

TREATMENT OF THE NEPHROTIC SYNDROME IN CHILDREN WITH TRIAMCINOLONE

By Freda M. Paul, M.B.,B.S., M.R.C.P. (Edin.), F.R.F.P.S. (Glas.), D.C.H. (Lond.)

(From the Paediatric Unit, General Hospital, Singapore)

The nephrotic syndrome in children is characterised by the presence of oedema, massive albuminuria, hypoproteinaemia and hyperlipaemia and is commonly met with in the Paediatric Unit. In recent years, steroid therapy seems able to bring about a diuresis, and maintenance steroid therapy seems to keep the patient in a state of clinical remission. Wong (1960) in a comparison of children here with the nephrotic syndrome without and with steroid therapy states that at the end of two years, 57% remitted as compared with 16.8% in the non-steroid group. He further states that only one-seventh as many may develop renal failure with steroids and the death rate is lowered to 9.2% with steroids, as compared with 42% without steroids.

At present when the patient is first seen in the Paediatric Unit and a diagnosis of the nephrotic syndrome is made clinically and biochemically, the child is warded and intensive steroid therapy is started, prednisolone being given in a dose of 1.5 mgm. to 2.0 mgm. per kilogram body weight per day for two to three weeks and then gradually tailed off. The child is then followed in the outpatient clinic fortnightly, while he is on a maintenance dose of 2.5 mgm. to 5 mgm. daily. Should a relapse occur, as characterised by gross oedema and a rise in the urinary protein, the dose of prednisolone is stepped up and early recurrence may be reversed. Unfortunately in those cases with recurrent relapses increasing the dose of prednisolone may fail to produce a diuresis. In such cases the use of one of the newer more potent steroids proves effective.

Triamcinolone (9 alpha-fluoro-16alpha hydroxy-delta¹ hydrocortisone) a synthetic steroid is a recent product of the search for corticosteroids which are more potent and have fewer undesirable side-effects than hydrocortisone. It differs from hydrocortisone by having a fluorine atom at C₉, a double bond between C₁ and C₂ and a hydroxyl group at C₁₆. This compound is of particular interest because the parent substances, flourine, hydrocortisone, and delta¹ fluoro-hydrocortisone are potent salt-retainers whereas the addition of the hydroxyl group at C₁₆ abolishes the salt retention without interfering with the anti-inflam-

matory and glucocorticoid properties of the compound. Metabolic and clinical studies have shown that Triamcinolone has no salt-retaining or hypertensive effects in doses of 10 to 20 mgm. per day, which is sufficient to produce desirable therapeutic responses in a variety of disease. Accordingly this compound was tried on six children with the nephrotic syndrome in the paediatric unit.

MATERIAL AND RESULTS

As seen in Table I, all the patients were males which is not surprising as the nephrotic syndrome predominantly affects males. Their ages varied from two to seven years. The cases chosen were those with recurrences of gross oedema and gross proteinuria while on a maintenance dose of Prednisolone. Table I shows the average length of history before admission.

The relapses while on Prednisolone therapy are also indicated, and the time Triamcinolone was begun is also shown.

Case I relapsed twice during three months and was therefore put on Triamcinolone on the 3rd admission. Case 4 had recurrences of oedema and proteinuria five times over a period of nine months and responded dramatically to Triamcinolone on the 6th admission, as seen in Figures 1 and 2, with a weight loss of ten pounds.

Case 2 was given a trial of Prednisolone for a month and when diuresis failed to occur, Triamcinolone was tried. Figures 3 and 4 show the patient before and after treatment with Triamcinolone. This child lost eight pounds after therapy.

Case 6 was given a trial of Prednisolone and later tried on Triamcinolone. Unfortunately as will be seen later, this child did not do well.

