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Acute poststreptococcal glomerulo-nephritis in general practice: the contribution of infection to its onset and course

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SUMMARY

Twenty-one patients considered to have acute poststreptococcal glomerulo-nephritis were encountered during 35 years of general practice. In ten of them good evidence of active streptococcal infection at the time of discovery of nephritis was recorded. The more complete the data the more convincing was the evidence of active infection.

In over half of those whose urines were routinely cultured pathogens were isolated and over a third were treated for infection of the urinary tract. Such infections were associated with adverse effects and prolonged illness.

As compared with children, adults in general had a longer history of ill-health, were less likely to present with acute infections and more likely to have urinary tract infections and prolonged illness.

Vigorous antistreptococcal treatment was followed by rapid recovery in those patients so treated whose illnesses were not complicated by urinary tract infections.

Concurrent streptococcal infection and secondary infection of the urinary tract may contribute more to the onset of acute poststreptococcal glomerulo-nephritis and to its course than is currently believed.

INTRODUCTION

Why acute nephritis follows some infections with group A streptococci (GAS) is not known [1]. Current theories postulate that glomerular damage is the result of an antigen-antibody reaction the nature and location of which are matters of debate [1–3].

A similar pathogenesis is postulated for rheumatic fever. The origin of these theories lies in the similarity between the latent interval noted in experimentally induced serum sickness and the asymptomatic period between a streptococcal infection and the appearance of signs of either rheumatic fever or nephritis [3]. However, the latent interval tends to be shorter in acute poststreptococcal glomerulo-nephritis (APSGN) than in rheumatic fever [4]. Although usually quoted as 10 days it may be 6 days [5] or less [6].

In former times it was well known that in patients with scarlet fever nephritis developed mainly in those with some septic complication such as suppurating cervical glands [7, 8] mastoiditis, peritonsillar abscess, otitis media or sinusitis from which streptococci could be cultured [9]. Two-thirds of patients with nephritis had such infections [10]; if the infection cleared the patient recovered [7, 9].

In recent years it has been claimed that once the process that leads to nephritis is initiated persisting streptococcal infection is not necessary to sustain it [11], that penicillin treatment of the streptococcal infection has not been shown to reduce the risk of nephritis [12–14] and that penicillin given after the

onset of nephritis does not alter the course of the disease [11, 15]. There is one report of a dramatic improvement in some children following treatment with penicillin but bacteriological and serological data were not provided [16].

Current knowledge of APSGN is based upon patients admitted to hospital. This paper describes 21 cases seen over 35 years in general practice, all but one of them between 1954 and 1965 in a population with a high incidence of streptococcal infection.

I joined a practice in a mining area in the Midlands in December 1953. In January 1954 I saw a man of 41 who complained of sore throat and fever. He mentioned that his urine was 'dark and muddy' and was found to have nephritis. Thereafter, I routinely asked patients with sore throats to provide specimens of urine. Urines were tested for protein and sugar and microscoped before transmission to the laboratory. Up to 1960 specimens were sent by post; from 1960 specimens were transported to the laboratory by van on weekdays. All urines were routinely cultured.

During the 12 years from 1954 to 1965 inclusive the number of patients on my list grew from nil to 3292. In the early years all my patients, and in the later years about half of them, lived on a new Coal Board estate. In 1959 the consultation rate for patients with sore throats associated with a positive culture for GAS among my patients on that estate was 7·8 per 100 persons per year, and among my patients elsewhere, 3·8 per 100 persons per year [17]. The lower figure is more than twice the rate, 1·5 per 100 persons per year (range 0·4–2·9), over the 10 years from 1962 in another practice in England [18] and more than three times the rate, 1·1 per 100 persons per year (range 1·04–1·47), derived from studies in 27 practices in Holland between 1959 and 1965 [19]. The latter figure may be slightly understated since children under 5 years of age and patients with coughs and colds were excluded.

