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December 23, 1999

David Feigal, M.D.
Director CDRH
HFZ-001
Food and Drug Administration
3200 Corporate Boulevard
Rockville, Maryland 20850

Re: Docket No. 99N-4491

Dear Dr. Feigal:

I am writing this letter in response to "The FDA's proposed strategy on reuse of single use devices", 64 Fed. Reg. 59782 (November 3, 1999).

I have had the opportunity to review the literature in this field while preparing an invited editorial for **PACE**, the official journal of the North American Society of Pacing and Electrophysiology. Although there is no consensus at the present time for catheter reuse, there is a great deal of confusion promulgated by multiple different guidelines and regulations at a local, regional, state and national levels. Unfortunately, cardiac electrophysiologists as a group have failed to perform the necessary prospective studies to document the safety and reliability of catheter reuse.

I continue to strongly urge NASPE to design, organize and perform prospective studies that document the reliability and safety of catheter reuse before it is considered acceptable policy by the FDA and practicing physicians. More scientific study is required on the safety of the cleaning and resterilization process before it becomes adapted by physicians. There are few studies examining in a detailed fashion testing of catheter function, catheter reliability and catheter performance during electrophysiolgy studies and ablation following catheter reuse. Importantly, serious issues regarding the transmission of infectious diseases by catheter reuse are equally important and my be more difficult to assess. In addition, multiple ethical and legal questions remain regarding catheter reuse. These can not be thoroughly discussed in this short letter.

The FDA has been entrusted to protect the safety of patients. Catheter reuse can only be condoned by the Federal government when all parties (e.g., manufacturers, patients, physicians and regulators) are convinced that patient safety concerns are satisfied. I believe that until these questions can be definitively answered, there should be one policy encouraged by the FDA. This policy should be the

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prohibition of catheter reuse until these scientific questions are answered. Then, each individual physician can make a decision taking into account the scientific merits of catheter reuse, along with a cognizance of the ethical, legal and economic considerations of their own specific situations.

I encourage the FDA to carefully review our summary on catheter reuse found in our editorial published in PACE in December 1998.

Sincerely,

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GUEST EDITORIAL

Catheter Reuse: Boon or Boondoggle?

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In this issue of PACE, Blomstrom-Lundqvist reports on the reuse of radiofrequency ablation (RFA) catheters.[1] This article is a welcome addition to an important and little studied area of clinical practice in cardiac electrophysiology. Reuse of electrophysiology catheters has been widely practiced because these catheters, without a lumen, have been amenable to cleaning and sterilization and proven resilient with reuse. The reuse of electrophysiology catheters is one part of the controversial field of medical device reuse.

The frequency of catheter reuse in cardiac electrophysiology is not known but appears to be relatively common. A survey of 12 major medical centers in the United States by O'Donoghue and Platia[2] in 1988 found that 9 of 12 centers reused diagnostic electrophysiology catheters. It is our impression that in the 1990s, with increasing cost constraints, many more laboratories in the USA have considered reuse. Catheter reuse may be even more common in other countries where health care is delivered via a nationalized health care system with fixed budgets for medical devices.[3] There is no consensus at international, national, or state levels with regard to catheter reuse, but various agencies have produced guidelines and regulations concerning reuse, especially in countries outside the USA. In the USA, the Food and Drug Administration (FDA) policy on medical device reuse states, "... the institution or practitioner who reuses a disposable medical device should be able to demonstrate: (1) that the device can be adequately cleaned and sterilized; (2) that the physical characteristics or quality of the device will not be adversely affected; and (3) that the device remains safe and effective for its intended use."[4] Therefore, cardiac electrophysiologists must address these issues of catheter reuse at their institution. If reuse is practiced or contemplated, physicians should consider the cost effectiveness, efficacy, and safety of resterilization, catheter functional integrity, ethics, patient consent, billing and legal responsibility, and ensure that applicable local and national guidelines are being followed.

