

CASE REPORT

Joseph H. Davis,¹ M.D. and Roger E. Mittleman,² M.D.

In-Vivo Glutaraldehyde Fixation of the Brain Stem and Spinal Cord After Inadvertent Intrathecal Injection

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ABSTRACT: A 64-year-old diabetic man underwent total maxillectomy with orbital exenteration because of recurrent carcinoma. In order to decrease pressure at the surgical site, 50 mL of cerebrospinal fluid were withdrawn. After the procedure was completed, 5% glutaraldehyde was inadvertently injected into the subarachnoid space instead of reinjection of the original cerebrospinal fluid. The patient suffered hypotension and coma culminating in death five days after the procedure. Postmortem examination revealed exquisite fixation of the outer cortical shell of the spinal cord and brain stem. The mishap occurred because an unlabeled vial was mistaken for the withdrawn cerebrospinal fluid. Graicunas' theory and formula on relationship complexities in organizations is exemplified by this occurrence. One may calculate the theoretical potential for 24,708 miscommunications during such a complex and lengthy surgical procedure. Proper operating room procedures must be developed and followed in order to prevent such tragedies.

KEYWORDS: forensic science, glutaraldehyde, surgery, poisoning, fixation (in-vivo), Graicunas Theory, management concepts, miscommunication

A total maxillectomy with orbital exenteration was performed for a recurrent malignancy of the maxillary sinus. After the exenteration, 5% glutaraldehyde was inadvertently injected into the subarachnoid space because of a surgical mishap. This report presents the results of in-vivo fixation of the central nervous system and the events leading up to this tragedy. The theoretical potential for such a mishap is calculated by use of the Graicunas Theory and formula (1).

Case Report

A 64-year-old diabetic man was admitted for treatment of recurrent malignant papillomatosis of the maxillary sinus. The surgical procedure consisted of a total maxillectomy with exenteration of the normal eye. The patient had previously agreed to experimental

laser surgery to the retina and donation of the extracted eye for study. An unlabeled widemouth vial of 5% glutaraldehyde was brought to the operating room by an ophthalmology resident to preserve the donation which would then be processed for pathologic study in a university-affiliated eye institute. This surgical procedure had never been performed at the medical center.

The patient was taken to the operating room where both endotracheal tube and anesthesia were properly administered. Prior to the surgical procedure, the chief surgeon ordered 50 mL of cerebrospinal fluid be withdrawn via a lumbar puncture. The purpose of the fluid withdrawal was to decrease pressure on the dura mater at the surgical site. The lumbar puncture was performed prior to surgery and access to the subarachnoid space was maintained throughout the procedure by tubing running under the patient with access to the nurse anesthetist. The operation proceeded without complication until it was time for the withdrawn cerebrospinal fluid to be reinjected into the spinal canal.

The unlabeled vial (approximately 50 mL volume capacity) with 35 mL of 5% glutaraldehyde had previously been brought to the operating room in a knotted rubber glove by an ophthalmology resident and left inside the doorway of the operating room. The circulating nurse inquired about the contents of the vial, whereupon one of the doctors informed her that it contained the cerebrospinal fluid that was originally removed via lumbar puncture. The doctor instructed the nurse to give the vial to the stand-in nurse anesthetist, who then wrote "CSF" on the label. Upon return from lunch, the original nurse anesthetist was informed that there was another 35 mL of CSF.

When the chief surgeon ordered the "CSF" reinjected into the spinal column, profound hypotension resulted within minutes. The operating room team did not realize their mistake until one hour later when the ophthalmology resident returned to the operating room and inquired about his glutaraldehyde. At that time, the surgeons tried to withdraw as much spinal fluid as possible in order to diminish the effect of the chemical. The patient remained on the ventilator for five days. Despite cessation of respiratory function due to brain stem and spinal cord damage from direct toxicity, the patient's cardiac function was sufficient to last for several days until the development of pneumonia and then death.

The cause of death was then presumably related to the spinal injection of glutaraldehyde, a variable independent of the disease process or expected risk of the surgical procedure. The manner of death was, therefore, considered to be potentially accidental, mandating medical examiner investigation in Florida. Had death

¹ Chief medical examiner (retired), Miami-Dade County Medical Examiner Department, and professor of pathology emeritus, University of Miami School of Medicine, Miami, FL.

