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ACUTE NEPHRITIS IN NON-EUROPEAN CHILDREN, WITH SPECIAL REFERENCE TO THE TREATMENT OF HYPERTENSION WITH MAGNESIUM SULPHATE

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Acute nephritis is a fairly common condition in paediatric practice but as far as we are aware no comparable series of the disease in the non-European community in South Africa has been published. The only available literature is a paper by Uys[1] on the pathology of renal disease in the Bantu on the Witwatersrand.

The paediatric out-patient department of the Coronation Hospital deals with children of African, Indian and Coloured (i.e. mixed) descent up to the age of 12 years. The average annual attendance is 65,000, out of which 2,100 patients are admitted to the wards.

The series now reported comprises 83 cases of acute nephritis admitted to the paediatric wards during the period January 1951 - December 1958 (inclusive). The diagnosis was based on the 4 factors: history, oedema, oliguria, and hypertension, in various combinations, as well as urinary findings of haematuria, albuminuria and granular casts in all cases.

Sex, age and race. Of the 83 cases, 45 were males (54%) and 38 females (46%). There were 46 Africans (55%), 30 Coloured (i.e. of mixed descent) (36%), and 7 Indians (9%). The ages ranged from 2 to 12 years, the greatest incidence being at 3 - 5 years (Tables I and II).

TABLE I. CASES BY AGE (IN YEARS) AND SEX

	1 - 2	*2 - 3*	*3 - 4*	*4 - 5*	*5 - 6*	*6 - 7*	*7 - 8*	*8 - 9*	*9 - 10*	*10 - 11*	*11 - 12*	*12 - 13*
Male	—	3	8	6	10	3	4	2	4	2	2	1
Female	—	1	5	8	11	4	3	2	1	2	1	—
Total	—	4	13	14	21	7	7	4	5	4	3	1

TABLE II. CASES BY RACE

	Bantu	*Mixed*	*Indian*	*Total*
Male	24	18	3	45
Female	22	12	4	38
Total	46	30	7	83

Stay in hospital. This ranged from 3 to 68 days, with an average of 3½ weeks (Table III).

TABLE III. DURATION OF STAY IN HOSPITAL (IN DAYS)

	0 - 7	*8 - 14*	*15 - 21*	*22 - 28*	*29 - 35*	*36 - 42*	*43 - 49*	*50 - 56*	*57 - 63*	*64 - 70*	*Total*
Male	3	9	10	10	8	2	3	—	—	—	45
Female ..	2	9	5	7	6	2	—	2	3	2	38
Total	5	18	15	17	14	4	3	2	3	2	83

Predisposing illnesses. In only 40 cases could a history of predisposing illness be elicited. Twenty gave a history of sore throats, 15 of impetigo, 4 of acute otitis media, and 1 of infected burns.

Presenting symptoms. Although oedema and haematuria were the commonest symptoms, not all of the 83 cases presented with them. There were 72 with initial oedema, while only 52 presented with haematuria. Only 43 patients, however, presented with both symptoms together. In 8 cases there was a history of oliguria. Cerebral symptoms as a presenting feature occurred in 22 cases. Other presenting symptoms are shown in Table IV.

TABLE IV. PRESENTING SYMPTOMS

Symptoms		*Number of Cases*
Oedema		72
Haematuria		52
Cerebral symptoms		22
Headache	18	
Vomiting	11	
Drowsiness	6	
Irritability	2	
Convulsions	1	
Blurring of vision	1	
Urinary symptoms		8
Oliguria	8	
Dysuria	8	
Polyuria	4	
Backache	3	
Anorexia		14
Pyrexia		10
Abdominal pain		7
Epistaxis		4
Diarrhoea		2
Dyspnoea		2

Clinical Findings

1. *Oedema.* A history of oedema was given in 72 cases, but on examination this was only found in 67; and of these 3 did not give a history of oedema. This indicates that at least 75 patients had had oedema during the course of their illness.

