form precisely to the accounts given by Chagas[3] and others in morphology, attachment to corpuscles, and tissue invasion. The Leishmania-like stages of the trypanosome occur in heart muscle and are accompanied by the typical degenerative processes.

We therefore conclude that the trypanosome (*Trypanosoma triatomae,* Kofoid and McCulloch) of the cone-nose bug (*Triatoma protracta*) in California is identical with that found in *Triatoma megista* and in other Reduviidae of South and Central America known to be vectors of Brazilian human trypanosomiasis.

The determination of this identity extends the geographical range of the infected insect vector into the Southwestern United States. Mammals naturally infected have not as yet been discovered in this region, but further investigation by splenectomizing suspected mammals in regions where infected bugs are found may be expected to reveal the infection.

6542

Comparative Physiological Action of Quaternary Ammonium Salts of the Epinephrine Series.*

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The classical studies of Barger and Dale[1] on the relationships between chemical constitution and physiological action of compounds related in structure to epinephrine included 3 quaternary ammonium salts, hordenine methiodide, 3:4-dihydroxyphenylethyl trimethyl ammonium chloride and trimethylaminoacetocatechol chloride. These compounds were found to resemble nicotine, rather than epinephrine, in their physiological actions and the conclusion was tentatively drawn that the relative intensity of these effects paralleled the relative intensity of the sympathomimetic action of the corresponding amino or methylamino derivatives. It became of interest to see if this generalization would hold for other quaternary ammonium salts of the epinephrine group of com-

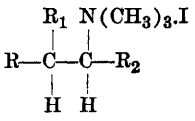
[3] Chagas, C., *Mem. Inst. Oswaldo Cruz,* 1909, **1**, 158.

* Supported in part by the Christine Breon Medical Research Fund.

[1] Barger, G., and Dale, H. H., *J. Physiol.,* 1910, **41**, 19.

pounds, since it might be considered to indicate a close similarity in the processes by which nicotine and epinephrine act upon their respective cellular mechanisms.

Sixteen compounds of this type have been synthesized and studied. Their structures may be represented by the general formula, where R is C_6H_5-,



p-HO-C_6H_4-, p-CH_3O-C_6H_4-, p-CH_3COO-C_6H_4-, or m, p-$(HO)_2$-C_6H_3-; R_1 is H, OH, $OCOCH_3$ or $OCOC_6H_5$ and R_2 is H or CH_3.

In general, all of these compounds exert a certain degree of activity resembling that of nicotine, with regard to their central nervous system and circulation effects as indicated by the respiratory and pressor responses in dogs following their intravenous injection. Many of these compounds are intensely active, some more active than nicotine on injecting molecularly equivalent concentrations, and the circulatory effects of almost all these compounds in comparison with their central nervous system effects seem to be relatively greater than observed with nicotine. Secondary depression following the stimulant action of this class of compounds appears to be less marked than observed with nicotine, which was also commented upon by Barger and Dale.

Certain generalizations seem to be quite constant in the series of compounds studied and often indicate a lack of parallelism of the effects of substitution with the quaternary ammonium compounds and the corresponding substitution effects with the amino or methylamino compounds. With the present series of compounds, it was observed that: (1) The introduction of a phenolic hydroxyl group in the para position to the side chain has little effect upon the intensity of the action of the quaternary ammonium salts, while two phenolic hydroxyl groups, one in the meta and the other in the para position more than double the activity of the parent phenyl compound. (2) Acetylation of a phenolic hydroxyl group does not markedly change the action of these quaternary ammonium compounds. (3) Methylation of a phenolic hydroxyl group decreases the activity a hundred times or more. (4) The introduction of a α-methyl group, resulting in a 3 carbon atom side chain, increases the activity by 2 times or more. (5) The introduction of an alcoholic hydroxyl group into the β-position of the side chain decreases the

activity from 50 to 100 times, or more. (6) Acetylation or benzoylation of a β-hydroxyl group does not markedly alter the activity. (7) The activity of stereoisomers involving asymmetry of the β-carbon atom of the side chain, caused by hydroxyl substitution, are not very different.

No analysis has been made of the exact mechanisms of action of these various compounds other than their general correspondence of effect with that of nicotine. Probably certain differences in the mechanisms of their effects will be found after further study but the quantitative picture of total respiratory and circulatory activities seems to be clearly related to the structure of the compounds studied and further work is in progress to define more completely these relationships.

6543

Methylene Blue as an Antidote to CO Poisoning.*

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This paper is a continuation of the study of the use of methylene blue in antagonizing the effects of CN and CO poisoning in whole animals[1,2].

In these experiments CO was administered to rabbits which had been tracheotomized. A cannula was inserted in the trachea which was then directly connected with the vessel containing the measured CO. The inspired air was separated from that expired by means of a valve. The experiments were done in two parts:

1. Injections of 1 cc. of .01% methylene blue in Ringer solution per kilo body weight were made intravenously a few minutes before CO was administered. CO (10% by volume in air) was then given until the animal stopped breathing. It was found that the peak of the variation curve for control animals was at 4.5 minutes where 39% stopped breathing, whereas the peak of the curve for those animals receiving methylene blue treatment, was at 6.5

* Aided by grants from the Board of Research of the University of California and by Dr. J. C. Geiger, Director of Public Health of City and County of San Francisco.

[1] Brooks, M. M., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1228.

[2] Brooks, M. M., *Am. J. Physiol.*, 1932, **102**, 145.