17257. Effect of Febrile Plasma, Typhoid Vaccine and Nitrogen Mustard on Renal Manifestations of Human Glomerulonephritis.

HERBERT CHASIS, WILLIAM GOLDRING, AND DAVID S. BALDWIN.*

From the Department of Medicine, New York University College of Medicine, and Third (New York University) Medical Division, Bellevue Hospital.

Remissions have been observed to occur spontaneously in patients with chronic diffuse glomerulonephritis in the nephrotic phase. Blumberg and Cassady[1] and Janeway[2] have reported that patients with diffuse glomerulonephritis after accidental or induced measles show transient reduction in protein excretion and significant diuresis, confirming the generally accepted opinion that remissions in this disease may be occasioned by intercurrent infection. Since the febrile phase of infection may be accompanied by profound disturbance in renal hemodynamics[3,4] it seemed possible that both decrease in proteinuria and diuresis might be directly attributable to alteration in renal hemodynamics.

On the other hand, Becker[5] has shown that administration of HN_2 prevents the development of the Schwartzman phenomenon in rabbits.† Since there is reason to believe that diffuse glomerulonephritis may be the result of immunological alteration in renal tissue, it seemed conceivable that a common factor might be operative in infection and following the administration of these agents. In this view it was conceivable that reactive factors might be present in the plasma of patients with acute infections which would produce remission of the nephrotic syndrome.

To test these possibilities, we have explored the effects of 1) pyrogenic reaction, 2) infusion of plasma from patients acutely ill with pneumococcal and hemolytic streptococcal infections, and 3) one of the nitrogen mustards, methyl bis(B-chloroethyl)amine hydrochloride (HN_2), on protein excretion, diuresis, and rate of glomerular filtration in patients with diffuse glomerulonephritis.

Methods. Observations were made on daily weight, 24 hour urinary volume and urinary protein excretion, rate of glomerular filtration (C_{IN}) as measured by the inulin clearance, and renal plasma flow (C_{PAH}) as measured by the p-aminohippurate clearance in 4 patients with chronic diffuse glomerulonephritis in the nephrotic phase.

Urinary protein was determined by the micro-Kjeldahl and biuret methods[8] and inulin and p-aminohippurate by methods previously described.[9]

Results. The pyrogenic reaction was induced in one patient with marked renal functional impairment on 2 occasions with intravenously administered typhoid vaccine. On both occasions there was marked decrease in proteinuria, accompanied in the one instance in which it was measured by decreased filtra-

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† Since our investigations were initiated, Janeway *et al.*[6] have reported that experimental nephritis produced in rabbits by the administration of bovine gamma globulin can be prevented by HN_2 and Dammin and Bukantz[7] have shown that HN_2 inhibits antibody production, Arthus reaction, and vascular lesions in rabbits produced by horse serum antigen.

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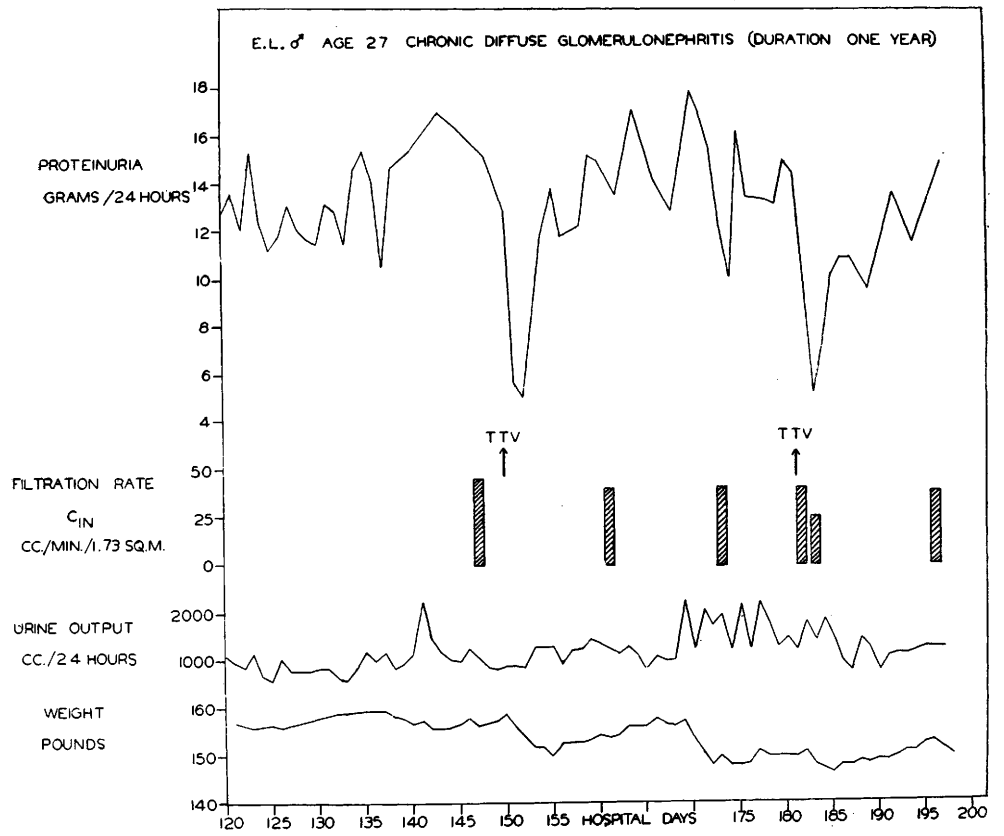

FIG. 1.

Effect of pyrogenic reaction on proteinuria and rate of glomerular filtration.

tion rate. No diuresis occurred (Fig. 1). It is our tentative opinion that the decrease in proteinuria was related to the renal hemodynamic alteration as manifested in part by decrease in filtration rate.

