paracentesis and thoracentesis. He received transjugular intrahepatic portosystemic shunt procedure for increasing ascites. Past serologic workup was negative for autoimmune diseases and infections hepatitis. The patient was scheduled for liver transplantation. He presented with unstable condition, lethargy, confusion, drowsiness, and orthopnea and was transferred to intensive care unit where he died after complicated course. Autopsy showed that all organs of the abdominal and thoracic cavity were encased in a thick, hyalinized fibrous tissue. Histologic findings revealed bland paucicellular subserosal fibrocollagenous tissue with focal chronic inflammation (Figure 53). Liver showed chronic passive congestion without evidence of cirrhosis. A stable radiologic abnormality in the upper lobe of left lung was a 0.8-cm, well-differentiated pulmonary adenocarcinoma with no evidence of metastases. Massive upper gastrointestinal bleeding was the terminal event. Cases of sclerosing encapsulating peritonitis have either silent clinical course or acute presentation with intestinal obstruction. In our case, the process was insidious, restrictive-causing multiorgan failure due to the constrictive effect of fibrosis. We term this case idiopathic sclerosing polyserositis in view of the above findings and absence of recognized clinical causes of sclerosing encapsulating peritonitis.

Intrauterine Fetal Demise Caused by Thymic Hyperplasia and Cardiovascular Compromise (Poster No. 4)

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The thymus is normally large at birth and continues to grow until puberty. Whether enlarged thymus can cause pediatric morbidity and mortality (so-called thymic asthma and thymic death) has been subject to controversy since thymic death was first described 400 years ago. We report a case of intrauterine fetal demise caused by a severely enlarged thymus. The pregnancy was induced when the male fetus was at 30-week gestational age. The 36-year-old mother was gravida 1, para 0, with a history of hypothyroidism. Her thyroxine medication was reduced at admission because of clinical hyperthyroid symptoms. Serum autoantibody studies showed high titer of thyroglobulin antibody (25250 U/mL) and thyroid peroxidase antibody (2204 U/mL). At fetal autopsy, the thymus was found to be markedly enlarged, weighing 19 g (reference range, 2.8–4.1 g). It showed thymic hyperplasia on histology; it occupied most of the chest cavity, encompassing the anterior heart. There was also evidence of cardiovascular compromise, including severely congested hepatosplenomegaly and severe congestion in the umbilical cord vein. This is the first reported case of intrauterine fetal demise due to thymic hyperplasia in which the mother was diagnosed with hypothyroidism. Thymic hyperplasia is relatively common in patients with hyperthyroidism and Graves disease, and thyroid autoantibody can cause thymic hyperplasia. Thyrotrpin receptors have been identified in human thymus. However, thymic hyperplasia is rare in patients with hypothyroidism. There is one report of thymic enlargement during thyrxine treatment for primary hypothyroidism. The etiology of the severe thymic hyperplasia in this case merits further investigation.

Transfusion-Related Iron Overload in Diamond-Blackfan Anemia: An Autopsy Case Report (Poster No. 5)

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Diamond-Blackfan anemia (DBA) is a rare heterogeneous genetic disorder characterized by red cell aplasia. The degree of anemia, presence of other congenital anomalies, and response to therapy varies significantly among affected individuals. While as many as 80% of patients with DBA respond to corticosteroid therapy, a small group of patients require lifelong blood transfusion therapy and ultimately develop an iron overload syndrome. We report the case of a 27-year-old man with transfusion-dependent DBA who had an atrial septum primum defect corrected during infancy. The patient developed cirrhosis and polycyndocrinopathy and eventually died of a cardiac arrhythmia. Autopsy examination confirmed the presence of iron-induced polycyndocrinopathy, hepatic cirrhosis, and a dilated cardiomyopathy (see Figure 54), all of which were consequences of his lifelong dependence on blood transfusions. The study of DBA is important because of the dramatic clinical impact the disease has on af-
affected patients and their families. The autopsy findings in this patient illustrate how critical iron chelation therapy is in managing patients with transfusion-dependent DBA. The clinical and genetic heterogeneity of DBA prompted the Schneider Children's Hospital (New Hyde Park, New York) to establish the Diamond-Blackfan Anemia Registry of North America in 1993 in an attempt to create a reliable demographic, clinical, and laboratory database of affected patients.

**Novel Mutations in Glycogen Branching Enzyme in Glycogen Storage Disorder Type IV or Andersen Disease**

(Poster No. 8)

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Glycogen storage disease type IV (type IV GSD), or Andersen disease, is a genetic disease with variable expressivity. This rare autosomal recessive disorder (0.3% of glycogenoses) is caused by a deficiency of the glycogen branching enzyme (GBE1) and presents in childhood as a classic hepatic form or later in life as neuromuscular disease. We report a novel GBE1 mutation in a type IV GSD case of a 4-month-old male infant with hepatomegaly. Liver biopsy demonstrated cirrhosis with hepatocytes and Kupffer cells containing distinctive cytoplasmic, periodic acid-Schiff-positive, Lafora body-like inclusions and amylopectin-like ultrastructure. The patient died shortly after liver transplantation. Autopsy revealed diffuse myocardial and reticuloendothelial system involvement, including infiltration of lymph nodes, spleen, and lungs by foamy macrophages containing cytoplasmic inclusions of similar tinctural quality to the hepatocytes and suggesting partially degraded amylopectin-like material. GBE activity in cardiac muscle was undetectable. Analysis of the GBE1 gene revealed compound heterozygosity for c.1279G>A, resulting in a novel G427R missense mutation of an evolutionarily conserved glycine residue, and a previously reported frameshift mutation c.1292delT, leading to premature truncation and likely a null allele. Previously reported mutations in GBE1 displayed marked allelic heterogeneity, including more than 15 alleles associated with different clinical presentations and variable enzyme activities. Diffuse reticuloendothelial system involvement in type IV GSD occurs infrequently. It is unclear whether diffuse reticuloendothelial system involvement represents a worse prognosis with severe enzymatic deficiency resulting from null mutations. This is the first report correlating molecular defects in GBE1 with this presentation.

**Particularly Well-Demarcated Field Effect of Known Developmental Genes: A Case of Otocephaly-Agnathia Complex**

(Poster No. 9)

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Otocephaly-agnathia complex is a rare, lethal malformation, including hypognathia or agnathia, synotia, microstomia, and hypoglossia. Estimated prevalence is 1/70,000, with 80 published cases. A 17-year-old G1P0 adolescent girl presented at 32 weeks’ gestation with ruptured membranes and chorioamnionitis. Results from a 21-week obstetrical ultrasonography were normal. She gave birth to a premature male infant with low birth weight (1260 g). Because of multiple head and neck anomalies, he died within an hour. Postmortem imaging and autopsy focused on the pattern and extent of anomalies. Autopsy revealed absent mandibular arch, hemipalate, hypoplastic facial bones, low-set ears, microstomia, and microglossia. Imaging showed malformed hyoid bone, wide sella turcica, and multiple vertebral and rib abnormalities. Dissection demonstrated unusual rostral insertion of neck musculature and inferiorly displaced eustachian tubes. Anterior pituitary was present; nasopharynx and salivary glands were absent. Cardiac atrial septal defect was present. Neuropathologic examination showed arthrichyencephaly, lissencephaly and Arnold-Chiari type 1 malformation. Associated anomalies, including synotia, external nose malformation, and situs inversus, were absent. Other findings included hypoplastic lungs, visceral herniations, and dilated heart with normal cytogenetic study (Figure 55: clockwise: absent mandible, upon face and gross examination; arthrichyencephaly; vertebral ribs clefts). This rare congenital defect is characterized by the association of otocephaly-agnathia complex with atrial septal defect. Developmentally, a maxillary process derived from first pharyngeal arch. Fail-
ure of sonic hedgehog (chromosome 7q36) signaling system and pair-related (non-HOX) homeobox Prx-1/Prx-2 expression were implicated. Continued eye development drew a rostral limit to the affected field. However, prosencephalic and vertebral-rib anomalies suggested a more caudal Lim1 transcription factor involvement. Other findings were secondary to hypoxia.

Epithelioid angiosarcomas (EASs) of the adrenal gland are extremely rare neoplasms. The diagnosis is difficult due to lack of conclusive radiographic and endocrinologic findings, unusual location, and histologic features. The differential may include chromophotography, primary adrenal epithelial neoplasms, and metastatic disease. Because of the small number of reported cases, we know little about clinical course and prognosis. Our case of adrenal EAS had an unusual clinical presentation and was diagnosed at autopsy. The patient was a 65-year-old woman with a history of melanoma. During evaluation of lower back pain, we discovered a 5-cm, nonfunctioning adrenal mass. The patient underwent laparoscopic adrenalectomy; however, she died postoperatively before diagnosis of the surgical specimen. Microscopic examination of the hemorrhagic retroperitoneal tissue revealed residual adrenal gland with nests and cords of pleomorphic epithelial cells demonstrating prominent nucleoli and high mitotic activity throughout the cortex and medulla and interspersed with anastomotic vascular spaces. Metastatic foci with identical morphology were also identified in multiple retroperitoneal lymph nodes and in bone marrow. Tumor emboli were noted in the lungs. Immunohistochemical analysis was negative for Melan-A, HMB-45 and S100 and positive for vimentin, CD31, CD34 and factor VIII. We report a case of adrenal EAS that was diagnosed at autopsy. Immunohistochemical analysis helped to rule out metastatic melanoma and to diagnose EAS. The presence of extensive metastatic foci indicates an extremely aggressive course. This report contributes to a better understanding of the natural history of this rare entity.

Agnathia-Otocephaly With Alobar Holoprosencephaly and Visceral Anomalies: A Case Report and Immunohistochemical Study
(Poster No. 12)

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Agnathia-ofocephaly with alobar holoprosencephaly and visceral anomalies is a very rare and lethal congenital disorder. Since 1717, less than 30 cases have been reported in the literature. Most cases are sporadic and of normal karyotype. Etiology is unknown and might be related to a mutation of sonic hedgehog, ZIC2, SIX3, and paired-related homeobox genes. The current case is that of a male infant who was born at 35 weeks' gestation to a 16-year-old G2P2 mother. The infant died shortly after birth. We performed autopsy and cytogenetic examinations and immunostaining for chromogranin and inhibin on adrenal glands. Macroscopically, facial dysmorphism showed trigonocephalic microcephaly, cyclopia with anophthalmia, tiny central skin tags, absence of nose and nostrils, microstomia and microglossia, agnathia and hypoplasia of the maxilla, and centrally displaced low-set ears. Alobar form, pancakelike holoprosencephaly showed pachygria with an 80-mL fluid-filled dorsal sac and undivided thalami and corpora striata. We found no olfactory tracts and bulbs, optic nerves, chiasm and optic tracts, pituitary gland and pineal gland, or corpus callosum. Medulla showed olive hypertrophy and pyramidal hypotrophy. Both lungs were hypoplastic with massive hemorrhage. Spleen was blushed and accesorized. Microscopically, adrenal glands demonstrated cortical hypoplasia and medullar hypertrophy and were positive for inhibin and chromogranin. The thyroid gland was hypoplastic, and the testes were small and undescended. Cytogenetics indicated normal male karyotype 46, XY. This rarely reported phenotype suggests that temporal and spatial damage of the anterior embryonic disc occurs during early embryonic development (Carnegie stage 10, embryonic days 22 or 23).

Hyphal Coccidioidomycosis of the Brain in a Patient With Central Nervous System Lymphoma
(Poster No. 13)

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Coccidioidomycosis is an opportunistic infection caused by the dimorphic fungi Coccidioides immitis and Coccidioides posadasi. At body temperature, the organism almost always assumes a characteristic spherical morphology. The hyphal morphology has been observed in human tissue, but almost exclusively in the lung. A review of the literature revealed 3 previously reported cases of parenchymal brain disease. We describe the first known case occurring with concurrent lesions of diffuse large B-cell lymphoma of the brain. The patient was a 22-year-old Hispanic woman who presented with dyspnea, weight loss, and fatigue. A workup revealed diffuse large B-cell lymphoma involving the bone marrow, mediastinum,
characteristic hyphae and barrel-shaped alternating arthroconidia. Several small arrow feet are present consistent with invasion by a fungal mold. Hyphal coccidioidomycosis is exceedingly rare in tissues other than the lung. Only 3 cases of parenchymal brain infection have been previously reported. They include 2 men (ages 26 and 43) with human immunodeficiency virus and one 46-year-old woman with a history of kidney transplantation due to diabetic nephropathy. This is the first known case associated with central nervous system lymphoma and bone marrow transplantation.

**Characterization of Triamcinolone in Formalin-Fixed and Paraffin-Embedded Tissue Specimens by Using Infrared Micro-Spectroscopy**

(Poster No. 14)

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Corticosteroid injection sites have to be differentiated microscopically from other conditions, including rheumatoid nodules, gouty tophi, myxomas, and injection sites of other materials. Infrared microspectroscopy is a noninvasive technique that allows for the molecular characterization of unidentified materials in histopathology specimens. We evaluated 2 specimens for the presence of steroids. In case 1, we received formalin-fixed wet tissue from a postavsectomy sponamic cord stump that contained a pale nodule that was sampled for infrared microspectroscopy. In case 2, we received a formalin-fixed, paraffin-embedded shave biopsy of skin. Consecutive unstained sections were placed on an aluminized glass slide, a carbon disc, and a glass slide. The latter was hematoxylin-eosin-stained, and the areas of interest were located for analysis of the unstained sections, which were deparaffinized and examined by infrared microspectroscopy and by scanning electron microscopy with energy dispersive x-ray analysis. In both cases, infrared spectra characteristics of triamcinolone acetone were obtained. A clinical history of multiple prior triamcinolone injections was provided for case 1 but not for case 2. In case 2, scanning electron microscopy with energy dispersive x-ray analysis identified carbon, oxygen, and fluorine in an area of interest. Fluorine is a constituent of triamcinolone. Triamcinolone may be identified by infrared microspectroscopy in both formalin-fixed wet tissue and in formalin-fixed, paraffin-embedded tissue. Fluorine may be identified by scanning electron microscopy with energy dispersive x-ray analysis. This analysis can help in the differential diagnosis of steroid injection sites and can have broader applications in forensic and medico-legal investigations.

**Generational Differences in Coronary Artery Atherosclerosis in Women: An Autopsy-Based Study**

(Poster No. 15)

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**Context:** Heart disease remains the leading cause of death for women in the United States, with coronary disease being the most common form. Many studies characterize coronary artery atherosclerosis by autopsy and by in vivo methods, but very few studies in the recent literature focus on women.

**Design:** This was a retrospective review of autopsy reports from 2003–2008. We abstracted patient age, sex, height, weight, and cause of death and heart weight and degree of coronary atherosclerosis in the left anterior descending coronary artery, left circumflex coronary artery, and right coronary artery. All autopsies included histologic examination of coronary arteries with grading of stenosis (1 = <25%, 2 = 26%–50%, 3 = 51%–75%, 4 = >75%). These data were compared to similar data compiled at our institution and published in 1950.

**Results:** We included 726 women ranging in age from 30–99. Cases with at least 1 grade 3 lesion in at least 1 coronary artery included 49% of women aged 30–39, 61% aged 40–49, 55% aged 50–59, and 71% aged 60–69. Of these groups, 12%, 15%, 18%, and 18%, respectively, had grade 3 lesions in all 3 arteries. Patients older than 70 years had comparatively lower grade lesions occurring in fewer arteries; this trend was not statistically significant. In 1950, less than 30% of women under age 70 had 1 grade 3 disease in any vessel.

**Conclusions:** Potentially significant (>50%) coronary stenosis was found at autopsy in a surprisingly high number of premenopausal women dying from any cause. This represents a major shift from data published 60 years ago.

**Abdominal lymphomatosis**

(Poster No. 16)

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Confronted with a gross pathologic finding of massive tumor infiltration of the omentum as shown in the figure below (Figure 56) and a radiologic diagnosis of abdominal carcinomatosis, most pathologists would be very confident that this is an epithelial or mesothelial malignancy; this, however, was a disseminated peritoneal B-cell lymphoma in a 51-year-old woman who presented with severe abdominal pain. Computed tomography showed extensive peritoneal infiltration of tumor, bilateral adnexal masses, and right pleural effusion, results which prompted the radiologic diagnosis of peritoneal carcinomatosis with possible ovarian primary tumor. The patient died of massive pulmonary thromboembolism before biopsy could be performed. Microscopic examination revealed sheets of intermediate-sized blastlike cells with scant cytoplasm and round nuclei with a fine chromatin pattern. Immunoreactivity was demonstrated for B-cell markers, CD10, CD22, and CD79a, with little to no expression of T-cell or epithelial markers, leading to the diagnosis of B-cell lymphoid neoplasm with high-grade features. This case serves to raise awareness of the entity, abdominal lymphomatosis, which is radiologically difficult to differentiate from peritoneal carcinoma.
A Case Report on Sirenomelia: Theories of Pathogenesis (Poster No. 18)

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Sirenomelia is a congenital birth defect that is defined as a fusion of the lower extremities. Sirenomelia is also associated with other anomalies. It is a rare defect that has an incidence of approximately 1 in 60,000 to 1 in 100,000 births. There is a male predominance of nearly 3:1. Some consider that sirenomelia represents the most severe end of the spectrum known as caudal dysgenesis. A full autopsy was performed on a nonmacerated, stillborn, female fetus born at 31 weeks’ gestation by induced labor. We found multiple anomalies, including a fused single inferior limb with a poorly formed lumbosacral spine, Potter phenotype with complete renal agenesis and severely hypoplastic lungs, agenesis of the external genitalia, agenesis of the vagina and uterus, anorectal atresia, a persistent left superior vena cava, and a single umbilical artery with an aberrant abdominal aorta connection. These findings represent many of the classic features associated with sirenomelia. There are 2 main hypotheses regarding the pathogenesis of sirenomelia. One hypothesis involves an axial mesoderm defect and the other a vascular developmental defect. The axial mesoderm hypothesis suggests that sirenomelia arises from a blastogenesis or developmental field defect. The vascular hypothesis suggests that the single umbilical artery is a remnant of the vitelline artery and contributes to caudal vascular steal syndrome. However, there is still disagreement as to whether the vascular anomaly is the cause or consequence of the sirenomelia sequence because an axial mesoderm defect could preclude the development of normal umbilical arteries.

Severe Phenotype of HFE-Associated Hemochromatosis (Poster No. 19)

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Hereditary hemochromatosis (HH) is the most common inherited disorder in individuals of Northern and Central European ancestry, affecting approximately 1 in 200. Left untreated, HH can result in widespread tissue injury and early death. We describe the case of a 37-year-old man with a 2-year history of progressive fatigue, darkening skin, intermittent leg swelling, and occasional heart palpitations. He had cardiomegaly, atrial fibrillation, and hepatosplenomegaly. Pertinent laboratory data were as follows: serum iron levels 194 μg/dL (reference range, 50–160 μg/dL); serum transferrin saturation 99% (reference range, 25%–45%); and serum ferritin levels 3260 μg/dL (reference range, 27–285 μg/dL). A liver biopsy disclosed cirrhosis and grade 4 iron deposition. Genetic testing revealed homozygosity for Cys282Tyr in the HFE gene. No mutation was detected in the HAMP, HJV, TJR2, and FRN genes. The patient was treated with frequent phlebotomies, digoxin, amiodarone, spironolactone, and furosemide. After brief clinical improvement, he suffered rapid decline and fatal cardiac complications. Autopsy findings included massive hemosiderin deposition in myocardial fibers, hepatocytes, pancreas, follicular epithelial cells of the thyroid, adrenal zona glomerulosa, and gastric mucosa. HFE mutations are associated with most HH cases. However, many individuals with HFE mutations do not express clinical disease, and early fatalities of HFE-associated HH are very rare. The latter are often associated with hepatotoxic insults, such as alcohol abuse, hepatitis B, or hepatitis C. This case is significant for absence of confounding environmental factors and mutations in other known HH-associated genes. This case highlights the persistent gap in our understanding of the complex pathophysiology and genetics of HFE-associated HH.

Hereditary Systemic Amyloidosis With a Novel Arg50 Mutation in an African American Man (Poster No. 20)

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A 44-year-old African American man was newly diagnosed with systemic amyloidosis, which was initially thought to be of light-chain origin. He presented with chronic diarrhea, peripheral neuropathy, and lower extremity edema. The hospital course was complicated by S. aureus infection and pulseless electrical activity cardiac arrest, leading to the patient’s death. Exploration of his family history revealed a mother who died before age 50 of amyloidosis and 2 aunts who also likely had the disease. The major finding at autopsy was diffuse amyloid deposition in nearly all organs examined. Congo-red staining of representative slides confirmed the diagnosis of amyloidosis. A genetic mutation of serine to arginine at position 50 (S50R) in transthyretin was identified. This mutation has been previously reported only 3 times and in Japanese and European patients. Mutations in transthyretin are the most common cause of hereditary amyloidosis, and there are more than 80 amyloidigenic mutations identified, each of which is associated with particular clinical features and geographic regions. This mutation has not been previously reported in an African American person. The most common mutation in African Americans (approximately 3% of population) is Val122Ile, which typically causes restrictive cardiomyopathy in patients older than 60 years. This patient had an unusual presentation, and the diagnosis was initially missed. These clinical and autopsy findings represent a novel case of hereditary amyloidosis in an African American man, with clinical implications for his offspring. This case emphasizes the underdiagnosed nature of this hereditary disease and argues for more widespread genetic testing in patients with systemic amyloidosis.
Congenital Intracranial Teratoma: A Case Report With Autopsy Findings and Literature Review

(Poster No. 21)

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Congenital intracranial teratoma is extremely rare and accounts for 0.5% to 1% of all pediatric brain tumors. These tumors grow rapidly, are destructive, and have a poor prognosis. We report a case of congenital intracranial teratoma in a 5-week-old female neonate who was born with normal Apgar scores at 38 weeks' gestation by elective cesarean delivery. At birth, she was macrocephalic with increasing hydrocephalus. Cranial ultrasonography and magnetic resonance imaging showed a large heterogeneous cystic and solid midline tumor with multiple calcifications and obstructive hydrocephalus. The lesion was unresectable, and she received palliative care until her death. Autopsy findings showed significantly increased occipitofrontal circumference (greater than 98th percentile) with wide open anterior and posterior fontanelles. An 8 × 8 × 6-cm, gray-tan, solid and cystic midline tumor with areas of necrosis and hemorrhage occupied most of the supratentorial compartment. The epicenter of the tumor was in the region of the third ventricle and hypothalamus. The tumor stretched and attenuated the corpus callosum, inferiorly displaced the thalamus, and occupied most of the supratentorial compartment. The epicenter of the tumor was in the region of the third ventricle and hypothalamus. The tumor stretched and attenuated the corpus callosum, inferiorly displaced the thalamus, and occupied most of the supratentorial compartment. The epicenter of the tumor was in the region of the third ventricle and hypothalamus. The tumor stretched and attenuated the corpus callosum, inferiorly displaced the thalamus, and occupied most of the supratentorial compartment. The epicenter of the tumor was in the region of the third ventricle and hypothalamus. The tumor stretched and attenuated the corpus callosum, inferiorly displaced the thalamus, and occupied most of the supratentorial compartment.

Hepatocerebral Syndrome With Mitochondrial DNA Polymerase γ Compound Heterozygous Missense Mutations

(Poster No. 23)

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Mitochondrial DNA polymerase γ mutation is related to several disorders of mitochondrial metabolism that have a broad range of clinical presentations. We report the case of a female infant with compound mitochondrial DNA polymerase γ mutations. Clinical presentation was consistent with hepatocerebral syndrome (Alpers syndrome). At 7 months of age, the patient started having seizures, failure to thrive, hypotonia, and renal tubular acidosis. She subsequently developed fulminant liver failure with significant coagulopathy, and she died 3 months later. An autopsy revealed massive liver necrosis with diffuse hepatic parenchymal fibrosis. Occasional glial nodules were noted in the brain stem, and there was significant loss of Purkinje cells in the cerebellum. There were degenerative changes in the cerebral gray matter. The thymus was atrophied, and bone marrow was hypocellular with diffuse erythroid precursor dysplasia. Scattered bilateral cytomegalovirus-positive cells were identified in the lungs. Electron microscopy showed no specific inclusion bodies associated with mitochondrialopathies. Premortem blood molecular tests revealed heterozygous mitochondrial DNA polymerase γ mutation A467T, which has been previously linked to Alpers syndrome, and heterozygous R807H mutation, which is a novel missense mitochondrial DNA polymerase γ polymorphism. Because heterozygous A467T mutation is unlikely to cause clinically significant disease, R807H is probably a relevant novel mutation contributing to this clinical syndrome; however, the type and extent of the contribution is not clear. This case shows the important diagnostic role that autopsy pathologists can have in cases of infant death preceded by a metabolic syndrome when premortem workup was incomplete.

Inner Ear and Eye Pathology in Wolfram or DIDMOAD Syndrome: Clinicopathologic Correlation

(Poster No. 22)

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Wolfram or DIDMOAD syndrome is a neurodegenerative disease that is characterized by diabetes mellitus and optic atrophy leading to blindness. Most patients also suffer from some degree of diabetes insipidus and deafness. While blindness and deafness are major aspects of this syndrome, previous histopathologic studies have not described the eye and inner ear. We present postmortem neuropathologic findings, including histologic examination of retinas and ears, for a man with Wolfram syndrome. His disease course included blindness, high-frequency hearing loss, diabetes insipidus, diabetes mellitus, and episodes of central hypoventilation leading to aspiration pneumonia and eventually death at the age of 24 from acute respiratory distress syndrome. Findings on histologic examination of the brain were similar to previously reported neuropathologic descriptions of Wolfram syndrome, including atrophy and loss of myelinated axons in the optic tracts and nerves and loss of neurons in the pontine base and lateral geniculate, paraventricular, supraoptic, and inferior olivary nuclei. Histochemical examination of the cochlea revealed bilateral loss of the organ of Corti in the basal turns and focal atrophy of the stria vascularis (Figure 58). These findings correlate clinically with the high-frequency hearing loss seen in our patient and typically seen in Wolfram syndrome. Histologic examination of the retina revealed marked loss of neurons in the retina ganglion layer, suggesting that neuron loss in the retina leads to subsequent degeneration of the axons in the optic nerves and tracts. These findings provide new insight into the underlying pathology of blindness and hearing loss in Wolfram syndrome.

Congenital Cerebral Arteriovenous Malformation Identified at Autopsy: Associated Findings and Implications for Prenatal Screening

(Poster No. 24)

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Cerebral arteriovenous malformations are uncommon phenomena that can present at any age, but they rarely occur during the perinatal period. We present a case of unexpected perinatal death secondary to asystole that occurred after emergency cesarean delivery due to fetal heart rate abnormalities. Prenatal ultrasonography showed no anatomic anomalies. At autopsy, the heart was found to occupy nearly the entire thoracic cavity with subsequent pulmonary hypoplasia. Upon opening the cranium, a 4.5 × 3.0-cm arteriovenous malformation was identified, connecting the basal artery and the vein of Galen with vessels completely encircling the midbrain. Subarachnoid and subdural hemorrhages were also present. Identification of such a lesion is imperative because it may indicate hereditary disease, such as the autosomal dominant capillary malformation—
Black Esophagus With Histopathologic Description and Characterization
(For the No. 25)

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Black esophagus, or acute necrotizing esophagitis, is a thickening of the esophagus that is usually distal with a sharp demarcation at the gastroesophageal border. On histology, the mucosa is necrotic with underlying deranged muscle fibers in the absence of causative agents. Black esophagus is known to the gastroenterology community and carries a 36% mortality rate according to its literature; however, it is virtually unknown in the pathology literature with only 1 instance described in 1967.

Coagulopathy with a tendency toward severe bleeding is a well-recognized complication of acute promyelocytic leukemia. However, deep vein thromboses and fatal thromboembolism are rarely associated with acute promyelocytic leukemia. We report an autopsy case of a 36-year-old woman with multiple deep vein thromboses and a fatal pulmonary embolism occurring during all-trans retinoic acid (ATRA) therapy for relapsed acute promyelocytic leukemia. No significant thrombotic events had been documented during her initial induction with ATRA and idarubicin 1 year earlier. After a month of ATRA therapy for relapse, the patient’s platelet count increased from less than 20000 to 252000. She subsequently experienced sudden cardiopulmonary arrest the day after an ultrasonography revealed a nonocclusive jugular vein thrombus. A complete autopsy revealed the following: multiple right pulmonary thromboemboli with occlusion of the right main pulmonary artery, bilateral internal jugular venous thromboses, a remote portal vein thrombus, and leukemic cells throughout the marrow and in other organs. ATRA is now widely accepted as a first line induction therapy for acute promyelocytic leukemia, and it greatly reduces bleeding complications. However, low-grade disseminated intravascular coagulation and procoagulant activity may persist during ATRA therapy. With the recovery of peripheral blood platelets, the chance of thrombotic events increases, presenting an underrecognized, potentially fatal risk in clinically promising induction therapy. This case suggests that close monitoring of the hypercoagulable state might be required during ATRA induction therapy.

Adult-Type Gangliosidosis Diagnosed at Autopsy
(For the No. 26)

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Gangliosidoses (GM), a group of autosomal recessively inherited lysosomal storage diseases, are characterized by the accumulation of gangliosides primarily in neurons. Two types have been described: GM1 results from a deficiency of acid β-galactosidase, and GM2 results from defects in the β-hexosaminidase A or β-subunit or the GM2 activator protein. An enzyme assay on peripheral blood leukocytes demonstrating decreased acid β-galactosidase or hexosaminidase A activity is diagnostic of GM1 or GM2, respectively. We report a case of gangliosidosis diagnosed at autopsy. Our patient was a 37-year-old white woman with a history of developmental delay that was first noted at 5 years of age. She developed slowly progressive dementia, proximal muscle weakness, dysphagia, and ataxia, with acceleration of her symptoms 3 years before her death from pneumonia. The clinical differential diagnosis included Huntington disease, fragile X-associated tremor/ataxia syndrome and spinocerebellar ataxia, each of which had negative genetic evaluations. A central nervous system—only limited autopsy revealed moderate cerebral atrophy with histologic demonstration of numerous swollen neurons containing periodic acid-Schiff–positive, granular storage material in the brain and spinal cord (Figure 59). Ultrastructural studies demonstrated multiple small, electron-dense inclusions containing concentrically arranged and curved lamellar structures in the swollen perikarya of the affected neurons. The clinical, histologic, and ultrastructural findings were consistent with adult-type GM1 or GM2 gangliosidosis. Although a central nervous system–only examination provided a diagnosis in this case, a full autopsy would have been of significant value in elucidating the unusual etiology of this patient’s progressive neurologic disorder.

Deep Vein Thromboses and Fatal Pulmonary Thromboembolism During All-Trans Retinoic Acid Induction Therapy for Relapsed Promyelocytic Leukemia
(For the No. 27)

Linseng Zhang, MD, PhD; Laura S. Spruill, MD, PhD; Susan E. Presnell, MD. Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston.

Coagulopathy with a tendency toward severe bleeding is a well-recognized complication of acute promyelocytic leukemia. However, deep vein thromboses and fatal thromboembolism are rarely associated with acute promyelocytic leukemia. We report an autopsy case of a 36-year-old woman with multiple deep vein thromboses and a fatal pulmonary embolism occurring during all-trans retinoic acid (ATRA) therapy for relapsed acute promyelocytic leukemia. No significant thrombotic events had been documented during her initial induction with ATRA and idarubicin 1 year earlier. After a month of ATRA therapy for relapse, the patient’s platelet count increased from less than 20000 to 252000. She subsequently experienced sudden cardiopulmonary arrest the day after an ultrasonography revealed a nonocclusive jugular vein thrombus. A complete autopsy revealed the following: multiple right pulmonary thromboemboli with occlusion of the right main pulmonary artery, bilateral internal jugular venous thromboses, a remote portal vein thrombus, and leukemic cells throughout the marrow and in other organs. ATRA is now widely accepted as a first line induction therapy for acute promyelocytic leukemia, and it greatly reduces bleeding complications. However, low-grade disseminated intravascular coagulation and procoagulant activity may persist during ATRA therapy. With the recovery of peripheral blood platelets, the chance of thrombotic events increases, presenting an underrecognized, potentially fatal risk in clinically promising induction therapy. This case suggests that close monitoring of the hypercoagulable state might be required during ATRA induction therapy.

Touch Preparations of Myxoid Soft Tissue Lesions: A Retrospective Study of 20 Cases
(For the No. 28)

Lisa Pitelka, MD (Lisa.Pittelka@rush.edu); Vijaya Reddy, MD; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Fine-needle aspiration biopsy findings of myxoid soft tissue lesions are rarely described. We report cytologic findings for 20 cases of myxoid lesions of the soft tissue, with emphasis on spectrum of cytologic findings.

Design: Twenty cases underwent frozen section, and touch preparations were performed at that time. All touch preparations, surgical pathology slides, and clinical data were reviewed.

Results: There were 13 men and 7 women, ranging in age from 26 to 83 years (mean, 49 years). Lesions were located in the thigh, calf, para-vertebral and perianal areas, neck, foot, groin, and shoulder. The surgical diagnoses were as follows: myxoid liposarcoma, myxoma, low-grade fibromyxoid sarcoma, and extraskeletal myxoid chondrosarcoma. The myxoid liposarcomas on smears showed branching capillary networks with increased cellularity and lipoblasts with scalloped nuclei. The background showed myxoid material ranging from scant to abundant. The low-grade fibromyxoid sarcomas were highly cellular with oval to spindle cell nuclei...
with inconspicuous nuclei. The cytoplasm was fragile and wispy. Myxoid substance and naked nuclei were present in the background. Background myxoid material was pale, thin, and poorly defined.

Conclusions: We rendered a definitive diagnosis of myxoid liposarcoma, extraskelatal myxoid chondrosarcoma, and myxoma in cytologic material. However, a definitive diagnosis of low-grade fibromyxoid sarcoma can be challenging because other spindle cell tumors may cytologically mimic it.

Correlation of Proliferation and Apoptotic and Glucose Utilization Markers With [18F]Fluorodeoxyglucose Positron Emision Tomography Uptake in Peripheral Nerve Sheath Tumors

(Poster No. 29)

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Context: We analyzed 24 tumors (12 MPNSTs and 12 BPNSTs). The SUV-positive group had 11 MPNSTs and 2 schwannomas; the SUV-negative group had 1 MPNST, 2 neurofibromas, and 8 schwannomas. We studied histologic features (necrosis and intratumoral hemorrhage), proliferative indices (mitotic rate, Ki-67, and sp2), apoptotic rate by terminal deoxynucleotidyl transferase-mediated dUTP-biotin end labeling of fragmented DNA (TUNEL) indices, and expression of glucose utilization markers including glucose transporter (GLUT-1) and hexokinase II. Ki-67, p53, and TUNEL indices were estimated and quantified by automated image analysis software. Established scoring systems were used for GLUT-1 and hexokinase II staining. Tumors with more than 10% staining were classified as high (sp2) or positive (p53).

Results: Necrosis and hemorrhage were not statistically different between groups. Proliferative indices were higher in the SUV-positive group. Apoptotic rate was higher in the SUV-negative group. SUV-positive tumors had more GLUT-1 staining; hexokinase II stained all but 1 SUV-positive tumor. The difference in mitotic rate and TUNEL was significant on 2-way analysis of variance. GLUT-1 score and SUV status demonstrated significant correlation. SUV-positive and SUV-negative BPNSTs showed no differences in the above factors.

Conclusions: Compared to SUV-negative tumors, SUV-positive peripheral nerve sheath tumors were associated with higher mitotic rate and GLUT-1 scores and lower apoptotic rate.

A Framework for Computer-Assisted Pathologic Diagnosis of Well-Differentiated Liposarcoma

(Poster No. 30)

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Context: Increased digitalization of microscopic images provides a unique opportunity for studying the utility of image analysis as an adjunct to microscopic diagnosis. In particular, image analysis may facilitate arriving at diagnoses that are dependent on identification of relatively rare cytologic or histopathologic features. By using MATLAB software (The MathWorks, Inc, Natick, Massachusetts), we identified atypical lipoblasts in well-differentiated liposarcoma, we hope to determine if screening by image analysis could provide diagnostically useful information.

Design: We identified 10 cases of benign lipoma and 10 cases of well-differentiated liposarcoma in the surgical pathology and consultation files at East Carolina University. Glass slides were digitized using the Aperio system (Aperio Technologies, Inc, Vista, California). MATLAB software was used to identify cells with enlarged, hyperchromatic nuclei by using k-means segmentation and subsequent filtering based on size and color. Images from 20 cells, selected by software screening from each case, underwent blind review. A diagnosis was rendered in each case, and then was compared to the light microscopic diagnosis. Sensitivity, specificity, and predictive values were calculated.

