The development of multiple primary malignancies in an individual is rare and unfortunate, and the care of such a patient presents specific challenges. We report the diagnosis and progression of 3 histologically different primary cancers in 1 patient over the course of 15 years. At age 50 years, the patient received a diagnosis of transitional cell carcinoma of the bladder; treatment was successful. When the patient was 64 years old, mesothelioma of the tunica vaginalis was diagnosed, and computed tomography performed for staging purposes revealed a lung lesion, which was later diagnosed as adenocarcinoma. Treatment for the adenocarcinoma was also successful, but the patient continues to have recurrence of mesothelioma. To our knowledge, the present report is the first description of a case of 3 primary cancers that includes a mesothelioma of the tunica vaginalis. Because mesothelioma of the tunica vaginalis is rare, we reviewed the literature on its prevalence, presentation, management, and prognosis.

In the diagnosis of cancer, recognition of early warning signs is primarily the responsibility of the primary care physician (PCP). Physicians in almost every medical specialty play a role in the detection of cancer, but the PCP is best positioned to recognize the earliest warning signs of neoplasm and is most often the individual who refers the patient to the appropriate specialist. In addition to having a role as a gatekeeper—as patients’ initial point of contact and as one who refers patients for further medical treatment by specialists—the PCP is also the patient’s only consistent and familiar guide through the complicated landscape of cancer care in the 21st century.

We present a case report describing a patient with 3 separate primary cancers: transitional cell carcinoma of the bladder, mesothelioma of the tunica vaginalis, and adenocarcinoma of the lung. In addition to discussing a novel combination of cancers, the wealth of specialists involved in the present report highlights the importance of the PCP, who is not focused on a particular body region, in the provision of holistic care to the patient. The case also illustrates the enormity of the effort required to coordinate with consulting physicians regarding a complicated case.

Report of Case

In March 2007, a 64-year-old man presented to his PCP with left-sided scrotal swelling and testicular discomfort. The patient reported that the swelling had been present for several weeks. During physical examination, a mass was detected on palpation of the left side of the scrotum, which was slightly tender and was neither erythematous nor warm to the touch. Findings of the remainder of the physical examination were normal.

The patient’s medical history revealed no weight loss, night sweats, urinary irregularities, or sexual dysfunction. It was, however, clinically significant for transitional cell carcinoma of the bladder that had initially manifested as painless hematuria 14 years previously in January 1993. Results from cystoscopy performed at that time demonstrated a fungating mass. Biopsy results confirmed the mass to be grade I/III papillary transitional cell carcinoma. The mass was excised and fulgurated. Routine, annual observational cystoscopy was recommended and continues to this day. The patient’s medical history also included hyperlipidemia and a 40-pack-year smoking history.

Occupational history included a brief period during which the patient worked on a naval vessel, where he may have been exposed to asbestos. Family history included no known instance of cancer. The patient’s father died at the age of 65 years of causes unknown to the patient; however, the patient’s mother was alive and healthy in her mid-90s at the time that the patient presented with symptoms.

When the patient presented to his PCP with scrotal...
swelling in March 2007, he was also found to be overdue for routine surveillance cystoscopy; therefore, he was referred to a urologist for evaluation. Results from a testicular sonogram ordered by the urologist suggested the presence of a cyst, which could not be clearly characterized by the study. Results of magnetic resonance imaging showed a hydrocele, but a cyst was not identified.

In April 2007, the PCP performed a preoperative medical evaluation on the patient, and a urologist conducted an exploratory scrotal surgery. Frozen section analysis demonstrated the presence of a tumor, which was identified as mesothelioma of the tunica vaginalis. A time line of the present case beginning with this diagnosis is shown in Figure 1. A cardiothoracic surgeon performed a left orchietomy, which is the treatment of choice for patients with mesothelioma under these conditions. Results of local lymph node biopsy were negative for disease.

