PREDNISOLONE THERAPY OF ACUTE GLOMERULONEPHRITIS. "INTERRUPTION SYNDROME"

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Prednisolone has been found favourable to influence acute glomerulonephritis taking a protracted course, as well as the acute exacerbation of chronic nephritis. If the hormone treatment is discontinued abruptly in the early phase of improvement, microhematuria will mostly increase in severity. In some cases the complement titre decreases, and exceptionally the NPN value increases for a time. The relapse is accompanied by headache, vertigo, anorexia, nausea and weakness.

The "interruption syndrome" is ascribed to an iatrogenic adrenocortical insufficiency.

The reactive microhematuria and the reactive decrease of the complement titre suggest that adrenocortical glucocorticoid secretion is a significant factor in the mechanism of glomerulonephritis.

On the basis of the clinical evidence obtained, steroid treatment is believed to be justified in acute glomerulonephritis.

The three problems subject to most debates in the treatment of acute glomerulonephritis are

(1) the use of antibiotics;

(2) the composition of the diet;

(3) the value of steroid therapy.

While concerning the first two questions a more or less uniform view has been adopted, opinions concerning the value of steroid therapy are contradictory.

REUBI [13] regards adrenocortical hormone therapy as contraindicated. The views of American authors are not uniform. DANOWSKI and MATEER [4] claim high doses of ACTH and cortisone to be indispensable for reducing the incidence of chronic forms, while other authors [3, 10, 11, 14] are less enthusiastic. FISHBERG [5] believes the use of cortisone to be dangerous, because sometimes it promotes the development of hypertension. There are few data concerning the modern forms and modifications of steroid hormones. The clinical results have not been confirmed by statistical evaluation, which, in view of the great tendency to spontaneous healing of glomerulonephritis, would require a very large number of cases.

We have been studying since five years the effects of prednisone and prednisolone on the various forms of glomerulonephritis. The results were in some cases astonishingly favourable, in others disappointing. Our observations

have not made it possible to rule out the possibility that the pathological process continues with its original dynamics [6, 7, 8, 9].

In the present study we have attempted to approach the problem from a new angle.

Materials and methods

The observations have been made in 9 patients. Steroid therapy was indicated by an acute exacerbation of chronic nephritis in 1 case, and by acute glomerulonephritis in 8 cases. In every case the clinical picture was characterised by the persistence, or eventually a progression, of hematuria, after antibiotic treatment had been terminated. Prednisolone was used in daily doses of from 40 to 60 mg by mouth, together with 3 g KCl and alkali, according to need. Steroid treatment was abruptly interrupted in the early phase of improvement. In one case treatment was interrupted twice (zig-zag therapy).

The course of the illness was controlled by the following methods.

Urine was analysed daily. Protein excretion was determined by means of Esbach and Shevky—Stafford tubes; the sediment was examined quantitatively according to ADDIS [1]. Blood pressure and body weight were measured every day. The serum complement titre was determined several times a week by the method of LANGE et al. [12]; the same applies to the antistreptolysin titre, NPN, serum cholesterol and serum cholesterol esters. At intervals, we examined the nasal and pharyngeal bacterial flora, the eye fundus, performed different capillary tests (according to LANDIS, RUMPEL-LEEDE, GÖTHLIN, BORBÉLY), as well as the antistreptolysin cutaneous test. Serum total protein (by refractometry) and the serum protein fractions (by paper electrophoresis) were determined repeatedly. Renal function was appraised on the basis of the inulin and PAH clearances in most cases, but at least on grounds of the endogenous creatinine clearance. Finally, we examined also the diluting and concentrating power of the kidneys (our patients were not markedly oedematous).

Results

In a day or two after discontinuing the prednisolone, microhematuria invariably increased, and in two cases gross hematuria developed. In two patients a transient decrease in the complement titre was noted. In the patient with an acute exacerbation of chronic nephritis, the NPN value increased temporarily. In almost every case the relapse was accompanied by complaints of weakness, anorexia, headache and vertigo.

Fig. 1 shows the natural course of the "interruption syndrome". After discontinuance of prednisolone administration the Addis count rose steeply, and the complement level decreased for a while, to 0.67 U, as compared with the lowest limit of normal: 1.0 U. The duration of reactive hematuria was about two weeks.

