and without any infection, such as was occasionally noted in cases in which ethyl chloride had been used. In all the above cases the concentrations of the benzyl alcohol employed ranged from 0.5 per cent. to 4 per cent. and such solutions were never found to be noticeably irritant to the tissues. As far as the authors have been able to learn none of the other commonly used local anesthetics such as cocaine, novocain, alypin, etc., can be said to possess antiseptic properties. It is therefore interesting to call attention to the antiseptic properties of benzyl alcohol as a desirable concomitant of its anesthetic action.

18 (1393)

On the action of opium alkaloids on Trypanosoma brucei.

By D. I. MACHT and J. WEINER.

[*From the Pharmacological Laboratory of Johns Hopkins University and James Buchanan Brady Urological Institute, Baltimore, Md.*]

In a paper on the "Toxic Action of Opium Alkaloids Individually and in Combination with Each Other on Paramecia," by Macht and Fisher,[1] it was shown that some of the opium alkaloids were very toxic for that organism while others produced very little effect on it. It was found that the benzyl-isoquinolin group of alkaloids of which papaverin is the principal representative killed paramecia very quickly; whereas the pyridin-phenanthrene group of which morphin is the principal member was comparatively non-toxic. A further analysis of the papaverin action proved that the toxicity of that alkaloid was to be ascribed to the presence of the benzyl radicle in its molecule. Following the above investigation, it was interesting to inquire into whether the opium alkaloids are also toxic for other forms of protozoa, and especially for trypanosomes. The present authors have accordingly undertaken the study of the action of various opium alkaloids and their derivatives on *Trypanosoma brucei.* The organisms were obtained through the kindness of Dr. Wade Brown, of the Rockefeller Institute for Medical Research.

[1] Macht and Fisher, *Jour. of Pharmacol. and Exp. Therap.*, 1917, x., 95.

Experiments in vitro revealed as in the case of paramecia that the papaverin group of opium alkaloids was very toxic for trypanosomes. Papaverin itself in dilutions of 1 to 10,000 markedly inhibited the movements of the organisms in a few minutes and killed them completely within thirty minutes. Similarly the alkaloids narcotin and narcein were also found to be very toxic for trypanosomes in vitro.

Contrary to expectations however the morphin group of alkaloids while not as toxic as papaverin was also found to be deleterious to the trypanosomes, but in a much lesser degree. Dilutions of morphin sulphate 1 to 2,000 did not kill the organisms within an hour but were found to inhibit slightly their movements after the lapse of some ten minutes. Stronger solutions of morphin, for example 1 to 2,000, inhibited the movements and killed the parasites in less than half an hour. A similar action was noted in cases of codein and thebain. Heroin was found to be more toxic than morphin and killed the organisms in about fifteen minutes.

A comparative study of various alkaloids in addition to those already mentioned, namely, benzyl morphin or peronin, cotarnin, hydrastin, hydrastinin, and others seemed to point as in the case of paramecia to the benzyl grouping as the toxophoric portion of the papaverin molecule.

Having studied the effect of papaverin on trypanosomes in vitro some experiments were made on infected rats to ascertain whether that alkaloid could be employed in curing the infection with trypanosomes *in vivo*. It was found that small doses of papaverin had no effect in shortening the course of the disease when injected into rats. Neither were small doses of benzyl benzoate or benzyl alcohol efficient in this respect. These findings were not at all surprising as it is well known that experimental results with anti-syphilitic drugs in vitro can not at all be taken as an index to the clinical use of the same.