Dear Doctor: This is to alert neurosurgeons to the potential risk of transmitting Jakob-Creutzfeldt disease to surgical patients through possibly contaminated batches of human dura mater transplant material, and to ask that you check your stocks for these batches.

The material in question is an imported, commercially prepared dura mater of human origin, Lyodura, processed by B. Braun Melsungen AG of the Federal Republic of Germany and distributed by Tri Hawk International of Montreal, Canada. The batches of concern were packaged in 1982, and can be identified by a first digit of "2" in their four-digit lot numbers. One of these lots, No. 2105, has been associated with the first identified case of Jakob-Creutzfeldt disease following the use of a human dura mater graft, as reported by the Centers for Disease Control (CDC) in the February 6, 1987, issue of Morbidity and Mortality Weekly Report.

To diminish the risk of transmitting Jakob-Creutzfeldt disease, a rare but lethal disease, we recommend that you dispose of all Lyodura from packages bearing lot numbers beginning with the digit "2," as well as any unmarked pieces of this product that may remain in stock. We are also requesting that you or your staff report to the FDA any other cases of Jakob-Creutzfeldt disease that may be associated with the use of human dura mater grafts.

To report cases, or further information, please contact Gordon C. Johnson, M.D., Center for Devices and Radiological Health, FDA, 8757 Georgia Avenue, Silver Spring, Maryland 20910, or telephone 301-427-7034.

John C. Villfirth
Food and Drug Administration
Rockville, Maryland

References

Editor's Note: Recently the Food and Drug Administration (FDA) issued a safety alert regarding possibly contaminated dura mater. Because of the importance of this announcement and the exchange of letters in this month's Neurosurgical Forum, segments from the FDA letter to physicians are reproduced below.

Percutaneous Discectomy
To the Editor: Drs. Maroon and Onik, in their technical note on percutaneous discectomy (Maroon JC, Onik G: Percutaneous automated discectomy: a new method for lumbar disc removal. J Neurosurg 66:143-146, January, 1987), are quite correct in their premise that surgeons have struggled for 25 years to eliminate the complications of lumbar disc surgery. Fortunately, many of them have succeeded. Unfortunately, much surgery is still being performed without appropriate indications, and this is the major reason for the tremendous cost of hospitalization, compensation, and prolonged disability related to this disease.

As a result of the zeal to find a "less invasive means" of treatment, it is entirely predictable that many patients who previously had inappropriate lumbar disc surgery will be subjected to percutaneous discectomy and then have surgery in addition. Sadly, the same prediction 8 years ago did not prevent the unwarranted excessive use of chemonucleolysis.

Intradiscal therapy has never been adequate for the patient who truly requires surgery, since most of the disc fragment responsible for neural compression is in the spinal canal. Furthermore, such a fragment, whether fully extruded or (more commonly) subligamentous, may lie partially within the disc space but has no direct continuity with residual disc tissue. Having burst mushroom-like through a small opening or marginal tear in the anulus, the fragment is incarcerated, figuratively speaking, at the stem of the mushroom. The most typical operative experience is that, during dissection from the longitudinal ligament and epidural tissues, the intraspinal fragment breaks away with outward traction, and then the opening must be enlarged so as to retrieve the small additional portion and enter the disc space. Such a maneuver from within the disc space is obviously impossible.

The authors correctly point out that there is no satisfactory radiological or imaging technique to demonstrate this pathology. Indeed, four of their first 20 patients subsequently required surgery. While it seems likely that intradiscal removal of the protruding disc demonstrated in their Fig. 2 will produce a satisfactory result, spontaneous recovery from this type of lesion is of course quite common. Such recovery has in fact now been well documented, even with ruptured and extruded discs. An arbitrary time period of 6 weeks fails to satisfy the requirement of adequate nonoperative treatment since many patients improve after 6 weeks, even while they are waiting to be scheduled for surgery.
Drs. Maroon and Onik have incorrectly assumed that open surgery may be more complicated and require prolonged hospitalization. More than half of our patients who require operation for ruptured disc are in the hospital 1 night and the remainder seldom more than 2 nights.

I have commented previously on percutaneous discectomy following publication of Friedman’s paper, but the authors omitted reference to that communication in their bibliography. At a time when there are so many studies and so much effort is being exerted to improve on the embarrassing state of therapy for spinal disorders, and when it finally appears that chemonucleolysis may soon fade into oblivion, Maroon and Onik’s procedure is clearly less effective in cases in which surgical intervention is essential and it may well prove to be more costly. Thus, it has little to recommend it.

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References

RESPONSE: We acknowledge the healthy skepticism reflected in Dr. Fager’s letter. However, we strongly disagree with his conclusions. He fears that “many patients who previously had inappropriate lumbar disc surgery will be subjected to percutaneous discectomy.” However, “inappropriate surgery” or the consequences of inappropriate patient selection was not the subject of our paper. We believe it “inappropriate” to impugn the procedure itself because of postulated poor clinical judgment in patient selection — be it for open surgery, chemonucleolysis, or percutaneous discectomy.

We have no argument with his (and our) recommendation for open surgical removal of extruded lumbar discs. As we stated, percutaneous discectomy “cannot be used in patients with extruded or free fragments of disc in the spinal canal.” Although it is not possible in 100% of cases to be certain of the precise location of herniations (that is, whether they are under or through the posterior longitudinal ligament), in the majority of patients it is now possible to make this determination with magnetic resonance imaging and intrathecal enhanced computerized tomography scans. Admitting that errors can still be made, we believe that percutaneous discectomy is nevertheless a reasonable alternative to surgery in appropriately selected patients.

