NEPHRITIS IN CHILDREN AND ITS PROGNOSIS.

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Being in some doubt as to the prognosis of nephritis in childhood, and hesitating to base our beliefs upon observations of too short a duration, we have endeavoured to form our conclusions on this subject from a more protracted investigation. With this object in view we have followed up 64 cases, all of which have been re-examined at least twice in a period of three and a half to five and a half years after the onset of the renal symptoms.

The majority of our cases were first observed in the acute stages, so that an attempt has been made to classify them by the symptoms which they then presented. Subsequent examinations have served to show in which type of acute nephritis the largest proportion of recoveries can be expected.

Classification and Symptomatology of Acute Cases.

For the purposes of this paper acute nephritis in children has been divided into two main groups, the parenchymatous or "exudative," and the hæmorrhagic. Parenchymatous is taken to include all cases of tubulo- and glomerulo-nephritis, post-scarlatinal nephritis being the best known example of the latter. It is not intended to discuss these two sub-groups separately, as symptomatically they present essentially similar features, and in the clinical state it is usually a matter of conjecture whether the glomeruli or the tubules are chiefly affected. In either case the urine is blood stained at the onset of the illness, and traces of blood may be detected either microscopically or chemically for several weeks afterwards. The quantity of albumen passed is usually considerable, and is much in excess of that attributable to the amount of blood present in the urine. Casts, granular, epithelial, and hyaline are numerous, and blood casts may also be found. A variable degree of oliguria is common in the early stages, the obstruction to the urinary outflow resulting either from swelling of the endothelium lining the capillaries of the Malpighian tufts, or from blocking of the tubules by cellular debris. Other symptoms often associated with acute parenchymatous nephritis are headache, vomiting, abdominal pain, a slight rise of temperature, and œdema. Œdema is the most constant symptom of this type of nephritis, very often becomes generalised, and is not infrequently the only indication of the occurrence of the renal trouble.

Acute hæmorrhagic nephritis⁽⁶⁾ on the other hand can usually be distinguished from the above type. Its chief characteristic is the sudden onset of hæmaturia, in most cases without reduction in the quantity of urine passed. The hæmaturia occurs during, or follows at a short interval after, some acute or subacute infection, especially of the naso-pharynx. There may be little or no evidence of constitutional disturbance when the hæmaturia commences during the subsidence of the primary infection, but in those cases where the two conditions exist synchronously general symptoms such as headache, vomiting, abdominal pain and pyrexia are often present. The quantity of blood passed is greater than in the acute parenchymatous type, and the colour of the urine may vary in the initial stages between the bright red of arterial blood and a "smoky" brown. The albumen present can largely be accounted for by the degree of hæmaturia. In many cases the blood and albumen disappear almost synchronously from the urine in a few days or weeks, but may persist sometimes intermittently for several weeks. It is not uncommon, however, for a trace of albumen to be present in the urine for a considerable time after the passage of red blood corpuscles has ceased. It is important to note that œdema is seldom generalised, and in most cases consists of no more than a slight puffiness round the eyes. Blood and other casts are met with, but are not so numerous as in the parenchymatous type.

As a rule in hæmorrhagic nephritis there is no increase of cardiac dulness nor of the blood pressure, the blood urea is not raised, and the power to concentrate urea is within normal limits. In parenchymatous nephritis, on the other hand, a disturbance of one or other of these features is commonly present in the acute stages.

Ætiology.

As to the causation of acute nephritis the belief is growing that it is more commonly secondary to some naso-pharyngeal infection, especially tonsillitis, than to any other cause. Streptococcal infections appear to be the commonest precursors of acute nephritis, but pneumococcal and staphylococcal infections must also be mentioned. In the parenchymatous type the presence of toxins in the circulation is generally held responsible for the renal injury. In the hæmorrhagic type, on the other hand, it is possible that the condition is of embolic origin affecting a proportion of the glomeruli in a scattered uneven manner. This type of nephritis is described by Muir⁽³⁾ as a complication of subacute endocarditis due to streptococci. Allison⁽¹⁾ in making some observations on acute nephritis in children was impressed by the sudden appearance of hæmaturia in several of his cases, and suggested infarction as a cause. Cultures of the urine, which were made in six of our hæmorrhagic and in seven of our parenchymatous cases, were all negative.

