slow and erratic, while the injection itself is often painful.

Unfortunately, diazepam is insoluble in water. The injectable solution contains diazepam compounded with propylene glycol and ethyl alcohol as solvents, sodium benzoate and benzoic acid as buffers, and benzyl alcohol as a preservative, all irritant to veins and fraught with the hazards of thrombosis, phlebitis, and sclerosis. The manufacturer's warnings state, "The solution should be injected slowly . . . do not use small veins, such as those on the dorsum of the hand or wrist . . . if it is not feasible to administer Valium directly iv, it may be injected slowly through the infusion tubing as close as possible to the vein insertion."*

The "puff technic," somewhat at variance with these warnings, is nevertheless uniquely designed to obviate the hazards. A 22-gauge needle attached to a syringe containing the drug is inserted into the most proximal (*i.e.*, furthest from the patient) injection port of a rapidly flowing iv line. After commenting to the patient, "This may feel slightly warm at the hand (or wrist)," the anesthesiologist holds the barrel of the syringe in one hand and proceeds to tap rapidly and forcefully with the index or middle finger of the other hand on the plunger of the syringe. Because of the viscosity of the solution and the deliberately chosen small bore of the needle, only an infinitesimal amount of diazepam is extruded with each tap, perceptible in the infusion solution as a tiny opalescent cloud (the "puff") quickly swept along in the flowing stream. Indeed, the individual puffs are so small that at the first the plunger is seemingly immobile. Only after repeated puffs does its slow advance become perceptible. Several minutes of this tapping are required to deliver the desired dose, maximally diluted, with minimal discomfort to the patient (the slight warmth at hand or wrist sites is usually absent if larger veins in the forearm or antecubital fossa are used) and minimal incidence of undesirable sequelae.

The puff technic is not new. Its use is well established in our Department of Anesthesiology at the Columbia–Presbyterian Medical Center (and elsewhere); but its conception is shrouded in mystery. If any reader knows with certainty the originator of this peerless method, a brief note to the address below would be much appreciated. Let's give credit where credit is due!

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* Package insert, Valium® injectable (diazepam/Roche). Hoffmann–La Roche, Nutley, New Jersey, May, 1983.

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Hydrogen Peroxide May Cause Venous Oxygen Embolism

To the Editor:—The following case report illustrates the cause of an air embolism from the gas being liberated from surgical packs impregnated with H_2O_2.

A 53 year old, 66-kg female underwent a transphenoidal resection of a large pituitary adenoma in a 5 degree reverse Trendelenberg position. Anesthesia was maintained with N_2O–O_2 and isoflurane and monitoring consisted of an arterial line, CVP catheter in the right atrium, and esophageal stethoscope. The Doppler was not used at the request of the surgeon, for the operation was being videotaped and the Doppler interfered with the sound quality of the tape.

The tumor had eroded and was protruding into the sphenoid sinus. Unusual bleeding was encountered and strips soaked in 3% H_2O_2 were packed into the surgical field in an attempt to maintain hemostasis. Immediately thereafter, two separate, approximately 3-s-long, "tinkling" sounds were heard via the esophageal stethoscope. The $FETCO_2$ dropped from 30 to 27 mmHg, mean CVP increased from 2 to 5 mmHg, and airway pressure increased from 15 to 24 mmH_2O. N_2O was discontinued immediately and the surgeon notified. The hydrogen peroxide packs were removed and the surgical field flooded with saline. Aspiration from the right arterial catheter did not reveal any gas. Arterial blood pressure and heart rate were unchanged, and the $FETCO_2$ and airway pressures returned to previous values within 4 min. The remainder of the case was uneventful and the patient made an uneventful recovery.

Since the surgical field was a small confined space, the tumor large and eroding, it is likely that surgical disruption of the dura and a venous sinus occurred. We believe the use of hydrogen peroxide via packs effectively forced the liberated oxygen to be vented into the cavernous sinus.

Use of hydrogen peroxide in the surgical field for cleansing and vasoconstriction is well known. H_2O_2 in the presence of organic material yields $H_2O + O_2$. The

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amount of oxygen liberated is not known precisely. The manufacturer states that in 35% hydrogen peroxide the amount of active oxygen is approximately 16.5%.

Venous air embolism is a serious potential complication of transphenoidal resections especially if the cavernous sinus is eroded. The tinkling sound heard via the esophageal stethoscope, the sudden though small drop in $FETCO_2$, the rise in airway pressure, and the increase in CVP occurring immediately after placement of the packs soaked with hydrogen peroxide raise strong suspicions of either a venous oxygen or venous air embolism. Circumstantial evidence suggests venous oxygen embolism. Air emboli expands 30 times in size under nitrous oxide anesthesia, and therefore its presence is readily detectable and its complications pronounced. Since the changes in the parameters we monitored occurred in the same direction as with venous air embolism, but were of shorter duration and lesser magnitude, we speculate that an oxygen embolus may have been produced from the hydrogen peroxide reaction with tissue.

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Benzodiazepines and Polymorphonuclear Leukocyte Oxidative Activity

To the Editor:—Goldfarb *et al.* recently published the results of a study in which they showed that diazepam, flunitrazepam, and clorazepate inhibited human polymorphonuclear leukocyte oxidative activity.[1] Although they were suitably circumspect about the clinical relevance of these findings, there are a number of issues in their article that need to be addressed. First, there is no indication of how many subjects were studied. We are told that "three measurements were carried out at each concentration." It is not clear whether this means triplicate measurements on one individual's leukocytes or one measurement on three individual's leukocytes. Would it have been preferable if blood from a number of healthy subjects was studied and, to assure us of the reproducibility of the measurement techniques, duplicate or, preferably, triplicate measurements done on each individual's blood at each concentration?

Although there are large differences in the therapeutic plasma concentrations of these drugs, the authors studied each drug at identical concentrations. This makes comparison of the toxic effects of the three drugs difficult in the context of what may be found clinically. In addition, it is the unbound drug rather than the total plasma concentration that is clinically effective. Ten per cent serum was added to the Krebs–Ringer's solution. To what extent would this bring the free plasma concentrations more closely in line with what is found in clinical practice?

The clinical relevance of this study might have been enhanced by studying clinically relevant drug concentrations rather than evaluating concentrations significantly greater than those found in clinical practice. The authors argue that this was done because the cells were exposed to the drugs for only 15 min, a period shorter than may be seen clinically. Does exposing cells to high drug concentrations for a short period have the same effect as exposing cells to smaller concentrations for a longer period?

An intriguing observation made in this study was that, despite the fact that the cells were washed after incubation, there was a significant depression in oxidative activity. This is in contrast to other studies that have shown that washing will reverse the depressant effects of thiopentone, Alfathesin®, and tetracaine.[2,3] What is the explanation for this difference? Do the benzodiazepines studied have prolonged or permanent effects on leukocytes, or is this a cytotoxic effect from the relatively high drug concentrations employed? Goldfarb *et al.* have the technical ability to answer this important question and I would urge them to do so.

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