# EFFECT OF PREDNISOLONE ON SERUM PROTEIN FRACTIONS IN EXPERIMENTAL GLOMERULONEPHRITIS

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In rats with glomerulonephritis caused by injection of kidney emulsion with Freund's adjuvant, hypertension, hypoproteinemia, hypoalbuminemia, and an increase in the concentration of $\beta$- and $\gamma$-globulins in the blood are observed. Administration of prednisolone in the early stage of the disease improves the general condition of most animals and reduces the changes in total protein content and in the composition of the serum protein fractions.

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After experiments [10] which demonstrated the inhibitory action of hormonal preparations on autoantibody production in animals, steroid hormones have been successfully used for treatment of nephritis [9].

A correlation exists between changes in the blood protein fractions and the formation of autoantibodies which play a role in the pathogenesis of immunoallergic diseases and, in particular, of glomerulonephritis. It has been shown [4, 6, 7], that marked changes in the content of the serum protein fractions take place in animals with experimental glomerulonephritis: The albumins are decreased while at the same time the $\beta$- and $\gamma$-globulins are increased to twice their previous level or more. Changes in the serum protein concentrations have also been observed clinically in patients with a nephrotic syndrome [3].

In clinical practice nowadays administration of large doses of steroid hormones during treatment of nephritis is used with caution because of complications which have been observed, notably hypertension and ulcer hemorrhages [2, 5], although these have not reduced interest in this problem.

The object of this investigation was to study changes in the composition of the serum protein fractions in experimental autoimmune nephritis during administration of steroid hormones.

## EXPERIMENTAL METHOD

Experiments were performed on 40 male August rats weighing 120-130 g, ten of which were controls, while 30 animals received injections of Freund's adjuvant with 20% kidney emulsion and streptomycin, in doses of 1 ml at four separate points subcutaneously (in the auxiliary and inguinal regions). A second injection of the adjuvant was given intraperitoneally in a dose of 1 ml two months later.

The experimental rats were divided into two groups: group 1 (18 rats) not receiving prednisolone; group 2 (12 rats) receiving prednisolone in a dose of 2.5 mg, given in three courses each lasting three weeks with intervals of two weeks between them.

Periodically the rats were weighed, their blood pressure was measured in the caudal artery, and the total blood protein and serum protein fractions were determined. Blood for determination of total protein and for electrophoretic investigations was taken from the jugular vein when the animal was sacrificed on the 120th day.

## EXPERIMENTAL RESULTS

The animals of group 1 developed experimental glomerulonephritis, accompanied by hypertension (arterial pressure raised by 35-40 mm over normal), azotemia (121.7±5.4 mg%), and marked edema.

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TABLE 1. Serum Protein Fractions of Rats with Experimental Glomerulonephritis Treated with (Prednisolone, Untreated, and under Normal Conditions

| Serum protein fractions | Healthy rats (N) | Rats with nephritis (Group 1) | Rats with nephritis receiving prednisolone (Group 2) | P(N – Group 1) | P(N – Group 2) | P(Group 1 – Group 2) |
|---|---|---|---|---|---|---|
| Albumins | 44.2±1.86 | 26.0±2.28 | 40±2.17 | < 0.001 | > 0.10 | < 0.01 |
| Globulins | | | | | | |
| $\alpha_1$ | 14.4±0.99 | 16.1±1.14 | 13.9±1.015 | > 0.10 | > 0.10 | > 0.10 |
| $\beta_2$ | 10.3±0.05 | 14.7±0.87 | 12.3±0.85 | < 0.001 | > 0.05 | > 0.05 |
| $\beta$ | 14.4±1.45 | 20.7±1.02 | 19±1.16 | < 0.01 | > 0.05 | > 0.10 |
| $\gamma$ | 16.1±0.38 | 22.3±2.46 | 14.8±0.9 | < 0.001 | > 0.10 | < 0.01 |
| Total protein | 6.74±0.15 | 3.5±0.23 | 6.3±0.34 | < 0.01 | > 0.10 | < 0.01 |

