precipitated in this case by the prolonged presence of a cardiac catheter in the pulmonary outflow tract. The diminution of the intensity of the systolic murmur indicated diminished flow across the pulmonary valve, but that this was not due to decreased systemic arterial resistance is shown by the sustained systemic blood pressure. Tachycardia was not responsible for the changes, as the heart rate remained rapid for some time after the disappearance of cyanosis and the return of a loud systolic murmur.

Thus the findings in this case confirm Wood's (1958) hypothesis that the cyanotic attack is precipitated by temporarily increased obstruction at the pulmonary outflow tract, with greatly increased shunting of blood from right ventricle into aorta. Unlike Wood's cases, our patient showed only a slight drop in pulmonary artery pressure during the attack with no change in the pulse pressure, and deep coma was present with an arterial oxygen saturation of 52.5% (Wood states that coma ensues when the arterial oxygen saturation falls to about 20%).

It would seem that the level of arterial desaturation at which the patient loses consciousness is, at least partly, dependent on the resting level of saturation, which in this patient was presumably normal or almost normal, in view of the absence of clinical cyanosis. The fact that the pulmonary artery pressure diminished only slightly might suggest that the obstruction to the pulmonary flow in our patient was less marked than in Wood's cases. It is significant, however, that the pulmonary artery pressure did not rise, which one would have expected were the obstruction to pulmonary flow produced by an increased pulmonary arterial resistance.

The findings in this case indicate that the dangerous cyanotic attack may occur in those patients with Fallot's tetralogy with no clinical cyanosis, a finding which we have observed in other such cases (to be published).

When faced with a cyanotic attack the practitioner may use procaine intravenously as an emergency measure, but for a sustained effect morphine would appear to be more suitable. It must be mentioned, however, that we have had patients in whom morphine has failed to stop the attack. Other narcotics might presumably be efficacious, and Wood has recommended cyclopropane anaesthesia. It must be stressed that oxygen administration is not, by itself, effective therapy.

Summary

A patient with "acyanotic Fallot's tetralogy" developed a cyanotic (syncopal) attack during cardiac catheterization. The attack was probably precipitated by the prolonged presence of the catheter in the pulmonary outflow tract. The condition was studied haemodynamically, and it was believed that the attack was due to increased resistance to the flow of blood through the narrowed infundibulum. The treatment of the attack was difficult, and procaine intravenously was found to be effective, although the effect was not sustained. Morphine proved effective in relieving the attack.

We thank Drs. M. J. Meyer, W. Scott, and K. Jooste for their assistance during the cardiac catheterization. Dr. B. Senior suggested the use of procaine intravenously, and we are grateful to him for this advice.

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CASE OF LATENT NEPHRITIS TREATED WITH PREDNISOLONE

BY

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It is now accepted that the nephrotic syndrome is often amenable to treatment with steroids and corticotrophin (Arneil and Wilson, 1952; Arneil, 1956). The newer steroid preparations, especially prednisolone, seem to be particularly useful, and cases of nephrosis have been reported to respond to prednisolone after failure to respond to cortisone and prednisone (Holland *et al.*, 1958).

Cortisone and corticotrophin have also been used to treat acute and latent nephritis (Thorn *et al.*, 1950; Burnett *et al.*, 1950), but the results have generally been disappointing. Some workers (Michaels and Walters, 1953) found an increase of haematuria during treatment, and Philpott and Briggs (1953) concluded that cortisone and corticotrophin were valueless in the treatment or prevention of subacute nephritis complicating the Schönlein-Henoch syndrome.

A case of acute nephritis occurred in a general practice, and it became evident that the disease was progressing into a latent phase with persistent albuminuria, haematuria, and cast formation. I decided to observe the effect of prednisolone treatment.