Before starting therapy the blood urea, the blood cholesterol, the serum protein, and the serum electrolytes were checked. The blood urea was normal in all except the last case. The latter was in the "haematuric" or "mixed phase" of the nephrotic syndrome and had an elevated blood urea and hypertension. The blood cholesterol and

TABLE I

No.	Age	Sex	Length of History	Date of admission	Date of first relapse while on Prednisolone	2nd relapse while on Pred-nisolone	3rd relapse while on Pred-nisolone	4th relapse while on Pred-nisolone	5th relapse while on Pred-nisolone	Length of disease before Triamcinolone started
1.	2 years	M	3 weeks	22. 6.60	15. 7.60	20.9.60				3 months 3 weeks
2.	4 years	M	2 months	21. 4.60						4 months 3 weeks
3.	4 years	M	2 months	5.10.59	7.12.59	1.3.60				7 months
4.	7 years	M	2 weeks	22. 1.58	1. 2.58	2.3.58	5.1.58	5.4.59	1.8.60	2½ years
5.	5½ years	M	3 months	30. 1.60	6. 6.60					9 months
6.	2 years	M	2 weeks	9. 4.60						3 weeks



Fig. 1(a)



Fig. 2(a)



Fig. 1(b)



Fig. 2(b)

Figs. 1(a) & 1(b). Show the patient on his sixth admission with gross ascites, oedema of limbs and puffiness of face.

Figs. 2(a) & 2(b). Note the loss of ascites and oedema 10 days after treatment with Triamcinolone.



Fig. 3(a)

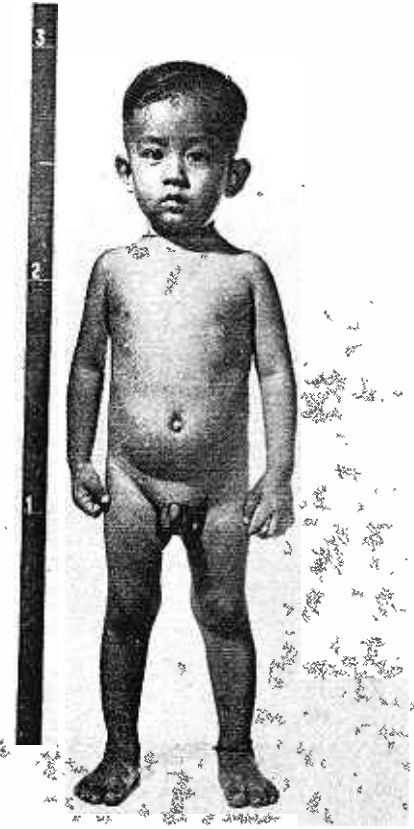


Fig. 4(a)



Fig. 3(b)

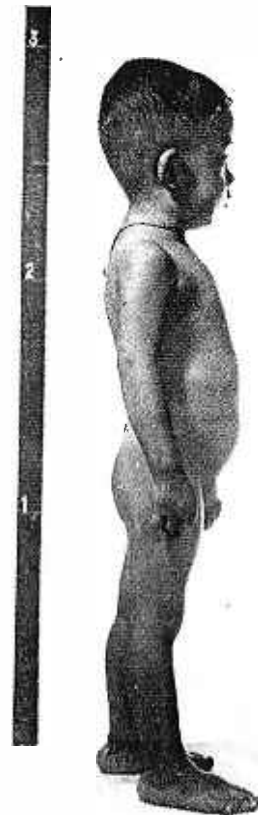


Fig. 4(b)

Figs. 3(a) & 3(b). Note the puffy eyes, sagging abdomen and oedema of feet.

Figs. 4(a) & 4(b). Note the loss of oedema after ten days treatment with Triamcinolone.

the serum protein in all the cases had the typical findings of the nephrotic syndrome.

The initial dose of Triamcinolone was 16 mgms. daily in doses of 4 mgm. each. This dose was continued until diuresis occurred and until proteinuria improved when the dose was gradually tailed off and the maintenance dose of either 4 mgm. or 2 mgm. given daily.

The typical response was an abrupt diuresis beginning 10-12 days after the start of therapy and resulting in complete disappearance of retained fluid in the next three to four days. The loss of weight due to the diuresis was so great that it was sometimes difficult to recognise the same patient after his diuresis. Most of the patients showed a little increase in weight in the "lag period" prior to diuresis.

URINARY ABNORMALITIES

One of the striking features following therapy is the reduction of urinary protein even before diuresis occurred. During the period of diuresis, the urinary excretion of protein decreased rapidly and by the time diuresis was complete, the urinary

findings were within normal limits. Table II shows the urinary findings before and after Triamcinolone therapy.

SODIUM AND POTASSIUM BALANCE

There were no definite changes in the serum concentration of sodium and potassium and although one expected to get a fall in the serum potassium, this was not the case. No potassium supplement were given nor required.

SERUM ALBUMIN AND GLOBULIN

At the onset of diuresis, albumin began to increase and globulin showed a lesser rise. It usually requires three to five weeks of Triamcinolone therapy before these values return to normal.

