tions gives rise to a substance capable of producing purpuric reactions in mice and in rabbits but the presence and location of these reactions is dependent upon the condition of the capillaries in the various cutaneous areas.

9500 P

Differentiation of Glomerular and Tubular Function in Glomerular Nephritis.

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It was recently shown that at low plasma levels about 94% of the phenol red clearance in the normal human kidney is accomplished by tubular activity.[1] In view of this fact this clearance is a sensitive index of tubular excretion, and when observed simultaneously with the inulin clearance, affords evidence of the respective functional activities of the tubules and of the glomeruli. The present investigation concerns the study of these clearances together with the urea clearance in 21 subjects with glomerular nephritis either during a first attack, during an exacerbation, or in the chronic stage.

We have endeavored to maintain the urine flow above the augmentation limit wherever possible so that the urea clearances would be physiologically comparable. The urea clearance has ranged from 64.6 to 5.4, the inulin clearance from 131 to 6.2 cc. per minute; the urea/inulin clearance ratio has ranged from its normal value of 0.55 to a value of 0.88. In no case has the urea/inulin clearance ratio been observed to fall significantly below the normal value in any stage of the disease. In general it tends to rise, so that in advanced chronic glomerular nephritis it has a value of 0.85 or higher. Our observations do not bear out the belief that in renal disease there is increased back-diffusion of urea, or that the elevation of the blood urea is due to such back-diffusion.

A full discussion of the behavior of the phenol red clearance and its relation to the inulin clearance in various stages of disease must be deferred to a later time, but a few interesting features may be noted here. In general, in those individuals in whom renal impair-

[1] Goldring, W., Clarke, R. W., and Smith, H. W., *J. Clin. Invest.*, 1936, **15**, 221.

ment is not too far advanced, the phenol red/inulin clearance ratio tends to maintain its normal value (above 3.0), suggesting that injury of glomeruli and tubules progresses in a parallel manner, as might be expected from the anatomical structure of the nephron. But in more advanced cases this ratio tends to fall below normal, reaching such low values as 0.60, indicating almost complete loss of the capacity of the tubules to excrete the dye. (Values less than 1.0 are to be expected in theory since much of the plasma phenol red is rendered unfilterable by being bound to plasma proteins.) In no case has there been evidence of the persistence of functioning aglomerular tubules in advanced chronic glomerular nephritis, as judged by the excretion of phenol red.

In a few subjects observed early in the course of the disease the phenol red/inulin clearance ratio has so far exceeded the normal range as to suggest a dissociation of glomerular and tubular function of another nature. One subject, first observed early in an initial attack of acute glomerular nephritis, showed an inulin clearance of 72%, a phenol red clearance of 156%, and a phenol red/inulin clearance ratio of 210% of our average normal figures. During the next 3 months the inulin clearance rose to 109% while the phenol red clearance fell to 132%, so that the ratio decreased to 119% of normal. In interpreting this phenomenon it must be recognized that, physiologically or functionally, the phenol red clearance might rise to excessively high absolute values because of an increase in the specific capacity of the tubules to excrete the dye, or an increase in the quantity of plasma presented to the tubules. The latter circumstance might arise from renal hyperemia due to gross delivery of an increased quantity of blood to the kidneys, or from dilatation of either the afferent or efferent glomerular arterioles, or both. On the other hand, structural alterations in the kidney might increase the phenol red/inulin clearance ratio, as when the permeability of the glomerular membranes is reduced without obstruction to blood flow, or when some glomeruli have been obliterated and a blood supply to the tubules has been reëstablished either by channalization of the fibrosed glomeruli or by new extraglomerular routes. There is at the moment no evidence that will permit a final selection from these possibilities. Since dilatation of the efferent glomerular arterioles would tend not only to increase the phenol red clearance by permitting an increase in renal blood flow, but also to decrease the inulin clearance by reducing the effective glomerular filtration pressure, this functional disturbance could explain the observations on the subject mentioned above. Whether or not efferent dilatation is the

only factor involved, our observations suggest that renal hyperemia may exist during a phase of acute glomerular nephritis.

Evidences of reversible renal ischemia have been obtained in an exacerbation of chronic disease during the period of subsidence. Further discussion of this and other aspects of the problem are postponed in the hope that information may be gained on the relative importance of reversible functional as compared to irreversible structural changes in renal activity at various stages of the disease.

9501

Further Investigations of the Effect of Tissues on Autonomic Drugs.

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In previous papers[1, 2] it was established that epinephrine and acetylcholine are destroyed by tissues (in this case the scales of *Fundulus heteroclitus*); it was found also that 50% deuterium oxide inhibits this destruction. Using the same technique and method of recording as previously, the destructive effect of the same tissues has now been investigated on atropine, pilocarpine, physostigmine and mecholyl.

Three kinds of solutions were made in each case: (1) solution of the drugs used, (2) the same solution + fish scales, and (3) the same solution + fish scales + 50% deuterium oxide. All solutions were tested 4 times: immediately after they had been made, 12 hours later, 24 hours later, and 48 hours later. The test objects were melanophores of isolated scales of *Fundulus heteroclitus* freshly removed from the fish.

A. Atropine. One-half percent solution of atropine sulphate was used; in this concentration, atropine fully expands the melanophores. The solutions of atropine sulphate to which fish scales were added showed a much slighter effect after 12 hours. After 24 and 48 hours the same solutions were ineffective. If, however, 50% deuterium oxide were added together with the scales, the atropine solu-

1 Barbour, H. G., and Bogdanovitch, S. B., *J. Pharm. and Exp. Therap.*, 1937. In press.

2 Bogdanovitch, S. B., and Barbour, H. G., *J. Pharm. and Exp. Therap.*, 1937. In press.