² Chief medical examiner, Miami-Dade County Medical Examiner Department, and clinical associate professor of pathology, University of Miami School of Medicine, Miami, FL.

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been a consequence of a reasonable risk, e.g., improperly placed endotracheal tube, or dysrhythmic effects of anesthetic agents, then the manner of death would be considered to have been natural. We encourage physicians to report any operating room mishap to the medical examiner in order to determine proper disposition. In this case, the independent variable was similar to an explosion from anesthetic gases in the operating room. Therefore, the case was accepted by the Miami-Dade County Medical Examiner Department in accordance with Florida Statute 406.

At autopsy, the pathologic features of anoxia were evident in the brain and spinal cord. The centers of the spinal cord, medulla and pons were necrotic. However, there was a thin external rim of well-preserved tissue having a parchment-like gross appearance and microscopic perfect fixation secondary to the inadvertent fixation by glutaraldehyde (Figs. 1–3). In addition, there was focal similar preservation of the cerebellar cortex.

An additional finding at autopsy was metastatic squamous cell carcinoma to the lung from the malignant maxillary sinus tumor. No tumor was found at the site of resection.

Discussion

Glutaraldehyde is a 5-carbon dialdehyde which is utilized as a tanning agent, fixative, anti-microbial and a dermatological treatment modality for warts and various skin disorders. It is also employed in the preparation of grafts and bioprostheses. Because of its ability to crosslink proteins and change the surface characteristics of tissues, glutaraldehyde has been employed as a fixative for electronmicroscopy and cytochemistry since 1960. Workplace

toxicity is a concern since respiratory distress and secondary infections have been reported during airborne exposure in humans. In addition, inflammation of the skin, gingiva and eyes has been reported during medical applications (2). Colitis from contamination by residual glutaraldehyde for disinfection of the colonoscope has also been reported (3).

In the present case, the inadvertent introduction of glutaraldehyde into the cerebral spinal fluid caused spinal shock with cerebral anoxia and resultant swelling. The swollen brain precluded a normal inflammatory response due to vascular compression. Hence, the exposed brain stem, spinal cord and cerebellum were fixed as would happen if they were removed from their bony encasement and placed in a vat of fixative. The interior of the spinal cord and brain stem autolyzed because of compromised circulation and further dilution of the 5% glutaraldehyde by cerebrospinal fluid. Computerized Medline search from 1966 to 1997 (April) failed to produce any reported similar cases of in-vivo fixation with glutaraldehyde or formaldehyde.

The mishap occurred because of failure to create special operating room management procedures for this unique operation. Likewise, numerous personnel requiring two shifts were in the operating room during the 12-h procedure. A total of 13 men and women (chief surgeon, assistant surgeons, anesthesiologists, nurse-anesthetists, nurses and a technician-observer) were present in the operating room at various times.

The cause of death was listed as “anoxic cerebral degeneration due to intrathecal injection of glutaraldehyde following craniofacial resection for recurrent squamous carcinoma of the maxillary sinus.” The manner of death was listed as accident since the injection of glutaraldehyde was well above and beyond a reasonable and foreseeable complication of such an operation. It is important to realize that the pronouncement of the cause and manner of death in such cases requires clinical consultation. The death certifier is certainly not knowledgeable in all aspects of medicine and most certainly the pathologist is almost never an expert in the administration of anesthesia. The pronouncement of “therapeutic misadventure” (implying fault or negligence) is best proven in the courtroom. Accordingly, such phraseology was avoided on the death certificate.

This specific surgical procedure had never been performed in the hospital. None of the participants had ever seen such a procedure except the chief surgeon. Two teams were involved due to the extended time. Until the morning of the operation, team members were not all familiar with each other, nor had tasks been clearly defined and practiced. The supervising anesthesiologist was also supervising anesthetists in other operating rooms. The stage was set for miscommunication.

