1) routine tourniquet use
2) avoidance of insufflation during entry of the joint (may lead to dissection of tissue planes)
3) close monitoring of the ET_{CO_2} tension
4) intraoperative assessment of the thigh for the presence of subcutaneous emphysema

In conclusion, laser arthroscopy of the knee, despite having possible advantages, can result in serious complications. Our cases demonstrate that it is possible for gas to dissect not only from the shoulder joint but also from the knee joint, producing hypercapnia, subcutaneous emphysema, and pneumoperitoneum.

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Epidural Injection of a Phenol-containing Ranitidine Preparation

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As the popularity of a continuous epidural infusion for postoperative analgesia has increased, so too have the reports of accidental administration of unintended drugs into the epidural space. A case is presented here in which a ranitidine preparation (Zantac, Glaxo) was inadvertently infused into the epidural space. Although the patient was unaffected, the potential for neurologic damage certainly is present since the ranitidine hydrochloride solution is prepared with phenol as a preservative.

Case Report

A 36-yr-old woman (weight, 64 kg; height 160 cm; ASA physical status 2) was scheduled for a right dismembered pyeloplasty. Her medical history was remarkable for a 28 pack year smoking history as well as a suspected mitral valve prolapse. Admission laboratory data were within normal limits. Prior to her arrival in the operating room, she received 10 mg diazepam by mouth as well as 30 ml clear antacid (Bicitra).

Prior to induction of general anesthesia, an epidural catheter was inserted at the L3–L4 interspace with an 18-G Touhy-Schliff needle and a loss-of-resistance technique. Proper positioning of the catheter was verified with a test dose of 3 ml 2% lidocaine with 15 μg epinephrine. General anesthesia was induced with thiopental and intubation was facilitated with vecuronium. Anesthesia was maintained with isoflurane, nitrous oxide, and oxygen as well as with sufentanil. The surgery proceeded uneventfully, and 1 h prior to the end of the procedure the patient received 100 μg fentanyl *via* the epidural catheter. At the end of the procedure the trachea was extubated and the patient was taken to the intensive care unit for recovery and observation.

On arrival to the intensive care unit an epidural fentanyl infusion in a concentration of 10 μg/ml was initiated at 60 μg/h *via* an infusion pump. The infusion pump was connected to the epidural catheter with an infusion set tubing with an injection port between the pump and the epidural catheter. The pump was labeled "epidural" and the distal end of the catheter was labeled "epidural catheter". The injection port in the connecting tubing was not marked. The patient was also to receive intravenous ranitidine administered *via* an infusion pump into a peripheral intravenous infusion. Neither this pump nor the intravenous tubing was marked to indicate a ranitidine infusion.

Six hours into the postoperative period, notification was received of the accidental administration of the ranitidine solution into the epidural catheter. The ranitidine solution was prepared from a 2-ml single dose vial; each milliliter of the solution contained 25 mg ranitidine (as the hydrochloride) as well as 0.96 mg monobasic potassium phosphate, 2.4 mg dibasic sodium phosphate, and 5 mg phenol. This solution has a *p*H of between 6.7 and 7.3.‡ For intravenous administration, it was diluted in 50 ml 5% dextrose and water. Approximately 30 ml of the 50-ml total volume had been administered when the error was noted. After notification, the epidural catheter was flushed with 10 ml normal saline, and the epidural fentanyl infusion was discontinued. The patient's subsequent analgesic regime included 2-mg boluses of intravenous morphine sulfate titrated to pain relief. The patient required a total of 8 mg over the next 9 h and was reported to be comfortable. This is a seemingly small amount of morphine considering the patient's incision. Immediately after the incident, the patient was free of neurologic symptoms and a neurologic examination at that time was normal, as were daily neurologic examinations performed for the next week. The patient was discharged home with no untoward sequelae.

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‡ Trissel LA: Handbook on Injectable Drugs, ed 5. Bethesda, American Society of Hospital Pharmacists, 1988, p 622

TABLE 1. Morphine Preparations[15]

Name	Manufacturer	Phenol	Other Preservatives
Duramorph (1 mg/ml)	Elkins Sinn	None	None
Morphine sulfate (15 mg/ml)	Eli Lilly	None	Chlorobutanol 0.5% Sodium bisulfite 0.1%
Morphine sulfate (15 mg/ml)	Wyeth	None	Chlorobutanol 0.5% Edetate sodium 1%
Morphine sulfate (15 mg/ml)	Winthrop	5 mg/ml	Sodium biphosphate 8 mg Sodium metabisolfite 1 mg
Morphine sulfate (15 mg/ml)	Elkins Sinn	2.5 mg/ml	Formaldehyde 2.8 mg
Morphine sulfate (25 mg/ml)	IMS	None	Sodium bisulfite

DISCUSSION

There are numerous case reports in which various drugs have been inadvertently injected into the epidural space. The drugs injected include thiopental,[1–3] potassium chloride,[4,5] diazepam,[4] magnesium sulfate,[6] paraldehyde,[7] and ephedrine.[1] The errors result primarily from either a mislabeled or unlabeled syringe or, as in this case, inadequately marked tubing. The occurrence of this incident late in a shift and at the end of a busy week suggests that fatigue also played a role in the event. Since the patient was otherwise healthy and was being observed in the intensive care unit only because of her epidural opioid infusion, there may have been some diminution of nursing vigilance.