While parenchymatous nephritis frequently occurs without any apparent cause, yet in hæmorrhagic nephritis it is possible in most cases to associate the condition with some definite focus of infection. In the present series of 64 cases, 49 were examples of acute nephritis, and of these 22 were classified

as parenchymatous, and 27 as hæmorrhagic. In only two of the hæmorrhagic cases could no focus of origin be traced, while in nine of the parenchymatous cases the causation was quite obscure. Table I. shows the nature and proportion of the probable causes in each group.

TABLE I.

Analysis of Infective Conditions associated with 49 cases of Acute Nephritis.

<i>Parenchymatous.</i>				<i>Hæmorrhagic.</i>			
Tonsils found enlarged	...	...	5	Tonsillitis or large unhealthy	...	...	...
Cervical adenitis	...	...	1	tonsils	...	...	7
Scarlet fever	...	...	4	Tonsillitis and chorea	...	...	1
Measles	...	...	1	Cervical adenitis and tonsillitis	...	...	9
Gastro-enteritis	...	...	1	Otitis media	...	...	6
Bronchitis	...	...	1	Pneumonia	...	...	2
Origin obscure	...	...	9	Origin obscure	...	...	2
Total				Total			
22				27			

The figures in the above table suggest that tonsillar infections and associated conditions such as cervical adenitis and otitis media are of more importance in the causation of the hæmorrhagic than of the parenchymatous type of nephritis; 85·5% as compared with 27·2% in the present series. The proportion of cases in the two sexes was fairly evenly distributed; 11 boys and 11 girls in the parenchymatous type, and 15 boys and 12 girls in the hæmorrhagic. As regards the age incidence in our series all the hæmorrhagic cases occurred between the third and tenth years, 16 being between the third and fifth years. The majority of the parenchymatous cases occurred between the third and eleventh years, while seven were between the ages of one and three. Nine cases occurred in the period three to five.

Clinical Features of Each Group.

Some of the main features in each group of 22 cases of parenchymatous and 27 cases of hæmorrhagic nephritis are given in tabular form in Table II.

TABLE II.

Œdema :—

				<i>Parenchymatous.</i>	<i>Hæmorrhagic.</i>
Generalised	...	...	...	14	2
Slight general	...	...	...	3	3
Legs swollen	...	...	...	1	1
Face swollen	...	...	...	2	9
No œdema	...	...	...	2	12
				22	27

Albumen present on discharge	...	13	7
„ absent	„	5	20
		—	—
		18	27
		—	—
Heart enlarged	...	6	2 (1 chorea)
Optic neuritis	...	1	0
Deaths	...	4	0

Table II. clearly shows the greater tendency to œdema in the parenchymatous type, as in the nine hæmorrhagic cases marked “ face swollen ” there was only some puffiness round the eyes. The length of stay in hospital for the cases of the parenchymatous type was roughly one to five months, while that for the hæmorrhagic cases was relatively shorter. A trace of albumen was present in the urine in seven cases of the latter type when discharged, while in 13 of the parenchymatous type albumen was present on leaving hospital in quantities from a trace to a fairly dense cloud. In about half of the hæmorrhagic cases the blood and albumen disappeared from the urine almost simultaneously, and in only one were red blood corpuscles still found on microscopical examination when the patient left hospital. This case (W.B.) will be referred to again. Allowing for the number of days elapsed after the onset of symptoms before the patients entered hospital the urine remained obviously blood stained for a rather longer time in the hæmorrhagic cases, and microscopically red blood corpuscles were found in the urine for one week to three months ; three weeks in 12 cases. In the parenchymatous cases, also, erythrocytes were present any time up to three months, but more often were absent after a few days, and in five cases no red cells were seen at all while in hospital.

