The dogs were trained to run freely on a treadmill whose belt speed was 450 feet per minute. Rest periods at varying intervals during the exercise permitted the drawing of blood samples from the heart, and allowed the animals to regain their normal breathing. The total actual exercise varied from 30 minutes to 240 minutes.

The results from 10 experiments on 3 dogs showed:

1. Inorganic phosphorus in the blood of starved dogs taking standard exercise, at first decreased considerably (65 per cent in 90 minutes exercise), and then with continued exercise, rose towards the normal. During recovery, inorganic blood phosphorus rose to values approximately 60 per cent above normal. Total acid-soluble phosphorus of the blood paralleled its inorganic fraction during exercise and recovery. Sugar, calcium, and the percentage of corpuscles in the blood remained relatively constant.
2. Dogs that had not been starved showed very much less marked blood phosphorus changes with exercise. (30 per cent initial decrease in 60 min. exercise.)
3. A given duration of exercise produced a definite inorganic phosphate concentration in the blood.
4. Changes in the concentration of blood inorganic phosphate during recovery from exercise were independent of the duration of exercise.

This is a preliminary report.

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Scarlatinal Nephritis Experimentally Induced in the Dog.*

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Since the publication[1] of the results of our studies upon experimental nephritis in the rabbit with the toxic principle of *Streptococcus scarlatinae*, we have found that the dog is a more satisfactory animal for the purpose of causing nephritis with this particular injurious agent. This animal has proven to be not only highly susceptible to infection but developed regularly a severe and often fatal form of acute glomerulonephritis following the injection of the specific streptococcal toxin alone. None of the animals showed at any time an exanthem; however, it is significant that the induced

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kidney lesions completely correspond histopathologically to the glomerular and acute interstitial scarlatinal nephritis of man.

This communication is a brief report of the effects upon the kidneys of the dog produced by the viable culture and also the pure toxin of *Streptococcus scarlatinae*.

All dogs employed in the experiment were healthy and under three years of age. The animals were kept under close observation for a period of ten days prior to inoculation, during which time daily analysis of the urine was made and the blood chemistry determined. Only dogs that showed normal kidney function throughout this period were selected for the experiment. The preliminary study of the urine and blood was carried out by our colleague, Professor Denis, of the department of biochemistry.

Infectivity of the Dog. Six full-grown, healthy dogs were inoculated with living cultures of *Scarlatinal streptococcus*. Two animals received the injection intravenously, two subcutaneously and two intraperitoneally. In each instance the dosage was 10 mills of the surface growth from slanted sheep-serum agar which had been washed off and suspended in 50 mils of sterile normal saline. All animals of the series promptly developed a generalized infection and died in 2 to 5 days following the inoculation. Daily urine examination showed pus, blood, albumin and casts. At autopsy there was revealed the usual signs of sepsis, and in addition a markedly acute hemorrhagic nephritis.

Toxin Effects upon the Kidney of the Dog. Eight young, healthy dogs were injected intravenously with 5 mils each of filtered streptococcal "lysate" which had been prepared *in vivo* after the method described by us in a previous publication.[2] The animals developed within 4 to 6 hours symptoms of toxemia, and 24 hours later were extremely ill. The urine macroscopically was bloody and analysis showed quantities of albumin, granular casts, bile and blood. Two of the animals died on the fourth and 3 on the fifth day following the inoculation. The others survived, and though apparently well have continued to show, at intervals, albumin and casts in the urine. Two months later these survivors were sacrificed and the kidneys revealed varying degrees of chronic diffuse nephritis.

The Kidney Pathology Induced in the Dog. Constant and significant structural changes occur in the kidney of the experimentally produced nephritis with *Streptococcus scarlatinae*. The lesions are primarily glomerular or interstitial, the determining factor depending upon the character of the material employed. For example, the glomeruli are first affected where the toxic principle alone is used,

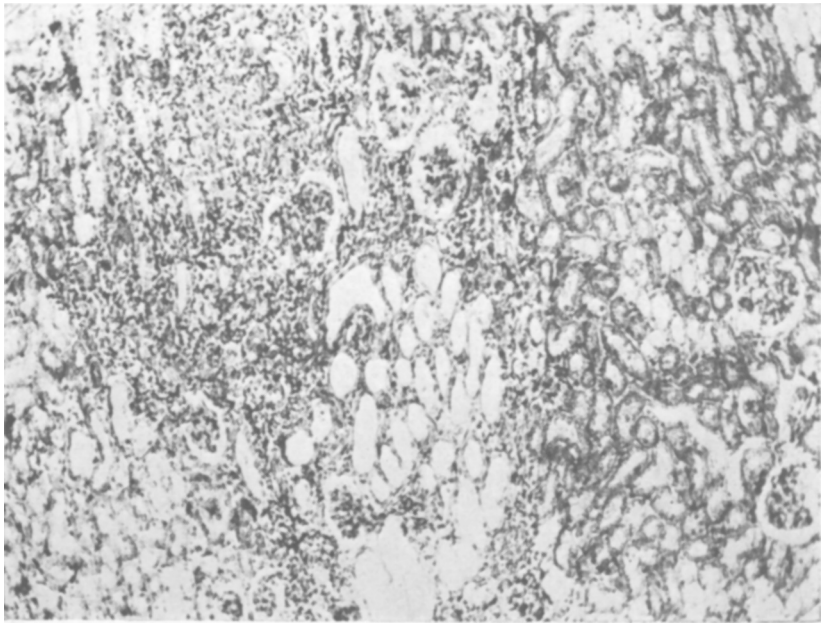
and regardless of whether the injection is made intravenously or subcutaneously. On the other hand the primary interstitial lesion occurs in the animals inoculated with the living culture, and in which a generalized infection has resulted.