Cost Effectiveness

The primary motive for catheter reuse is to reduce costs, and in the current health care climate this is a very powerful one. Questions relate to how much are the actual cost savings, who gains, and who loses? Cost savings appear considerable but may be difficult to accurately calculate. In a typical electrophysiology study 2–4 diagnostic catheters are used. If an RFA procedure is performed, then at least one ablation catheter is also used. The cost of these catheters varies, with ablation catheters costing approximately five times that of diagnostic catheters. Other special purpose catheters such as "halo" catheters may cost up to $1,000 each. Indeed, the cost and frequency of electrophysiology procedures is predicted to increase when RFA for atrial fibrillation becomes a clinically practical procedure. Simple calculations of catheter reuse overestimate savings. For instance in a laboratory with 200 diagnostic electrophysiology studies per annum, averaging three diagnostic catheters per case at $120 per catheter, the cost for single use would be $72,000 versus $14,400 for the prorated cost of catheters reused five times. However, to this prorated cost must be added the cost of cleaning, packaging, sterilization, and testing of catheters, the staff time and overhead involved in these activities, and the cost to the hospital of maintaining a reuse policy with

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the attendant risk of litigation. These costs are more difficult to quantify, many are "hidden," and no study has adequately addressed these costs with regard to electrophysiology catheters, although it has been attempted with coronary angioplasty.[5] As an alternative to reprocessing of catheters within the hospital, independent companies have emerged that perform resterilization and testing of catheters, assume the legal responsibility for reuse, and "sell" the catheters back to the hospital at a reduced price.

Who gains from the savings associated with catheter reuse? In many countries, cost savings from reuse allows a much larger number of patients to have electrophysiology studies and curative RFA procedures performed within a fixed budget; single use would result in some patients not having these procedures. Cost savings may be passed on to the patient, insurance carrier, and ultimately society as a whole. Catheter reuse may also be performed on a for-profit basis without any immediate benefit to the individual patient or the population being cared for. Clinicians should be aware of the motivation behind reuse at their institutions.

Manufacturers would appear to be the financial losers from reuse. The various manufacturers of electrophysiology catheters do not support catheter reuse, and they label the packaging and/or the actual device as single use only (however, catheter cables are labeled reusable). Manufacturers argue that catheters are not tested for their ability to undergo resterilization and repeated use. In recent years, in the USA, manufacturers have reduced catheter prices significantly to make reuse less cost effective. This price reduction is welcome and may be partly successful at stemming catheter reuse. The effects of widespread catheter reuse are unpredictable. Manufacturers might increase catheter prices to recoup losses, and thus negate the cost effectiveness of reuse. Catheter manufacturers might test and promote reusable devices. Reduction of expenditure in the area of electrophysiology catheters might also discourage industry investment in research and development in this field.

Adequacy and Safety of Resterilization

Patient safety is paramount, and, therefore, there should be no detectable increase in the risk of infection with reused, as opposed to single use, catheters. The available data on reuse of catheters suggests that there is no increased infection risk using ethylene oxide (EtO) sterilization.[1,2,6,7] O'Donoghue and Platia[2] found an incidence of bacteremia following electrophysiology study of $< 0.05\%$ in 1,245 single use studies and 13,395 reused catheter studies. However, it can be argued that, as infection related to electrophysiology studies is uncommon, insufficient patient numbers have been reported. Until further data is available, current best resterilization practices should be used.

Adequate catheter cleaning is critical. After contact with blood, a biofilm consisting of cells, cell debris, proteins, etc. forms on catheters and may become contaminated with bacteria or viruses. Catheters to be reused must be meticulously cleaned as sterilization may be ineffective if biofilm remains. One of the primary reasons that cardiac electrophysiology catheter reuse is possible is that these catheters are solid catheters without a lumen to which blood is exposed. This lack of a lumen allows for effective, complete cleaning. The problem of cleaning and sterilizing a lumen catheter is one of the problems in reuse of balloon angioplasty catheters.[8] All studies of catheter reuse in a cardiac electrophysiology laboratory include a thorough cleaning process.[1,6,7] This is often performed in the electrophysiology laboratory by the laboratory staff, and is a combination of washing and soaking in detergent with subsequent rinsing off of all detergent. This process needs to be evaluated for adequacy of cleaning, removal of detergent, and staff safety. Catheters are then typically packaged and sent to the local sterile processing department for sterilization.

There are a variety of established sterilization techniques. Because catheters cannot withstand the extreme heat of autoclaving, sterilization has been performed with chemicals, usually EtO. Although there are some problems associated with its use (see below), EtO sterilization is well established, widely available, and prior studies have used this agent.[2,6,7,9] Newer techniques are also available, such as the hydrogen peroxide vapor technique used by Blomstrom-Lundqvist,[1] which may be suitable for catheters without lumens.

