No significant change in blood sugar level was noted. In the one instance when the insulin was placed beneath the positive pole there was no important change in blood sugar level.

On 6 occasions insulin was placed beneath the negative pole and in each experiment there was a drop in blood sugar. The smallest fall was 12 mg per 100 cc; the largest 32 mg per 100 cc. In one dog the level of blood sugar dropped from 59 mg per 100 cc to 33 mg per 100 cc and at this period the animal showed signs of an hypoglycemic reaction.

It was not possible to predict when the sugar would fall. At times it occurred within an hour or two after the termination of iontophoresis. In other experiments it occurred later.

The thought naturally occurs as to the propriety or advisability of using such a form of administration in the treatment of diabetes in man. The data we have obtained do not permit us to draw any conclusions. However, it might be pointed out, as we have noted not only in these experiments but in those in which acetyl beta methylcholine was used in man, that there is apparently considerable variation in skin resistance in different individuals. It is conceivable that a technic might be developed which could control the variable skin resistance and deliver a known amount of insulin to the body. Such a method would offer the particularly desirable condition of providing a slowly absorbable supply of insulin.

Summary. A fall in blood sugar in dogs has been demonstrated following cathode iontophoresis with insulin.

9937 P

Physiological Effects of Some Thio-Esters of Choline.

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The effects on blood pressure and respiration produced in cats and dogs under morphine-urethane, nembutal and chloralose anesthesias, by intravenous injections of thio-acetyl choline chloride, thio-acetyl-gamma-homo-choline chloride and thio-acetyl-beta-methyl choline chloride have been observed and recorded.* Eighteen

*The chemistry of these compounds will be reported separately.

animals (10 cats and 8 dogs) have been used in these experiments. Records were taken of the results of over 200 injections, of which approximately one-third was of each of the 3 compounds. The results of the administration of each compound were constant.

Thio-acetyl-choline chloride and thio-acetyl-gamma-homo choline chloride are almost identical in their effects. Immediately following injection the blood pressure falls slightly, then rises rapidly to 60 to 90 mm Hg above the normal level. During this rapid rise the heart rate increases but upon reaching the peak pressure the rate slows and large vagal beats appear. The duration of this bradycardia varies from one to 5 minutes depending upon the amount of the compound injected. During this period the blood pressure gradually falls to normal, which level is reached in 2 to 10 minutes. Hyperpnea of short duration immediately follows injection. This hyperpnea is followed by depression with gradual return to normal.

Thio-acetyl-beta-methyl choline chloride produces a moderate depressor action but has no effect upon the respiration. B.P. falls 30-50 mm Hg and is not accompanied by changes in heart rate.

The minimum effective dose is of the order of .016 mg/kg. When larger dosages are used (.5-1 mg/kg) the animals rapidly pass into a fatal apnea.

Atropine sulphate abolishes neither the pressor response nor the hyperpnea caused by thio-acetyl choline chloride and thio-acetyl-gamma-homo choline chloride, but eliminates the bradycardia. The depressor action of thio-acetyl-beta-methyl choline chloride is abolished by atropine. Physostigmine does not augment the action of any of these compounds. Section of the vago-sympathetic trunk alone does not eliminate the pressor responses to thio-acetyl choline chloride and thio-acetyl-gamma-homo choline chloride but diminishes the hyperpnea. Denervation of the carotid sinuses alone does not affect the hyperpnea of thio-acetyl choline chloride or of thio-acetyl-gamma-homo choline chloride. No carotid sinus denervation has been carried out with thio-acetyl-beta-methyl choline chloride.

After denervation of the carotid sinus and section of the vago-sympathetic trunk in the neck, thio-acetyl choline chloride and thio-acetyl gamma-homo choline chloride have no effect upon respiration but still produce their pressor effect which is preceded by a slightly augmented depressor response.

The duration of the action of these compounds indicates that they are probably destroyed rather rapidly by the blood. Thio-acetyl-beta-methyl choline chloride is very evanescent in its action and is probably hydrolyzed more rapidly than the other two thio-esters.

When thio-acetyl choline is placed in freshly drawn blood and allowed to stand at room temperature for 30 minutes to one hour, its action is greatly reduced and in some cases reversed.

The results suggest that thio-acetyl choline chloride and thio-acetyl-gamma-homo choline chloride have a nicotine-like action; however, when respiratory failure occurs, stimulation of the phrenic nerve still causes tetanic contraction of the diaphragm. Thio-acetyl-beta-methyl choline chloride has a muscarine-like action; however, its action is not augmented by physostigmine.

9938 P

Attenuation of Toxins by Interfacial Adsorption.*

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The writer has previously demonstrated that crystalline insulin[1] can be attenuated by interfacial adsorption. In the same communication reference was made to the fact that bacterial toxins can also be attenuated by a similar procedure. It has been found by additional experimentation that ricin, tetanus toxin, staphylococcus toxin and snake venom may be completely detoxified by this method and still retain antigenic properties adequate for purposes of immunization, as demonstrated with rabbits and mice. The following data are representative of the results which have been obtained.

"C.P. ricin" which will produce a pronounced erythema, induration and necrosis when 0.2 cc of a solution of 1 part of ricin in 25,000,000 parts of saline are injected intradermally into rabbits will produce only a faint erythema when equal volumes of the same ricin in dilutions of 1 part of ricin in 1,000 parts of saline are injected after 2 treatments of 48 hours each with chloroform. When triple injections of untreated ricin in dilutions of 1 part ricin in 1,000,000 parts of saline were injected intradermally into rabbits which had been immunized with completely detoxified ricin, only a faint erythema was produced at the site of each injection. When

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1 Johlin, J. M., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 523.