Results: Ten of 10 liposarcomas were correctly classified. One of 10 lipomas was misclassified as a liposarcoma. Sensitivity was 100% and specificity 90%. Negative predictive value was 100% and positive predictive value was 91%. The degree of cellularity and the presence of lipoblasts of the tumor and fibromuscular tissue caused difficulty with software screening and interpretation in some cases.

Conclusions: Screening by image analysis can assist in diagnosis through identification of infrequent cytologic or histopathologic features of selected pathologic processes.

Leiomyosarcoma ARISING FROM THE Pancreatic Duct: A Case Report And Review Of Pancreatic Sarcomas

(Poster No. 31)

Nicole M. DeMers Riddle, MD1 (ndemers@health.usf.edu); Brian Quigley, MD2; Irwin Browarsky, MD. 1Department of Pathology and Cell Biology, University of South Florida, Tampa.

Leiomyosarcomas are rare malignant smooth muscle tumors that may arise in any organ or tissue that contains smooth muscle. They are most commonly found in the stomach, large and small intestine, and retroperitoneum. Primary pancreatic leiomyosarcoma is extremely rare. To the best of our knowledge, only 30 cases have been reported in world literature since 1951. However, no cell of origin has ever been clearly shown. The prognosis is poor, and treatment consists of alleviating symptoms and pain management. In this case, a pancreatic tail mass was identified by computed tomography scan. Histopathologic evaluation showed large pleomorphic and spindle-shaped cells. Immunohistochemistry and vimentin and smooth muscle actin was positive. Results with all remaining immunohistochemical markers used were negative. There was a clear origination from the pancreatic duct, with expansion of the wall by a tumor with overlying benign duct epithelium lining the constricted lumen. This case represents the first reported pancreatic leiomyosarcoma to clearly arise from the main pancreatic duct wall.

Sclerosing Rhabdomyosarcoma as a Metastasis of Embryonal Variant or Vice Versa: A Clinicopathologic, Immunohistochemical, and Molecular Case Study

(Poster No. 32)

Cristian Ortiz Villalon, MD, PhD1 (cortizv@gmail.com); Miguel Martorell, MD, PhD2; Rosa Barbella Aponte, MD1; Jose Garcia, MD, PhD3; Pablo Mucientes, MD3. 1Department of Pathology, Hospital General Universitario de Valencia, Spain; 2Department of Pathology, Hospital Clinico Regional de Concepcion, Chile.

Sclerosing rhabdomyosarcoma (SRMS) is a recently described rare variant of rhabdomyosarcoma that is characterized by extensive hyaline fibrosis. We report a case of a 37-year-old man with coexisting tumors: a 2-cm soft tissue tumor located in the right elbow and a 3-cm right testicular tumor. Histopathologically, the tumor in the right elbow was located in the deep soft tissue, with a richly collagened matrix corresponding to an SRMS and a microscopic focus of embryonal rhabdomyosarcoma. The testicular tumor was reported as a pure embryonal rhabdomyosarcoma. Both tumors were immunohistochemically negative for desmin and positive for MYOD1. In both tumors, genomic study results with reverse transcription–polymerase chain reaction were negative for alveolar rhabdomyosarcoma–mutated genes PAX3, PAX7, and K-RAS wild type. Six months after tumor resection, the patient presented with metastatic disease in lung and bone. We present a rare case of 2 coexisting subtypes of rhabdomyosarcoma: embryonal rhabdomyosarcoma and SRMS. Despite their different locations, it was difficult to determine the primary tumor from the metastatic one. This case shows a clear relationship between SRMS and embryonal rhabdomyosarcoma. Furthermore, our case suggests that SRMS is a subtype of embryonal rhabdomyosarcoma and that they share a common origin, with one being the primary tumor and the other being the metastatic one.

Metastatic Osteosarcoma Presenting 28 Years After Primary Diagnosis

(Poster No. 33)

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We report an unusual case of metastatic osteosarcoma presenting in the lungs 28 years after the primary diagnosis. The patient was a 45-year-old woman who presented with a persistent cough for 3 months. She also had a past medical history of low-grade osteosarcoma of the right proximal tibia, which occurred at the age of 17 and was treated with a right above-the-knee amputation only. Computed tomography scan revealed an approximately 16 × 12-cm, large, multiloculated, predominantly solid mass occupying the right lung and extending into the right hilum with encasement of the bronchus. Bronchoscopy and endobronchial biopsy were performed. Histologic sections of the biopsy revealed infiltrating, poorly differentiated, highly pleomorphic neoplastic cells. Immunohistochemical staining was performed on the biopsy specimen, and the neoplasm was strongly positive for vimentin and very focally and weakly positive for desmin. Results with pan-cytokeratin, CAM 5.2, thyroid transcription factor-1, epithelial membrane antigen, and S100 were negative, and sarcoma was favored. A pneumonectomy with node dissection was subsequently performed. Consistent with metastatic osteosarcoma, the histologic appearance of the mass was that of a highly cellular pleomorphic sarcoma with focal osteoid production and extensive necrosis. Subsequent histologic, immunohistochemical, and molecular techniques demonstrated the mass as a metastatic osteosarcoma, confirming the previous diagnosis of osteosarcoma made after the limb amputation 28 years earlier. Histologic examination of the lesion demonstrated a highly cellular pleomorphic sarcoma with focal osteoid production and extensive necrosis. Our patient was a 78-year-old man who presented at our institution with a metastatic papillary thyroid carcinoma involving a metastatic papillary thyroid carcinoma and an enchondroma. Our patient was a 78-year-old man who presented at our institution for a restaging positron emission tomography scan after total thyroidectomy for papillary thyroid carcinoma. The scan revealed multiple supravacular lesions that were suggestive of metastatic disease. A subsequent radiograph of the right humerus revealed a mixed lytic and sclerotic lesion, with imaging features of an aggressive-appearing cartilaginous tumor. Intraoperative core biopsy of the lesion before definitive resection demonstrated a low-cellularity cartilaginous tumor with scattered foci of dark brown discoloration. The lesion involved the humeral metaphysis and epiphysis with focal, mild, endosteal erosion. Microscopic examination of the lesion demonstrated a low-cellularity cartilaginous tumor that was consistent with an enchondroma. Sections also revealed the presence of metastatic papillary thyroid carcinoma, a morphologic diagnosis supported by immunohistochemical positivity for thyroglobulin and thyroid transcription factor-1. Our knowledge, only one prior case report of a collision tumor involving an enchondroma and carcinoma exists. That case report described an enchondroma and metastatic lung carcinoma. Prior cases of enchondroma receiving a metastatic papillary thyroid carcinoma have not been reported in the literature. Synthetic thyroid hormone can alter the importance of good clinical history and surveillance.

A Collision Tumor Involving a Primary Humeral Enchondroma and a Metastatic Papillary Thyroid Carcinoma
(Forer No. 34)

Thomas R. Fennell, MD* (fennellthomas@hotmail.com); Wendy N. Wiesend, MD; Jon D. Wilson, MD; Aron M. Trochia, MD, Departments of Anatomic Pathology and Orthopaedic Surgery, William Beaumont Hospital, Royal Oak, Michigan.

Tumor-to-tumor metastasis, also known as “collision tumor,” is a rare phenomenon. This entity is defined as 2 histologically distinct neoplasms occurring in the same anatomic region. In this report, we discuss a collision tumor involving a metastatic papillary thyroid carcinoma and an enchondroma. Our patient was a 78-year-old man who presented at our institution for a restaging positron emission tomography scan after total thyroidectomy for papillary thyroid carcinoma. The scan revealed multiple supravacular lesions that were suggestive of metastatic disease. A subsequent radiograph of the right humerus revealed a mixed lytic and sclerotic lesion, with imaging features of an aggressive-appearing cartilaginous tumor. Intraoperative core biopsy of the lesion before definitive resection demonstrated a low-cellularity cartilaginous tumor with scattered foci of dark brown discoloration. The lesion involved the humeral metaphysis and epiphysis with focal, mild, endosteal erosion. Microscopic examination of the lesion demonstrated a low-cellularity cartilaginous tumor that was consistent with an enchondroma. Sections also revealed the presence of metastatic papillary thyroid carcinoma, a morphologic diagnosis supported by immunohistochemical positivity for thyroglobulin and thyroid transcription factor-1. Our knowledge, only one prior case report of a collision tumor involving an enchondroma and carcinoma exists. That case report described an enchondroma and metastatic lung carcinoma. Prior cases of enchondroma receiving a metastatic papillary thyroid carcinoma have not been reported in the literature. Electron Microscopy Ultrastructural Study as an Adjunct to Fine-Needle Aspiration Biopsy in Establishing a Definitive Diagnosis of Soft Tissue Tumor
(Forer No. 35)

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Context: Making a specific diagnosis by fine-needle aspiration biopsy (FNA) is often difficult; nevertheless, the screening role of FNA cannot be overemphasized because of its low cost, quick turnaround time, and low incidence of complication. The use of FNA on soft tissue tumors is becoming more widespread because of advanced immunohistochemistry and molecular and cytogenetic techniques. However, electron microscopy (EM) ultrastructural studies of FNA material have mainly been reported in case studies.

Design: Cytopathology files from 2001 to 2007 were searched for cases of soft tissue FNA with corresponding EM ultrastructural studies. We retrieved the results of cytology and EM and reviewed the corresponding tissue diagnosis cases.

Results: Ten soft tissue FNA materials were submitted for EM during this period. Six cases had an EM diagnosis; 3 cases had no malignant cells; and 1 case yielded only degenerated tumors cells. EM was subsequently performed on 2 of the 4 unsuccessful cases by using histology material. The EM diagnostic cases included 2 Ewing sarcomas, 1 monomorphic synovial sarcoma, 1 lymphoma, 1 osteosarcoma, and 1 poorly differentiated carcinoma. In addition, computed tomography revealed wide-
spread metastatic lesions in the lung, liver, breast, and pelvic wall with involvement of multiple lymph node groups. This observation highlights the fact that morphologic features alone are not reliable in distinguishing atypical from malignant GCT.

Ossifying Fibromyxoid Tumor of Soft Parts Presenting as a Parapharyngeal Mass
(Poster No. 38)

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Ossifying fibromyxoid tumor of soft parts (OFTSP) is a rare mesenchymal neoplasm of intermediate malignant potential. The tumor is of possible Schwann cell origin and commonly occurs in adult men with preferential localization to the subcutis of upper and lower extremities. Nine cases of OFTSP occurring in submucosal and subcutaneous tissues of the head and neck region have been previously reported. A 35-year-old man was being evaluated for sudden abdominal pain when multiple ossifying fibromyxoid tumor with multiple lung metastases. A 34-year-old man was being evaluated for sudden abdominal pain when multiple...

High-Grade Sarcoma Arising in an Ossifying Fibromyxoid Tumor
(Poster No. 40)

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Ossifying fibromyxoid tumor of soft parts is an uncommon neoplasm that typically has a benign to uncertain or low-grade behavior. However, atypical and malignant forms that potentially behave more aggressively have been described. Conventional ossifying fibromyxoid tumors have the potential for local recurrence, but they pose little to no risk for metastasis. We present a rare case of a high-grade sarcoma arising from a conventional ossifying fibromyxoid tumor with multiple lung metastases. A 34-year-old man was being evaluated for sudden abdominal pain when multiple...

Activation of Mammalian Target of Rapamycin in Soft Tissue and Bone Tumors: Study of 141 Cases
(Poster No. 39)

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Context: Malignant target of rapamycin is a serine/threonine kinase of the PI3K/AKT signaling pathway that is known to play an important role in tumor growth. It is also a potential therapeutic target. Phosphoribosomal S6 protein is a downstream molecule and a surrogate marker for mammalian target of rapamycin activation. Several malignant targets of rapamycin inhibitors are in clinical trials. We examined phosphoribosomal S6-protein reactivity in a wide variety of sarcomas and mesenchymal tumors.

Design: We reviewed 141 cases of sarcomas. Cases included 19 categories of soft tissue and bone tumors: synovial sarcoma (10), Ewing sarcoma (5), chordoma (8), leiomyosarcoma (20), pleomorphic undifferentiated sarcoma (5), malignant solitary fibrous tumor (5), low-grade fibromyxoid sarcoma (5), clear cell sarcoma (2), alveolar soft parts sarcoma (3), angiosarcoma (12), desmoplastic small round cell tumor (3), liposarcoma (12), malignant peripheral nerve sheath tumor (14), chondrosarcoma (5), extraskeletal myxoid chondrosarcoma (8), osteosarcoma (5), desmoid type fibromatosis (7), rhabdomyosarcoma (3), and angiomylipoma (9). Sections were stained with antibody to phosphoribosomal S6 protein and were scored on a 3-point scale: 0 (negative), 1+ (less than 25%), 2+ (less than 50%), 3+ (greater than 50%). High expression was defined as tumors with at least 50% of 2+ or 3+ staining; low expression was defined as a 1+ score.

Results: Expression pattern was stratified naturally into high and low expressers (Table). Conclusions: High expression of phosphoribosomal S6 protein was observed in several sarcoma subtypes, suggesting a potential benefit from targeted mammalian target of rapamycin therapy. Clinical trials are needed to confirm clinical utility.

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<tr>
<th>p56rp Expression in Soft Tissue and Bone Tumors</th>
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<tr>
<td><strong>High Expressors (2+ or 3+ score), Tumor (%)</strong></td>
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<td><strong>Rhabdomyosarcoma (100)</strong></td>
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tiple incidental bilateral lung nodules were identified. Physical examination and further radiologic evaluation revealed a large intramuscular mass in his left axilla, with distinctive peripheral and focally central bone formation. After resection, we identified a firm, white, well-circumscribed, encapsulated mass that had a white, fibrous cut surface and that was partially encapsulated (50%) by hard bone. Microscopically, cords of medium round cells arranged within a hyaline background and surrounded by a shell of lamellar bone were present (Figure 62, A and B); these findings were consistent with an ossifying fibromyxoid tumor of soft parts. In other areas, the sections resembled a sclerosing osteosarcoma (Figure 62, C) and a high-grade round cell sarcoma. The metastatic lesions in the lung were clearly high grade, consisting of undifferentiated round cells (Figure 62, D). This case provides the first reported clinical and pathologic evidence that high-grade transformation can occur in ossifying fibromyxoid tumors and that the risk for metastasis is present, albeit only after transformation.

Williams syndrome (WS) is an autosomal dominant disorder caused by deletion of chromosome 7q11.23, which encodes the elastin gene. Phenotypic manifestations include abnormalities in epidermal and subcutaneous tissues; however, no known tumor predisposition is currently recognized. We report on a patient with WS who developed a proximal-type epithelioid sarcoma. A 26-year-old man who was diagnosed with WS by metaphase fluorescence in situ hybridization analysis, which identified a deletion at the WS critical region, presented with a firm, painless perianal mass of 8 weeks’ duration. His medical history was significant for aortic and renal artery stenosis. A computed tomography scan showed a solid 3.2 × 2.9-cm soft tissue mass located between the scrotum and anus. Needle-core biopsy demonstrated poorly differentiated tumor cells that were strongly immunoreactive against broad spectrum cytokeratin, epithelial membrane antigen, and myoglobin and focally positive for calretinin, p53, and CK7. The cells were negative for p63, TTF-1, desmin, myogenin, MART-45, and CK20. Ki-67 labeled 25% of nuclei. These findings are consistent with the diagnosis of proximal-type epithelioid sarcoma. The patient received neoadjuvant radiation with evidence of tumor necrosis, and then, underwent an excision with administration of intraoperative radiation. Rarely have tumors been reported in patients with WS. These include epithelial and hematologic malignancies. A case of fibrous hamartoma of infancy has also been reported in a patient with WS, suggesting a link between abnormal elastin synthesis and development of certain soft tissue tumors. To our knowledge, this is the first report of a sarcoma of any type in a patient with WS.

Expression of MTA1, FIP1, RBM9, and CTR9 in Small Blue Cell Tumors in Children

(Poster No. 43)

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Context: Metastasis-associated protein 1 (MTA1) is an oncosite that regulates epithelial to mesenchymal transition and metastasis and may indicate progression to metastatic state. Factor interacting with poly(A) polymerase (FIP1), RNA-binding motif protein 9 (RBM9), and Paf1/RNA polymerase II complex component homolog Ctr 9 (CTR9) are c-myc pathway oncogenes that are important in controlling tumorigenesis. The purpose of this study was to evaluate the expression of these novel growth tumor markers in small blue cell tumors in children.

Design: A tissue microarray was constructed using paraffin-embedded samples from 7 Ewing sarcomas, 6 rhabdomyosarcomas, 6 neuroblastomas, 2 Wilms tumors, and 2 desmoplastic small round cell tumors. Immunohistochemistry was performed with rabbit polyclonal antibodies to MTA1, FIP1, RBM9, and CTR9. Immunoreactive scoring was based on stain intensity (2+ to 3+ were positive) and percentage of positive tumor cells.

Results: MTA1 and RBM9 were moderately to strongly expressed in most of the small blue cell tumors. FIP1 had stronger expression in desmoplastic small round cell tumors and Wilms tumor. CTR9 had stronger expression in Wilms tumor than in other small blue cell tumors (Table).

Conclusions: FIP1 is a potential diagnostic marker for desmoplastic small round cell tumors, and CTR9 is a potential diagnostic marker for
Wilms tumor. MTA1 and RBM9 are important c-myC pathway oncogenes expressed in all small blue cell tumors, and they may become important for prognostic and targeted therapy treatment. However, analysis of a larger number of cases is necessary.

**Amyloidoma of Bone and Peripheral Nerve: Report of 2 Cases and Review of Literature**  
(Poster No. 44)

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Amyloidosis is the extracellular deposition of the fibrous protein amyloid with resultant tissue damage. Amyloidosis may be systemic, organ limited, or localized. Amyloidoma, also known as tumoral amyloidosis, is defined as a solitary localized deposit of amyloid in the absence of plasma cell dyscrasia or abnormal serum proteins. Although uncommon, amyloidomas have been reported in various anatomic sites, including respiratory, genitourinary, and gastrointestinal tracts. We report 2 distinct cases of amyloidomas in very unusual locations. The first case was that of a 42-year-old man who presented with a mass lesion in his arm. At the time of surgery, the peripheral nerve seemed to be encased in a sheath of abnormal firm tissue, which was submitted for pathologic evaluation.

The second case was that of a 55-year-old man who presented with an 18-cm pelvic mass that was eroding the sacroiliac joint and sacrum. After subsequent pathologic evaluation, both of the lesions were diagnosed as amyloidomas. Involvement of peripheral nerves by amyloidoma is extremely uncommon. Most prior cases of amyloidomas of the central nervous system have involved the triginemal nerve. Tumoral amyloidosis of bone is even rarer, with only 34 cases reported in the literature. Previously reported cases often involved the spine and skull. To our knowledge, this is the only report of amyloidoma with involvement of the pelvis. Additionally, there are no reports of amyloidomas of such large size. We discuss the clinical and pathologic findings of the amyloidomas in these 2 patients and review the prior literature.

**Rare Metastatic Site for a Malignant Fibrosarcoma**  
(Poster No. 45)

Suman Goel, MD, MPH (sgoei@usuhealth.edu); Jeffery S. Sosnowski, MD, PhD. Department of Pathology, University of South Alabama, Mobile.

Of the soft tissue sarcomas that occur in adults, malignant fibrous histiocytoma is the most common. The 2 main sites of metastases are lung and bone. The brain is a rare and unusual site for metastasis. We report a case of a 52-year-old man who presented with a 1-week history of left arm weakness and dizziness. The patient’s medical history was significant for left lower extremity, soft tissue, high-grade, malignant fibrous histiocytoma with lung metastasis and recurrence for which he underwent left above-the-knee amputation. Magnetic resonance imaging and computed tomography scan showed a large homogenous enhancing lesion in the right occipitoparietal region extending into the corpus callosum. Surgery was performed in the form of craniotomy with biopsy, decompression, and/or removal. Microscopic sections showed a malignant neoplasm containing pleomorphic nuclei with multiple mitotic figures compatible with metastatic malignant fibrous histiocytoma. The neoplasm was immunoreactive for vimentin but not for glial fibrillary acidic protein. Postoperative magnetic resonance imaging showed resolution of the occipitoparietal mass with residual tumor burden signal along the inferior and lateral aspect of the right lateral ventricle. The patient gradually improved neurologically. He also showed improvement in left upper extremity weakness and was ambulatory at discharge 4 days after surgery. Although the diagnosis of cerebral metastasis is a terminal event, this case represents early detection of a rare metastatic site, with successful tumor decompression as a reasonable therapeutic approach.

**A Rare Case of Adrenal Cavernous Hemangioma**  
(Poster No. 46)

Anna T. Vischio, MD, MPH (annavischio@gmail.com); Salman B. Ayub, MD; Steven Sieber, MD. Department of Pathology and Laboratory Medicine, Danbury Hospital, Danbury, Connecticut.

Cavernous hemangiomas of the adrenal gland are extremely rare, benign, vascular lesions composed of large cavernous blood vessels lined by endothelial cells. Patients may present with complaints of dull pressure or mass-related symptoms. Imaging with computed tomography revealed a predominantly hemorrhagic, 9.1-cm mass with small foci of peripheral enhancement. The mass was surgically excised and postoperatively diagnosed as a cavernous hemangioma of the adrenal gland with secondary thrombosis and extensive hemorrhage (Figure 63). Adrenal hemangiomas remain a rare entity and are challenging to diagnose postoperatively. However, they should always be included in the differential diagnosis of adrenal masses.

**A Case of Spondyloepiphyseal Dysplasia Congenita With Additional Findings of Bilateral Simian Creases and Tracheoesophageal Fistula**  
(Poster No. 47)

Nawaal M. Nasser, MD (mmnass@gmail.com); Orlando R. Gonzalez, MD. Department of Pathology, Orlando Health, Orlando, Florida.

Spondyloepiphyseal dysplasia congenita is a rare disorder that is characterized by short limbs, large head, flattened facies, short neck and trunk, and protuberant abdomen. It less often includes myopia or retinal detachment, hearing loss, cleft palate, and inguinal hernias. This primarily autosomal dominant condition is due to defects in type II collagen and has a genetic linkage to COL2A1 (12q13.11-q13.2). We report a case of spondyloepiphyseal dysplasia congenita that was first diagnosed in a 3-month-old, 46, XY male infant who presented at birth with rhizomelia, platyspondyly, short neck, flattened facies, retrorenal fibrolipoma, Pierre Robin sequence, protuberant abdomen, bilateral inguinal hernias, bilateral simian creases, and a tracheoesophageal fistula that was repaired early in life. The diagnosis was established by radiographic findings and genetic testing that showed a defect in the transition of amino acids involving exon 20 of the COL2A1 gene. Unfortunately, the patient developed Pseudomonas and Streptococcus culture-positive bronchopneumonia, and his condition deteriorated. Additional findings at autopsy included poor ossification of the calvarium and pubic bones. Microscopic examination of the vertebrae and femur were remarkable for disorganization of the physeal growth zone and scattered cytoplasmic inclusions in chondrocytes. These findings were consistent with established descriptions of this disease. This is the first reported case of spondyloepiphyseal dysplasia congenita with concomitant bilateral simian creases and tracheoesophageal fistula, findings which may indicate additional manifestations and clinical implications of this disorder.

**The Utility of Perivascular Lymphocytic Infiltrates as a Diagnostic Feature of Atypical Lipomatous Tumor**  
(Poster No. 48)

Adam A. VanRegenmorter, MD (adamvr@gmail.com); Vladimir Osipov, MD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

Context: Atypical lipomatous tumor (ALT), also known as well-differentiated liposarcoma, is an uncommon tumor with predilection for the thigh and retroperitoneum. Morphologically, ALT is differentiated from lipoma by the presence of atypical cells with hyperchromatic nuclei. The diagnosis can be missed when diagnostic cells are inconspicuous or unidentifiable.
**Design:** We tested the sensitivity and specificity of perivascular lymphocytic infiltrates as a novel histologic feature for differentiating ALT from lipoma. We assessed 30 ALTs and 68 lipomas for the presence or absence of perivascular lymphocytic infiltrates. This feature was defined as the presence of at least 15 lymphocytes surrounding at least two-thirds of one or more blood vessels. The ALTs included specimens from 6 biopsies and 24 resections that were selected from cases diagnosed at our institution since 2001. All selected lipomas were resected specimens.

**Results:** Among ALTs, 23 of 24 resected specimens (95.8%) and 3 of 6 biopsy specimens (50%) contained perivascular lymphocytic infiltrates. Among lipomas, 3 of 68 cases (4.4%) contained perivascular lymphocytic infiltrates. In cases of perivascular lymphocytic infiltrate, all ALTs showed multiple foci of perivascular lymphocytic infiltrate, while only lipoma showed multiple foci. In most cases, the number of perivascular lymphocytic infiltrates was directly proportional to the number of atypical cells present.

**Conclusions:** Perivascular lymphocytic infiltrates are a useful diagnostic feature when differentiating lipoma from ALT. One should strongly consider a diagnosis of ALT when perivascular lymphocytic infiltrates are present in a fatty tumor. In such cases, additional sections, deeper sections, or immunohistochemical staining to search for atypical cells is warranted.

**Extranodal Rosai-Dorfman Disease of Right Calcaneus Without Lymphadenopathy in a 2.5-Year-Old Girl**

(Poster No. 49)

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Rosai-Dorfman disease (RDD) is characterized by massive painless cervical lymphadenopathy, which is caused by accumulation of proliferating histiocytes in the sinusoids of lymph nodes. We present a unique case of extranodal RDD without systemic lymphadenopathy in the right calcaneus of a 2.5-year-old girl. Imaging studies demonstrated a fairly defined lytic focus involving the posterior portion of the right calcaneus with no adjacent periosteal reaction or soft tissue swelling. There were no other distant lesions. Based on imaging, the differential diagnosis included osseous myelitis, eosinophilic granuloma, bone cyst, or chondroblastoma. Excisional curettage was performed, and histologic examination demonstrated bone fragments with a polymorphous inflammatory cell infiltrate composed of lymphocytes, plasma cells, neutrophils and large vacuolated histiocytes with intracytoplasmic lymphocytes, and neutrophils (emperiploic). The foamy histiocytes were S100 positive and CD1a negative by immunohistochemical staining. This combination of morphology and immunohistochemical findings is characteristic of RDD histiocytes. To our knowledge, only 12 cases, 7 of which were pediatric (Table), have been reported to date of extranodal RDD as a solitary lesion in bone without systemic lymphadenopathy. Our case is the first reported case in the right calcaneus in the pediatric population. There is no specific therapy for RDD; however, a solitary lesion in the bone may be treated with local excision or corticosteroid therapy.

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<th>Rosai-Dorfman Disease as Solitary Bone Lesions in Pediatric Population: Case With Literature Review</th>
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Spinal Bone Tumors: A Review of 100 Cases Collected From 2000 to 2009

(Poster No. 50)

Rachel Pevsner, DO1 (rachelcrun@yahoo.com); Phillip Robinson, MD; N. Henry Pevsner, MD2; Deborah Pevsner, MD2; Christopher R. Hancock, MD2.

1 Department of Radiology, Mount Sinai Medical Center, Miami Beach, Florida; Departments of 2Pathology, 3Musculoskeletal Section, and 4Radiology, University of Miami School of Medicine, Miami, Florida.

**Context:** We reviewed 100 spinal bone lesions that were biopsied from 2000-2009 in the musculoskeletal section. We present histopathologic findings of common and uncommon spinal lesions with a review of the pertinent radiographic findings.

**Design:** Lesions fell into 6 general categories based on frequency and pathologic and radiographic findings: infections, benign and malignant bone lesions, metastatic bone lesions, traumatic bone lesions, and neural neoplasms.

**Results:** Metastatic lesions included breast (8), squamous cell (5), thyroid (3), prostate (1), lung (1), hepatocellular (1), and gastrointestinal/genitourinary (5). Benign bone lesions included aneurysmal bone cyst (1), giant cell tumor (1), brown tumor (1), osteoid osteoma (1), osteoblastoma (5), giant cell granuloma (1), hemangioma (5), and traumatic lesions (19). Neural lesions included schwannoma (5), ganglieneuroma (1), and ependymoma (1). Primary malignant bone lesions included osteosarcoma (1), lymphoma (3), treated lymphoma (1), multiple myeloma (1), plasma cell dyscrasia (8), chondrosarcoma (1), osteosarcoma (1), chondroma (5), and possible yolk sac tumor (1). Pathologic findings for infectious cases (13) were nonspecific or showed mild acute or chronic inflammation. Cultures yielded results for Staphylococcus aureus (1), tuberculosis (1), and Pseudomonas osteomyelitis (1). Positive culture results were obtained in 23% of cases.

**Conclusions:** Benign lesions (34) were most numerous and were commonly posttraumatic. Metastases (25) were the most common spinal bone tumor, with breast tumors being the most common followed by squamous carcinoma. Primary malignant lesions (21) accounted for 21% of cases, with myeloma and chordoma being the most common. Neural lesions (7) were mostly schwannomas. Histopathologic appearance and correlation with clinical history and radiographs is paramount for diagnosis.

**Malignant Granular Cell Tumor: Case Report With a Novel Karyotype**

(Poster No. 51)

Haitham Nasser, MD (haitham.nasser@stjohn.org); Robert D. Danforth, MD; Mohamad Sunbuli, MD. Department of Pathology, St John Hospital and Medical Center, Detroit, Michigan.

Granular cell tumor is an uncommon benign neoplasm that arises in all body sites with predilection for the head and neck region. Rare case reports and small series describe the metastatic potential and adverse prognosis of malignant granular cell tumors. To our knowledge, no specific karyotype characterizes these tumors. We report a case of malignant granular cell tumor arising in the subcutaneous tissue of the thigh in a 56-year-old woman. There was metastasis to the abdominal wall and both lungs, and the patient experienced dyspnea. Grossly, the tumor was ulcerated, homogeneously gray-white, ill-defined, and firm. Microscopically, it was composed of sheets and nests of pleomorphic epithelioid and spindle cells with eosinophilic and granular cytoplasm. There were scattered karyorrhexis. Mitotic count was up to 7/10 high-power fields. Immunohistochemically, the tumor cells were diffusely and strongly positive for S100. Sixty per cent of tumor cells displayed the following karyotype: 46,XX, t(5;15)(p14;q25). Malignant granular cell tumor is a rare and difficult tumor to diagnose and treat. The histologic criteria of malignancy proposed by Fanburg-Smith et al are still debated among pathologists, with metastasis being the only criterion unanimously agreed upon. We report an interesting case of malignant granular cell tumor with multiple metastases and a novel karyotype. Detecting characteristic cytogenetic alterations in these tumors is important because they might serve as an aid in diagnosis or therapy.

**Retroperitoneal Fibrosis Associated With Widely Disseminated Anaplastic Large Cell Lymphoma Identified at Autopsy**

(Poster No. 52)

Suntrea Hammer, MD (sugoudaeu@med.umich.edu); Megan S. Lim, MD, PhD. Department of Pathology, University of Michigan Health System, Ann Arbor.

Retroperitoneal fibrosis is a fibroinflammatory condition involving the abdominal aorta, iliac vessels, and ureters. This rare phenomenon, with an incidence of 0.1 cases per 100,000 people, carries a strong correlation with the autoimmune condition such as scleroderma, systemic sclerosis, systemic lupus erythematosus, primary sclerosing cholangitis, Reidel thyroiditis, autoimmune pancreatitis, and orbital pseudotumor. Most cases are idiopathic; however, as many as one-third of cases can be attributed to a secondary cause. We present a case of secondary retroperitoneal fibrosis arising in a 29-year-old woman with anaplastic large cell lymphoma identified at autopsy. The patient presented with a 2-month history of early satiety, abdominal discomfort, constipation, and progressive fatigue. Abdominal
magnetic resonance imaging revealed a peripancreatic soft-tissue mass, which on open biopsy revealed fibroadipose tissue with acute inflammation and fat necrosis. A bone marrow biopsy was unremarkable. Despite steroid therapy, the patient declined during the ensuing 8 months, experiencing failure to thrive and then death. At autopsy, diffuse fibrosis surrounded the abdominal aorta from the level of the renal arteries to the origin of the iliac vessels. The fibrosis encased the pancreas, bilateral ureters, and the inferior mesenteric artery. Histologic examination revealed a CD2/3/4/7/8/9/10/11/14/15/20/25/27/30/43-negative and CD30/ALK-1-positive infiltrate of large lymphoid cells with wreath-shaped nuclei infiltrating most organs and fibrotic areas. To our knowledge, this represents the first association between anaplastic large cell lymphoma and retroperitoneal fibrosis reported in the English literature. This case illustrates the importance of both patient demographics and adequate surgical sampling for patients with retroperitoneal fibrosis.

A Case and Review of Osseous Sarcoidosis of the Distal Clavicle and Proximal Humerus

(Poster No. 53)

Bryan Keenan, MD (bryan.keenan@med.navy.mil); Sean Hussey, MD. Department of Pathology, National Capitol Consortium, Bethesda, Maryland.

A 51-year-old white man with known pulmonary sarcoidosis presented with a 1-year history of right shoulder pain during strenuous activity. Plain radiographs of the right shoulder were unremarkable, but a magnetic resonance imaging study showed multiple low-intensity foci in his right proximal humerus, acromion, and distal clavicle. Shoulder arthroscopy with open distal clavicle excision was performed. Histologic evaluation of the right distal clavicle and right acromium revealed multiple noncaseating granulomas comprised of compact epithelioid histiocytes and multinucleated giant cells. Special stains for acid-fast bacilli and fungi were negative. Given the histologic findings, these lesions were consistent with osseous sarcoidosis. Bone involvement in patients with sarcoidosis can occur in up to 30% of cases and typically affects the vertebrae and bones of the hand and foot. Bone involvement is often asymmetrical and discovered incidentally by radiographic studies. Plain radiographs may fail to reveal the osseous lesions, and are identified on magnetic resonance scan or nuclear scintigraphy. Histologic evaluation of the involved bone established the diagnosis and demonstrated aggregates of epithelioid histiocytes, multinucleated giant cells, and macrophages surrounded by lymphocytes and fibroblasts with no evidence of caseating necrosis. In this patient, the clinical history, in conjunction with the radiographic and histologic findings, was consistent with osseous sarcoidosis limited to the distal clavicle and proximal humerus. This is a previously undocumented isolated osseous location for this disease.

Autoimmune Hemolytic Anemia After Small-Bowel Transplantation May Represent Graft Versus Host Disease

(Poster No. 54)

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After observing 2 cases of autoimmune hemolytic anemia after small-bowel transplants, we reviewed Transfusion Service records of all solid organ transplants during the prior 12 months for serologic evidence of autoimmune hemolytic anemia. Positive direct antiglobulin test results were identified for 3/21 patients with multiorgan transplants including small bowel, 0/90 patients with liver transplants, and 0/6 patients with kidney transplants (+/- pancreas). A 1-year-old boy with microvillus inclusion disease received liver, pancreas, and small-bowel transplants. On day 137 posttransplant, we observed a positive direct antiglobulin test (anti- IgG: 2+ /anti-C3d: 1+) and an eluate panagglutinin (hematocrit = 32.9%) for the first time. A 4-year-old boy with microvillus inclusion disease received small bowel, liver, pancreas, and spleen transplants. On day 141 posttransplant, we detected a positive direct antiglobulin test (anti-IgG: 3+ /anti-C3d: 1+) and an eluate panagglutinin (hematocrit = 28.0%) for the first time. These cases of autoimmune hemolytic anemia appear to distinguish small-bowel transplants from other solid organ transplants. In theory, all transplanted organs have the potential for expressing graft versus host disease by cellular and/or humoral immune mechanisms. However, the presence of a major site of the donor’s humoral immunity versus host disease by cellular and/or humoral immune mechanisms.

Utility of the Disseminated Intravascular Coagulation Scoring System by International Society on Thrombosis and Haemostasis in a Pediatric Setting

(Poster No. 56)

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The International Society on Thrombosis and Haemostasis (ISTH) has a scoring system in which a score of greater than or equal to 5 can determine the presence of disseminated intravascular coagulation (DIC). Five values are used: predisposing condition, prothrombin time, fibrinogen level, D-dimer, and platelet count. There have been a few studies on the accuracy of the ISTH system, but none have shown the scoring system’s utility in the pediatric population.

Design: We reviewed 2136 DIC panels and 25 autopsy reports in which DIC was suspected. The patients were monitored by using a panel of coagulation assays that included prothrombin time, activated partial thromboplastin time, fibrinogen levels, thrombin time, D-dimer, and platelet count. Difference in diagnosis was compared between the ISTH scoring system and our hospital by isolating data specific to ISTH criteria from the DIC panels and then entering it in the ISTH algorithms.

