In addition to the morphologic data herein reported, we have observed that the urine from animals in shock frequently contained large quantities of R. B. C., hyaline, and granular casts. Conclusive evidence of an hemoglobinuria was not obtained.

It must be emphasized that the intravenous injection of concentrated trypsin solutions (2% to 4%) in rabbits results in rapid death, within a few minutes after the injection, or even while the injection is in progress. Examination of such animals reveals extensive intravascular clotting, all chambers of the heart being filled with thrombus. In some respects this response is similar to the anaphylaxis-like syndrome produced by trypsin as described by Roche e Silva[3] and Dragstedt[4] although they do not attribute the collapse and death to the intravascular clotting which we have observed.

Data not yet reported lend support to the possibility that with extensive tissue damage some proteolytic enzyme is released or activated which in turn may be responsible not only for changes at the site of injury, but also for the production of catabolic factors whose effects may be reflected in renal, hepatic, and other systemic functional and structural depressions.

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Paroxysmal Pulmonary Edema: A New Experimental Method.

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We have studied pulmonary edema following rapid infusion of massive doses of fluid into the circulation of dogs. Infusion into either the femoral or the jugular veins, or the femoral arteries was tried in 14 dogs with inconstant results. The rapid infusion of fluid into the carotid arteries toward the brain was therefore used to induce pulmonary edema constantly.

Technique. Experiments were performed on 18 dogs weighing from 8 to 20 kg, under morphine (3 mg/kilo)-urethane (1 g/kilo) anesthesia. Infusions were given simultaneously into both carotid arteries under a pressure of 280-300 m/m Hg. The total quantity of fluid injected amounted to 2.3 times the animal's estimated blood volume (on the basis of an assumed blood volume equal to 10% of body weight). A first infusion amounted to 85% of the blood volume and required from 1 to 2.5 minutes. A second infusion equivalent to 80% was given 10 minutes later. A third infusion equivalent to 65% of the blood volume was given 5 minutes after the end of the second. If the animal survived, it was sacrificed 7 minutes after the end of the last infusion.

Edema of the lungs was evaluated by: (a) weighing the lungs and calculating the lung/body index; (b) examining the gross appearance of the lungs and the presence of foam in the trachea; (c) studying the fluid pouring out of the cut parenchyma. Venous pressure, arterial pressure, X-ray of the chest and electro- and phonocardiograms were studied in some animals.

Results. 16 of the group of 18 dogs studied developed severe pulmonary edema after infusion with: (a) Tyrode solution; (b) physiologic salt solution; (c) bovine albumin solution; (d) oxygenated dog's blood.

Pulmonary edema occurred in all 4 types of infusion, with increasing severity from (a) to (d), but dyspnea was more severe with saline than with the other fluids.

Having obtained a reliable technique, we

have studied the effect of different surgical and mechanical procedures, and drugs, on the occurrence and severity of the edema. These studies are continuing and, therefore, only a brief summary of the results is given here.

Procedures useful in preventing or minimizing the edema were: (a) Intratracheal positive pressure; (b) bleeding during the infusion, and (c) denervation of the carotid sinus.

Useful drugs were: (a) Drugs inhibiting the sympathetic system (883 Fourneau,* ergotamine); (b) Curare; (c) Narcotics (barbital, phenobarbital, morphine, chloral); (d) Procaine (subcutaneous injections); (e) A combination of atropine and physostigmine.

Comment. A definitive interpretation of the results will be possible only after completion of the study. However, the experiments appear to show that stimulation of the cardiovascular receptors (chiefly those of the carotid sinus) has a prominent part in the genesis of our type of experimental pulmonary edema by increasing in a reflex way the permeability of the lung capillaries.

* 2-diethylamin-ethyl-1,4-benzodioxan is the formula of 883F.

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Experimental Alloxan Diabetes in Hooded Rats.

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Following the demonstration of Shaw Dunn and his collaborators[1,2] that alloxan, administred intravenously, produces rapid necrosis of the islets of Langerhans in rabbits, various investigators have observed the same effects on the islets and the development of persistent diabetes following parenteral injections of alloxan in rabbits,[3-6] white rats,[7,8] and dogs.[9,10] Gomori and Goldner[8] failed to produce these effects in 5 hooded rats given intraperitoneal injections of alloxan in doses of 200 mg per kg of body weight and, accordingly, they considered hooded rats resistant to alloxan.

On the contrary, we have found islet lesions and disturbances of blood sugar levels without exception in more than 60 hooded rats injected subcutaneously with alloxan (Eastman) in doses of 175 to 350 mg per kg of body weight. In these experiments a single injection of a 5% solution of alloxan was employed in each case. Blood sugar determinations were made by a modified Folin micro method as frequently as every 1 or 2 hours during the first 12 hours, every 3 to 6 hours up to 48 hours and at longer intervals thereafter. The animals either died, were killed when moribund or were sacrificed at desired intervals. Complete autopsies were performed in every instance and tissues appropriately fixed for histological staining with haematoxylin and eosin, Best's carmine stain for glycogen and Gomori's stain for granules in islet cells of the pancreas.

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