Fig. 2 illustrates that the reactive hematuria is abolished by the resumption of prednisolone administration.

The consequences of a repeated interruption of treatment are shown in Fig. 3. The first interruption was followed by an increase of microhematuria, the second by gross hematuria. At the end of the figure it is visible that the relapse may be prevented by a gradual reduction of steroid dosage.

Fig. 4 is illustrative of the course of the reactive transitory uremia.

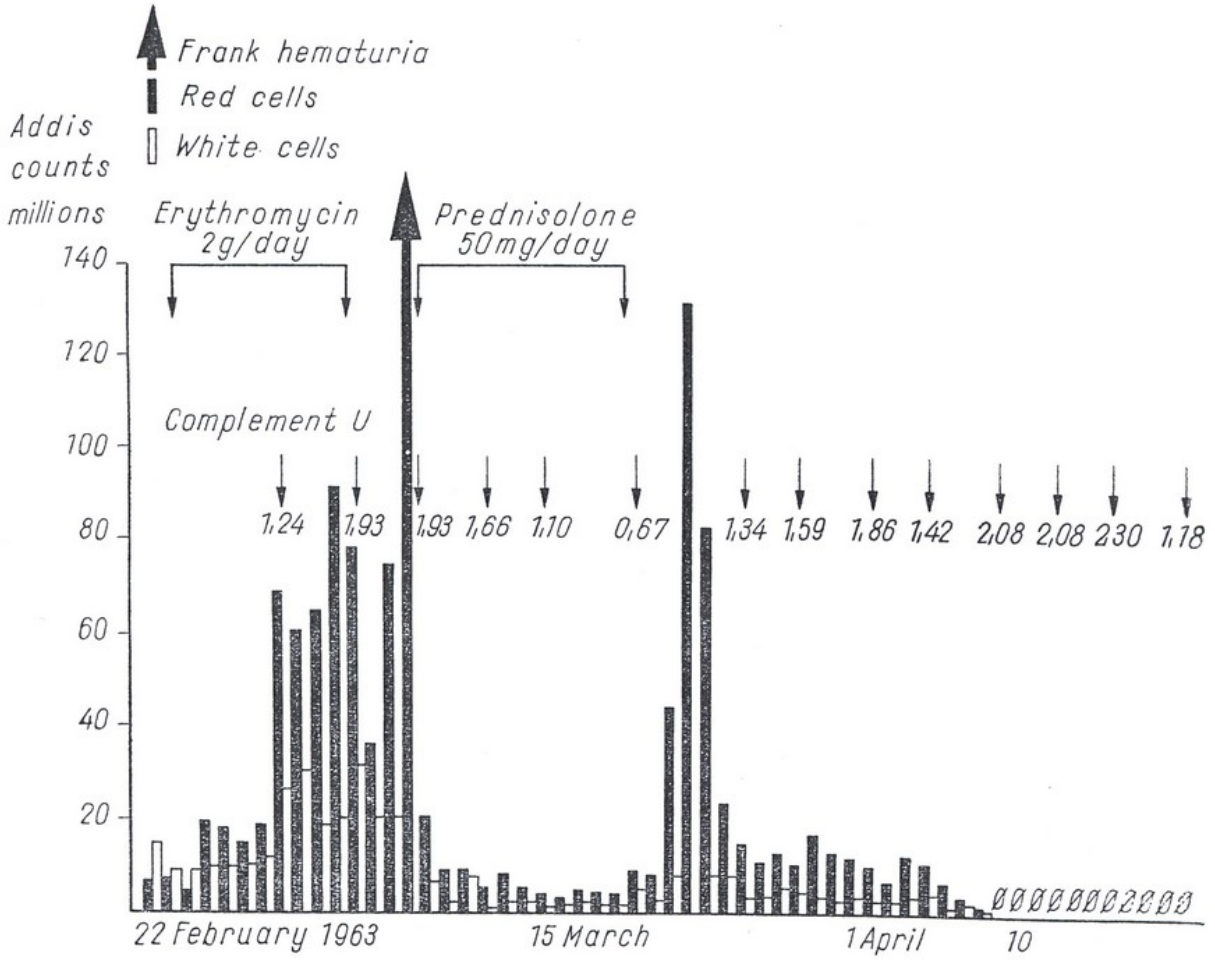

Fig. 1. Male, 58 years. "Interruption syndrome". Diagnosis, acute glomerulonephritis

The "interruption syndrome" can be explained by adrenal cortical insufficiency developing during prednisolone therapy and promoted by the feedback mechanism. The reactive hematuria and the reactive fall in complement level seem to indicate that the adrenal cortical hormones play a major role in th econtrol of the inflammatory processes associated with glomerulonephritis.

