GENERAL GYNECOLOGY

The perils of commercially driven surgical innovation

L. Lewis Wall, MD, DPhil; Douglas Brown, PhD

The practice of gynecological surgery is being reshaped by commercial interests that are promoting the use of trochar-and-mesh surgical kits for the treatment of stress incontinence and pelvic organ prolapse. In this article, we review the recent history of these surgical innovations and discuss the implications of changes in surgical practice that are driven by commercial interests of this kind. We situate this phenomenon within the general "life cycle" of surgical innovation and point out the dangers inherent in the adoption of new procedures without adequate evidence to support their safety and efficacy. We highlight the ethical responsibilities surgeons and their professional organizations have in making sure such innovations are safe and effective before they come into widespread use. Finally, we offer some policy suggestions to ensure that this process has proper oversight.

Key words: ethics, medical devices, prolapse, sling operations, surgical ethics, surgical innovation, surgical mesh

Cite this article as: Wall LL, Brown D. The perils of commercially driven surgical innovation. Am J Obstet Gynecol 2010;202:30.e1-4.

Conflicts of interest are commonplace in all areas of life. From time to time, everyone finds himself or herself forced to choose between potential self-interest or personal advantage and other obligations. Physicians are no exception to this rule. "Physicians have a conflict of interest when their interests or commitments compromise their independent judgment or their loyalty to patients."[1] Surgeons face particularly challenging conflicts of interest, since they determine both who needs surgery and also who performs the operations once that decision is made. As the Irish playwright George Bernard Shaw wrote sardonically in *The Doctor's Dilemma*, "That any sane nation, having observed that you could provide for the supply of bread by giving bakers a pecuniary interest in baking for you, should go on to give a surgeon a pecuniary interest in cutting off your leg, is enough to make one despair of political humanity."[2]

This reality raises important ethical questions for individual surgeons as well as for their professional associations. Are there appropriate indications for surgery? If so, is an operation in the patient's best interest rather than just in the financial interest of the surgeon? Which operation should be performed?

There is a constant tension in the practice of surgery around these issues. For the most part, surgeons handle these tensions well. Unfortunately, there are egregious examples of surgeons who have gone ethically awry when faced with competing interests of this sort. Perhaps the most notable recent example is the cardiothoracic surgeon in California who (in collusion with a local cardiologist who performed coronary angiography on nearly every patient he saw with even minimal complaints of chest pain) conspired to make false diagnoses of coronary artery disease and performed cardiac bypass surgery on hundreds of patients with normal hearts. (It goes without saying that most of these patients "did well" after surgery, having had no coronary pathology in the first place!)[3]

These ethical problems have accelerated recently in gynecologic surgery, as commercial interests that have previously paid little attention to the details of gynecologic operations have become intensely interested in the details of specific surgical procedures. The reason for this reversal has been the development of operation-specific "kits" for surgical use, which provide everything you need to operate (except technical skill and good clinical judgment) right in the box. These kits hold out the promise of quick, easy, standardized operations; higher surgical volumes; and increased profits for both the surgeon and the device manufacturer. What could be better?

This trend toward prepackaged surgical procedures originated with operations for urinary stress incontinence but has now expanded into the related field of surgery for vaginal prolapse. A wide variety of "trochar-and-mesh" kits for repositioning prolapsed female genitalia are now available, with new variations attempting to elbow their way into the medical marketplace almost every month. As long as you have a strong right arm and a long enough spike, you can thread an artificial mesh through almost any cavity in the female pelvis. What remains to be seen is whether or not this trend is good for patients and not just for the balance sheets of medical device manufacturers and the surgeons who use their products. As yet, there have been very few appropriately powered clinical trials with follow-up long enough to judge the outcomes. Nevertheless, it is clear that powerful commercial interests are reshaping the field of pelvic surgery. These surgical procedures are being promoted by groups that stand to benefit directly from their increasing use. As yet, we do not know if these procedures are better than the operations they are re-

From the Departments of Obstetrics and Gynecology and Anthropology, Washington University in St. Louis (Dr Wall) and Barnes-Jewish Hospital Ethics Program (Dr Brown), St. Louis, MO.

