

OVER THE LIPS AND PAST THE GUMS COULD BE THE NEXT BIG THING IN SURGERY:

No need for general anesthesia // Virtually pain-free // Speedy discharge from the hospital //

No unsightly scars to show you were ever there.

Down the Hatch

■ BY CHARLES SLACK

Generations of American children have drawn their first impressions of surgery trying to save the life of Sam, a patient in the iconic board game Operation. Using metal tweezers, players try to remove body parts (wishbone, butterflies in the stomach) without touching the metal sides of body cavities. Slip up, and Sam's red nose flashes. The game bears little resemblance to real surgery except in one crucial regard—it recognizes that there are serious penalties for setting off the body's alarms.

In an actual patient, of course, the alarm systems are infinitely more sensitive and complex. And now the analogy shifts from a children's board game to a museum guarded by lasers and sophisticated motion detectors. Surgeons targeting organs in the abdominal cavity traverse a delicate, complicated network of nerves, antibodies and chemical messengers designed to recognize and attack all invaders—bacteria, a surgeon's scalpel—with lightning speed. To get past these defenses, surgeons rely on stealth and subterfuge. They make ever-smaller incisions and employ less invasive equipment. In that sense, the entire history of surgery is a quest for the perfect crime.

While the internal organs themselves are relatively free from nerves, getting at them, even with minimally invasive techniques such as laparoscopy, requires cutting through the nerve-laden abdominal wall and parietal peritoneum. That's where most of the pain from abdominal surgery comes from. But what if a surgeon could find another way into the body,

and thus avoid cutting through the abdominal wall at all? Advances in endoscopy already provide close-up views of the entire digestive tract, utilizing probes and cameras not just to diagnose but also to treat a variety of gastrointestinal disorders. What if the next logical step were to approach the heavily guarded bodily museum through the mouth or anus and then sneak into the abdominal cavity, gaining access to internal organs, through an incision in the stomach wall?

To a growing group of proponents, this has become much more than a pipe dream. Already the new procedure has a name—NOTES, for natural orifice transluminal endoscopic surgery—and several American surgeons have been honing their techniques on test animals. Meanwhile, two surgeons in India have reportedly done limited experiments on humans, using a combination of laparoscopic and natural orifice surgery. (A few U.S. researchers have seen a short video of the procedures, but the results haven't been published and few details are known.) Estimates for when human trials will begin in the United States range from two years to five or more.

For natural orifice surgery to succeed, surgeons will have to win over critics, who contend that the new approach offers scant improvement over laparoscopic technology and may not be worth the risks, which include fatal infection. But supporters say the procedure, if perfected, could offer a revolutionary prospect to patients suffering from problems of the gallbladder, appendix, spleen or other organs: abdominal surgery with no pain, no scars and almost no recovery time.



To reach deep within the twisting confines of the digestive tract, surgeons thread flexible tools such as (left to right) an IT knife, Coagrasper, triangle tip knife, hook knife and Hot Claw through their endoscopes to grasp and snip tissue. For natural orifice surgery to succeed on humans, surgeons will need even smaller and more flexible instruments, possibly including voice-activated controls and tiny robots.

16

In an operating room at Brigham and Women's Hospital in Boston, gastroenterologist Christopher Thompson is feeding a black endoscope down the throat of a morbidly obese man. The man had undergone gastric bypass surgery, in which doctors fashion a new, smaller stomach pouch that bypasses part of the small intestine to promote weight loss. Since the first operation, though, the patient has been in considerable pain, and his weight hasn't gone down. Doctors have found a fistula, or small hole, between his new stomach and the old one, and it's Thompson's job to repair it.

Watching his progress on a video screen beside the operating table, Thompson manipulates the endoscope with controls at its base. One knob moves the scope left and right; another makes up and down adjustments. But as Thompson probes the sleeping man's gut for the fistula, he discovers an unexpected

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complication. Scarring has dangerously narrowed the hole created to serve as the new passageway to the man's intestines.

So Thompson must widen one hole even as he closes another. It takes two hours, twice as long as he had expected. The scope slithers up, down and around inside the moist orange cavity of the man's esophagus and gut; on the screen, the movements look like some endless, slightly deranged amusement park ride. Finally, the work is done, and an exhausted Thompson and his assistant exchange high fives. Thompson takes a last admiring look at the inside of his 57-year-old patient's gut, noting, as only a gastroenterologist would, "That's just beautiful, man."

Of Anthony N. Kalloo, chief of the division of gastroenterology and hepatology at Johns Hopkins Hospital, has his way, the stomach or colon will someday no longer be the destination of endoscopic surgery but, rather, an access route,

a portal to the many organs of the abdominal cavity. Kalloo is credited with having originated that concept during the late 1990s. But when he first broached the idea of what would later be called NOTES, many physicians felt it bordered on malpractice. "To any gastroenterologist, making a hole in the stomach is about the worst thing you can do to a patient in terms of complications," Kalloo says. "And here I was saying you should intentionally create a perforation to treat disease processes that seemed to be well managed by laparoscopic surgery."