SERUM CHOLESTEROL

The serum cholesterol showed a marked fall after the diuresis and it took 4 weeks before the cholesterol reached normal values of 250 mgm. per 100 cc.

TABLE II
LABORATORY TESTS BEFORE AND AFTER TRIAMCINOLONE

Patient No.	1	2	3	4	5	6
Weight (Pre.)	28 lbs.	34 lbs.	28½ lbs.	41 lbs.	45½ lbs.	31 lbs.
Weight (Post)	23 lbs.	26 lbs.	22 lbs.	31 lbs.	38 lbs.	28 lbs.
U. Prot. (Pre.)	1000 mgm.%	2000 mgm.%	3000 mgm.%	3000 mgm.%	3000 mgm.%	1800 mgm.%
U. Prot. (Post)	10 mgm.%	10 mgm.%	50 mgm.%	35 mgm.%	40 mgm.%	100 mgm.%
Blood Proteins (Pre.)	4.8 gm.%	5.3 gm.%	4.03 gm.%	4.96 gm.%	4.8 gm.%	3.88 gm.%
Proteins (Post)	5.6 gm.%	8.0 gm.%	6.98 gm.%	8.5 gm.%	4.7 gm.%	4.46 gm.%
Albumen (Pre.)	1.1 gm.%	4.30 gm.%	3.23 gm.%	4.60 gm.%	3.2 gm.%	3.03 gm.%
Albumen (Post)	2.6 gm.%	4.8 gm.%	3.49 gm.%	3.8 gm.%	3.7 gm.%	3.23 gm.%
Globulin (Pre.)	2.5 gm.%	1.04 gm.	0.80 gm.%	0.30 gm.	1.6 gm.	0.83 gm.%
Globulin (Post)	2.0 gm.	3.2 gm.%	3.49 gm.%	4.7 gm.	1.0 gm.	1.23 gm.%
Cholesterol (Pre.)	600 mgm.%	512 mgm.%	488 mgm.%	408 mgm.%	544 mgm.%	460 mgm.%
Cholesterol (Post)	408 mgm.%	280 mgm.%	233 mgm.%	270 mgm.%	412 mgm.	412 mgm.%
Sodium (Pre.)	135 mEq.	128 mEq.	320 mgm.%	127 mEq.	not done	130 mEq.
Sodium (Post)	137 mEq.	130 mEq.	350 mgm.%	129 mEq.	not done	152 mEq.
Potassium (Pre.)	4.4 mEq.	4.3 mEq.	19.5 mgm.%	4.3 mEq.	not done	5.7 mEq.
Potassium (Post)	4.5 mEq.	4.2 mEq.	17.0 mgm.%	4.2 mEq.	not done	3.3 mEq.
Chloride (Pre.)	104 mEq.	98 mEq.	358 mgm.%	96 mEq.	not done	90 mEq.
Chloride (Post)	104 mEq.	97 mEq.	350 mgm.%	97 mEq.	not done	122 mEq.

CHART OF CASE 4

A CASE OF NEPHROTIC SYNDROME TREATED WITH PREDNISOLONE AND TRIAMCINOLONE

(NOTE DRAMATIC LOSS OF WEIGHT WITH TRIAMCINOLONE THERAPY)

