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!

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

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 H₂O₂.

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 N₂O–O₂ 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% H₂O₂ 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 FETCO₂ dropped from 30 to 27 mmHg, mean
CVP increased from 2 to 5 mmHg, and airway pressure
increased from 15 to 24 mmH₂O. N₂O 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 FETCO₂ 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. H₂O₂ in
the presence of organic material yields H₂O + O₂. The
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 FETCO₂, 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 technique, 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 percent 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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