2. *Hypertension.* This was recorded as being present in any child with a diastolic blood-pressure reading of 10 mm.Hg (or more) above the normal for the corresponding age-group given by Lyon and Kaplan in Nelson's *Textbook of Pediatrics.*[2] On this criterion, 61 cases (73·5%) of whom 32 were males and 29 females, showed variable degrees of hypertension (Table V). Under treatment this persisted for 1 - 29 days (average 7·1 days). Of the 46 African cases 71·7% showed hypertension, and of the 30 Coloured, 70%. All the 7 Indians were hypertensive. Associated with the hypertension were 13 cases in con-

TABLE V. TREATED AND UNTREATED HYPERTENSIVE CASES

Age Groups	Cases	Diastolic BP in mm.Hg								Total
		70 - 80	>80 ^	>90 ^	>100 ^	>110 ^	>120 ^	>130 ^	>140 ^	
4 years and under*	All	4	5	2	4	2	3	2	1	23
	Treated	1	2	1	3	1	3	1	1	13
5 - 8 years†	All	2	2	8	8	6	2	2	—	30
	Treated	1	1	6	8	5	1	1	—	23
9 - 12 years‡	All	1	1	—	3	3	—	—	—	8
	Treated	—	1	—	3	3	—	—	—	7
Total	All	7	8	10	15	11	5	4	1	61
	Treated	2	4	7	14	9	4	2	1	43

* Mean normal blood pressure, systolic 85, diastolic 60.
† Mean normal blood pressure, systolic 87 - 95, diastolic 60 - 62.
‡ Mean normal blood pressure, systolic 98 - 108, diastolic 64-69.

gestive cardiac failure, of whom 1 was hyperpotassaemic with complete heart block, dying in uraemia soon after admission. Two were cases of hypertensive encephalopathy with bizarre and changing signs.

3. *Infections.* Acute infections were present on admission in 56 patients — in 36 acute tonsilitis and pharyngitis, 11 impetigo, 5 acute otitis media, 3 pneumonia, and 1 carbuncle of the anterior abdominal wall. One child was found to have pulmonary tuberculosis.

Investigations

1. In all the cases proteinuria, haematuria, and granular casts were found in the urine.

2. The urinary output was measured in every patient. In those showing an initial oliguria the output soon became normal, except in one who was anuric on admission and died in uraemia.

3. The blood urea was measured in 78 cases. In 36 (46%) it was found to be above normal, i.e. above 40 mg. per 100 ml. In all these the blood urea reverted to normal on improvement of the clinical condition.

4. The erythrocyte sedimentation rate was measured in 55 of the children and was found to be raised in 48 (87%).

5. Haemoglobin estimations were carried out in 73 cases. Anaemia was recorded if the level of haemoglobin found was 1 g. per 100 ml. (or more) below the normal given for the corresponding age and sex by Whitby and Britton.[3] On these criteria, 30 patients (41%) were found to be suffering from different degrees of anaemia.

6. Leucocyte counts were carried out in 72 patients. In 39 of these a reading of over 11,000 WBCs per c.mm. was recorded.

7. Serum-protein and serum-cholesterol estimations were carried out in some cases and as the results were all within normal limits, these investigations were not made in the rest of the cases. The actual results in the cases where the estimations were carried out were as follows: Serum-cholesterol estimations were carried out in 35 cases; 8 had levels between 100 - 150 mg. per 100 ml., 17 between 151 - 200, and 10 between 201 - 260 mg. per 100 ml. Serum-protein estimations showed the usual reversal of albumin-globulin ratio which is found in the non-European population, except in 1 case. The albumin-globulin ratio in this case was 4·4 : 3·1 g. per 100 ml.

8. In the 31 cases where throat swabs were taken haemolytic streptococci were isolated on culture in only 2 cases. Other organisms cultured were non-haemolytic streptococci (2 cases), *Streptococcus viridans* (11 cases), *Staphylococcus aureus* (1 case) and *pneumococci* (2 cases). In 13 cases no pathogenic organisms were found.

9. Streptococcal antihaemolysin-O titres were only estimated (in 26 cases) during the latter years of this series. In 16 cases (62%) the titre exceeded 200 units.

TREATMENT AND RESULTS

General Treatment

All cases were treated with bed rest, salt-free and low-protein diet, and a regulated fluid intake for a variable period depending on the clinical improvement. Every case received parenteral penicillin for at least 5 days.