Received April 23, 2009; accepted May 14, 2009.

Reprints not available from the authors.

0002-9378/$36.00

doi: 10.1016/j.ajog.2009.05.031

TABLE 1
The 7 stages in the career of a medical or surgical innovation

1. The "promising report" —an interesting observation that prompts further, similar case reports.
2. Professional adoption—widespread use of the procedure by physicians and surgeons.
3. Public acceptance without formal critical evaluation—third-party payers begin to cover the procedure, but it still usually remains without formal critical evaluation.
4. Acceptance as a "standard procedure"—the procedure has now become entrenched. Case series accumulate, but formal critical evaluation still does not exist. Powerful forces—both surgical egos and commercial interests—champion the procedure and discourage criticism.
5. The randomized controlled trial—inquiring minds finally decide to evaluate the procedure in a formal study.
6. Professional denunciation of the procedure—the randomized controlled trial finds the procedure wanting.
7. Erosion of support and discredit—the procedure falls from favor and is replaced, usually with a new procedure at the beginning of its own life cycle, and thus also unevaluated.

Wall. Commercially driven surgical innovation. Am J Obstet Gynecol 2010.

placing and whether or not this trend is in the best long-term interests of the patients who undergo them. We contend that these issues are not being adequately addressed by the community of pelvic surgeons, by their professional organizations, or by the federal government.

The ProteGen Sling: prototype of a continuing problem

The ProteGen pubovaginal sling was 1 of the earliest "kit" operations to make its way onto the market. It was a woven polyester mesh impregnated with pressure-injected bovine collagen that was intended for use in treating women with urinary stress incontinence. The product was implanted underneath the affected woman's urethra through a transvaginal incision using a surgical kit that included the Vesica bone-anchor system for fixing the sling in place with surgical screws that were drilled into the back of the pubic symphysis. The ProteGen sling turned out to be a disastrous marriage of 2 bad ideas[4] and produced catastrophic consequences in many patients who underwent this operation. The product was conceived in haste and rushed to market for financial reasons without adequate premarket clinical trials.

Two investigative journalists who wrote about this fiasco several years later recorded that the manufacturer of the ProteGen Sling (Boston Scientific/Urology) anticipated sales of over 35,000 kits in the first year of use, with an annual sales growth of 80-100% per year over the next 5 years.[5] In 1997, the Food and Drug Administration cleared the ProteGen Sling for marketing as being "substantially equivalent" to other devices already on the market. After receiving permission to introduce the device, Boston Scientific sales representatives aggressively marketed the device and uncritical surgeons adopted it rapidly.

Unlike drugs—which must be shown by clinical trials to be both safe and effective prior to their release—current regulations in the United States do not require medical devices such as the ProteGen Sling to meet this burden of proof.[6] The collagen-injected polyester mesh from which the sling was manufactured had never been used in urological operations or implanted in a human vagina prior to its clearance, release, and marketing. Boston Scientific relied on a 90-day study in rats and the fact that the mesh was already being used for cardiovascular grafting to gain approval from the FDA.[5] The results were disastrous.

The ProteGen Sling turned out to have an extremely high erosion rate within 8 months of implantation. Anecdotes concerning eroded slings, bleeding ulcers, and infections quickly spread among the community of pelvic surgeons who specialized in the treatment of incontinence, and eventually this experience made its way into the peer-reviewed urological literature.[7] Less than 2 years after its introduction, the ProteGen Sling was withdrawn from the market by Boston Scientific in January 1999. The FDA found that the product was associated with a "higher than expected rate of vaginal erosion and dehiscence" and did "not appear to function as intended."[8] Over 23,000 unused (unimplanted) kits were recalled, but patients who had already had a ProteGen Sling implanted were "left to their own devices." At the time of the recall, the ProteGen Sling had not been the subject of a single randomized, controlled clinical trial published in a peer-reviewed journal. The fact that no data on the product's safety and efficacy as a suburethral sling existed prior to its sale and marketing did not deter commercial exuberance. Boston Scientific executive Bill Martin enthusiastically wrote to a colleague in March 1996 that, "We need to continue moving quickly and steadily on this project so we can begin realizing our market potential very soon."[5] However, the financial bonanza that resulted from the ProteGen Sling largely fell to trial lawyers, who have been aggressively pursuing malpractice claims over the device and who continue to solicit cases from the general public over the Internet (eg, www.protegen-vaginal-sling.com).

