

been calculated preoperatively. Use of an assumed  $Ca_{O_2}-C\bar{v}_{O_2}$  of 4.5 vol per cent, as is frequently done, would have led to both over- and underestimation of shunt by more than 50 per cent in several instances. **Summary:** Measurement of both  $Cc_{O_2}-Ca_{O_2}$  and  $Ca_{O_2}-C\bar{v}_{O_2}$  is necessary if a meaningful estimation of shunt is to be made in individual cases. Intrapulmonary ( $Cc_{O_2}-Ca_{O_2}$ ) and systemic ( $Ca_{O_2}-C\bar{v}_{O_2}$ ) oxygen content differences determine the intrapulmonary shunt:  $\dot{Q}_s/\dot{Q}_t = Cc_{O_2}-Ca_{O_2}/(Cc_{O_2} - Ca_{O_2}) + (Ca_{O_2}-C\bar{v}_{O_2})$ . With  $Cc_{O_2}-Ca_{O_2}$  on the Y axis and  $Ca_{O_2}-C\bar{v}_{O_2}$  on the X axis, the relative influence of pulmonary and systemic factors on shunting can be readily determined. A series of straight lines representing per cent shunt are determined by substitution in the above formula; these radiate from the XY intercept. Since shunt values obtained using oxygen content differences as coordinates are not affected by the absolute value of the inspired oxygen tension, serial plotting of shunt values allows better assessment of cardiopulmonary therapy.

**A Safer Method for Measuring Body-fluid Compartments in Patients.** D. R. COOK, M.D., S. J. GALLA, M.D., and W. S. GUALTIERE, PH.D., *Departments of Anesthesiology and Physical Education, University of Pittsburgh, Pittsburgh, Penna.* Measurement of body-fluid compartments requires the administration of relatively high doses of radioactive tracers. Ordinarily, 10  $\mu$ c of  $^{131}$ iodine are used to measure plasma volume; 20  $\mu$ c of  $^{51}$ chromium are used to measure erythrocyte mass; 70-100  $\mu$ c of  $^{35}$ sulfur are used to measure extracellular fluid volume; 1.0 of tritium is used to measure total body water. Although this represents a total body radiation exposure of only 0.402 rems, the testicular and thyroid exposure from the radioactive sulfur and iodine is 2.925 rems. Recently, liquid scintillation spectrometry has provided increased simplicity and accuracy in the measurement of the activity of the weak beta emitters. **Methods:** We devised a technique to reduce radiation exposure significantly, using a double-labeling liquid scintillation technique with quench cor-

rection. **Results:** We were able to reduce the  $^{35}$ sulfur dose to 10  $\mu$ c and the tritium dose to 0.5 mc per subject. Plasma volume and blood volume were measured with the Evan's blue-microhematocrit method, eliminating  $^{131}$ iodine and  $^{51}$ chromium. Total body radiation was reduced 72 per cent and the radiation exposure to the testes and thyroid was reduced 93 per cent. Our method was validated by measuring body fluid compartments in young men. The volumes obtained were comparable to those reported by Moore for men in the same age group. (Supported in part by USPHS Grant GM-13965.)

**Cardiovascular Effects of Cyclopropane in Man.** D. J. CULLEN, M.D., E. I. EGER, II, M.D., and G. GREGORY, M.D., *Department of Anesthesia, University of California, San Francisco Medical Center, San Francisco, California.* Simultaneous cardiac and peripheral vascular effects of cyclopropane were determined in nonmedicated volunteers, at normal  $Pa_{CO_2}$  and body temperature. **Methods:** Measurements were made with the subjects awake during controlled ventilation ( $Pa_{CO_2}$  34 mm Hg) and at 15-20, 25-30 and 35-40 per cent alveolar cyclopropane ( $Pa_{CO_2}$  38-40 mm Hg). **Results:** Cardiac output ( $\dot{Q}$ ), heart rate (HR) and stroke volume (SV) remained at or near control values except at 35-40 per cent cyclopropane, when a 15 per cent decrease in  $\dot{Q}$  occurred ( $P < 0.05$ ). Mean arterial pressure (MAP), total peripheral resistance (TPR) and mean right atrial pressure (MRAP) rose significantly with onset of cyclopropane anesthesia. TPR and MRAP continued to rise as cyclopropane concentration increased. The peripheral vasculature showed arterial and venous constriction because forearm vascular resistance (FVR) increased while forearm venous compliance (FVC) decreased. When cyclopropane was acutely reduced from 35 per cent to 15 per cent, an overshoot of  $\dot{Q}$ , MAP and SV developed in the first two minutes. This overshoot reversed itself as MRAP continued to fall at ten minutes. **Summary:** We suggest that ventricular function is altered by cyclopropane because of the profound rise in