Among the parenchymatous cases four are included in which a recent history of scarlet fever was obtained, all of which showed general œdema, and a trace of albumen was still present at the time they left hospital.

Other Forms of Nephritis in Series of 64 Cases.

(B) Chronic Parenchymatous Nephritis. Eight cases were encountered which had already passed into the chronic state, including two cases of scarlatinal origin. Two were without œdema, and the other six had generalised œdema. The albuminuria was persistent in all. In five of the eight cases red blood corpuscles were present in the urine, often in considerable quantity, during exacerbations of the renal trouble.

(C) Syphilitic Nephritis. There were four examples of this type, in each of which the Wassermann reaction of the blood was positive. One was 4 months and two 6 months old, and albuminuria and œdema had been present from two weeks to two months. All died except the fourth case, a child of 5½ years with a slightly positive Wassermann reaction, who had had

œdema and albuminuria intermittently for two years. Her mother had a strongly positive Wassermann reaction.

(D) Chronic Interstitial Nephritis. There were two cases of this type. Both showed bony changes of the character met with in renal dwarfism⁽⁴⁾. Their ages were $4\frac{1}{2}$ and 6 years. Frequency of micturition with a low specific gravity of the urine (1006-1008) was present in both instances, and their blood ureas were 108 and 76 mgm. per 100 cc. respectively. Both showed an increase in the area of cardiac dulness and a diminished urea concentration power (below 2·0).

(E) Stone in the Kidney. The following case has been included as the history resembles in many ways that of a case of hæmorrhagic nephritis. A boy of 6 had intermittent attacks of hæmaturia for four months, each attack being accompanied by pain in the back. At the time of examination the urine contained albumen, a few red blood corpuscles and one or two casts per field. Radiographic examination for calculus was negative. His subsequent history discloses that a year after leaving hospital he passed a stone in the urine with much pain, and three years later was stated to have had no further renal trouble.

Results of Re-examination.

(A) Tables III. and IV. give the results of examinations of the cases of acute parenchymatous and hæmorrhagic nephritis at three and a half to five and a half years after the onset of the symptoms.

TABLE III.

Re-examination of 18 Surviving Cases of Parenchymatous Nephritis.

Case.	Dates.	Urine.	B.P. Heart enlarged = +	Maximum Urea Conc.	Remarks.
J. W. ♀ 16 years	1920 1922 1925	Alb. trace Alb. 0 Alb. trace Cells +	— B.P. 100 B.P. 118	— — 3·12	Pallor, puffy face Looked healthy Drowsy and languid
J. P. ♂ 9 years	1922 1925	Alb. 0 Alb. v.s t.* Cells +	B.P. 100 B.P. 103	— 3·6	Tonsils + + Looked healthy
J. B. ♀ 8½ years	—	—	—	—	Died
A. G. ♀ 15 years	1922 1925	Alb. + + + Alb. + + + Cells	B.P. 120 B.P. 120	2·1 2·9	Sometimes puffy Looked healthy

* alb. v.s.t. = very slight trace albumen.