Seven stages in the life of a medical or surgical innovation

The unfortunate case of the ProteGen Sling was not an anomaly; rather, it was typical of the life cycle of most surgical procedures. In a classic but underappreciated article, J. B. McKinlay described the 7 stages in the career of a medical or surgical innovation as it moves from initial "promising report" to become a "standard procedure," then on to ultimate abandonment once critical data have finally been collected from randomized controlled trials of the procedure's effectiveness (Table 1).[9] Anyone familiar with the history of the surgical treatment of urinary incontinence can recognize this pattern, perhaps most notably in the life history of the multitude of needle-suspension procedures that were commonly performed on women for stress incontinence until they fell out of favor a decade ago.[10] As McKinlay lamented ". . . it is wasteful and perhaps unethical that proper evaluations of in-

novations should be postponed until the penultimate stages in their career. Imagine the potential for harm that could be avoided, and the resources saved, if innovations were routinely evaluated during earlier stages in their careers— certainly well before they become 'standard procedures.'"[9] Nonetheless, this "extraordinarily wasteful" process still continues as "innovation after innovation begins its slow, costly journey through the stages described only to end up—in the overwhelming majority of cases— either discarded or discredited."[9]

As McKinlay correctly noted, the only way to abort this cycle of innovation, premature adoption, and subsequent discredit is through the systematic collection of data. Not only does this carefulness make good economic sense, but, more importantly, it is the only ethically justifiable way to introduce new products and innovative techniques into practice. Sutherland et al put it succinctly when they wrote, "'Good' science is a prerequisite for 'good' ethics."[11]

Modern bioethics requires practitioners to uphold 4 interlocking ethical principles:[12] (1) nonmaleficence, the duty to avoid harm wherever possible; (2) beneficence, the duty to put the best interests of the patient ahead of other considerations, to act as a fiduciary for the patient[13] (3) respect for persons, the duty to take a patient's preferences into consideration and to respect her autonomy with regard to her health care decisions; and (4) justice, the duty to act fairly toward patients. When new types of treatment are begun, when new drugs are introduced, when innovative surgical procedures are taken up by practitioners, or when new medical devices are released—one cannot uphold these fundamental ethical obligations to patients without access to data. The weighing of risks and benefits cannot be undertaken without data on outcomes and complications. The patient's preferences cannot be respected, because she has nothing to guide her aside from a surgeon who also has no data and who may be unduly (perhaps unconsciously) influenced by the potential financial gain of performing the procedure or the prestige of being the first in his or her practice to adopt the "newest thing." Behaving in this way clearly cannot be considered fair. As an anonymous author in *The Lancet* commented over 20 years ago, "The true demarcation between the practice of scientific medicine and the lunatic fringe lies in the quality of evidence available in support of the remedy, rather than the nature of the remedy itself."[14] To be introduced into practice in an ethical manner, surgical innovations should not become widely practiced until there is reliable scientific knowledge to support their use. Stirrat et al correctly called this "a fundamental ethical imperative," not some "optional extra."[15]

History repeats itself: the mentor ObTape

The life-cycle fiasco of the ProteGen Sling is not a unique event. The same process was repeated again within the ensuing decade. Following the success of the trochar-and-mesh operation developed by Ulmsten ("intravaginal slingplasty"),[16] which was marketed as the Tension-Free Vaginal Tape or "TVT" procedure,[17] hordes of imitators rushed to market "equivalent" products by creating new, potentially lucrative variations on the same theme. The Mentor Corporation of Santa Barbara, CA, offered up its ObTape device as part of this process—a nonwoven polypropylene mesh that was threaded underneath the uretha, through the vagina, and out through the obturator foramen as a treatment of stress incontinence. The FDA determined that the ObTape was "substantially equivalent" to the predicate devices in Mentor's application, and it allowed the release of ObTape into the market in July 2003. Sales boomed. Mentor's Women's Health Products division posted fourth-quarter sales figures of $5.6 million in 2004, an increase of 89% over the fourth-quarter of the year before.[18] According to the company, this strong growth in Women's Health Products "was driven by sales of Mentor's ObTape device, an innovative treatment for stress incontinence," which by the time these sales figures were reported had already been used in over 20,000 cases.[18]