Results: Our hospital and ISTH showed 59.4% concordance for suspected DIC diagnosis. The autopsy reports confirmed that 96% of patients suspected of having DIC had DIC (Table). Three autopsy cases with significantly elevated prothrombin time, positive D-dimer, and low platelet

Comparison of Disseminated Intravascular Coagulation Scoring System by International Society on Thrombosis and Haemostasis in a Pediatric Setting

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<tr>
<th>Disseminated Intravascular Coagulation Panels</th>
<th>Autopsy Reports</th>
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<tr>
<td>Our Hospital, No. (%)</td>
<td>ISTH, No. (%)</td>
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<tr>
<td>Positive diagnosis</td>
<td>3167 (64)</td>
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<tr>
<td>Negative diagnosis</td>
<td>769 (36)</td>
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<tr>
<td>Total</td>
<td>2136 (100)</td>
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counts scored below a 5 under ISTH guidelines. The ISTH scoring system more closely represented D-dimer and platelet counts but underrepresented elevated prothrombin time and higher levels of fibrinogen when indicating DIC. ISTH criteria suggest fibrinogen counts lower than 100 mg/dL are significant; however, these values are rarely seen in DIC cases at our hospital.

Conclusions: We recommend comparative analysis of all DIC-related assays until the ISTH system is revised.

Risk of Hemolytic Transfusion Reactions After Emergency Release Red Blood Cell Transfusion (Poster No. 57)

Pamela P. Goodell, MD (pgoodell@rics.mh.harvard.edu); Lynne Uhl, MD; Mostafa T. Mobbly, MD, MS(ASCP); SBB; Amy Powers, MD, Department of Pathology, Division of Laboratory and Transfusion Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Context: Patients requiring urgent red cell blood (RBC) transfusion may receive one by using emergency release (ER) RBCs before completion of routine blood bank testing. To avoid ABO-incompatible hemolytic transfusion reactions (HTRs), group O RBCs are typically issued. Identification of alloantibodies to other clinically significant RBC antigens requires performance of an antibody screen, and ER of RBCs before completion of the screen places the recipient at risk for HTRs due to non-ABO alloantibodies. We performed a retrospective review of ER RBC transfusion recipients to determine the likelihood of prior alloimmunization in this population and risk of HTRs after ER transfusion.

Design: We reviewed ER RBC transfusions performed during a 2-year period at a tertiary medical center. Data collected included recipient demographics, ER indication, number of units, and blood bank laboratory and clinic data.

Results: In total, 1002 ER RBC transfusions involving 265 ER episodes (262 recipients) were analyzed. A positive antibody screen was found upon completion of testing in 29 episodes (10.9%). Clinically, significant antibodies were identified in 17/29 (6.4%) ER episodes. The remaining seven recipients with clinically significant alloantibodies received a transfusion, with a total of 15 antigen-incompatible units. One incompatible unit resulted in a clinically apparent HTR due to anti-c.

Conclusions: Transfusion of ER RBCs before completion of routine blood bank testing carries a low but real risk of non-ABO alloantibody-mediated HTRs (0.4% of ER episodes) and receipt of antigen-incompatible RBCs (2.6% of ER episodes).

Management of Membranoproliferative Glomerulonephritis Type II—Related Complement-Mediated Glomerular Injury With Plasmapheresis Postrenal Transplant (Poster No. 58)

Christina M. Bagby, DO1 (christina.Bagby@UHospitals.org); Joshua J. Augustine, MD2; Greta H. Jacobs, MD; Katharine A. Downes, MD1. Departments of Pathology and Nephrology, University Hospitals Case Medical Center, Cleveland, Ohio.

Membranoproliferative glomerulonephritis type II (MPGN II) is a rare kidney disease that is characterized by ribbonlike electron-dense deposition within the glomerular basement membrane. More than 80% of patients with MPGN II have circulating C3 nephritic factor (C3NF), an autoantibody directed against the C3dβb convertase involved in the complement cascade. We present the case of a 36-year-old man who was diagnosed with MPGN II at age 16 and who had bilateral native nephrectomies and a failed cadaveric renal transplant because of rapid recurrence of disease. After 17 years of dialysis, he received a second cadaveric renal transplant in October 2008 and required dialysis for persistent oliguria (>100 cc/d) posttransplant. Ten days posttransplant, a renal biopsy revealed abnormal C3 immunofluorescent staining, which was suggestive of early recurrence of MPGN II; however, electron-dense deposition was not seen. High levels of C3NF were detected, and plasmapheresis (PE) was initiated for possible removal of this autoantibody.

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was 46%. A negative EIA predicted a negative SRA with 96% accuracy. The average OD per stratum was correlated with the percentage of positive SRA results ($r^2 = 0.991$). However, the percentage of agreement between positive EIA and positive SRA ranged from only 7% to 67%, depending on the OD stratum (Figure 64).

**Conclusions:** As used clinically in our setting, the OD of the EIA correlates with the percentage of positive SRA results. However, the degree of correlation is not sufficient enough to override clinical judgment when an SRA is felt to be indicated.

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**Nurse Issue of Red Blood Cell Units Remotely Stored at a Level I Trauma Center Emergency Room Is Safe and Clinically Effective**

(Yoshiyuki Kikuchi, DO; Michael Craun, MD; Walter Linz, MD, MBA; Departments of Pathology and Trauma and Critical Care Surgery, Scott and White and Texas A&M Health Science Center College of Medicine, Temple, Texas.

**Context:** At our level I trauma center, red blood cell (RBC) units have been previously issued exclusively from the blood bank by medical technology staff. However, our emergency department (ED) recently relocated and is now at a substantial distance from the blood bank. As a result, there is now an approximately 15-minute emergency-release RBC transport time. We hypothesized that RBCs properly stored in the ED would be both appropriately used and safely issued by the ED nursing staff.

**Design:** We purchased a small blood bank refrigerator and a remote monitoring system that was controlled by the blood bank for the ED. The transfusion service created standard operating procedures for nurse issue of uncrossmatched RBCs. The ED charge nurses were given extensive training in the proper issue and handling of blood products, including training regarding cyclic guanosine monophosphate. Quality and utilization parameters were monitored for all activations.

**Results:** During the first 6 months, the ED’s refrigerator was activated 29 times. The patients ranged in age from 17 to 88 years. All activations were for serious injuries and/or acute medical blood loss. The injury severity score ranged from 8 to 50. All activations were considered appropriate. To date, we have documented 3 minor occurrences. No issue errors or product loss were recorded, and the blood supply was continuously monitored.

**Conclusions:** Emergency release RBCs stored at a remote location can be safely issued by nursing staff, thus eliminating unnecessary blood transit time and improving the potential for benefit from transfusion therapy.

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**Increase in Likelihood of Donating Blood After Being Offered a Topical Anesthetic**

(Kyle M. Watanabe, MPH (kylewatanabe@hotmail.com); Jeffery Jay, RN, MPH; Christopher Alicko, RA; Loren G. Yamamoto, MD, MPH, MBA. Department of Pediatrics, University of Hawaii, John A. Burns School of Medicine, Honolulu.

**Context:** Because pain experienced during blood donation is likely to deter individuals from donating blood, we used a survey to study the potential increase in likelihood of participants donating blood when presented with the option of a topical anesthetic cream before donation.

**Design:** During a 3-month period, 316 adults (convenience sample) completed a 1-page survey consisting of 12 questions regarding blood donation in which they were asked about their likelihood of donating blood in the near future (no possibility, possible, likely, certain). They were then informed about the possibility of using a topical anesthetic cream before donation. Subsequently, their likelihood of donating blood was reassessed. Data were analyzed by using Epi-Info version 3.3.2.

**Results:** Fifty of 316 subjects (16%) reported an increased likelihood of donating blood when offered a topical anesthetic ($P < .001$). Of these 50 respondents, 11 increased their likelihood by 2 or more categories. Among 169 participants who never donated blood, 34 (20%) increased their likelihood of donating blood after being told about the topical anesthetic cream, and 16 of 147 subjects (10%) who had previously donated blood increased their likelihood of donating blood after being told about the topical anesthetic cream ($P = .02$).

**Conclusions:** In this study, offering a topical anesthetic cream had a positive effect on the likelihood of participants donating blood. This increase in likelihood was greatest among those who had never donated blood before.

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**Prospective Review Improves Compliance for Blood Component Transfusion**

(Christina M. Mancini-Flegel, BS (cmancin1@jhmi.edu); Bonnie K. Hammond, BS; Stanley J. Podlasek, MD. Department of Pathology, Johns Hopkins University, Baltimore, Maryland.

**Context:** Life-saving blood component therapy still has residual risk of immune reactions, clerical accidents, mechanical or thermal damage to components, and transmission of infectious contaminants. Despite vast improvements in transfusion safety, clinicians must weigh benefits against these risks. To assure best practice, protocols have been implemented, and blood transfusions have been reviewed retrospectively on the basis of well-established transfusion indications.

**Design:** We hypothesized that prospective review of transfusion indications would lead to improved compliance with protocols in comparison to retrospective review. Indications for packed red blood cells, frozen plasma, apheresis platelets, and cryoprecipitate were simplified and adjusted to comply with former transfusion indications at Howard County General Hospital and The Johns Hopkins Hospital. We collected data on retrospective compliance by medical chart review from a representative sample of blood transfused in 2007–2008. For prospective review, the same indication criteria for each blood component were displayed as choices on a physician order sheet, which was completed by the ordering physician and was sent to blood bank before blood was issued. Prospective review was introduced in September 2008.

**Results:** Prospective blood review demonstrated 194/194 (100%) compliance with the transfusion protocol indication criteria. In contrast, retrospective blood review showed that 36/39 (92.3%) of blood components transfused in 2008 and 142/146 (97.3%) of blood components transfused in 2007 successfully met the protocol criteria.

**Conclusions:** Prospective blood review gives better compliance with transfusion indications than does retrospective blood review. American Association of Blood Banks designated our procedure as a commendable practice.

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**Burkitt Lymphoma Mimicking Thrombotic Thrombocytopenic Purpura in a Woman With Postpartum Gigantomastia**

(Smita Krishnamurthy, MD (skrishnamurthy@path.wustl.edu); Nina Wagner-Johnston, MD; Charles Eby, MD. Departments of Pathology, Internal Medicine, and Clinical Pathology, Washington University in St Louis, Missouri.

A 35-year-old gravida 1, para 1 woman with a medical history of migraines presented 10 days postpartum with unexplained thrombocytopenia, anemia, and elevated levels of hepatic transaminases. Her pregnancy was complicated during the third trimester by preeclampsia and progressive breast enlargement attributed to gigantomastia. Physical examination revealed bilateral massive breast enlargement with prominent purple discoloration and exquisite tenderness requiring narcotic analgesia. Breast ultrasonography showed no hemorrhage or other abnormality. Peripheral blood smear was nonspecific, with 1 to 2 possible schistocytes/high-power field, markedly diminished platelets, and no abnormal or im-

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mature leukocytes. A few days into the hospitalization, she developed mild confusion, headaches that were not consistent with her previous migraines, and left facial numbness. The initial differential diagnosis was HELLP syndrome versus postpartum thrombotic thrombocytopenia purpura. Her platelet count continued to decline after 3 daily 1.5-volume plasma exchanges with fresh frozen plasma. Given her worsening symptoms, lack of response to plasma exchange, low reticulocyte count in the presence of anemia, and return of a normal ADAMTS13 activity, bone marrow biopsy and aspirate were performed, with findings diagnostic of Burkitt lymphoma. Chemotherapy was begun with rapid diminishment of breast enlargement. This case illustrates the importance of having a high index of suspicion in diagnosing these rare cases. The role of plasma exchange is not clearly established for atypical HELLP. However, since the differential diagnosis of HELLP in the postpartum period includes thrombotic thrombocytopenia purpura, plasma exchange may have a role in these cases, especially when thrombocytopenia lasts more than 3 days postpartum.

Familial Combined Factor V and Factor VIII Deficiencies
(Poster No. 65)

Michael E Sinnott, MB, BCh, BA; (sinnottm@ccf.org); Michael Levian, MD; Andrew E. Schade, MD, PhD. Departments of Clinical Pathology and Pediatric Hematology and Oncology, Cleveland Clinic, Cleveland, Ohio.

A 6-year-old girl presented with minor head trauma with bleeding that responded to intravenous desmopressin. She bruised easily but had no complaints of epistaxis or mucosal bleeding. No other bleeding problems were noted; she had never had surgery. Testing revealed a prothrombin time of 15.6 seconds, an international normalized ratio of 1.4, and an activated partial thromboplastin time of 64.1 seconds. Further workup for the prolonged activated partial thromboplastin time revealed a corrected mixing study. Factor assays were significant for a factor VIII level of 12% and a factor V level of 13%. Other factors were within normal reference ranges. Her 4-year-old sister had a history of easy bruising but no significant bleeding history. Testing revealed a prothrombin time of 17.0 seconds, an international normalized ratio of 1.5, and an activated partial thromboplastin time of 78.4 seconds. This girl’s mixing studies corrected with normal plasma and factor assays were significant for a factor VIII level of 6% and a factor V level of 8%; other factors were normal. Low factor VIII levels in females may indicate a rare hemophilia A, which is caused by a particular lyonization or a carrier mother and affected father, resulting in a homozygous state. Type 2N von Willebrand disease is a consideration. The prolonged prothrombin time suggested a possible defect in the common pathway as well. Combined factor V and VIII deficiencies are a rare autosomal recessive bleeding disorder that is associated with plasma levels of coagulation factors V and VIII that are approximately 5%–30% of normal.

Applications of Sanctions by the Centers for Medicare and Medicaid Services and Accrediting Organizations for Proficiency Testing Failure: A 7-Year Study
(Poster No. 66)

Amy B. Karger, MD, PhD (karger026@umn.edu); Anthony A. Killeen, MD, PhD, FACP. Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota.

Context: Proficiency testing (PT) is a requirement for laboratories that hold certificates for nonwaived testing under the Clinical Laboratory Improvement Amendments of 1988. There has been little published analysis regarding sanctions levied against laboratories with unsuccessful PT performance.

Design: Data from the Laboratory Registry, which are published annually by the Centers for Medicare and Medicaid Services (CMS), were examined for a 7-year period (2001–2007) to determine the incidence of sanctions by CMS or an accrediting organization for unsuccessful PT performance. We reviewed the type of sanctions that were imposed on laboratories that failed PT. In addition, the current certification status of these laboratories was determined by searching the CMS Laboratory Demographic Information Report database.

Results: During the period examined, 272 laboratories were sanctioned for unsuccessful PT performance. Of these laboratories, 67% received a principal sanction, the most severe penalty imposed by CMS. Of the laboratories receiving a principal sanction, 24% are no longer operating. Of the laboratories that received a sanction, 63% now have a Certificate of Waiver. PT failures have increased in recent years, and most laboratories cited were penalized with a principal sanction.

Conclusions: Most laboratories that failed PT received a principal sanction, most are currently operating with CMS Certificates of Compliance or Accreditation. Therefore, most laboratories took the required corrective actions to regain a CLIA Certificate of Operation. Further investigation is needed to determine whether the increasing application of sanctions is the result of deteriorating laboratory performance in PT or increased enforcement by CMS or accrediting agencies.

POSTER SESSION 500: TUESDAY, OCTOBER 13, 2009, 7:00 AM–9:30 AM

Cytology; Dermatopathology; Neuropathology; Practice Management; Cardiovascular Pathology

Fine-Needle Aspiration Biopsy of Salivary Gland Lesions: Comparing On-Site Rapid Interpretation With the Final Cytologic Diagnosis
(Poster No. 1)

Ami Bhalodia, MD (abhalo@lsuhsc.edu); Jessica Bagby, BS; Fleurette Abreo, MD; Songlin Zhang, MD, PhD. Department of Pathology, Louisiana State University Health Sciences Center, Shreveport.

Context: Fine-needle aspiration biopsy (FNAB) has been used for evaluation of salivary gland lesions during the past several decades, and FNAB has been documented to have very good sensitivity and accuracy for differentiating neoplastic lesions from reactive processes. Most FNABs were performed in outpatient clinics by clinicians without on-site rapid interpretation, so the accuracy and efficiency of on-site rapid interpretation has not been documented in the literature.

Design: We searched our cytology files from 2003 to 2007 for salivary gland aspiration and the corresponding surgical resection reports. The on-site rapid interpretation, the final cytologic diagnosis, and the corresponding histology diagnosis were compared.

Results: One hundred ninety-nine salivary gland FNABs were performed during the 5-year period; 94 cases had surgical resection follow-up (49.5%). A total of 168 cases had on-site cytology evaluation (88.4%), 159 cases had on-site rapid diagnosis, and 9 cases were deferred for permanent diagnosis (deferring rate 5.4%). One hundred forty-one (88.7%) cases had the same on-site and final diagnosis, and 18 (11.3%) cases had variable-degree differences. Thirteen cases were upgraded, and 5 cases were downgraded in final diagnosis. Eleven of the 18 cases had surgical follow-up, and final diagnosis was confirmed in 9 cases.

Conclusions: On-site rapid interpretation has a high (88.7%) diagnosis agreement with final cytology diagnosis, and only a few cases (5.4%) were deferred for the permanent diagnosis. We encourage providing on-site rapid interpretation, and the advantage of on-site cytology evaluation includes decreasing patient’s anxiety and waiting time, providing training opportunity for pathology residents/fellows, and increasing interaction and trust between pathologists and clinicians.

Deletion of 9p21 Is a Rare Finding in Urine Specimens Collected From Patients With a History of Hematuria and Bladder Cancer
(Poster No. 2)

Junqi Qian, MD; Milliani Medina, MS; Karen Crewell, MS; Deena Weber, MS; Deloar Hossain, MD; David G. Bostwick, MD, MBA (mmdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

Context: Fluorescence in situ hybridization (FISH) of voided urine is a sensitive and specific test for the detection of urothelial carcinoma. Common FISH testing consists of 4 DNA probes to chromosomes 3, 7, and 17 and to band 9p21. We sought to determine the incidence of these chromosomal anomalies in urine specimens because their patterns are not well documented.

Design: Urine samples from 13284 patients with a history of hematuria and/or bladder cancer were studied. FISH was performed using probes to chromosomes 3, 7, and 17 and to band 9p21; cytology was also performed.

Results: The FISH positive rate was 5.7% (691 of 12 163) of the samples sufficient for FISH. Gains of chromosomes 3 and 7 (56.5%), 7 and 17 (51.6%), and 3 and 17 (36.9%) were most frequent. Deletion of 9p21 was observed in 12% of cases; however, only 1% was more sensitive than cytology for the detection of urothelial carcinoma (77.4% vs 53.5%, respectively; P < .05), but specificity was nearly equal (68% vs 71.6%, respectively; P > .05).

Conclusions: Gains of chromosomes 3 and 7 were the most common anomalies detected, whereas deletions of 9p21 only was rare and never seen in isolation. FISH was significantly more sensitive than cytology for the detection of urothelial carcinoma with equivalent specificity.
Primary Intrathyroid Paraganglioma Mimicking Hürthle Cell Neoplasm on Fine-Needle Aspiration Cytology: Unique Cytomorphologic Presentation in a Rare Entity (Poster No. 3)

Arvind Rishi, MBBS (arishti@nshs.edu); Yan Shi, MD, PhD; Patricia Wasserman, MD. Department of Pathology, North Shore Long Island Jewish Health System, New Hyde Park, New York.

Primary intrathyroid paraganglioma of thyroid is extremely rare and offers significant diagnostic challenges on fine-needle aspiration cytology (FNAC). Cytologic features are diverse, and important differential diagnosis includes Hürthle cell neoplasm, paraganglioma-like medullary carcinoma, hyalinizing trabecular adenoma, follicular carcinoma, parathyroid gland lesions, and carcinoid tumor. We report an unusual case of primary intrathyroid paraganglioma, mimicking Hürthle cell neoplasm on FNAC, in a 21-year-old euthyroid woman presenting with a solitary left thyroid nodule. Cytology showed moderately cellular specimen composed of polygonal, round to spindle cells with moderate amounts of amphophilic finely granular cytoplasm, focal intracytoplasmic vacuoles, eccentrically located nuclei with mild nuclear pleomorphism, and conspicuous eosinophilic nuclei. FNAC was suggestive of Hürthle cell neoplasm. Histology on partial thyroidectomy specimen showed nests of polygonal to round cells arranged in a characteristic “zellballen” neuroendocrine pattern. Mitosis, necrosis, or capsular infiltration was absent. The tumor cells were immunopositive for CD56, chromogranin and synaptophysin, and immunonegative for TTF-1 and calcitonin. S100 protein immunopositive tumor cells were immunopositive for CD56, chromogranin and synaptophysin. Mitosis, necrosis, or capsular infiltration was absent. The low-power examination revealed many dyshesive to loose clusters of cells with metaplastic features and apparent high nuclear to cytoplasmic ratios. However, at high-power, many of these cells demonstrated bichromatic logic presentation on FNAC of this rare entity. Based on our experience and literature review, the most helpful cytomorphologic features for differential diagnosis include the color of cytoplasmic granules, intracytoplasmic vacuoles, admixed spindle cells, and background of bare nuclei (Table). Also discussed are the other cytomorphologic features reported in primary thyroid paraganglioma and the diagnostic pitfalls of paraganglioma in all body sites.

Cytologic Features of Hailey-Hailey Disease in an Anal ThinPrep: Pitfalls in the Diagnosis of Squamous Intraepithelial Lesions in Liquid-Based Cytology Specimens (Poster No. 4)

Sarah E. Frost, MD1 (sarah.frost@msmss.edu); Marie A. Ramer, DDS2; Jeffrey S. Freed, MD2; Arnold H. Szporn, MD1. Departments of 1Pathology and 2Surgery, The Mount Sinai School of Medicine, New York.

Pemphigus has long been known as a pitfall in the diagnosis of squamous intraepithelial lesions arising in squamous mucosa, but its presentation in liquid-based cytologic preparations is not well described. Hailey-Hailey disease (benign familial chronic pemphigus) is a rare, dominantly inherited dermatosis not previously described in the cytology literature. We present the case of a 56-year-old woman with a known personal and family history of Hailey-Hailey disease and previous high-risk human papilloma virus–positive tests who was diagnosed by another laboratory as having a “high-grade squamous intraepithelial lesion with gland involvement” in an anal ThinPrep. We received for review one Papanicolaou-stained ThinPrep slide originally prepared from an anal brushing. Low-power examination revealed many dysesive to loose clusters of cells with metaplastic features and apparent high nuclear to cytoplasmic ratios. However, at high-power, many of these cells demonstrated bichromatic logic presentation on FNAC of this rare entity. Based on our experience and literature review, the most helpful cytomorphologic features for differential diagnosis include the color of cytoplasmic granules, intracytoplasmic vacuoles, admixed spindle cells, and background of bare nuclei (Table). Also discussed are the other cytomorphologic features reported in primary thyroid paraganglioma and the diagnostic pitfalls of paraganglioma in all body sites.
Conclusions: Although AGCTs and JGCTs show many similarities, CEBs and grooves are only seen in AGCTs. Cellular atypia is more striking in JGCT than AGCTs (REC or NREC). Careful evaluation is necessary when examining fluids because tumor cells of AGCTs can be easily overlooked. Our series suggests that AGCTs with cytoplasmic vacuoles, PN, increased mitoses, and necrosis correspond to clinically aggressive behavior and should, therefore, be conveyed in cytology reports of ovarian tumors.

Endoscopic Ultrasound-Guided Fine-Needle Aspiration of Pancreatic Mucinous Neoplasm: Diagnostic Accuracy and Pitfalls

Ilike Nalbantoglu, MD1 (inanalbantoglu@yahoo.com); Mohammad Bara- wi, MD2; Basim M. Al-Khafaji, MD1 Departments of ‘Pathology and ‘Internal Medicine, St. John Hospital and Medical Center, Detroit, Michigan.

Context: Pancreatic mucinous neoplasms (PMNs) are rare tumors, characterized by a mucin-producing epithelium, which includes intraductal papillary-mucinous neoplasm, mucinous cystic neoplasms, and mucinous adenocarcinoma. Most PMNs are evaluated with endoscopic ultrasound-guided fine-needle aspiration (EUFNA). The diagnostic accuracy of the cytomorphologic criteria of PMNs is evaluated.

Design: Our institution’s files from January 2003 to March 2009 were reviewed to identify EUFNA of PMN. Two independent reviewers evaluated the cytologic features: background, cellularity, and nuclear and cytoplasmic features, noting the corresponding histologic diagnosis and/or clinical follow-up when available.

Results: Four hundred sixty FNAs of pancreatic lesions were identified, 25 had a cytologic diagnosis of PMN, all obtained by EUFNA, and 13 had a histologic diagnosis. Patients’ age ranged between 33 and 80 (average 58), including 6 women and 7 men. There were 10 true-positive (6 PMNs, 2 ductal adenocarcinomas, 1 adenoma with high-grade dysplasia, and 1 metastatic renal cell carcinoma), and 2 false-positives (chronic pancreatitis). True-positive cases showed a thin mucinous background in all 10, whereas 3 had areas of thick mucin. Most (9 of 10; 90%) were moderately to densely cellular. However, review of the 2 false-positives showed similar features, except for the lack of thick mucin, epithelial sheets of cells, and increased cellularity.

Conclusion: The presence of a thin/thick mucinous background, honeycomb sheets, and increased cellularity would raise the possibility of a PMN. Samples obtained by EUFNA were adequate in reaching a cytologic diagnosis. Additional studies are suggested to identify further cytologic criteria to differentiate false-positive cases.

Follow-up Biopsy Results for Women 30 Years and Older With LSIL

HPV/HP-16 2–3, CIN 1, No. (%) HPV/CIN 2, No. (%) Negative, No. (%) No HPV, No. (%)

Positive 1 (0.9) 12 (10.9) 15 (13.6) 62 (57.4)
Negative 0 (0.0) 12 (10.9) 14 (12.8) 79 (72.7)
Not done 9 (7.6) 34 (30.9) 16 (14.8) 157 (142.7)
Total 2 (1.7) 61 (53.9) 45 (41.0) 293 (268.7)

Conclusions: Among women 30 years and older with LSIL PT, those known to be HPV-negative have a much higher likelihood of harboring high-grade dysplasia. Our study suggests that HR-HPV testing may be useful for colposcopy triage of LSIL in women 30 years and older; the HR-HPV positive rate is relatively low in this age group, and few women with high-grade dysplasia are HPV-negative.

C-MYC Protein Is a Useful New Diagnostic Marker for Prostate Cancer

Michael J. Thrall, MD (mjthrall@tmhs.org); Debbie A. Smith, CT(ASCP); Dina R. Mody, MD. Department of Pathology, The Methodist Hospital, Houston, Tex.

Context: High-risk human papillomavirus (HR-HPV) testing for colposcopy triage of the Papanicolaou test (PT) category of low-grade squamous intraepithelial lesion (LSIL) is not cost effective in young women because of high positive rates (~80%). It remains unclear whether HR-HPV may be a useful test for triage of older women.

Design: We compiled HR-HPV data for women aged 30 years and older with LSIL who were seen in clinics requesting adjunctive HR-HPV testing from April 1, 2006, to March 31, 2008. Follow-up cervical biopsy information was collected for the period April 1, 2006, to August 15, 2008. The annual PT volume for the clinics used in this study is about 30,000. Dysplasia clinics were excluded. HR-HPV tests were ordered either adjunc-tively or for reflex testing of a different PT. We used the Hybrid Capture 2 test performed on residual material from liquid-based PT (98% ThinPrep, 2% SurePath).

Results: Women positive for HR-HPV had a significantly greater likelihood of high-grade dysplasia than women who were HR-HPV negative (P < .01) or who were not tested (P = .01; Table). The overall HR-HPV positive rate in women aged 30 years and older with LSIL was 56.7%. The ages of the HR-HPV positive women (mean, 43.4; median, 41.3) were similar to the untested women (mean, 43.4; median, 41.9).

Reconsidering Human Papillomavirus Triage for Low-Grade Squamous Intraepithelial Lesion in Women Older Than 30 Years

(POSTER No. 7)

Meena S. Parab, MD (meenaparab1@hotmail.com); Daniza Mandich, MS; Richard W. Cartum, PhD; Saverio Ligato, MD. Department of Pathology, Hartford Hospital, Hartford, Connecticut.

Context: Human papillomavirus (HPV) triage for low-grade squamous intraepithelial lesions (LSIL) is not cost-effective in women younger than 30 years of age because of high positive rates (~80%). However, it is unclear whether HPV testing for women older than 30 years is a useful triage test.

Design: We compiled HPV testing data for women aged 30 years and older with LSIL who were seen in clinics requesting adjunctive HPV testing from April 1, 2006, to March 31, 2008. Follow-up cervical biopsy information was collected for the period April 1, 2006, to August 15, 2008. The annual PT volume for the clinics used in this study is about 30,000. Dysplasia clinics were excluded. HPV tests were ordered either adjuc-tively or for reflex testing of a different PT. We used the Hybrid Capture 2 test performed on residual material from liquid-based PT (98% ThinPrep, 2% SurePath).

Results: Women positive for HPV had a significantly greater likelihood of high-grade dysplasia than women who were HPV negative (P < .01) or who were not tested (P = .01; Table). The overall HPV positive rate in women aged 30 years and older with LSIL was 56.7%. The ages of the HPV positive women (mean, 43.4; median, 41.3) were similar to the untested women (mean, 43.4; median, 41.9).
Biliary brush cytology is an important diagnostic tool in the evaluation of patients with bile duct strictures. In this study, we evaluated the immunocytochemical expression of insulin-like growth factor (IGF) mRNA-binding protein 3 (IMP3), also known as h-khomology domain containing protein overexpressed in cancer (KOC/L125S), to assess the performance of this marker for the detection of malignant cells in bile duct-brushing specimens.

Design: Sixty-four patients who underwent endoscopic retrograde cannulation of the pancreatic duct and bile duct brushing for bile duct stricture were studied. Diagnoses were 37 cases negative for malignancy; 14 cases atypical, not diagnostic for malignancy; and 13 cases suspicious/positive for malignancy. Alcohol-fixed, Papanicolaou test–stained slides were immunostained with monoclonal antibody to IMP3 (Dako). Results were recorded as negative (<5% cells positive) or positive (>5% cells positive). The atypical, not diagnostic cytology cases were considered negative for statistical analysis.

Results: Thirty-nine of the 64 patients were diagnosed with malignancy based on biopsy, fine-needle aspiration, or clinical progression of disease. The sensitivity of routine cytology for the detection of malignancy was 33.3% (13 of 39), immunocytochemical-IMP3 expression was 61.4% (25 of 39), and the combined sensitivity was 71.8% (28 of 39) (P < .001). The specificity of both tests was 100%.

Conclusions: Our study shows that IMP3 improves significantly the sensitivity of routine cytology for the detection of malignancy in bile duct specimens. The combined use of biliary brushing cytology and IMP3 provides the highest yield for diagnosing malignancy in the pancreatobiliary system.

Quantification of Atypical Squamous Cells of Undetermined Significance (ASC-US) on ThinPrep and SurePath Papanicolaou Tests: Is Total Number of ASC-US Cells/Clusters per Slide or One ASC-US Cell/Cluster Significant? (Poster No. 10)

Ognjen Kosarac, MD1 (okosarac@mhhs.org); Debora A. Smith, CT(ASCP)2; Hidehiro Takei, MD1, Dina R. Modly, MD2; Department of Pathology, The Methodist Hospital, Houston, Texas; 2Department of Pathology, Weil Cornell Medical College, Houston.

Context: Few reports are available on a quantitative analysis of atypical squamous cells of undetermined significance (ASC-US) on Papanicolaou (Pap) tests.

Design: ASC-US Pap tests were compared for the mean of ASC-US cells/clusters (c/c) per slide and cases with only one ASC-US c/c between the following groups: age, high-risk (HR) human papillomavirus (HPV) status, presence (+) versus absence (−) of bacterial vaginosis, Candida, and inflammation, and ThinPrep versus SurePath Pap methods.

Results: ASC-US cases (184 cases; mean, 40.9 y/o) consisted of 138 ThinPrep and 46 SurePath Pap tests. Forty-seven (25.6%; mean, 33.5 y/o) and 138 (mean, 43.5 y/o) c/c were HR-HPV+ and HR-HPV−, respectively. Bacterial vaginosis, Candida, and inflammation were present in 37 (20.1%), 20 (10.8%), and 121 (65.7%) cases, respectively. The total number of ASC-US c/c per slide was 2.5 on average (range, 1–14) with no significant association with HR-HPV status, presence or absence of microorganisms, or inflammation. ASC-US c/c were significantly more present on ThinPrep slides (average, 2.8) than on SurePath slides (average, 1.6) (P = .001). Results of ASC-US cases with one c/c per slide are summarized in the Table.

<table>
<thead>
<tr>
<th>Analysis of Number of Cases With One ASC-US Cell/Cluster Per Slide</th>
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<tbody>
<tr>
<td><strong>No. of Cases With</strong></td>
</tr>
<tr>
<td>Total, n = 184</td>
</tr>
<tr>
<td>&gt;30 y, n = 138</td>
</tr>
<tr>
<td>≤30 y, n = 46</td>
</tr>
<tr>
<td>SurePath, n = 46</td>
</tr>
<tr>
<td>ThinPrep, n = 138</td>
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</tbody>
</table>

Abbreviations: ASC-US, atypical squamous cells of undetermined significance; PPV, positive predictive value for HR-HPV+ tests.

Conclusions: Quantification of ASC-US c/c had no correlation with HR-HPV status, bacterial vaginosis, Candida, or inflammation. One c/c of ASC-US cases were associated significantly more often with HR-HPV status, patients age older than 30 years, and the SurePath method. Given the high PPV for HR-HPV+ status, one ASC-US c/c is clinically significant, particularly in patients who are 30 years old or younger.

Type-Specific Human Papilloma Virus Testing on Liquid-Based Cytology Samples in Routine Clinical Practice (Poster No. 11)

Brian J. Sutton, MD; Jennifer Laudadio, MD (jlaudadi@wubmc.edu), Department of Pathology, Wake Forest University, Winston-Salem, North Carolina.

Context: Routine type-specific human papilloma virus (HPV) testing, as opposed to pooled high-risk detection, can be useful in monitoring the persistence of HPV infections and is increasingly important for patient management. The purpose of this study is to determine the positivity rate, type-specific prevalence, and number of persistent HPV infections detected in routine clinical testing of cytology samples.

Design: DNA extracted from liquid-based cytology samples was amplified using consensus HPV primers. Positive samples were typed by restriction enzyme digestion. HPV test results were retrospectively correlated with cytopathologic diagnosis, biopsy result, and prior Papanicolaou test result.

Results: During a 10-month period, 765 HPV tests were performed on cytology samples from 747 patients aged 14 to 85 years. Of the 765 HPV tests, 377 (49.3%) were positive: 273 high risk (72.4%), 52 low risk (13.8%), and 52 unclassified risk (13.8%). HPV positivity rate was 51.6% in atypical squamous cells of undetermined significance (ASC-US) cases versus 21.8% in cytology-negative cases (P < .001). Almost 65% (64.9%) of patients younger than 30 years old were positive for HPV compared with 35.9% of patients 30 years old and older (P < .001). Overall, 35 different HPV types were detected with types 16 and 52 being most common; 279 single-type HPV infections were detected. Twenty-eight persistent infections, 27 of which were high risk, were identified with corresponding dysplasia on 50% of the available biopsies.

Conclusions: Of cytology samples routinely sent for HPV testing, 49% were positive, with HPV types 16 and 52 being the most common; 28 persistent infections were identified.

Cytologic Analysis of Residual Fixative From Prostate Biopsy Vials (Poster No. 12)

Deenar Hossain, MD; Harpreet Singh, MS; Suman Banerjee, MD; Junqi Qian, MD; David G. Bostwick, MD, MBA (mmcdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

Context: Malignant cells may be shed into the transport media from prostate biopsy specimens, and cytopathologic evaluation may increase the cancer yield. We studied the yield of cytologic examination of residual-trans- port fixative in prostate biopsy vials.

Design: Prostate biopsies were routinely collected and processed from 64 previously untreated patients, in vials containing StatFix (BBC Biochemical, Seattle, Washington), an alcoholic/formalin fixative. All residual-transport fixative in vials from the left and right sides were separately pooled and processed through cytospin centrifugation and acid hematoxylin staining, creating 2 slides per case. Two cytopathologists, blinded as to biopsy findings, evaluated the cytology slides, and results were correlated with the biopsy findings. Triple stains (34BE12, p63, and racemase) were used in all cases with atypical cytologic findings.