Discussion

In the light of the clinical evidence, we consider the use of prednisolone to be justified in glomerulonephritis, although not without discrimination, in view of the eventual side effects. VÁLEK et al. [15] treated 18 patients suffering from nephrotic glomerulonephritis with prednisone and lost one owing to gastric perforation. Steroid treatment should be considered in the same way as surgery: benefits and hazards should be weighed. BROD et al. [2] recommended long-term corticoid therapy in chronic cases. It is difficult to delineate sharply acute from chronic nephritis. We think the use of prednisolone

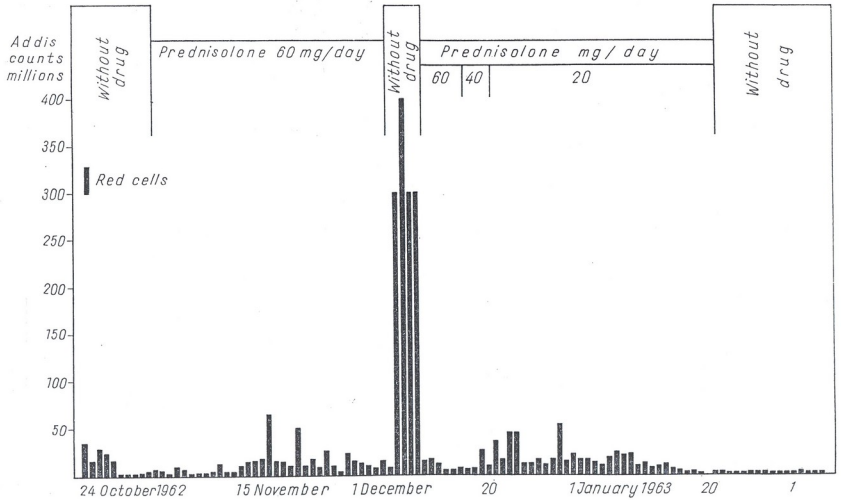

Fig. 2. Male, 40 years. Effect of prednisolone on reactive hematuria. Diagnosis, acute glomerulonephritis

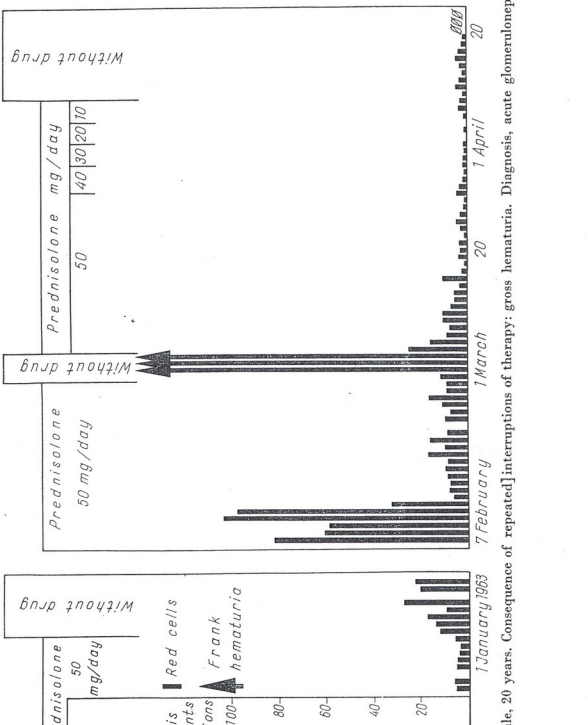

Fig. 3. Female, 20 years. Consequence of repeated interruptions of therapy: gross hematuria. Diagnosis, acute glomerulonephritis

