This problem is being pursued further by studying in humans, the changes in tone which occur in normal extraocular muscles following the intravenous administration of succinylcholine. These are detached from the insertion but the origins remain intact leaving normal blood and nerve supplies. In two subjects thus far studied, neither contracture nor contraction of the extraocular muscles has been obtained, probably as a result of too great a depth of thiopental-nitrous oxide anesthesia.

We conclude that succinylcholine can be used in ocular surgery in single doses for tracheal intubation preoperatively (except in patients with acute narrow angle glaucoma in remission) since any rise in ocular tension is dissipated by the time surgery is begun. It may be used with caution throughout an operation as an intravenous drip, if it is begun well before surgery starts and the patient's succinylcholine level is maintained throughout surgery (that is, kept completely paralyzed). It should never be started after actual surgery on the eyes is begun.

Depression of the Myocardium and of Total Body Oxygen Consumption by Fluothane Anesthesia in Man. J. W. SEVERINGHAUS, M.D., AND S. C. CULLEN, M.D., Division of Anesthesiology, State University of Iowa, Iowa City, Iowa.

ARTERIAL hypotension predictably occurs with the administration of (1,1,1 trifluoro-2,2-bromochlorethylene) Fluothane to man and animals. In man, the pulse slows, pupils are small, skin remains warm and dry, with good color, and capillary refill time is normal with pressure as low as 60/45 mm. of mercury. Some have suggested this hypotension is due to ganglionic blockade. The following experiments suggest, however, that the primary circulatory effect of Fluothane is myocardial depression, with no demonstrable component owing to ganglionic blockade in man.

Patients were paralysed with succinylcholine and artificially ventilated with 75 per cent nitrous oxide in an open circuit. Fluothane (1.5 per cent) was added for fifteen minutes, and the change in cardiac output, arterial pressure and central venous pressure determined. The Fluothane was stopped, the autonomic ganglia were blocked with an Arfonad infusion (in 2 patients high spinal sympathetic block was substituted), and the arterial pressure was returned to control levels with an infusion of phenylephrine; after stabilization, the phenylephrine infusion was held at constant rate to provide a constant vascular tone. Following at least forty-five minutes of washout of the previous dose, Fluothane was again given for fifteen minutes in 1.5 per cent concentration, and determinations made of cardiac output and arterial and venous pressure. If the Fluothane depressor effect had been ganglionic blockade in origin, the patients with blocked and stabilized sympathetic responses should have been less depressed by Fluothane. The results showed the contrary, the reductions in cardiac output and arterial pressure being 31 per cent and 21 per cent before blockade, and 42 per cent and 44 per cent in the presence of blockade (7 subjects). Central venous pressure and peripheral resistance rose with Fluothane administration, more in the presence of intact sympathetics. This suggests that myocardial weakening accounts for the major portion of the circulatory depression, and that the sympathetic nervous system tends to compensate partially for circulatory depression due to Fluothane. In a separate group of 6 subjects, oxygen consumption was determined before and during the spontaneous respiration of Fluothane in air, in an open circuit. The average reduction of oxygen consumption corresponding with 1.5 per cent Fluothane appeared to be 15 per cent to 20 per cent.

Cardiac Arrhythmias Produced by Mechanical Stimulation During Hypothermia. KARL L. SIEBECKER, M.D., AND JOHN E. STEINHAUS, M.D., Department of Anesthesiology, University of Wisconsin Medical School, Madison, Wisconsin.

MECHANICAL stimulation of the heart is one of the factors precipitating ventricular fibrillation during hypothermia for cardiac surgery. This factor has been studied under

conditions which simulate those of the operating room, with special attention to the anesthetic agent, the acid-base balance and oxygenation.

One hundred twenty dogs were anesthetized with either cyclopropane, diethyl ether, thiopental and nitrous oxide, or a combination of thiopental, lidocaine and nitrous oxide at either normal body temperature, 27 C. or 20 C. Endotracheal anesthesia was maintained by the to-and-fro absorption technique. A respirator was used throughout all experiments and adequate ventilation was carefully maintained. Hypothermia was produced by surface cooling, and rectal temperature was determined by a thermocouple. After the desired body temperature was reached, the thorax and pericardium were opened. After a 30-minute control period, during which the anesthetic state of the dog was maintained by the anesthetic agent and oxygen, an arterial blood sample was drawn and analyzed for pH, carbon dioxide and oxygen. The surface of the ventricle was then stroked ten times with a blunt probe, followed by cardiac massage for two 30-second periods, one minute apart. After recovery the absorption canister was removed and 10 per cent carbon dioxide was added to the anesthetic atmosphere. Adequate oxygenation was maintained during this period. After thirty minutes the blood sampling and mechanical stimulation were repeated. The canister was then replaced in the circuit, absorbing the carbon dioxide, and a mixture of the anesthetic agent, nitrogen and 15 per cent oxygen was given for a 30-minute period, after which the sampling and stimulation were again repeated.

At normal body temperature, one dog's heart fibrillated after the cardiac massage during the administration of oxygen and cyclopropane and one dog exhibited cardiovascular failure during hypoxia with thiopental, lidocaine and nitrous oxide. We believe it worthy of mention that during the administration of cyclopropane at normal body temperatures, we produced blood pH values as low as 6.84 and pCO_2 values as high as 104 without demonstrating significant cardiac arrhythmias or fibrillation.