I left that practice in 1966 and, after two years in another practice in the Midlands during which my list grew from nil to 5400 patients, I moved to start up a new practice in London. My list of patients was around 1000 over the 20 years from 1969–88 inclusive. After 1965 I encountered only one patient with APSGN: in 1981. In that year my consultation rate for sore throats yielding GAS was 1 per 100 persons. In all three practices there was, as compared with the general population, about double the proportion of families in which the father was engaged in unskilled or semi-skilled work and in the first and third practices double the proportion of children under 15 years of age. In general my patients in the first practice were in poorer circumstances than were my patients in the other two practices.

Table 1. *Patients with acute nephritis by age and sex: all cases*

		Age group (years)			
	No.	0–4	5–9	10–19	20–49
Male	12 (8)	3 (3)	3 (3)	2 (2)	4 (1)
Female	9 (8)	3 (2)	4 (4)	0 (0)	2 (1)
Total	21 (16)	6 (5)	7 (7)	2 (2)	6 (2)

Note: Figures in parentheses are my patients.

Between 1954 and 1965, 16 individuals on my list, 11 of them from the Coal Board estate, were considered to have APSGN. One, a boy 3 years old, was sent into hospital by a colleague. About him I know only that APSGN was diagnosed and that haematuria continued for 49 days. He is not included in the cases described here. The incidence of APSGN, based upon the number of patients on my list (2167) in January 1960, the midpoint of those years, was 6·1 per 10000 persons per year. At least nine fulfilled the criteria for APSGN used in the Dutch studies [19], an incidence of 3·5 per 10000 per year compared with 2·0 per 10000 per year in Holland (range 1·0–5·9).

During those years I saw 5 patients, 4 adults and 1 child, not on my list who were considered to have APSGN. The total number seen was therefore 21 of whom 20 were in the first practice and 1 in the third practice.

Seven patients were identified in 1959 during a study by the whole practice of urinary abnormalities following sore throat [20]. Five were on my list, an incidence of 24·5 per 10000 persons for that year. The rest were distributed fairly evenly over other years.

Five patients were seen from January 1954 to February 1959; three I sent into the nearest general hospital for reasons that I did not consider valid after that date: oliguria for 24–48 h in two children, oedema and breathlessness in an adult. All patients seen from March 1959 to December 1965 were treated personally, 11 (all under 15 years of age) at home, 6 (all but 1 over 14 years of age) in the local cottage hospital. The patient seen in 1981 was sent into hospital by a colleague.

The age and sex distribution is given in Table 1. Four patients were 30–39 years of age, one 29, one 41.

Protein and red cells were found in the urines of all but one patient, RaW, who has been described in

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detail elsewhere [21]. Casts were found in the urines of 19 patients: granular and/or cellular casts in 18, hyaline casts in 1 (PhA).

Patients have been separated into three categories (Table 2). Category A1 consists of 8 patients, all of whom had facial swelling; 3 also had swelling of the ankles. In 5 patients the systolic pressure was high for their age and fell by 30 mmHg or more. For 5 the results of serial blood urea estimations are known; in all temporary impairment of renal function was demonstrated. Two are recorded as having oliguria.

Category A2 consists of 8 patients whose notes record either swelling round the eyes (DoP, MaS, JoT) or impairment of renal function (JoN, KeE, ErG) or both (JaB, ReW). The systolic pressure was 160 mmHg or higher in all 3 adults in this category and in 2 it fell by more than 30 mmHg. Four patients are recorded as having oliguria.

Category B consists of 5 patients with no discernible oedema or evidence of impairment of renal function.

In 9 cases, including 4 of the 5 in category B, the urine was recorded as being coffee coloured or greyish.

Presenting symptoms

Twelve patients presented with symptoms of acute infection. Six had signs of a localized inflammatory process: in 1 a peritonsillar abscess, in 1 a discharging otitis media (plus sore throat), in 4 a single enlarged and painful tonsillar gland. Five had a sore throat and 1 a feverish cold. Four also complained of passing dark or red urine. Eight patients had no symptoms or signs of nephritis. In 4 of them a routine urine test within 3 days of presentation revealed nephritis. In the other 4 signs of nephritis appeared 2–5 days later; in 2 of these patients the first urine test was normal:

JoT, male, aged 4 years, presented with ear ache and swelling of one tonsillar gland of 1 day's duration. Throat swab: no growth. Urine normal. Two days later: T40.3 °C, periglandular swelling; puffy eyes, sore back, sore penis. He had passed very little urine over the preceding 18 h. Urine: protein 45 mgm/100 ml, numerous red cells, granular and cellular casts, no excess of white cells, no bacterial growth. Blood: 12400 wbc/cmm (neutrophils 80%); ASL 580 u/ml. Penicillin i.m. started. TN (temperature normal) next day. Urine normal 4 days later. A few red cells in one specimen 15 days later.

