

of human serum albumin. In seven of these subjects the actual renal plasma flow was measured by the ratio

$$\frac{\text{PAH Excretion}}{\text{Arterial PAH conc.} - \text{Renal Venous PAH conc.}}$$

samples obtained from the right renal vein by catheterization being compared with simultaneous samples from the femoral artery.

The hematocrit fell in all subjects after albumin (average fall = 16 per cent of control) and the plasma protein concentration rose less than 1 Gm. per cent. In nine of the ten subjects an immediate increase in inulin (average rise 14 per cent) and PAH (average rise 37.4 per cent) clearances was found, with a fall in filtration fraction in every case. The PAH clearance was found not to be a valid measure of renal plasma flow, however, since the percentage extraction of PAH ( $\frac{A_{\text{PAH}} - R_{\text{VPAH}}}{A_{\text{PAH}}}$ ) fell after albumin in each of the seven subjects in which it was measured (average fall = 19.6 per cent). The increase in actual renal plasma flow after albumin (average 44.3 per cent) was therefore greater than would be indicated by the PAH clearance (average 33.9 per cent) and the fall in filtration fraction correspondingly greater. In a control series of eight normal subjects under basal conditions consecutive determinations of renal PAH extraction at ten to fifteen minute intervals for one to two hours have shown a maximum variation of  $\pm 1.8$  per cent from the mean for each individual.

An immediate increase in urine flow in all subjects and in chloride excretion in the four subjects in which it was measured was found. The two patients with nephrosis differed from the others only in showing a greater rise in filtration rate and less fall in filtration fraction.

#### 17. EFFECT OF SALINE CATHARSIS ON URINE SPECIFIC GRAVITY

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Methods used in concentration tests of kidney function fail to produce a consistent effect on urine specific gravity unless the subject has undergone water deprivation for at least twenty-

four hours. Even after such a long fast, wide variations have been observed in normal controls. A method capable of producing a consistent high elevation of urine specific gravity would be of value.

Observations of urine specific gravity have been made in normal subjects at fifteen minute intervals following administration of a sodium phosphate solution. In seven subjects the cathartic was administered thirty minutes after breakfast. Within two hours the mean urine specific gravity was 1.027. In eleven subjects the cathartic was given after an eight to twelve hour fast and the mean specific gravity in ninety minutes was 1.035, ranging from 1.030 to 1.039. In six series of observations in a single subject the urine specific gravity ranged from 1.034 to 1.039 at the end of 120 minutes.

It would seem that the rapid dehydration produced by saline catharsis is an effective means of increasing urine concentration and might prove a reliable test of renal function.

#### 18. EFFECT OF ORAL STREPTOMYCIN AND PHTHALYLSULFATHIAZOLE ON BLOOD PHENOL CONCENTRATIONS AND SURVIVAL IN EXPERIMENTAL UREMIA

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Blood phenol (tyrosine standard) determinations were made daily on five mongrel dogs. On the second day oral phthalylsulfathiazole (0.5 to 0.6 Gm./Kg. per day in divided doses) was started. On the fifth day bilateral nephrectomy was performed. The dogs diet in from two to eight days postoperatively with phenol levels from 3.70 to 7.35 mg./100 cc.

A similar experiment was performed on four dogs using oral streptomycin\* (0.48 Gm./day in divided doses). The dogs died two to three days postoperatively with phenol levels from 1.54 to 2.14 mg./100 cc.

On five control dogs blood phenol levels were determined for four days (1.05 to 2.19 mg./100 cc.). On the fifth day bilateral nephrectomy was done. These dogs died two to five days post-

\* Kindly supplied by Dr. D. F. Robertson of Merck and Co., Inc.

operatively with determined phenol levels from 3.69 to 6.60 mg./100 cc.

Stool cultures showed that both drugs reduced gas-forming organisms.

There were no differences in the symptoms of uremia exhibited by the three groups of animals.

*Conclusion.* Intestinal organisms other than the coliform group were responsible for blood phenol production; blood phenol levels were of minor importance in producing the symptoms of experimental uremia.

#### 19. STUDIES OF HUMAN CARBOHYDRATE METABOLISM BY THE LIVER CATHETERIZATION TECHNIC

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Animal experimentation has proved the importance of the liver in carbohydrate metabolism. Although clinical experience has tended to confirm in humans the findings of the physiologists in animals, direct observations relating to the rôle of the liver have not heretofore been possible in man.

By the use of the cardiac catheter technic one can obtain samples of blood from the hepatic veins. If simultaneous arterial and hepatic venous samples are analyzed for glucose, it is possible to determine whether the liver is extracting glucose from the circulation or breaking down glycogen to contribute glucose to the blood.

The data obtained show that under fasting conditions the human liver contributes glucose to the peripheral circulation. After the administration of glucose intravenously, the arterial glucose level exceeds the hepatic level, indicating that glucose is being stored. As the arterial glucose level drops, the hepatic venous level drops less rapidly until it again exceeds the arterial level, indicating that the liver is releasing glucose and "braking" the descending blood glucose curve.

When peripheral venous glucose levels are obtained, they are lower than the hepatic venous level at the peak of the glucose tolerance curve, indicating that the peripheral tissues extract a greater portion of glucose from the blood flowing through them than does the liver. In the absence of measurements of peripheral

blood flow, however, it is impossible to determine whether a greater absolute quantity is removed.

As the glucose tolerance curve falls, the arterial level often falls below the peripheral venous level, thus showing that glucose is being contributed to the circulation by the peripheral tissues. This phenomenon probably arises from the back-diffusion of glucose from intercellular fluid as the blood level falls below that in the tissue spaces. The possibility must also be considered that part of the glucose may be contributed by skin, bone and other connective tissues which, unlike muscle, contain phosphatase.

Blood inorganic phosphate was also determined during the glucose tolerance tests. After the injection of glucose there was a reduction of the phosphate level of the blood drawn from arterial, hepatic and peripheral venous sources. This reduction could not be related quantitatively to the glucose level or to the rate of change of the glucose levels.

By application of the liver blood flow technic described by Bradley et al. (*J. Clin. Investigation*, 24: 890, 1945), one can estimate the actual amount of glycogen deposited or broken down in the liver.

The possible application of the technic to the elucidation of problems of the rôle of the liver in amino acid and fat metabolism are discussed.

#### 20. ESTIMATION OF THE HEPATIC BLOOD FLOW AND SPLANCHNIC OXYGEN CONSUMPTION IN HEART FAILURE

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The hepatic blood flow has been measured in a group of patients with cardiac decompensation using the bromsulphalein technic of Bradley et al. The hepatic arteriovenous oxygen differences and cardiac outputs by the direct Fick method were determined in the same patients.

The hepatic blood flows in cardiac failure have been found between 200 and 700 ml. per minute per square meter (normal range, 600 to 1200 ml.). The degree of reduction in flow is in proportion to the reduction in cardiac output,