Undeterred by these concerns, Kalloo forged ahead, and in 2004 he and his Johns Hopkins team published a report in the journal *Gastrointestinal Endoscopy* describing their experiments on pigs. The NOTES concept began to attract adherents at major medical schools around the United States.

But with additional animal studies under way, it has become increasingly clear that existing surgical and endoscopic devices won't be adequate for NOTES procedures on people. "We don't have the appropriate tools yet," says Jeffrey Ponsky, chairman of surgery at Case Western University School of Medicine and

University Hospitals of Cleveland. "We're still working with instruments that were designed for a different purpose."

Among the greatest needs: better ways to close the hole that surgeons must punch through the stomach wall. Conventional stapling and suturing techniques work moderately well, but in those tight, dark, twisting confines, doctors need greater flexibility and maneuverability. In a trial in which Thompson operated on more than 20 pigs, two developed potentially fatal peritonitis when holes failed to seal properly. New suturing systems now being developed may solve that problem.

Operating inside the peritoneal cavity is greatly complicated by the distance between surgeon and subject. "We're working several feet away from our hands," Ponsky says. "That's triple or quadruple the distance of laparoscopic surgery, and here we're performing very complex, intricate maneuvers." To succeed, surgeons need what they call a better "platform" of

PHOTOGRAPH BY JOHN OFFENBACH



Quest for the Perfect Crime //

Surgeons targeting organs in the abdominal cavity rely on stealth and subterfuge to sneak past the body's complicated network designed to recognize and attack all invaders. First using endoscopes, then laparoscopes (and maybe someday the new instruments of natural orifice surgery), they make ever smaller incisions and employ less invasive equipment— inching toward surgery's age-old goal to leave no trace at all.

Endoscopy

In 1853 the French surgeon Antoine Jean Desormeaux used a "Lichtleiter" to look inside patients. The device used lenses and mirrors and was lit by a turpentine-and-alcohol-burning lamp outside the body. In the early 1900s, lightbulbs allowed physicians to insert the light source into a patient, through the mouth or anus. The introduction of fiber optics (which transmit light and pictures around curves) in the 1950s and '60s made it possible for surgeons to peer deep inside the stomach and intestines.

Today, sophisticated probes, cameras and monitors enable physicians to diagnose and treat such gastrointestinal problems as tumors and bowel disease. Still, most endoscopy is confined to the digestive tract.

Laparoscopy

In the early twentieth century, physicians began using small scopes to diagnose liver disease and other ailments. But it was not until the 1980s that minimally invasive laparoscopic surgery made its great advance, when surgeons began inserting instruments (including digital cameras that produced clear, real-time images) through small incisions in the abdominal wall. Laparoscopic gallbladder removal, first performed in 1987, is now routine.

Because incisions are small, laparoscopy patients experience significantly less pain than they would with open abdominal surgery. Hospital stays have dropped from several nights to overnight for many procedures, and recovery is swift.

Natural Orifice Surgery

During the late 1990s, Anthony N. Kalloo of Johns Hopkins came up with the idea of inserting an endoscope through the mouth or anus and cutting a hole in the stomach or colon to reach other organs that required surgery. Initial trials on pigs show successful recovery from surgery performed on gallbladders, ovaries and other organs. But the tests also highlight the need for further advances such as better tools and improved methods for closing the stomach hole.

If human trials (beginning in two to five years) succeed, NOTES could be used for many procedures now done laparoscopically. Benefits for patients may include no external scarring, less pain and faster recovery than with current techniques.

tools—meaning the ability to perform multiple tasks at once, such as holding organs securely apart while they cut or stitch. Possible solutions lie in more precise scissors and knives, better grasping forceps and perhaps even voice-activated controls and small robots. “A robot could duplicate human hand motion at a distance through a very tiny incision,” Ponsky suggests.

Yet another challenge involves spatial orientation. Because of the stomach’s configuration, feeding instruments down the esophagus and through the stomach may require a 180-degree turn to reach the upper part of the abdominal cavity. That reverses the images surgeons see, essentially requiring

Yet Salky has serious reservations about natural orifice surgery. “When you consider the retooling that would have to occur for surgeons to learn how to do this, what kind of advantage would there really be for the patient?” he wonders. “And what kinds of risks would we be subjecting patients to?”

Salky thinks that two major selling points of natural orifice surgery—no visible scars and less post-operative pain—may not even represent much of an advance over the current state of the art. Barring infection, laparoscopic scars are nearly invisible after a year, according to Salky. And in terms of pain reduction, “after a laparoscopic gallbladder removal, most patients just need one or two Percocets and a heating pad,” he says. “That’s about it.” Moreover, he worries about cutting into the stomach or colon. “Now you’ve got an incision in a piece of intestine that is potentially contaminated with bacteria,” says Salky.

The risk of spreading infection into the abdominal cavity is a major concern of NOTES proponents as well. Learning to control that risk is a chief focus of animal studies, they say. Yet they also point out that infection is an issue with any surgery.

