

abdominal, 23 percent total vaginal, 10 percent total laparoscopic, and 2 percent subtotal abdominal or laparoscopic.<sup>11</sup> It is not clear whether all types of hysterectomy result in similar outcomes.

Subtotal abdominal hysterectomy has increased in popularity in recent years. It is thought that conservation of the cervix minimizes neurologic and anatomical disruption and that it therefore also helps to minimize potential adverse effects on bladder, bowel, and sexual function. In addition, it is theorized that subtotal abdominal hysterectomy decreases the incidence of posthysterectomy prolapse of the vaginal vault by preserving connective-tissue support of the upper vagina. This procedure is now widely used in Europe and in parts of the United States, although few data are available to support its efficacy.

In this issue of the *Journal*, Thakar et al. report results of the largest and most comprehensive randomized trial to date comparing the effects of total and subtotal abdominal hysterectomy.<sup>12</sup> One year after surgery, no significant differences were found between the two treatment groups with respect to bladder, bowel, or sexual function. These results, together with the 6.8 percent incidence of cyclical vaginal bleeding after subtotal hysterectomy, suggest that subtotal abdominal hysterectomy confers no advantage over total abdominal hysterectomy. This study, however, does not address the issue of posthysterectomy vaginal-vault prolapse. Since prolapse may occur years after hysterectomy, long-term follow-up is needed to assess whether cervical preservation results in better support of the vaginal vault.

An important finding of the study by Thakar and colleagues is that urinary function improved in both groups after hysterectomy, in terms of the measured decreases in urinary stress incontinence, urgency, frequency, and nocturia. These results suggest that the conditions that may lead to hysterectomy adversely affect lower urinary tract function. The study also provides evidence that hysterectomy, whether total or subtotal, does not cause deterioration in sexual function.

Hysterectomy has been a mainstay of gynecologic therapy for 100 years. It continues to be performed frequently because it is tremendously effective for the treatment of abnormal uterine bleeding and pelvic pain. The report by Thakar et al. provides solid evidence that hysterectomy performed with the use of either technique has a beneficial effect on lower urinary tract symptoms. Hysterectomy will probably continue to be common until other treatments are developed that provide similar results.

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## INSTITUTIONS, CONTRACTS, AND ACADEMIC FREEDOM

CLINICAL research in the United States is commonly performed under contracts between institutions and commercial sponsors. Often the investigator who actually does the research is not a direct party to the contract, but its language will govern the investigator's behavior with respect to the performance of the research. No matter how altruistic the motive, investigators must recognize that research performed under these contracts is a business transaction. It is imperative that the terms of such contracts guarantee the safety and confidentiality of patients while preserving the academic independence of participating investigators.

This issue of the *Journal* contains several articles about the academic-industrial interface and academic freedom. One of these is a Sounding Board article that revisits the case of Nancy Olivieri, a Canadian hematologist who entered into a research contract with a drug company and was later sued for breach of contract when she tried to publish findings that could have been construed as damaging to the company.<sup>1</sup> This is a complex and controversial case, in-

volving accusations and counteraccusations by all parties, including Olivieri's research collaborators, the sponsoring company, and the institution where the work was performed. It will probably never be resolved to everyone's satisfaction.

Indeed, on the basis of the evidence published to date, we cannot be sure whether, in the end, Olivieri's concern about the safety and efficacy of the drug she was studying will be validated. But the eventual outcome of this ongoing scientific debate is not the reason to revisit the case; rather, it is to reiterate the importance of good contracting in research. In their article, Nathan and Weatherall<sup>1</sup> advocate the formation of a national appeals panel to resolve conflicts between investigators and sponsors. This is a reasonable idea if there are disputes about the meaning of language in a contract, but it would be far preferable if standard language to protect the rights of patients and researchers could be adopted, thus minimizing the need for such appeals.

Research performed under a contract that gives the investigators full access to the data and the right to publish their findings, without interference from the sponsor, lets the peer-review system and the scientific process of replication eventually get to the truth. Had Olivieri's research been performed under such a contract, it is likely that the entire crisis could have been averted. Particular problems can arise when the contracting party — the institution — is both in a position to profit from the sale of the drug or device under study and the employer of the scientist doing the work. In such a case, there is even greater need for ironclad contractual protection for the investigator.

Are academic centers effectively negotiating such contracts? In this issue of the *Journal*, Schulman et al. report the results of a national survey of research contracting officers at academic medical centers.<sup>2</sup> This survey paints a bleak picture of the state of academic-industrial contracting. According to the results, very few centers included standard language in their contracts that guaranteed the investigators at a given center access to the primary data from the entire study. Without such a guarantee, the entities sponsoring the research can effectively implement a "divide and conquer" strategy that allows each group of investigators access to their own data, but makes analysis of all the data in a multicenter trial a virtual impossibility. The one encouraging piece of news is that nearly all centers incorporated into their contracts language that gives investigators the right to submit data from their own center for publication.

The study by Schulman et al. is imperfect. Contracting officers were surveyed retrospectively and thus the results are subject to recall bias; investigators (who may be more aware of the terms of their contracts than contracting officers) were not surveyed; and many of

the questions focused on issues more applicable to the collective outcome of the research than to the work performed at a given center. Nevertheless, the study gives us an important first look at this issue, and it seems unlikely that better methods will vitiate its core findings.

This past summer the Pharmaceutical Research and Manufacturers of America, an association of major drug manufacturers, promulgated voluntary guidelines for the performance of clinical research.<sup>3</sup> These are an important step in the right direction, but the system would be better served if there were universally accepted contractual language that protected patients' confidentiality and any proprietary aspects of the data, while ensuring that academic investigators participating in clinical trials have full and unfettered access to the data. If universally adopted, such language would help safeguard the integrity of the research process.

Contracting for research is only one of many difficult issues at the academic-industrial interface. Other problems, such as the academic status of the investigator-entrepreneur and the testing of treatments by their inventors, need to be addressed and resolved in a way that preserves the academic freedom of the investigator, protects the integrity of the research process, and fosters the scientific and intellectual collaborations that will bring new biologic findings to the bedside. In another Sounding Board article in this issue of the *Journal*, Moses and colleagues point out that there are achievable solutions to these and other problems, but that we must have the will to implement them.<sup>4</sup>

As new ideas are brought from the bench to the bedside, there will be more translational clinical research. There will be unexpected toxic effects and poor results with treatment strategies that initially seem promising. It is not a failure of the research system when such unexpected events occur. Rather, it is a failure of the system when a summons to court or the threat of being fired silences the voice of an investigator.

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