Two weeks after biopsy, the PCP referred the patient to an oncologist for tumor staging and treatment recommendations, at which time the patient also underwent computed tomography (CT) of the chest, abdomen, and pelvis. A suspicious mass identified in the lower lobe of the left lung was initially thought to be metastatic disease. Positron emission tomography results revealed hypermetabolic activity. For further evaluation of the mass, the oncologist referred the patient to a thoracic surgeon, who removed the mass by means of a video-assisted thoracic surgery procedure performed 3 months after the diagnosis of mesothelioma of the tunica vaginalis was made. The patient was seen preoperatively by cardiology and pulmonary consultants and underwent an uneventful procedure. Surprisingly, the pathologic examination did not reveal mesothelioma; however, the histologic pattern was indicative of adenocarcinoma.

In August 2007, 1 month after the video-assisted thoracic surgery procedure was performed, a surgical oncologist conducted an exploratory abdominal surgery involving lymph node dissection as well as hemiscrotectomy in the patient. No cancer was discovered, and abdominal ascites that emerged postoperatively eventually resolved with rest and diuresis. In December 2008, 20 months after mesothelioma of the tunica vaginalis was initially diagnosed, a lump in the left groin was discovered. One month later, the mass was excised and found to be local recurrence of mesothelioma. The patient underwent radical groin dissection in February 2009, 22 months after the initial diagnosis. All groin operations were performed by a surgical oncologist. Six months after radical groin dissection, issues related to lymphedema of the left leg and mild ankle ulceration were addressed by the PCP and resolved with medical treatment.

The patient was seen by the PCP in October 2010 (42 months after diagnosis), at which time results of a CT scan revealed that the patient once again had local recurrence of mesothelioma in the left groin. Despite diminishment of the size of the lymph nodes in the groin, the patient opted to undergo a 6-week course of radiation therapy targeting the left groin region.

Forty-four months after mesothelioma was initially diagnosed, results from a CT scan revealed 2 new pulmonary nod-
ules and evidence of peritoneal implantation. Since the submission of the present report, the patient underwent surgical groin exploration with lymph node biopsy by a surgical oncologist for the new growths, which were confirmed to be metastases resulting from the mesothelioma. The patient received a 6-month course of chemotherapy, which just recently ended. The patient is alive and enjoying a fairly normal lifestyle. His psychological outlook remains positive.

Comment
To our knowledge, the present report is the first to discuss a rare case of 3 primary cancers that includes an equally rare mesothelioma of the tunica vaginalis. Multiple primary neoplasms are uncommon clinical entities that often require highly specialized, intensive medical care. The prevalence of this phenomenon has been increasing in recent years, perhaps because of the increased survival rate associated with cancers previously considered to be fatal (ie, allowing the patient time to develop a second or third malignancy).

Because the only available data on the prevalence of multiple neoplasms come from case reports and studies based on case report data, accurate determination of prevalence is difficult. Koutrisopoulos et al tabulated the results of an extensive literature search for multiple primary cancers and found 42 cases of 3 or more cancers reported between 1949 and 2003, proving that the entity is rare. Important epidemiologic parameters, such as incidence, prevalence, and prognosis, would almost certainly depend on the particular combination of cancers considered. Therefore, the particular combination of cancers should be examined in an attempt to explain the occurrence through elucidation of a common risk factor or, perhaps, genetic predisposition.

Mesothelioma of the tunica vaginalis can also be classified under the slightly broader term “paratesticular mesothelioma,” which defines a group of neoplasms that also includes mesothelioma of the spermatic cord and epididymis, although the contribution of these two entities is minimal. Through 2009, paratesticular mesothelioma was reported only 223 times in the literature, with publication of the earliest report, by Barbera and Rubino, occurring more than 50 years ago. These malignancies account for 0.3% to 1.4% of reported cases of mesothelioma. To date, the only known risk factor for mesothelioma is asbestos, with a history of direct contact with or familial exposure to asbestos reported in 35% to 40% of cases.

Preoperative diagnosis of mesothelioma of the tunica vaginalis is extremely rare, because clinical symptomatology is diverse and often appears to be benign. This type of tumor most commonly occurs in the elderly patient with a hydrocele for which operative repair is attempted and in whom mesothelioma is encountered. Diagnosis requires a tissue sample and pathologic examination. The limited available evidence suggests that surgery is the most beneficial treatment modality, with radiation therapy and chemotherapy having little—if any—effect on survival. A highly aggressive cancer with the potential for local, lymphatic, or hematogenous spread, mesothelioma of the tunica vaginalis has a 60% chance of recurrence in the first 2 years after diagnosis. Plas et al reported that the median duration of survival was 23 months, or 14 months in the event of a recurrence.

