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3444

Induced Large Variations in the Urinary Proteins in Bright's Disease, Particularly in Nephrosis.

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In a previous report[1] some of the factors influencing the albumin output through diseased kidneys in chronic nephrosis and in animal experiments were discussed. The present work is a continuation of this investigation, using three patients with chronic nephrosis.

With two of the patients the same sudden rise under high protein diet (130 gm. daily) occurred as in the previous experiments, with immediate fall to the original level upon return to a low protein diet (30 gm. daily). The globulin to albumin ratio in the urine remained approximately constant.

During a period of fever (body temperature about 38.5°) of one of the patients, the urinary proteins increased to a still higher level, and the globulin to albumin ratio also increased, indicating a greater permeability of the kidney. That the kidney was probably damaged was indicated by the slow return of the urinary proteins to their former level, as contrasted with the sudden fall after high protein feeding.

The third patient was a case of myxedema combined with nephrosis and showed a metabolic rate of —30 at the beginning of the experiment. The induced increase of urinary protein was insignificant as compared with the results in other cases. After a short period on high protein intake, the patient was given thyroid extract daily, whereupon there occurred an immediate large rise in the protein output followed by a gradual decline during the ensuing period. This sudden increased output of protein is interpreted as a confirmation of the theory of Boothby[2] that the body contains part of its

protein in the form of storage protein, which, in non-nephritic cases of myxedema is being mobilized by thyroid medication and eliminated as urinary non-protein nitrogen. In the case studied by us, the whole extra nitrogen output following the thyroid medication was in the form of urinary protein.

The urinary protein in nephrosis consists of at least two proteins of marked difference in solubility. The so-called globulin fraction is chiefly precipitated between concentrations of Na_2SO_4 of 1.0 *M* and 1.25 *M*. The so-called albumin fraction, which always is much larger than the globulin fraction, shows a higher solubility than the serum albumin of the blood plasma, practically nothing coming down before a Na_2SO_4 concentration of 1.7 *M*. Comparisons between the globulin concentrations in plasma and urine as well as between the albumin in plasma and urine are therefore futile.

The large variation in urinary proteins induced in several successive cases of chronic nephrosis by sufficiently large variations of the protein intake is looked upon as far as the kidney is concerned as a passive process, not indicative of any variation in the degree of the existing kidney damage.

The excess protein coming out in the urine on a high protein feeding was finally discussed in its relation to protein digestion, amino acid absorption and protein synthesis and the hypophysis was advanced that the urinary protein under discussion represents an escape through the leaking kidney of new protein formed in the organs of the highest amino acid concentration during the post absorptive period,[3] this new protein being on its way to other parts of the body. The possibility of such a more or less unfinished protein is suggested by the high solubility found by the so-called albumin fraction of the urine. Purification of this protein is under way.

This is a preliminary report.

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[1] Berglund, H., Scriver, W., and Medes, Grace, *Proc. 18th Annual Meeting Am. Soc. for Clin. Invest.*, p. 612.

[2] Boothby, Walter, and co-workers (personal communication).

[3] Van Slyke, D. D., *Harvey Lectures*, 1915-16, xi, 146.