

of Physicians and Surgeons, New York, N. Y. In current analysis of the uptake and distribution of metabolically inert anesthetic gases, it has been assumed that the solubility of these substances in body fluids is constant and obeys Henry's Law. This assumption has been challenged recently by H. J. Lowe (personal communication), who found an increased apparent solubility at low gas phase concentrations of cyclopropane. This variation of solubility can be attributed to the simultaneous processes of physical solution and adsorption to proteins of the gas. Previously we have reported significant, persisting differences in the rates of approach to equilibrium of nitrous oxide and cyclopropane administered simultaneously in man (Rackow, H., Salanitre, E., Epstein, R. M., Wolf, G. L., and Perl, W. J.: *Appl. Physiol.* 20: 611, 1965). By standard tests, these gases have been found to have nearly identical blood solubilities. In our study cyclopropane, particularly, was administered in very low concentration, so we must consider the possibility that the difference in uptake rates reported might be attributable to concentration-dependent differences in blood solubility. **Methods:** The effect of concentration dependence of solubility in blood upon predicted uptake patterns for cyclopropane was subjected to theoretical analysis. The solubility function was represented as a sum of two processes: "true" Henry's Law solubility (constant) plus a variable quantity expressed as a Langmuir adsorption isotherm. At high concentrations this formulation becomes a substantially constant solubility. The concentration function was fitted to produce an apparent Ostwald coefficient of 0.46 at 100 per cent cyclopropane, rising to 0.63 at 1 per cent cyclopropane. In tissues the solubility was taken to be constant both for simplicity and because no data is available to suggest the extent of any concentration dependence. Ventilation, circulation and body composition values were taken from those of the subject analyzed in detail in Rackow *et al.*, cited above. **Results:** The differential equations resulting from this formulation are non-linear and cannot be solved analytically. Numerical solution was effected by a step-wise Runge-Kutta integration procedure using an IBM 7094 computer. At the same time the

classical (not variable with concentration) equations were solved for comparison, using a blood Ostwald coefficient of 0.46. In comparison with standard models, concentration-dependent solubility resulted in a small slowing of equilibration in the lung when the inspiratory concentration was as low as 1 per cent. There was also a distortion of the uptake pattern at high concentrations arising from the early period when alveolar gas tension passes through the low range. The difference in rates of equilibration between high and low concentrations tended to diminish with time and therefore did not resemble the more constant difference between cyclopropane and nitrous oxide in our earlier studies. **Discussion:** Concentration dependence of solubility is potentially significant in the use of cyclopropane or other gases for tracer experiments. Further evaluation of the chemical evidence for such dependence seems important. Direct measurement of the uptake changes appears unprofitable because the pharmacological action of the gas produces other more gross changes in the systems which control uptake rates during inhalation of high concentrations. (Performed in part during the tenure of a Fellowship of the John Simon Guggenheim Memorial Foundation at the Department of Pharmacology, Oxford University, and supported in part by USPHS grant GM-09069-05.)

The Vasopressor Effect of Indigo Carmine. J. C. ERICKSON, M.D., and B. A. WIMMER, B.A., *Woman's Medical College of Pennsylvania and Temple University School of Medicine, Philadelphia, Penna.* Since the introduction of indigo carmine, or sodium indigotin disulfonate, in 1904, it has been regarded as pharmacologically inert. Appearing in fresh urine eight to ten minutes after intravenous administration, it aids in identification of ureteral orifices during cystoscopy. The blue dye may also be used to demonstrate divided or damaged ureters during lower abdominal surgery. We have observed that the systolic and diastolic blood pressures increase and that bradycardia usually occurs two to three minutes after injection. Having found this phenomenon in a series of 60 consecutive