Two patients were given 1975 and 1280 cc of plasma intravenously respectively from patients with hemolytic streptococcal and pneumococcal infections in amounts of 125 to 500 cc at intervals in one patient over a period of one month and in the other over a period of 4 months. In neither patient was there a decrease in proteinuria or diuresis.

HN_2 was administered intravenously to 3 patients in 2 doses of 0.2 mg per kilo on successive days. In all 3 proteinuria decreased. In patient B.D. whose control C_{IN} and C_{PAH} were 13.9 cc and 66.3 cc per minute respectively, daily excretion of protein during a control period of 28 days ranged from 21.4 to 14.5 g, averaging 17.0 g. Protein excretion decreased to 2.3 and 10.6 g in the 24 to 48 and the 48 to 72 hour periods following the administration of HN_2, after which it returned to the pretreatment level. Diuresis did not occur. In patient L. G. whose control C_{IN} and C_{PAH} were 10.9 and 236 cc per minute, the daily excretion of protein during a control period of 113 days ranged from 9.1 to 4.2 g, averaging 7.0 g. Following administration of HN_2 proteinuria decreased to 4.0 g per day, the decrease being first observed during the first 24 hours of HN_2 administration, and persisting for 4 days. Diuresis did not occur.

Patient J.H., whose control C_{IN} and C_{PAH} were 116 and 839 cc per minute, was given HN_2 on 2 separate occasions. As shown in Fig. 2, in each instance there occurred diuresis and marked decrease in protein-

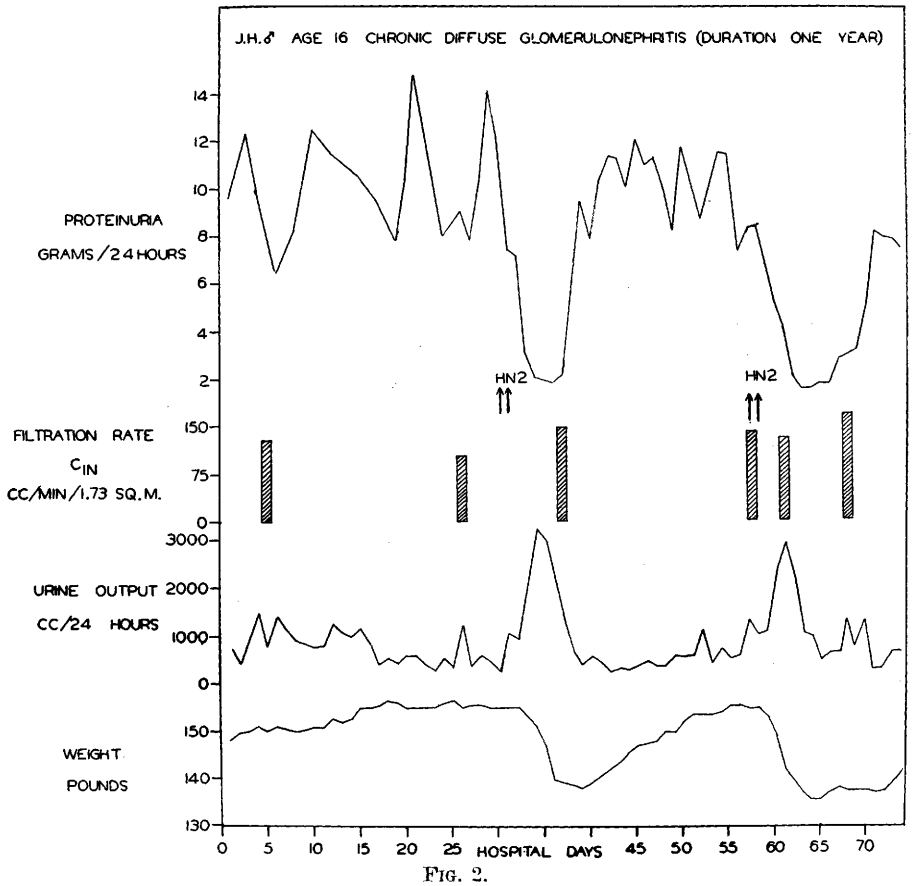

FIG. 2.
Effect of nitrogen mustard on proteinuria and rate of glomerular filtration.

uria, accompanied by an increased filtration rate. The diuresis was associated with disappearance of edema.

Summary. Administration of plasma from patients acutely ill with pneumococcal and streptococcal infections failed to decrease proteinuria or induce diuresis in 2 patients with chronic diffuse glomerulonephritis.

Induction of the pyrogenic reaction was accompanied by decrease in proteinuria on 2 occasions in one patient. We are inclined to attribute this result to the concomitant decrease in the rate of glomerular filtration.

Therapeutic doses of HN_2 reduced proteinuria but diuresis failed to occur in 2 patients with advanced chronic diffuse glomerulonephritis with marked renal functional impairment. However, in one patient with minimal renal functional impairment, administration of HN_2 was followed on 2 separate occasions by diuresis, marked reduction in proteinuria and concomitant increase in filtration rate, a combination of effects consistent with a return of glomerular function towards normal.‡

Our observations indicate that reversal of renal manifestations of human glomerulonephritis can be induced by HN_2.

This study is being extended to include patients in earlier phases of glomerulonephritis.

‡ It is of interest in this connection that in dogs the filtration rate may be substantially increased 40 to 72 hours after intravenous administration of HN_3.[10]

[10] Houck, C. R., Crawford, B., Bannon, J. H., and Smith, H. W., *J. Pharm. and Exp. Therap.*, 1947, **90**, 277.

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