Treatment of Hypertension

Hypertension was treated in cases where it persisted for more than 24 hours after admission, or the blood pressure continued to rise, and in cases with complications (congestive cardiac failure or encephalopathy).

In our opinion the treatment of choice in cases of uncomplicated hypertension is intramuscular magnesium sulphate (0·1 c.c. of a 50% solution per kg. body-weight) given every 4 - 6 hours until the blood pressure readings became normal. These were taken every 2 - 4 hours.

Cases in which congestive cardiac failure is present are treated with digoxin as well as intramuscular magnesium sulphate. The digitalizing dose of digoxin is 0·025 - 0·04 mg. per lb. body-weight for the first 24 hours.

In patients with encephalopathy magnesium sulphate is given by slow intravenous infusion (15 c.c. of a 1% solution per kg. body-weight) over 12 - 24 hours. The blood pressures should be checked every half hour. As clinical improvement occurs, the treatment should be changed to intramuscular magnesium sulphate until the blood pressure has become normal.

The following 2 cases are reported as examples of this regime of treatment:

Case 1

P. J., a 10-year-old Coloured girl was admitted to hospital on 13 September 1956 with a history of headache and vomiting of increasing severity for 3 weeks. On the day before admission she developed generalized convulsions lasting from 2 - 5 minutes without loss of consciousness. There was no history of previous convulsions and no family history of epilepsy.

Examination. On the day of admission the child lay curled up in bed, ill, mentally confused, and irritable. Temperature 99·8°F, pulse rate 100 per minute, respiration rate 24 per minute, blood pressure 180/120 mm.Hg. Further examination negative. The next day peri-orbital oedema and left hemiparesis were noted. The fundi showed vascular spasm. The urinary output during the first 24 hours was slightly diminished. Urinalysis showed marked proteinuria with innumerable erythrocytes, a moderate number of pus cells, and granular and hyaline casts. Blood urea 62 mg. per 100 ml.

Treatment with 1% intravenous magnesium sulphate (3 g. in 300 c.c. of 5% invert sugar) was commenced. Within 30 minutes the blood pressure started to fall and in 5 hours it was 120/90 mm.Hg; the headache had disappeared and the neurological examination was normal, the fundi showing no vascular spasm. After 9 hours' treatment intramuscular magnesium sulphate (5 c.c. of 50% solution 4 hourly) was instituted. No further cerebral symptoms were observed and the blood pressure remained normal. The patient made an uneventful and complete recovery, and was discharged from hospital on 16 October 1956.

Case 2

C.T., a 9-year-old Coloured boy was admitted on 10 March 1957 with a 1 week's history of headache, swelling of the face and black urine.

Examination. On admission the child looked ill, temperature 101°F, pulse rate 100 per minute, respiration rate 24 per minute, blood pressure 180/120 mm.Hg. Peri-orbital, scrotal and ankle oedema were present. There were no neurological signs. Urinalysis showed a marked proteinuria, numerous erythrocytes, a few pus cells, and hyaline and granular casts. Blood urea 49 mg. per 100 ml. Urinary output normal.

Treatment with intramuscular magnesium sulphate (3 c.c. of 50% solution 4 hourly) was started. The following morning the headache was severer and vision was blurred. The blood pressure was then 170/130 mm.Hg. As intravenous magnesium sulphate (6 g. in 600 c.c. of 5% dextrose water) was about to be commenced, the child had a generalized convulsion. The infusion, however, brought the blood pressure under control with dramatic improvement of symptoms, the blood pressure falling to 140/90 mm.Hg within 4 hours. After 8 hours, intramuscular therapy was recommenced for another 2 days with no further rise in blood pressure. The patient was discharged on 13 April 1957 with a blood pressure of 110/60 mm.Hg.