Alas, however, the honeymoon was not to last. A cascade of complications soon followed, and the product was withdrawn from the market in 2006.[19-25] As in the case of the ProteGen Sling, the damage was largely done before reports of the complications reached the peer-reviewed medical journals. Once again, a defective product was cleared for sale without clinical proof of its safety and efficacy, and, as a result, it entered the market, where it was pushed relentlessly by commercial interests, doing immeasurable harm to patients. Once again, the beneficiaries of this process were the commercial manufacturers, who foisted the product upon uncritical surgeons, and the trial lawyers, who have come in to clean up the resulting mess (eg, www.obtape.com, www.obtapeinjury.com, etc).

Solving the problem

There are clear differences between what is legal and what is ethical with regard to the use of surgical devices such as the ProteGen Sling, the Mentor ObTape, or the ever-expanding number of trochar-and-mesh kits now being marketed for the surgical treatment of prolapse and urinary incontinence. A regulatory body such as the FDA grants legal permission to introduce a drug or device into the marketplace. This is largely a political decision, with no guarantee that such decisions are based on high-quality evidence of the product's safety and efficacy. Legal permission to market a product is not the same as using that product in an ethical manner. The recent (since withdrawn) ACOG Practice Bulletin no. 79 on pelvic organ prolapse got this distinction exactly right when the committee members stated that, "Given the limited data and frequent changes in marketed products (particularly with regard to type of mesh material itself, which is most closely associated with several of the postoperative risks, especially mesh erosion), the procedures should be considered experimental and patients should consent to surgery with that understanding."[26] What has happened in this country is the development of a disjunction between legal permission to sell a product and the prudent, ethical use of those products by surgeons. We are operating under a rule of caveat emptor: "Let the buyer beware," rather than the

kind of careful scientific scrutiny that the public health demands. The evidence for problems with these trochar-and-mesh procedures has now become so compelling that the FDA issued a public health notification in October 2008 on "Serious complications associated with transvaginal placement of surgical mesh in repair of pelvic organ prolapse and stress urinary incontinence" (http://www.fda.gov/cdrh/safety/102008-surgicalmesh.html). Caveat emptor, indeed.

Vaginal mesh products for prolapse and incontinence—or any other new medical or surgical devices—should not be cleared for release or endorsed by professional organizations until there is clear evidence of their safety and efficacy on the basis of properly designed, properly powered clinical trials.[27] Rather than endorsing a policy that favors commercial interests, we should protect patients by pushing for more stringent regulatory control of the medical device industry. Before new devices are released, manufacturers should be required to prove that they are efficacious in treating the conditions for which they are promoted in randomized, controlled clinical trials. After initial permission to market such products is granted on the basis of this preliminary efficacy data, their safety should be monitored by requiring that all patients in whom such devices have been implanted are tracked in a mandatory product registry until the safety of the device has been finally ascertained. Industry should bear the costs of this process.[28] We must remember Santayana's famous admonition that, "Those who cannot remember the past are condemned to repeat it."[29] It is time to break the cycle. Our patients deserve better. ■

REFERENCES

1. Rodwin MJ. Medicine, money, and morals: physicians' conflicts of interest. New York: Oxford University Press; 1993:9.

2. Shaw GB. Preface on doctors. The doctor's dilemma. New York: Penguin Books; 1946: 9-88.

3. Klaidman S. Coronary: a true story of medicine gone awry. New York: Scribner; 2007.

4. Glowacki CA, Wall LL. Bone anchors in urogynecology. Clin Obstet Gynecol 2000:43: 659-69.

5. Nygaard I. What does "FDA approved" mean for medical devices? Obstet Gynecol 2007; 111:4-6.

6. Cohen R, Orr JS. A surefire profit-maker could cost its maker dearly. NJ Star-Ledger, August 11, 2002.

7. Kobashi KC, Dmochowski R, Mee SL, et al. Erosion of woven polyester pubovaginal sling. J Urology 1999;162:2070-2.

8. FDA enforcement report. Recall notice of microvasive urology products ProteGen collagen impregnated sling and Vesica sling kits with ProteGen. March 17, 1999.