Case Report

A boy aged 16 was referred to me in March, 1957, albuminuria having been detected at a medical examination held for prospective employees of the urban district council. About two weeks before this examination he had complained of a sore throat and his temperature was said to have been over 100° F. (37.8° C.) for two days. His throat symptoms resolved in a few days, but he then noticed slight backache.

On examination there was slight facial oedema but no ankle oedema; the blood pressure was 145/95. The urine was reported to contain albumin ++, red blood cells +++, and cellular and granular casts ++. The blood urea was 38 mg./100 ml.

A diagnosis of acute nephritis was made, and the patient was confined to bed and given a low-protein diet. After 12 weeks of absolute bed rest there was no improvement.

On June 8, 1957, he was transferred to a hospital, where the regime of bed rest and low-protein and low-salt diet was continued. He was discharged on October 1, still excreting red cells, casts, and albumin, but the blood pressure had fallen to 125/80. He was sent for two weeks' convalescence.

He returned home on October 16 and was then having a normal diet. Two days later he developed gross haematuria, the urine being the colour of port wine, albumin ++++; blood pressure 135/80. There was no oedema. His temperature was 99° F. (37.2° C.). Bed rest was again enforced.

On October 21 his temperature was normal, E.S.R. (Westergren) 32 mm./hour, blood pressure 130/80. The urine was slightly "smoky" to the naked eye. There was gross microscopic haematuria, and granular and cellular casts were abundant. The blood urea was 38 mg./100 ml. During the day he complained of toothache, and on closer questioning admitted having had intermittent pain several times before.

By October 31 the E.S.R. had fallen to 5 mm./hour, blood pressure 120/80, temperature normal. His general condition was satisfactory apart from the persistence of

albumin (1 g./litre); red cells, and cellular casts in the urine. The blood urea, serum proteins, and serum cholesterol were normal.

During the first week in November he developed a dental abscess; culture showed the organism to be an alpha-haemolytic streptococcus sensitive to penicillin. A 10-day course of crystalline penicillin, 0.5 mega unit twice daily, was started on November 14 and the next day the carious tooth was extracted under general anaesthesia. There was no improvement following this procedure; the clinical and laboratory findings remained unchanged.

On November 30 he developed an *Escherichia coli* urinary infection. The organism proved to be sensitive to sulphamylamide, streptomycin, and chloramphenicol. The infection responded to a six-day course of sulphadimidine, 2 g. every six hours. The excretion of albumin, red cells, and cellular casts persisted as before.

Investigations

Twelve days before starting steroid therapy the following routine was established. All fluid taken was carefully measured and recorded, the urinary output for each 24-hour period being similarly recorded and the albumin content estimated by the Esbach method. The urea clearance test was normal, and after 24 hours of fluid deprivation the urine specific gravity was 1030. The blood pressure was recorded daily. A Mantoux jelly test was negative. Weekly estimations of the serum electrolytes and bicarbonate reserve were carried out. The E.S.R., serum proteins, haemoglobin, blood urea, and urinalysis were determined weekly as before.

Paper electrophoresis of the serum and urinary proteins was carried out on three occasions: firstly, during treatment on January 3, 1958; secondly, four weeks after treatment, on February 25; and, finally, 34 weeks after treatment, on August 8. A modification of the method described by Flynn and Mayo (1951) was used and bromocresol-green was chosen as the protein dye. Readings were made by a photoelectric scanner. The urinary electrolytes were removed by an ion-exchange resin ("amberlite" monobed resin MB-1). The solution was then freeze-dried *in vacuo* at -4°C . and the proteins were redissolved.

The patient was given a high-protein (126 g. a day), low-salt diet; the total salt intake did not exceed 2 g. a day.

Treatment

Prednisolone was started on December 16, 1957: 60 mg. daily for 10 days, then 40 mg. daily for 10 days, followed by 20 mg. for 10 days, and finally 10 mg. for 10 days. While he was receiving hormone treatment oral benzathine penicillin, 1 mega unit daily, was administered together with 1.5 g. of potassium chloride a day as the serum potassium was only 3.5 mEq/l. before treatment.