Results: In total, 25 of 64 patients (39%) were diagnosed with prostate cancer on routine biopsy review by pathologists; 14 had unilateral cancer, and 11 had bilateral cancer. An additional 6 cases (9.4%) had high-grade prostatic intraepithelial neoplasia (PIN) and/or atypical small acinar proliferation (ASAP) suspicious for cancer, and 33 cases (51.6%) were benign. Cellularity in the cytologic preparations was invariably low. After triple stain, 8 of 64 cytologic cases (12.5%) had at least 1 of 2 slides diagnosed as abnormal (at least suspicious for malignancy). Correlation with biopsy findings (assuming PIN and cancer findings are positive) revealed sensitivity of 16.6% and specificity of 100%, with a false-positive rate of 0%.

Conclusions: Cytologic analysis of residual fixative from prostate biopsy vials has 100% specificity and 0% false-positive rate for the detection of prostate cancer.

Fine-Needle Aspiration Biopsy of Thyroid Nodules in the Pediatric Population: A 10-Year Experience (Poster No. 13)

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MD. Department of Pathology, North Shore/Long Island Jewish Medical Center, Glen Oaks, New York.

Context: Thyroid nodules are uncommon in the pediatric population, and the prevalence of malignancy is higher than in adults. The clinicopathologic studies in the pediatric population are limited. The National Cancer Institute (NCI) recently published a 6-tier thyroid fine-needle aspiration (FNA) classification scheme for cytologic diagnosis of thyroid lesions. The purpose of the present study was to analyze our thyroid FNA experience in the pediatric population.

Design: Thyroid FNA performed in patients younger than 21 years from January 1998 through December 2008 were retrieved retrospectively. The cytologic diagnoses were classified according to the new NCI diagnostic categories, and clinical follow-up information was reviewed.

Results: From 1998 to 2008, 11,718 cases of thyroid FNA were received. One hundred sixty-seven cases (1.4%) were from patients younger than 21 years. These cases were classified into one of following NCI diagnostic categories: nondiagnostic (9.6%), benign (69%), atypical follicular cells of undetermined significance (5.4%), suspicious for follicular neoplasm (22.2%), suspicious for malignancy (1.8%), and malignant (13.2%). Fifty-five patients had surgical follow-ups, including 5.5% nondiagnostic; 14.5% with atypical follicular cells of undetermined significance, 40% with suspicious for follicular neoplasm, 9% with suspicious for malignancy, and 59% with malignant results. The sensitivity and specificity of thyroid FNA for malignancy in pediatric population were 100% and 100%, respectively.

Conclusions: Thyroid FNA provides a sensitive and specific diagnostic tool for the evaluation of thyroid nodules in the pediatric population. NCI classification standardizes the diagnostic terminology, which is beneficial for clinical management of pediatric patients.

Clinicopathologic Investigation of Metastatic Tumors to the Liver Diagnosed by Fine-Needle Aspiration

(Poster No. 14)

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Context: Colorectal adenocarcinoma is generally regarded as the most common secondary hepatic tumor. The data supporting this assertion are outdated because most of the analyses come from 3 autopsy series published before 1990. With improvements in screening and treatments, the incidence of secondary liver tumors has likely increased. We present a comprehensive analysis of consecutive liver metastases and report an updated incidence of the originating tumors.

Design: One hundred forty patients who underwent fine-needle aspirations of secondary hepatic tumors were retrospectively identified from 2004 to 2007. Two pathologists, one experienced in cytology, correlated morphology with clinical notes, radiology, and autopsy data to confirm the origin of each metastasis.

Results: For all histologic types, the order of incidence was pancreas (34 of 140; 24.3%), lung (29 of 140; 20.7%), colorectal (25 of 140; 17.9%), unknown (17 of 140; 12.1%), and breast (7 of 140; 5.0%) (Figure 66). Adenocarcinomas were the most common metastases (93 of 140; 66.4%), followed by neuroendocrine (22 of 140; 15.7%), undifferentiated (6 of 140; 4.3%), melanomas (5 of 140; 3.6%), and squamous cell carcinomas (4 of 140; 2.9%). Secondary hepatic adenocarcinomas most frequently originated from the pancreas (25 of 93; 26.9%), whereas secondary neuroendocrine and squamous cell carcinomas most frequently originated from the lung (12 of 22; 54.5% and 2 of 4; 50.0%, respectively; Figure). The incidence of metastatic pancreatic cancer was significantly higher in our study compared with the combined incidence of the 3 prior autopsy series (24.3% vs. 6.2%; P < 0.001).

Conclusions: In our sample, pancreas and lung cancers were more common secondary hepatic tumors than colorectal cancers. The incidence of secondary hepatic tumors originating from the pancreas is significantly higher than previously reported.

Interobserver and Intraobserver Variability in the Measurement of Colombo Index: Implications for the Evaluation of Aspiration in Children

(Poster No. 15)

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Context: Chronic aspiration in children is a diagnostic challenge with no gold standard for assessment. The Colombo index (COLIN) is a quantitative test that measures lipid-laden macrophages in bronchial washings/lavages in cases of suspected aspiration. It is not universally accepted and cannot be readily performed. We evaluated interobserver (IROV) and intraobserver variability (IAOV) in calculating COLIN and correlated the results with clinical findings.

Design: Using established COLIN measurement standards, 49 oil red O-stained bronchoalveolar lavages were scored (twice) by 3 pathologists at 2-week intervals and by a cytotechnologist (once). Lipid content/100 macrophages was quantified and graded, and data were entered into a log form. Based on clinical diagnosis patients were classified as group 1 (no diagnosis), group 2 (dyspnea/cough/cardiac or immune dysfunction), group 3 (reflux disease/cystic fibrosis/asthma or recurrent pneumonia), and group 4 (any 2 diagnoses from group 3 vs group 4). Three pathologists included. There was no significant difference in the mean COLIN between groups (smallest P = 0.20, group 2 vs group 3).

Conclusions: Although there was no IAOV in COLIN measurement, there was significant IROV both between pathologists and between cytotechnologists. This challenges the reproducibility and reliability of COLIN at predicting aspiration in children. COLIN measurement does not reliably correlate with clinical diagnosis.

CD10 Expression in Metastatic Prostatic Carcinoma to the Liver

(Poster No. 16)

Alicia Calderon, DO (amcalder@uci.edu); Banafsheh Rashidi, MD; Jane Ellaine Tsongson-Ignacio, MD. Department of Pathology, University of California Irvine, Orange.

Although the loss of CD10 expression is a common early event in human prostate cancer, its expression appears in lymph node metastasis and in a subset of cases with high Gleason scores. Furthermore, studies suggest that prostate tumors with high Gleason scores express high levels of CD10, have a more aggressive biology, and frequently metastasize to the lymph nodes. CD10 positivity offers potential clinical utility for stratifying prostate cancer to predict the biologic behavior of the tumor. We recently encountered an unusual case of a prostatic carcinoma metastasizing to the liver, diagnosed by cytology via computed tomography (CT)–guided fine-needle aspiration biopsy. This is a case of a 53-year-old man with a past history of poorly differentiated prostatic adenocarcinoma, Gleason score 8, with local recurrence, including metastasis to the lymph nodes. He presented to our institution with a liver lesion and underwent a CT-guided liver biopsy. Cytomorphologically, the aspirated smears and cell block showed clusters of malignant cells with prominent nuclei and acinar formation. Immunohistochemical stains showed the malignant cells to be positive for protein-specific antigen, PSMA, and CD10 (Figure 67). Primary liver or possible metastatic lesions from the kidney, lung, and gastrointestinal tract were ruled out. Awareness that CD10 expression by
prostate cancer corresponds to a more aggressive phenotype with a higher malignant potential may help recognize the poorly differentiated metastatic prostatic adenocarcinomas.

Disseminated Blastomycosis Diagnosed by Fine-Needle Aspiration of the Thyroid
(Poster No. 17)

Aaron M. Harvey, MD (amharvey@mbhs.org); Dina R. Mody, MD; Morgan Amrikachi, MD. Department of Pathology, The Methodist Hospital, Houston, Texas.

Blastomycosis is an uncommon disease caused by the dimorphic fungus Blastomyces dermatitidis. It can manifest as chronic pulmonary symptoms or disseminated disease. Only 3 previous cases of blastomycosis involving the thyroid have been reported, of which only 2 were diagnosed by fine-needle aspiration. We present a case of disseminated blastomycosis initially diagnosed by thyroid fine-needle aspiration. Our case involved a 47-year-old man, with past medical history significant for diabetes, hyperlipidemia, and chronic pancreatitis, who presented with a 2-week history of fever, chills, rigors, constipation, and 10-pound weight loss. Abdominal computed tomography (CT) revealed chronic pancreatitis and a calcified mass in the pancreas. Chest CT revealed a single 1.5 to 2 cm thyroid mass and innumerable small (2-3 mm) pulmonary nodules bilaterally. Fine-needle aspiration of the thyroid demonstrated 10- to 20-μm, broad-based, budding yeasts with thick-walled, refractile capsules amidst a background of granulomatous inflammation and was diagnosed as a fungal infection consistent with blastomycosis. The patient was started on treatment with itraconazole based upon the fine-needle aspiration diagnosis. Concurrent lung biopsy demonstrated rare possible yeast forms on histology. A specimen from the lung was sent for culture and was positive for Blastomyces dermatitidis, confirming the diagnosis. Disseminated blastomycosis rarely involves the thyroid. However, the thyroid is amenable to fine-needle aspiration. Fungal and mycobacterial cultures and special stains for fungal organisms should be requested on all thyroid fine-needle aspiration biopsies with granulomatous inflammation.

Efficacy of Cell-Block Preparations of Thyroid Fine-Needle Aspiration Biopsies
(Poster No. 18)

Stephanie D. Simmons, MD (stephanie.simmons@bhsala.com); Al Rector, MD. Department of Pathology, Baptist Health Systems, Birmingham, Alabama.

Context: Fine-needle aspiration biopsies (FNABs) are routinely used in the initial evaluation of thyroid lesions. The objective of the study was to determine the usefulness of cell-block preparations of thyroid fine-needle aspirates.

Design: Papanicolaou smears were made, and cell blocks were made on 343 FNABs performed by clinicians between January 2007 and January 2009. The cases were divided into 4 groups: (1) the cell block was not contributory; (2) the cell block provided information when the smear was insufficient for analysis; (3) the cell block provided a diagnosis of atypia, which was not seen on the smear; (4) the smear demonstrated atypia, but the cell block showed only benign tissue.

Results: Cell blocks were contributory in 7% of thyroid FNABs. In 2 of these cases (0.6% of all cases), the cell block changed a benign diagnosis from the smear to a diagnosis of atypia. The surgical specimens for these cases were benign. There were 54 smears that were nondiagnostic. In 38.9% of these cases (n = 21; 6.1% of all cases), the cell blocks contributed to the diagnosis. One of these cases was diagnosed as carcinoma on histologic sections. In 1.2% of cases (n = 4), the smear showed atypia, and the cell block showed only benign tissue. Two of these cases were diagnosed as carcinoma on histologic sections.

Conclusions: We conclude that it is not cost effective to routinely prepare a cell block for every thyroid FNAB. It would be cost effective to order a cell block on insufficient smears only.

Does Polyomavirus Infection in Urine Specimens Cause False-Positive Fluorescence In Situ Hybridization Results?
(Poster No. 19)

David Hull, MD; Deloar Hossain, MD; Mililani Medina, MS; Karen Crewell, MS; Harpreet Singh, MS; Janqi Qian, MD; David G. Bostwick, MD, MBA (mmcdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

Context: In urine specimens, polyomavirus-infected cells (decoy cells) may be misinterpreted as malignant. Urine cytology alone, although specific, suffers from suboptimal sensitivity. Multicolor fluorescence in situ hybridization (FISH) assay allows separation of diploid and nondiploid (aneuploid) cells. We sought to characterize the coincidence of polyomavirus and positive FISH results in urine specimens and to identify whether polyoma cells specifically were aneuploid by FISH analysis.

Design: The study group consisted of 101 urine specimens with polyomavirus-infected cells. Cytology slides were prepared in duplicate: one was stained with hematoxylin-eosin, and the other was used for FISH assay to chromosomes 3, 7, and 17, and to band 9p21 (p16/Cdkn2A gene).

Results: Among the 101 specimens with polyomavirus infection, the mean number of decoy cells per case was 4.1 (range, 1–31), with a mean of 2.5 urothelial cells per high power field (HPF; 400×; range, 1–16). Ninety-eight of 101 specimens (97%) had normal diploid FISH results, whereas 3 (3%) had abnormal, nondiploid FISH results. These 3 specimens consisted of 2 with urethelial cancer cells and 1 with normal suspicious urothelial cells. FISH was invariably negative in polyoma-infected cells.

Conclusions: Polyomavirus infected cells were not a source of false-positive FISH results using FISH criteria. Polyomavirus infection does not appear to involve findings of abnormal or malignant urothelial cells.

An Improved, Buffered, Alcoholic Fixative for Urine Cytologies
(Poster No. 20)

Harpreet Singh, MS; Karen Crewell, MS; Mililani Medina, MS; David G. Bostwick, MD, MBA (mmcdonald@bostwicklaboratories.com). Bostwick Laboratories, Glen Allen, Virginia.

Context: The sensitivity and specificity of urine cytology for bladder cancer detection are improved by multitarget fluorescent in situ hybridization (FISH). We previously described an improved method for preparing urine FISH slides in Saccomanno fixative (Arch Pathol Lab Med. 2007; 131:1574–1577). One limitation of this method was filter clogging in cases with abundant particulate debris. To overcome this limitation, we investigated using a different fixative.

Design: Urine samples from 36 healthy individuals were split into a traditional, nonbuffered, alcoholic fixative (Saccomanno) or a novel, buffered, alcoholic fixative (NuCyte, QC Sciences). Samples were routinely processed for bright-field microscopy. One hundred twenty-five additional urine specimens were collected in the novel fixative and analyzed by FISH using probes to chromosomes 3, 7, and 17 and to band 9p21. FISH slides were screened using the Metafer automated-imaging system (MetaSystems, Inc.). Results were compared with 125 sequential FISH cases received in traditional fixative.

Results: Bright-field slides were evaluated by a cytotechnologist blinded as to fixative. The novel fixative showed reduction of crystals compared with an additional fixative (0% vs 33% of cases, respectively, P < .001), reduction in background (3% vs 22%, P = .01), and improved staining contrast (69% vs 0%, P < .001); also, FISH results showed a reduction in insufficient cases (6 vs 10) and an increase in the number of cases readable by automated imaging (82 vs 69).

Conclusions: The new, buffered, alcoholic fixative was superior to traditional Saccomanno fixative for bright-field and FISH analyses by virtually eliminating crystals, reducing background, and improving the overall diagnostic value of difficult urine specimens.

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Spectrum of Histologic Findings After Fine-Needle Aspiration Diagnosis of Hürthle Cell Neoplasm

(Poster No. 21)

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Context: Fine-needle aspiration (FNA) is the standard procedure for evaluation of thyroid nodules. Cytologic aspirates containing predominantly Hürthle cells are often problematic for both cytopathologists and clinicians. Large oncocytic cells may be present in nonneoplastic conditions or in benign or malignant neoplasms. Because many clinicians regard all Hürthle cell lesions as at least potentially malignant, most patients with Hürthle cell neoplasm (HCN) by FNA are referred for surgical excision. This study examines the final histologic findings in 30 patients who underwent surgical resection after FNA diagnosis of Hürthle cell neoplasm.

Design: We reviewed reports from FNAs of thyroid lesions examined by the Department of Pathology, University of Miami/Jackson Memorial Hospital during a 5-year period. Thirty patients with HCN subsequently underwent surgical resection. HCN was defined by FNA when Hürthle cells comprised at least 70% of the cellularity. Slides and reports were reviewed, and the final diagnoses and results of special stains and immunohistochemistry were noted.

Results: Among the 30 FNA cases designated as HCN, there were 13 Hürthle cell adenomas, 10 carcinomas, and 7 nonneoplastic thyroid lesions. Thyroid carcinomas included 3 Hürthle cell carcinomas, 2 oncocytic variant papillary carcinomas, 2 medullary carcinomas, 2 insular carcinomas, and 1 squamous cell carcinoma. Nonneoplastic benign lesions were 3 cases of chronic lymphocytic thyroiditis, 3 cases of nodular hyperplasia, and 1 case with both features.

Conclusions: HCN by FNA may indicate Hürthle cell adenoma or carcinoma. Papillary and medullary thyroid carcinomas may also show oncocytic features on FNA smears. Surgical resection remains essential for definitive classification.

The Role of Multimodality Approach in a Bone Fine-Needle Aspiration of a Patient With Lymphoma

(Poster No. 22)

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A 62-year-old woman presented with left leg pain. Computed tomography (CT) scan showed a lytic lesion in the left femur and diffuse lymphadenopathy. Fine-needle aspiration (FNA) of the right paratracheal lymph node was performed. Flow cytometry (FC) using cluster analysis revealed CD5+/CD10- x-restricted, large B-cell lymphoma (red cluster, Figure 68) in addition to a lesser population of CD5+/CD10+ x-restricted, B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (blue). Morphologically, variously sized atypical lymphocytes were present. CT-guided FNA and core biopsy of the lytic lesion in the left femur was performed. FC showed the B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The large B-cell lymphoma component present in the prior FC was not identified. Morphology and an extensive immunohistochemical panel revealed only the diffuse large B-cell lymphoma component. The small CD5+ B-cell population identified by both the accompanying and the previous FC was not apparent. A staging bone marrow showed involvement by the B-cell small lymphocytic lymphoma/chronic lymphocytic leukemia by both morphology and FC. The relatedness between the 2 processes may represent Richter syndrome or 2 independent diseases, in light of the synchronous presentation and opposite light chain restriction. In addition, we discuss the sensitivity of FC and FNA in bone samples. The case reinforces the understanding that an accurate pathologic diagnosis is a multimodality approach, and a clinically significant component may be potentially missed when a single modality is employed.
Strongyloides Hyperinfection/Disseminated Disease: An Unexpected Cytologic Diagnosis With Autopsy Follow-up  
(Poster No. 24)

Timothy R. Pal, MD (tpal@notes.cc.sunysb.edu); Sonya Hwang, MD, Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

Infection by Strongyloides stercoralis is common worldwide, but it is relatively rare in the United States. Most chronically infected patients are asymptomatic; however, severe clinical manifestations, including hyperinfection and disseminated disease (increase in worm burden without or with spread to organs beyond normal migration pattern, respectively) have been reported in up to 2.5% of infected patients, with high mortality rates. The most commonly reported risk factor for hyperinfection and disseminated disease is immunosuppression secondary to steroid use. We present the case of a 67-year-old man, originally from Guyana, with neu-rololgic deficits secondary to severe vertebral degenerative joint disease, for which he received multiple courses of dexamethasone. During the patient’s last admission, he developed shortness of breath and hemoptysis. Radiologic studies demonstrated diffuse nodularity of the lungs, compatible with infectious etiology. A bronchial lavage was performed to rule out Pneumocystis pneumonia. Although Pneumocystis organisms were not present, parasites morphologically consistent with Strongyloides were seen in the lavage fluid (ThinPrep, Figure 70, left). Strongyloides stercoralis was subsequently identified in the patient’s stool. Despite appropriate therapy, the patient died. At autopsy, histologic examination demonstrated Strongyloides in various organs, including pancreas, gastrointestinal tract, lungs (Figure, right), and heart, consistent with disseminated disease. In our case, the unexpected cytologic identification of Strongyloides was the primary diagnosis of infection. Although Strongyloides hyperinfection/dissem-inated disease is rare, it should be included in the differential when examining cytologic specimens (ie, lavage or sputum) from patients with a history of immunosuppression and travel to endemic areas.

Bile Duct Brush Cytology: Indeterminate Diagnosis Is Essential  
(Poster No. 26)

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Context: Bile duct brush cytology is often the primary diagnostic procedure for treatment decisions of biliary lesions. These samples are often difficult to interpret because of reactive changes. Indeterminate (atypical or suspicious) diagnoses are frequent, although not as useful as a malignant or benign diagnosis. We conducted this study to determine whether the indeterminate diagnoses can be reduced by refining diagnostic criteria.

Design: Bile duct brush ThinPrep cases with atypical/suspicious diagnoses and follow-up were selected during a 200-day period in 2008. Five cytopathologists, blinded to the diagnosis, reviewed the slides independently. Each case was diagnosed as malignant, benign, or nondiagnostic and evaluated for 19 morphologic features.

Results: Twenty-eight cases, 25 atypical and 3 suspicious, were included. Of the 16 cases with malignant follow up, 5 (31%) were upgraded to malignant, and 1 was downgraded to benign by at least 3 of 5 pathologists. Two remained nondiagnostic. Of the 12 cases with benign follow up, 4 (33%) were downgraded to benign, 5 (42%) were upgraded to malignant, and 2 remained nondiagnostic by the majority. In the remaining cases, there was no majority agreement. In the 5 false-positive cases, 3 patients had had stents, 1 had stones, and 1 had gallstones with cholangitis. Features that showed significant difference between benign and malignant lesions were single, atypical cells and irregular nuclear membranes (P < .05).

Conclusions: Indeterminate categories are necessary to avoid false-positive and false-negative diagnoses. Single, atypical cells and irregular nuclear membranes may be the most useful features in recognizing malignancy in difficult cases.

Angiosarcoma Mimickers on Fine-Needle Aspiration Cytology  
(Poster No. 27)

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The cytologic diagnosis of angiosarcoma is challenging because the morphology may simulate that of nonvascular malignant tumors. The incidence of this neoplasm is increasing in cases of breast-conserving therapy for breast carcinoma. Cytologic evaluation of patients with a pertinent clinical history requires careful on-site screening of slides for proper triaging of cellular material, allowing for allocation of material for immunocytochemistry, immediate additional sampling, and preparation of cell blocks for appropriate special studies. An 80-year-old woman with a history of prior surgeries for breast cancer presented with cervical lymphadenopathy. Fine-needle aspiration of the lymph node revealed a hypercellular specimen with dispersed, isolated malignant cells with prominent macronucleoli, raising the suspicion of a lymphoproliferative disorder. Rare “cell in cell” appearance was noted. On flow cytometry, the cells were positive for CD30 and CD34 and were negative for other hematopoietic markers. Review of the breast lesion showed features of high-grade angiosarcoma with abundant mitoses and necrosis, strong, diffuse positivity for CD31 and CD34, and lacking expression of pancytokeratin (AE1/3). The fine-needle aspiration findings were cytomorphologically identical to the prior angiosarcoma. In patients with a pertinent clinical history, it is important to consider angiosarcoma in the differential diagnosis of lesions with epithelioid morphology. Recognizing the cytologic features during adequacy assessment would allow appropriate im

Basaloid Squamous Cell Carcinoma of Tonsil Presenting With Metastatic Cystic Squamous Cell Carcinoma and Positive Human Papillomavirus 16: Case Report and Review of the Literature  
(Poster No. 25)

Bela H. Dalwadi, MD (Bela.Dalwadi@DrexelMed.edu); Xiaoli Chen, MD. Department of Pathology, Drexel University College of Medicine, Philadelphia, Pennsylvania.

The cytologic diagnosis in fine-needle aspiration (FNA) of a squamous cystic mass can be difficult, especially between branchial cleft cyst and metastatic cystic squamous cell carcinoma. Human papillomavirus (HPV) 16 infection has been detected in squamous cell carcinoma of the head and neck but not in branchial cleft cyst. We report a case of a 64-year-old man who presented with a 3-cm, enlarging left neck mass with a recent diagnosis suspicious of epithelial neoplasm on FNA. A repeat FNA was requested by clinician. The specimen showed nests of small- to medium-sized, oval-shaped tumor cells with hyperchromatic nuclei and scant cytoplasm. There was no prominent degree of anaplasia. The background showed a few lymphocytes, histiocytes, and multinucleated giant cells. A diagnosis of metastatic squamous cell carcinoma was made in the context that this most likely represented a metastatic cystic squamous cell carcinoma. Three weeks later, the patient underwent panendoscopy with tonsillectomies and random biopsies. The left tonsil showed invasive squamous cell carcinoma with basoloid features. An HPV in situ hybridization test showed positivity for high-risk HPV including type 16. After literature review, we conclude that HPV may prove to be a useful test in differentiating metastatic squamous cell carcinoma from branchial cleft cyst. Extra passes should be obtained when the diagnosis is difficult, and HPV testing should be considered. Also, the relationship between the metastatic cystic squamous cell carcinoma of the oropharynx and basoloid squamous cell carcinoma with HPV-16 should be studied; this may help in understanding the pathogenesis of cystic lymph node metastasis.
muhistochemical testing and diagnosis. Comparison with prior lesions can be crucial in differentiating metastasis from a new lesion. A literature review of cytomorphologic criteria of angiosarcoma and its diagnostic pitfalls will be summarized in this report (Figure 71).

**Primary Uterine Diffuse Large B-Cell Lymphoma Detected in a Cervicovaginal Papanicolaou Test: A Case Report and Review of the Literature**

Jian-Feng Wang, MD, PhD; Xiangrong Zhao, MD, PhD; Teri Cooper, MD. Department of Pathology, Berkshire Medical Center, Pittsfield, Massachusetts.

Hematologic malignancies are rarely encountered in the female genital tract, either as a primary malignancy or as systemic dissemination. Without known clinical history, the cytomorphologic diagnosis of these neoplasms may be very challenging. Here, we report a case with primary uterine diffuse large B-cell lymphoma, which was first detected by liquid-based cervicovaginal Pap test (Pap) test. A 75-year-old, white woman underwent a Pap test for vaginal bleeding and endometrial thickening. On SurePath Pap test, numerous atypical mononuclear cells were present singly or admixed with groups of squamous cells and inflammatory cells. These atypical cells varied in size and had irregular hyperchromatic nuclei, coarse chromatin, and minimal cyttoplasm. Some of the cells showed cytologic features that mimicked high-grade squamous intraepithelial lesion with convoluted nuclei, thickened nuclear membranes, and one or several nucleoli (Figure 72). Subsequent endometrial biopsy demonstrated diffuse large B-cell lymphoma, which was confirmed with a panel of immunohistochemistry stains. Further workup by computed tomography and magnetic resonance imaging, bone marrow biopsies, and flow cytometry did not show evidence of lymphoma in other sites, supporting the diagnosis of primary uterine diffuse large B-cell lymphoma. Hematologic malignancies in female genital tract may be undiagnosed in Pap test because they are rare, usually unexpected, and may be misdiagnosed as inflammatory lesions, squamous intraepithelial lesions, or other types of malignant tumors. Therefore, it is critical to keep these malignancies in the differential diagnosis and initiate further diagnostic workup when they are suspected.

**Significance of hrHPV Testing in Women Age 50 Years or Older With Low-Grade Squamous Intraepithelial Lesion and High-Grade Squamous Intraepithelial Lesion Cytology**

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**Context:** Older women are considered a special population. The 2006 American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines support reflex high-risk human papillomavirus (hrHPV) testing as an option for postmenopausal women with low-grade squamous intraepithelial lesions (LSIL). The data of hrHPV infection and its association to histologic cervical intraepithelial neoplasia (CIN) 2/3 in older women with LSIL and high-grade squamous intraepithelial lesion (HSIL) cytology are limited.

**Design:** A computer-based search of Copath files at our institution was performed for the period between July 1, 2005, and June 30, 2008, to retrieve cases of women aged 50 years or older reported as LSIL or HSIL cytology who also were tested for hrHPV DNA (Hybrid Capture 2 [HC2] test). The HPV testing result, Papanicolaou test, and histologic follow-up results were recorded.

**Results:** hrHPV DNA was detected in 25 of 28 women (89.3%) age 50 or older with HSIL cytology, and in 154 of 217 women (71.0%) age 50 or older with LSIL cytology. The average interval between SIL cytology and an initial diagnosis of CIN 2/3 was 2.6 months (range, 0–22 months) in women with HSIL cytology and was 10.4 months (range, 0–35 months) in women with LSIL cytology. The histologic findings are listed in the Table.

**Histologic CIN Lesions Between hrHPV+ and hrHPV Testing Results in Older Women With LSIL**

<table>
<thead>
<tr>
<th>Cytology</th>
<th>Follow-up, No.</th>
<th>CIN 1, No (%)</th>
<th>CIN 2, No (%)</th>
<th>CIN 3, No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>hrHPV+</td>
<td>21</td>
<td>2 (9.5)</td>
<td>9 (42.9)</td>
<td>10 (47.6)</td>
</tr>
<tr>
<td>LSIL</td>
<td>82</td>
<td>48 (58.5)</td>
<td>6 (7.3)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>hrHPV</td>
<td>HSIL 21</td>
<td>2 (9.5)</td>
<td>9 (42.9)</td>
<td>10 (47.6)</td>
</tr>
<tr>
<td>LSIL</td>
<td>82</td>
<td>48 (58.5)</td>
<td>6 (7.3)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>LSIL</td>
<td>3</td>
<td>0</td>
<td>1 (33.3)</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>LSIL</td>
<td>24</td>
<td>11 (45.8)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Conclusions:** The incidence of histologic CIN 2/3 was markedly higher in women with HSIL cytology than in women with LSIL cytology. No CIN 2/3 was noted in older women with LSIL cytology and negative hrHPV testing. hrHPV testing might be helpful for risk assessment for older women with LSIL cytology but not for older women with HSIL cytology.

**Langerhans Cell Histiocytosis: E-Cadherin and Cyclin D1**

Jie Ouyang, MD, PhD; Xuchen Zhang, MD, PhD; Constantine Axiotis, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

Epidermal Langerhans cells (LCs) account for 3% to 5% of all nucleated cells in the epidermis and constitutively express E-cadherin, which anchors LCs to keratinocytes. Langerhans cell histiocytosis (LCH) is a clonal proliferative disorder of LCs and often occurs in children as a cutaneous disease. The course of disease is characterized by either spontaneous regression or multisystemic dissemination with poor prognosis. The mechanisms of migration of LCs from epidermis to dermis, proliferation, and dissemination are unclear. We report one case of multisystemic LCH and investigate the pathogenesis by observing expressions of E-cadherin and cyclin D1. A 15-month-old girl presented with multiple papules and splenomegaly for 1 week. Skin and bone biopsies revealed that the dermal and bone marrow lesional cells were positive for CD1a and S100. Furthermore, the lesional cells were negative or weakly positive for E-cadherin but demonstrated strong nuclear positivity for cyclin D1. E-cadherin is an important cell-adhesion molecule and is essential for the homing of LCs to epidermis. Decrease of E-cadherin expression has been related to...
LCH dissemination and poor prognosis. Cyclin D1 involves cells prolif-
eration. The expression of cyclin D1 in LCH has never been reported. Down-regulation of E-cadherin may explain the migration of LCs and dissemination of LCH, and overexpression of cyclin D1 may explain the proliferation of LCs in LCH. The data demonstrated that decrease of -cad-
erin and increase of cyclin D1 expression play important roles in the pathogenesis of LCH and might be markers for evaluating disease dis-
semination and prognosis.

**Lymphomatoid Granulomatosis in a Patient With Granulomatous-Type Mycosis Fungoides**  
(Poster No. 31)

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ham, North Carolina.

Lymphomatoid granulomatosis (LG) is a rare Epstein-Barr virus (EBV)-
driven B-cell lymphoproliferative disorder that occurs in the lungs or oth-
er extranodal sites in the setting of immunodeficiency. We report a case of LG that developed after chemotherapy for granulomatous mycosis fun-
goides (MF). A 35-year-old, white man with granulomatous MF was ini-
tially treated with topical preparations but failed initial therapy and pro-
gressed to extracutaneous disease (stage III). High-dose systemic che-
motherapy (cyclophosphamide and prednisone) was then administered
during a 9-month period. The MF was in clinical remission 2 years after
therapy when he developed an omental mass. Excisional biopsy demonstrated polymorphous lymphoid infiltrate with angiodestruction, focal
carcinosis, primarily B-cell phenotype, and EBV positivity, consistent with grade I LG. He was then treated with rituximab with complete re-
sponse; however, 4 years later, the patient developed a 10-cm lung mass, which, on lobectomy, revealed EBV- monomorphic large B cells consistent with grade III LG. Although EBV- B-cell lymphoma has been reported in rare cases of MF, no reports have linked its occurrence to corresponding treatment. This case seems best to fit into the category of iatrogenic immu-
nodeficiency-associated lymphoproliferative disorder by the new 2008 World Health Organization criteria.

**Seboplastic Carcinoma: A Rare Histologic Variant of Sebaceous Carcinoma**  
(Poster No. 32)

Kamaljeet Singh, MD (kosingh@lifespan.org). Department of Pathology, Brown University, Providence, Rhode Island.

Sebaceous carcinoma masquerades clinically and histologically as a va-
riety of lesions. Histology shows basaloid and squamous differentiation that can be misdiagnosed as basal or squamous cell carcinoma. Apocrine differentiation in sebaceous carcinoma is rare. It consists of glands lined by cuboidal cells expressing epithelial membrane antigen (EMA) and other apocrine markers. A 78-year-old man presented with an enlarging nod-
ular lesion at the right upper eyelid. The lesion started as an itch and developed into an ulcer. He underwent wide excision of the eyelid with ad-
ditional surgical scar. The lesion appeared as a 1-cm, mollicute, pigmented lesion and grew into a 2-cm nodule during 10 months. His renal and pancreatic function remained normal, and no additional lesions were identified radiographically. An excisional biopsy was performed. A hema-
toxylin-eosin stained section shows a nodular aggregate of plasma cells in the dermis. Most plasma cells were well to moderately differentiated,
whereas a few were multinucleate or multilobated giant cell forms (Fig-
ure 74). The plasma cells, including giant cell forms, were positive for CD138, CD56, and κ light-chain isotype. In situ hybridization for EBV-
encoded RNA was positive in plasma cells. The plasma cells were nega-
tive for λ light chain, CD30, CD20, CD3, S100, and pancytokeratin. Ki-67 demonstrated a proliferation index of 30% in plasma cells. Giant cell plas-
macytoma has been described in patients without history of organ trans-
plant or being immunocompromised. In the setting of PTLD, plasmacy-
toma-like lesions have been well-documented; however, primary cutane-
ous plasmacytoma of giant cell type, in the setting of PTLD, has not been
reported in the English literature. The clinical significance of this mor-
phologic variant remains to be further studied.

**Desmoplastic Malignant Melanoma With Myofibroblastic Differentiation**  
(Poster No. 34)

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Desmoplastic malignant melanoma (DMM) is an uncommon melano-
cytic lesion. DMM has been reported, in some cases, to have an association with cells with smooth muscle differentiation, without being clear wheth-
er this is due to melanoma cells with smooth muscle differentiation or to a proliferation of reactive myofibroblasts. A right breast lesion from a 68-
year-old woman was excised and demonstrated a poorly circumscribed
a proliferation index of 30% in plasma cells. Giant cell plas-
macytoma has been described in patients without history of organ trans-
plant or being immunocompromised. In the setting of PTLD, plasmacy-
toma-like lesions have been well-documented; however, primary cutane-
ous plasmacytoma of giant cell type, in the setting of PTLD, has not been
reported in the English literature. The clinical significance of this mor-
phologic variant remains to be further studied.

**Cutaneous Giant Cell Plasmacytoma in an Organ Transplant Recipient: A Rare Presentation of a Posttransplant Lymphoproliferative Disorder**  
(Poster No. 33)

Maggie Stoecker, MD; John Papalas, MD; Endi Wang, MD, PhD (endi.wang@duke.edu). Department of Pathology, Duke University Med-
ical Center, Durham, North Carolina.

Posttransplantation lymphoproliferative disorder (PTLD) comprises a spectrum of lymphoid diseases, ranging from early stage infectious mono-
ucleosis-like lesions to monomorphic, including plasmacytoma-like, le-
sions. Although PTLD may involve a variety of organs, primary cutaneous
PTLD, particularly the plasmacytoma-like subtype, is rare. We report a case of a 56-year-old man, status postkidney and pancreas transplant,
who 4 years later, developed a cutaneous lesion near a previous abdom-
inal surgical scar. The lesion appeared as a 1-cm, mollicute, pigmented
lesion and grew into a 2-cm nodule during 10 months. His renal and
pancreatic function remained normal, and no additional lesions were
identified radiographically. An excisional biopsy was performed. A hema-
toxylin-eosin stained section shows a nodular aggregate of plasma cells
in the dermis. Most plasma cells were well to moderately differentiated,
whereas a few were multinucleate or multilobated giant cell forms (Fig-
ure 74). The plasma cells, including giant cell forms, were positive for
CD138, CD56, and κ light-chain isotype. In situ hybridization for EBV-
encoded RNA was positive in plasma cells. The plasma cells were nega-
tive for λ light chain, CD30, CD20, CD3, S100, and pancytokeratin. Ki-67 demonstrated a proliferation index of 30% in plasma cells. Giant cell plas-
macytoma has been described in patients without history of organ trans-
plant or being immunocompromised. In the setting of PTLD, plasmacy-
toma-like lesions have been well-documented; however, primary cutane-
ous plasmacytoma of giant cell type, in the setting of PTLD, has not been
reported in the English literature. The clinical significance of this mor-
phologic variant remains to be further studied.
thesis, when fibroblasts and melanoma cells were in close proximity. Demonstration of double staining in some of the malignant cells with S100 and SMA with negativity for desmin is very suggestive of a true myofibroblastic differentiation in this neoplasm. These facts, along with a stimulus of normal fibroblastic cells to grow and produce collagen, by melanoma cells, suggests a double mechanism for the fibrosis and the positivity of SMA, which is a true myofibroblastic differentiation and a stimulus of myofibroblasts and fibroblasts to produce collagen.

