"in situ" gastric cancer that they consider not terribly uncomfortable for the patient. Endoscopic mucosal resection, a technique developed about 15 years ago in Japan, but rarely used in the West, borrows conceptually from endoscopic removal of polyps of the colon. Used to treat lesions of less than 2 cm, it involves first the injection of a layer of saline below the mucosal layer to elevate the lesion, and then the lopping of the lesion by a snare.

For Schlemper and others, universal terminology is a critical step toward universal application of stage-specific treatments. "Western surgeons treat lesions diagnosed as severe dysplasia by open surgery," wrote Mitsuru Sasako, M.D., a surgeon at the National Cancer Center Hospital in Tokyo, in an editorial that appeared in the October issue of the Japanese Journal of Clinical Oncology. "The Japanese diagnose them as cancer, but treat them by endoscopic mucosal resection." According to Schlemper, Western patients who may not officially have cancer may lose their stomachs; Japanese patients who are diagnosed with early gastric cancer are treated with a minimally invasive procedure.

Sasako likens the goal of the pathologist to the task of being able to tell an ostrich from a dinosaur — before it has hatched. An ostrich egg, in this lexicon, is an apparently non-invasive lesion that, like the bird to which Sasako likens it, will never become aggressive. A dinosaur egg may look very similar, but with time will give rise to an aggressive, invasive monster. "Japanese pathologists believe they can recognize the difference between the eggs of a dinosaur and the eggs of an ostrich," he explained.

Schlemper expects the new consensus nomenclature to be published in peer-reviewed journals any month now. But even if the new classification is widely accepted, as Schlemper hopes it will be, other controversies continue to rock the international gastric cancer community.

**Other Controversies**

How much of a causal role does *Helicobacter pylori* play? Schlemper argues that past Japanese research showing that eradication of the bacteria prevented stomach cancer is suspect because it used "cancer" cases as defined by Japanese criteria. What is the optimal surgical treatment for advanced stomach cancer? The results of two European trials, soon to be published, show no survival advantage for the more radical surgery typically practiced by Japanese. But McCulloch says the studies' investigators themselves concede that flaws in the study leave the validity of their results open to debate.

And does Japan's mass screening program reduce gastric cancer mortality? Many Japanese adamantly defend screening, while Westerners tend to dismiss it in the absence of prospective trials proving its effect.

Even in the diagnostic arena the debate has not ended. Schlemper has reported diagnostic differences across the Pacific for colon and esophageal cancer, and suggests there may be more of the same kinds of differences in liver, uterine and perhaps other cancers.

Those who dream of a common language have their work cut out for them.

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**Tired Out: Patients Find Few Easy Answers for Cancer-Related Fatigue**

Imagine straining your legs and lungs just to walk into the kitchen for a cup of tea. Or panting as a trip to the bathroom drags into a 15-minute ordeal. Or missing a phone call because you are unable to reach your desk in ten rings or less.

Cancer patients face these obstacles every day. Several surveys show upwards of 75% of these patients suffer from anemia and other kinds of fatigue — physical, emotional, mental. Many times the fear and frustration of cancer is compounded by exhaustion brought on by the very drugs and radiation that are meant to cure it.

A touring virtual reality road show is bringing this fatigue experience to doctors, family members, and others. After strapping on a video-display helmet and an input glove (which works like a mouse), simulator-goers experience a typical morning in the life of a cancer patient.

**Real Exhaustion**

The moves are simple, but taxing: pump your legs constantly on stairmaster-type pedals while navigating your virtual home. Then get used to being thwarted at each turn, frustrated at each uncontrollable mishap. Everything happens too quickly — that trip to the front door seems to take hours of pumping, and when you get there, the pharmacy delivery truck is already gone.

A spokesperson for Ortho Biotech Inc., Raritan, N.J., said the company
developed the simulator so doctors can “really understand what their patients are going through.” Surveys peg fatigue as the most common, most debilitating symptom cancer patients face. But no standard treatment exists, and unlike more visible side effects of chemotherapy and radiation such as hair loss and nausea, fatigue has traditionally received scant attention.