Results

Throughout treatment the blood pressure remained at 125/80; the E.S.R., blood urea, and haemoglobin remained normal. There was no evidence of sodium retention; indeed, the salt intake was increased after three weeks' treatment as the serum sodium had fallen from 138 to 120 mEq/l. The serum potassium remained at 3.5 mEq/l. in spite of the potassium chloride, but rose to 4.5 mEq/l. when the oral dose was increased to 2 g. a day. While on steroid treatment the serum cholesterol rose from 195 to 260 mg./100 ml., falling again to 180 mg./100 ml. after cessation of treatment.

Little effect on the albuminuria was observed, 1 to 2 g. of albumin being excreted in the urine a day: occasionally this value was exceeded and sometimes it was less than 1 g. a day. Seven months after treatment the albumin excretion averaged 1 g. a day.

On the fourth day of treatment the number of red cells in the centrifuged urinary deposit was reported as + (previously +++), and no casts were seen. At the end of the course the urine was either reported as free from

red cells or "an occasional red cell seen" in the centrifuged deposit. Casts were always reported absent. No red cells or casts have been demonstrated in repeated samples during the seven months period following treatment.

The patient complained of epigastric pain on three occasions while receiving the larger doses of prednisolone. These attacks lasted one to ten minutes. They were not associated with nausea or vomiting and no abdominal tenderness was elicited.

The serum and urinary protein electrophoretic patterns are shown in Figs. 1-6, and the quantitative values are given in the Table.

Results of Electrophoresis of Serum and Urinary Proteins, Together with Some Biochemical Findings, and the Results of Microscopical Examination of the Centrifuged Urinary Deposit

	Jan. 3, 1958	Feb. 25	Aug. 28
Serum proteins (g./100 ml.):			
Total	8	8.2	7.0
Albumin	3.52 (44%)	4.51 (55%)	3.64 (52%)
Globulin α_1	0.4 (5%)	0.57 (7%)	0.28 (4%)
" α_2	1.76 (22%)	1.23 (15%)	0.86 (12%)
" β	1.28 (16%)	0.82 (10%)	0.96 (14%)
" γ	1.04 (13%)	1.07 (13%)	1.26 (18%)
Urinary proteins (g./100 ml.):			
Total	0.14	0.43	0.1
Albumin	0.062 (44%)	0.38 (87.5%)	0.085 (85%)
Globulin α_2	0.046 (33%)		0.003 (3%)
" β	0.032 (23%)	0.04 (10%)	0.012 (12%)
" γ		0.01 (2.5%)	
Blood urea (mg./100 ml.)	39	24	37
Serum cholesterol (mg./100 ml.)	260*	220	160
E.S.R. (mm./hour)	2	2	1
Urine:			
R.B.C.	Nil	Nil	Nil
Casts	"	"	"

* Estimated on January 21.

At the time of writing the boy was working as a labourer, and, apart from slight proteinuria, all clinical and biochemical examinations have failed to reveal any abnormality.

Discussion

Rennie (1958) defines latent nephritis as the persistence of albumin, blood, and casts in the urine six months after acute nephritis. Spontaneous recovery is possible, and 82% of those who recover do so within the first two years (Addis, 1948).

From a study of the electrophoretic patterns (Figs. 1 and 2) it will be seen that the serum shows a significant rise in the α_2 -globulin. There is a slight fall of albumin

FIG. 1.—Serum protein electrophoresis on January 3, 1958.

FIG. 2.—Urine protein electrophoresis on January 3, 1958.

FIG. 3.—Serum protein electrophoresis on February 25, 1958.