What constitutes “adequate” conservative therapy is a function of many factors and perhaps is related to “whose cow is getting gored.” The severity of the patient’s pain, his financial and job constraints, and the limitations on his activities are all major considerations. If one can afford not to work, the cost of medication and therapy, and the interdiction of many of life’s enjoyable activities for several months, certainly a small percentage of patients with herniated lumbar discs may improve, as we have all observed. However, most of our patients, who now include many physicians, cannot afford such luxury and believe 6 to 8 weeks of vigorous conservative measures to be an adequate trial period.

Since Dr. Fager’s patients spend 1 or, at the most, 2 nights in the hospital following disc surgery, he states that we “have incorrectly assumed that open surgery may be more complicated and require prolonged hospitalization.” What we have assumed is what Dr. Fager himself wrote and which we also believe to be true: “But all too frequently patients are seen suffering from varying degrees of paralysis, saddle sensory loss, poor sphincter function, and impotence — they testify to the hazards of spine surgery. No longer present to lend testimony are those who have sustained fatal damage to the iliac vessels during lumbar disc operations. Many patients with adhesive arachnoiditis are condemned to a life of pain.”

Perhaps our most significant disagreement with our colleague is philosophical rather than technical. We acknowledge that many new techniques heralded as scientific advances turn out to be ineffective, inappropriate, or even harmful. We truly believe, however, that complete satisfaction with present surgical techniques will never lead to scientific progress. In a few years, on the basis of a longer follow-up period, we ourselves may write that the procedure “has little to recommend it,” but we would remind Dr. Fager of his own initial reluctance to accept the transsphenoidal approach to pituitary tumors over open craniotomy and of his persistent resistance to the anterior approach to herniated midline cervical discs in favor of his posterior cervical technique. We respect Dr. Fager for his healthy skepticism toward acceptance of new techniques, which we also share. However, as William Osler advised, “we should neither be the first to accept changes in medicine nor the last.”

Finally, we concur with Dwight Parkinson’s response to a letter Dr. Fager wrote to the editor of the Journal of Neurosurgery in which he criticized Dr. Parkinson’s report on chemonucleolysis. Parkinson stated that if he had a ruptured non-extruded disc that failed all conservative therapy, he would have chemonucleolysis, and if that failed, he would go to Dr. Fager for surgery. If we had the same problem, we would first have a percutaneous discectomy, and if that failed, we would be on the next flight to Boston!

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Cytodifferentiation in Cerebellar Medulloblastoma


The question of cytodifferentiation in cerebellar medulloblastoma is a formidable one. Indeed, differentiation does exist in this tumor; however, its elucidation has required conducting systematic in vitro studies, in addition to extensive pathological investigations. Accordingly, in this rapidly evolving era of applied tumor biology, such statements as "fused egg" appearance are no longer acceptable as sufficient evidence to define neoplastic differentiation. Even on purely morphological grounds, such reminiscent artificial figures may be encountered in areas of tumor infiltration into the adjoining cerebellar internal granular layer, and also in incomplete (transitional) "follicles" in the desmoplastic medulloblastoma. By the same token, utmost caution should be exercised not to interpret as evidence of glial differentiation such "secondary histoarchitectures" as tumor cells infiltrating white matter fascicles and/or the cerebellar cortex, thus imparting pseudospongiosplastic and "comb" appearances. These and other related caveats have also been reiterated by Schindler and Gullotta, and even though not entirely agreed upon they ought at least to be acknowledged as plausible arguments. The Homer Wright rosettes, which are universally recognized as expressions of neuroblastic differentiation, do not confer (by virtue of their abortive differentiating potential) a crucial importance to the biological behavior of this neoplasm. Furthermore, the presence of rare mature neurons in the tumor cannot be accepted as an a priori indication of neuroblastic differentiation, an issue previously addressed by Professor Zülch. It would be more reasonable to consider these well-differentiated neurons as preexisting entrapped elements that are native to the region, unless there is overt evidence to the contrary. Tumor necrosis, albeit an important pathological parameter, has no direct bearing on the question of cell differentiation. The authors' closing statements in reference to differentiation of the peripheral neuroblastoma draw a poor analogy to the principal issue under discussion; that is, cerebellar medulloblastoma.

The ultimate discrepancy in the conclusions of Caputy, et al., as opposed to those of Packer, et al., may well be a reflection of the overly simplified, yet ill-defined histological criteria used by Rorke in describing primitive neuroectodermal tumors. This "classification" is nowadays viewed with utmost circumspection by authorities on both sides of the Atlantic, because: 1) it offers no conceptual contribution to the fundamental pathobiology of cerebellar medulloblastoma and central nervous system (CNS) embryonal tumors in general; 2) it sets the stage for erroneous and inconsistent interpretations concerning differentiation and, therefore, for the creation of potentially spurious and impaired biostatistical data (particularly during a declining period for in-depth postmortem correlation); and 3) it disregards the diverse taxonomy of embryonal central neuroepithelial tumors, an area presently undergoing intensive scientific exploration.

Thus, unless standardized criteria are to be established for assessing cell differentiation in medulloblastomas and other CNS embryonal neoplasms (and hopefully adopted by the World Health Organization Tumor Registry), it would be utterly hazardous to attempt to advance prognostic extrapolations based on ambiguous and poorly reproducible findings. In the context of cytodifferentiation in medulloblastoma, the only nosologically significant variant thus far is the pure desmoplastic medulloblastoma, as was originally defined by Foerster and Gagel and was subsequently reappraised and brought forward in its prevailing nomenclature by Rubinstein and Northfield. This subtype sui generis warrants distinction from the leptomeningeal desmoplastic reaction induced by contiguous infiltration by the classic medulloblastoma. It is especially surprising that the desmoplastic variant did not deserve attention in a study advocating the prognostic importance of cell differentiation in medulloblastoma.

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