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Glucose Pool Size, Turnover Rate and $C^{14}O_2$ Production During Halothane Anesthesia in Dogs. STEPHEN J. GALLA, M.D., *University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.* Previous studies have shown that although the plasma glucose concentration is not significantly altered during halothane anesthesia in dogs, after an exogenous glucose load the plasma glucose disappearance rate is reduced (Galla, S. J., and Wilson, E. P.: ANESTHESIOLOGY *25:* 96, 1964). To define more specifically the effects of halothane anesthesia on carbohydrate metabolism, glucose pool size, turnover rate, and utilization were estimated using a radio-isotope dilution technique. *Methods:* Healthy, mongrel dogs were prepared by chronically implanting polyvinyl catheters into the aorta and right atrium through the neck vessels. When the animals resumed normal activity, studies were performed either, (1) in the conscious state, or, (2) anesthetized with halothane (1–1.5 per cent) administered through an endotracheal tube in a non-rebreathing system with 40 per cent oxygen–60 per cent nitrogen. After a 2 hour stabilization period a priming-infusion dose of glucose-U-C^{14} (90–210 mc./m*M*) was administered following the principles outlined by Steele *et al.* (Amer. J. Physiol. *187:* 15, 1956). Experiments were randomized to lessen residual effects and each dog was used as its own control. At least a 3 week interval elapsed between experiments on the same animal to insure adequate elimination of isotope. Extracellular fluid space (ECF) was measured with sulfate-35. Blood volume was calculated from the plasma volume (Evans blue) and arterial hematocrit. Glucose-C^{14} was determined by liquid scintillation after oxidation and precipitation as the gluconate. Expired $C^{14}O_2$ was trapped and counted in hyamine by liquid scintillation. Glucose pool size and turnover rate were calculated from the plasma glucose specific activity between 60–180 minutes after the beginning of the isotope infusion. Erythrocyte transketolase activity was measured by a modification of Brin's method (Brin, and others: J. Nutr. *71:* 273, 1960). *Results:* Seventeen experiments were performed on six dogs (C = conscious group; H = halothane group). During halothane anesthesia blood volume decreased slightly (C = 11.6 per cent of body weight; H = 25.5 per cent of body weight). Glucose pool size decreased significantly (C = 0.183 vs. H = 0.142 g. glucose C/kg.) as did the turnover rate (C = 0.0411 vs. H = 0.0324 g. glucose C/m.²/minute). Total carbon dioxide production remained unchanged (C = 75 vs. H = 79 ml./m.²/minute) but cumulative $C^{14}O_2$, expressed as a per cent of the injected dose of radioactivity expired after 180 min., increased significantly (C = 9.3 per cent vs. H = 10.8 per cent). Erythrocyte transketolase activity increased significantly after halothane (C = 2,190 vs. H = 2,360 μg./ml./hr.). *Discussion:* Reduction in glucose pool size could have been due either to decreased hepatic glucose output or increased peripheral uptake. Since turnover rate was also reduced it appears that decreased hepatic glucose output effected the reduction in pool size during halothane. The increased conversion of glucose C^{14} to $C^{14}O_2$, while the total CO_2 production was unchanged, suggested that glucose was oxidized to a greater degree during halothane anesthesia than in the conscious group. The increase in transketolase activity (an indicator of function in the pentose phosphate pathway) is in agreement with increased glycolysis. The reduction in blood volume probably resulted from sampling blood loss. *Summary:* Radioisotope studies of glucose metabolism during halothane anesthesia suggest that although the tissue uptake of glucose may be reduced a larger fraction is oxidized to carbon dioxide. There appears to be no impairment of glucose metabolism. (Supported by Grants HE-06967-05 and GM 13965-01, National Institutes of Health, Bethesda, Maryland.)