9. McKinlay JB. From 'promising report' to 'standard procedure': seven stages in the career of a medical innovation. Milbank Memorial Fund Quarterly–Health and Society 1981;59: 374-411.

10. Bodell DM, Leach GE. Needle suspension procedures for female incontinence. Urol Clin NA 2002;29:575-84.

11. Sutherland HJ, Meslin EM, Da Cunha R, Till JE. Judging clinical research questions: what criteria are used? Soc Sci Med 1993; 37:1427-30.

12. Beauchamp TL, Childress JF. Fundamentals of biomedical ethics, 5th ed. New York: Oxford University Press; 2001.

13. Chervenak FA, McCullough LB. The moral foundation of medical leadership: the professional virtues of the physician as fiduciary of the patient. Am J Obstet Gynecol 2001;184:875-9.

14. Anonymous. The epistemology of surgery. Lancet 1986;1:656-7.

15. Stirratt GM, Farrow SC, Farndon JF, Dwyer N. The challenge of evaluating surgical procedures. Ann Royal Coll Surg Engl 1992;74:80-4.

16. Ulmsten U, Petros P. Intravaginal slingplasty (IVS): an ambulatory surgical procedure for treatment of female urinary incontinence. Scand J Urol Nephrol 1995;29:75-82.

17. Ulmsten U, Johson P, Rezapour M. A three-year follow up of tension-free vaginal tape for surgical treatment of female stress urinary incontinence. BJOG 1999;106:345-50.

18. Mentor Corporation. Mentor reports record sales for the fourth quarter and year. Press release dated May 18, 2004. Available at: http://ir.mentorcorp.com/phoenix.zhtml?c=76343&p=irol-newsArticle&ID=614762&highlight=. Accessed March 5, 2009.

19. Domingo S, Alama P, Ruiz N, Perales A, Pellicer A. Diagnosis, management and prognosis of vaginal erosion after transobturator suburethral tape procedure using a nonwoven thermally bonded polypropylene mesh. J Urol 2005;173:1627-30.

20. Siegel AL. Vaginal mesh extrusion associated with use of Mentor transobturator sling. Urology 2005;66:995-9.

21. Babalola EO, Famuyide AO, McGuire LJ, Gebhart JB, Klingele CJ. Vaginal erosion, sinus formation, and ischiorectal abscess following transobturator tape: ObTape implantation. Int Urogynecol J 2006;17:418-21.

22. Abdel-Fattah M, Sivanesan K, Ramsay I, Pringle S, Bjornsson S. How common are tape erosions? A comparison of two versions of the transobturator tension-free vaginal tape procedure. BJU Inter 2006;98:594-8.

23. Robert M, Murphy M, Birch C, Swaby C, Ross S. Five cases of tape erosion after transobturator surgery for urinary incontinence. Obstet Gynecol 2006;107:472-4.

24. Yamada BS, Govier FE, Stefanovic KB, Kobashi KC. High rate of vaginal erosions associated with Mentor ObTape™. J Urol 2006;176: 651-4.

25. Geoffrion R, Murphy M, Mainprize M, Ross S. Closing the chapter on Obtape: a case report of delayed thigh abscess and a literature review. J Obstet Gynecol Can 2008;30:143-7.

26. American College of Obstetricians and Gynecology. ACOG practice bulletin no. 79. Pelvic organ prolapse. Washington, DC: ACOG; February 2007.

27. Strasberg SM, Ludbrook PA. Who oversees innovative practice? Is there a structure that meets the monitoring needs of new techniques? J Am Coll Surg 2003;196:938-48.

28. Wall LL, Brown D. Commercial pressures and professional ethics: troubling revisions to the recent ACOG practice bulletins on surgery for pelvic organ prolapse. Int Urogynecol J In press. doi: 10.1007/s00192-009-0864-3.

29. Santayana G. The life of reason, volume I: reason in common sense. New York: Scribner; 1905:284.