This tragic event is the direct result of miscommunication within an organization. People tend to be poor communicators. Supervisors cannot directly manage each and every detail of subordinate activity and communication. This case event exemplifies the problems of subordinate-superior relationships and increasing complexities as the number of subordinates increases. This becomes aggravated when one considers the complexities of major surgical procedures, the focus of the chief surgeon upon the techniques of the procedure, the unique nature of this operation within the institution, plus the additional experimental procedures involving the exenterated eye.

In a paper first published in 1933, management consultant V. A. Graicunas developed a mathematical formula based upon the geometric increase in complexities of management as the number of subordinates increases (1). Even if not directly applicable

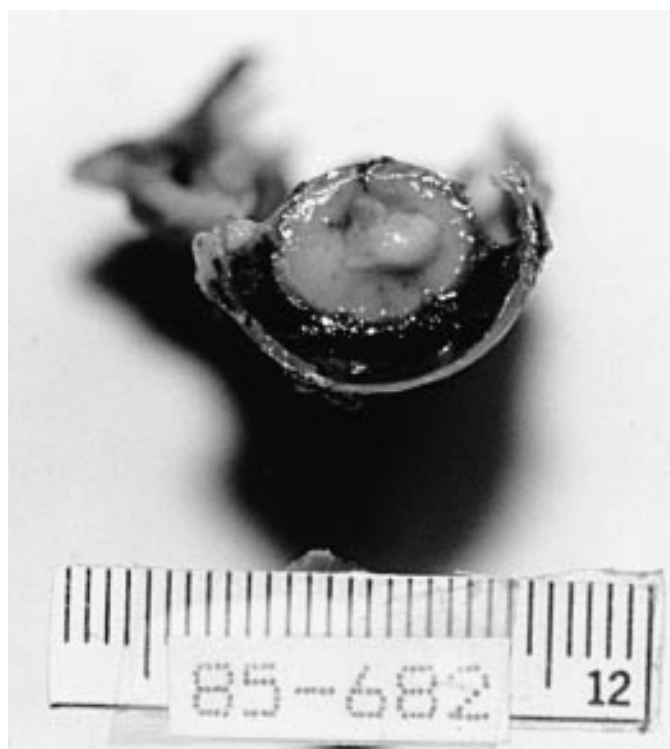


FIG. 1—Transverse section of formalin-fixed spinal cord with glutaraldehyde preserved outer shell and toothpaste-like autolyzed central cord. The dark layer between cord and dura represents fixation effect causing proteinaceous coagulation. Measurement in mm.

