Rates of Uptake and Release of Thiopental by Human Brain; Relation to Kinetics of Thiopental Anesthesia. H. L. PRICE, M.D., J. W. DUNDEE, M.D., AND E. H. CONNER, M.D., Departments of Anesthesiology, Hospital of the University of Pennsylvania and Philadelphia General Hospital, and Harrison Department of Surgical Research, University of Pennsylvania, Philadelphia, Pennsylvania.

THE rate of uptake of thiopental by human brain after its injection into arm veins has been estimated. Simultaneous measurements of carotid arterial and jugular venous bulb thiopental concentrations were made by Brodie's method, and cerebral blood flow was estimated by the nitrous oxide method of Kety. The cerebral uptake rate of thiopental was calculated as equal to the cerebral blood flow rate times the arterio-venous concentration difference.

When amounts of thiopental ranging from 150 to 250 mg. were injected rapidly (5 seconds) into the antecubital veins of five subjects, the rate of brain uptake reached a maximum at fifteen to twenty seconds following the end of injection. Brain uptake ceased by the end of 40 to 50 seconds, by which time approximately five per cent of the injected dose was calculated to be in the brain. The concentration of thiopental in jugular venous blood reached a peak between 35 and 50 seconds and thereafter decreased. At the end of approximately 45 seconds the brain began to give up thiopental to blood. Five to seven minutes following the injection the brain content was only fifty per cent of that present at 45 seconds.

The interpretation of these results depends upon how rapidly thiopental taken up by brain reaches and acts upon cerebral neurons. If the effects of thiopental were always directly proportional to the amount present in the brain, the depth of anesthesia following each injection would be greatest 45 seconds after injection, and only half as great a few minutes later. To a large extent this is what actually occurs.

The "depth" of anesthesia at various times following the intravenous injection of thiopental was estimated by three criteria: 1) EEG level, 2) arterial blood pressure, and 3) respiratory tidal volume. In the dose range of 2.5 to 3.5 mg./Kg. body weight, the onset time of EEG level I varied between 14 and 20 seconds after the end of injection. Level II occurred 24 to 37 seconds after injection and persisted until after one minute. The curve of EEG level versus time was, therefore, similar in shape to that of the concentration of thiopental in jugular venous blood.

A more quantitative approach employed the relation between jugular venous thiopental concentration and the decrease in arterial pressure or tidal volume observed at various times after injection. By this method a straight line relationship was found between the concentration of thiopental in jugular venous blood and the degree of arterial hypotension. This relationship began as soon as brain uptake was complete. Similar results were obtained when tidal volume was measured.

It is concluded that the human brain rapidly takes up and equilibrates with thiopental entering it by way of arterial blood. The "depth" of anesthesia produced by thiopental therefore depends on the total volume in which the drug is distributed at various times after its injection. This volume is composed not only of fatty tissues with poor circulation which have a high thiopental capacity per gram, but also of watery tissues which have a large total volume and a relatively rapid equilibration rate.

Effects of Trifluoroethylvinyl Ether (Fluoromar®) on Some Organ Functions. MAX S. SADOVE, M.D., REUBEN C. BALAGOT, M.D., AND HARRY LINDE, PH.D., Division of Surgery, University of Illinois Research and Educational Hospitals, Chicago, Illinois.

ACCEPTED standard function tests were performed on patients before and after exposure to trifluoroethylvinyl ether. Tests were directed at the liver, the kidney, and the cardiovascular system to a limited extent.

Two liver function tests were employed, bromsulphalein excretion and thymol turbidity. The dose of BSP employed was 5 mg./Kg. body weight. Of 32 patients tested