JuJ, male aged 4 years, presented with sore throat of 1 day's duration. Throat swab: GAS type 12. Urine: trace of protein only. Four days later tonsillar glands enlarged and tender, facial swelling, T37.4 °C. Urine: protein 75 mgm/100 ml, numerous red cells, granular casts. BP 125/85. Throat swab: GAS type 12. Over the following 6 days facial swelling disappeared, urine output increased, BP fell to 95/65 and proteinuria decreased to 10 mg/100 ml. Casts and red cells persisted. 9th day: urine: protein 15 mgm/100 ml, numerous red cells, occasional casts, a few white cells. Penicillin i.m. for 12 days from the 10th day. 11th day: urine: trace of protein, a few red cells, no casts. Urine normal on the 19th day. Occasional red cells in most urines for 5 months.

In two others there is no record of an early urine test:

KeB, male aged 4 years, presented with an enlarged left tonsillar gland that had been noted for 24 h. Reported to have had a sore throat 2 weeks previously. Throat swab negative. Five days later the gland became larger and the mother noticed that his urine was dark. T38.4 °C. Periglandular swelling. Throat swab: haemolytic streptococci not of groups A, C or G. Urine: protein 300 mgm/100 ml, numerous red cells, granular casts, a few white cells. Oral penicillin prescribed. TN next day. Urine normal 9 days later (except for 10 mgm/100 ml of protein) and on three subsequent occasions but a few red cells were found in specimens tested 21 and 32 days after treatment began. ASL titre 560 u/ml at the time of discovery of nephritis and $>$ 800 u/ml 34 days later.

RaW, male aged 17 years, was prescribed oral penicillin for a sore throat by a colleague. A rash developed and penicillin was stopped. When I saw him the rash was extensive and appeared to be herpetic; a throat swab was taken for viral culture and yielded herpes simplex virus. The sore throat recurred 2 days later and a colleague prescribed tetracyline. When I saw him next day pus was discharging near one tonsil. Penicillin was given i.m. for 2 days and then an injection of long acting penicillin. Two days after treatment began he was much better. Eight days later he attended for a certificate to return to work and was noted to have swelling of the face and ankles. He reported that he had been short of breath for 5 days and that his face had been swollen for 4 days. His father reported noting swelling of his ankles at about the time that treatment with penicillin began. Thus oedema had been noted within 5 days of the diagnosis of peritonsillar abscess. He was admitted to the cottage hospital and put on a low salt diet. BP 180/100. Blood urea 65 mgm/100 ml. Urine normal though casts appeared during recovery. Urine output increased to 1·8 l per day and by the 8th day oedema had disappeared. ASL 580 u/ml 19 days after the first sore throat and 650 u/ml 19 days later. His recovery was complicated by infection of the urinary tract.

In two children, KeB and JoT, periglandular swelling (described elsewhere [22]) was noted when nephritis developed. When it was noted subsequently in another child, MaS, the urine was tested and found to be abnormal.

Nine patients did not present with symptoms of infection though one, RaK, was reported to have had a sore throat 3 days previously. Three, AmB, DoB,

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Table 2. *Clinical findings by category*