The concurrence of the 3 cancers in the patient described in the present report raises suspicion that environmental exposure increased his risk of cancer. The patient’s history of smoking and his uncertain status regarding exposure to asbestos are the 2 most apparent risk possibilities (Figure 2). Smoking is a primary risk factor for bladder cancer and adenocarcinoma of the lung, with data indicating that smoking is associated with an approximately 3-fold increase in the risk of bladder cancer among heavy smokers, compared with nonsmokers. Asbestos exposure increases the risks of both mesothelioma of the tunica vaginalis and adenocarcinoma of the lung.

Table 1. Comparison characteristics of 3 primary cancers.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Transitional Cell Carcinoma</th>
<th>Mesothelioma of the Tunica Vaginalis</th>
<th>Adenocarcinoma of the Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known Risk Factors</td>
<td>Smoking, exposure to aniline dyes, external beam radiation</td>
<td>Asbestos exposure</td>
<td>Smoking, asbestos (working synergistically)</td>
</tr>
<tr>
<td>Average Patient Age at Onset, y</td>
<td>65</td>
<td>55-74</td>
<td>55-65</td>
</tr>
<tr>
<td>Age-Adjusted Prevalence, No. of cases per 100,000 Population</td>
<td>20</td>
<td>Rare*</td>
<td>17</td>
</tr>
<tr>
<td>Survival After Diagnosis</td>
<td>NA</td>
<td>90†</td>
<td>NA</td>
</tr>
<tr>
<td>5-Year rate, %</td>
<td>23</td>
<td>NA</td>
<td>17‡</td>
</tr>
</tbody>
</table>

*Age-adjusted prevalence of mesothelioma of the tunica vaginalis was not calculated, but the age-adjusted prevalence of general mesothelioma was estimated to be 1 case per 100,000 population. †Calculated for cases of superficial disease. ‡Calculated using data for cases of all subtypes and all stages. Abbreviation: NA, not available. Sources: Bisceglia et al; Fauci et al; and Travis et al.

Figure 2. Comparison of the epidemiologic characteristics of 3 primary cancers.
noma of the bladder. Age is a risk factor for all 3 cancers and is considered a risk factor for multiple malignancies. The patient’s age, 64 years, at the time of diagnosis of mesothelioma is very close to the age at which presentation of symptoms of all 3 cancers is most common. An unknown risk factor may have increased this patient’s likelihood of developing the cancers, but because there is such a small sample of patients who have multiple primary cancers that cannot be classified as known polycancer genetic disorders, hypotheses are many and firm answers are few.

Communication among several physicians, with the PCP acting as liaison, throughout the patient’s treatment was essential. In addition to the specialists mentioned, many other healthcare professionals (eg, general oncologist, radiotherapist, radiologist, nuclear medicine professionals, supporting hospital staff) were involved in the diagnosis and management of the presenting cancers. In fact, the patient in the present report saw more than 12 different physicians from multiple specialties in at least 2 major hospital institutions. A 2009 study in Annals of Internal Medicine found that for every 100 Medicare patients monitored, a PCP must coordinate with an average of 99 consulting physicians in 53 practices. We believe that a patient with a complicated case, such as the one discussed in the present report, represents an extreme case in this regard.

Conclusion
The present case report provides a powerful statement about the role of the PCP in modern medicine, highlighting the role of the PCP as a coordinator of physicians from various medical specialties. In an era when most physicians’ offices still use handwritten notes to record details about patient visits and use the telephone to coordinate consultation, the time required for healthcare coordination is staggering. Clearly, coordination of care and communication between physicians, patients, and families are crucial.

References

JAOA Online Archives
Archives of JAOA—The Journal of the American Osteopathic Association content as far back as 1950 are available online at http://www.jaoa.org/contents-by-date.0.shtml. Beginning with the January 2000 issue, JAOA articles, letters, and other contributions are available in full text, PDF documents, or both. In addition, members of the American Osteopathic Association and JAOA subscribers can access content from the past 12 months free of charge.