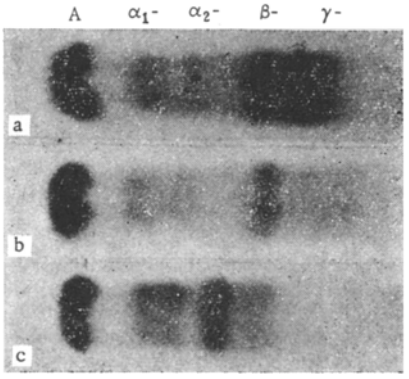


Fig. 1. Electrophoresis of serum protein fractions of rats. a) Rats with experimental glomerulonephritis, untreated (group 1); b) rats with experimental glomerulonephritis, receiving prednisolone concurrently (group 2); c) healthy rats. A – albumins; $\alpha_1$-, $\alpha_2$-, $\beta$-, and $\gamma$-globulin fractions.

Morphological investigations of the kidneys of the group 1 rats revealed a picture of intracapillary glomerulonephritis, and were described in our previous paper [1].

Hypoproteinemia accompanied by hypoalbuminemia and by a marked increase in the $\alpha$- and $\gamma$-globulin fractions was observed in this group (see Table 1 and Fig. 1a).

In the rats of group 2 with experimental glomerulonephritis and receiving prednisolone, clinical signs of the disease were found in only four of the twelve animals: azotemia, hypoproteinemia (one animal had edema and marked changes in the serum protein fractions similar to those in group 1; see Fig. 1).

In the remaining eight animals of this group the disease was accompanied by minimal clinical manifestations: slight proteinuria (from traces to 0.83%), moderate azotemia (59.5 ±3 mg%), and absence of edema.

The histologic changes in the kidneys of the group 2 rats likewise were very slight (Fig. 2b), apart from in the 4 rats mentioned above in which the picture of intracapillary nephritis was well defined, just as it was in the animals of group 1 (Fig. 2a).

The total protein level of these 8 rats of group 2 was near to normal, and their serum protein fractions corresponded to the normal pattern. Comparison between these indices and those for group 1 showed a statistically significant difference (see Table 1 and Fig. 1).

The results show that the development of experimental glomerulonephritis is accompanied by hypertension, hypoproteinemia, hypoalbuminemia, and by an increase in the $\beta$-globulin and $\gamma$-globulin fractions, correlated with the severity of the clinical picture of glomerulonephritis and the morphological changes.

Administration of prednisolone in the early stage of experimental glomerulonephritis considerably improved the general state of most animals and had a positive effect on the total protein level and the composition of the serum protein fractions, which were close to normal.

Evidently, as noted previously [8], prednisolone has a beneficial action on immunobiological processes in the body, suppressing autoantibody formation; the absence of effect of prednisolone in 4 animals of group 2 may be explained by individual differences between animals, by their increased reactivity, and, possibly, by the inadequate dose of prednisolone in that particular case.

The results obtained are in agreement with data in the literature concerning changes in the serum protein fractions of rats with experimental cytotoxic nephritis [4].

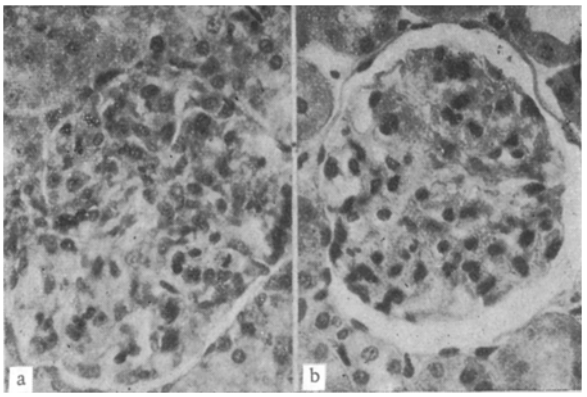

Fig. 2. Changes in kidneys in autoimmune glomerulonephritis. a) Severe intracapillary glomerulonephritis in untreated rats; b) minimal changes in the glomeruli of rats treated with prednisolone. Hematoxylin-eosin, 500 ×.

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