Category		Sex	Age (years)	Oedema	Blood urea*† mgm/100 ml 1	Blood urea*† mgm/100 ml 2	Blood pressure*‡ mmHg 1	Blood pressure*‡ mmHg 2	Comments
A1	RaK	M	5	+	50	26 (42)	110/60	100/60 (18)	Admitted to hospital
	WiP	M	36	+	55	26 (32)	180/110	130/80 (57)	Admitted to hospital
	LoG	F	8	+	—	—	155/95	102/72 (135)	Admitted to hospital
	JuJ	M	4	+	—	—	125/85	95/65 (5)	—
	DoB	F	5	+	—	—	105/70	95/70 (5)	—
	PhA	M	8	+	95	42 (21)	140/90	120/60 (2)	—
	RaW	M	17	+	68	35 (20)	180/100	125/80 (18)	—
	NoF	F	31	+	73	41 (17)	160/100	120/80 (10)	—
A2	DoP	F	3	?	—	—	—	—	Admitted to hospital
	MaS	F	$1\frac{11}{12}$	?	—	—	—	—	—
	JoT	M	4	?	—	—	95/60	—	—
	JaB	F	6	?	42	—	95/65	85/55	—
	JoN	M	14	—	37	22 (28)	130/70	—	—
	KeE	M	25	—	80	40 (10)	160/100	125/70 (9)	—
	ReW	M	36	?	45	27 (13)	210/110	170/100 (12)	—
	ErG	M	41	—	87	48 (7)	166/90	154/90 (42)	—
B	AmB	F	4	—	—	—	—	—	—
	RiC	M	4	—	23	—	110/90	105/60 (3)	—
	MaH	F	6	—	26	—	105/60	—	—
	KeB	M	6	—	28	—	110/60	105/55 (5)	—
	PaB	F	29	—	—	—	140/90	—	—

* Figures in parentheses, number of days between 1 and 2.
† 1, first result; 2, next result.
‡ 1, maximum level; 2, subsequent minimum level within the period stated.

KeE, complained only of passing red or dark urine. Three, NoF, RaK, WiP, presented with oedema. The child seen in 1981 presented with a tight feeling in her face. In the remaining two patients a urine test revealed nephritis; the urine was tested in one, ReW, because he had been unwell since a sore throat 17 days previously (urine normal at that time) and in the other, PhA, because he had had a sore throat 14 days previously. Thus in 6 of the 21 patients nephritis was revealed by a urine test performed because they either had or had had an acute infection.

As compared with the 12 patients who presented with acute infections more of the 9 who did not were over 17 years of age (4/9 *v.* 3/12), more had a history of sore throat 2 weeks or more previously (6/9 *v.* 1/12) and more were recorded as having felt unwell for 2 or more weeks (4/9 *v.* 2/12). As compared with children under 15 years of age more of the adults (over 17 years of age) had been ill for more than a week (4/6 *v.* 2/14) and more had had a sore throat 2 or more weeks previously (4/6 *v.* 3/14).

Seven patients (including the child with otitis media) presented with sore throat; one, RaW, had a peritonsillar abscess, in the other six the notes record only slight injection of the throat.

Laboratory results

The results of culture of swabs from throat or ear are recorded for 17 patients; 10 yielded GAS within 3 days of the discovery of nephritis. In 6 cases the streptococci isolated were typed: 3 yielded type 12, 2 type 1 and 1 type 4. In 2 of the 4 patients with nephritis seen between 1962 and 1965 swabs were taken for viral culture. RaW yielded herpes simplex virus and AmB yielded adenovirus type 5 (together with GAS type 12).

Antistreptolysin O (ASL) titres were not assayed in the five patients seen before March 1959, ErG, PhA, RaK, DoP, WiP, nor in three young children seen after that time, JuJ, AmB, MaS. For all the remaining 13 patients the titre at the time nephritis was discovered is known. In 11 it was over 400 u/ml, indicating a streptococcal infection that had begun more than a week before the patient presented and that might or might not still be active. In two, JoN