At 27 C. there were no ventricular fibrillations or cardiac failures with any of the agents under any condition. When cyclopropane was used at 20 C., all 10 dogs had ventricular fibrillation before hypercarbia or hypoxia could be established. Six dog's hearts fibrillated during cooling, 2 more while the pericardium was being opened and the remaining 2 following the first 30-second massage.

Of the 10 dogs given ether, 6 dog's hearts fibrillated in the control period, 4 spontaneously during cooling and 2 after mechanical stimulation. During the hypercarbic phase of the experiment, one heart fibrillated spontaneously and 2 failed after mechanical stimulation. One dog withstood all insults.

During the administration of thiopental and nitrous oxide anesthesia at 20 C., 4 dogs hearts fibrillated in the control period, 2 during cooling and 2 after stimulation. One cardiac asystole and failure occurred after stimulation in the control period. During the hypercarbic period 3 hearts fibrillated, one spontaneously and 2 after stimulation. Two dogs survived the complete experimental procedure. With the addition of lidocaine intravenously in equal amounts with thiopental and using nitrous oxide supplement, 6 dogs hearts fibrillated during the control period, 5 spontaneously during cooling and one after stimulation. The addition of hypercarbia caused one ventricular fibrillation with stimulation and one spontaneous cardiac arrest. The production of hypoxia in the remaining 2 dogs caused no further demonstrable cardiac damage.

During deep hypothermia a large diphasic deflection of the T–U segment of the electrocardiogram was noted in all dogs that subsequently developed ventricular fibrillation. This type of wave, described by Osborn in 1953, was observed in some dogs whose hearts did not fibrillate, but none had ventricular fibrillation during hypothermia without exhibiting a similar T–U deflection. In one instance of fibrillation at normal body temperature, this type of wave was not recorded.

A "current of injury" manifested by an elevated S–T takeoff was noted frequently following mechanical stimulation, but seemed to have no prognostic value as far as the onset of ventricular fibrillation was concerned. Various abnormalities such as bundle

branch block, mild deviations of the S-T segment, bradycardia and occasionally premature systoles occurred, but with no consistency or prognostic value. (This work was accomplished in the Cardiopulmonary Research Laboratory of the University of Wisconsin Medical School and was supported in part by a grant from the Wisconsin Heart Association and in part from Air Force Contract AF 41(657) 87, Alaskan Air Command, Arctic Aeromedical Laboratory.)

Studies on Newer Analeptics and the Comparison of Their Action with Pentylenetetrazole, Nikethamide and Picrotoxin. BOBBY SMITH, M.D., AND JOHN ADRIANI, M.D., Department of Surgery, Louisiana State University School of Medicine, and Department of Anesthesia, Charity Hospital, New Orleans, Louisiana.

A CONTROLLED clinical evaluation of some of the newer analeptics in comparison to pentylenetetrazole (Metrazol), nikethamide, and picrotoxin was conducted on human subjects. The drugs used were methylethylglutarimide (Megimide), piperidyl acetate (Ritalin), and Win 7969. Thirty-two subjects were included both as controls and as subjects for methylethylglutarimide. They were given 150 mg. of secobarbital, intravenously, two times three days apart. With the second injection, methylethylglutarimide was administered twenty to forty minutes after the secobarbital. Respirations were stimulated both in rate and depth within thirty seconds to sixty-five seconds, and other vital signs returned toward normal. The subjects were completely recovered in two to five minutes. Relapses to the drowsy state occurred in 12 subjects; however, another dose of 50 mg. of methylethylglutarimide restored them to the awakened state.

With piperidyl acetate the same procedure was followed with 33 subjects. In these subjects, all vital signs were stimulated in thirty seconds to ninety seconds. Complete recovery occurred in ten to twenty-three minutes. Side effects noted were nausea in 7; disorientation after recovery in 6; and garrulousness in 8; and relapses occurred in 9 subjects. The dose of this drug was based on 0.2 mg. per pound of body weight.

Win 7969 proved to be a poor over-all analeptic as compared to the other drugs, but was found to be a good respiratory stimulant. In the controlled studies pentylenetetrazole was effective as methylethylglutarimide in activity and time of stimulation; however, the majority of this group relapsed and required subsequent therapy. Nikethamide proved to be less effective than pentylenetetrazole in that 500 mg. provided only mild stimulation for a short period of time. Pictrotoxin had a latent period and side effects similar to piperidyl acetate. Its margin of safety is, however, much narrower.

In addition to this controlled series, methylethylglutarimide was used to treat 35 patients with barbiturate intoxication. These included long acting, intermediate acting, and short acting barbiturates. The majority of these patients (ages ranged from 13 months to 84 years) were comatose. A total of 125 to 1,925 mg. of methylethylglutarimide was given in 50 mg. doses to adults and 25 mg. doses to children. All patients were brought to the point where their reflexes had returned and they could respond to painful stimuli. This required from eighteen minutes to four hours and fifteen minutes in 19 patients. Of the remaining 16 patients, awaking time ranged from twelve to thirty-four hours with regressions in 9 patients who required additional drug.

Twenty-six patients with barbiturate intoxication were treated with 60 mg. to 1,100 mg. of piperidyl acetate. Nine of the patients were awakened in twenty-two minutes to six hours and thirty-five minutes. The remaining 17 were awakened fairly well in the next twelve to forty-eight hours. Some side effects as previously noted were seen. Nine relapses occurred and more treatment was required.

Both methylethylglutarimide and piperidyl acetate have proved more effective than the older analeptics in mild and severe barbiturate intoxication. They tend to shorten the period of depression and reduce complications.