TABLE III.—*continued.*

Case.	Dates.	Urine.	B.P. Heart enlarged = †	Maximum Urea Conc.	Remarks.
J. B. ♂ 11 years	1922 1925	Alb. trace Alb. v.s.t.* Cells +	B.P. 120 B.P. 110	— 4.0	Face puffy Pallor, short of breath
F. H. ♂ 10 years	1922 1925	Alb. 0 Alb. v. s. t.* Cells	B.P. 120 Heart† B.P. 110	— 3.5	Edema legs Developed hepatic cirrhosis
C. L. ♀ 7 years	1922 1925	Alb. 0 Alb. v. s. t.* Cells	B.P. 93 Heart†	— 3.2	Looked healthy Looked healthy
G. G. ♂ 15 years	—	—	—	—	Died
J. D. ♂ 11 years	1922 1925	Alb. 0 Alb. 0	B.P. 110 B.P. 90	— 3.9	Looked healthy Looked healthy
L. S. ♂ 13 years	1922 1925	Alb. 0 Alb. 0	Heart† B.P. 120 Heart†	— 3.3	Puffy Looked healthy
E. P. ♂ 12 years	1922 1925	Alb. ++ Alb. +++ Cells +	B.P. 110 Heart† B.P. 140	2.6 2.6	No complaints Looked healthy
V. C. ♀ 12 years	1922 1925	Alb. 0 Alb. ++ Cells +	Heart† Heart†	— 2.4	Very pale Looked healthy
F. L. ♀ 8 years	1922 1925	Alb. 0 Alb. 0	B.P. 80 B.P. 120	— 2.8	Looked healthy Looked healthy
J. H. ♂ 11½ years	1922 1925	Alb. trace Alb. v.s.t.* Cells +	— B.P. 120	— 3.3	Looked healthy Looked healthy
H. P. ♂ 6 years	1922 1925	Alb. ++ Alb. 0	B.P. 80 B.P. 90	— 3.4	— Looked healthy
F. B. ♀ 7 years	1922 1925	Alb. 0 Alb. 0	— B.P. 90	— 3.4	Looked healthy Looked healthy
L. L. ♀ 14 years	1922 1925	Alb. trace Alb. + Cells +	B.P. 110 B.P. 105	2.0 3.1	— Puffy in mornings
P. W. ♀ 5½ years	1925	—	—	—	Too ill to come to hos- pital. Headaches and vomiting

* alb. v.s.t. = very slight trace albumen.

TABLE IV.

Re-examination of 27 Cases of Hæmorrhagic Nephritis.

Case.	Dates.	Urine.	B.P. Heart enlarged = +	Maximum Urea Conc.	Remarks.
J. D. ♂ 12½ years	1922 1925	Alb. 0 Alb. 0	— B.P. 100	— —	Looked healthy Looked healthy
D. K. ♀ 16 years	1922 1925	Alb. 0 Alb. trace Cells +	Heart† Heart† B.P. 85	— 3·2	Chorea Chorea
A. N. ♀ 11 years	1922 1925	Alb. 0 —	— —	— —	Looked healthy Looked healthy
G. A. ♀ 16 years	1922 1925	Alb. 0 Alb. 0	— B.P. 105	— 3·4	Looked healthy Looked healthy
B. U. ♀ 9 years	1922 1925	Alb. 0 —	— —	— —	— Intermittent hæmaturia (not seen)
J. D. ♂ 9 years	1922 1925	Alb. 0 Alb. v.s.t.* Cells +	— B.P. 85	— —	Looked healthy Looked healthy
H. H. ♂ 9½ years	1922 1925	Alb. 0 Alb. 0	— B.P. 110	— 2·9	Looked healthy Looked healthy
W. W. ♂ 8 years	1922 1925	Alb. 0 Alb. 0	— B.P. 110	— 3·19	Looked healthy Looked healthy
A. R. ♂ 14 years	—	—	—	—	Died. T.B. Meningitis
E. E. ♂ 15 years	1922 1925	Alb. 0 Alb. 0	B.P. 100 B.P. 100	2·7 3·15	2 attacks hæmaturia, cystoscopy negative Looked healthy
N. P. ♀ 8½ years	1922 1925	Alb. 0 Alb. v.s.t.* Cells +	B.P. 100 B.P. 120	— 2·8	Looked healthy, hæmaturia before tonsillectomy 1923 Looked healthy
M. F. ♀ 13 years	1922 1925	Alb. 0 Alb. s.t.** Cells +	B.P. 100 B.P. 130	— 3·3	Thin child Delicate
T. B. ♂ 7½ years	1922 1925	Alb. 0 Alb. 0	— B.P. 90	— 2·7	Looked healthy Looked healthy

* alb. v.s.t. = very slight trace albumen.