Table 3. *Evidence of concurrent streptococcal infection*

Evidence	P	Sex	Age	Category	Presenting symptoms*	Culture†	ASL 1	ASL 2	Preceding illness	Notes‡
Suppuration	RiC	M	4	B	ST, ear discharge, red urine	GAS§	460	—	Fever, discharge 3/52	Ear swab
	RaW	M	17	A1	ST (peritonsillar abscess)	Not done§	580	650	—	On antibiotics
Rising ASL	JoN	M	14	A2	ST	GAS	65	200	—	—
	KeB	M	4	B	GL	Neg	560	> 800	ST 2/52 previously	—
	LoG	F	8	A1	Facial swelling	GAS	640	10240	ST 2/52 previously	H
ST, GAS	JaB	F	6	A2	ST	GAS	> 800	—	Fever, earache 4/52	—
	JuJ	M	4	A1	ST	GAS	—	—	—	—
	PaB	F	29	B	ST	GAS	110	No record	—	—
GL, ASL > 300 u/ml	JoT	M	4	A2	GL	Neg	580	—	—	—
	MaH	F	6	B	GL + dark urine	GAS	400	—	—	—
ASL > 800 u/ml	NoF	F	31	A1	Swelling face and ankles, dark urine	GAS	> 800	—	ST 7/52 previously	—
	ReW	M	36	A2	Unwell after ST	b.h.s.	> 800	—	ST 3/52 previously	—
ASL > 300 u/ml	DoB	F	5	A1	Fever, cold, dark urine	b.h.s.	550	—	—	—
	KeE	M	25	A2	Unwell + dark urine	No record	460	—	ST 4/52 previously	—
GAS+	RaK	M	5	A1	Facial swelling	GAS	—	—	ST 3 days previously	H
	AmB	F	3	B	Dark urine	GAS§	—	—	—	+ adenovirus
No evidence	DoP	F	3	A1	Red urine	Neg	—	—	—	H
	WiP	M	36	A1	Swelling of face	Neg	—	—	ST 5/52 previously	H
	ErG	M	41	A1	ST + dark urine	Not done§	—	—	Fever 10 days previously	On penicillin
	MaS	F	$1\frac{11}{12}$	A2	GL	Not done§	—	—	—	On penicillin
	PhA	M	8	A1	None§	b.h.s.	—	—	ST 2/52 previously	Routine urine test

* ST, sore throat; GL, single enlarged tender tonsillar gland.
† b.h.s., beta-haemolytic streptococci.
‡ H, Admitted to district hospital.
§ See note.

and PaB, who presented with sore throat, it was below 200 u/ml, the level considered to be the upper limit of normal [23]; in JoN a rise in titre (60 to 200 u/ml) was demonstrated despite treatment with long-acting penicillin intra-muscularly.

The evidence for streptococcal infection concurrent with the discovery of nephritis is set out in descending order of significance in Table 3. Two patients, RiC and RaW, had suppurative conditions which resolved soon after the start of treatment with penicillin. Aural discharge yielded GAS in the former; in the latter the ASL titre rose. Rising titres were also demonstrated in the three other patients who were tested both initially and in convalescence; two also yielded GAS. In these five patients there is strong clinical and/or laboratory evidence of active streptococcal infection at the time when nephritis was discovered.

Three patients who complained of sore throat, JaB, JuJ, PaB, yielded GAS. In the population from which they came isolation of GAS from a person with sore throat was associated with serological evidence of streptococcal infection in 5 out of 6 cases [17]. PaB yielded GAS type 4 when she presented and when sore throat and haematuria recurred. Two others, JoT and MaH, presented with an active inflammatory process in one tonsillar gland. In both the ASL titre was raised and one, MaH, yielded GAS. In these five patients there is good evidence of active streptococcal infection at the time of discovery of nephritis.

In two adults, NoF (who yielded GAS) and ReW, the ASL titre was over 800 u/ml 3 and 10 days respectively after the discovery of nephritis. This is compatible with streptococcal infection at or shortly before the onset of nephritis.

For two patients, DoB and KeE, the only evidence of streptococcal infection is a raised ASL titre. In two others, RaK and AmB, the only evidence is a positive culture plus, in RaK's case, the history of a sore throat 3 days previously.

In five patients no evidence of streptococcal infection was obtained. In two, ErG and MaS, it was not sought. In three others, swabs were taken but did not yield GAS; in none were ASL titres assayed.

Excluding the two in whom evidence was not sought, in a quarter (5/19) there was strong evidence and in half (10/19) strong or good evidence of streptococcal infection at the time of discovery of nephritis. Excluding those seen in the early years, in a third (5/16) there was strong and in two-thirds (10/16) strong or good evidence of concurrent infection. The more complete the data the stronger the evidence of concurrent streptococcal infection.

