that agent, as far as an acceptable anesthesia goes, and that a patient who is outspoken against the use of a certain agent will have a 'rough' anesthesia if given that one." It may be better to bypass the agent and method of choice and select one less desirable to the anesthesiologist but more desirable to the patient.

During the operative period one must provide the maximum of safety and pain relief for the patient, and as ideal working conditions for the surgeon as possible.

Postoperatively the anesthesiologist is available for consultation and treatment of complications, such as atelectasis or paralytic ileus, and for advice concerning pain relief and fluid administration.

For all of this the anesthesiologist's training must include a general knowledge of medicine, knowledge of the basic sciences, as well as technical training.

The national organization is The American Society of Anesthesiologists, Inc., which publishes ANESTHESIOLOGY bi-monthly. The specialty also has its certifying board and its Scientific Section in the A.M.A.

The specialty's future appears brilliant and its goal is the wider application of safer and better anesthesia.

From the findings of the Anesthesia Study Commission of The Philadelphia County Medical Society, it was determined that 47 per cent of the deaths resulting within twenty-four hours of surgery were preventable. Physicians trained in the specialty were responsible for 29 per cent of these; physicians training, for 38 per cent; others legally permitted, 58 per cent.

There will be more accepted residences; more satisfactory economic arrangements are being made; newer agents and more efficient equipment are anticipated; and the general anesthetic care of the patient will continue to improve. 5 references.

J. R. H.

EVERETT, G. M.: *Pharmacological Studies of d-Tubocurarine and Other Curare Fractions.* J. Pharmacol. & Exper. Therap. **92**: 236–248 (Mar.) 1948.

This report deals with the action of d-tubocurarine, intocostrin (Squibb) and the dimethyl ether iodide of d-tubocurarine in rats, mice, rabbits, guinea pigs, cats, and dogs, with reference to toxicity, excretion, and effects on the cardiovascular and central nervous systems.

The dropping forward of the head, due to the selective paralysis of the neck musculature, is referred to as "head drop" (H.P.) and is a useful sign of curarization. The margin between L.D. and H.D. is the difference in the paralyzing dose for the intercostal and diaphragmatic muscles, particularly those of the neck. As might be expected, this difference is small and consequently there is a narrow margin between effective curarization and respiratory paralysis.

In the rabbit a significant number of head drops appear at 0.125 mg/kg. At the higher dose of 0.175 mg/kg., the number of head drops and complete paralysis increases and more animals require artificial respiration. Because of the clear cut differences observed in the range of 0.125 to 0.175 mg/kg., this range has been utilized in formulating the bioassay for determining curarizing potency of d-tubocurarine.

The toxicity in other species indicates that rats and guinea pigs are more sensitive, having a H.D. of 0.075 and 0.035 mg/kg. respectively.

In a series of 20 rabbits the antagonism of d-tubocurarine by neostigmine methyl sulfate was investigated. From these experiments it appears that neostigmine is more effective when given

prior to curare and is of limited usefulness as an antagonist, since it is effective against just paralytic doses but is ineffective against higher doses. In other experiments it was found that pentamethylentetrazol was also ineffective as an antidote and did not affect the head drop dose.

The fate of curare in the body has been generally accepted to involve partial destruction in the liver and excretion by the kidneys. It was surprising to find, therefore, that in a group of 8 double nephrectomized rats there was no increase in sensitivity to or duration of action of d-tubocurarine given intravenously. Likewise, in 9 hepatectomized rats (70 to 90 per cent of liver removed) no increase in duration was noted. Another group, with both double nephrectomy and hepatectomy, also showed no prolongation of curare action. The present studies do not imply that the kidney and liver may not play a part in excretion or metabolism of d-tubocurarine, but rather indicate that these mammals can detoxify curare without kidney or liver function. This was further supported by the observation that upon injection of the second curare dose, two hours after the first dose, there was no indication of residual curare from the first injection.

The action of d-tubocurarine on blood pressure was investigated. Small doses caused small drops in blood pressure, while with large doses, which produce respiratory paralysis, a more profound fall of blood pressure occurred. The fall in blood pressure is most probably due to peripheral effects with poor venous return resulting from the complete loss of muscle tone, lack of diaphragmatic movements and dilatation of peripheral blood vessels as contributing factors. Injection of a vasopressor agent in most instances produces some increase in blood pressure. Epinephrine was found to be the most reliable.

