4. Carbon appears to exert a mild aggressin-like action upon the subcutaneous tissues, making it possible for these bacteria to maintain their existence and multiply locally in spite of the defensive mechanism of the animal body.

5. The serum of the carbon-plus-proteus animals agglutinated the organisms up to a dilution of 1-100, the same as did that from animals receiving the proteus alone, indicating that the presence of the carbon did not modify the agglutinative power of the serum.

6. The method developed has reduced the initial mortality of animals, after injection of *B. proteus* x 19, and has enabled the organisms to resist the bactericidal powers of the body for relatively long periods of time.

180 (2412)

The action of ephedrine, an alkaloid from Ma Huang.

By K. K. CHEN and CARL F. SCHMIDT.

[*From the Laboratory of Pharmacology, Peking Union Medical College, Peking, China.*]

Ma Huang, identified as *Ephedra vulgaris* var. *helvetica,* has been known to Chinese medicine since about 3100 B. C., when it was one of the herbs tested and approved by Emperor Shen Nung. According to the Pen Tsao Kang Mu (the Chinese Dispensatory, 1596) it improves circulation, causes sweating, stops cough, reduces fever, etc.

Nagai[1] obtained from the plant an alkaloid which he named ephedrine, and which he[2] found to possess a mydriatic effect. Amatsu and Kubota[3] described a rise in blood pressure and relaxation of the intestines after ephedrine. Merck[4] isolated from the European variety of *E. vulgaris* an alkaloid named pseudoephedrine isomeric with ephedrine.

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[1] Nagai, *Pharm. Z.,* 1887, xxxii, 700.

[2] Nagai, *Chem. Z.,* 1888, 755.

[3] Amatsu, H., and Kubota, S., *Kyoto, Igaku, Zosshi,* 1917, xiv, 77, through *Chem. Abs.,* 1918, xii, 2019.

[4] *Merck's Ber.,* 1893, 13.

In our preliminary investigation an intravenous injection of a simple extract of the crude drug to an anesthetized dog caused a sustained rise in blood pressure, accompanied by prolonged acceleration of heart and constriction of kidney vessels. An alkaloid was soon isolated from the drug and found to have the same effects. This alkaloid has been identified as ephedrine.

The injection of 0.25 to 10 mg. of the alkaloid into a vein of a dog or cat always causes a prolonged rise in blood pressure, cardiac acceleration, and constriction of peripheral vessels. In addition, intestines are relaxed and peristalsis inhibited, uterine tone is increased—these effects are the same in surviving tissues as in those in situ—pupils are widely dilated, and bronchial muscle is relaxed.

After the destruction of the brain and cord the drug acts as before, so that its effects are peripheral. A direct muscle action is eliminated by the tonic action on uterus and blood vessels and inhibitory action on gut and bronchi—effects that point to parasympathetic depression or sympathetic stimulation. That the parasympathetic is not paralyzed is shown by electrical stimulation of the vagus, for the weakest current that slowed the heart continues to be effective during the acceleration produced by ephedrine. Also, the pupil dilated by ephedrine, or the gut inhibited by it, is contracted by pilocarpine.

The most striking effects are those on the circulation. The myocardiograph shows greatly increased strength of contractions when acceleration occurs following the drug, but the isolated mammalian heart is only moderately stimulated by very dilute solutions and stronger concentrations cause pure depression. Application of the drug directly to the stellate ganglion causes a marked increase in rate and strength of contractions comparable to the first effect of local application of nicotine, but ephedrine does not paralyze after stimulating; after local application of nicotine to the ganglion, ephedrine applied locally has no effect, so that its action is not due to absorption from the pleura. The cardiac and blood pressure effects of application of ephedrine to the stellate ganglion are less marked than those of intravenous injection. Intravenous injection of toxic doses of nicotine does not prevent the typical ephedrine effects on heart and blood pressure in dogs.

The action of ephedrine on the heart appears to be (1) stimulation of accelerator ganglia; (2) stimulation of accelerator endings; (3) direct depression of heart muscle.

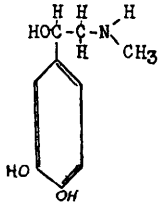
Peripheral vessels are constricted by ephedrine, but this effect is relatively weak and is often overcome by cardiac stimulation. The vessels of the perfused kidney show definite and prolonged constriction, while those of the perfused lung are affected only slightly. These effects are apparently not concerned with ganglia, for the volume of the kidney in situ is not affected by application of the drug to the thoracic ganglia, and after intravenous injection of nicotine ephedrine causes marked vasoconstriction.

The circulatory effects of one injection of ephedrine persist for 10 to 15 minutes. Repeated injections soon fail to cause further acceleration or augmentation of the heart, but a progressive rise of pressure occurs as a result of progressive vasoconstriction until a maximum is reached, often at a sustained pressure level of over 200 mm. Hg, even in a spinal animal. Beyond this, further injections cause pure cardiac depression.

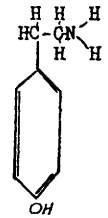
The other effects of the drug—on gut, uterus, pupil, bronchial muscle—are apparently due entirely to the stimulation of sympathetic endings. After nicotine the isolated gut is inhibited and relaxed by ephedrine, while pilocarpine stimulates after nicotine and ephedrine. The pupil is widely dilated when ephedrine is applied to the conjunctiva, while application to the superior cervical ganglion has no effect. The light reflex is not abolished by ephedrine, and pilocarpine action is not prevented. Bronchial spasm due to physostigmine is relaxed by ephedrine.

The action of ephedrine is therefore similar to that of adrenaline. Compared to adrenaline, ephedrine action is much more persistent; its cardiac effects are relatively stronger than its vascular action, which may be due to simultaneous stimulation of accelerator ganglia and endings; its action on the circulation soon reaches a maximum beyond which repeated doses fail to stimulate, and may cause depression.

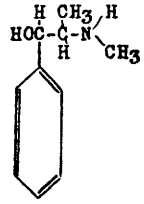
The similarity of the effects of ephedrine to those of tyramine and adrenaline is especially interesting in view of the similarity in chemical structure.



Adrenaline
Jowett[6]



Tyramine
Barger-Dale[6]



Ephedrine
Ladenburg[5]

It properly belongs to the group of "sympathomimetic amines" of Dale.[6]

The acute toxicity of ephedrine is low, the m.l.d. lying between 100 and 145 mg. per kilo in rats. These doses cause cocaine-like convulsions, which are probably the cause of death.

Further chemical and histological investigations of the plant are being made and a method of assay has been devised.

181 (2413)

The experimental transmission of leishmaniasis to animals.

By H. JOCELYN SMYLY and CHARLES W. YOUNG.

[*From the Department of Medicine, Peking Union Medical College, Peking, China.*]

On December 18th, 1922, an autopsy (No. 3853) was performed on a patient who had died of kala-azar that day in the Peking Union Medical College Hospital. The spleen was found to be unusually heavily infected with *Leishmania donovani*, spleen smears showing hundreds of organisms in every field under the 1.9 mm. oil immersion objective. A portion of the spleen was taken, using sterile precautions, ground in Rosenow's tissue crusher, and mixed with 0.85 per cent salt solution to make an emulsion which easily passed through a fine hypodermic needle. The same suspension was used to inject the following series of animals, all of which were injected intraperitoneally except the dogs which were injected intravenously:

[5] Ladenburg, A., and Oelschaegel, C., *Ber.*, 1889, xxii, 1823.

[6] Barger, G., *The Simple Natural Bases*, 1914.