**Facial and Extremity Spitz Nevi in Childhood: Architectural and Immunohistochemical Features, Similarities, and Differences**  
*Vinay Prasad, MD (vinay.prasad@nationwidechildrens.org); Sue Hammong, MS; Emily Chenever, MS; Anna Hughes, MS; Ronald Houston, MS; Kathleen Nicol, MD. Department of Pathology, Nationwide Children’s Hospital, Columbus, Ohio.*

**Context:** Spitz nevi (SN) occur frequently in prepubertal children and at birth, with a predilection for the face and neck. SN may be junctional, compound, or intradermal. This is a review of 21 childhood SN.

**Design:** The clinical features and biopsies of 21 children with SN were reviewed. Twelve were from extremities, and 9 were from the face/neck. Patients with facial SN ranged from 7 weeks to 14 years with 6 males and 3 females. Patients with extremity SN ranged from 1 year to 15 years with 6 males and 6 females. Hematoxylin-eosin slides were reviewed. Melan-A, HMB-45, and Ki-67 slides were reviewed when available.

**Results:** All cases showed melanocytic lesions with confluent distribution of spindled and epithelioid nevus cell nests and Kamino bodies. Five of 9 facial SN (56%) were compound; 4 of 9 (44%) were junctional. All facial SN immunostained, showing Melan-A, HMB-45, and Ki-67 slides were reviewed when available. Five of 9 facial SN (56%) were compound; 4 of 9 (44%) were junctional. All facial SN immunostained, showing Melan-A, HMB-45, and Ki-67. Twelve were from extremities, and 9 were from the face/neck.

**Eccrine Porocarcinoma of the Vulvar**  
*Patrick A. Adegbuyega, MD (padбег@lsuhsc.edu). Department of Pathology, Louisiana State University Health Sciences Center, Shreveport.*

Eccrine porocarcinoma (EPC) is a rare skin adnexal tumor, with less than 200 cases reported in the English literature. Involvement of the vulva by EPC is even rarer, with only 5 previously reported cases. This case study was observed in a 48-year-old woman who presented with a 5-cm, verrucous, polypoid, pedunculated left vulvar mass, which she reported had been increasing in size during the preceding 6 months. The mass was excised and histopathologic examination of the lesion showed features diagnosing malignant eccrine porocarcinoma (EPC) on the basis of the histologic findings. The lesion was negative for carcinoembryonic antigen, epithelial membrane antigen, and an increased Ki-67 proliferation index (19% and 75%, respectively) (Figure 75). Strong diffuse membranous staining for EGFR was present. Both tumors were negative for Ki-67, p53, cytokeratin, estrogen receptor, and progesterone receptor while negative for carcinoembryonic antigen, epithelial membrane antigen, and S100. To our knowledge, the expression profile for the predictive immunohistochemical (IHC) studies have shown these lesions to be positive for Ki-67, p53, cytokeratins, estrogen receptor, and progesterone receptor while negative for carcinoembryonic antigen, epithelial membrane antigen, and S100. To our knowledge, the expression profile for the predictive IHC marker, epidermal growth factor receptor (EGFR), vascular endothelial growth factor, HER2/new, and CD117, has not been determined. We present 2 new cases of malignant acrospiroma and the IHC staining patterns for common therapeutic targets.

**Design:** Two new cases of malignant acrospiroma were diagnosed on the basis of the histologic findings. The lesion was negative for carcinoembryonic antigen, epithelial membrane antigen, and an increased Ki-67 proliferation index (19% and 75%, respectively) (Figure 75). Strong diffuse membranous staining for EGFR was present. Both tumors were negative for Ki-67, p53, cytokeratins, estrogen receptor, and progesterone receptor while negative for carcinoembryonic antigen, epithelial membrane antigen, and S100. To our knowledge, the expression profile for the predictive IHC markers, epidermal growth factor receptor (EGFR), vascular endothelial growth factor, HER2/new, and CD117, has not been determined. We present 2 new cases of malignant acrospiroma and the IHC staining patterns for common therapeutic targets.

**Predictive Immunohistochemical Staining Pattern in 2 New Cases of Malignant Eccrine Acrospiroma**  
*Claire M. Pollard, MD (pollard.claire@gmail.com); John B. Carpenter, MD; Fangu Lian, MD; William H. Leyva, MD. *Department of Pathology, University of Arizona, Tucson; Department of Pathology and Dermatology, Southern Arizona Veterans Affairs Health Care System, Tucson.*

**Context:** Malignant acrospiroma, also called malignant hidradenoma or hidradenocarcinoma, is a rare aggressive neoplasm of the eccrine sweat gland for which no consensus treatment strategy exists. Since first described in 1954, fewer than 100 cases have been reported. Previous immunohistochemical (IHC) studies have shown these lesions to be positive for Ki-67, p53, cytokeratins, estrogen receptor, and progesterone receptor while negative for carcinoembryonic antigen, epithelial membrane antigen, and S100. To our knowledge, the expression profile for the predictive IHC markers, epidermal growth factor receptor (EGFR), vascular endothelial growth factor, HER2/new, and CD117, has not been determined. We present 2 new cases of malignant acrospiroma and the IHC staining patterns for common therapeutic targets.

**Design:** Two new cases of malignant acrospiroma were diagnosed on the basis of the histologic findings. The lesion was negative for carcinoembryonic antigen, epithelial membrane antigen, and an increased Ki-67 proliferation index (19% and 75%, respectively) (Figure 75). Strong diffuse membranous staining for EGFR was present. Both tumors were negative for Ki-67, p53, cytokeratins, estrogen receptor, and progesterone receptor while negative for carcinoembryonic antigen, epithelial membrane antigen, and S100. To our knowledge, the expression profile for the predictive IHC markers, epidermal growth factor receptor (EGFR), vascular endothelial growth factor, HER2/new, and CD117, has not been determined. We present 2 new cases of malignant acrospiroma and the IHC staining patterns for common therapeutic targets.

**Immunohistochemical Staining Pattern of Malignant Melanoma With Coexisting Melanocytic Nevus**  
*Smita Krishnamurthy, MD (skrishnamurthy@path.wustl.edu); Dongsi Lu, MD, PhD. Department of Pathology, Washington University in St Louis/Barnes-Jewish Hospital, St Louis, Missouri.*

**Context:** Although malignant melanoma and melanocytic nevi often coexist, the relationship between them remains unclear. We investigated immunohistochemical staining patterns of 3 novel markers that have recently been reported in the literature: glypican 3 (GPC-3), p16, and insulin-like growth factor II mRNA binding protein 3 (IMP-3) to further evaluate this relationship.

**Design:** Twenty-four cases of malignant melanoma with coexisting melanocytic nevi were identified through a database search of May 2003 to February 2008 Barnes-Jewish Hospital files. Monoclonal antibodies to GPC-3, p16, and IMP-3 were used to evaluate differential staining patterns between nevus and melanoma cells. All slides were independently reviewed by 2 pathologists and graded according to intensity and proportion of staining.

**Results:** Discordant staining was noted between malignant melanoma and melanocytic nevus cells in 4 cases for GPC-3, 6 cases for p16, and 2 cases for IMP-3. In most discordant cases, GPC-3 and IMP-3 stained melanoma cells and not nevi. However, one case showed no GPC-3 staining in melanoma and focal, weak staining in nevus cells. Most discordant cases showed p16 staining in nevus cells and no staining in melanoma; however, one case showed weak p16 staining in melanoma and no staining in nevus cells.

**Conclusions:** Immunohistochemical staining for GPC-3, p16, and IMP-3 has limited value in evaluating the relationship between malignant melanoma and coexisting melanocytic nevi. In general, when a discordant staining pattern was observed, GPC-3 and IMP-3 were positive in melanoma cells more often than nevi, whereas p16 was positive in melanocytic nevi more often than melanomas.
Rapidly Progressive Fatal Dementia Secondary to Lymphomatosis Cerebri

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Lymphomatosis cerebri is a term indicating a diffusely infiltrating form of primary central nervous system lymphoma without evidence of a mass lesion. This is a rare entity, with only a few cases described in the literature. We report a unique, autopsy–diagnosed lymphomatosis cerebri case with widespread infiltration of the brain by rod-shaped, microglial-appearing tumor cells. The patient was a 71-year-old, immunocompetent, independently living woman who developed rapid-onset dementia. She had a complete intracranial workup. Magnetic resonance imaging showed a nonspecific, ill-defined signal in the white matter diffusely. The cerebrospinal fluid lymphocytosis showed nonspecific, diffuse encephalopathy. She was clinically thought to have Lewy body dementia. Her dementia progressed to coma, and palliative care was offered. She died 2 months after onset of the disease. Grossly, the postmortem brain showed no mass lesions. There were widespread, poorly delineated areas of gray disorganization with focal softening, mainly in the white matter. Microscopically, CD20 and PAX5 immunohistochemistry showed medium-sized B cells widely infiltrating the cortex and white matter from frontal to occipital lobe, basal ganglia, thalamus, and midbrain. Most of the infiltrating tumor cells were rod-shaped, with few nuclei, resembling microglia. However, focal, perivascular, round lymphoid infiltrates were also present. There was no evidence of degenerative brain disease or lymphoma elsewhere. This case illustrates that lymphomatosis cerebri should be included in the differential diagnosis of rapidly progressive dementia, especially when there is no mass lesion, so that pathologists should be aware of the existence of atypical morphology of central nervous system lymphomas.

Anaplastic Meningioma With Carcinomatous Differentiation

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A 77-year-old man presented with a 4-month history of visual impairment, memory problems, and headache. Magnetic resonance imaging of the head showed a 6.9 \( \times \) 6.2 \( \times \) 3.5-cm, heterogeneously enhancing, hypervascular, dural-based, right posterior falcine mass, which invaded through the right parietooccipital calvarium into the scalp. The patient underwent right parietooccipital craniotomy with resection of the tumor and overlying skull. Histologically, the neoplasm showed 2 basic patterns, which merged with each other. Some areas had features of atypical meningioma, whereas others had sheets of malignant cells with brisk mitotic activity and focal squamous differentiation. The differential diagnosis included anaplastic meningioma with carcinosomatous features versus metastatic carcinoma to a meningioma. Immunohistochemical studies showed strong immunoreactivity for AE1/AE3 in about 50% of frankly malignant areas and in rare cells with meningothelial features. Both components were strongly, diffusely immunoreactive for vimentin and focally for CK7 and P63. CK5/6 was focally immunoreactive in the malignant areas and negative in meningothelial areas. Epithelial membrane antigen was strongly, diffusely immunoreactive in the malignant epithelial component and 10% to 40% of cells in meningothelial areas. MOC31 was immunoreactive in up to 40% of the malignant epithelial component and negative in meningothelial areas. About 12% of neoplastic cells were positive for PR, CK20, CEA, S100, ER, and TTF-1 were negative throughout. The above findings support the diagnosis of anaplastic meningioma with carcinosomatous differentiation for which cytologic features are described in the most recent World Health Organization Tumors of the Central Nervous System.
Composite Tumors and Cortical Dysplasias in the Brain of a Patient With Chronic Epilepsy (Poster No. 44)

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Tumors in patients with epilepsy are not uncommon. This case report describes a rather rare composite tumor of a ganglioglioma and dysembryoplastic neuroepithelial tumors (G-DNT tumors) with cortical dysplasia and the diagnosis was dysembryoplastic neuroepithelial tumor. Few cases have been described with such features. At autopsy, the brain revealed multifocal cysts and free tachyzoites of Toxoplasma gondii with diffuse microglial nodules and no necrosis (Figure 76, A through D). To the best of our knowledge, this case represents the first report of the encephalitic form of toxoplasmosis in a non-AIDS-associated patient.
potential, and expression of some carcinogenic markers in adult medulloblastomas.

**Design:** We analyzed the immunohistochemical expression of survivin, c-Kit, BCL2, fascin, p53, and Ki-67 (all antibodies, Neomarkers, Fremont, California) in 18 adult (older than 16 years) patients with medulloblastomas.

**Results:** Study included 14 men and 4 women (mean age, 22.9 ± 8.2 years). Fourteen cases were classical, 2 desmoplastic/ nodular, and 2 large cell medulloblastomas. Moderate to high nuclear survivin expression was observed with high percentages (55%–100%) in all medulloblastomas. However, BCL2 was mildly positive in only one case. Interestingly, mild to moderate cytoplasmic c-Kit expression was demonstrated in 16 cases (89%) without membranous immuno staining. Fascin expression was observed in 13 medulloblastomas (72%) with moderate to high immune activity in 9 tumors. Mild p53 expression was present in 4 cases (22%). Mean Ki-67 index was 20.6% (range, 8%–55%).

**Conclusions:** Frequent nuclear survivin expression indicates the predominance of antiapoptotic factors in carcinogenesis of adult medulloblastomas. It may also be a potential therapeutic target for adult medulloblastomas. Although BCL2 immunoreactivity was reported in approximately 30% of medulloblastomas, it was rarely expressed in the present series of adult medulloblastomas. This is the first study to demonstrate fascin expression in medulloblastomas. It may be related to the neuronal differentiation. Mild to moderate cytoplasmic c-Kit immunoreactivity without membranous staining in adult medulloblastomas may support the previous studies reporting low level of c-Kit protein expression with a lack of activating mutations in medulloblastomas. It seems p53 is rarely involved in the carcinogenesis of adult medulloblastomas.

**Supratentorial Primitive Neuroectodermal Tumor With an Unusual Translocation t(14;19)**

(Alexa Siddon, MD) (alexa.siddon@yale.edu); Anita Huttner, MD. Department of Pathology, Yale, New Haven, Connecticut.

Navajo neurohepatopathy is an autosomal recessive disease affecting 1 in 1600 live births in the Navajo population of the southwestern United States. The clinical features previously described include hepatopathy, corneal anesthesia, progressive sensorimotor neuropathy, failure to thrive, and cerebral leukoencephalopathy. We report a case of a 2-year-old boy, status postorthotopic liver transplantation for Navajo neurohepatopathy, who presented with a small patent ductus arteriosus and pulmonary hypoplasia. While vascular coiling of the ductus arteriosus was being performed, a right ventricular heart biopsy was taken to evaluate his cardiac muscle for mitochondrial disease, which may have led to left ventricular hypertrophy. The cardiac biopsy showed immature muscle fibers of varying sizes, many containing subsarcolemmal and intermyofibrillar aggregates (ragged red fibers). Nicotinamide adenine dinucleotide (NADH) histochemical staining illustrated an abnormal intermyofibrillar network. Electron microscopy revealed a significant increase in the number of mitochondria, which appear large and diffusely swollen, in addition to pressure amplification of cristae with focal condensations. This is the first reported description of mitochondrial disease within cardiac muscle in a patient with Navajo neurohepatopathy.

A Malignant Peripheral Nerve Sheath Tumor of the Cauda Equina Mimicking Myxopapillary Ependymoma: A Case Report With Emphasis on Differential Diagnosis

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Malignant peripheral nerve sheath tumors can be diagnostic dilemmas, especially when these tumors present in unusual locations. These tumors are usually subcutaneous and may have nonspecific gross and microscopic presentations. Immunohistochemistry and electron microscopy may be beneficial to render a precise diagnosis. An example of such a dilemma involves a 49-year-old woman who presented with back pain that had become severe during the course of a month. An L5 disk herniation and a spinal cord tumor at the level of L2 were found by magnetic resonance imaging. During surgery, an intraoperative frozen section was suggestive of myxopapillary ependymoma, which was also the clinical impression. The tumor was found to be encapsulated and to involve a single nerve root and was completely excised. Examination of hematoyxlin–eosin–stained sections at low power demonstrated a lobular morphology. Higher magnification revealed delicate, spindle-shaped cells separated by a myxoid matrix. Foci of spindled cells without myxoid change and areas of loose stellate cells were also observed. Pallisading of tumor cells was not identified. Based on these findings, myxopapillary ependymoma was ruled out, and the diagnoses considered included neurothekeoma, nerve sheath myxoma, and schwannoma. Immunohistochemical staining for S100 was strongly positive, glial fibrillary acidic protein showed weak, focal cell positivity, and epithelial membrane antigen was negative. Ultrastructural evaluation demonstrated long, intertwined cell processes lined by basal lamina and numerous Luse bodies, consistent with Schwannian differentiation.

**Presacral, Immature Teratoma With Predominant Medulloepithelioma Component Accompanied By Sacrococcygeal Bone Defect and Intradural Extension**

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Presacral teratomatous tumors combined with sacral bone defects are uncommon. We report a rare case that contains medulloepithelioma component. An 11-month-old female infant presented with several weeks’ history of constipation and flacid lower extremities. Magnetic resonance imaging of the lumbar spine revealed a large mass (5.5 × 4.8 × 4.5 cm) in the presacral space, accompanied by a defect of the fourth and fifth sacral and coccygeal bone spines. The mass extended posteriorly into the spinal canal, surrounded the cauda equina, and extended superiorly to the eighth thoracic spine. The patient underwent excision of the presacral and intradural portion of the mass. On microscopic examination of the resected mass (25 of 26 blocks, entirely submitted) was composed largely of immature, neural parenchymal tissue at different stages of maturation, admixed with benign connective tissue, within which was a solitary area of pure medulloepithelioma-like component up to 2.5 cm on greatest dimension. A small portion of the tumor (1 of 26 cassettes) contained mature skin with hair and respiratory mucus-secreting glands. These features are consistent with a diagnosis of immature teratoma with predominant medulloepithelioma component. This patient was treated with surgery only. At 5 years follow-up, there was no evidence of recurrence. Thorough search in the English literature, the combination of teratoma with medulloepithelioma-like component with sacral bone defects has not been reported.

**Navajo Neurohepatopathy: First Description of Cardiac Mitochondrial Disease**

(Alexa Siddon, MD) (alexa.siddon@yale.edu); Anita Huttner, MD. Department of Pathology, Yale, New Haven, Connecticut.

Navajo neurohepatopathy is an autosomal recessive disease affecting 1 in 1600 live births in the Navajo population of the southwestern United States. The clinical features previously described include hepatopathy, corneal anesthesia, progressive sensorimotor neuropathy, failure to thrive, and cerebral leukoencephalopathy. We report a case of a 2-year-old boy, status postorthotopic liver transplantation for Navajo neurohepatopathy, who presented with a small patent ductus arteriosus and pulmonary hypoplasia. While vascular coiling of the ductus arteriosus was being performed, a right ventricular heart biopsy was taken to evaluate his cardiac muscle for mitochondrial disease, which may have led to left ventricular hypertrophy. The cardiac biopsy showed immature muscle fibers of varying sizes, many containing subsarcolemmal and intermyofibrillar aggregates (ragged red fibers). Nicotinamide adenine dinucleotide (NADH) histochemical staining illustrated an abnormal intermyofibrillar network. Electron microscopy revealed a significant increase in the number of mitochondria, which appear large and diffusely swollen, in addition to pressure amplification of cristae with focal condensations. This is the first reported description of mitochondrial disease within cardiac muscle in a patient with Navajo neurohepatopathy.
Diffuse Leptomeningeal Oligodendrogliomatosis Diagnosed at Autopsy
(Poster No. 52)

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Widely disseminated subarachnoid involvement by oligodendroglioma in the absence of a clinically apparent intraparenchymal focus is rare; only 12 cases have been reported in the English literature. We describe an autopsy case of a 37-year-old woman who presented with new onset of seizures and a 6-month history of headaches. Imaging demonstrated diffuse intracranial leptomeningeal thickening, as well as a mass lesion in the distal thoracic spinal cord and conus medullaris. She developed refractory intracranial hypertension and died 2 days after hospital admission. At autopsy, the lumbosacral leptomeninges and spinal cord were involved by a glistening, white mass, which extended throughout the length of the posterior spinal cord. Microscopic examination revealed a well-differentiated oligodendroglioma in the subarachnoid space surrounding the spinal cord, spinal nerve roots, parietal and temporal lobes, medulla, and optic chiasm. Tumor also infiltrated the lumbosacral spinal cord. Tumor cells were immunoreactive with glial fibrillary acidic protein and were negative for epithelial membrane antigen, NeuN, synaptophysin, and chromogranin. The MIB-1 labeling index was approximately 2%. Fluorescence in situ hybridization markers for 1p19q (1p36/1q25, 1p32/1q13), and 19p13 were intact. Another unusual finding in this case was a pleomorphic adenoma arising within the choroid of the left eye. To our knowledge, this represents the first case of diffuse leptomeningeal oligodendrogliomatosis in a young adult patient. These findings are consistent with giant cell arteritis and rule out a neurodegenerative disorder characterized by eosinophilic intranuclear inclusions.

Fatal Cerebral Infarction in a Young Man Secondary to Disseminated Giant Cell Arteritis
(Poster No. 53)

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GIant cell arteritis is unusual in patients younger than age 50, and concurrent intracranial and visceral involvement in this disease is extremely rare. We report the case of a rapidly progressing, disseminated giant cell arteritis in a 24-year-old man who presented with a history of severe headache leading to collapse. Computed tomography studies showed filling defects involving both middle cerebral arteries and infarcts in multiple arterial territories. Results of routine blood work, cultures, serologies, and autoimmune and hypercoagulability workups were unremarkable. Attempts at recanalization failed, and the patient died of multiple cerebral infarctions. Postmortem examination showed arteritis composed of multinucleated giant cells, lymphocytes, and histiocytes causing thrombosis in segments of both middle and anterior cerebral arteries and one posterior cerebral artery. Both carotid siphons and one renal artery segment were also involved. The arteritis was circumferential with many CD4+ and CD8+ lymphocytes in the adventitia and fragmentation of the internal elastic lamina by invading giant cells (Figure 78). The arteries affected ranged from 2.0 to 3.5 mm in diameter, and all lesions were the same age as the little fibrinoid necrosis. Special stains for fungi, bacteria, β-amyloid, and in situ hybridization for varicella-zoster virus were negative. These findings are consistent with giant cell arteritis and rule out a primary central nervous system vasculitis. To our knowledge, this is the first reported case in the literature of disseminated giant cell arteritis in an atypical age group with concurrent involvement of the anterior, middle, and posterior cerebral arteries and extracranial visceral arteries.

A Rare Neoplasm of the Extramedullary Intradural Spinal Canal
(Poster No. 54)

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The most common extramedullary intradural spinal tumors in adults include meningioma, schwannoma, metastasis, and secondary lymphoma/leukemia. A 30-year-old man presented after several months of progressive weakness and sensory deficit in his left lower extremity. Magnetic resonance imaging revealed an ovoid well-defined extramedullary intradural mass at the T11 to T12 level, which avidly enhanced following contrast administration. Following a complete staging workup that was negative for additional masses, the patient underwent surgical excision of the tumor. Intraoperative findings revealed a firm extramedullary tumor underlying the left-sided distal thoracic nerve roots. The tumor was diagnosed as a probable nerve sheath tumor (schwannoma vs neurofibroma) by intraoperative cytology. On submission of the mass in formalin for routine permanent sections, the tumor was grossly identified as an ovoid, well-circumscribed, firm, tan-white mass. Histologic study revealed a tumor with a patternless architecture, and numerous small to medium-sized, branching “stag-horn” blood vessels. Many spindle-shaped and uniform cells with little cytoplasm, indistinct borders, and vesicular bland nuclei were dispersed among abundant thick bands of hyalinized collagen (Figure 79). Immunohistochemistry revealed the spindle-shaped cells to be positive for CD34 and BCL2 and negative for S100 and epithelial membrane antigen. Morphologic and immunophenotypic features supported the diagnosis of solitary fibrous tumor. A solitary fibrous tumor of the spinal canal is a rare entity that should, nevertheless, be considered in the differential diagnosis of an extramedullary intradural spinal tumor.

Neuronal Intranuclear Inclusion Disease Diagnosed Incidentally at Autopsy
(Poster No. 55)

Wendy N. Wiesend, MD (wendy.wiesend@beaumont.edu); Joseph E. Parisi, MD; Jon D. Wilson, MD.1 Department of Anatomic Pathology, William Beaumont Hospital, Royal Oak, Michigan; 2Department of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota.

Neuronal intranuclear inclusion disease (NIID) is an exceedingly rare neurodegenerative disorder characterized by eosinophilic intranuclear inclusions in neurons and glia of the central nervous system and neurons of the peripheral nervous system. The clinical features of the disease are highly heterogenous. In adult-onset cases, in which dementia may be a prominent feature, inclusions are seen more frequently in glial cells than...
neurons. Most cases are sporadic; however, familial cases have rarely been reported. NIID is suspected to be a trinucleotide repeat (CAG) disorder, but this has not been proven definitively. We present a case of NIID diagnosed incidentally at autopsy in a 71-year-old woman who died of sepsis. Gross examination of the brain revealed only mild frontal-parietal cortical atrophy, commensurate with age. Microscopic examination revealed characteristic intranuclear inclusions in neurons and glial cells throughout the neuraxis. Inclusions were also identified in other central and peripheral nervous system cells, including myenteric plexus and celomic ganglion neurons. The inclusions were decorated by ubiquitin, but were negative for Gallyas and other markers, including β-amyloid, and neurofilament protein. On electron microscopy, the inclusions demonstrated filamentous ultrastructure. Subsequent discussion with a family member revealed that the patient had 2 children with mental retardation of unknown etiology. The patient had previously functioned well as a nurse. This case demonstrates that NIID may be asymptomatic and present late in life. The more clinically apparent symptoms seen in this patient's children are suggestive of "anticipation," which is characteristic of trinucleotide repeat disorders.

**Metastatic Cranioopharyngioma**

(Poster No. 56)

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A 51-year-old man was treated 2 years prior at another institution for a suprasellar cranioopharyngioma with subtotal resection and postoperative radiation therapy. One year following the initial resection, he underwent a second surgery at our institution for gross total resection of a suprasellar recurrence. Follow-up magnetic resonance imaging 1 year after this second surgery showed a new mass in the right temporal convexity. The new tumor was distinct from the primary tumor bed or the tract of prior surgical resection. The tumor was dissected free of the temporal cortex via a right temporal craniotomy. All tumor was removed, the field irrigated, and the craniotomy closed. Histopathology confirmed cranioopharyngioma in the subarachnoid space. Metastatic recurrence of cranioopharyngioma is a rare complication of tumor resection. Cranioopharyngioma tumor cells seeded to the cerebrospinal fluid intraoperatively have metastatic potential. Analysis of post reports shows these tumors recur at a median of 2 years following the most recent operation. Long-term neuroimaging follow-up is indicated.

**Early and Late Solvent-Related Neuropathology**

(Poster No. 57)

Zahra Al-Hajri, MD (zalajri@hotmail.com); Marc R. Del Bigio, MD, PhD, FRCP(C). Department of Pathology, University of Manitoba, Winnipeg, Manitoba, Canada.

**Context:** The neuropathology of solvent inhalation (especially toluene) has characteristic features, consisting of patchy myelin loss with white matter macrophages that contain granular inclusions.

**Design:** A retrospective study from 1985 to 2008 including 73 autopsy cases with documented history of solvent abuse. Among these are 6 fetuses and infants with history of maternal exposure; 15 children, age 12–17 years; and 52 adults, age 18–86 years. Circumstances of death included 22 acute intoxications, 15 hangings, 7 traumas, 7 sepsis/aspirations, 4 fire/burns, and 3 hypothermias. Paraffin blocks from 61 cases were recut and stained with solochrome cyanin to demonstrate myelin and periodic acid-Schiff (PAS) to highlight the characteristic inclusions. All slides were examined in a blinded manner by the senior author. Patchy loss of myelin and the prevalence of inclusions were documented semiquantitatively.

**Results:** Eleven patients (age, 23–49 years; median, 40 years) had well-established leukoencephalopathy with multilocular perivascular myelin loss and inclusion-containing macrophages. Five patients (age, 15–53 years; median, 22 years) had mild changes consisting of rare inclusion-containing cells but no obvious myelin change. All parts of brain, but not cranial or spinal nerves, are potentially involved.

**Conclusions:** Given the sociologic nature of solvent abuse, actual exposure is impossible to ascertain. However, it would appear that there is a duration-dependent effect. Interaction with alcohol and possible other risk factors need to be considered to explain why not all heavy users develop the disease.

**Rare Intradural Extraosseous Chordoma in a 51-Year-Old Woman:** Case Report and Literature Review

(Poster No. 58)

Lorna L. Ogden, MD (ogdenlorna@gmail.com); Steven A. Drexler, MD. Department of Pathology, Winthrop University Hospital, Mineola, New York.

We report on a 51-year-old woman who underwent brain tumor resection after presenting with altered mental status. On computed tomography scan before the resection, the patient was found to have a large suprasellar mass encroaching on her third ventricle. At the time of surgery, the tumor was in the suprasellar region with no connection to the sella. The histology showed tumor cells arranged in cords and nests with abundant eosinophilic cytoplasm and irregular nuclei floating in a mucinous matrix. A focal area of matrix with osteoid and calcification was present. Immunohistochemical stains demonstrated the patient's tumor was positive for calretinin and S100. Epithelial membrane antigen and S100 were focally positive. Occasional lymphocytes on leukocyte common antigen were positive. Glial fibrillary acidic protein was negative. Based on the clinical history, permanent histologic findings, and the immunohistochemical profile, the final diagnosis was an intradural, extraosseous chordoma. Only 16 previous cases of intradural chordoma have been reported with only 3 reported in the past 17 years. A suprasellar location is even rarer, being reported in only 2 of the above-mentioned 16 cases. Unique to this case is the finding of osteoid formation and calcification, which to date has not been reported in the literature for intradural chordomas.

**SOX2 Is a Glioma-Specific Marker and Potential Target for Therapy**

(Poster No. 59)

Jennifer Eschbacher, MD (jenny.eschbacher@chwu.edu); Val Felton, BS; Anna Joy, PhD; Burt Feuerstein, MD, PhD; Stephen Coons, MD. Department of Neuropathology/Pathology, Barrow Neurological Institute, Phoenix, Arizona.

**Context:** It is becoming increasingly apparent that biologic pathways active during tumorigenesis often parallel developmental pathways. SOX2 is a well-characterized transcription factor expressed during the early neuroectodermal stage of human central nervous system (CNS), where expression is lost during neuronal differentiation but maintained during gliogenesis. We hypothesized that SOX2 would be expressed in gliomas, but not in neuronal tumors, and that inhibition of SOX2 would negatively affect glioma growth in vitro.

**Design:** One hundred twenty-eight gliomas and 47 nonglial primary CNS tumors were evaluated by immunohistochemistry for SOX2 protein expression. Published gene RNA expression microarray data were analyzed for SOX2 in grade II to grade IV astrocytomas, grade II and III oligodendrogliomas, and medulloblastomas. We further evaluated the effects of inhibition of SOX2 with small, interfering RNA on 5 glioma cell lines.

**Results:** SOX2 protein was expressed in 95% (122 of 128) of gliomas, including astrocytomas (World Health Organization [WHO] grades I–IV), oligodendrogliomas (WHO grades II, III), ependymomas (WHO grades I–III), and oligoastrocytomas (WHO grade II). Of the 47 nonglial primary CNS tumors, 83% (39 of 47) were nonreactive for SOX2 protein, including 81% (29 of 36) of tumors with neuronal features. RNA expression microarrays indicated strong SOX2 expression in astrocytomas and oligodendrogliomas and less in medulloblastomas, consistent with immunohistochemistry. We found a significant decrease in cell number (up to 50%) in all 5 cell lines.

**Conclusions:** Our results suggest that inhibition of SOX2 or one of its upstream or downstream factors may be a good target for glioma therapeuic treatment. SOX2 may also serve as a adjuvant marker for gliomas in the diagnostic setting.

**MALT Lymphoma of the Dura Mater**

(Poster No. 60)

Jyoti Kapil, MD1 (jpkapil01@gmail.com); Haipeng Shao, MD2; Robert Jones, MD1; Mark Raffeld, MD; Elaine Jaffe, MD. 1Department of Pathology, George Washington University Hospital, Washington, DC; 2Department of Hematopathology, National Institutes of Health, Bethesda, Maryland.

We present the case of a 61-year-old woman who sought medical attention for vertebral headaches and vertigo lasting a few months in duration. Magnetic resonance imaging (MRI) showed a diffuse dural-based isointense, contrast-enhancing, extra-axial lesion in the right posterior fossa along the right lateral wall, thought to be an en-plaque meningioma. During a 6-week preoperative interval, the patient was maintained on dexamethasone and a repeat MRI on day of surgery showed significant shrinkage of the mass. Intraoperative evaluation of the specimen showed a proliferation of small, round lymphocytes with admixed plasma cells. Permanent sections displayed dura infiltrated by small lymphocytes, marginating B cells, plasmacytoid cells, plasma blasts, marginal zone B cells, and transformed B cells. Proliferating cells were immunopositive for CD20 and CD79a and immunonegative for CD5, CD10, CD43, and CD23. Many of
these B cells were MUM1+ and showed a light-chain restriction. Epstein-Barr virus LMP-1 immunostain was negative. These features were consistent with a diagnosis of extranodal marginal-zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) type. Polymerase chain reaction (PCR) for immunoglobulin heavy-chain gene rearrangements showed a polyclonal rearrangement pattern. However, PCR has an approximately 20% false-negative rate in detecting clonal immunoglobulin \( \text{H} \) gene rearrangement. Primary lymphomas of the dura are rare, with most cases falling within the spectrum of MALT lymphoma. Overlap with plasmacytoma may exist, although it is not a factor in our case. With correct diagnosis and treatment, dural extranodal marginal zone lymphomas of MALT-type have a very favorable prognosis. This entity deserves wider recognition among pathologists responsible for diagnosis of neurosurgical material.

**Neuropathologic Causes of Medically Intractable Epilepsy in Magnetic Resonance Imaging–Negative, Anterior Mesial Temporal Lobe Resections Other Than Hippocampal Sclerosis**

*(Poster No. 61)*

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**Context:** Among a pool of 388 anterior mesial lobe neurosurgical resection specimens from 1997 to 2008, 86 were designated as patients with magnetic resonance imaging (MRI)–negative, medically intractable seizures. Thirty-eight cases were neuropathologically classified as hippocampal sclerosis (HPC-S). Twenty-five were negative for HPC-S. Five patients had MRI-negative, neuropathologic causes of intractable epilepsy other than HPC-S.

**Design:** Histologic sections were reviewed with 2 observers rating 12 neuropathologic criteria and scoring 1 to 3 (mild-moderate-severe). Observers were blinded, except to MRI-negative status. Neuropathology criteria scored were presence of glissis or pyramidial cell neuronal loss in \( \text{CA}4 \); outer rim of \( \text{CA}4 \)/layer 3 dentate cortex; \( \text{CA}3 \); proximal \( \text{CA}1 \); Sommer sector; distal \( \text{CA}1 \), with sparing of \( \text{CA}2 \); presence of cortical dysplasia/migration defect; lesions of dentate gyrus/entorhinal cortex; amygdala; and vascular hyalinization/endothelial hyperplasia. MRIs were reviewed separately by 2 neuroradiologists, the neurosurgeon, and epilepsy team.

**Results:** Five patients had neuropathologic causes of temporal lobe-localized epilepsy, other than primary HPC-S. Patients had (1) adult polyglucosan body (Lafora disease); (2) cortical dysplasia; (3) glial-neuronal migration defect; (4) viral encephalitis; and (5) cavernous hemangioma (Table).

**Conclusions:** The patients with Lafora disease and viral encephalitis had HPC-S pattern disease suggesting the possibility of secondary HPC-S developing in association with viral infections and neurodegenerative diseases, whereas developmental (cortical dysplasia/migration defect) and vascular lesions did not produce a HPC-S pattern. Neurosurgical intervention was effective, resulting in patients who were seizure-free (n = 3) and nearly seizure-free (n = 2). Inflammatory, vascular lesions, polyglucosan bodies with calcifications may be MRI-negative causes of temporal lobe epilepsy; other localizing modalities may be needed before surgical intervention.