Viruses, such as HIV and Hepatitis B and C, are very sensitive to sterilization. Incomplete ster-

ilization could lead to transmission of bacteria or spores, but all sterilization departments should have safeguards and quality assurance tests to prevent such problems. Lipopolysaccharide endotoxins from bacterial cell walls are not destroyed by EtO sterilization, and if catheters become contaminated with endotoxin, then pyrogenic and/or hypotensive episodes could result. Such an occurrence has been described for catheters in a cardiac catheterization laboratory in the past but again modern quality control of sterilization should include testing for pyrogens.[10]

More recently, concern has been raised about the possibility of transmission of Creutzfeldt-Jakob or related prion diseases.[11] Although the prevalence of such diseases is extremely low (estimate 1 per million), the outbreak of Bovine Spongiform Encephalopathy in Britain, with its possible transmission to humans, has greatly increased awareness of these diseases. It has been recognized for some time that these infectious proteins are not destroyed by standard sterilization techniques, and require special autoclaving procedures. This raises the possibility of patient to patient transmission via reuse of medical devices such as catheters. In animals, the infectious capacity of human blood has been demonstrated by intracerebral injections but not by intravascular injections.[11] In 1997, the Canadian Conseil de'Evaluation des Technologies de la Sante evaluated this issue and stated, "... the currently available knowledge indicates that, although there are no known cases of Creutzfeldt-Jakob disease attributable to the reuse of devices contaminated via blood or to the transfusion of blood or blood products, the hypothesis that Creutzfeldt-Jakob disease can be transmitted via these routes cannot be ruled out at this time."[11] Because of this concern, the Conseil, which has studied the issue of device reuse in detail and approved the practice in the past,[12] announced a change in policy and withdrew support for reuse of catheters and pacemakers.[11] We are unaware of any other major regulatory body taking this position, but clearly this issue has affected the Canadian reuse policy.

A further area of concern regarding sterilization is that residual levels of EtO or its chemical derivatives on electrophysiology catheters might be harmful. Our attention was drawn to this by a report from Barnes Hospital, St. Louis, Missouri,[13] which found that at 24–48 hours following resterilization, electrophysiology catheters had residual EtO levels that exceeded 25 parts per million, a limit set by the FDA for residual EtO concentration on implantable devices.[14] High doses of EtO may be toxic.[15] More controversial is the association between low dose EtO exposure and certain carcinomas in humans,[16] although it is a well-recognized mutagen and carcinogen in animals.[17] Therefore, we investigated our own practice and found that at 48 hours after standard resterilization with aeration, the levels of EtO on resterilized catheters were twice the FDA limit.[9] These levels dissipated with shelf time, and were consistently < 25 parts per million by day 14 following resterilization or at day 2 when a 15-hour detoxification process followed sterilization with EtO.[9] Institutions reusing catheters may wish to measure the levels of EtO residuals on their catheters to determine if these results are applicable.

Maintenance of Functional Integrity

For successful reuse, a catheter must clearly be able to perform its recording, pacing, and ablation (if applicable) functions just as well on repeated use as on its initial use, and it should be possible to test for functional integrity before each reuse. Because the design of diagnostic electrophysiology catheters is relatively simple, it is not surprising that studies and clinical experience to date have demonstrated that they do maintain functional integrity with repeated use.[2,6] The protocols described in the literature usually include gross visual inspection of the catheter, and inspection under magnification especially of the junctions between the electrodes and the catheter.[6,7,9] This is important because one report suggests that the most common defect that precludes further reuse is electrode glue separation.[7] Laboratories also used impedance testing of each pole to ensure that there was no break in the electrical integrity of the catheter cables.[1,6,7] Catheters with steering mechanisms such as ablation catheters and some multipolar diagnostic catheters add an additional component (the steering mechanism) that must stand up to repeated use. Failure of delicate deflection mechanisms may be one of the biggest problems limiting ablation catheter reuse. Fortunately, the steering

mechanism can easily be tested by the operator before the catheter is placed in the circulation, and thus satisfactory function ensured before the catheter is reused. Avitall et al.[7] have previously shown for Mansfield-Webster (Watertown, MA, USA) ablation catheters that an average of five uses could be obtained before deflection failures. However, failure rates may vary with different catheter manufacturers. It has been our experience that some newer catheters with a more complex steering mechanism may not withstand reuse or even last with undiminished mechanical properties after a single long ablation case.

