greatly helped by the Wellcome Historical Medical Museum, both in the arrangement of the museum and by the loan of several exhibits.

Members and associates of the Royal College of General Practitioners may care to visit the Museum and 'The Temple of Vaccinia' (open 1 May–30 September (except Mondays), 2.30 p.m.–5.30 p.m.) It may well be included with visits to Berkeley Centre and Church, and Slimbridge Wildfowl Trust, a few miles away.

Acknowledgement

I am grateful to Mr John Eatough for allowing me to use his photograph of 'The Temple of Vaccinia'.

CLINICAL NOTE

ACUTE NEPHRITIS PRESENTING WITH A NORMAL URINE

Report of a case

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THAT THE URINARY FEATURES OF acute nephritis may be found without other evidence of renal disease is well known (McCrae 1913, Lyttle 1933, Weinstein *et al.* 1950, Stetson *et al.* 1955) and renal biopsy studies (Hutt and White 1964) have shown that in some patients signs are absent and urinary abnormalities minimal.

Less familiar is the claim that patients may manifest the systemic signs of this disease—oedema and hypertension—yet excrete a urine with either few abnormalities or none at all.

Whether dropsy without proteinuria ever followed scarlet fever has been a subject of discussion since 1844 (*Lancet* 1844, Thomson 1886, Tirard 1909, McCrae 1911, Nonnenbruch 1916). Fenini, in 1872, described a series of cases of acute nephritis (some fatal) in which at some stage proteinuria was either absent or slight. Other authors have claimed that oedema, or a rise in blood pressure, or both, sometimes preceded the appearance of proteinuria (Mohammed 1874, Kylin 1929, Keefer 1939, Hahn 1948, Osman 1948). Manser and Wilson (1952), investigating an epidemic of sore throats associated with a high incidence of acute nephritis, found that, late on in the outbreak, a few patients had hypertension without proteinuria and over 30 had oedema, with only a trace of protein in the urine.

It has been claimed that abnormalities of the urinary deposit may also

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be absent or slight or delayed (Burke and Ross 1947, Sharpey-Schafer 1955, Fleisher 1963).

Actual case reports have been recorded by Fenini (1872), Henoch (1899) (who included a case of Litten's), Quincke (1906), Schick (1912), Wickbom (1928), de Wesselow (1934), Zischinsky (1936), Keefer (1939), Allessandri and Roeschmann (1942), Crofton and Truelove (1948), Brod (1949), Blumberg and Fieldman (1962), Berman and Vogelsand (1963), Cohen and Levitt (1963) and Albert *et al.* (1966). In addition, Wilson (1942) described two patients who developed short-lived oedema after a respiratory tract infection. One also had a raised blood pressure but in neither was the urine abnormal.

Unfortunately, few of these case reports are both complete and convincing. Some (e.g. those recorded by Litten, Quincke, and Zischinsky) seem unlikely to have been cases of acute nephritis and in others the period of observation was too short. Those that are reasonably well-documented are summarized in the table. The most recent, and best attested, reports derive from hospital experience. A further case, seen in general practice, is here reported.

Case report

R.W., aged 17, male; no relevant past history. On 8 December 1963, he developed a sore throat; oral penicillin was prescribed but stopped on 10 December when a rash appeared. He was first seen by the author on 11 December; extensive localized patches of herpes simplex were present on forehead, cheek and neck; herpes simplex virus was isolated from a throat swab but, as he had received penicillin, bacterial culture was not attempted. On 16 December the sore throat recurred; he was seen late at night by a colleague who prescribed tetracycline. Next day his mouth was full of sticky yellow discharge and pus could be seen coming from a point just above the left tonsil. Tetracycline was stopped and I.M. penicillin ordered (800,000 units of mixed procaine and soluble penicillin daily for two days, followed by benzathine penicillin).

On 18 December his temperature was normal and he made an uninterrupted recovery. On 27 December he attended for a certificate of fitness to resume work and his face was seen to be swollen. He was fairly well but admitted to some shortness of breath for five days and headaches for one day. Micturition was normal. He claimed that the oedema of his face began on 24 December but his father stated subsequently that his ankles became swollen at about the time parenteral penicillin was instituted (i.e. about 17 December).

He was admitted to the local cottage hospital and treated with bed rest and low salt diet. The main findings are recorded on the accompanying chart. The blood pressure was 180/100, the fundal arteries thin and tortuous, and he had pitting oedema of both ankles. ASLO titre was 580 u/ml and a complement fixation test was positive for herpes simplex at 1/80. Blood urea was 65mg/100ml, Hb 99 per cent, ESR 19mm in one hour, white cells 9,000/cm.