FIG. 4.—Urine protein electrophoresis on February 25, 1958.

and γ -globulin. Analysis of the urine shows that less than one-half of the total protein content consists of albumin and that one-third is made up of α_2 -globulin. Squire (1953) gives a figure of 300,000 for the molecular weight of α_2 -globulin compared with 69,000, the molecular weight of albumin. The leakage of the large globulin molecule indicates loss of selective permeability and therefore gross damage to the glomerular membrane (Hardwicke and Squire, 1955).

Two months after steroid therapy it is apparent that the serum proteins show a slight rise of the albumin fraction (Fig. 3). The general pattern is, however, unchanged. The urine picture is markedly different (Fig. 4). Only 12.5% of the total protein is globulin; the rest consists of albumin. This could be interpreted as a recovery of the selective permeability of the glomerular membrane.

The third analysis, made seven months after treatment, supports this view. The serum proteins (Fig. 5) are almost within normal limits, apart from a rather high α_2 -globulin. The bulk of the urinary protein again consists of albumin; only 15% is made up of globulin (Fig. 6).

FIG. 5.—Serum protein electrophoresis on August 28, 1958.

FIG. 6.—Urine protein electrophoresis on August 28, 1958.

Too much emphasis cannot be laid on the absolute values of the individual protein fractions estimated by paper electrophoresis (Wolstenholme and Millar, 1956). Furthermore, it is conceivable that some denaturation of the urinary proteins may occur as a result of the extraction methods. Only marked changes in pattern are therefore considered significant.

The fact that both red cells and casts were present in the urine for a period of nine months prior to treatment, but were suddenly reduced, and finally disappeared during and after treatment, suggests that the improvement was directly due to the hormone.

It would be tempting to suppose that prednisolone treatment had prevented the stage of latent nephritis from progressing into the chronic phase, and that the albuminuria was a legacy of permanent renal damage. Such an optimistic view is difficult to entertain on the result of one case, and past experience has shown that steroids rarely succeed in curing pathological processes. If it could be shown, however, that treatment prolonged the transition into the chronic phase then it would be worth while. Latent nephritis may smoulder for many years with little apparent deterioration in the patient's general condition, so the results of any form of treatment would be difficult to assess. Nevertheless, at the present time there is no known treatment which will directly influence the course of the disease, and it does seem that a trial of the newer synthetic steroid preparations would be justified.

Summary

In a patient with latent nephritis blood and casts disappeared from the urine during treatment with

prednisolone. Evidence is given to suggest that the drug had a direct effect on the improvement of glomerular permeability.

It is considered that more extensive trials would be justified.

I thank Dr. D. G. Bennett for permission to publish this account and for his encouragement; Dr. J. Gibson and the staff of the Bath Central Laboratory for the biochemical investigations; and Messrs. Pfizer Ltd., who provided a generous supply of "delta-cortril" (prednisolone).

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SPONTANEOUS HAEMARTHROSIS IN OSTEOARTHRITIS OF KNEE

A REPORT OF FIVE CASES

BY

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Haemarthrosis of any joint, if associated with trauma, is usually coupled with a severe intra-articular injury. Spontaneous bleeding occurs in cases of blood dyscrasia, and sometimes will result from tumour invasion. It is known that small intra-articular haemorrhages occur in arthritic knees from time to time, often as the result of minor strain (DePalma, 1954); but it is not widely appreciated that these haemorrhages may be very extensive. Within the past two years I have been able to collect the details of five cases of spontaneous haemarthrosis of the knee. The history has been so characteristic that in two of the cases a firm diagnosis was possible before it was confirmed by aspiration. Although a "doughy" consistency is sometimes thought to be characteristic of a haemarthrosis, difficulty often arises in distinguishing it from an acute effusion. It is felt that the condition may often go undiagnosed and that, if recognized, early aspiration might reduce the period of disability.

Case Reports

Case 1.—A married woman aged 64 was admitted to hospital with a history of sudden swelling of the left knee while she was standing. She stated that three weeks previously there had been a similar incident. The second attack was described "as if the muscles tightened into a knot and the knee swelled." On the first occasion she