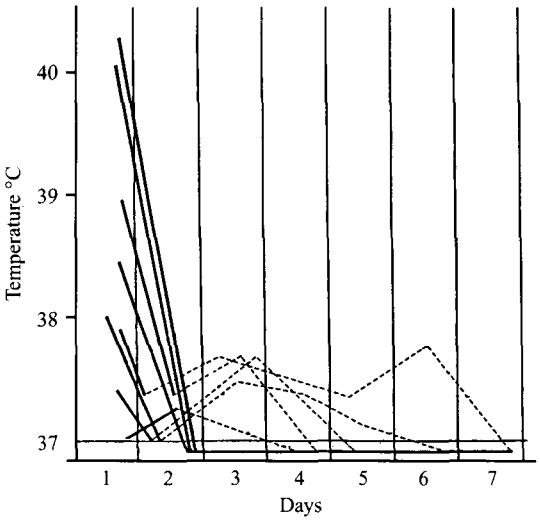

Fig. 1. Temperature after penicillin.

Comparing those who presented with symptoms of infection and those who did not there is little difference in the yield of GAS (6/9 v. 4/8) or in the proportions with rising ASL titres (3/3 v. 1/1) or with a single titre over 300 u/ml (4/5 v. 4/4).

Management and outcome

In addition to the usual dietary restrictions all 17 patients treated personally received penicillin. Two, RaW and JoN, were treated with long acting penicillin when they presented with sore throat. The remaining 15 patients were treated when nephritis was diagnosed. In 14 patients treatment began within 4 days of diagnosis; in one, JuJ, treatment was not started until the 10th day after diagnosis. The 14 patients seen after February 1959 are recorded as having received penicillin for at least 10 days, in all but one by intramuscular injection. In the six patients with localized inflammation the condition resolved soon after treatment was initiated.

In 17 patients treatment began within 24 hours of diagnosis. In 8 an oral temperature over 37 °C was recorded; in 7 it fell sharply the next day (Fig. 1). Fever after the third day was recorded in 9 of the 17 patients; in 6 pathogens were cultured from the urine (see later).

Red cells disappeared from the urines of 12 of the 16 patients with haematuria within 14 days of the start of penicillin treatment. In only 3 patients were red cells present in all specimens tested for more than 21 days (Table 4) and in only 2, ErG and KeE, for more than 6 weeks.

In three patients red cells were found again in all or

Table 4. *Duration of haematuria by age group: patients treated personally*

	Days				
Age	1–7	8–14	15–21	Over 21	Total
< 15	3	6	1[3]	1	11
15+	1	2	0	2	5
Total	4	8	1[3]	3	16

Notes:
1. Duration, period from the start of treatment with penicillin to the first urine free of red cells.
2. RaW omitted (no haematuria).
3. RiC: urine not tested between 6th and 20th days.

most specimens after the urine had been free of them. Thus after 6 weeks haematuria in all or most specimens tested was recorded in 5 of the 17 patients treated personally. Two were children, JuJ and DoB; three were adults, ErG, KeE, NoF. JuJ was the only child who did not receive early penicillin; the other four patients had secondary infections of the urinary tract (see later).

One patient, KeE, was followed up by his own doctor and the ultimate outcome is not recorded. The other 16 patients treated personally recovered though in ReW the blood pressure remained high for at least 2 years.

Haematuria persisted for more than 6 weeks in all five patients admitted to a general hospital. Red cells were consistently found in WiP's urine for 324 days. It is known that WiP was treated with tetracycline and dexamethasone but information about the three children admitted to the same hospital is not available. The child, LoG, received penicillin.

Pathogenic bacteria in the urine

All urines were routinely cultured in the 17 patients treated personally and in WiP when he was out of hospital. What follows is therefore based upon 18 patients. All were treated before the results of culture were expressed in quantitative terms. A diagnosis of urinary tract infection was based upon fever plus white cells in the urine plus isolation of a pathogen in pure culture.