“I think fatigue has a bigger impact than a lot of the other symptoms and side effects,” said Mary Pat Lynch, an oncology nurse at the University of Pennsylvania, Philadelphia. “But only in the past few years have we started to recognize it.”

Part of the problem is a communication breakdown. Like a married couple ignoring the obvious signs of a downhill relationship, doctors and patients conspire to avoid dealing with the issue. Patients tend to not tell their doctors about it, and doctors often don’t ask.

“In general, doctors feel they can’t do anything about fatigue,” said Gregory Curt, M.D., clinical director at the National Cancer Institute. “And doctors don’t ask about things and don’t want to know about things they can’t help.”

In turn, patients tend to put on a game face and not report symptoms like exhaustion, foggy-headedness, and depression.

After breast and ovarian cancer survivor Susan Scherr underwent surgery and chemotherapy two decades ago, taking a shower or answering the phone became tests of will, measures of patience. But even then she did not report it to her doctors. “Sometimes fatigue seems so insignificant in the big scale of things. You don’t want to seem like a whiner or a complainer,” said Scherr, who heads community liaison activities at the National Coalition for Cancer Survivors in Silver Spring, Md.

Curt illustrates both sides of the communication gap with a story he cites as a typical exchange: A surgeon suffering from cancer and his wife are waiting for a post-treatment visit with their oncologist. The oncologist comes in and says, “How are you feeling?” The surgeon replies, “I feel great.” Then the wife, ribbing her husband, says, “You do not, what are you saying? Tell him what you just told me.” The reticent surgeon admits he’s feeling tired. And the doctor says, “You’re tired! I’m tired too. Do you know how overworked I am?”

Simple Prescription

Nurses are notoriously overworked, but as front-line workers in oncology wards, they are leading the war against fatigue. Lynch said although there are not “a whole lot of interventions available,” nurses and doctors, guided by feedback from patients, are finding ways to ameliorate fatigue.

Lynch works with patients to develop realistic daily schedules that include rest periods and restructured work times. She also gives them energy-saving tips, such as drying off by donning an absorbent robe instead of scrubbing with a towel.

Mild exercise is the first prescription many nurses and doctors give their fatigued patients, and it can turn enervation into energy, said Bernadine Pinto, Ph.D., of the Miriam Hospital, Providence, R.I. Pinto, who studies whether exercise boosts quality of life for breast cancer survivors, said patients often resist exercising because of how tired
they get during chemotherapy and radiation treatments.

"But I am trying to get patients to do something very moderate," she said. "We want to help them establish the habit and keep them going."

For people whose daily accomplishment is, say, a struggling, draining trip to the shower, a 10-minute jaunt around the block may sound impossible.

"People usually say, 'I'm too tired to exercise. How will it make me feel any better?'" said Pinto. But often it does, a message that Pinto said doctors should emphasize before, not after, patients complain about fatigue.

Both Curt and Pinto said a healthy diet, perhaps prepared with a nutritionist, can yield more energy. Relaxation techniques like self-hypnosis can also help. Keeping a fatigue journal, noting when it lifts and when it lingers, can aid patients when arranging a new schedule that boosts their energy. And one is likely needed, because according to a Fatigue Coalition survey, 75% of chemotherapy patients had to drop work responsibilities or limit their working hours.

Some cancer patients suffer fatigue caused by anemia. If tests show a low red cell count, a drug called epoetin-alfa is often prescribed. Approved for cancer-related fatigue in 1993, epoetin-alfa, made by Amgen Inc. of Thousand Oaks, Calif., and marketed by Ortho Biotech, boosts red blood cell production by mimicking a bone marrow growth hormone. (Leukemia patients cannot take the drug.)

Though research is limited, patients appear to fare better when they try these interventions. "The real surprise [about the Fatigue Coalition survey] was that when doctors actually did suggest something, the patients pretty uniformly found it useful and effective," said Curt.