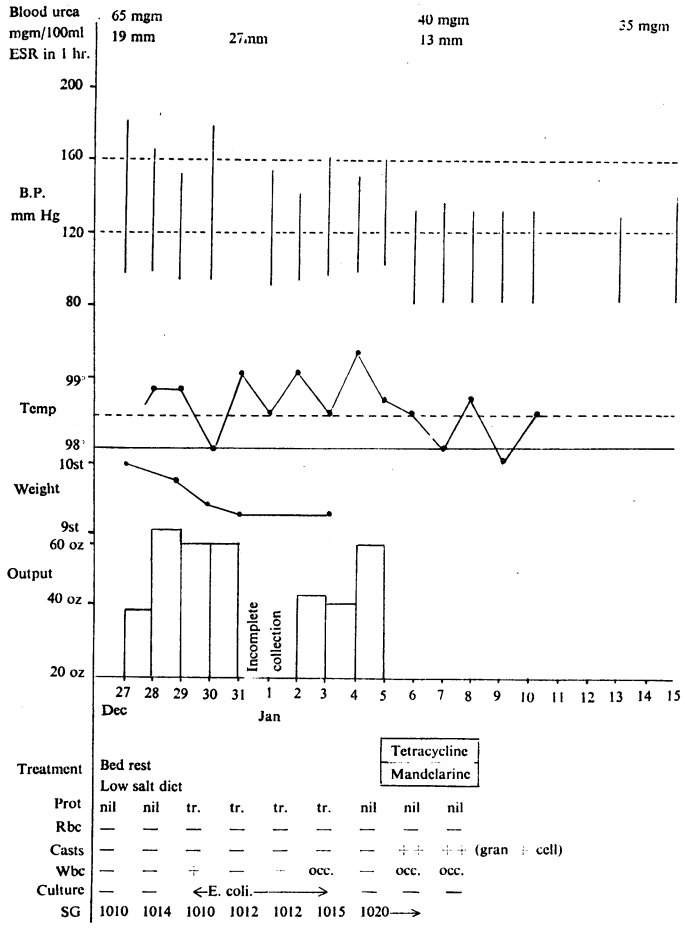
On 30 December the serum Na was 14 mEq/1;K was 4.5 mEq/1; chlorides 112 mEq/1. The urine contained no protein and no cells or casts. The urinary output rose, the blood pressure began to fall, he lost 8 lb in weight and the oedema disappeared, all within four days. A trace of protein was then found in the urine, with a few white cells, and *Escherichia coli* was grown on culture; at the same time the ESR went up and the temperature rose. The *E. coli* isolated was sensitive only to mandelamine; this was, therefore, started on 4 January, together with tetracycline, in the hope that this might control any intrarenal infection. There was

TABLE I

SUMMARY OF SOME PREVIOUS CASE REPORTS

Author	*Year*	*Age*	*Sex*	*Preceding infection*	Str. pyogenes *isolated*	*ASLO*[1] *raised*	*Nitrogen retention*	*Urine*			*Renal biopsy or PM*	*Outcome*
								Prot	*Rbc*	*casts*		
Wickbom ..	1928	24	F	Sore throat			+	—	+	+		Recovered
de Wesselow..	1934	26	M	Quinsy			—	—	?	—		Recovered
Allessandri ..	1942	32	?	Acute tonsillitis	—			—	—	—	+	Died[2]
Crofton ..	1948	16	F	Sore throat	—		—	—	—	—		Recovered
Brod	1949	34	M					—[3]	—	—		Recovered
Blumberg ..	1962	2	M	Impetigo	+	+	—	—	—	—	+	Recovered
Cohen ..	1963	20	M	Sore throat		+	—	—[4]	+	?	+	Recovered
		39	F	Sore throat	—	+	—	—[3]	—[5]	?	+	Recovered
Berman ..	1963	15	F	Sore throat	6 ?	+		—	+	+	+	Recovered
Albert ..	1966	10	F	Sore throat	+ (type 3)	+	—	—[3]	—[5]	—	+	Recovered

All cases had oedema and raised blood pressure; oliguria recorded in cases reported by Wickbom, Allessandri, Brod and Blumberg.



KEY TO TABLE

1. ASLO titre over 400u/ml.
2. Died following ether test after 48 hours observation. Five other cases described but with insufficient details.
3. Trace of protein noted later.
4. Urine before admission contained protein + +; trace noted occasionally subsequently.
5. A few red cells noted later.
6. Beta-haemolytic streptococcus isolated; group not stated.

an immediate improvement; the temperature fell and the blood pressure became normal for the first time; protein and white cells disappeared from the urine, the output rose and the specific gravity of the urine reached 1020. On 7 and 8 January, granular and cellular casts were seen in the urine for the first and only time. At no stage were red cells seen.