In all but one of these patients white cells, often in large numbers, were found in most urines with other abnormalities. In 4 of the 11 children aged under 15 and 6 of the 7 patients aged over 16 urines yielded pathogenic bacteria at some time. Three of these 10 patients did not receive specific treatment; in two, coliforms were cultured on one occasion only and in the third, *E. coli* was isolated on the first day of the illness and together with enterococci on the 11th day but intermediate and subsequent specimens did not yield pathogens.

Seven of the 18 patients were treated for infection of the urinary tract. Two were children whose illnesses were short. Five of the 7 patients aged over 16 were treated and in 4 deterioration in the clinical state was demonstrated. In three, RaW, KeE and WiP, the blood pressure and blood urea level rose and then fell after treatment of the infection; in one, NoF, haematuria recurred and the ESR rose sharply. In four, ErG, RaW, KeE, WiP, the illness was prolonged and in NoF it recurred. RaW has been reported in detail elsewhere [21]. Two other case histories are given as illustrations:

NoF, female aged 30 years, 14 weeks pregnant, attended for antenatal care and complained of swelling of face and ankles and dark urine for a few days. Tonsillitis (treated with penicillin) 7 weeks previously. Not well since. Fever, cough and backache 4 weeks previously; urine normal at that time. T37.7 °C; BP 160/100; urine: protein + +, numerous white cells, cellular casts, *E. coli* on culture; throat swab GAS; ASL > 800 u/ml; blood urea 73 mgm/100 ml. Penicillin i.m. for 12 days. TN second day. Slight fever on third, fourth and fifth days. Fourth day urine: red cells, white cells and casts, *E. coli* on culture. Tetracyline from the fifth day. Nitrofurantoin from the 8th day. Diuresis began on the 8th day; weight reduced by 12 kg over 6 days. 10th day urine: trace of protein, a few red cells, moderate number of white cells, no growth on culture. 13th day: urine normal except for trace of protein; BP 120/80. 17th day: blood urea 41 mgm/100 ml; ESR 59 mm; discharged from cottage hospital. Readmitted 23rd day, vomiting and unwell, urine red. T37.2 °C; urine: protein + +, red cells + + +, no white cells. *E. coli* on culture. Blood urea 37 mgm/100 ml; ESR 60 mm. Streptomycin from the 26th day, nitrofurantoin from the 30th day. 37th day: urine culture negative. ESR 110 mm on the 45th day. Red cells noted in the urine up to the 37th day and on the 45th day. Premature delivery of a normal child 14 weeks later. Two years later she had an acute sore throat treated with i.m. penicillin. Swab yielded GAS type 12; ASL titres 50 and 470 u/ml; urines normal.

WiP, male aged 36 years, presented with vomiting, swelling of face and breathlessness 5 weeks after a sore throat treated for 1 week with oral penicillin. Throat swab: no growth; BP 180/110; urine: protein + + +, frequent red cells, hyaline and granular casts; blood urea 55 mgm/100 ml; ESR 42 mm. Admitted to district hospital and treated there with dexamethasone and tetracycline. Discharged after 32 days: BP 160/98; blood urea 26 mgm/100 ml; ESR 19 mm. Persistent proteinuria and haematuria. 88th day: urine: protein 250 mgm/100 ml, red cells + + +, white cells + +, enterococci sensitive to chloramphenicol on culture; BP 180/106. Following treatment with chloramphenicol culture was negative and BP 164/98. Three weeks later he developed

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fever, vomiting and rigors and was readmitted. BP 190/88; urine: trace of protein, numerous red cells, casts, white cells, enterococci on culture; wbc 35200/cmm (neutrophils 92%); ESR 40 mm in 1 h. Pyelo-nephritis diagnosed. Treated again with dexamethasone and tetracycline. Fourth day: BP 130/80; treatment with streptomycin began. 11th day: blood urea 60 mgm/100 ml. Discharged 15th day: BP 136/90; urine: protein ++ red cells ++, occasional casts, white cells +. 13 days later the urine yielded coliforms: BP 174/100; blood urea 30 mgm/100 ml; ESR 39 mm in 1 h. Treated with sulphatriad. 12 months after the illness began the urine was normal and BP 140/80. Four years later he presented with sore throat; swab yielded GAS type 1; urine: protein +, moderate numbers of granular casts. Treated with i.m. penicillin; subsequent urines normal.