The acute interstitial lesion is a focal infiltration of the intertubular tissues with cells of the lymphocytic variety. As a rule the neutraphiles are absent or only few in number; however, in some of the more advanced lesions they occur but are not as numerous as the lymphoid and plasma cells. Associated with the interstitial lesion are viable streptococci which are readily demonstrable in stained sections and recoverable in pure culture from the fresh tissues.

The absence of fibroblasts or any other evidence of stromal activity in the early interstitial lesion is of significance. This fact clearly indicates that the lymphocytic infiltration is a true reaction on the part of the host to the injurious agent and in no sense reparatory, from which it may be inferred that acute interstitial scarlatinal nephritis of man is the same kind of reaction.

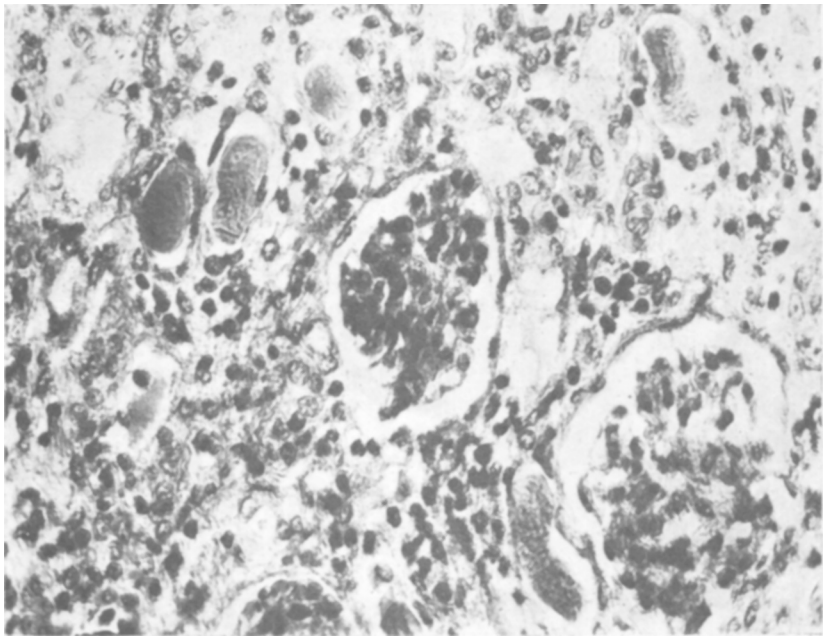
In regard to the primary glomerular lesion in the dog, the streptococcal toxin affects especially the capillaries of the kidney tufts, producing various alterations in the whole glomerular structure.

FIG. 1.



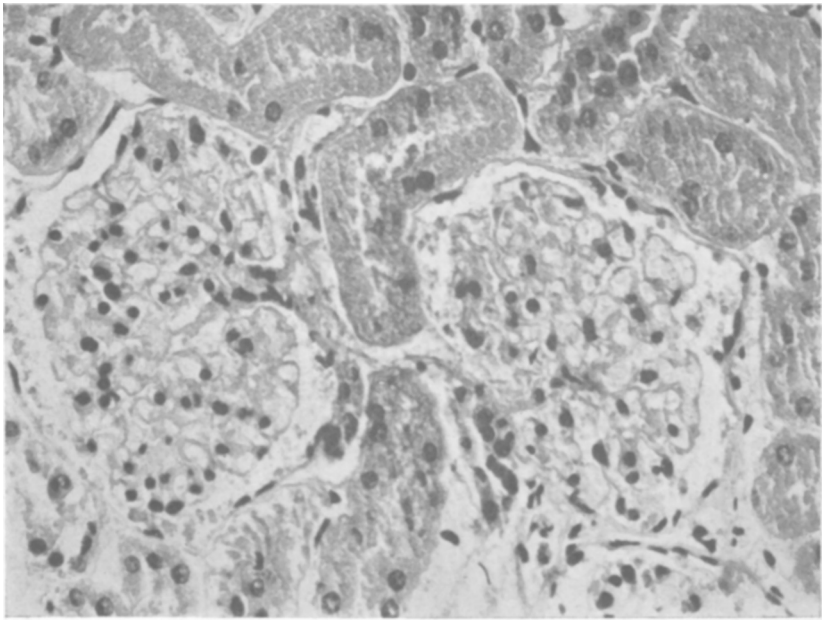
Acute Interstitial, Non-suppurative (induced by the injection of specific culture).