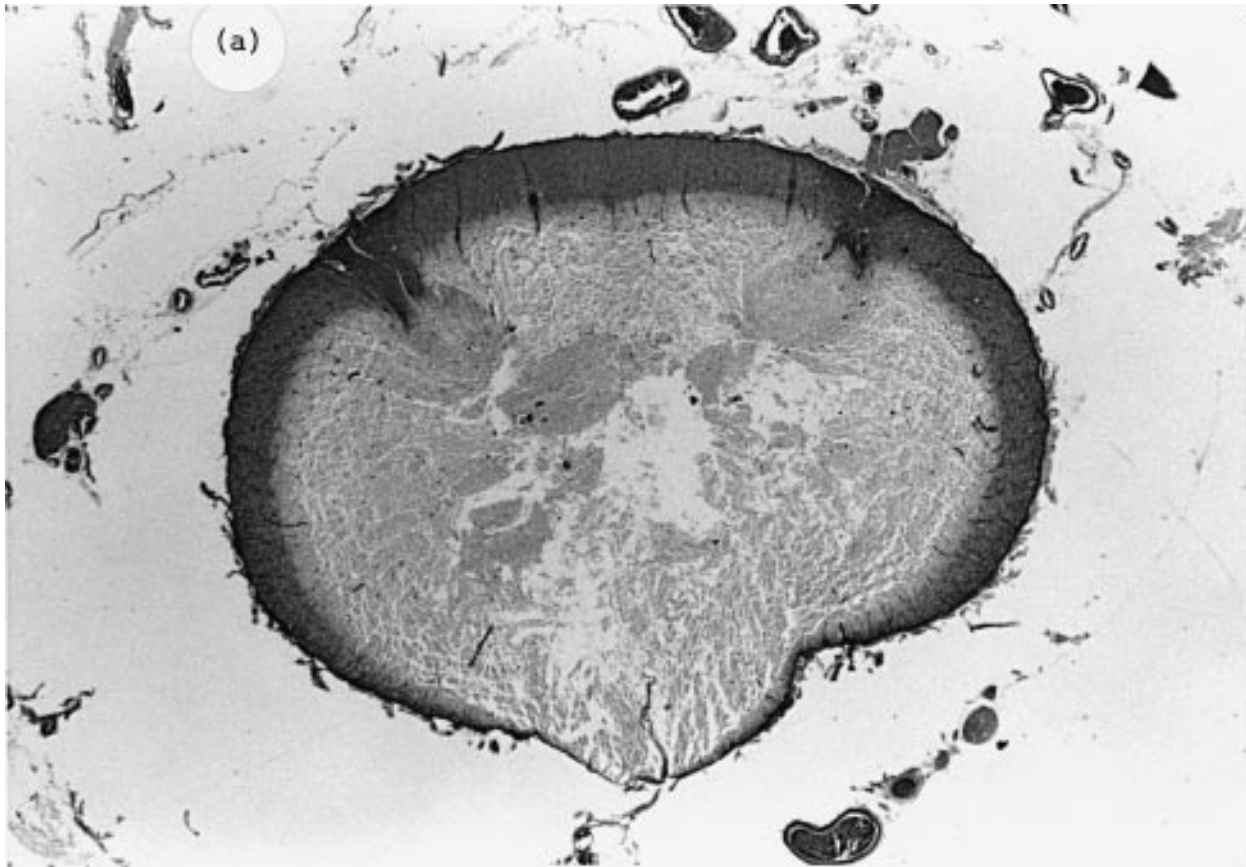


FIG. 2—Transverse sections of spinal cord after in-vivo exposure to glutaraldehyde. The “fixed” outer shell of remaining tissue is in contrast to the autolyzed central cord: (a) bodian, $\times 12.5$; (b) hematoxylin and eosin, $\times 100$).

due to the nature of an operating room and the surgical procedure, the principles apply. Graicunas recognized three types of subordinate-superior relationships: (1) direct single relationships, superior to one subordinate; (2) direct group relationships, superior to a group of subordinates; and (3) cross-relationships between subordinates. He developed a formula to demonstrate the geometric increase of potential communication relationships as the number of subordinates increases

$$\text{Potential relationships} = n \left(\frac{2^n}{2} + n - 1 \right)$$

where n equals the number of subordinates.

In this case we have 14 people in the operating room, the patient plus a chief surgeon and 12 supporting personnel. Accordingly, 12 subordinates create a potential for 24,708 relationships, one or more of which may result in a miscommunication. Complicating the issue was the fact that the stand-in nurse anesthetist labeled the glutaraldehyde as CSF. Perhaps the original nurse anesthetist would have suspected the error.

As a result of this tragedy, new hospital policies were established. These include: (1) visitor controls making it impossible for unapproved personnel to come into the operating room; (2) maintenance of signature logs of personnel entering the operating room; (3) policy of never reinjecting anything but blood; and (4) policy of never permitting an unlabeled bottle into the operating

room. It is obvious that containers of any sort inside an operating room must be properly labeled. However, even when properly labeled, a neurotoxic drug was accidentally administered in another reported case (4). A bottle of vincristine was inadvertently placed with other medications for intrathecal injection during an operation on another patient with carcinoma of the maxillary sinuses. The container was labeled “intravenous/not for intrathecal use”; instead, the label was incorrectly read as “for intrathecal use” and thereby injected intrathecally resulting in paralysis. It is also interesting to note that the practice of reinjecting cerebrospinal fluid is described as part of the operative procedure for craniofacial exenteration (5). The reinjection is to detect any dural defects (e.g., leaks) incurred during surgical repair of the cranial floor during the operative procedure.

In summary, a unique set of surgical circumstances and procedural errors in the operating room permitted inadvertent administration of glutaraldehyde into the spinal subarachnoid space. In-vivo fixation of the outer shell of the brain stem, spinal cord and portions of the cerebellum occurred. Proper operating room procedures would have prevented this tragedy.