MRAP with only small decreases in  $\dot{Q}$ . However, from these data we cannot define the shape or slope of change in ventricular function. The peripheral vasculature demonstrates intense sympathetic activity, perhaps instrumental in maintaining filling pressure and cardiac function. Thus, with SV maintained by an increase in filling pressure and HR remaining constant,  $\dot{Q}$  remains normal.

**Block of Pain Transmission by Halothane in the Spinal Cord of the Cat.** R. H. DE JONG, M.D., R. ROBLES, M.D., and K-I. MORIKAWA, M.D., *Department of Anesthesiology, University of Washington, Seattle, Wash.* Melzack and Wall (*Science* 150: 971, 1965) proposed that the passage of impulses related to pain is affected by a presynaptic gating mechanism residing in the dorsal horn of the spinal cord. Because general anesthetics suppress the response to pain, we investigated the effects of halothane on the rate of discharge of dorsal horn neurons. These cells characteristically discharge at a rapid rate when the innervated skin is stimulated mechanically, as by stroking of hairs or by pinching a fold of skin. *Methods:* Under endotracheal halothane anesthesia, cats were decerebrated and the spinal cords transected at C<sub>7</sub>. Therefore, the lungs were ventilated mechanically with oxygen. Arterial blood pressure, end-expired CO<sub>2</sub>, temperature and urinary output were monitored continuously. Partial pressure of halothane in arterial blood was measured chromatographically. The lumbar spinal cord was exposed via a laminectomy and a metal-filled microelectrode advanced hydraulically into the dorsal horn until it recorded potentials from a single cutaneous afferent neuron. Most neurons discharged slowly and irregularly at rest. When the skin of the foot or leg was stimulated, the firing rate increased ten to 20 times. Following measurement of controls, 1 to 3 per cent halothane in oxygen was delivered to the nonbreathing system. *Results:* In the first one or two minutes halothane usually accelerated the firing rate of an afferent neuron. Thereafter, the rate slowed progressively, and firing ceased eventually. Rest-

ing discharge was suppressed at an average arterial halothane content of 1.3 per cent, the response to stroking of hairs at 1.6 per cent and that to skin pinching at 2.2 per cent. *Summary:* Earlier we showed that halothane affects neither the discharge of cutaneous receptors nor the conduction of impulses to the spinal cord. Halothane thus blocks these impulses from the skin in the dorsal horn of the spinal cord. Hence, analgesia may be attributed, at least in part, to blockade by halothane of impulse transmission at the first synapse of the extralemniscal pathway.

**Immediate Circulatory Effects of Anesthesia in Conscious Dogs.** J. H. EISELE, M.D., D. TRENCHARD, M.D., J. STUBBS, M.D., and A. GUZ, M.D., *Department of Medicine, Charing Cross Hospital Medical School, Fulham Hospital, London, England, and Department of Anesthesia, University of California, San Francisco Medical Center, San Francisco, Calif.* The time course of circulatory changes during induction with halothane and/or nitrous oxide was studied in six healthy awake dogs. *Methods:* Beat-to-beat changes in cardiac performance were measured with implanted ascending aortic electromagnetic flowmeters. Pressures were recorded from right and left atria, pulmonary artery, and descending aorta. The dogs were trained to breathe anesthetic gases from a mask. *Results:* Both 3 per cent halothane and 60 per cent nitrous oxide reduced peak aortic flow and maximum acceleration within eight to 12 seconds after inhalation of the first breath of either anesthetic. These changes were greater with halothane than with nitrous oxide, and were even more marked when the combination of halothane and nitrous oxide was inhaled. Cardiac acceleration decreased before any reduction in cardiac output, aortic or central pressures occurred, thus indicating that these anesthetics have a direct depressant effect on the myocardium. This was confirmed in three of the dogs that were studied after surgical denervation of the heart, when halothane and nitrous oxide alone and in combination produced a rapid cardiac depression similar to that in the nondenervated dogs.