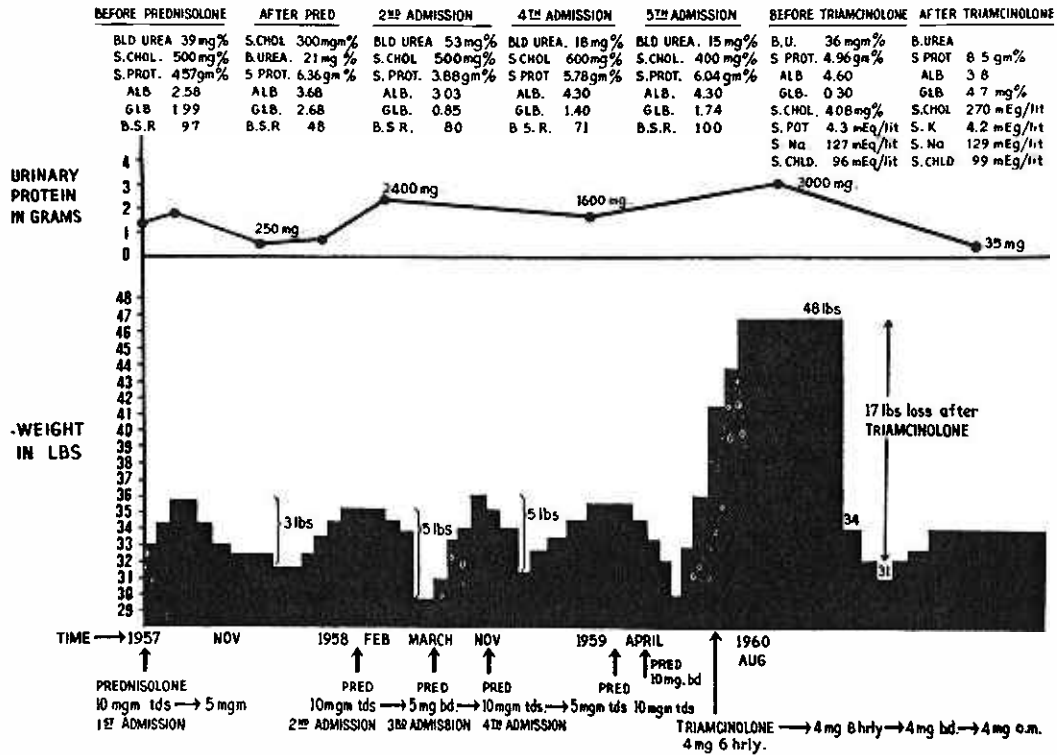


Fig. 5. Note: (a) the loss of 17 lbs. during the phase of maximum diuresis during Triamcinolone therapy.
 (b) the drop of urinary protein from 3.000 mgm. to 35 mgm.%.
 (c) the reduction of serum cholesterol to normal values after therapy.
 (d) the elevation of the serum protein to 8.5 gm.%. after therapy.

CHART OF CASE 2

TREATMENT OF THE NEPHROTIC SYNDROME WITH PREDNISOLONE AND TRIAMCINOLONE.

(NOTE THE MODERATE LOSS OF WEIGHT WITH PREDISOLONE THERAPY AND THE MARKED LOSS WITH TRIAMCINOLONE THERAPY)