**Clinical and Neuropathologic Data of the 5 MRI-Negative Medically Intractable Epilepsy Patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Engel Classification</th>
<th>PET/SPET</th>
<th>Main Pathology</th>
<th>Finding</th>
<th>HPC-S</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>II</td>
<td>Normal</td>
<td>Lafora disease</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>II</td>
<td>Cavernous hemangioma</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>II</td>
<td>Migration defect</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>I</td>
<td>Normal</td>
<td>Viral encephalitis</td>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>I</td>
<td>Positive</td>
<td>Cortical dysplasia</td>
<td>Negative</td>
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</tbody>
</table>

**Immunohistochemical Analysis of Interleukin-27 (WSX-1/TCCR) Receptor Expression in Human Neuronal Cell Bodies**

*(Poster No. 62)*

John H. Irlam, DO (john.irlam@utoledo.edu). Department of Pathology, The University of Toledo Medical Center, Toledo, Ohio.

**Context:** Interleukin-27 is a newly identified interleukin-12 related cytokine that has demonstrated the ability to induce proliferation and differentiation of naïve CD4+ T cells into a Th1 population as well as attenuating and suppressing cytokine production. In addition, interleukin-27 has demonstrated potent antitumor effects as well as playing a role in the regulation of hematopoietic stem cell differentiation. To date, there has been limited reporting on interleukin-27 receptor (WSX-1/TCCR) expression in the human central nervous system. Through immunohistochemical analysis of interleukin-27 receptor expression was qualified by light microscopy and compared with splenic T lymphocytes with known receptor expression.

**Results:** Examination of neural tissue demonstrated strong cytoplasmic staining in neuronal cell bodies without significant staining in neuronal axons or other cells of the brain, including astrocytes, microglial cells, or oligodendrocytes.

**Conclusions:** Preliminary results demonstrate a strong positive staining pattern in neuronal cytoplasm for interleukin-27 receptor (WSX-1/TCCR) expression in the human brain without significant expression in astrocytes, microglial cells, or oligodendrocytes. To our knowledge, this has not been previously reported in human neurons. We submit that the importance of this expression has yet to be determined and that further evaluation is needed.

**Concurrent Oligodendroglioma and Hemangioblastoma in the Brain of a 49-Year-Old Man**

*(Poster No. 63)*

Jonathan L. Klein, MD (kleimmd@gmail.com); Steven Dreixler, MD. Department of Pathology, Winthrop University Hospital, Mineola, New York.

We report a case of a 49-year-old man who presented with generalized tonic-clonic seizure. The patient was found to have enhancing right cerebellar and nonenhancing right parietal masses on magnetic resonance imaging. The right cerebellar mass was resected, and the histology showed 2 distinct cell populations; one population consisted of interstitial cells with intracytoplasmic fat vacuoles, and a second population consisted of endothelial cells forming vascular channels. A Giemsa stain showed scattered mast cells. The findings were consistent with a World Health Organization (WHO) grade I hemangioblastoma. Eighteen days later, the patient returned for a biopsy of the parietal nonenhancing mass. The histologic sections at this time showed a tumor composed of a homogeneous cell population of intermediate-sized cells with prominent chromatin, occasional small nucleoli, and perinuclear clearings. There was no vascular endothelial hyperplasia, necrosis, or observable mitoses. Fluorescence in situ hybridization studies revealed the tumor to have deletions of 1p and 19q. The findings were consistent with a WHO grade II oligodendrogloma. The occurrence of 2 concomitant primary brain neoplasms is extremely rare and may represent an antibody to the interleukin-27 receptor (WSX-1/TCCR), we hope to further elucidate and qualify interleukin-27 receptor expression in the human brain.

**Pending Case Reports: Tools for Reducing Turnaround Time and for Practice Improvement**

*(Poster No. 64)*

Meenakshi Singh, MD (meenakshi.singh@stonybrook.edu); Kathleen Dasilva, BS; Sui Zee, MD; Kenneth Shroyer, MD, PhD. Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

**Context:** Turnaround time (TAT) is an important quality measure. Laboratory information systems can provide TAT and pending case reports (PCRs).

**Design:** We sought to use PCRs to evaluate practice performance, identify areas for improvement, allocate resources, and evaluate impact of these measures. We reviewed weekly PCRs during 21 weeks to identify sources contributing to overdue/pending cases. Weekly overdue charges were reviewed.

Eight of four contributing sources were identified. (1) Equipment failure (electron microscope [EM]); an alternate EM was identified within the institute, cases were completed, and a mechanism was established for...
ongoing use. Pending EM cases went from 27 to 0. (2) We process 250+ placentas each month. A backlog of cases was successfully cleared (from 138 to 2 cases) with changes made to histology work distribution and to a backup service plan. (3) A slow decalcification process replaced with a rapid method markedly reduced pending bone cases (from 16 to 1). (4). Thyroid fine-needle aspiration (FNA) cases were traditionally signed out in a longer timeframe than other cytology cases. Instead of submitting all thyroid FNAs to one cytopathologist on a given day, cases were distributed with direct notification to all practicing cytopathologists. This has reduced TAT from 4.5 to 2.4 days. The overall pending list was significantly reduced (from a maximum of 154 cases in a week to 2 cases in a week). Overdue charges significantly decreased (from $70.5 K to $1K).

Conclusions: FCRs are a valuable tool for practice assessment. Using them enabled our service to achieve and even exceed TAT benchmarks.

### Voice Recognition Software Use Enhances Surgical Pathology Work Flow

**Poster No. 65**

Tim Pal, MD; Mark Hersh, MS, MT(ASCP); Meenakshi Singh, MD (meenakshi.singh@stonybrook.edu). Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

**Context:** Based on experience with voice recognition software (VRS) for gross descriptions, we initiated a pilot study to determine its efficacy in surgical pathology sign-out.

**Design:** Dragon Naturally Speaking software (Version 10) enhanced by a pathology VRS (VoiceOver from VoiceBrook) was used. After 1 hour of training, pathologists used VRS for surgical pathology reports. A second group of similar cases was submitted in the routine manner for typing (RMT). The time it took to sign-out different types of cases by both methods was tracked.

**Results:** A significant time benefit was obtained with VRS use versus RMT (mean, 1.6 vs 747 minutes; median, 2 vs 495 minutes for a total of 62 cases). The VRS reports became available in the hospital information system within minutes of viewing the slides. VRS misinterpretations were uncommon and were corrected in real-time before electronic release of reports. Errors related to handwriting with the RMT were avoided. A seamless flow from looking at the slides under the microscope, dictating using VRS, and submitting VRS reports using VRS.

**Conclusions:** VRS tailored for surgical pathology reports can be a valuable tool for a pathologist. We have decided to incorporate VRS for sign-out of surgical pathology cases.

### Multiplex Polymerase Chain Reaction Diagnosis of Viral Respiratory Infections: Projected Cost Savings and Effect on Patient Admission Length

**Poster No. 66**

Ian M. Bovio, MD (boviim@pathology.ufl.edu); Howard Rampersaud, BS, MT; Kenneth Rand, MD. Department of Pathology, University of Florida, College of Medicine, Gainesville.

**Context:** Viral respiratory infections (VRI) account for numerous hospitalizations. Viral culture is hampered by prolonged turnaround time and suboptimal sensitivity, potentially resulting in extended length of stay (LOS). Multiplex polymerase chain reaction (PCR) is a sensitive, rapid technique that simultaneously detects multiple viruses in 24 hours or less. As molecular technology approaches the market, expenses must be justified by demonstrating the ability to economically improve patient care. We sought to project cost savings and LOS impact by implementing multiplex viral PCR.

**Design:** We analyzed LOS for inpatients tested for influenza or RSV by direct antigen testing (DAT) or culture from June 2003 to June 2008. To exclude significant comorbidities, we included only patients younger than 16 years with LOS of 10 or fewer days. LOS was divided into 4 subgroups depending on result (positive or negative) and type (rapid or nonrapid) of test. Number and relative percentages of patients discharged on days 0 through 10 for positive/rapid, positive/nonrapid, negative/rapid, and negative/nonrapid were calculated. The assumption is LOS by DAT can serve as a surrogate indicator for LOS by other rapid (ie, multiplex PCR) diagnostic modalities.

**Results:** LOS in admission days per 100 patients was as follows (Figure 80): positive/rapid (301.7), positive/nonrapid (360.8), negative/rapid (339.8), negative/nonrapid (431.5). For positive groups, χ² was 0.31; however, rapid versus nonrapid influenza was 0.0038. For negative groups, χ² was 3.35 x 10⁻²⁰. With multiplex PCR implementation, it is assumed (regarding LOS) that nonrapid groups shift to rapid groups, resulting in $276 000 annual variable admission cost savings.

**Conclusions:** VRI multiplex PCR has potential for cost savings and improved patient care.

### Cardiac Epithelioid Angiosarcoma With Pulmonary Metastases Presenting as Primary Pulmonary Epithelioid Hemangioendothelioma

**Poster No. 68**

Mark Podberezin, MD (markp@uic.edu); Thitiwat Sriprasart, MD2; Eugene DeGuzman, MD; Sangeeta Mehendale, MD; Carey August, MD3; Department of Pathology, University of Illinois, Chicago; Departments of Internal Medicine and Pathology, Advocate Illinois Masonic Medical Center, Chicago.

**Abstracts**

**Cardiac Epithelioid Angiosarcoma With Pulmonary Metastases Presenting as Primary Pulmonary Epithelioid Hemangioendothelioma**

**Poster No. 68**

Mark Podberezin, MD (markp@uic.edu); Thitiwat Sriprasart, MD; Eugene DeGuzman, MD; Sangeeta Mehendale, MD; Carey August, MD. Department of Pathology, University of Illinois, Chicago; Departments of Internal Medicine and Pathology, Advocate Illinois Masonic Medical Center, Chicago.

Arch Pathol Lab Med—Vol 133, October 2009
We report a case of a cardiac epithelioid angiosarcoma with pseudoaneurysmal communication with right atrium and bilateral lung metastases, presenting as primary pulmonary epithelioid hemangioendothelioma. To the best of our knowledge, this is the first case of this kind of cardiac tumor with pseudoaneurysmal communication with the right atrium. The patient was a 43-year-old, previously healthy man, who presented with a 6-month history of progressive dyspnea on exertion, hemoptysis, and severe right-sided chest pain. Computed tomography of the chest showed multiple subcentimeter pulmonary nodules, and open lung biopsy confirmed the presence of circumscribed, but ill-defined, nodules, comprising cells with a mixed epithelioid and spindled morphology and numerous extravasated erythrocytes frequently in a myxoid or hyalinized background. Mitotic activity was not prominent, but the nuclei were moderately atypical, with vesicular chromatin and occasional prominent nucleoli. Within the myxomatous and hyalinized areas, cells often contained intracytoplasmic vacuoles. The lesional cells were immunoreactive with vascular markers CD31, CD34, and factor VIII. The morphologic findings were thus most consistent with a primary epithelioid hemangioendothelioma. Magnetic resonance imaging revealed a 4-cm, right atrial mass with pseudoaneurysmal cavity. Considering the presence of a solitary cardiac mass accompanied by multiple pulmonary nodules with foci of cytologic atypia, the final diagnosis was primary cardiac epithelioid angiosarcoma with multifocal pulmonary metastases. This case illustrates the morphologic overlap between epithelioid hemangioendothelioma and epithelioid angiosarcoma and emphasizes the importance of correlating pathologic findings with clinical data and imaging studies.

POSTER SESSION 600: TUESDAY, OCTOBER 13, 2009, 11:00 AM–1:30 PM
Endocrine Pathology; Head, Neck and Oral Pathology; Informatics; Microbiology; Ophthalmic Pathology; Molecular Pathology; Pathology Education; Quality Assurance

Morphoxygenic Confirmation of an Activated Nuclear Factor–κB Pathway in Follicular Thyroid Carcinoma (Poster No. 1)
Jing Liu, MD, PhD (Jing.Liu1@uth.tmc.edu); Robert E. Brown, MD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center, Houston Medical School, Houston.

Context: Follicular thyroid carcinoma is the second most malignant thyroid neoplasm. The role of the nuclear factor–κB pathway in the pathogenesis of follicular thyroid carcinoma has not been fully investigated.

Design: We retrieved 10 cases of follicular thyroid carcinoma from our files. Tissue microarrays were constructed using 2.0-mm cores from formalin-fixed, paraffin-embedded tissue blocks. Tissue microarray sections were immunohistochemically stained for p-nuclear factor–κB (Ser 536), interleukin 8 (IL-8), and glutathione S-transferase–pi. Staining intensity (0 to 3+), extensiveness (0%-100%), and subcellular compartmentalization were evaluated. The positive staining intensity was graded as weak (1+), moderate (2+), or strong (3+).

Results: Both nuclear and cytoplasmic immunoreactivities with p-nuclear factor–κB (Ser 536) were observed in all 10 cases, including moderate to strong nuclear staining intensity with a range of extensiveness from 20% to 100% of tumor cells. Moderate or strong cytoplasmic expression of IL-8 was present in 50% to 100% of tumor cells in all cases. Glutathione S-transferase–pi diffusely (70%-100%) and moderately or strongly stained the tumor cytoplasm in all cases (except in one case with insufficient tissue). Three of these cases also demonstrated nuclear positivity.

Conclusions: Morphoxygenic analysis revealed the constitutive activation of the nuclear factor–κB pathway in follicular thyroid carcinoma (phosphorylation at Ser 536 with nuclear translocation and with correlation expression of transcriptionally active gene products, IL-8, and glutathione S-transferase–pi). These results provide some insight into the biology of follicular thyroid carcinoma and a potential therapeutic target.

Incidental Papillary Thyroid Microcarcinoma With Lung Metastasis, an Autopsy Case Study: Should We Adopt the Term Papillary Micro-Tumor of the Thyroid Instead of Microcarcinoma? (Poster No. 2)
Oleksandr N. Kryvenko, MD (okryven1@hfhs.org); Osama Alasi, MD. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.

Papillary thyroid microcarcinoma (PTMC) is defined by the World Health Organization as a tumor measuring less than 10 mm and demonstrating cytologic features of conventional papillary thyroid carcinoma. Most tumors in this group are indolent and are found incidentally. Occasionally, they may present as cervical lymph node metastasis. Some suggest using the term papillary micro-tumor instead of PTMC for intra-thyroid tumors with favorable prognosis. We discuss the case of a 58-year-old woman who presented with loss of consciousness secondary to bilateral cerebellar infarcts. Suboccipital craniotomy was performed in an effort to decompress the posterior fossa. However, the patient died shortly thereafter. Routine gross examination of the internal organs and microscopic slides with immunohistochemical stains were performed. The cause of death was bilateral cerebellar and frontotemporal infarcts. The thyroid was symmetric and nonenlarged, with an 8-mm solid nodule in the right lobe. Microscopic examination of the thyroid revealed PTMC with extrathyroid extension and no vascular or lymphatic invasion. The lung sections revealed microscopic foci of thyroid papillary carcinoma in 2 lobes, which were confirmed by positive thyroglobulin immunostain (Figure 81). Although the primary focus of this PTMC did not demonstrate high-risk histologic features, such as vascular invasion and extrathyroid extension, pulmonary metastases were seen. It is unlikely that these metastases contributed to the patient’s death; however, this case demonstrates the potential for widespread dissemination of PTMC and possible adverse outcome.
Expression of Matrix Metalloproteinase 7 and Fibronectin in Papillary Thyroid Cancer: Gene Expression Profiling Using Real-Time Polymerase Chain Reaction

(Poster No. 4)

Malak Abedalthagafi, MD (mxa212@gunet.georgetown.edu). Department of Pathology, Georgetown University Hospital, Washington, DC.

Context: Papillary thyroid cancer (PTC) is usually indolent with a high frequency of lymph node metastasis. Rarely, PTC behaves in a more aggressive fashion; however, the mechanisms of invasion and metastasis in thyroid cancer remain poorly understood. We recently encountered a case of aggressive PTC with metastasis to the spine that prompted us to study molecular profiles of PTC with aggressive behavior.

Design: We studied 5 cases of PTC for which fresh-frozen tissue was available. In 3 cases, there was a distant metastasis to the lung and bone; the other 2 cases had only local disease. We used the human tumor metastasis RT2 Profiler PCR Array (SA Bioscience, Frederick, Maryland) and a high-performance SYBR green LightCycler real-time PCR (Roche, Indianapolis, Indiana). The array represents 84 genes known to be involved in metastasis. Statistical analysis was performed using the PCR Array Data Analysis Web Portal.

Results: Analysis of the 2 PTCs without hematogenous metastasis showed down-regulation of matrix metalloproteinases and fibronectin. Significant over-expression of metalloproteinases, especially MMP7, and fibronectin were found in 3 PTCs with hematogenous metastasis (group 1; Figure 83). Compared with normal control and PTC without hematogenous metastasis, the ratios of fibronectin and MMP7 expression were 1066.5 and 700.3, respectively.

Conclusions: Metalloproteinases, particularly MMP7, and fibronectin were over-expressed in PTC with hematogenous metastasis. Metalloproteinases are a family of proteolytic enzymes that degrade protein components of extracellular matrix; thus, these enzymes are believed to play an important role in tumor progression, invasion and metastasis.

Anaplastic Carcinoma of the Thyroid With Osteoclast-Like Giant Cells

(Poster No. 5)

Lea A. Filippone, BA (lealexa@mail.med.upenn.edu); Virginia A. Li-Volsi, MD. Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia.

We report a case of a 64-year-old woman with anaplastic carcinoma of the thyroid occurring in association with 2 distinct, differentiated thyroid carcinomas. The patient presented with a neck mass causing trachea deviation and internal jugular vein narrowing. The histology showed anaplastic undifferentiated carcinoma that was composed of spindle and epithelioid cells with osteoclast-like giant cells. Additionally, we identified 2 areas of differentiated tumor. The first area had papillary architecture with ground-glass chromatin and nuclear grooves that were consistent with papillary carcinoma (Figure 84). The second area exhibited a nest growth pattern with finely granular oncocytic cytoplasm and round nuclei, which was consistent with Hurthle cell carcinoma. The Hurthle cell carcinoma was metastatic to one lymph node. The anaplastic carcinoma was not present in any lymph nodes but exhibited high mitotic activity, extracapsular extension, and lymphovascular invasion with tumor emboli. Immunohistochemical stains for cytkeratins were positive in the Hurthle and papillary components and focally positive in the anaplastic component. Thyroid transcription factor-1 and thyroglobulin were positive in the Hurthle and papillary components and negative in the anaplastic component. The osteoclast-like giant cells were positive for CD68 but not for cytkeratin. Anecdotal case report data in the literature suggest that some thyroid papillary carcinomas can progress to Hurthle cell carcinoma. However, this is the first case report of anaplastic thyroid carcinoma with osteoclast-like giant cells and 2 separate well-differentiated components. This observation raises the possibility of a progression from a well-differentiated papillary carcinoma to Hurthle cell and then to anaplastic carcinoma.

Oncocytic Adrenocortical Neoplasm as an Incidental Finding

(Poster No. 6)

Brad E. Chaser, MD (brad-chaser@ouhsc.edu); Jeffrey S. Bender, MD; Kar-Ming Fung, MD, PhD. Departments of Pathology and Surgery, University of Oklahoma, Oklahoma City.

Although adrenocortical neoplasms are not uncommon, oncocytic adrenocortical neoplasms are rare. We report an incidental case of an oncocytic adrenocortical neoplasm. The patient was a 58-year-old woman with diabetes, hypertension, and osteoarthritis who presented with vague back pain of uncertain duration. Further workup showed a 5.0-cm, left adrenal mass. Her laboratory workup was within normal limits. The tumor was laparoscopically removed. The tumor was received as several irregular pieces, intermixed with fat and normal-appearing adrenal tissue. The largest, intact piece of tumor measured 7.4 cm, and because of the presence of a thin fibrous capsule, appeared to be an accurate approximation of the tumor size. Light microscopy revealed tissue composed of homogenous oncocytic cells with minimal nuclear atypia. The cells were arranged in nests and displayed a tubular pattern. Tumor cells were immunoreactive for vimentin and synaptophysin and negative for inhibin. Ultrastructurally, the cytoplasm was largely filled with numerous mitochondria. A diagnosis of adrenocortical neoplasm was made. Several classification systems have been proposed, but true categorization remains elusive. One system suggests using major and minor criteria to predict biologic behavior of the tumor. Major criteria for malignant classification include a mitotic rate greater than 5 of 50 high-power fields, atypical mitoses, and venous invasion. Minor criteria include large size, necrosis, and capsular/sinusoidal invasion. This tumor lacked all major and minor criteria, and therefore, it was diagnosed as benign.
Papillary Thyroid Carcinomas in the Pediatric Age Group and the Significance of Pathologic Parameters

(Poster No. 7)

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Context: Pediatric thyroid carcinomas are relatively rare, and most are papillary carcinomas with an excellent prognosis. Our study aimed to identify those pathologic parameters that could influence the prognosis of papillary thyroid carcinomas in children.

Design: Twenty-four cases of papillary thyroid carcinomas in the 0- to 18-year-old age group were retrieved from the databases (1989 to 2007) of Long Island Jewish Medical Center and North Shore University Hospital. Hematoxylin-eosin slides were reviewed. The documented clinicopathologic features included age at diagnosis, sex, radiation exposure, treatment, relapse, follow-up duration, histologic subtype, tumor size, tumor follicular, vascular invasion, extrathyroidal extension, margin status, additional pathologic findings, nodal metastases, extranodal extension, distant metastases, and pTNM staging. Statistical analysis was performed using the Fisher exact test. The overall survival rate was derived from a Kaplan-Meier plot.

Results: The most common histologic subtypes were as follows: 16 cases (66.7%) of papillary carcinoma, not otherwise specified, 7 cases (29.2%) of follicular variant, and 1 case (4.2%) of diffuse sclerosing variant. Nineteen cases (79.2%) had nodal metastases at diagnosis. Four patients (16.7%) relapsed with regional lymph node recurrence. A comparison of pathologic parameters between cases with and without recurrence is depicted in the Table. The mean follow-up duration was 8 years. The overall 5-year survival rate was 100%.

Conclusions: Our study confirms the excellent prognosis in cases of pediatric papillary thyroid carcinomas. Positive surgical margins were the only statistically significant pathologic parameter associated with relapse. This finding indicates a need for more frequent follow-up.

### Comparison of Pathologic Parameters Between Cases With and Without Recurrence

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group With Recurrence</th>
<th>Group Without Recurrence</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologic subtype of papillary carcinoma, not otherwise specified</td>
<td>4</td>
<td>12</td>
<td>.26</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td>2</td>
<td>64</td>
<td>.25</td>
</tr>
<tr>
<td>Extrathyroidal extension</td>
<td>3</td>
<td>4</td>
<td>.06</td>
</tr>
<tr>
<td>Extramural extension</td>
<td>2</td>
<td>1</td>
<td>.10</td>
</tr>
<tr>
<td>Positive surgical margins</td>
<td>3</td>
<td>0</td>
<td>.002</td>
</tr>
</tbody>
</table>

* P < .05 was considered statistically significant.

Demographics and Long-term Follow-up of Ductal and Endocrine Carcinomas of the Pancreas

(Poster No. 8)

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Context: Of all human malignant neoplasms, ductal carcinoma (DC) of the pancreas is one of the most lethal, whereas endocrine pancreatic carcinomas are considered to be low-grade malignant tumors. Few studies of endocrine carcinomas (ECs) of the pancreas with long-term follow-up have been published.

Design: Using data (1973 to 2005) from the National Cancer Institute’s Surveillance, Epidemiology, and End Results program, we compared the demographics and long-term survival rates in cases of DC and EC of the pancreas. Logarithmic transformation plots of age-adjusted incidence rates were analyzed.

Results: We identified 114761 cases of pancreatic DC. Of these, 49% were men; 51% were women. We identified 2864 cases of EC. Of these, 54% were men; 46% were women. The mean age of diagnosis was 70.3 years for DC and 58.8 years for EC. Gastrinoma (40.7%), insulinoma (29.6%), glucagonoma (19.6%), and vipoma (10.1%) were the most common functioning ECs. The 10-year relative survival rates for pancreatic EC and DC were 27.6% and 2.5%, respectively. For distant stage at time of diagnosis, 59.6% of cases were EC; 49.6% of cases were DC. Logarithmic transformation plots revealed pancreatic EC and DC as having separate carcinogenic pathways.

Conclusions: DCs of the pancreas were slightly more common in women. ECs were more common in men and presented at younger ages. Gastrinoma, insulinoma, and glucagonoma were the most common functioning ECs. Although pancreatic EC is considered to be of low-grade histology, it does not have a favorable long-term survival rate. Pancreatic EC and DC arise from different cells and have separate carcinogenic pathways.

The Use of Human Papillomavirus Polymerase Chain Reaction in the Histopathologic Diagnosis of Florid Oral Papillomatosis Associated With Malignant Acanthosis Nigricans Versus Multifocal Epithelial Hyperplasia or Heck Disease

(Poster No. 9)

Marina Santos, DDS, MS1; Elizabeth Kerr, MD2 (ehanson@uab.edu); Marietta Alvarez, DDS3; Patricia De Villiers, DDS, MS4; Aleodro Andea, MD5; Helen Rivera, DDS, MS. 1Department of Oral Medicine, Universidad de Carabobo, Valencina, Venezuela; 2Department of Oral Medicine, Universidad Santa Maria, Caracas, Venezuela; 3Department of Anatomic Pathology, University of Alabama, Birmingham; 4Department of Oral Medicine, Universidad de Carabobo, Valencia, Venezuela; 5Department of Oral Pathology, Universidad Central de Venezuela, Caracas.

Multifocal epithelial hyperplasia or Heck disease and oral papillomatosis have similar clinical presentations, including multiple small papules or nodules in the oral mucosa and histologic features of parakeratized, stratified squamous epithelium with marked acanthosis. Although multifocal epithelial hyperplasia is associated with human papillomavirus (HPV) infection, oral papillomas associated with malignant acanthosis nigricans. We present 2 patients, a 24-year-old and a 47-year-old, who sought dental treatment for lesions covering the oral mucosa. In addition to the oral lesions, clinical examination revealed skin lesions that were consistent with acanthosis nigricans. The biopsies for both patients revealed papillomatosis with mild hyperkeratosis, marked acanthosis, and focal koilocytes. Human papillomavirus DNA polymerase chain reaction analysis (Maxim Biotech, Inc., Rockville, Maryland) was negative in both biopsies. Both patients underwent gastric and colonic biopsies. The first patient, age 24, was diagnosed with colonic and gastric polyposis with more than 100 polyps, including some with dysplasia. This patient was not aware of intestinal problems before the biopsies. The second patient, age 47, had a history of untreated vomiting and weight loss during a 6-month period. Following a gastric biopsy, she was diagnosed with advanced-stage gastric adenocarcinoma. In conclusion, human papillomavirus DNA polymerase chain reaction analysis is useful in the histopathologic differential diagnosis of florid oral papillomatosis associated with acanthosis nigricans and multifocal epithelial hyperplasia or Heck disease.

Malignant Pindborg Tumor

(Poster No. 10)

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Calculating epithelial odontogenic tumors account for less than 1% of all odontogenic tumors. Malignant calcifying epithelial odontogenic tumor, also known as malignant Pindborg tumor, is an even rarer entity. We describe the case of a 40-year-old man who self-extracted his right mobile third maxillary molar tooth and sought consultation for a nonhealing extraction site. Imaging studies revealed a destructive mass involving the floor and lateral wall of the right maxillary sinus with extension into the pterygoid plate and soft tissue. An incisional biopsy was performed, and histologic review identified a malignant epithelial neoplasm. Squamous cell carcinoma and malignant Pindborg tumor were top considerations in the differential diagnosis. The patient subsequently underwent a right partial maxillectomy, and gross examination revealed a 2.0 × 1.5 × 1.3 cm, tan-white, fleshy, lobulated tumor involving the floor and lateral wall of the maxillary sinus. The tumor also grossly invaded the alveolar bone and associated molar tooth. Microscopically, the tumor had an infiltrative pattern and was composed of sheets, islands, and strands of polygonal...
The Significance of Intranuclear Pseudoinclusions in Fine-Needle Aspiration of Papillary Carcinoma of the Thyroid: Can We Count on Them?  
(Poster No. 12)

Kilik Kesha, MD (kilik.kesha@danhaps.org); Mary S. Chacho, MD; Carol Schneider, MS; Elizabeth Carr, CT (ASCP). Department of Pathology, Danbury Hospital, Danbury, Connecticut.

Context: Our objective was to identify the significance of intranuclear inclusions and other cytologic features on fine-needle aspiration biopsy that were signed out as “suspicious” for papillary carcinoma of the thyroid.

Design: We conducted a retrospective slide review of fine-needle aspiration biopsies that were signed out as “suspicious” for papillary carcinoma of the thyroid during a 2-year period at Danbury Hospital. We also reviewed 20 random cases. The following cytologic features were graded from 1 to 3: nuclear grooves, overall cellularity, and cell overlap. We counted the total number of intranuclear pseudoinclusions.

Results: A total of 58 fine-needle aspiration biopsy cases were identified. Diagnoses for papillary carcinoma of the thyroid included the following: “suspicious” (n = 52), “worrisome” (n = 2), “possibility of” (n = 2), “cannot rule out” (n = 1), and “indeterminate” (n = 1). Twenty-four cases had no surgical follow-up at our institution and were excluded from the study. The age of the patients ranged from 37 to 80 years. There were 27 women and 7 men. The 34 cases with surgical follow-up included 20 papillary carcinoma of the thyroid (59%), 6 multinodular hyperplasia (18%), 5 nodular hyperplasia (15%), 2 follicularadenoma (6%), and 1 hialinizing trabecular tumor (3%). Statistically significant features included intranuclear pseudoinclusions, nuclear grooves, and overall cellularity. Cell overlap was not statistically significant.

Conclusions: Our study used a semiquantitative system to assess the likelihood of papillary carcinoma. Although no single cytologic characteristic is diagnostic of papillary carcinoma, the presence of intranuclear pseudoinclusions, nuclear grooves, and overall cellularity help in making this diagnosis with a high level of certainty.

Nuclear Protein in Testis-Associated Carcinoma in the Salivary Gland of a Pediatric Patient  
(Poster No. 13)

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Nuclear protein in testis (NUT) midline carcinomas (NMCs) are a rare and recently described class of poorly differentiated tumors that exhibit highly aggressive clinicopathologic behavior. Although NMCs carry a pathognomonic BRD4-NUT fusion gene, they frequently go unrecognized because of their rarity and lack of distinguishing histologic features. Such tumors rarely affect pediatric patients and have never been reported in the salivary glands. We report the first case of NMC involving the salivary gland in an adolescent. A previously healthy, 15-year-old, adolescent boy presented with a left submandibular mass of 3-month duration. He reported waxing and waning pain and episodes of swelling and regression of the mass. Ultrasound showed no evidence of cystic degeneration, hemorrhage, or invasion. He underwent submandibular sialadenectomy with histopathologic evaluation and subsequent left neck dissection. Grossly, the tumor was circumscribed and white and firm, mimicking a pleomorphic adenoma. On histology, tumor cells were predominantly undifferentiated with high mitotic activity, atypical mitoses, and nondescript immunoprofile. Perineural and perivascular invasion were noted. Tumor cells were positive for NUT translocation by fluorescence in situ hybridization. Left neck dissection revealed that 1 of 33 lymph nodes was positive for metastatic tumor. This case identifies salivary gland NMC as a diagnostic consideration in poorly differentiated salivary gland carcinomas affecting pediatric patients. Because poorly differentiated tumors lack distinguishing histologic or immunohistochemical features, molecular diagnosis is essential for accurate categorization and treatment. Any such midline or head and neck tumors that do not exhibit lineage-specific differentiation markers should be considered for NUT rearrangement testing.

Differential Expression of Cytokeratins, p63, and Epidermal Growth Factor Receptor in Spindle-Cell (Sarcomatoid) Squamous Cell Carcinoma of the Head and Neck  
(Poster No. 14)

Fadi Habib, MD1 (fhabib1@hfhs.org); Tarek Hammour, MD1; Mitul Amin, MD; Dhananjay Chitale, MD; Frank Torres, MD. 1Department of Clinical and Anatomic Pathology, Henry Ford Health System, Detroit, Michigan; 2Department of Clinical and Anatomic Pathology, William Beaumont Hospital, Royal Oak, Michigan.

Context: Spindle-cell squamous cell carcinoma (sSCC) of the head and neck frequently lacks expression of typical immunohistochemical markers of conventional squamous cell carcinoma (sCC), making it difficult to diagnose, especially in the absence of sCC component and/or in limited biopsy specimens. We aimed to characterize the immunohistochemical profile of sSCC.

Design: We identified 20 cases of sSCC and 17 cases of sCC from our files. The microscopic features were reviewed. Tissue microarray blocks were constructed from formalin-fixed, paraffin-embedded tumor blocks containing 0.6-mm cores of each tumor. Immunohistochemistry was performed for high- and low-weight molecular cytokeratins (CKs), including AE1/AE3, CAM 5.2, CK-super cocktail (CAM 5.2, AE1/AE3, CK903, and MAk6), CK5/6, and CK903, and for p63, p67, and epithelial growth factor receptor. Intensity of staining for CKs was recorded as high or low and was scored semiquantitatively on a 0 to 5 scale: 0%, less than 10%, 10% to 25%, 26% to 50%, 51% to 75%, and 76% to 100%. Epithelial growth factor receptor immunostain was scored (0 to 3+) based on membranous staining pattern, and 2+ or 3+ was recorded as positive. Greater than 20% nuclear staining for p63 and p67 was considered positive.

Results: We excluded 2 cases of sSCC because of tissue loss (Table).

Conclusions: Our study highlights the differential expression of CKs between sSCC and sCC. Lack of immunostaining for keratin super-cocktail and p63 in many of the cases of sCC emphasizes the need to use a CK-panel approach to diagnosis. Underexpression of p63 and epithelial growth factor receptor in sSCC indicates different biology compared with sCC and thus different potential therapeutic targets.

<table>
<thead>
<tr>
<th>Immunostain Results</th>
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<tbody>
<tr>
<td>Stain</td>
</tr>
<tr>
<td>AE1/AE3</td>
</tr>
<tr>
<td>CK5/6</td>
</tr>
<tr>
<td>CK903</td>
</tr>
<tr>
<td>CK-super cocktail</td>
</tr>
<tr>
<td>p63</td>
</tr>
<tr>
<td>p67</td>
</tr>
<tr>
<td>Epidermal growth factor receptor</td>
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</tbody>
</table>
Chernobyl-Related Thyroid Carcinoma
(Poster No. 15)

Keith D. Bohman, MD (kbobman14@aol.com); Robert L. Booth Jr., MD. Department of Pathology, University of Toledo, Ohio.

On April 26, 1986, the Chernobyl nuclear accident exposed millions of people to significant radiation in Belarus, Russia, and the Ukraine. The environment quickly became contaminated with radioactive isotopes, leading to an increase in the incidence of papillary thyroid carcinomas in these nations. Papillary thyroid carcinomas in Chernobyl victims were first reported 3 to 4 years after the accident, and these tumors have tended to be of the solid histologic subtype. It has been proposed that the occurrence of the solid-type of papillary thyroid carcinoma in these cases may be, in part, due to the amount of iodine in the Russian diet, a characteristicistically iodine-poor diet. A 58-year-old Caucasian woman of Eastern-European descent, who lived approximately 100 miles from Chernobyl during the 1986 nuclear reactor accident, presented with an enlarging neck mass in 2006 (Figure 85). Histologic examination of the tumor showed a very distinct and well-formed, solid-type papillary carcinoma, which merged almost imperceptibly with anaplastic areas. There appears to be a variable period between the time of radiation exposure and the onset of papillary thyroid carcinoma in Chernobyl victims, and a significant number of cases are occurring in individuals who were children at the time of exposure. With the increase in world travel, Chernobyl victims may be encountered in a variety of nations outside the former Soviet Union. Therefore, when presented with a papillary thyroid carcinoma, one must take a thorough history, including nation of origin, to investigate a possible association with the Chernobyl accident.

Evaluation of Microsatellite Instability in Mucoepidermoid Carcinoma
(Poster No. 17)

Mark Podberezin, MD (markp@uic.edu); ShriHari Kadkol, MD, PhD; Elizabeth Wiley, MD; Grace Guzman, MD. Department of Pathology, University of Illinois at Chicago.

Context: Microsatellite instability (MSI) is a replication/repair genetic error resulting from aberrations in the following mismatch repair genes: MLH1, MSH2, MSH6, and PMS2. The most commonly involved genes are MLH1 and MSH2. MSI has been detected in both hereditary and sporadic tumors, including colorectal, pancreatic, gastric, and endometrial adenocarcinomas. Studies addressing the role of MSI in mucoepidermoid carcinogenesis (MEC) are limited. We aimed to determine whether MSI contributed to the pathogenesis of MEC.