FIG. 2.



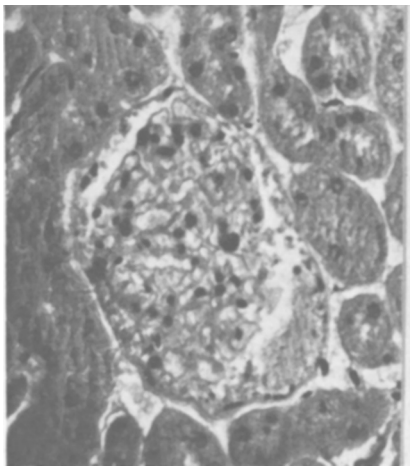
Acute Interstitial, Non-suppurative (induced by the injection of specific culture).

FIG. 3.

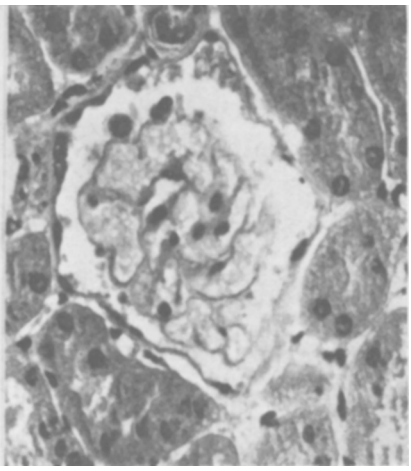


Glomerular and Capsular Lesions.

FIG. 4.

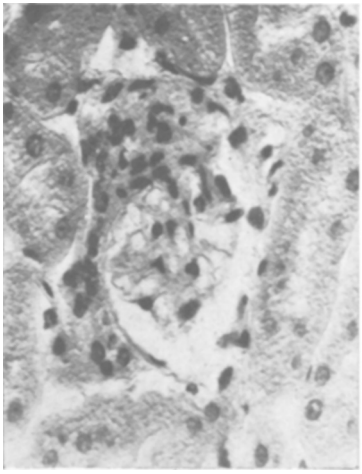


Glomerular Lesion.



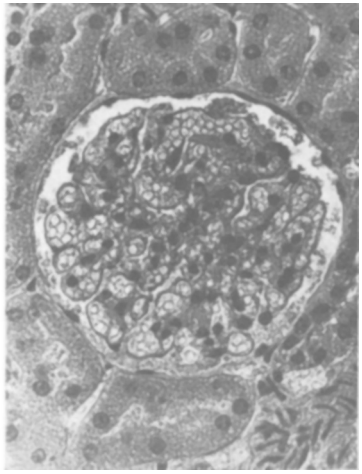
Degeneration of Tuft.

FIG. 5.



Glomerular and Capsular Lesions. (Early epithelial "crescent" formation.)

FIG. 6.



Early Glomerular Lesion. (Intracapillary dilatation and engorgement.)

There are lesions in the wall of the capillaries which cause the formation of thrombi, in consequence of which the vascular loops become greatly dilated, occluded and later adherent to Bowman's capsule. Other glomerular tufts become enlarged through the appearance of quantities of endothelial cells in the lumina of the capillaries.

Bowman's capsular spaces generally contain blood in the form of hyalin masses, also albuminous material and desquamated epithelium. Later, in those capsular spaces where hemorrhage has occurred, early epithelial proliferation ("crescent" formation) is noted. All these structural changes cause the glomeruli to undergo further and more serious alteration through replacement by fibrous tissue of the destroyed capillary loops.

While tubular changes are not an early feature in either the glomerular or interstitial type of experimental scarlatinal nephritis, they occur later in the process and appear in the form of epithelial degeneration, especially of the convoluted portion of the tubules. Here the lining cells become swollen through the presence of fluid, granules, fat and hyalin droplets. Often the lumen is filled with blood, desquamated epithelium, granular and hyalin casts.

The acute lesions of the experimental nephritis in the dog are recognized macroscopically by an increase in size of the kidney, by swelling of the glomeruli which project above the cut surface, and by pinhead and smaller discrete yellowish white foci in the cortical substance and by sprinkling throughout the organ with hemorrhages.

Summary. The various types of glomerular and also the acute interstitial nephritis of human scarlet fever can be regularly produced in the dog with the culture and with the pure toxic principle of *Streptococcus scarlatinae.*

The experimentally induced acute nephritic lesions are of two forms, glomerular and interstitial, and these are alike in kind and variety to the acute scarlatinal nephritis of man.

The complete analogy of the experimental nephritic lesion in the dog to that in man is of unusual interest since it affords the opportunity to study the acute lesions in the order of their related sequence and is a means of tracing the changes that lead to a progressive diffuse nephritis.

This is a preliminary report.

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[1] Duval, C. W., and Hibbard, R. J., *J. Exp. Med.*, 1926, xliv, 567.

[2] Duval, C. W., and Hibbard, R. J., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiii, 850.