Pyribenzamine prior to d-tubocurarine in anesthetized cats decreased the transitory drops in blood pressure which follows immediately after curare injection. This transitory fall may be due in part to a release of histamine by curare. The overall gradual decline in blood pressure with increasing larger doses of curare is not prevented however.

The electrocardiographic records made on cats, dogs, and rats indicated no marked change in rate or in the P-QRST complex with large doses of d-tubocurarine. The relatively low cardiotoxic properties of d-tubocurarine was also ascertained in Straub and Langendorf heart preparations.

The electroencephalogram in unanesthetized rats, rabbits, and cats remained unchanged with 5 to 50 times the paralytic dose of curare given intravenously. No signs of central nervous stimulation or depression were seen. When curare is given intracisternally to rabbits it produces violent convulsions even with small amounts.

The results from these experiments may have certain clinical implications with regard to overdosage. The importance of adequate oxygenation and positive artifical respiration to eliminate the effects of anoxia is emphasized. Curare should be used with caution in cases where damage to blood vessels might allow the drug direct access to the brain or cord. 23 references.

R. J. G.

POPKIN, R. J.: *Experiences with a New Synthetic Analgesic, Amidone. Its Action on Ischemic Pains of Occlusive Arterial Disease.* Am. Heart J. **35**: 793–799 (May) 1948.

Pain due to ischemia in occlusive arterial disease is usually severe and prolonged, and the anxiety, restlessness, and general deterioration of pain

resistance undermine the patient's body strength and increase vasoconstriction. As a result, vasodilatation and development of collateral circulation are interfered with and the ischemic process spreads.

Narcotic analgesia has not been too satisfactory. The results of surgical procedures have been disappointing, as have recent methods, such as intravenous ether in saline, intravenous alcohol, and the histidine-ascorbic acid treatment.

Amidone (6-dimethylamino-4, 4-diphenyl-3-heptanone hydrochloride) gives promise of value in this condition. It was given to 18 patients suffering from occlusive arterial disease associated with pain. One or more of the following symptoms were present: rest pain, nocturnal cramps, intermittent claudication, paresthesias, ulceration, and gangrene. The following therapeutic procedures had been tried at various times: intermittent venous occlusion, reflex heat, ionization, histidine-ascorbic acid, intravenous ether and saline, intravenous alcohol, codeine, barbiturates, aminophyline, etc. The drug was given in 5 to 15 mg. capsules or tablets orally. Five mg. per cc. distilled water was used for intramuscular administration.

RESULTS AND DISCUSSIONS

Pain relief was prompt and satisfactory, lasting as long as sixteen hours. Pharmacologic activity appeared within forty minutes after receiving Amidone. Intermittent claudication and pains of dependency and weight bearing were unaffected, but other symptoms mentioned were relieved. Apparently there was some sedative action, but no euphoria. There was no addiction or increase in tolerance. As pain subsided, administration became less frequent.

Pain relief was not due to any increase in peripheral arterial circulation. Blood studies showed no change. There were no changes in pulse, temperature, blood pressure, etc.

Reactions were frequent when patients were upright, but rare when recumbent. Lightheadedness, nausea and vomiting occurred in these, and it was felt it should not be used in ambulatory cases. The more nausea, the less effective the analgesia. If given with meals, nausea was more frequent.

In two patients with bronchial asthma they had difficulty in expectoration after Amidone, indicating a possible codeine-like action.

After seventeen days one patient developed hemorrhagic urticaria. She had a long history of allergic reactions.

SUMMARY AND CONCLUSIONS

Amidone appears to act on the central nervous system, its action resembling morphine. It was well tolerated by the majority of cases when the patient was in the recumbent position. Satisfactory doses were 5 to 15 mg. It was ineffective in intermittent claudication and pain of dependency and weight bearing. There was one case of hemorrhagic urticaria. Blood pressure, pulse, respirations, temperature and oscillometer readings were not affected. There was no increase in arterial circulation. The occurrence of lightheadedness, nausea and vomiting in ambulatory patients who are receiving Amidone appears to be a safeguard in the control of patients suffering from ischemic lesions in peripheral vascular diseases in which bed rest is a very important factor.

J. R. H.