Discussion

This boy of 17 presented with oedema, hypertension and raised blood urea 19 days after a sore throat first began and 11 days after it had recurred. The urine—examined within a few hours of voiding—was then entirely normal. Subsequent specimens were sent by post to the laboratory and the consequent delay might have accounted for the inability to demonstrate red cells and casts, though not for the absence of protein. Like other recently reported cases, therefore, this patient displayed the systemic signs of disordered renal function without the urinary evidence of an inflammatory process involving the glomeruli that normally accompanies those signs.

In general it seems that this dissociation of signs has been noted at two stages—at the onset of acute nephritis, and during recovery. The earlier writers, carefully observing cases of scarlet fever for the first signs of nephritis, were preoccupied with the first stage. Unfortunately the evidence they present is insufficient to decide if oedema and hypertension do indeed ever precede other signs. The better documented reports of recent years, on the other hand, are of patients who, once admitted to hospital, quickly recovered. This patient also was probably recovering when first discovered; the ESR was then only 19 mm in one hour and he responded speedily to simple measures.

It has generally been accepted that the last signs of acute nephritis to disappear are the urinary abnormalities (see, for example, Fishberg 1939). The problem is to explain why in some patients this sequence is reversed. Moreover it is possible that this reversal may be a relatively new phenomenon. The number of reports since 1942 presents a contrast with the literature of the 1930's, a search through which failed to reveal any cases of this kind, apart from the three already quoted, only one of which seems likely to have had acute nephritis (de Wesselow 1934).

There is some evidence that penicillin shortens the course of some cases of acute nephritis (Moncrieff 1944, Shore 1944, Suckeki 1945, Sen 1946, Razzaz 1949). Most of the recently reported cases are known to have had penicillin before admission to hospital and in the patient reported here penicillin was given at a time possibly coincidental with the onset of nephritis. In one instance it does appear that an antibiotic was not given (Albert *et al.* 1966) and while that case, and de Wesselow's patient in 1934, suggest that acute nephritis may resolve spontaneously in the manner here described, if the early administration of penicillin does in some way cut short the inflammatory phase, leaving function to recover more slowly with the gradual resumption of normal blood flow, then this might account for any increase in such cases in recent years.

There is one further point of interest in the patient reported here: the

evidence of both viral and streptococcal infection preceding the onset of acute nephritis. A subsequent case seen by the author also yielded both *Streptococcus pyogenes* (type 12) and a virus (adenovirus type 5).

Summary

A case of acute nephritis presenting with hypertension, oedema, raised blood urea, and a normal urine, 19 days after a sore throat treated with penicillin, is described. There was evidence of infection with both *Str. pyogenes* and herpes simplex.

The possibility that penicillin might be responsible for the dissociation of signs in this patient and in other recently reported cases is discussed.

Acknowledgements

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PERSONAL POINTS OF VIEW

PRESCRIBING COSTS

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SINCE 1955, THE CLERK TO THE Executive Council has sent out to each of his flock of general practitioners a roneoed form on 'Prescribing Costs'. This gives certain statistics for one month's prescribing, for example the total number of prescriptions, their total cost, the average cost per prescription, and for comparison your partners' figures, the average figures for your area and for England. Figures below the average pass without commendation, yet figures above the average merit a visit from the regional medical officer. As I remember from schooldays, there should be as many figures below as above this mythical 'average'.

Analysis of these figures and their changing pattern over seven years is interesting.

TABLE
PRESCRIBING COSTS

Year Mnth	*Partnership figures*			*Area*	*England*	*No. of prescriptions per person on N.H.S. list*		
	No. of pre-scrip-tions	*Total cost £*	*Cost per pre-scrip-tion s. d.*	*Average cost s. d.*	*Average cost s. d.*	*Practice*	*Area*	*England*
1961 Mar	3,820	1,313	6 10½	8 3	7 10½	.235	.310	.400
1961 Nov	3,634	1,294	7 1	8 8	8 2¾	.223	.297	.372
1963 June	3,207	1,182	7 4	9 2	9 0¾	.196	.264	.335
1964 June	3,856	1,377	7 2	9 2	9 6	.239	.309	.375
1965 May	4,820	1,862	7 9	9 9	10 3	.295	.386	.439
1966 Mar	5,933	2,281	7 8	9 10	10 6	.363	.466	.512
1967 Jan	5,765	2,320	8 1	10 1	10 7	.357	.435	.506