Design: Subjects consisted of 12 patients who underwent surgical resection for primary MEC of the parotid gland. Hematoxylin-eosin–stained slides were reviewed for confirmation of diagnosis. A section containing malignant and nonneoplastic salivary gland tissue was selected from each case. Three 5-μm, unstained sections were obtained from the corresponding formalin-fixed, paraffin-embedded tissue blocks. DNA was extracted from microdissected tumor and normal tissue. Five mononucleotide loci (BAT26, NR21, NR24, BAT25, NR22) were amplified in 2 multiplex polymerase chain reactions using fluorescently labeled primers. Products from polymerase chain reaction were subjected to capillary electrophoresis on an ABI Prism 3100 Genetic Analyzer (Applied Biosystems Inc., Foster City, California) followed by fragment analysis using Genotyper 4.0 software (Applied Biosystems, Inc.). Tumor and matched normal tissue were compared at each locus to determine instability.

Results: MSI was not present in 12 of 12 primary MECs of the parotid gland.

Conclusions: This preliminary study suggests that replication error is an unlikely mechanism in the pathogenesis of MEC. A larger cohort study using additional methods to determine MSI will be necessary to determine its potential involvement in MEC.

Improved Frozen-Section Diagnosis of Mucormycosis
(Poster No. 18)

Harvey E Sasaki, MD1 (hsasaken@gmail.com); Rita Roure, MD2; Ronaldo Zamuco, MD; Amy Paul, MD. Departments of Pathology and Otolaryngology, Lincoln Medical Center, Bronx, New York.

Context: Acute fulminant fungal rhinosinusitis caused by Mucor is a not-uncommon, life-threatening infection that is associated with poorly controlled diabetes, ketoacidosis, or immunosuppression. Characteristically, it invades blood vessels and rapidly spreads along nerves and across tissue planes to involve the orbit or the brain. The reported mortality rate is approximately 50%. Immediate diagnosis by frozen section has been suggested as an aid in rapidly instituting appropriate therapy. Frozen sections cut at 5 to 10 micra reveal only small fragments of fungal organisms. If the organism fragments are identified, the diagnosis is established; however, because they may be difficult to identify, there is a strong potential for a false-negative diagnosis. The addition of a rapid Wright stain (Poly Scientific, Bay Shore, New York) or metachromatic stain on a touch preparation reduces this danger.

Design: Four cases of suspected mucormycosis were submitted for diagnosis using hematoxylin-eosin–stained frozen sections that were cut at 5 micra. The specimens consisted of a debridement of necrotic tissue. They were examined by routine frozen sections that were hematoxylin-eosin–stained and cut at 5 micra and by touch preparations stained with either a metachromatic or rapid Wright stain.

Results: The touch preparations revealed easily identifiable, large, unbroken masses of fungal elements. The routine frozen sections showed fragments of fungus with their association with the blood vessels and native tissues preserved.

Conclusions: The use of routine frozen section (hematoxylin-eosin) and touch preparations (rapid Wright or metachromatic stain) provides the necessary criteria for the diagnosis of mucormycosis and reduces the danger of a false-negative diagnosis.
Phyllis T. England, MD, PhD, FRCPath1; Sarah E. Houlston, PhD2; John L. Armsby, MD1; Stephen E. Seltzer, MD3; Paul Klonowski, MD1; Peter H. Dobbertin, MD1; Elizabeth Crowther, MD1; Edward A. Frank, MD2; Brian J. Skarda, MD2; Daniel C. Dim, MD. Department of Pathology and Cytopathology, Washington University School of Medicine, St. Louis, Missouri.

Context: Merkel cell carcinoma (MCC) and high-grade neuroendocrine carcinoma (HGNEC) are rare tumors with similar morphology, arising in the skin and mucosa, respectively. MCC cases are split, with approximately 50% showing angulated or molding nuclei with crush artifact, whereas only 13% showed round, regular nuclei with fine chromatin. HGNEC cases, on the other hand, are characterized by another 50% showing angulated or molding nuclei with crush artifact, whereas only 30% showed round, regular nuclei. The histopathology, cytologic, and immunohistochemical features of these two entities are well described, with MCC being negative for neurofilament and thyroid transcription factor 1, and HGNEC being positive for both. However, the distinction between the two entities can be challenging, especially in cases with overlapping features.

Conclusions: Based on these findings, MCC and HGNEC should be considered as separate entities, with MCC being more common in the skin and HGNEC being more common in the mucosa. The distinction between the two entities can be challenging, and further research is needed to better understand the clinical and biological implications of these findings.

Clinicopathologic Correlation and Microvascular Density

Clinicopathologic Correlation and Microvascular Density Counts in Sinonasal Melanomas

Elizabeth Kerr, MD1 (ehanson@uab.edu); Omar Hameed, MD1; Alfred Bartolucci, PhD2; Dezhi Wang, MD2; Nasser Said-Al-Naief, DDS, MS1. Departments of 1Pathology and 2Biostatistics, University of Alabama, Birmingham.

Context: Microvascular density (MVD) in cutaneous malignant melanomas has a significant negative correlation with survival; however, this has not been well-studied in mucosal melanomas. This study evaluated MVD in relation to the clinicopathologic features and survival in sinonasal melanomas.

Design: The clinicopathologic features of 7 cases of primary sinonasal melanoma were reviewed. MVD was evaluated in each case by immunostaining with CD31 antibody (Dako, Glostrup, Denmark) and by using Bioquant Image Analysis software (R&M Biometrics, Nashville, Tennessee). We examined the relationship between the MVD and various clinicopathologic features.

Results: We have evaluated 7 cases to date, including 5 men and 2 women, ranging in age from 35 to 72 years (mean, 54 years; median, 50 years). One patient died in the immediate postoperative period. A median follow-up period of 36.5 months (range, 9 to 63 months) was obtained. All patients developed recurrences and/or distant metastases, except in the case of one patient, who died of disease. The MVD of the tumors ranged from 0.2 to 400 vessels/mm² (mean, 207.7 vessels/mm²). There was no significant correlation between the MVD and various clinicopathologic features. The most common histologic patterns were spindle and epithelioid.

Conclusions: Although the findings confirm the aggressive nature of sinonasal melanoma, the clinicopathologic features and survival in sinonasal melanomas remain to be determined. Accrual of additional cases is ongoing, and further evaluation is ongoing.

Neuroendocrine Carcinoma?

Fine-Needle Aspiration Diagnosis in a Case of Follicular Dendritic Cell Sarcoma

Xiaohong Wang, MD, PhD (zwang@lsuhsc.edu); Jaiyeola Thomas, MD; Songlin Zhang, MD, PhD. Department of Pathology, Louisiana State University Health Science Center, Shreveport.

Follicular dendritic cell (FDC) sarcoma is a rare, neoplastic proliferation of follicular dendritic cells. Although the histopathology and immunophenotype have been fairly well characterized, FDC sarcoma remains underrecognized, and one-third of extranodal cases are initially misdiagnosed. Cytology features of FDC sarcoma have been reported in only 4 cases. A 24-year-old woman presented with a painless neck mass of a few weeks' duration. Physical examination revealed a deeply located, firm, 3.6-cm mass in the right posterior neck. Diff-Quik-stained slides showed many large, oval- to spindle-shaped neoplastic cells singly or in loosely

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cohesive or syncytial groups. Tumor cells had a moderate amount of cytoplasm and indistinct cell borders. Nuclei were variable in size with irregular nuclear membrane and conspicuous nucleoli. A significant small lymphocytic infiltration was noted in the tumor tissue. A malignant neoplasm was favored for site-on-site interpretation. Cell block showed fragments of neoplastic spindle cells with prominent whorling, mimicking meningioma (Figure 87). Small lymphocytes were scattered throughout the tumor. Tumor cells were positive for CD21, CD35, vimentin, and epithelial membrane antigen and were negative for S100 and keratin. A diagnosis of FDC sarcoma was rendered, and excision of the neck mass confirmed this diagnosis. The differential diagnosis for FDC sarcoma in cytology smears includes thymic neoplasm, germ cell tumor, nasopharyngeal carcinoma, and meningioma. A prominent, whorling pattern and epithelial membrane antigen positivity can lead to a misdiagnosis of extracranial meningioma. Although some cytology features are helpful, awareness of FDC sarcoma is most important in rendering the correct diagnosis.

Concurrent Plasmablastic Lymphoma and Classic Hodgkin Lymphoma Arising in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Treated With Fludarabine: An Unusual Presentation of Iatrogenic Immunodeficiency–Associated Lymphoproliferative Disorder

(Poster No. 23)

Wen-Chi Foo, MD (foo00001@mc.duke.edu); Charles B. Hutchinson, MD; Endi Wang, MD, PhD. Department of Pathology, Duke University Medical Center, Durham, North Carolina.

A 73-year-old man with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) was treated with fludarabine and later with rituximab. He experienced clinical remission for 16 months following completion of fludarabine therapy. He then developed a nasopharyngeal mass and cervical lymphadenopathy. Although biopsy of the nasopharyngeal mass revealed necrosis, the cervical lymph node demonstrated scattered Hodgkin-like cells in a mixed inflammatory background and residual CLL/SLL. The large Hodgkin-like cells were positive for CD30, dim Pax-5, and Epstein-Barr virus (EBV)-EBNA-2 and were negative for CD15, CD3, EBV-LMP-1, and ALK-1. These findings supported a diagnosis of classic Hodgkin lymphoma in a background of residual CLL/SLL. After 5 cycles of chemotherapy, the nasopharyngeal mass persisted; biopsy showed monomorphic, large plasmacytoid cells with frequent apoptosis and focal necrosis. These large cells expressed dim CD45, CD138, and MUM-1 and were negative for CD20, CD79a, PAX-5, CD56, and T-cell antigen markers. Proliferation index was 90%. Although EBV−LMP-1 and EBV−EBNA-2 were negative, in situ hybridization for EBV-encoded RNA was positive in many large cells. These findings were consistent with plasmablastic lymphoma. Polymerase chain reaction-based immunoglobulin gene rearrangement studies on the nasopharyngeal mass and the cervical lymph node detected 2 distinct rearranged products, suggesting that the plasmablastic lymphoma was clonally unrelated to the CLL/SLL. Although EBV− lymphoproliferative disorders, including classic Hodgkin lymphoma, have been documented in association with fludarabine treatment for low-grade B-cell neoplasms, plasmablastic lymphoma concurrent with classic Hodgkin lymphoma is unique to our case and has not been previously reported in a setting of CLL/SLL treated with fludarabine.
Context: Pathology researchers often use locally obtained specimens because there is no easy way to search for and locate specimens outside a laboratory or institution. The ability to aggregate similar specimens from various sites would expand the validation of pathology research findings and more quickly affect patient care. The Common Biorepository Model (CBM) is an information model that interfaces with systems by sharing key specimen information, enabling a single search across multiple biobanks. The goal is to reduce the time and effort required by researchers to locate a biobank that has needed specimens. This model is part of the National Cancer Institute's cancer BioInformatics Grid initiative to develop methods and models to support and fast-track research.

Design: With a CBM, data fit a standardized, simple domain model to promote sharing. CBMs can define infrastructure and enable a dynamic way to develop methods and models to support and fast-track research. It is part of the National Cancer Institute's cancer BioInformatics Grid initiative to develop methods and models to support and fast-track research. CBMs can define infrastructure and enable a dynamic way to develop methods and models to support and fast-track research.

Results: Representatives of biobanking software vendors and the National Cancer Institute stakeholders convened to develop CBM 1.0. Currently, CBM 1.0 is an evolving, searchable catalog of basic specimen information that is simple, mutually understood, and community supported. By establishing a new system-independent model, the team seeks to gain the widest possible adoption through consensus.

Conclusions: CBM provides an information model that has been developed with researcher and vendor input to enable high-level sharing of specimen information that could speed up research efforts; CBM is also an example of interoperability efforts in the community.

Media-Enhanced Reporting (Poster No. 27)

Daniel J. Cowden, MD (Daniel.Cowden@yahoo.com); Dave Romer, BSEE; Peter C. Kolbeck, MD. Department of Nephropathology, PathLogic, Carmichael, California.

Context: Information enthusiasts continue to profess the benefits of digital microscopy and whole-slide imaging; however, in practice, this type of virtual microscopy has not come to full fruition. Perhaps video streaming, a simple technology for viewing digitized slides, is more feasible. To date, no study has compared these 2 technologies and how they can be effectively used in pathology reporting systems. In this study, the use of these technologies in pathology reporting systems was designated medical reporting.

Design: Using data extracted from Aperio ScanScope (Aperio Technologies, Inc., Vista, California) and CamStudio, we compared whole-slide imaging and audio/video streaming by marginal-cost curve analysis, production times for .AVI media files (Aperio ScanScope and CamStudio) and XML annotation (Aperio), and number of hits generated for each URL-hyperlink. Finally, a user opinion poll was collected.

Results: Video streaming had significantly lower start-up costs than whole-slide imaging; however, both had similar hardware and storage requirements. Neither technology had a sustainable business model; however, video streaming was the preferred media based on opinion polls (90%). Video streaming was preferred for 3 reasons: (1) 85% of clinicians preferred an audio-guided video review of the diagnosis versus annotations, (2) 100% of clinicians considered video streaming a more familiar technology, and (3) 70% of clinicians preferred that all diagnostic information be presented to them on the same report (media-enhanced reporting).

Conclusions: Neither form of digital imaging has a sustainable business model; however, video streaming may be a better solution for digital imagery than whole-slide imaging.

Use of Telepathology Technology in Computed Tomography–Guided Biopsy Specimen Evaluation (Poster No. 28)

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Context: The use of telepathology systems has been evaluated in routine practice and in intraoperative consultation for histology specimens. We assessed the utility of real-time telepathology in determining the adequacy of cytology fine-needle aspiration biopsy specimens.

Design: Residents prepared and evaluated slides for microscopic adequacy. We used the Olympus America, Inc. (Center Valley, Pennsylvania) telepathology system. A pathologist accessed live images of the microscopic images as seen by the resident. The pathologist recorded adequacy and diagnostic impressions based on the live digital images and light microscopy. After routine processing, a final diagnosis was rendered. The efficacy of the telepathology system was analyzed using 3 categories: Adequate vs Not Adequate for Diagnosis, Benign vs Malignant, and Change in Diagnostic Category.

Results: We made 61 touch preparations and 156 smears using aspirated materials and core biopsies from 150 cases. The Adequate vs Not Adequate category had 170 determinations, with 165 (97%) showing no change. The remainder changed from Not Adequate to Adequate. We analyzed 91 cases in the Benign vs Malignant category; 77 (85%) of these showed no change from the initial telepathology images to the final diagnosis. We analyzed 91 cases for Change in Diagnostic Category; 68 (75%) of these showed no change from the preliminary telepathology images to the final diagnosis.

Conclusions: The telepathology system demonstrated high concordance between digital images and light microscopy in adequacy determination, confirming that the system is useful for remote adequacy determinations. However, the diagnostic capabilities were suboptimal, possibly because of image quality or the inherent limitations of cytology.

This research was supported by a College of American Pathologists Telepathology Grant, which was purchased by the Olympus of America (Center Valley, Pennsylvania) equipment.

Genetics Café: A Web-Site Consortium for Genetic Information (Poster No. 29)

Elizabeth Howe, MPH (bhowe@access-genetics.com); Ronald McGlennen, MD. Department of Research, Access Genetics, Minneapolis, Minnesota.

Context: Molecular diagnostic testing is a growing field that lacks standard methodologies; consequently, test results may vary between different laboratories and test platforms, and no central database exists to compare results of population-level analyses. Access Genetics provides expertise in molecular diagnostic operations and test interpretation through an integrated Web portal, which includes tools for abstracting and correlating analytic results from distinct laboratories and testing technologies. Genetics Café is a Web database designed to facilitate comparisons of real-time genetic data on a population level.

Design: Access Genetics has developed an interactive Web site using web-based widgets; abstractions of analytic results can be used to compare one laboratory’s findings to the cumulative group results. The Web site, Genetics Café, presents real-time displays of these data, including features for uploading adjunctive demographic and anatomic test results to create a consortium of genetic information.

Results: The Web site is designed as a series of laboratory widgets that are compiled from results obtained from more than 75 laboratories and one million tests. One featured widget set compares the analytic performance of 3 human papillomavirus (HPV) test platforms, including findings from more than 50 clinical laboratories using genotype-specific HPV detection, a geographic HPV-type heat-map (Figure 88), and a normalized HPV use rate based on common clinical HPV testing patterns.

Conclusions: Genetics Café is a unique way to compare genetic-testing information and to improve the quality of clinical test results. Advantages include interlaboratory, interplatform, morphologic, and molecular correlations. This Web site adds value for researchers and the industry.

Genetics Café: A Web-Site Consortium for Genetic Information (Poster No. 29)
Laboratory Information System-Based Synoptic Reporting Tool for Genitourinary Cancer Resection Specimens: A 6-Year Experience With More Than 3700 Specimens
(Poster No. 30)

Shveta Hooda, MD (dshveta@gmail.com); Anthony Piccoli, BS; Anil V. Parwani, MD, PhD. Department of Pathology, University of Pittsburgh Medical Center, University of Pittsburgh, Pennsylvania.

Context: Cancer checklists comprising standardized data elements are valuable tools that clinicians can use for guidance in managing patients. We describe our experience with the use of the Synoptic Worksheet entry tool for genitourinary cancer resections and also describe the use of synoptics in providing reports in our clinical environment of multiple academic and community centers.

Design: We used a synoptic reporting tool as part of our existing laboratory information system, CoPathPlus, from Cerner DHT Corp. We modified the College of American Pathologists’ checklists into worksheets for select genitourinary organ system malignancies. The synoptics have been in use for 40 months in our laboratory information system. The data were present as discrete data elements. A data element, that is, tumor type, is in the value dictionary under the value of tumor type, allowing users to search for cases that have that value point populated.

Results: A total of 3736 genitourinary resection specimens in our network had a synoptic report completed. Prostate (n = 2811), kidney (n = 833), urinary bladder (n = 281), kidney pelvis (n = 110), testsis (n = 86), ureter (n = 34), and penis (n = 11) were the most used templates in the system. See Table.

Conclusions: Use of the new synoptic report enables quicker access to information and improves communication for cancer management. Such uniformity lends itself to ease of data viewing and extraction, as demonstrated by rapid production of standardized, high-quality data from these genitourinary cancer resection specimens.

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Mycobacterium Vertebral Osteomyelitis in a Patient With a History of Bacillus Calmette-Guérin Intravesical Therapy
(Poster No. 31)

Hannah H. Wong, MD (hhwong@llu.edu); Anwar Raza, MD. Department of Pathology and Laboratory Medicine, Loma Linda University Medical Center, Loma Linda, California.

Bacillus Calmette-Guérin (BCG) intravesical immunotherapy using Mycobacterium bovis has been used in the treatment of low-grade bladder cancers since the 1970s. Complications are generally limited to cystitis, fever, hematuria, and prostatitis. Cases of Mycobacterium bovis vertebral osteomyelitis following BCG therapy are rare, with fewer than 10 cases reported in the literature. A 79-year-old man presented with vertebral osteomyelitis 14 years after a diagnosis of bladder cancer and BCG therapy. He had received a 1-month course of dexamethasone for idiopathic thrombocytopenia a month prior, and he subsequently developed leukocytosis. Magnetic resonance imaging revealed multiple paraspinal abscesses and a 5.2 × 0.9-cm abscess in the T11 to T12 disk space. He rapidly developed paraplegia requiring decompression laminectomy. Microscopic examination revealed an acute and chronic necrotizing granulomatous inflammation with acid-fast-positive bacillary forms. Cultures revealed acid-fast bacilli, which were identified as Mycobacterium tuberculosis complex organisms using the Gen-Probe (San Diego, California) Amplified Mycobacterium Tuberculosis Direct test. The organisms identified by this method were Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium bovis BCG, Mycobacterium africanum, Mycobacterium microti, and Mycobacterium canetti. Standard mycobacterium therapy was initiated, and further specification was not pursued. Despite therapy, the patient remains a paraplegic and in critical condition. Careful review of his clinical history revealed no other Mycobacterium exposures, favoring the possibility of Mycobacterium bovis osteomyelitis secondary to BCG therapy. Vertebral osteomyelitis due to acid-fast bacilli is a rare entity and should be considered in patients with a history of intravesical BCG therapy because early therapy may significantly reduce complications.

Chronic, Recurrent Epiglottitis in a Young Adult With Actinomyces israeli infection
(Poster No. 32)

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Actinomyces israeli is a common inhabitant of the oral cavity. This gram-positive microorganism is normally nonpathogenic, but there have been reported cases in which an infection ensued at the site of injury following a traumatic insult to the oral mucosa. Rarely, this microorganism can cause a chronic infection to a traumatized part of the oral cavity. These rare occurrences have been described in immunocompetent patients who are older than 60 years but not in young adults. We present a case of a 34-year-old, immunocompetent woman with good dental hygiene who presented twice at our institution within a 2-month period. She had shortness of breath, a sore throat, and dysphagia related to both solids and liquids. Her symptoms had progressively worsened during several weeks.

Results: A 34-year-old, immunocompetent woman was evaluated in our emergency department for a 2-month history of shortness of breath, a sore throat, and dysphagia. She was afebrile, with no other significant complaints. Physical examination revealed a 34-year-old, immunocompetent woman with good dental hygiene who presented twice at our institution within a 2-month period. She had shortness of breath, a sore throat, and dysphagia related to both solids and liquids. Her symptoms had progressively worsened during several weeks.

Conclusions: We conclude that physicians should be aware of, and have a high degree of suspicion regarding, this atypical presentation of Actinomyces.

Is the QuantifERON TB Gold In-Tube Method a Good Replacement for the Tuberculin Skin Test in Tuberculosis Screening: A Pilot Study at Berkshire Medical Center
(Poster No. 33)

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Context: QuantifERON TB Gold In-Tube method (QFT-GIT; Cellestis, Inc., Valencia, California) is an interferon-γ release assay that was recently approved by the US Food and Drug Administration to detect tuberculosis infection, which has been screened for using a tuberculin skin test (TST) for nearly a century. We report on a pilot study comparing the QFT-GIT and TST results in screening health care workers at Berkshire Medical Center, the second hospital in Massachusetts to employ QFT-GIT.

Design: We screened 40 health care workers at Berkshire Medical Center using the QFT-GIT test. Of the 40 workers, 20 had TST-positive results, and 20 had TST-negative results.

Results: All 20 subjects with TST-negative results also had QFT-GIT-negative results, whereas only 10 of 20 subjects with TST-positive results also had QFT-GIT-positive results. The overall agreement between the QFT-GIT and TST results was 75% (k = 0.5; 95% confidence interval, 0.268–0.732).

Conclusions: The suboptimal agreement was partially due to a higher specificity of QFT-GIT. Confounding factors (eg, bacillus Calmette-Guérin vaccination status and birthplace) are discussed, and literature regarding interferon-γ release assays in comparison to TST is reviewed in detail.

Human Pythiosis in a Bone Marrow Transplant Recipient
(Poster No. 34)

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Pythium insidiosum is an aquatic pseudofungus belonging to the class Oomycetes. Pythium rarely causes human infection but has been reported in animals. We describe a case of human pythiosis in an immunocompromised patient. A 52-year-old man with acute lymphoblastic leukemia had undergone allogeneic stem cell transplantation 6 months before admission. He presented with a complicated soft tissue infection of the right lower extremity after having sustained trauma from...
strikings his leg on the edge of a chlorinated swimming pool. The wound appeared as multiple indurated nodules. After surgical debridement, the infected tissue was sent for culture and pathology. The surgical pathology revealed extensive epidermal erosion with suppurative and deep perivascular inflammation, necrosis, and hemorrhage. In tissue sections, the organisms appeared as hyaline, pauci-septate hyphae (6–7 μm wide). There were some branching forms; these, however, were infrequent. The organism stained strongly with Gomori methenamine-silver and was also positive with periodic acid-Schiff (Figure 89). The hyphal forms were scattered throughout the mid and deep dermis, as well as in deep dermal blood vessels. Tissue cultures grew a septate hyphal organism that failed to sporulate on traditional media. Fluorescent anti–Pythium insidiosum staining positively identified the organism. Western blot analysis on the patient’s serum sample positively detected all Pythium insidiosum antigens. We describe the first case of cutaneous human pythiosis occurring in a patient with acute lymphocytic leukemia 6 months after allogeneic hematopoietic stem cell transplantation.

Human Protothecosis: Lethal, Disseminated Infection by Prototheca zopfii in a Pediatric Patient With Leukemia

(Poster No. 35)

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Prototheca species, or achlorophyllic algae of the genus Prototheca, have rarely been identified as causative agents in lethal human infections. Of the few reported cases of disseminated protothecosis, only 2 were due to Prototheca zopfii, and both were in adult posttransplant patients. We report a case of a lethal, disseminated infection by Prototheca zopfii, causing multisystem organ failure in a 9-year-old boy with no transplant history, as with nonendosporulating cells (Figure 90). The cells of containing endospores, some arranging into morula formations, admixed with nonendosporulating cells (Figure 90). The cells of Prototheca were positive for standard histologic stains commonly used for fungal organisms. Electron microscopy revealed dense granules and needle-shaped structures, which are typically found in Prototheca. Cytomegalovirus and Aspergillus were also identified. In conclusion, disseminated protothecosis is an uncommon but deadly infection in humans that is caused by a group of algae of the genus Prototheca. Immunocompromised individuals are most susceptible to systemic protothecosis and are more likely to be infected with other organisms. In this case, the extensive damage to multiple organs speaks to the potential lethality of infection by Prototheca zopfii.

Increased Prevalence of Antimicrobial-Resistant Organisms in Urinary Tract Infections in Patients at Long-term Care Facilities

(Poster No. 36)

Rita H. Khoury, MD (rkhoury@aculabs.com); Shakira Gibbs, BS; B. P. Salmon, MS; Asha Gandhi, BS; Peter Gadaitis, BS; Dauna Gadaitis, BS. Aculabs, Inc., East Brunswick, New Jersey.

Context: Urinary tract infection is the most common bacterial infection in the elderly. The emerging thread of the antimicrobial-resistant organism is making it a major health problem, especially in long-term care facilities where it is associated with higher mortality rates and longer hospital stays.

Design: We collected 2805 specimens (1184 from 2007 and 1621 from 2008) for urine cultures from residents in long-term care facilities. The cultures were done using MicroScan Walkaway 96 conventional panels. No growth or fewer than 10,000 colony-forming unit (CFU)/mL were considered negative. Cultures with more than 50,000 CFU/mL were considered positive. If a specimen was collected from a catheter, any growth was considered positive. The positive cultures were segregated further by the isolated organisms.

Results: More than 70% of the patients were women (72.3% in 2007 and 73.9% in 2008). Of the total number of cultures, 46.5% and 55.0% were positive in 2007 and 2008, respectively; the large increase was mostly among male patients. Of the positive cultures, 13.27% in 2007 and 15.7% in 2008 were drug resistant. No changes were observed in the methicillin-resistant Staphylococcus aureus during the test period (Table).

Conclusions: Urinary tract infection occurs at a high rate in the elderly; the prevalence of antimicrobial-resistant organisms is increasing among residents in long-term care facilities. Although many believe that methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci are more common, we found that cases of extended-spectrum β-lactamase account for more than 60% of multiresistant organisms. This finding indicates that nursing homes or acute care settings are a reservoir for cases of extended-spectrum β-lactamase.
Blood Culture Contamination in Long-term Care Facilities
(Poster No. 37)

Rita H. Khoury, MD (rkhoury@aculabs.com); Shakira S. Gibbs, BS; Asha Gandhi, BS; B. P. Salmon, MS; Peter Gadaitis, BS; Dauna Gadaitis, BS. Aculabs, Inc., East Brunswick, New Jersey.

Context: Blood cultures are among the most important tests performed in the laboratory for the diagnosis of serious infection; and because clinicians rely on culture results to diagnose and monitor their patients, contaminated blood cultures are as important as positive cultures. They are, however, very costly and, at times, confusing for physicians.

Design: We received 438 sets of blood cultures from residents in long-term care facilities during February 2009. Every set included 2 vials (aerobic and anaerobic). Cultures were analyzed using Microscan Walkaway 96. Positive blood cultures were considered contaminated when one or more of the following organisms were identified in at least one of a series of blood culture specimens: coagulase-negative Staphylococcus species, Propionibacterium acnes, Micrococcus species, viridans streptococci, Corynebacterium species, or Bacillus species.

Results: Twenty-eight of the cultures (6.4%) were positive. The contamination rate was 2.5%: the contaminants represented 35.7% of the positive cultures. Coagulase-negative Staphylococcus species accounted for 80% of the contamination, and Staphylococcus epidermidis was responsible for 60% of the cases. Seventy percent of contaminated cases occurred with patients who were older than 70 years.

Conclusions: The contamination rate for blood cultures was lower than most of the reported rates, which may be due to the extensive training and strict aseptic technique used by our phlebotomists when taking blood specimens. Clinicians should pay attention to the number of blood culture sets that are positive. When more than one culture is positive with the same organism, even if contaminated, it may represent a real disease.

Increased Incidence of Multidrug-Resistant Acinetobacter baumannii Complex in a Midwestern, US, University Hospital
(Poster No. 38)

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Context: The emergence of multidrug-resistant Acinetobacter baumannii (MDRAB) has recently plagued health care institutions locally and globally. This has greatly challenged current strategies for successfully controlling the spread of this organism.

Design: To improve our understanding of the growth characteristics and extent of MDRAB infection at our institution, a retrospective study of MDRAB-associated wound infections was performed for the period of October 2007 to February 2009. Sixteen patients were identified with MDRAB wound infections. Their growth characteristics and susceptibility profiles were recorded and were compared with data from a year prior.

Results: The susceptibility percentages for MDRAB from the study period versus the year prior were as follows: ampicillin/sulbactam, 12.5% versus 62%; cefepime, 0% versus 25%; ciprofloxacin, 0% versus 33%; gentamicin, 12.5% versus 39%; piperacillin/tazobactam, 0% versus 54%; tobramycin, 31.2% versus 54%; imipenem, 7.1% versus 60%; levofloxacin, 0% versus 34%; and trimethoprim/sulfamethoxazole, 0% versus 33%. Additionally, tigecycline showed 10% susceptibility, 80% intermediate resistance, and 10% full resistance. Colistin showed 75% susceptibility, 8.3% intermediate resistance, and 16.7% full resistance. The mortality rate was 3 of 16 (19%). Many patients (58%) were diabetic or had increased glucose levels at the time of collection. Most isolates (75%) revealed polymicrobial infections, with the most frequent organisms being Enterobacteriaceae (53%), Enterococcus (31%), and Pseudomonas aeruginosa (19%).

Conclusions: Our data demonstrate a dramatic increase in the incidence of MDRAB. The medical community must facilitate changes in antimicrobial stewardship strategies and implement new control measures to prevent the emergence of pan-resistant Acinetobacter baumannii.

An Unusual Presentation of Focal Myositis With Bilateral Eyelid Swellings
(Poster No. 39)

Sonali P. Ayar, MD (sarayar@southal.edu); Sree Ravula, MD, Jeffrey Sosnowski, MD, PhD; Jack Polski, MD. Department of Pathology, University of South Alabama, Mobile.

Focal myositis is a rare, self-limiting inflammation of skeletal muscle. Fewer than 50 cases of focal myositis have been reported in the literature. Of these, most cases were located in the limbs. We report a unique case of myositis involving bilateral eyelid musculature and eyelid swellings. A 31-year-old woman presented with bilateral eyelid swellings and a medical history of fibromyalgia. Clinically, she was diagnosed with dermatomyositis and a bilateral upper eyelid edema that was not responsive. Microscopic examination revealed skeletal muscles with extensive, diffuse lymphocytic and other inflammatory infiltrates with muscle fiber atrophy. The immunohistochemistry and flow cytometry showed mixed T cell and polytrophic B cells, with a predominance of T cells. The clonality study was positive for clonal T cell receptor gene rearrangement and negative for clonal immunoglobulin gene rearrangement. Based on morphology, immunohistochemistry, flow cytometry, and the clonality study, a diagnosis of focal myositis was made. Focal myositis is a very rare, benign condition, and most patients improve without immunosuppressive therapy. Hence, this condition should be differentiated from other soft tissue tumors involving skeletal muscles. However, the presence of a clonal T cell population in myositis should not be confused with lymphoma. To our knowledge, this is the second case of focal myositis presenting with bilateral eyelid swellings.

100-Negative Metastatic Choroidal Melanoma
(Poster No. 40)

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The immunohistochemical stain 5100 is highly sensitive for metastatic melanoma and is positive in approximately 99% of these tumors. Although very few melanomas are negative for the 5100 stain, a dramatic increase in the high number of these melanomas are ocular in origin, including approximately 24% in one study. A 61-year-old man with ascites, large omental cake, and a 7-cm liver lesion presented with increasing abdominal girth and early satiety. Histologic examination of the peritoneal fluid revealed large, anaplastic, malignant cells in a discohesive pattern with a background of small, mature lymphocytes (Figure 91). Because of inadequate clinical history and nonspecific malignant cytologic findings, a panel of immunohistochemical stains was performed. Initial immunohistochemical staining of the cell block was negative for 5100, pancytokeratin, CD45, CD15, CD34, CAM5.2, CD31, placental alkaline phosphatase, CD117, and mucarmin. Scattered malignant cells stained weakly for carcinoma bryonic antigen and vimentin. After consulting additional electronic medical records, we discovered that 17 years ago the patient had undergone enucleation for choroidal melanoma. Immunohistochemistry for HMB-45 and MART-1 (Melan-A) was then performed on the peritoneal fluid (Figure). The results were interpreted as positive, and metastatic melanoma was diagnosed. We stained slides of the prior enucleation specimen; the primary tumor stained positively for 5100, pancytokeratin, CD45, CD15, CD34, CAM5.2, CD31, placental alkaline phosphatase, CD117, and mucarmin. Scattered malignant cells stained weakly for carcinoembryonic antigen and vimentin. Based on the clinical and other studies, additional melanoma markers, such as MART-1 or HMB-45, should be used in a poorly differentiated metastatic tumor with a differential diagnosis of melanoma, especially choroidal melanoma, or in a patient with a history of melanoma that stains negatively for 5100.

Mutations in Exons 12 to 16 of the Janus Kinase 2 Gene Are Rare in JAK2V617F-Negative Chronic Myeloproliferative Neoplasms
(Poster No. 41)

Rashmi Kanagal Shamanna, MD (r shamann1@hfhs.org); Lisa Whiteley, BA; Milena Cankovic, PhD; Dhananjay Chital, MD; Kedar Inamdar, MD,
**Context:** Constitutive activation of tyrosine kinases due to JAK2V617F mutation (exon 14) is central to the pathogenesis of chronic myeloproliferative neoplasms (CMPN). It occurs in 95% of polycythemia vera cases and in other CMNP cases less frequently. Pathogenesis of JAK2V617F-negative polycythemia vera is unclear. Recent studies have identified recurrent somatic mutations in exon 12 of the JAK2 gene. Similar mutations in other exons may contribute to kinase activation. We sought to identify them in patients at our hospital with JAK2V617F-negative polycythemia vera.

**Results:** Sequencing reaction was successful in 36 cases. In one case, we identified a novel exon 13 mutation causing substitution of glycine, a nonpolar amino acid to serine, which is a polar amino acid at position 571 (G571S). Known exon 15 single nucleotide polymorphism (ID rs2290728) between thymine and cytosine were identified in 2 cases. No mutations were identified in exons 12 (novel or previously reported), 14, and 16.

**Conclusions:** We report a previously undescribed exon 13 mutation in a subset of JAK2V617F-negative CMNP. Although functional significance remains to be elucidated, this finding may contribute to disease phenotype in similar cases. The low prevalence of the mutations outside JAK2V617F does not warrant routine clinical testing but may be targeted in clinically suspicious JAK2V617F-negative CMNP.

**Microarray-Based Determination of Estrogen Receptor, Progesterone Receptor, and HER2 Expression: TargetPrint**

(Poster No. 42)

Richard Bender, MD, FACP (richard.bender@agenda.com); Paul Roepman, PhD; Hugo Horlings, PhD; Jolien Bueno-de-Mesquita, MD, PhD; Sabine Linn, MD, PhD; Femke de Snoo, MD, PhD; Annuska Glas, PhD; Reinhard Büttner, MD, PhD; Uwe-Jochen Göhring, MD, PhD. 1Department of Medical Affairs, Agenda Inc., Huntington Beach, California; Departments of 2Bioinformatics and 3Medical Affairs, Agenda, Amsterdam, Netherlands; 4Division of Experimental Therapy, 5Department of Pathology, and 6Division of Medical Oncology, Netherlands Cancer Institute, Amsterdam; 7Department of Institut für Pathologie, Universitätssklinikum, Bonn, Germany; 8Department of Frauenklinik, Johanner-Krankenhaus, Bonn, Germany.