DISCUSSION

Such a large number of cases has not been reported from a general practice previously. Three factors contributed: the excess of children, the high rate of streptococcal infection and the search for cases. The incidence of APSGN declined sharply in the 1960's [2, 24] and it is unlikely that a single general practitioner will again be able to present such a picture of the early stages of the disease.

The first question is the validity of the diagnosis. Sixteen patients exhibited at least two of the following signs of acute nephritis: oedema, temporary hypertension, haematuria, temporary impairment of renal function. In five others only the urinary abnormalities were found; the histological features of acute post-streptococcal glomerulo-nephritis may be present in such cases [25, 26]; in four of them the urine had the characteristic coffee colour of acute nephritis. Membranous nephropathy and IgA nephropathy are alternative diagnoses. The former is uncommon in children and is usually associated with symptomless proteinuria [27]. The latter may present in children as macroscopic haematuria soon after an infection of the respiratory tract but affects mainly those in the second and third decades of life [28].

ASL titres were above normal in all but one of those tested. Four patients for whom significant information about ASL titres is lacking yielded GAS; three complained of sore throat. In my patients the isolation of GAS from those with acute sore throat was highly correlated with serological evidence of streptococcal infection at the time [17]. The age distribution, with most patients under the age of 10 years and a cluster of patients aged between 29 and 41 years, is similar to that for streptococcal sore throat in the population served [17]. I conclude that for all cases reported here the most likely diagnosis is acute poststreptococcal glomerulo-nephritis.

All but one of the cases were identified between 1954 and 1965. The higher rate of streptococcal infection in the population at risk is sufficient to account for the higher incidence of nephritis as compared with the practices in Holland. The very high incidence in 1959 suggests that the more systematic the follow up of patients with sore throat the greater the yield; the implication is that in other years many cases were not recognized.

Twelve patients presented with symptoms of infection within 2–5 days of the discovery of signs of nephritis. In 6 there were signs of a localized inflammatory process: in 2 a suppurative condition and in 4 a single swollen tender tonsillar gland. Six others complained of sore throat; 5 were swabbed and all yielded GAS but in none was exudate or more than sight redness of the throat noted. It is possible that in some or in all the sore throat was due to a virus infection occurring in a person with a subclinical streptococcal infection. Dual infection may increase the risk of developing haematuria [29].

There was little or no difference between those with and those without symptoms of infection in the proportions yielding GAS or having a high or rising ASL titre. Adults in general had a longer history of ill health than did children, were less likely to present with acute infections, were more likely to have infection of the urinary tract and took longer to recover. They may have presented at a later stage of the illness than did children.

This was not a planned study of acute nephritis. Interest grew with experience and investigative facilities improved over the years. The most significant finding is that the more complete the data the more convincing is the evidence of active streptococcal infection at the time of discovery of nephritis.

Patients with acute nephritis may have concomitant infections, often asymptomatic, of the urinary tract; catheterization or cystoscopy undertaken in the early stage of diagnosis may be the cause in some cases [30]. In over half of those patients whose urines were cultured pathogens were found at some stage. None had been subjected to catheterization or cystoscopy. Just over a third were treated for infections of the urinary tract. Such a high incidence, possibly the result of routine culture of all urines, has not been reported previously; it suggests that infections were secondary to kidney damage. Five of the seven patients aged over 16 years were affected and in four infection was asociated with adverse effects and

prolonged or recurrent illness. Children were less often affected and in them adverse affects were not demonstrated but they were not investigated as intensively as were adults.

Penicillin treatment was followed by a rapid subsidence of fever and a speedy recovery in most cases. Haematuria persisting for 6 weeks or recurring was associated with infections of the urinary tract, delay in starting penicillin and admission to hospital.

Active streptococcal infection of the upper respiratory tract and cervical glands and secondary infection of the urinary tract may contribute more to the onset of APSGN and to its course than is currently believed.

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