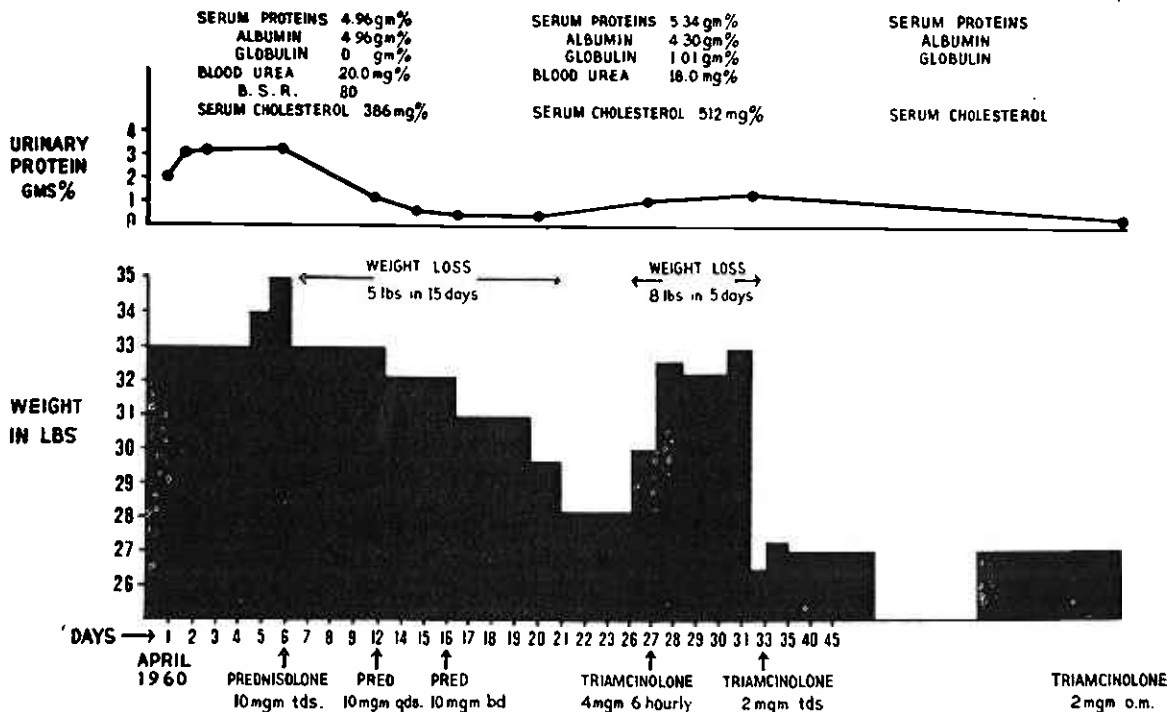


Fig. 6. Note: (a) the loss of 8 lbs. during Triamcinolone therapy.
 (b) the drop of urinary proteins from 2,000 mgm. to 10 mgm.%.
 (c) the return of the serum cholesterol from 512 mgm. to 280 mgm.%.
 (d) the elevation of the serum protein after treatment to 8.0 gm. (A/G= 4.8/3.2), which was not been indicated on diagram.

SIDE-EFFECTS

No clinical manifestations of the sodium and water retention generally associated with Corticosteroid therapy was seen. None of the patients showed the gross moon-face that develops with Prednisolone therapy.

Case 4 developed boils on the face which subsided with antibiotics. No psychic effects were noted.

Case 1 was noted to limp 4 weeks after Triamcinolone was started because of pain in the right ankle but there was no swelling nor redness of the ankle and as the pain subsided in spite of Triamcinolone being continued, the possibility of "Triamcinolone Arthritis" was dismissed. None of the patients developed hypertension due to the drug itself. In general, Triamcinolone was well tolerated.

Special mention must be made of Case 6, which was in the haematuric phase of the nephrotic syndrome. McCrory and Fleischner (1953) do not think that this "haematuric phase" is a contraindication to steroid therapy as many patients in this phase had no complications with steroid therapy. Wong (1960) reported hypertensive encephalopathy in 2 of 3 patients who were in the haematuric phase, when started on steroid therapy. Case 6 lost 3 lbs. while on Triamcinolone therapy but developed a fulminating B-coli gastroenteritis, strain 0119, which was not sensitive to any antibiotic, except Kantrex. This child eventually died of this secondary infection.

FOLLOW-UP

Of the 5 children who are alive and who have had a diuresis and who have had a marked improvement in the loss of urinary protein, all have remained in a state of remission. They have been followed from 4 to 11 months and so far no relapses occurred while on Triamcinolone therapy.

COMMENTS

Hellman (1959) on a trial of 15 children with the nephrotic syndrome report that Triamcinolone

is a highly effective therapeutic agent. With the 20 mgm. per day dose which they employed for 30-45 days in their series, side-effects were absent except for the occasional appearance of slight moon-face. 67% of their cases were in complete remission in the entire series. Of patients whose disease was less than 12 months in duration, and who did not have hypertension, 89% had a complete remission.

Daeschner et al (1960) states that the response to treatment is more consistent in patients whose proteinuria has been present for less than 4 months at the time treatment is instituted. He states that in patients with proteinuria of greater duration treatment may lead to a loss of oedema and reduction in the degree of proteinuria without complete clearing of the urine of protein.

In the present series though the cases were few, the results were satisfactory and comparable to those reported in the literature. Triamcinolone has the advantage of producing a more rapid diuresis and is therefore suitable for cases that relapse on Prednisolone therapy. The side-effects were few except for case 6, who contracted a severe gastroenteritis.

SUMMARY

The use and results of Triamcinolone in the Nephrotic syndrome in 6 children are described above.

ACKNOWLEDGEMENT

I wish to thank Mr. Ho Tat Seng for the photographs.

REFERENCES

- Daeschner, C. Wm., Dodge, W.F., and Leighton Hill, L. (1960) Nephrotic syndrome. Management with triamcinolone. *Journal of Paediatrics*, 56, 48.
- Hellman, L., Zumoff, B., Minsky, A., Kretchmer, N., and Kramer, B. (1959): Treatment of the nephrotic syndrome with triamcinolone. *Paediatrics*, 23, 686.
- McCrory, W.W., Fleischner, L.S. (1958): The nephrotic syndrome. Recent advances in Paediatrics, 2nd. Edition. P. 246. London. J. & A. Churchill Ltd.
- Wong, H.B. (1960) The nephrotic syndrome in Singapore children. *Journal of Singapore Paediatric Society*, 1, 19.