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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In reply:—Dr. Gelb asks for more details about the leukocytes we used in our experiments. We performed one measurement at each concentration on three individual's leukocytes for each drug. The control values all were within the normal range for our laboratory[1] and all the standard errors were small; thus, it seems inappropriate to conclude that triplicate measurements on each sample would be preferable.

Dr. Gelb raises the question of the application of our *in vitro* findings to clinical practice. It is a conceptual error to attempt any correlation between an *in vitro* study and a clinical conclusion. The purpose of our study was strictly analytic; were the tested drugs able to induce any change in leukocytes oxidative activity? We answered positively. Using lower concentration and another technique, Dr. Gelb and associates did not demonstrate any statistical difference in leukocyte oxidative activity under the influence of diazepam, although numerically the activity observed at a concentration of 2.5 $\mu g \cdot ml^{-1}$ was lower than the control value.[2] Concerning the leukocyte solutions used for *in vitro* experiments, these absolutely can not be compared with normal human blood. We totally ignore the amount of drug penetrating the leukocytes; since protein-bound and -unbound concentrations of diazepam were not measured either by us or by Dr. Gelb and his colleagues,[2] it seems impossible to draw any conclusions about the influence of the percentage of serum added to the Krebs–Ringer's solution. Concerning the inverse correlation between a drug's concentration and its incubation time on leukocyte's functions, this is a pharmacologic hypothesis used largely to study a drug's cytoxicity in the cancer research field; however, the viability of leukocytes is brief on account of aggregation, autolysis, spontaneous activation, or membrane modifications, and thus, this hypothesis cannot be tested for incubation times exceeding 30–60 min.

Concerning the noninfluence of washing on the leukocyte depression, there are different possible explanations. The time necessary to wash and to resuspend the leukocytes is short, about 15 min; it could be too short to cause an important decrease in the intracellular concentration of the drugs. Other possible explanations could be an irreversible binding between the drugs and some leukocyte receptors or a cytotoxic effect of the drug. Further studies are necessary to determine the mechanism of the depression of the leukocyte oxidative activity we have observed.

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Pulmonary Artery Catheter Sheath Malfunction with Sternotomy

To the Editor:—In their correspondence, Campbell and Schwartz[1] comment on the intraoperative failure of pulmonary artery catheter (PAC) placed via the right external jugular vein (EJV) as reported by Bromley and