Results

Forty-three of the 61 children who had hypertension associated with their acute nephritis were treated with magnesium sulphate. Forty-one, including 13 with congestive cardiac failure, were treated with intramuscular magnesium sulphate. A good response followed by complete recovery was obtained in every case but one. This case, mentioned above, was admitted with hypertension, congestive cardiac failure, anuria and hyperpotassaemia, and died in uraemia. The 2 cases with hypertensive encephalopathy were treated initially with intravenous magnesium sulphate, with dramatic improvement in the cerebral condition; intramuscular magnesium sulphate was then given until they became normotensive, and eventually they both recovered completely. The duration of therapy in the 41 cases was from 18 hours to 11 days with an average of 4·2 days. The remaining 18 hypertensive cases were not treated with magnesium sulphate because their blood pressure dropped to normal levels on bed rest alone. The 22 non-hypertensive cases in the series recovered completely without any specific treatment.

Socio-economic and racial factors made it difficult to follow up the 82 children who recovered. Amongst those who were seen there were no indications of progression to chronic renal disease.

DISCUSSION

In our series, acute nephritis accounted for 0·4% of admissions to the paediatric wards with a slight preponderance of males over females (Table I). The cases under the age of 7 made up 71% of the series. These figures are similar to those quoted by Rubin.[4]

Hypertension occurred in about 75% of all our cases. It was present in all 7 Indian patients which, although not of statistical significance, may indicate that they are more prone to hypertension in this disease than other races, or that dietary factors, viz. their high protein intake, may play an important part in the aetiology of this complication. Three other Indian cases of acute nephritis, which occurred during 1959 (not included in this series), were also found to have severe hypertension; follow-up has shown them to be progressing to the chronic phase of the disease.

The rise of blood pressure (like its fall) is often precipitous. It usually persists for the first week of the illness, but may continue for weeks before returning to normal levels. If the disease progresses to the subacute and chronic stages the hypertension will become permanent, but this did not occur in our series.

The hypertension is said to be caused by vasospasm following renal ischaemia.[4] The rise in blood pressure represents a compensatory attempt to increase the rate of glomerular filtration.[5]

The possibility that the hypertension may be complicated by encephalopathy and congestive cardiac failure necessitates close observation of the patient with immediate therapy upon detection of either of these complications. Hypertensive encephalopathy is a much more frequent complication in children than in adults.[6] Blackfan and Butler[7] reported an incidence of 8%. Cerebral symptoms occurred in 31·1% of Burke and Ross's cases.[8] In the present series 26·5% showed cerebral symptoms but only 2·4% had encephalopathy. Rubin[4] states that congestive cardiac failure occurs in 20% of cases. In this series 15·7% showed evidence of congestive cardiac failure.

A number of drugs have been employed in the treatment of hypertension in acute nephritis. Magnesium sulphate has been used for many years. It was introduced by Blackfan *et al.*[9] in 1923 and has been widely used ever since. It is most satisfactory in the treatment of hypertensive crises because it has the advantage of increasing the glomerular filtration rate, improving the effective renal plasma flow with a corresponding increase in the renal blood flow in the presence of vascular spasm. When encephalopathic symptoms occur the intravenous is the most useful method of administration,[10-12] because of its action in relieving cerebral arterial spasm.[13] In the presence of oliguria the excretion of the magnesium sulphate decreases, giving rise to toxic effects manifested by slowing of the respiratory rate.[11] It can be counteracted by the intravenous administration of 10% calcium gluconate, but this was not required in any of our cases.

Magnesium sulphate was the drug of choice in all our patients with hypertension which we considered necessitated treatment. The drug was effective in all cases and other hypotensive agents were found to be unnecessary.

Veriloid,[14,15] reserpine,[16] hydralazine,[17,18] reserpine with hydralazine,[19,20] and hexamethonium[19] have all been used in the treatment of hypertension of acute nephritis with variable results. We have had no experience with them.

Conclusion

We have found magnesium sulphate a very effective drug to use in the treatment of hypertension in acute

nephritis. We did not carry out routine control with electrolyte estimations and ECG tracings; nevertheless, none of our cases showed any signs of toxicity, and we recommend it as a safe and useful drug when hypotensive agents are indicated in this disease, provided it is used in the dosage suggested.

SUMMARY

1. Eighty-three cases of acute nephritis in non-European children admitted to hospital over a period of 8 years are analysed.

2. Special reference is made to hypertension, its complications, and its treatment with magnesium sulphate.

3. All cases where it was indicated were treated with magnesium sulphate with good results. No toxic effects followed its use.

4. There was only 1 fatality in the series.

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