**Context:** A number of interlaboratory comparison studies of hormonal receptor status showed strong correlation with immunohistochemistry as assessed with the Clinical Laboratory Improvement Amendments, and developed a microarray-based test called TargetPrint. By culturing only villi (skin, when available), the laboratory can save a rently study all tissue types from placenta, as well as skin, when available. Approximately 30% of patients studied with 5-FU/capcitabine develop a significant toxic response, which has been associated with single nucleotide polymorphisms (SNPs) in the dihydroorotidine dehydrogenase gene (DPYD). Other genes, including thymidine synthase (TYMS) and methylenetetrahydrofolate reductase (MTHFR) may also influence 5-FU/capcitabine response.

**Conclusions:** Using a multiplex microarray detection platform (Infiniti 5-FU, AutoGenomics, Inc., Carlsbad, California), we analyzed DNA samples from 25 colorectal cancer patients for specific genetic polymorphisms in DPYD (8S7T–C, IVS14 (+G–>A, 1390T>C, 1679T>G, and 2846A>T), MTHFR (677C>T and 1298A>C), and TYMS (ins/del TTAAAC in the 3′-untranslated region). SNPs in TYMS, DPYD, and MTHFR can be reliably identified using microarrays and may reliably identify patients susceptible to 5-FU/capcitabine toxicity.

**Optimum Tissue Type for Cytagenetic Analysis of Products of Conception**

(Poster No. 43)

Aarti Goswami, MD (goswami.aarti@danhsop.org); Richard Ligi, MS; Marilyn Arsham, BS; Laura Adomats, BS; Jennifer Kartz, BA; Julia De Layo, BS; Bina Siddiqui, MD. Department of Pathology, Danbury Hospital, Danbury, Connecticut.

**Context:** Chromosomal studies of products of conception (POC) are an important tool in determining cause of pregnancy loss. We explore selecting the appropriate POC tissue types for cytagenetic evaluation. Appropriate selection of tissue will streamline the process of specimen submission, reduce processing time, and reduce reagent/supply costs without compromising patient care.

**Design:** We retrospectively reviewed 100 cases of cytogenetically abnormal POC. Data included tissue type submitted for analysis and final karyotype. Salary expense and reagent/supply costs were also analyzed.

**Results:** We found 8 of 100 cases to have mosaic karyotypes. Of these, one proved to be true confined placental mosaicism with abnormal placentomes and normal fetal karyotype. Another case showed mosaicism among placenta tissues. A normal chromosome complement was seen in the cells studied from culture, whereas individually cultured villi and chorion each showed a low level of mosaicism. In 92 cases, we saw nonmosaic chromosomal abnormalities in all tissue types studied.

**Conclusions:** Because of its viability, villi are the overall preferred tissue for chromosome analysis of POC. Skin is the second choice because it is from the fetus proper. American College of Medical Genetics, College of American Pathologists, and New York State do not dictate which tissue type is the optimal source from POC for cytagenetic analysis. We currently study all tissue types from placentomes, as well as skin, when available. By utilizing only villi (skin, when available), the laboratory can save a minimum of $81 in salary expense and reagent/supply costs per case without compromising the quality of patient care.

**Microarray Evaluation of Single Nucleotide Polymorphisms Associated With 5-Fluourouracil Toxicity**

(Poster No. 44)

Delecia R. LaFrance, MD (delfra@lsuhsc.edu); Mary Nordberg, PhD; Erin Eaton, BS; Jack Waterman, HS. Department of Pathology, Louisiana State University Health Sciences Center, Shreveport.

**Context:** 5-Fluorouracil (5-FU)/capcitabine (its oral prodrug) is considered first-line treatment for colon cancer and is also used as chemotherapy for breast and head/neck carcinomas. Approximately 30% of patients treated with 5-FU/capcitabine develop a significant toxic response, which has been associated with single nucleotide polymorphisms (SNPs) in the dihydroorotidine dehydrogenase gene (DPYD). Other genes, including thymidine synthase (TYMS) and methylenetetrahydrofolate reductase (MTHFR) may also influence 5-FU/capcitabine response.

**Design:** Using a multiplex microarray detection platform (Infiniti 5-FU, AutoGenomics, Inc., Carlsbad, California), we analyzed DNA samples from 25 colorectal cancer patients for specific genetic polymorphisms in DPYD (85T>C, IVS14 (+A–>G, 1390T>C, 1679T>G, and 2846A>T), MTHFR (677C>T and 1298A>C), and TYMS (ins/del TTAAAC in the 3′-untranslated region). SNPs in TYMS, DPYD, and MTHFR can be reliably identified using microarrays and may reliably identify patients susceptible to 5-FU/capcitabine toxicity.

**Results:** SNPs genotyping using this microarray technology successfully identified mutations in TYMS, DPYD, and MTHFR of the selected patients. Most patients tested were heterogeneous carriers. However, homozygous mutations of TYMS (T5149A/ins), DPYD (85T>C), and MTHFR (677C>T and 1298A>C) were identified in several patients.

**Conclusions:** SNPs in TYMS, DPYD, and MTHFR can be efficiently and reliably detected using microarrays. Pretherapeutic SNP analysis may help clinicians choose a panel of mutations that is useful in screening 5-FU/capcitabine candidates to minimize severe toxicity, patient morbidity, and cost ineffectiveness.

**Mucolipidosis II With Skeletal or Pacman Dysplasia**

(Poster No. 45)

Rhea J. Birusingh, MD; Klass Wierenga, MD2; Car- los Parra-Herran, MD; Jocelyn Bruce, MD. Departments of 1Pathology and 2Medical Genetics, University of Miami, Florida.

Mucolipidosis II or inclusion cell disease is a rare, autosomal-recessive lysosomal trafficking disorder with a high mortality rate before 10 years. The molecular aberrations identified in this condition include mutations in the GNPTAB gene. As a result of the mutation, the lysosomes have a deficiency of multiple hydrolases. If bone abnormalities are also identified, Pacman dysplasia should be considered. We present a case of mucolipidosis...
Homzygous Deletion and Mutation of Exons 5 and 8 of the Fragile Histidine Triad Gene in Differentiated Thyroid Carcinoma (Poster No. 46)

De-tao Yin, MD, PhD; Elizabeth Plocharczyk, MD; (Elisabeth. Plocharczyk@osumc.edu); Jian-xin Gao, MD, PhD; Gang He, MD, PhD; 1Department of General Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; 2Department of Pathology, Ohio State University Medical Center, Columbus.

Context: Fragile histidine triad (FHIT) gene, which has been isolated in positional cloning, encompasses the most common human fragile site FRA3B at 3p14.2, a region involved in homozygous deletions in a variety of human tumors. It is considered a tumor-suppressor gene that is frequently inactivated in different types of cancer.

Design: To investigate the potential role of FHIT gene in thyroid tumorigenesis, we detected homzygous deletion and mutation of exons 5 and 8 of the FHIT gene in 65 cases of differentiated thyroid carcinoma and their matched, noncancerous epithelium by using exon-specific polymerase chain reaction amplification technique and polymerase chain reaction-single-strand conformation polymorphism technique.

Results: In differentiated thyroid carcinoma, the rate of homzygous deletion of exon 5 was 20 of 65 (30.8%), and it was related to tumor lymph node metastasis (P < .05). The rate of homzygous deletion of exon 8 was 19 of 65 (29.2%), and it was related to tumor pathologic grade, TNM stage, and lymph node metastasis (P < .05). There was a distinct correlation between homzygous deletion of exons 5 and 8 (P < .01). No point mutation was observed in exon 5 or exon 8.

Conclusions: Our results suggest that exons 5 and 8 might be important target regions of deletion in the FHIT gene, and homzygous deletion of exons 5 and 8 might be good biomarkers in evaluating the biologic behavior of differentiated thyroid carcinoma. Point mutation appears not to be an important factor in inactivation of the FHIT gene in differentiated thyroid carcinoma.

Validation of RNA Stability in Room Temperature–Stored Paraffin Blocks (Poster No. 47)

Stephen E. Vernon, MD (svernon@med.miami.edu); Jorge Torres-Munoz, PhD; Claire Lugassy, MD; Azorides Morales, MD. Department of Pathology, University of Miami Miller School of Medicine, Miami, Florida.

Context: Standard, routinely processed, formalin-fixed, paraffin-embedded tissues are generally unsuitable for recovery of RNA and investigation of gene expression. Alternative fixatives and processing methods have been demonstrated to preserve macromolecules in paraffin-block sections. The stability of the RNA in paraffin blocks stored at room temperature has not been previously documented.

Design: Human melanoma cells were inoculated onto a chicken chorioamniotic membrane. After 10 days, the chicken chorioamniotic membrane containing tumor cells was removed, fixed in a molecular-friendly fixative of overnight, processed on a Tissue-Tek Xpress ×120 (Sakura Finetek USA, Inc., Torrance, California), and embedded into paraffin blocks. Four-micron sections were cut for hematoxylin-eosin stains and for the laser-capture microdissection procedure. Unstained tissue sections were used for laser-capture microdissection, followed by total RNA extraction and qualitative and quantitative real-time reverse transcription-polymerase chain reaction analyses. After a 24-month interval, all steps were repeated on the same tissue blocks, which had been stored at room temperature.

Results: Routinely stained sections retained their morphology. Qualitative real-time reverse-transcription–polymerase chain reaction for the housekeeping gene GAPDH showed good-quality RNA. Quantitative real-time reverse-transcription-polymerase chain reaction for the LMA4, ITGB1, ITGB3, MMP2 and RSP4 genes demonstrated RNA of good quality that was suitable for gene expression quantification from the initial and 24-month interval experiments.

Conclusions: These results demonstrate that good-quality RNA can be extracted from formalin-fixed, microwave-processed tissue sections made from paraffin blocks stored at room temperature for at least 24 months after tissue processing and that this RNA remains suitable for gene expression profiling.

The research for this abstract was supported in part by a grant from Sakura Finetek USA Inc., Torrance, California.

Copresence of Epstein-Barr Virus and Human Papillomavirus Type 16 in lymphoepithelioma-like Carcinoma of the Uterine Cervix (Poster No. 48)

Nicolle Saviano, MD; Yi-Wei Tang, MD, PhD; Yong Kang, MD, PhD; (ykang@ssbcs.com). 1Department of Pathology, Monmouth Medical Center, Long Branch, New Jersey; 2Department of Pathology and Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.

Epstein-Barr virus (EBV) has been reported to play a role in the etiology of lymphoepithelioma-like carcinoma (LELC) of the uterine cervix in Asian women. LELC is rare in the Western world, where it is reported not to be associated with EBV. Human papillomavirus (HPV), however, has been detected in some cases in Western countries. We postulated that EBV varies geographically in the pathogenesis of LELC and that LELC in Western countries may have a different etiology. We studied a case of LELC by molecular method. A 37-year-old African American woman had a hystereomy because of LELC. Histologically, the tumor was poorly differentiated with a syncytial-like growth pattern and intense lymphocytic background, which is typical of LELC. A paraffin-embedded tumor-tissue block was deparaffinized, and DNA was extracted. Polymerase chain reaction amplifications were performed on the extracted DNA using HPV-negative–specific and HPV-negative–specific primers. HPV genotyping was further determined by DNA sequencing. EBV and HPV type 16 genomes were detected by polymerase chain reaction. By contrast, in situ hybridization failed to detect EBV or HPV in the tumor block. This negative finding implies that in situ hybridization is either less sensitive than polymerase chain reaction and/or that there is no active viral replication in tumor cells. This is the first reported case of LELC in the Western world in which both EBV and HPV were present. Whether EBV plays a role in the etiology of LELC in Western countries, as it does in the Orient, merits further investigation.

A Microarray-Based Gene Expression Test for Tumors With Uncertain Origins Using Formalin-Fixed, Paraffin-Embedded Specimens (Poster No. 49)

Raji Pillai, PhD (rpillai@pathworkdx.com); Rebecca Deeter, MS; MBA; C. T. Rigil, PhD; Meredith Halka-Miller, MD; Ljubomir Buturovic, MD; W. D. Henner, MD, PhD. 1Departments of 2Clinical Programs, 3Product Development, 4Laboratory, and 5Bioinformatics, Pathwork Diagnostics, Redwood City, California.

Context: Tumors with uncertain origins represent 5% to 10% of new cancer cases. The Pathwork Tissue of Origin Test is a gene expression test that aids in the diagnosis of tumors with uncertain origins using frozen specimens. It is the first test of its kind to be cleared by the US Food and Drug Administration. We validate a version of the test that works with formalin-fixed, paraffin-embedded (FFPE) specimens.

Design: Poorly differentiated and metastatic FFPE human tumor specimens with available diagnoses representing the 15 tissue-of-origin sites on the Origin-FFPE panel were blinded and processed at 2 independent laboratories to generate microarray data files. A prespecified classification model using more than 1500 genes was applied to each data file to yield similarity scores corresponding to the 15 tissues on the test panel. Results were blinded and compared with the available diagnoses.

Results: Of specimens processed, 352 of 405 (87%) yielded qualified data files. Based on the top similarity score, the overall agreement with available diagnoses was 89%. Metastatic and poorly differentiated primary specimens showed similar performance. Additionally, an average of 12 of 15 diagnoses for each specimen could be ruled out with greater than 99% probability.

Conclusions: The large size of this study allows for an accurate estimation...
mate of the confidence of test results for ruling in and ruling out tissues as likely sites of origin. The Origin-FFPE test makes the potential benefits of microarray-based gene expression tests for tumors with uncertain origins available for use with the most common type of histology specimen, FFPE.

An Investigational Prostate Cancer Methylation Assay Shows Predictive Value While Other Clinical Risk Factors Do Not
(Poster No. 50)

Jonathan Baden, MSc (jbaden@rvrus.inj.com); Jennifer Painter, MSc; Jadwiga Markiewicz, MSc; Jennifer Jones, MSc; Tara Astacio, BS; Susan Canning, BS; Jedidiah Quijano, MSc; Wilson Guinto, BS; Yixin Wang, PhD; George Green, PhD. Department of Assay Development, Veridex, Raritan, New Jersey.

Context: The ProCaM assay detects aberrant methylation in postdigital rectum examination urine of men with prostate-specific antigen values between 2.0 and 10.0 ng/mL. We compared the assay’s predictive performance to that of other clinical risk factors and determined its ability to detect aggressive cancer.

Design: The assay contains 3 methylation markers, GSTP1, RARβ2, and APC, and an endogenous control, β-actin, in a multiplexed format. This assay was evaluated on postdigital rectum examination urine samples prospectively collected from 185 (74 cancer, 111 noncancer) consenting subjects at 11 clinical sites. We obtained Institutional Review Board approvals. Assay results were not used for patient management.

Results: With univariate and multivariate analyses, the assay was the only significant independent predictor of positive biopsy (Table). The assay’s area under the curve (AUC) value for predicting subjects with positive versus negative biopsy results was 0.73, which was higher than the AUCs for the Prostate Cancer Prevention Trial risk calculator (AUC = 0.55, \( P = .001 \)) and for a nomogram consisting of prostate-specific antigen values, digital rectum examination result, and age (AUC = 0.60, \( P = .02 \)). The assay’s sensitivity was higher (\( P = .003 \)) when more than 30% of cores were histologically positive (76%) versus when fewer than 30% were positive (41%). It was also higher (\( P = .01 \)) when at least one core presented with more than 50% tumor (76%) versus no cores with more than 50% tumor (48%).

Conclusions: This assay shows high sensitivity for aggressive prostate cancers. Preliminary data suggest that the ProCaM assay may improve prostate cancer screening algorithms to more efficiently identify men with significant prostate cancer.

Independent Biopsy Predictors

<table>
<thead>
<tr>
<th>Source</th>
<th>Multivariate P Value</th>
<th>Univariate P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
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<td>.63</td>
</tr>
<tr>
<td>Race</td>
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<td>.59</td>
</tr>
<tr>
<td>Digital rectal examination</td>
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<td>.06</td>
</tr>
<tr>
<td>Prostate-specific antigen</td>
<td>.38</td>
<td>.08</td>
</tr>
<tr>
<td>Previous biopsy</td>
<td>.07</td>
<td>.07</td>
</tr>
<tr>
<td>Family history</td>
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<td>.28</td>
</tr>
<tr>
<td>Procam</td>
<td>&lt;.001</td>
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</tbody>
</table>

Mutational Surrogate for Acidification of Capsaicin Receptor, Transient Receptor Potential Vanilloid 1: Analysis of Influence on Ligand Recognition
(Poster No. 51)

Daniela Mihova, MD (damihova@yahoo.com); Alexandra Czap, BS; Noemi Kedei, MD; Peter M. Blumberg, PhD. Department of Molecular Mechanisms of Tumor Promotion, National Cancer Institute, Bethesda, Maryland.

Context: The transient receptor potential vanilloid 1 (TRPV1) is a non-selective cation channel that is predominantly expressed by peripheral sensory neurons and is known to play a key role in the detection of noxious and painful stimuli. TRPV1 receptors are activated by capsaicin, heat, low pH levels, and endogenous ligands. Previously, it has been reported that VR1 could be strongly activated by acidification of the extracellular milieu. To optimize drug selectivity for TRPV1, we wished to understand how a modeled acidic environment would affect ligand recognition and receptor response.

Design: To model the activity of TRPV1 in a chronic low pH setting, we generated an E600Q-TRPV1 mutant, substituting glutamic acid with glutamine. We created a noninducible system by transient transfection using HEK293 cells. We performed 45Ca2+ uptake functional assays 24 hours after the transfection, comparing the function of wild-type TRPV1 and mutated E600Q toward various full agonists (capsaicin, olvanil) and full antagonists (BCTC, AMG9810).

Results: The results from the 45Ca2+ uptake functional assays for wild-type versus mutant were as follows: capsaicin, partition coefficient (Kd) = 514 ± 7.7 versus Kd = 123 ± 24; olvanil, Kd = 49.9 ± 9 versus Kd = 136 ± 19; BCTC, inhibition coefficient (Ki) = 1.37 ± 0.28 versus Ki = 2.99 ± 0.1; AMG9810, Ki = 61.4 ± 9.9 versus Ki = 209 ± 20. \( P < .01 \) for all.

Conclusions: In contrast to what has been previously reported, we found that E600Q mutant receptors are less sensitive toward various agonists and antagonists. The explanation is that the receptors become desensitized over time in conditions of low pH stimulation because of either the effect of the environment or leakiness through the receptor.

The research for this abstract was supported in part by the Intramural Research Program of the National Institutes of Health, Center for Cancer Research, National Cancer Institute.

Recurrent of Breast Cancer in Women of Northwestern Mexico
(Poster No. 52)

Jose Manuel Ornelas-Aguirre, MD, MSc, PhD (jmoapat@yahoo.com.mx); Laura Maria Perez-Michel, MD; Mario Alberto Chavez-Zamudio, MD; Miguel Angel Ortiz-Martinez, MD. Departments of Research and Education, Oncology, Gynecology, and Pathology, Western Medical Center/Mexican Institute of Social Security, Cd. Obregon, Sonora, Mexico.

Context: We compared recurrence of breast cancer with the expression of estrogen receptor, progesterone receptor, and HER2 in women of northwest Mexico.

Design: This cross-sectional study included 397 cases of breast cancer. Correlation between clinical and pathologic factors, including estrogen receptor, progesterone receptor, and HER2 expression in the primary tumor, and the recurrence of disease were evaluated. Immunohistochemistry for estrogen receptor, progesterone receptor, and HER2 was interpreted; results were considered positive with 10% or higher expression in tumor cells. Variables with differences reaching statistical significance were incorporated into logistic regression analysis to predict the biomarker's effect in disease recurrence. A \( P \) value < .05 was considered statistically significant.

Results: The average age was 52 ± 12 years. Recurrence of disease occurred in 23% of patients (95% CI, 19–27; \( P = .001 \)) and for a nomogram consisting of prostate-specific antigen values, digital rectum examination result, and age (AUC = 0.60, \( P = .02 \)). The assay’s sensitivity was higher (\( P = .003 \)) when more than 30% of cores were histologically positive (76%) versus when fewer than 30% were positive (41%). It was also higher (\( P = .01 \)) when at least one core presented with more than 50% tumor (76%) versus no cores with more than 50% tumor (48%).

Conclusions: This assay shows high sensitivity for aggressive prostate cancers. Preliminary data suggest that the ProCaM assay may improve prostate cancer screening algorithms to more efficiently identify men with significant prostate cancer.
Development of interprofessional training programs. Therefore, faculty at the University of Arizona are creating innovative health care curriculum and are comparing various curricula. One option is offering pathology courses in undergraduate colleges.

Design: The Internal Review Board approved this study. We examined the ability of high school students with no prior exposure to premedical college courses to master medical school level pathology coursework. We enrolled 6 high school students in an experimental education program to test our hypothesis that high school students can master medical school pathology. Students participated in a 6-week immersion, simulated medical school curriculum, which was delivered in a college environment by tenured medical college faculty members. It included segments of a general pathology curriculum, including histopathology virtual slide laboratories.

Results: Students attended formal classes. Time was divided between classes as follows: 40.3% lectures, 13.8% virtual slide laboratories, 22.1% special projects, and 3.3% student assessment. Ten hours of faculty instruction were given by video conference distance education. Additionally, students conducted independent study projects involving a presentation on a specific disease, such as drug-resistant tuberculosis or Crohn disease. All students successfully completed the course achieving grades of B or A. Students rated the course 4.83 out of 5. On average, they rated their video conferencing seminars as 4.66 out of 5.

Conclusions: High school students essentially duplicated the performance of medical students on pathology subject material. This raises the possibility of introducing coursework in pathology at the college or high school level. Dr. Weinstein is co-founder of, and has equity in, DMetrix, Inc., Tucson, Arizona.

Implementing Digital Slides at Resident “Unknown” Conferences (Poster No. 54)

Brad E. Chaser, MD (brad-chaser@ouhsc.edu); Lewis A. Hassell, MD. Department of Pathology, University of Oklahoma, Oklahoma City.

Context: The use of digital slides appears imminent for routine diagnostic pathology workflow and research. They have already claimed a niche in medical school teaching and postgraduate education. However, the role of digital slides in residency training remains unexplored.

Design: Teaching conferences offered residents unknown slides in either a glass (centralized location only) or digital format (Imagescope/Webviewer) with online remote access. Following each conference, residents completed a questionnaire examining these 7 questions: (1) time previewing cases as a whole, (2) time per case, (3) slide availability, (4) quality of images, (5) ease of use of equipment, (6) value of conference to education, and (7) likelihood of postconference review.

Results: Survey results are presented in the Table below. Also, educational value ranked 7.8 for digital and 9.0 for glass. Likelihood of review scored 6.9 for digital and 6.5 for glass. Results are based on a 10-point scale ranging from poor to excellent.

Conclusions: Digital slides face several significant barriers before they can replace traditional microscopy for resident teaching. In general, residents spent approximately one-third more time per case when using digital slides. Follow-up surveys revealed that the digital media initially presented unknown slides in either a glass (centralized location only) or digital format (Imagescope/Webviewer) with online remote access. Following each conference, residents completed a questionnaire examining these 7 questions: (1) time previewing cases as a whole, (2) time per case, (3) slide availability, (4) quality of images, (5) ease of use of equipment, (6) value of conference to education, and (7) likelihood of postconference review.

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Anatomic Pathology and Its Role in the Development of the Health Care System in the Lao People’s Democratic Republic (Poster No. 55)

Moosa N. Khalil, MBBS, FRCP†. (moosa.khalil@cls.ab.ca); Anucha Tangthangham, MD‡; William W. Gorday, Technologist§; Phetsamone Arounlangsy, MD, PhD¶; John P. Whitelaw, MD, Hallgrimur Benediktsson, MD, FRCP. 1 Department of Pathology and Laboratory Medicine, University of Calgary, Calgary, Alberta, Canada; 2 Department of Pathology, Chest Disease Institute, Nonthaburi, Thailand; 3 Department of Pathology, Calgary Laboratory Services, Calgary, Alberta, Canada; 4 Department of Pathology, University of Health Sciences, Vientiane, Laos People’s Democratic Republic; 5 Department of Pathology and Laboratory Medicine, Nanao Hospital, Nanao, British Columbia, Canada.

Context: Anatomic pathology services are lacking in many developing countries. This deficiency negatively affects patient care and planning for the development of health care systems because of the absence of accurate statistics about the burdens of disease. Laos is a developing country with an urgent need for improvements in its health care system. Although it has modernized many of its hospitals, the country lags behind in providing pathology services, even at its biggest institutions.

Design: A team of pathologists and a laboratory technologist from Canada and Thailand visited Laos to assess the state of anatomic pathology in its hospitals and to determine potential areas for development. During a 4-week period, the team traveled between academic/urban centers and rural hospitals. They provided cytopathology diagnostic services and were involved in the development of a histopathology laboratory. They interacted with patients, pathologists, clinicians, technologists, students, and administrators. They provided practical training in cytopathology and laboratory technology.

Results: The main causes of poor pathology services in Laos are the insufficient number of well-trained pathologists and technologists, inadequate equipment maintenance, and unavailability of reagents. Training of pathologists is hampered by limited access to educational material because of logistic barriers and the absence of a pathology-training curriculum.

Conclusions: Sustained, structured collaboration between pathologists from developed countries and institutions in Laos is essential for development of that country’s medical education programs and health care system. Our data show that significant impact can be made using simple techniques. Customized training programs can make a significant impact on morbidity and mortality in this setting.

Transformative Resident Training: A Proposed Model for Pathology Resident Education in Coagulation (Poster No. 56)

Christina M. Wojewoda, MD (christina.wojewoda@uhospitals.org); Robert D. Hoffman, MD; Katharine A. Downes, MD. Department of Pathology, University Hospitals Case Medical Center, Cleveland, Ohio.

Context: Clinical pathology resident education requires an understanding of laboratory testing within the clinical context of the patient. Different

Redesigned Curriculum

<table>
<thead>
<tr>
<th>Educational Objective</th>
<th>Curriculum Content/Resident Required Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information integration (clinical and laboratory)</td>
<td>(1) Participation in clinical conferences and in pediatric hematology clinics with direct patient contact</td>
</tr>
<tr>
<td>(2) Review of coagulation test requests before testing for appropriateness and clinical correlation with direct communication with clinicians</td>
<td></td>
</tr>
<tr>
<td>(3) Preview of cases and rendering diagnostic interpretation before attending sign-out</td>
<td></td>
</tr>
<tr>
<td>Principles and practice of laboratory medicine (coagulation)</td>
<td>(1) Observation on the bench in coagulation/laboratory testing</td>
</tr>
<tr>
<td>(2) Daily review of quality control</td>
<td></td>
</tr>
<tr>
<td>(3) Performance of a mock College of American Pathologists coagulation laboratory inspection, presentation of findings, and recommendations for improvement</td>
<td></td>
</tr>
<tr>
<td>(4) Oral presentation to laboratory technologists on coagulation topic</td>
<td></td>
</tr>
<tr>
<td>Linkage among concepts, scientific literature, practical knowledge, and test taking</td>
<td>(1) Didactic lectures</td>
</tr>
<tr>
<td>(2) Written quizzes and final examination, including esoteric topics/cases that the resident may not have observed during rotation</td>
<td></td>
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</tbody>
</table>
forces in the health care environment may change the practice of medicine. These changes will require a transformation in how clinical pathology is practiced. We describe a novel approach to teaching pathology residents coagulation testing that could serve as a model for training future pathologists.

**Design:** During 2004 to 2005, the clinical pathology residency curriculum at our institution was restructured to dedicate 1 month to resident education in coagulation. The curriculum concept for this rotation was to educate pathology residents in the following: (1) integration of clinical context with laboratory testing, (2) laboratory coagulation testing, management and accreditation, and (3) linkage between concepts, scientific literature, practical experience, and test taking.

**Results:** The objectives and the redesign were achieved. The rotation teaching staff grew from 2 pathologists and 1 medical technologist in 2004 to 2005 to the current staff consisting of 2 pathologists, 3 pediatric hematologists, 2 hemophilia nurses, and 6 medical technicians. The 21 pathology residents who have completed this rotation have successfully passed the written evaluations; 33% required a make-up quiz on esoteric topics.

**Conclusions:** Clinical pathology resident training in coagulation provides an excellent opportunity to educate residents in the benefits of providing to clinicians value-added interpretation of laboratory results. Transforming pathology resident education to be more clinically comprehensive and integrative is an effective model to prepare pathology residents for future practice.

**Digital Cytology Images: A Multiplex Role With Potential as a Learning Tool for Pathology Residents**

(Deborah No. 57)

Meenakshi Singh, MD (meenakshi.singh@stonybrook.edu); Daniel Perez, MD. Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

**Context:** In our cytology laboratory, digital images of outgoing consultation material are collected and archived. We assessed the utility of digital images in resident education. We hypothesized that they could serve as a valuable tool in education and assessment.

**Design:** The images were reviewed, and a pilot set from 20 consecutive cases that included various organ sites were selected for teaching and assessing residents from all postgraduate years (n = 11). The residents were provided with a clinical history and had to assign a category (non-diagnostic, negative, benign, atypical, malignant) and a specific diagnosis, if feasible. The results were reviewed confidentially, correlated with postgraduate year, and shared with the residents.

**Results:** We had an average of 4 images per case. Negative and malignant cases were included. Image quality was excellent in 80% and acceptable in 20% of cases. A total of 215 diagnoses (97.7%) were rendered; there were 5 abstrained diagnoses. The 2-step discrepancy rate was 19 of 215 (8.8%). No discrepancies were identified between consultant review and the original diagnosis. Diagnostic accuracy was noted for small cell carcinoma and lymphoma, irrespective of organ site. We had a diagnosis accuracy goal of 75%. Five of 11 residents (45.4%) from the first 3 postgraduate years showed room for improvement in their cytology knowledge.

**Conclusions:** Digital images can have a multiplex role in cytology. We have found them to be useful for archiving outgoing consultation material. The same database can serve as a resource for cytology education and self-study and as a tool for prerotation and postrotation assessments.

**Virtual Slide Telepathology in a Breast Pathology Quality Assurance Program**

(Deborah No. 58)

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**Context:** Virtual slide telepathology represents a potential tool in providing quality assurance review of surgical pathology cases for a second hospital.

**Design:** The University of Arizona implemented a quality assurance program between 2 university hospitals. University Medical Center handles approximately 10 times the number of surgical pathology cases (about 20,000) than a smaller, affiliated hospital, University Physicians Healthcare Hospital (UPHH). UPHH is staffed by a rotating, part-time pathologist from University Medical Center. To provide same-day quality assurance review of breast surgical pathology cases, we installed a DMetrix DX-40 ultrarapid virtual slide scanner (DMetrix, Inc., Tucson, Arizona) at UPHH. Glass slides of breast cases are scanned on the same day as they are produced at the UPHH histology laboratory. The pathologist at UPHH generates a prompt return report based on light microscopy. At 3 pm each day, virtual slides of breast cases from UPHH are reviewed at University Medical Center by staff pathologists and residents on a 50-inch plasma monitor, using virtual slide viewer software.

**Results:** We analyzed 154 breast pathology cases. There was complete concurrence with the primary diagnosis in 139 cases (90.3%). There were 4 major discrepancies (2.6%), which would have resulted in different therapy, and 3 minor discrepancies (1.9%). Three cases (1.9%) were deferred for immunohistochemistry. Two cases (1.3%) were deferred for examination of glass slides. Discrepant cases incorporated the virtual slide diagnosis.

**Conclusions:** The quality assurance program found a small number of significant diagnostic discrepancies, promoted group decision making in a university subspecialty pathology practice, and increased job satisfaction for the pathologists.

Ms. Richter is a consultant for, and has equity in, DMetrix, Inc. Tucson, Arizona. Dr. Weinstein is cofounder of, and has equity in, DMetrix, Inc., Tucson, Arizona.

**Utility of Repeat Critical Value Testing**

(Deborah No. 59)

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**Context:** Critical values are routinely confirmed by a repeat run before being communicated to the patient's caregiver. This study was designed to answer a question frequently asked by clinicians and laboratorians: Is confirmation necessary in this era of new and improved automated technology?

**Design:** We selected 5 tests performed in the hematology laboratory: hemoglobin, white blood cell count, platelet count, prothrombin time, and activated partial thromboplastin time. Using institutionally established critical value limits, a minimum of 500 consecutive critical values were collected retrospectively for each test category. The absolute and percentage differences between the duplicate runs of each critical value were calculated and averaged for each category. Duplicate runs of individual critical values with absolute differences outside the mean range of plus/minus 3 standard deviations were tallied to determine the percentage of outliers in each category.

**Results:** The means obtained for the absolute and percentage differences between duplicate runs were as follows: 0.08 (1.4%) for hemoglobin, 0.05 (10.2%) for white blood cell count, 1.5 (9.9%) for platelet counts, 0.7 (14.3%) for prothrombin time, and 5.1 (4.4%) for activated partial thromboplastin time. The percentage of specimens with absolute differences outside 3 standard deviations (ie, outliers) ranged from 0.2 to 2.2 among the test categories (Table). The means of differences for each test category and the differences noted for individual outliers were not considered clinically significant from the standpoint of patient management.

**Conclusions:** Our findings indicate that repeat analysis of these tests is not necessary.
Using Amended Report Rates to Monitor Preanalytic and Postanalytic Errors in an Anatomic Pathology Laboratory (Poster No. 62)

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Context: There is currently national impetus to improve the quality of health care services. Logistic complexities exist in managing specimen receipt, processing, preparation, and reporting. Monitoring amended pathology reports provides a mechanism for assessing process improvement effects on error reduction.

Design: Report amendment data from 2007 and 2008 were collected. Department quality improvement minutes were reviewed. Classifications for preanalytic errors were as follows: missing clinical history, missing patient information, labeling error, or accessioning error. Postanalytic data were gathered from amended reports. Classifications for postanalytic errors were as follows: major diagnostic errors, diagnostic clarification, proofreading, missing or damaged specimens, and incorrect result assignment. Interventions identified sources of error; process improvement techniques were applied. Faculty, residents, and support staff participated in this exercise.

Results: The department issued an average of 24,000 surgical reports per year. Rates of corrected reports because of a lack of clinical history were reduced from 0.27% in 2007 to 0.11% in 2008. Significant typographic error rates were reduced from 0.21% to 0.04%, and incorrect patient assignment to a case decreased from 0.05% to 0.02%. The “diagnosis clarification” category increased from 0.07% to 0.14%. A “pathology time-out” on the specimen requisition helped to reduce patient labeling errors from 6 to 0 in the endoscopy suite.

Conclusions: Using the principles of manufacturing quality management, which involves systematically identifying and eliminating errors, we reduced the overall report amendment rate. An increase in diagnostic clarification was attributed to more involved participation in quality assurance sessions by faculty. These findings translate into improved delivery of quality health care.

The Effects of Formalin Fixation on the Immunolocalization of MLH1 and MSH2 Proteins (Poster No. 63)

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Context: Preanalytic factors, such as length of formalin fixation, can affect the quality of immunohistochemical staining. This study evaluated the effect of formalin fixation time on the immunohistochemical localization of human MutL Homolog 1 Protein (MLH1), and MutS Homolog 2 Protein (MSH2). Microsatellite instability is a genetic manifestation of defective MMR proteins. Loss of MMR function in individuals with microsatellite instability can lead to hereditary, nonpolyposis colorectal cancer. Monoclonal antibodies to MSH2 and MLH1 were evaluated on benign tonsil tissues fixed in formalin from 1 to 120 hours to determine the effects of fixation on the immunolocalization of the MMR proteins in routinely processed tissue specimens.

Design: Mouse monoclonal anti-human MLH1 (clones E505 and G168-15) and anti-human MSH2 (clones FE11 and G219-1129) were evaluated in immunohistochemistry on formalin-fixed, paraffin-embedded tonsil tissue fixed for 1, 4, 24, 48, and 120 hours. All tissue was pretreated with Tris/EDTA target-retrieval solution, and bound antibody was visualized with the Dako FLEX detection system.

Results: The highest staining intensity and most discrete nuclear localization were observed for MLH1 and MSH2 on tissue fixed in formalin for 4 and for 24 hours. Moderate to strong cytoplasmic staining was observed with antibodies to MLH1 and MSH2 in tissues fixed longer than 24 hours.

Conclusions: This study demonstrates that formalin fixation time is important for obtaining optimal immunohistochemical staining of the MMR proteins, MLH1 and MSH2. Standardization of preanalytic processing of tissue can help eliminate observed variations in the immunostaining intensity and cellular localization of proteins.