Spinal Fluid and Hyperventilation During Anesthesia in Man. BENNIE GEFFIN, M.D., *Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, Boston.* In neurosurgical anesthesia, hyperventilation is commonly employed as a means of decreasing the brain volume. This is achieved by the vasoconstrictor effect of a

reduced arterial carbon dioxide tension on the cerebral vasculature. This study was undertaken to note the acute effects of hyperventilation on the oxygen and carbon dioxide tensions, and the *p*H of lumbar cerebrospinal fluid. *Method:* The investigation was performed on patients undergoing various neurosurgical operations who required cerebrospinal fluid drainage by inlying spinal catheter. Premedications consisted of pentobarbital 100 mg. and atropine 0.6 mg. given intramuscularly one hour preoperatively. Anesthesia was induced with thiamylal sodium 2½ per cent and succinylcholine, followed by endotracheal intubation. The patients were then allowed to breathe spontaneously a mixture of nitrous oxide and oxygen (3:2 or 2½:2½ liters/minute) and halothane (0.5–1.5 per cent) for 20–30 minutes before cerebrospinal fluid and arterial blood samples were taken for analysis. Then the patients were curarized and hyperventilated by means of a positive pressure respirator, the tidal volume being approximately double that read off the "Radford Nomogram," the inspired gas concentration remaining unaltered. After a minimum of 45 minutes, sampling of arterial blood and cerebrospinal fluid was repeated, the dura still being intact. *Results:* With hyperventilation the mean arterial carbon dioxide tension fell from 50 ± 9 mm. to 29 ± 8 mm. of mercury, this being paralleled by the mean cerebrospinal fluid carbon dioxide tension dropping from 50 ± 8 mm. to 39 ± 12 mm. of mercury. Associated with this, the arterial *p*H rose from a mean of 7.34 ± 0.04 to one of 7.52 ± 0.07 and the cerebrospinal *p*H from 7.32 ± 0.04 to 7.44 ± 0.05. Although the mean arterial oxygen tension (128 mm. Hg) did not change with hyperventilation, the mean oxygen tension of the cerebrospinal fluid fell from 73 ± 18 mm. to 59 ± 13 mm. of mercury, a decrease occurring in eight out of the nine patients. *Discussion:* Cerebrospinal fluid neither uses oxygen nor produces carbon dioxide and its gaseous content is the result presumably of diffusion from the tissues surrounding it. Any variation in the tension of carbon dioxide and oxygen in the cerebrospinal fluid is likely, therefore, to be a reflection of similar variations in the brain, spinal cord and their blood vessels. *Summary:* It has been demonstrated in this study that with hyperventilation, a fall in arterial carbon dioxide tension was accompanied by a similar fall in the carbon dioxide tension of the lumbar cerebrospinal fluid, the *p*H changing appropriately. The associated fall in the oxygen tension of the cerebrospinal fluid in 8 out of 9 patients, in spite of no change in the mean arterial oxygen tension, would indicate a fall in the oxygen tension of those tissues with which the cerebrospinal fluid is in contact. This could be due either to reduced perfusion or increased oxygen utilization.

The Effect of Halothane on Neuromuscular Transmission. A. J. GISSEN, M.D., J. H. KARIS, M.D., and W. L. NASTUK, Ph.D., *Departments of Anesthesiology and Physiology, Columbia University, College of Physicians & Surgeons, New York City.* *Method and Results:* Halothane was studied in the amphibian nerve-muscle preparation to determine its effect on peripheral neuromuscular transmission and at what site it acts. The desired anesthetic concentration was obtained by equilibrating Ringer's solution with a gas mixture of halothane plus oxygen. The blocking concentrations of halothane were found to be: 1.5 per cent for the nerve stimulated twitch, 4 per cent for axonal conduction and 4 per cent for the directly stimulated muscle. From this it was concluded that the peripheral blockade produced by halothane occurs at the neuromuscular junction. The neuromuscular junction was studied by microelectrode penetration of single fibers. Transmembrane resting potential was unchanged following exposure to 4 per cent halothane although the neurally evoked action potential was completely blocked. This was entirely reversible. The magnitude of postjunctional depolarization produced by applied carbachol in a bath and iontophoretically applied acetylcholine (ACh) were decreased by exposure to halothane. Miniature endplate potentials (MEPPs), which reflect postjunctional depolarizations produced by random quantal release of ACh from the nerve ending, were rapidly decreased by application of halothane, and returned to previous levels following its removal. These experiments show postjunctional membrane desensitization by halothane.