** alb. s.t. = slight trace albumen.

TABLE IV.—*continued.*

Case.	Dates.	Urine.	B.P. Heart enlarged = †	Maximum Urea Conc.	Remarks.
A. B. ♀ 7 years	1922 1925	Alb. 0 Alb. trace Cells +	— B.P. 90	— 2·8	Looked healthy Looked healthy
B. S. ♀ 7½ years	1922 1925	Alb. 0 Alb. v.s.t.* Cells +	— B.P. 120	— 3·7	Looked healthy Looked healthy
J. T. ♂ 13 years	1922 1925	Alb. 0 Alb. 0	— B.P. 120	— 3·8	— Looked healthy
W. B. ♂ 9 years	1922 1925	Alb. + Alb. ++ Cells ++	— Heart† B.P. 105	2·3 1·6	Delicate Blood urea 53 Unhealthy
E. C. ♂ 8 years	1922 1925	— Alb. 0	— B.P. 85	— 3·24	— Looked healthy
G. W. ♀ 10 years	1922 1925	Alb. 0 Alb. trace Cells +	B.P. 80 Heart† B.P. 110	— 3·75	Tonsils + + Rheumatism
H. H. ♂ 14 years	1922 1925	Alb. 0 Alb. trace	B.P. 110 B.P. 110	— 3·1	Looked healthy Looked healthy
B. B. ♂ 9 years	1922 1925	Alb. + Alb. trace Cells +	B.P. 90 B.P. 108	— 2·5	Occasional vomiting Looked healthy
F. S. ♀ 7 years	1925	Alb. 0	B.P. 90	3·2	Looked healthy
F. T. ♂ 10 years	1922 1925	Alb. 0 Alb. 0	B.P. 120	— 3·6	Looked healthy Looked healthy
A. V. ♂ 6½ years	1922 1925	Alb. 0 Alb. v.s.t.*	B.P. 110 Heart† B.P. 110	— 3·06	Looked healthy Otorrhœa, looked healthy
P. O. ♀ 8 years	1922 1925	Alb. trace Alb. v.s.t.* Cells +	— B.P. 80	— —	Looked healthy Looked healthy
D. C. ♀ 10 years	1922 1925	Alb. 0 Alb. v.s.t.* Cells +	B.P. 95 B.P. 90	— 4·03	Looked healthy Looked healthy
J. M. ♂ 13 years	1922 1925	— Alb. + Cells +	— Heart† B.P. 130	— 2·5	— Looked delicate, easily tired

* alb. v.s.t. = very slight trace albumen.

A few comparisons of the after-results in the two types of acute nephritis, parenchymatous and hæmorrhagic, are worthy of separate mention.

1. Recoveries. Good physical condition and an absence of abnormal constituents in the urine—five parenchymatous and 10 hæmorrhagic. Two further cases of hæmorrhagic nephritis might be added to the list of recoveries, as although a trace of albumen was present there was no cellular deposit. As regards the presence of a slight trace of albumen in the urine we consider it of negligible importance except when accompanied by an abnormal number of leucocytes and epithelial cells in the centrifugalised deposit. The presence of an abnormal number of these cells in addition to a small trace of albumen is evidence in our opinion of renal damage.

2. Apparent good health, but with abnormal urinary constituents, consisting of albumen, a "very slight trace" to a dense cloud, and white blood corpuscles in the centrifugalised deposit—six parenchymatous and nine hæmorrhagic. In the latter group red blood corpuscles were present in only two, and the albumen did not amount to more than a trace in any of the nine cases. Three of the parenchymatous cases had enlarged hearts, and two of the hæmorrhagic, but both of these had developed rheumatism since the onset of the nephritis.

3. Deaths. Two of the parenchymatous cases had died of chronic nephritis, making a total of six deaths in the original group of 22. One hæmorrhagic case had died, but the cause of death was tuberculous meningitis.