Most modern RFA catheters use temperature monitoring to ensure adequate delivery of RF energy. Therefore, if considering reuse of ablation catheters, it is important to know if temperature monitoring remains reliable with repeated use and resterilization. The most important contribution of the report by Blomstrom-Lundqvist[1] is to show that temperature monitoring indeed remains reliable by testing catheters in water baths of varying temperatures prior to reuse. Of the 74 catheters tested during a mean of 7.6 ± 8.0 uses per catheter, inaccurate temperature measurement was the most common reason for catheter failure occurring in 14 (19%).[1] Failure of temperature measurement (and other failures) could occur after only one or after many uses. Indeed, two new catheters did not pass the testing protocol used.[1] If an institution is practicing reuse of RFA catheters, then a similar protocol would be important to demonstrate preservation of accurate temperature recording and identify failures.

Ethics, Consent, Billing, and Legal Issues

The ethics of device reuse concern the responsibilities of the parties involved (physicians, hospital administrators, government and private payers, and manufacturers) to the individual patient and to society. Different philosophical approaches and different economic realities are just two of the factors that will shape these arguments. For instance, a certain low level of risk to the individual from device reuse may be considered acceptable if reuse allows a much larger proportion of the population to benefit from that treatment.[3] Additional questions arise, such as which patients should receive new catheters and which patients reused catheters? In electrophysiology practice, this may be a minor problem, as many patients are likely to receive a mix of reused and new catheters during their study. Further professional and public debate is needed on these matters.

Should the fact that catheters are reused be included in the consent form for electrophysiology study in hospitals where reuse is practiced? If reused catheters are considered equivalent to new catheters in terms of function and safety without any increased risk, then there is no clear need to inform the patient. The reuse of catheters could be considered no different from the reuse of surgical instruments, where it is well understood by the medical profession and the lay public alike that such instruments are routinely reused, undergoing cleaning and sterilization between cases. However, given the issues described in the preceding sections, the difficulty in definitively stating that reuse has no increased risk, and the general level of public concern about issues of infection transmission, we feel that patients should be informed of catheter reuse practices.

In a private payer system, if catheters are reused and the cost of the procedure is significantly reduced, should this cost reduction be passed on to the patient and their insurer? We believe that it should, and that the charge for the procedure should reflect the savings from catheter reuse. We also believe that a hospital that charges patients full price for reused catheters is potentially guilty of fraud.

The legal issues regarding catheter reuse revolve around the fact that because a hospital resterilizes and repackages an item that was originally labeled for single use only, the hospital may become regarded as the manufacturer of this item, and thus become legally responsible for any defects in the item. In the USA, the FDA policy on medical device reuse states, "... since disposable devices are not intended by the manufacturer or distributor for reuse, any institution or practitioner who resterilizes and/or reuses a disposable medical device must bear full responsibility for its safety and effectiveness."[4] This is an onerous responsibility. Some institutions have opted not to consider reuse because of the risk of litigation. However, given the increasing cost constraints of the current health care system, hospital administrators may no longer be able to simply reject the option of catheter reuse.

Conclusions and Recommendations

There are many aspects of the reuse of catheters in electrophysiology about which more data is needed. We urge NASPE to address the practice of catheter reuse in cardiac electrophysiology. A survey of the current frequency of and trends in catheter reuse within the USA and internationally could be an initial step. A large database of electrophysiology laboratories comparing the outcomes of procedures using single use versus multiple use catheters would be useful. Careful cost effectiveness studies and, ideally, a randomized trial of single versus multiple use of catheters are called for. More scientific study is needed on cleaning and resterilization processes, their effectiveness, and minimizing chemical residue. Existing manufacturers or start-up companies should continue to develop reusable catheters.

In the meantime, we believe that any electrophysiology laboratory that reuses diagnostic and/or ablation catheters should have a written policy as part of an overall hospital or institutional policy on reuse and resterilization. The electrophysiology laboratory policy should address cleaning, resterilization, detailed testing of catheter function, staff safety and education, quality assurance, and ongoing review. Ideally, NASPE, in conjunction with the FDA, manufacturers, and other interested parties could design guidelines regarding the procedures to be followed with respect to appropriate cleaning, resterilization, and catheter testing. Uniform recommendations on these issues would largely eliminate the legal issues concerned with catheter reuse.

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