# The low-down on low-back surgery

Ralph Waldo Emerson didn't have an M.D., but the 19th-century essayist showed medical acumen when he wrote, "Nature abhors the old, and old age seems the only disease." One common age-related ailment is spinal stenosis, a condition in which the spinal canal narrows, causing tingling, weakness, and/or pain in the lower back. And spinal stenosis is often associated with degenerative spondylolisthesis, the slippage of one lumbar vertebra in front of another. Treatment of patients who have degenerative spondylolisthesis with spinal stenosis has been the subject of much discussion, with no clear long-term evidence for one treatment over another. But recently the DMS-led Spine Patient Outcomes Research Trial (SPORT) released the results of the first long-term study comparing the effectiveness of surgical and nonsurgical approaches to helping such patients.

**Conduit:** The spine forms a conduit for the spinal nerves, which exit through small openings between the vertebrae. Discs, resilient pads with gel-like centers, cushion the vertebrae. And laminae are bony structures on the vertebrae (see **http://www.dartmouth.edu/sport-trial/** for diagrams and more about the seven-year, $21-million SPORT study).

Wear may cause the discs to become thinner and the vertebrae to rub together. Or a disc's soft center may bulge (a condition known as a slipped disc) or rupture (a herniated disc). Or bone growths, called spurs, may form between vertebrae. Any of these may cause narrowing, or stenosis, of the spinal canal, leading to compression or irritation of nearby nerves and sometimes to slippage of the vertebrae as well.

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The standard surgical treatment for stenosis is a laminectomy—the removal of the lamina from the affected vertebra. It may be accompanied by spinal fusion to eliminate motion between the vertebrae. Alternatives to surgery are physical therapy, education, counseling, and/or nonsteroidal anti-inflammatory drugs.

**Pain:** A previous SPORT study showed that after two years, a laminectomy was more effective than nonsurgical treatment at relieving pain and improving function. The latest study, published in the *Journal of Bone and Joint Surgery*, reported that the benefits of surgery were still evident after four years. The study had 607 participants at 13 sites; 395 received a laminectomy, with or without spinal fusion, and 212 had only nonsurgical care. Those who got surgery showed "significantly greater improvement in scores for pain, function, satisfaction, and self-rated progress," the researchers reported.

"The rich data set collected from SPORT patients," says the trial's principal investigator, DMS's Dr. James Weinstein, is generating just the kind of comparative effectiveness research being called for nationally. Still, the decision to opt for surgery should not be made lightly, advises Weinstein, who notes that a spine treatment calculator is also available at **http://www.dartmouth.edu/sport-trial/**. ROGER P. SMITH, PH.D.

MARK WASHBURN

**Lionel Lewis tested the effect of taking a cancer drug with and without breakfast.**

# Eat, drink . . . and be wary of drugs

"Take at least one hour before or one hour after a meal" says the label on the breast-cancer drug lapatinib (which goes by the brand name Tykerb). Sounds simple. But behind that directive lies a complex story. GlaxoSmithKline (GSK), the maker of lapatinib, first noticed the profound effect of food on the drug during preclinical studies in animals, then later in humans before the drug was approved. In a cohort of six patients, for example, they found that taking lapatinib with a low-fat breakfast led to a three-fold increase in total drug exposure compared to fasting. GSK wanted, and needed, to know more about this effect before seeking approval from the Food and Drug Administration. So the company sought out a noted clinical pharmacologist, Dartmouth's Lionel Lewis, M.D.

**Surprising:** Lewis led a study in which 27 patients were given a 1,500-mg dose of lapatinib three times, one week apart. They took the drug three ways, in random order: after an overnight fast, with a low-fat breakfast, and with a high-fat breakfast. The results were "surprising," says Lewis. The low-fat breakfast produced a 2.67-fold average increase in lapatinib's concentration in the body over time compared to fasting. The difference was even greater—4.25-fold—with a high-fat breakfast. Lewis also found tremendous variability from one patient to another when food was involved. "This caused [GSK] a little bit of concern," says Lewis. Hence the instructions on the drug's label.

The fact that diet can affect a drug's concentration in the body is not a new revelation. Physicians have become increasingly aware of the role diet plays in how drugs work, says Lewis. Red wine and some juices, for example, are known to dramatically alter certain drugs' action. Sometimes the mechanism is easy to tease out. Other times, as with lapatinib, it's "very complicated," adds Lewis. In his study, published in the June issue of the *Journal of Clinical Oncology*, he was able to rule out several mechanisms but unable to pinpoint the exact mode of action. Nevertheless, as this study shows, it may not be as important for patients to know how food affects a drug's concentration, as it is to know how dramatically it does so. JENNIFER DURGIN