It's important for nurses and doctors to tailor their suggestions to the needs of each patient, said Pinto. Type and stage of cancer, as well as patients' dispositions and abilities, need to be accounted for. And then it's up to patients to find what works best.

Two years ago when a group of leading doctors, nurses, and patient advocates formed the Fatigue Coalition, cancer-related fatigue garnered little attention. But through the work of the coalition and others, notably Scherr's NCCS and the Oncology Nursing Society, Pittsburgh, the issue has jumped into oncologists' meetings and newspaper headlines.

One reason for the boost in publicity is Ortho Biotech's fatigue simulator, which has virtually fatigued 1,100 people since its debut earlier this year at an American Society of Clinical Oncology meeting. In September, five of the simulators arrived in Washington

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**Stat Bite**

**Fatigue in Patients Receiving Chemotherapy**

Fatigue following chemotherapy has an impact on patients' physical and emotional health and economic well-being. A recent survey in the United States showed that 76% of cancer patients undergoing chemotherapy consistently experienced fatigue. The most common cause was chemotherapy-induced anemia.

| Chemotherapy patients with fatigue who report: |
|-----------------------------------------------|----------------|
| Miss some days of work every month            | 71%            |
| Stop working altogether                       | 28%            |
| Fatigue is worst side effect                  | 60%            |
| Fatigue lasts at least a week after treatment | 45%            |
| Fatigue lasts 24 weeks after treatment        | 33%            |
| Treated with drugs or transfusions to correct anemia | 9% |

Percent

Note: From a 1998 study of 379 patients with cancer, including leukemia, lymphoma, and cancers of the breast, prostate, lung, and skin.

Source: Fatigue Coalition, from research by Withltn Worldwide. Underwritten by Ortho Biotech, Inc.
In Early Breast Cancer, Who Does NOT Need Chemo? The Hunt for Prognostic Markers

Recent large trials in early breast cancer all seem to lean in the same direction: towards chemotherapy. Nearly every group of patients has been shown to gain some survival benefit from adjuvant treatment, including those who fall into the traditional “good prognosis” categories. That means even patients who have small, localized tumors that are estrogen-receptor positive may do better, as a group, with chemotherapy.

The latest St. Gallen’s consensus conference, an international meeting on adjuvant therapy in primary breast cancer held every 3 years, confirms that trend (see page 1601). Joanne Zujewski, M.D., and Edison Liu, M.D., both of the National Cancer Institute, point out in their editorial (page 1587) that a major change since the last St. Gallen’s conference is “the recommendation that the majority of patients be considered candidates for chemotherapy.”

Burden of Proof

Does this mean it’s getting easier to make decisions about adjuvant therapy in early breast cancer? A better way to interpret this trend is not that it’s getting easier but that the burden of proof has shifted, according to one clinician, Alan Lyss, M.D., director of the Missouri Baptist Cancer Center in St. Louis, who spoke at last year’s annual meeting of the American Society of Clinical Oncology. “Instead of asking ‘why use chemotherapy?’ ” he said, “we now have to ask ‘why not?’ ”

When not to use chemotherapy is now a matter for individual patients and physicians to thrash out as they weigh survival odds vs. toxicity, using what clues they have about the risk of recurrence, such as tumor size and grade. For tumors less than 1 cm, the decision is often no and for those over 2 cm, it is often yes. For those in between, the decision is less clear-cut, said Nancy Davidson, M.D., of the Johns Hopkins Oncology Center, Baltimore. It depends on subjective factors, such as an individual’s tolerance of risk, as well as the objective data available.

In her own practice, Davidson said in a presentation at this year’s ASCO meeting, she would counsel patients with tumors less than 2 cm to forego chemotherapy only if their S-phase fraction was extremely low — at 1% or 2% — and if their hormone receptors were positive.

But the future, say Davidson, Zujewski, and others, may hold better clues in the shape of biomarkers.

In fact, one of the increasingly important questions in early breast cancer is whether new biomarkers now under study will someday serve as reliable...