Ranitidine is a histamine H-2 receptor blocker with polar, hydrophilic properties. Ranitidine acts at H-2 receptors and competes with histamine; it has virtually no H-1 blocking effects. It is without anticholinergic properties and is 4–10 times more potent than cimetidine. When administered orally, it is effective for 8–12 h. Ranitidine does not penetrate the blood–brain barrier well.[8] Approximately 15% of an intravenous dose is bound to serum proteins. Seventy per cent of an intravenous dose is recovered in the urine as unchanged drug; another 6% is found as metabolites in the urine; and the remainder is excreted in the stool.§ As a group, H-2 blockers have few significant side effects and in comparison to cimetidine, have even fewer side effects.[8]

Histamine H-2 receptors are widespread in the body, but their major function seems to be the regulation of gastric secretion.[8] In the central nervous system of the rat, H-2 binding sites are noted in the cerebellum, brain stem, and spinal cord; the sites are far more numerous in the brain stem and the spinal cord than in the cerebellum.[9] Histamine, as compared to other biogenic amines, is found in comparatively low concentrations in the brain; however, it appears more common in selected nuclei of the hypothalamus.[10] Although the precise roles of histamine and H-2 receptors in the central nervous system are not yet defined, they may be involved in the pain modulation process.[11]

There was concern about the presence of phenol in the solution infused into the epidural space. Phenol is used as a preservative in a number of opioid preparations (tables 1 and 2). Du Pen *et al.*[12] describe a patient in whom an epidural catheter had been inserted for control of cancer pain. As a cost-saving measure, the patient was given a morphine preparation containing phenol and formaldehyde as preservatives; at the time of maximum dosage, the patient was receiving 30 mg phenol and 33.6 mg formaldehyde each day. Because of deteriorating mental status the patient was hospitalized and his epidural morphine was replaced by an intravenous morphine infusion. The patient's mental status improved, and an epidurogram demonstrated flow restriction in the epidural space. The epidural morphine regime was restarted, this time with a preparation containing chlorobutanol 0.5% and edetate disodium 1% as preservatives. The patient's men-

TABLE 2. Meperdine Preparations*

Name	Manufacturer	Phenol	Other Preservatives
Demerol Carpuject (25 mg/ml)	Winthrop	None	None
Demerol Injectible (50, 100 mg/ml)	Winthrop	None	Metacresol 0.1% in multidose vials
Demerol Uniamp (50, 100 mg/ml)	Winthrop	None	None
Mepergan Injection	Wyeth	5 mg/ml	Edetate disodium 0.1 mg Formaldehyde 0.75 mg Sodium metabisulfite 0.25 mg
Mepergan Tubex	Wyeth	5 mg/ml	Edetate disodium 0.1 mg Formaldehyde 0.75 mg Sodium metabisulfite 0.25 mg
Meperidine HCl (25, 50, 75, 100 mg/ml)	Elkins Sinn	None	None

§ Glaxo Pharmaceuticals. Product information, Zantac. April 1989

* Compiled from Physicians' Desk Reference, Medical Economics Company, Oradell, NJ, 1989.

tal status remained clear, suggesting that the previous preservatives had a role in the mental status changes.[12]

In addition to its use as a preservative, phenol has long been used as a neurolytic agent in the treatment of intractable pain. The neurolytic properties of phenol depend on many factors, such as the volume of the injection, the speed of the injection, and the length of time the phenol is in contact with the structure. The concentration at which phenol causes neurolysis is contingent on the diameter of the nerve fiber; the thinnest fibers are the first to be damaged.[13] By our estimates, this patient received 30 ml 0.02% solution (6 mg) of phenol; when employed for intentional neurolysis, a 6–7% concentration is used.

Although the solution infused into the epidural space was far less concentrated, it was infused into a confined area in the epidural space over a 30-min period. Phenol causes neurolysis by denaturing proteins, and it penetrates tissues quite readily.[14] It is more potent in aqueous solutions than in glycerin. The systemic absorption and disposition of phenol are not well described; however, it is known that phenol is metabolized *via* oxidation and conjugation in the liver before undergoing renal excretion.[15]

A number of factors may have had a role in limiting neural damage to this patient. Perhaps the most important factor in minimizing any injury was that the low concentration and the slow rate of injection may have allowed the phenol to be absorbed before it could penetrate the dura. The reports of damage after the accidental injection of drugs into the epidural space involve bolus injections rather than infusions.[5,7]

Another factor limiting injury may have been the ability of the dura to resist chemical insults. Bromage[16] reported that 6.4% potassium chloride caused transient injury, and Lin *et al.*[4] likewise reported that 0.2% potassium chloride caused transient effects. Shankar *et al.*[5] reported that a bolus injection of 11.25% potassium chloride resulted in permanent neural damage.

The acute therapeutic interventions for this type of injury are not well defined. The efficacy of irrigation of the catheter and the epidural space is uncertain, especially if not initiated immediately. Irrigation may disseminate the irritant, as discussed by Lin *et al.*[4] Although epidural steroids have been administered in similar incidents,[3] their value is uncertain. The best treatment of this sort of accidental drug injection into the epidural space is prevention, and we have implemented measures designed of prevent a recurrence. We now place labels indicating an epidural infusion on the infusion bag, the pump, the tubing, and the tube epidural catheter connection. Injection ports in the tubing are blocked.¶ Epidural infusions are used only on nursing units familiar with this technique. We emphasize to the nursing staff that the use of an epidural catheter requires special vigilance. Most of these suggestions have already been made by other authors.[17,18]

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