4. The five remaining parenchymatous cases presented obvious signs of chronic nephritis. Of the remaining five hæmorrhagic cases one had had recurrent attacks of hæmaturia (one was not seen), and three looked unhealthy and had red blood corpuscles in the centrifugalised urinary deposit. One of these—W.B. already referred to—is worth mentioning in fuller detail, being a case which presented at the onset all the features of the hæmorrhagic type of nephritis. Subsequently he had frequent occurrences of hæmaturia with a gradual loss of health, cardiac hypertrophy and a diminishing power to concentrate urea, the final figure being 1·6. He had never been œdematous. When last seen the blood urea was 53 mgm. per 100 cc., and casts were present in the urine. This case demonstrates the possibility of the hæmorrhagic form developing into the chronic, possibly interstitial, type of nephritis.

5. Of the four post-scarlatinal cases included in the parenchymatous group two showed complete recovery and two had become chronic.

6. The figures for the urea concentration test performed in 21 of the parenchymatous cases and in 15 of the hæmorrhagic were all above or at the normal level (2·5), except in one case in each type.

(B) *Chronic Parenchymatous Nephritis.*

Four out of eight cases had died. Of the remainder only one appeared healthy, but had an enlarged heart and albumen and cells in the urine. The other three were obvious chronic renal cases; one had a blood urea of 119 mgm. per 100 cc., and urea concentration 1.3. Otherwise the urea concentration figures were above 3.0. Two of the four surviving cases were examples of post-scarlatinal nephritis.

(C) *Syphilitic Nephritis.*

The case which was first seen at 5½, when re-examined at 9½ years showed no cardiac enlargement and a urea concentration of 3.1. The urine contained a trace of albumen and some cells, but no casts. Œdema had appeared intermittently.

(D) *Interstitial Nephritis.*

Of the two cases of this type one died at the age of 6½, and the other, now aged 8, was too ill to come to hospital for examination.

Conclusions.

Following upon the appearance of nephritis in a child the question naturally arises as to whether an ultimate recovery or some permanent damage to the renal tissue may be expected. The answer to this question would seem to depend largely upon the type of nephritis present in each case. We agree with Hill⁽²⁾ that the prognosis is best in the acute hæmorrhagic type.

1. Six deaths occurred out of 22 cases of acute parenchymatous type, and one death, from other causes, in the 27 cases of acute hæmorrhagic nephritis.

2. The importance of re-examination at an interval of years is emphasised by the difference in the conclusions which may be based upon an immediate prognosis as compared with the results of later investigations. From a general examination the immediate prognosis seemed good in 13 cases of parenchymatous nephritis and in 26 cases of hæmorrhagic nephritis.

3. After a period of three to five years only five of the parenchymatous cases could be said to have recovered completely, as compared with 12 recoveries in the hæmorrhagic group.

4. Six of the parenchymatous and nine of the hæmorrhagic cases appeared to be in good health, but had albuminuria and abnormal cellular constituents in the urine. The degree of albuminuria and quantity of cells present was definitely less in the hæmorrhagic type than in the parenchymatous cases.

5. Four out of six cases of post-scarlatinal nephritis became chronic. This proportion rather opposes the general opinion that most cases of scarlatinal nephritis end in recovery, but the total figure is too small to be of much value.

6. We emphasise the importance in post-nephritis of the presence of even a very slight trace of albumen when it is associated with an excess of cells in the centrifugalised deposit. This we consider is of definite pathological significance.

The prognosis of syphilitic and interstitial nephritis is well known to be ominous and need not be discussed here. Dr. Still⁽⁴⁾ has suggested in the acute nephritis of children that it is "the minority of cases which ever make a complete recovery." In our own series of cases, even in its most benign form, the hæmorrhagic type of nephritis, recovery occurred in less than half the number of cases, namely 44.4%.

We wish to express our gratitude to Dr. G. A. Harrison for his kindness in carrying out the bio-chemical work connected with this paper.

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