Acknowledgment

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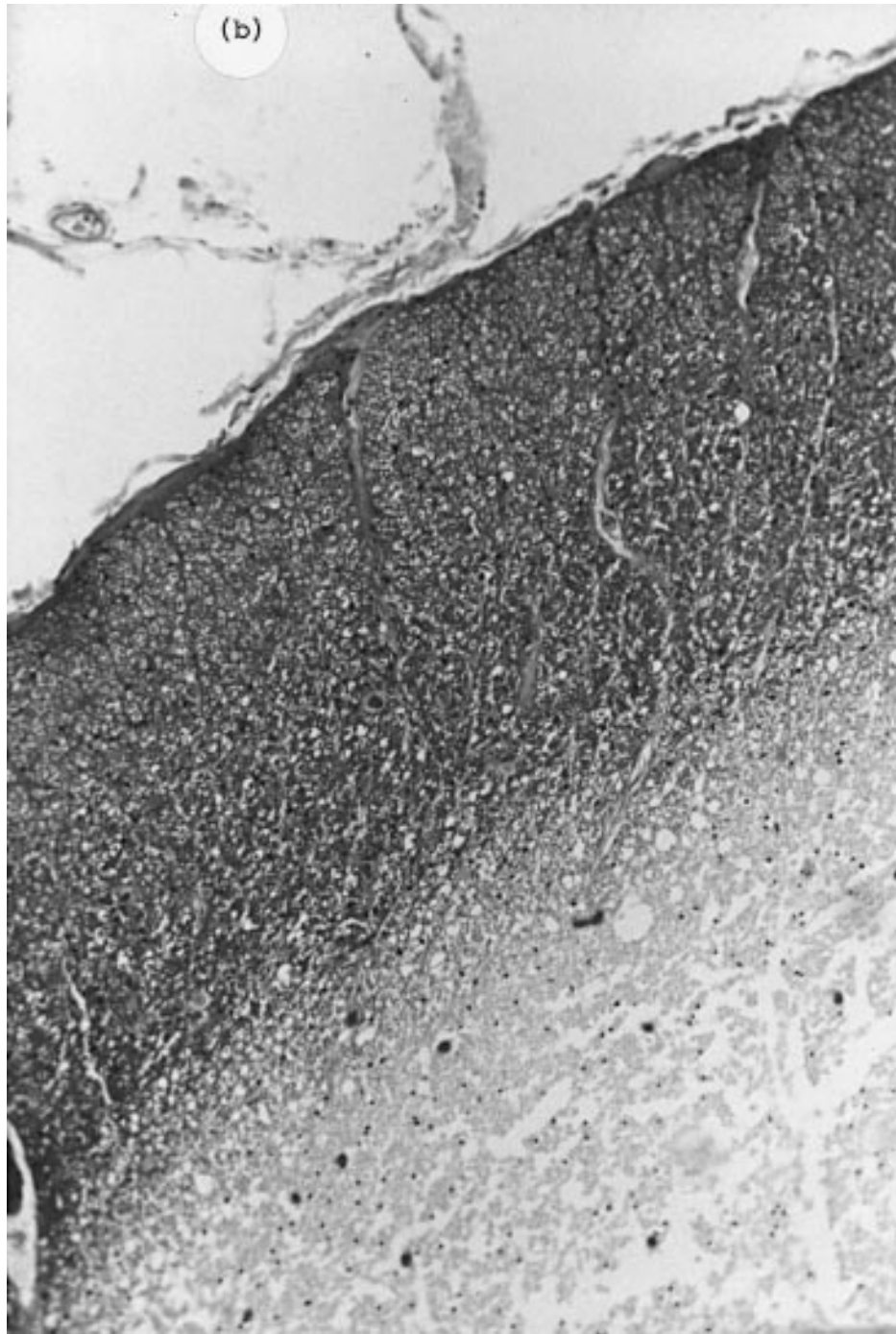


FIG. 2—(Continued)

