
"Since the early studies of Berger and Bradley... describing the skeletal muscle relaxing properties of mephenesin... presumably through its action on the central nervous system, a large number of chemical agents have been prepared with the intention of simulating the pharmacological action of this agent.... This agent has several shortcomings, among which are its short duration of action and its obvious lack of potency. Subsequent to the discovery of mephenesin a number of drugs have been described pharmacologically which in some respects are improvements over this drug....

"One of the purposes of our study was to compare all these agents [mephenesin carbamate... meprobamate... methocarbamol and zoxazolamine].... A second purpose of this investigation was to describe the properties of another therapeutically useful benzazole, chlorzoxazone....

"Zoxazolamine and chlorzoxazone appeared to be the most potent agents in inducing paralysis especially by the parenteral route. Meprobamate was a potent paralytic drug when administered orally. All the drugs tested with the exception of mephenesin were relatively long-acting compounds.

"Anticonvulsant studies carried out with these drugs indicate that chlorzoxazone possesses potent anti-strychnine activity while having virtually no protective action against pentylentetrazol. Meprobamate displays potent anti-pentylentetrazol activity and has relatively weak protective potential against strychnine. This suggests that chlorzoxazone may act principally at spinal levels and meprobamate at supraspinal levels."


"Indiscriminate use of 'general dilator' agents in the treatment of peripheral vascular disorders is contraindicated because of the possible diversion of blood flow away from already ischaemic tissues.... Several workers have recently reported successful treatment of night cramps, intermittent claudication and various vaso-spastic states with isoxsuprine....

"Thirty patients with peripheral arteriosclerosis involving the lower extremities and 10 normal subjects were studied. The patients had mild to moderate intermittent claudication and were all ambulatory....

"The cardiovascular effects of isoxsuprine have been measured in man. There is an increase in muscle circulation of the calf, with a smaller increase in the skin circulation of fingers and toes. Cardiac output is increased slightly. The agent is well tolerated in doses of 10 mg. intra-
venously or intramuscularly, or in oral doses of 10 mg. three times daily, providing other hypotensive agents are not given concomitantly and providing a tendency toward postural hypotension from other causes does not exist already."


"Oxymorphone (14-hydroxydihydromorphinone), a recently produced morphine derivative, has proved to be a potent analgesic both in animals and man. Although it possesses high addiction liability and is capable of producing hypotension and respiratory depression, oxymorphone has continued to arouse interest because of its reported low incidence of undesirable gastrointestinal actions. . . .

"Two groups of female patients who were awaiting elective surgical operation, most commonly gynecologic, were the subjects of this study. . . . Except for the effects drunk feeling, heavy feeling, itching, and dry mouth, the frequency of all subjective effects was higher after oxymorphone than after morphine. These differences were statistically significant only for the traits sleepiness, nervousness, dizziness, nausea and vomiting. . . .

"Only volunteered information was recorded. Sight difficulty included double vision, difficulty in focusing the eyes, and extreme dizziness. A heavy feeling usually referred to the extremities but at times to the head

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Volume 55

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or 'all over.' A hot feeling included most but not all the patients who perspired; some patients who perspired profusely did not complain of feeling hot.

"It was evident that oxymorphone did not possess lesser subjective side action liability than morphine and the claim of lesser gastrointestinal side actions after oxymorphone was not substantiated in this study."


"In an effort to reduce the flam-mability limits and also the expense of production, Fluoromar was mixed with 1, 1, 2-trifluoro-2, 2, 1-trichloroethane (Genetron 113) with which it forms an azeotropic mixture. . . . These studies describe the pharmacologic properties of this azeotropic mixture (AZT) and certain characteristics of Genetron 113. . . .

"Fluoromar and Genetron 113 form an azeotropic mixture which produced anesthesia in the rat, dog and monkey. AZT evokes an anesthetic syndrome similar to Fluoromar. These studies indicate that anesthesia with AZT does not produce deleterious effects upon the liver function or cardiac rhythm of the dog and, upon perfusion, the heart of the frog. Histologic studies revealed no pathologic findings in the lung, brain, kidney or bone marrow of the rat after 1/2-hour and 1-hour anesthesia with AZT over 7-day intervals. The multiple bursts of cerebral electrical activity evoked by anesthesia with Genetron 113 is not uncommon with certain fluorinated hydrocarbons or ethers. It appears that the depressant action of Fluoromar in AZT is sufficient to abolish the aberrant cerebral electrical activity.

"AZT, in its vaporized form at body temperature, retains the approximate composition of the azeotropic mixture in the liquid state. The two agents appear to exhibit synergistic anesthetic activity. The mixture affords the advantage of absence of explosive hazard and lower production cost.

"These experiments indicated that AZT exhibited desirable anesthetic properties in a variety of laboratory animals and in our opinion warranted trial by man. One of us (J. C. K., Jr.) administered AZT by the open-drop method to a patient requiring dilatation and curettage. She was premedicated with atropine sulfate and secobarbital sodium. The induction was smooth and rapid. Respiration and blood pressure remained essentially unaffected. Abdominal relaxation was good. The anesthesia was maintained for 30 minutes. Recovery was uneventful and occurred within 2 minutes after the discontinuance of the agent. There was no nausea or vomiting postoperatively. Constant observation of the hands and feet revealed no tremors as we had occasionally seen in animals."


"We have re-examined the problem of morphine-nalorphine action and interaction using a recently available apparatus which permits quantitative analyses of some of the parameters of the EEG. . . . All experi-
ments were performed on adult male albino rabbits. It has been found that the curves relating log-dose/effect are not the same for the effects of these drugs. The blocking action of nalorphine on morphine revealed an apparent all-or-none threshold of action and a proportionally longer duration of action for small doses of nalorphine than for large doses.


"It is now generally accepted that decamethonium may block neuromuscular transmission either by prolonged depolarization of the motor end-plate or by competition with acetylcholine. The purpose of the work described in this paper has been to investigate the action of decamethonium on neuromuscular transmission in the cat by a different technique from that used by Jewell & Zaimis. The preparatory operations were performed on 8 cats under ether anaesthesia.

"During continuous intravenous infusion of decamethonium it was found that this drug had a dual mode of action on both the tibialis anterior and the soleus muscles. Shortly after the infusion of decamethonium had begun, the neuromuscular block had the characteristics of a depolarization block. When the infusion of decamethonium had continued for some time, the neuromuscular block changed to a more curare-like block. This was found both in the tibialis anterior and in the soleus, but the change in mode of action occurred earlier in the soleus than in the tibialis."


"The glucan dextran, a polymerized glucose, when injected into rats induces the "anaphylactoid" inflammation. We reported that insulin administration sensitizes to this inflammation. Conversely, the lack of insulin, such as it exists during alloxan diabetes, totally inhibits the inflammation. However, in alloxan diabetic rats, the true hypoinsulinism results in a secondary relative glucose overdosage of the animal. The role of such an overdosage in the inhibition of the inflammation has been investigated now.

"Rats overdosed with glucose, and displaying a lasting glucosuria do not undergo the anaphylactoid inflammation when injected with the glucan dextran. The mechanism of insulin sensitization to the dextran anaphylactoid inflammation could be explained partly as follows. Insulin diminishes in various ways the amount of "free" monomolecular glucose in the organism of the rat, leaving the transport mechanisms freer to carry the glucan dextran across cell barriers, in larger amounts, to the sites of the anaphylactoid inflammation. The over-all effect of insulin is therefore a potentiation of the inflammation."