

of nucleosides and free amino acids in the extracellular space tend to equilibrate through the cell membrane with the soluble fraction in the cell.<sup>18</sup> In the present study, we have seen that halothane does not interfere with this process.

Future studies of DNA synthesis may be done with the knowledge that decreased <sup>3</sup>HT incorporation is not due to a block of its uptake by the exposure of the cell to halothane but rather to a more distal event in the sequence of steps in DNA synthesis.

Finally, the partition coefficient of about 1.1 indicates that our gas concentration of 2 per cent produced a liquid concentration of about 17 mg/100 ml. In our previous study this concentration caused about 60 per cent inhibition of <sup>3</sup>HT incorporation, so we may be assured that the present results refute any idea of a block in precursor uptake at the membrane level.

Miss Louise Owen gave expert technical assistance. Halothane was donated as Fluothane by Ayerst Laboratories, Inc.

## References

1. Bruce DL: Halothane inhibition of phytohemagglutinin-induced lymphocyte transformation. *ANESTHESIOLOGY* 36:201-205, 1972
2. Cullen BF, Sample WF, Chretien PB: *In vitro* effect of halothane on phytohemagglutinin (PHA)-induced human lymphocyte transformation. *ANESTHESIOLOGY* 36:206-212, 1972
3. Stewart CC, Ingram M: A method for counting phytohemagglutinin-stimulated lymphocytes. *Blood* 29:628-639, 1967
4. Hatch A, Balazs T: The use of Cetavlon in a diluent for counting leucocytes in the Coulter electronic counter. A comparison with some currently used diluents. *Am J Clin Pathol* 36:220-223, 1961
5. Larson CP, Eger EI, Severinghaus JW: The solubility of halothane in blood and tissue homogenates. *ANESTHESIOLOGY* 23:349-355, 1962
6. Cleaver JE: Thymidine Metabolism and Cell Kinetics. New York, American Elsevier, 1967, pp 70-103
7. Painter RB, Drew RM, Giaque BG: Further studies on deoxyribonucleic acid metabolism in mammalian cell cultures. *Exp Cell Res* 21:98-105, 1960
8. Feinendegen LE: Tritium-Labeled Molecules in Biology and Medicine. New York, Academic Press, 1967, p 245

## Drugs and Their Actions

**BRETYLIUM TOSYLATE AND PULMONARY HEMODYNAMICS** The effects of bretylium tosylate on pulmonary and systemic circulations were studied in four patients recovering from open-heart surgery for mitral-valve disease. Hemodynamic measurements were made at 30-minute intervals for two hours after administration of bretylium tosylate (5 mg/kg). The elevated pulmonary arterial pressure and vascular resistance increased progressively in three patients. Systemic arterial pressure, systemic vascular resistance, and left atrial pressure decreased in all patients; one sustained a continued decline in arterial pressure and cardiac arrest, successfully treated by closed-chest massage and large doses of norepinephrine. Cardiac output decreased in two patients, rose slightly in one, and was unchanged in the fourth. Caution is recommended when bretylium tosylate is needed for the patient with increased pulmonary arterial pressure and vascular resistance. (Cotter, S., and others: *Effect of Bretylium on the Pulmonary and Systemic Circulation in Patients with Mitral Valve Disease after Cardiopulmonary Bypass*. *J. Clin. Pharmacol.* 11: 409-416, 1971.) **ABSTRACTER'S COMMENT:** This paper confirms the known pulmonary vasopressor response to bretylium tosylate; the number of observations was small and the control of variables questionable (e.g., marginal pH  $P_{aO_2}$  and  $P_{aCO_2}$ ). Bretylium, formerly used as an antihypertensive agent and currently being investigated to treat ventricular arrhythmias, should be reserved for refractory, life-threatening arrhythmias, especially when pulmonary hypertension is present. Bretylium blocks norepinephrine release in response to adrenergic nerve stimulation, but does not impair the response to exogenous catecholamines. Therefore, norepinephrine is the preferred treatment when systemic hypotension ensues.