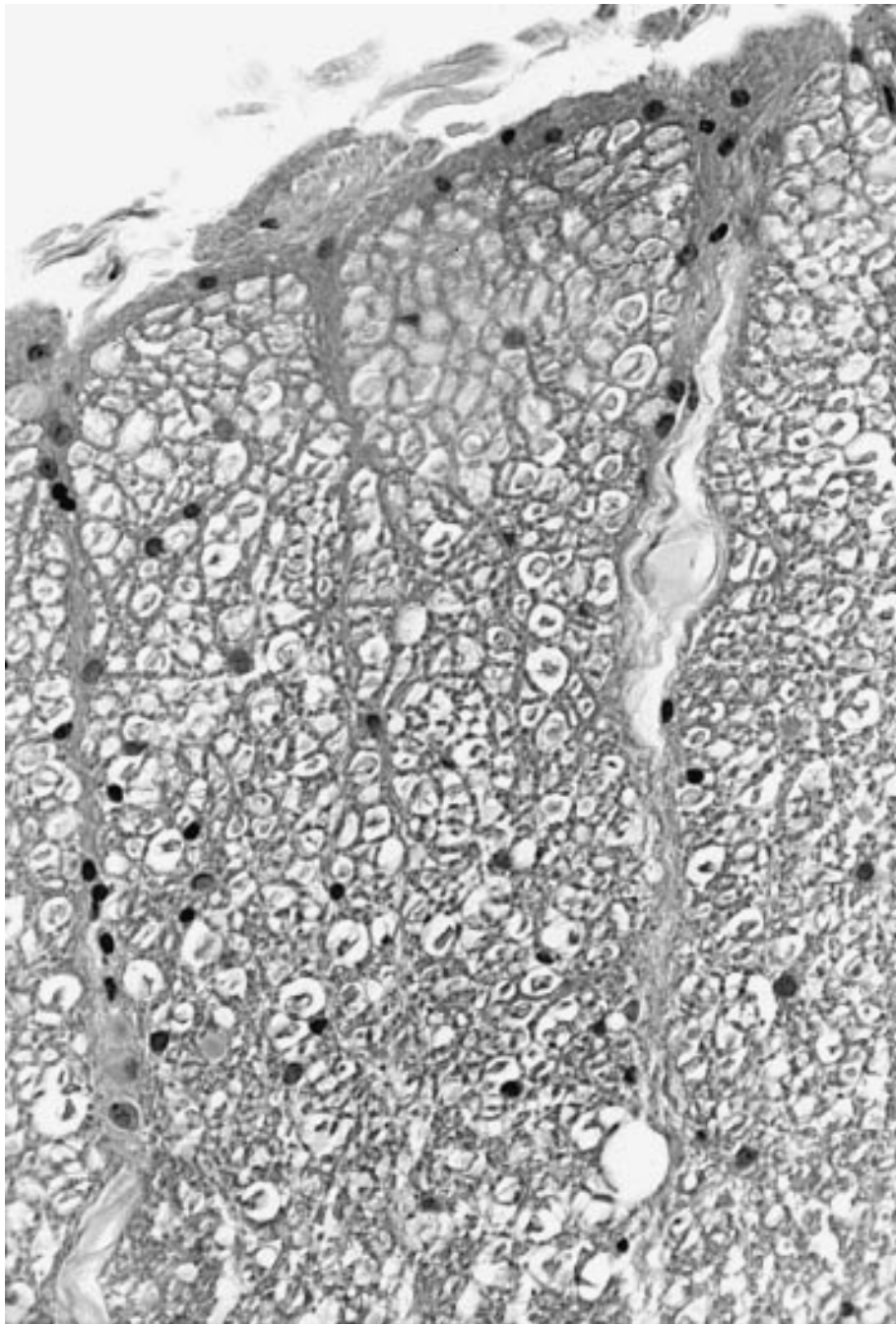


FIG. 3—Outer shell of spinal cord with good axonal preservation after in-vivo glutaraldehyde exposure (hematoxylin and eosin, $\times 400$).

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Additional information and reprint requests:
 Roger E. Mittleman, M.D.
 Chief Medical Examiner
 Miami-Dade County Medical Examiner Department
 Number One on Bob Hope Road
 Miami, FL 33136-1133