patients who undergoing surgery under various types of anesthesia, we collected similar data from 14 unanesthetized, unsedated subjects. *Methods:* After starting a slow intravenous infusion, blood pressure and pulse rate were recorded at two-minute intervals for one hour, thus establishing a steady state. When the dye was injected into the infusion tubing, most recipients were relaxed and drowsy. Systolic and diastolic pressure were obtained by auscultation of Korotkoff sounds and the pulse rate by palpation of a radial artery. After injection of 5 ml. of 0.8 per cent solution of indigo carmine, blood pressure and pulse rate were recorded every 30 seconds for ten minutes, and then every minute until they returned to previous levels. Similar determinations were made in three patients during cardiac catheterization, using arterial cannulas, an oscilloscope and a photographic recorder. Eight of the 14 subjects were anesthetized on the following day with similar measurements made by the indirect methods mentioned. *Results:* All systolic pressures of patients increased 4-50 mm. Hg and diastolic pressures rose 9-30 mm. Hg. Mean values were 17 mm. Hg and 19 mm. Hg, respectively. Pulse rate decreased by 8 to 20 beats per minute (mean 16 per minute) in all except one subject whose pulse was unchanged. Maximum alterations in pressures and pulse rate were attained within 1.5 to 3.0 minutes after injection. The duration of relative hypertension and bradycardia varied from two minutes to more than 30 minutes. There was no relationship between control values and increase in pressures or slowing of the pulse. All anesthetized patients developed hypertension and bradycardia. *Discussion:* These observations indicate that indigo carmine has a mild pressor effect. Whether the dye causes peripheral vasoconstriction or vasoconstriction plus a direct cardiac effect has not been ascertained. The bradycardia may be a reflex response from circulatory baroreceptors. The molecular structure of indigo carmine resembles two molecules of serotonin arranged as if one is a mirror image of the other. The similarity in structure to catecholamine compounds suggests a cardiovascular effect from its administration. The anesthesiologist who occasionally

administers this dye should exercise caution when administering it to hypertensive and cardiac patients.

Retinal Observations in Dying and Resuscitation. OSCAR FARMATI, M.D., STEPHAN KAMPSCHULTE, M.D., BULENT KIRIMLI, M.D., and PETER SAFAR, M.D., *Department of Anesthesiology, University of Pittsburgh School of Medicine, Pittsburgh, Penna.* Since the invention and introduction of the ophthalmoscope in clinical practice and research, the retina has been considered a mirror of intracranial events related to the cerebral blood circulation. Retinal and cerebral arteries have a common anatomic origin (i.e. internal carotid) and similar reactivity to PaO_2 and $PaCO_2$ changes in normal subjects. These vasomotor manifestations are concurrently and similarly altered also in atherosclerosis, diabetes, essential hypertension and glomerulosclerosis. Continuous retinoscopy and intermittent retinal photography were performed on lightly anesthetized, spontaneously breathing dogs which were subjected to rapid exsanguination, asphyxiation, and ventricular fibrillation. The observations were correlated with aortic pressure, PaO_2 , $PaCO_2$, pH_a , hematocrit, ECC and EEG. *Exsanguination* (8 dogs): Rapid arterial hemorrhage resulted in zero arterial pressure in 2-12 minutes (blood loss 30-60 ml/kg), which was followed by apnea. No apparent changes of retinal circulation occurred until mean aortic pressure was approximately 50 mm Hg. Sludging of the blood started when aortic pressure was near 40 mm Hg, and fragmentation of blood columns was complete at 15 mm Hg aortic pressure. The EEG became isoelectric after the aortic pressure had dropped to 8 mm Hg or less. After five minutes of clinical death (apnea and pulselessness) resuscitation was started. Five dogs were resuscitated with rapid venous infusion of blood or blood substitutes with epinephrine and sodium bicarbonate; intermittent positive pressure ventilation with oxygen (IPPV/ O_2) and external cardiac compression (ECC). Three dogs had intra-arterial transfusion without ECC. The rate of retinal filling during resuscitation was equally rapid with blood as with substitutes; but more rapid with arterial