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them to work backward. New cameras with automatic correcting technology might provide a head-on view, or multiple cameras could show the work area from several angles. Another solution would be to go through the anus or vagina to gain a straight-ahead shot.

There’s little doubt that the technical issues impeding NOTES will be resolved. But there’s a bigger question. Given the advanced state of laparoscopic surgery today, is a new approach even necessary? Barry Salky, chief of the division of laparoscopic surgery at New York City’s Mount Sinai Medical Center, isn’t sure. “I’m not against new technology,” Salky insists, noting that he was among the first surgeons to convert to doing only laparoscopic surgery, in 1992. “The difference between taking out a gallbladder with open surgery versus laparoscopy is pretty dramatic,” Salky says. “With open surgery, most people were in the hospital five to seven days because you had to cut the muscles of the abdominal wall. Laparoscopic cases are either ambulatory or involve an overnight admission. We’ve cut down length of stay tremendously.”

To Kalloo and Ponsky, many of the objections to natural orifice surgery bear striking resemblance to those presented decades ago against laparoscopy. Gallbladder removals and appendectomies had long ago become routine, and many doctors wondered why anyone would risk a radically new approach. Only in hindsight have the advantages come to be universally recognized. “Laparoscopy is a marvel,” Ponsky says. “Now we have to investigate what kinds of benefits, including unexpected ones, natural orifice surgery may offer.”

David W. Rattner, chief of the division of gastrointestinal general surgery at the Massachusetts General Hospital, has collaborated with Thompson on experiments funded by the Center for the Integration of Medicine and Innovative Technology, a Cambridge-based consortium linking several Harvard-affiliated hospitals, the Massachusetts Institute of Technology and Draper Laboratories. “The dream with natural orifice surgery is that you could have a procedure done and be back at work in a day or two, instead of the one or two weeks it takes after laparoscopic procedures or the month to recover from open surgery,” Rattner says.



The range of natural orifice procedures could be huge, suggest proponents such as Christopher Thompson of Brigham and Women's Hospital in Boston, who has been perfecting his technique on pigs.

To gastroenterologist Christopher J. Gostout of the Mayo Clinic, a chief advantage of natural orifice surgery is that it could reduce the need for general anesthesia, which is required to counteract the pain of open or laparoscopic surgery. Instead, patients could be deeply sedated, placed into a state of drug-induced relaxation that allows for quicker revival than anesthesia. Another possible advantage involves the body's immune system. Open surgery depresses natural defense mechanisms, making the patient more vulnerable to infection and disease. Laparoscopy offered a significant improvement, and NOTES could further reduce stress on the immune system.

The NOTES approach might work particularly well for certain procedures, Gostout explains, including gastrojejunostomies, in which surgeons attach a section of the small intestine directly to the stomach to create a new passageway when a tumor has blocked the existing passage. These surgeries carry a significant post-operative morbidity rate, Gostout says, requiring a lengthy recuperation for pancreatic cancer patients; NOTES could potentially get such patients out of the hospital sooner. NOTES could also be useful for operating on obese patients because it eliminates the need to slice large amounts of fat between the skin and the abdominal cavity.

When 14 surgeons and gastroenterologists met in New York City last July, they all “agreed that trans-luminal endoscopic surgery could offer such benefits to patients as less pain, faster recovery and better cosmesis than current laparoscopic techniques,” according to a white paper released in February. Still, the paper is laced with words of caution. “Bad outcomes by inadequately trained physicians could lead to regulatory intervention preventing development of a technology that would ultimately benefit many patients,” they wrote. Even proponents say that, in the early stages, NOTES procedures will have to be done in conjunction with laparoscopy and under general anesthesia. Moreover, says Rattner, co-chair of the group that wrote the white paper, early NOTES procedures would need to be monitored by institutional review boards.

Even if the procedures prove to be medically viable and offer clinical advantages, adoption may be slow. “Initially, there’s going to be a lot of risk involved and very little reimbursement,” predicts Rattner. “Most gastroenterologists aren’t going to want to have anything to do with this.”

Whether NOTES overcomes such resistance and takes its place as the next laparoscopy—or becomes a medical footnote, one among thousands of bright ideas that never panned out—may not be clear for years. Says Rattner, “For this new kind of surgery, you either have the religion or you don’t—I’ve got it.” He adds, “But I could be wrong.” ■

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1. “ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery,” *Surgical Endoscopy*, February 2006. This white paper by 14 gastroenterologists and surgeons offers a detailed description of the challenges facing NOTES.
2. “Flexible Transgastric Peritoneoscopy: A Novel Approach to Diagnostic and Therapeutic Interventions,” by Anthony N. Kalloo et al., *Gastrointestinal Endoscopy*, July 2004. Groundbreaking study by a NOTES pioneer and his Johns Hopkins team.
3. “Transgastric Surgery Panel.” Panel discussion to be held at the annual meeting of the Society of American Gastrointestinal and Endoscopic Surgeons, Dallas, April 28, moderated by David W. Rattner.