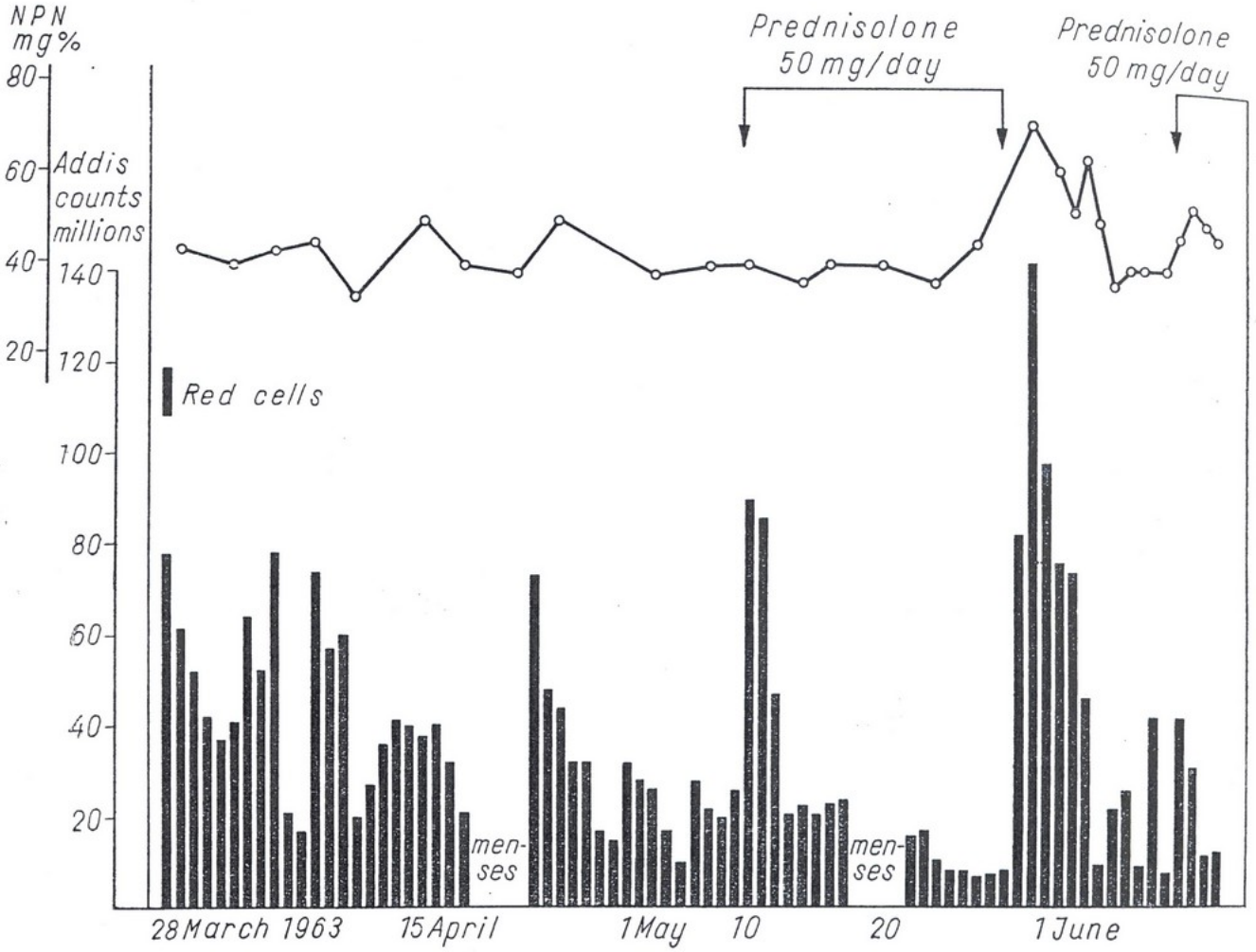

Fig. 4. Female, 21 years. Reactive uremia resulting after discontinuation of prednisolone administration. Diagnosis, acute exacerbation of chronic nephritis

to be justified in the acute stage already, i.e. in every clinically and/or immunologically active case when radiological examination rules out peptic ulcer. The most reliable signs of activity are microhematuria and a low complement level. Every harmful consequence of iatrogenic adrenal insufficiency can be prevented by a gradual reduction of the dose of prednisolone.

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