to account for this observation, only one of which implied that the spectral changes might be expressions of enzyme-substrate interaction. They offered as evidence of this concept a relationship between the spectral binding constant ($K_b$) and the Michaelis constant ($K_m$).

That the case of $K_b = K_m$ is unconvincing would be a charitable assessment, to say the least. Spectral shifts produced by binding of compounds to cytochrome P-450 do not provide evidence that the compounds are substrates for the enzyme. Phenobarbital and SKF 525-A produce Type I binding spectra, but are not metabolized at all; the same holds for pyridine, which is inert but produces a classic Type II binding spectrum. Imai and Sato demonstrated that organic solvents cause shifts in difference spectra due to nonspecific binding and disruption of the lipid environment contiguous to P-450. Binding is not equated with metabolism.

By use of $K_b$, Takahashi et al. deduced that anesthetics cause competitive inhibition of biotransformation of other "fixed" drugs. Competitive inhibition is not found if this interaction is studied in the proper manner—assay of metabolites of various fixed drug concentrations in the presence of an anesthetic and construction of a Lineweaver-Burk plot. Inhalation anesthetics actually inhibit Type I drugs in a noncompetitive fashion.

In summary, many investigators believe cytochrome P-450 is indeed integral in the biotransformation of anesthetics, but the paper of Takahashi et al. sheds little light on this concept.

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REFERENCES

The Critical Coronary Disease Patient

To the Editor.—In their article, "Intra-aortic Balloon Counterpulsation in a High-risk Cardiac Patient Undergoing Emergency Gastrectomy" (Anesthesiology 42:103-105, 1975), Miller and Hall describe the survival of a patient who was fortunate to have been in a hospital where counterpulsation equipment was available and the medical staff were knowledgeable and imaginative in its use. The usual utilization of intra-aortic counterpulsation has been to support the circulation in critical myocardial ischemia, i.e., shock, impending infarction, and refractory ventricular arrhythmia prior to diagnostic angiography and, where possible, myocardial revascularization.

In addition, it has been employed prophylactically before induction of anes-

esthesia in patients with significant multivessel disease including the left main coronary artery, and therapeutically to permit weaning from cardiopulmonary bypass when myocardial ischemia was detected during valve replacement or coronary grafting.

Two points in the management of this patient provoke comment. Intraoperatively, loss of counterpulsation due to "jamming" of the ECG (R wave), which triggers the timing mechanism and which occurs with use of the electro surgical unit, may sometimes be circumvented by triggering instead from the pressure wave transduced from the pulmonary artery. Triggering may also be achieved during electric pacing of the heart if the signal is simultaneously supplied to the timing mechanism.
In view of the elevated postoperative pressures reported (systemic 150/160/80 torr; pulmonary capillary wedge pressure 18 torr) and the subsequent development of left ventricular failure with an A-aDp of 586 torr, one wonders whether, in addition to counterpulsation, the beneficial effects of vasodilator therapy, such as with sodium nitroprusside iv, would not, in lessening ventricular afterload and preload, have accelerated this patient's recovery.

The anesthesiologist without benefit of mechanical circulatory assistance can still do much to manage the critical coronary disease patient successfully by rigorous attention to the factors that contribute to the balance between myocardial oxygen supply and demand.

Comment on the Critique

To the Editor:—We wish to comment on the critique prepared by Drs. Walts, Forsythe, and Moore (Anesthesiology 42:608-611, 1975) relative to the Ad Hoc Committee report on Occupational Disease among Operating Room Personnel (Anesthesiology 41:321-340, 1974). We support the effort by these individuals to offer a critical analysis of the report and would encourage similar attempts by other interested scientists. In a footnote to the original publication attention is called to the complete raw data file available by application from the National Institute for Occupational Safety and Health in Cincinnati.

In the interest of editorial brevity, we respond here only to the major areas of concern expressed by Walts et al. Detailed discussion of each of the points raised by these authors, has, however, been prepared and forwarded directly. Interested individuals may obtain a copy of these comments by writing to the undersigned.

Walt et al. refer to our decision to consider p 0.05 statistically significant; they would prefer to use a significance level of 0.01. They correctly point out that when 30 tests of significance are done (independently) at the 5 per cent level, there is a 79 per cent probability that one or more will be significant by chance alone. They should have noted, however, that of the 30 tests they refer to in our report, six were significant at the 1 per cent level, another six at the 5 per cent level, and 17 of the 30 were significant at the 10 per cent level; the probability of such small levels of P occurring by chance alone in 30 tests is less than one in a million. Furthermore, this tabulation does not include the six intra-group analyses comparing spontaneous abortions and congenital abnormalities.

However, the problems of multiple inference in such a complex set of data, including sex-specific comparisons among and within a number of different groups, are difficult, and the fitting of the pieces into a cogent whole involves considerable judgment. The Committee is aware of these problems and, in addition to carrying out extensive and thorough statistical summaries and analyses of the data, took two additional steps: 1) we reported as much of the data as possible by sex of respondent, by society, by exposure within society, etc., with standard errors and exact P values, so that the reader could, if he chose, undertake supplementary statistical evaluation; 2) we consulted many experts and submitted the paper in draft form to epidemiologists, biostatisticians, anesthesiologists, and other scientists, to be certain that their evaluation of the evidence was in line with our conclusions. We have drawn our conclusions cautiously and with qualifications, and believe strongly that the results, weighed against the risks of various actions, call for...