have been the source of infection in a case reported by Wheeler and Borchers.⁷

In conclusion, it seems that campylobacters (*C jejuni* and *C coli*) are an important addition to the growing list of known enteric pathogens. Indeed, if the samples received in this laboratory are typical of those in the rest of the country they are the commonest identifiable cause of infectious diarrhoea. Moreover, the fact that these organisms are highly sensitive in vitro to the aminoglycoside and macrolide antibiotics (less so to the penicillins) means that chemotherapy is likely to be effective. Erythromycin has the advantage of a narrow spectrum of activity, and the stearate is a logical choice on account of its acid-resistance and incomplete absorption, which should provide therapeutic concentrations of the antibiotic in the gut as well as in the blood.

The development of a selective culture medium has now made the isolation of campylobacters from faeces a simple matter requiring only a vacuum jar and an incubator set at about 43°C. Although it may seem burdensome to laboratory staff to add yet another medium to those already in regular use for detecting enteric pathogens, the returns are likely to be great.

I thank Mr J Benjamin and Mr R V Waters for technical help, and the general practitioners and their patients for such willing co-operation, without which this study would not have been possible.

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(Accepted 29 April 1977)

Prognosis of Henoch-Schönlein nephritis in children

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British Medical Journal, 1977, **2**, 11-14

Summary

All the survivors of a series of 88 patients with Henoch-Schönlein nephritis were examined after a follow-up of six and a half to 21 years (mean 9.9). Sixty-one patients had no demonstrable abnormality; six had minor urinary abnormalities; five had hypertension without urinary abnormality or renal dysfunction; four had heavy proteinuria; eight were in chronic renal failure, three of whom were on regular dialysis; and four patients had died within 25 months of onset. Neither corticosteroids nor immunosuppressive drugs alone or in combination appeared to influence the outcome. A clinical presentation with a combination of acute nephritis and

a nephrotic syndrome and a high proportion of crescents in renal biopsy specimens was associated with a poor outcome. Neither the clinical presentation nor the renal morphology were, however, precise determinants of outcome. Outcome was not related to age, associated streptococcal infection, or recurrences of the rash. The clinical state two years after presentation was compared with the state six and a half years or more after presentation in 76 patients. The clinical state had changed in 32 patients, in 17 of whom it had deteriorated. It was not possible to identify with any certainty the patients who would deteriorate (or improve). Patients who have had Henoch-Schönlein nephritis should be followed up for at least five years.

Introduction

The clinical course and outcome in 88 children with Henoch-Schönlein nephritis were reported by Meadow *et al*¹ in 1972. Follow-up information was then available for 62 patients, who had been followed for two or more years. Since that study we have traced all the survivors and reassessed their outcome six and a half to 21 years after presentation. Our purpose was to re-evaluate clinicopathological correlations after this longer follow-up. We have also introduced a new renal histological grading system.

Patients and methods

With the permission of the general practitioner each of the 84 survivors was examined by one of us or, in a few patients who pre-

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ferred it, by the general practitioner or referring paediatrician. Symptoms, abnormal signs, and blood pressure were recorded. Urine was tested for blood and protein with reagent strips (Hema-Combistix or Labstix), and abnormal findings were confirmed by microscopical examination of the urine and timed overnight protein excretion (sulphosalicylic acid method). Plasma creatinine concentration was measured by autoanalyser on every patient and, if abnormal, the glomerular filtration rate (GFR) was estimated by ^{51}Cr EDTA single injection slope clearance.² The clinical status of the patients was then classified as in the original paper.¹

State A—Normal: the patient was normal on physical examination, with normal urine and renal function.

State B—Minor urinary abnormality: the patient was normal on physical examination, with microscopic haematuria or proteinuria < 1 g/24 hours (or < 40 mg/hour/m²), or both.

State C—Active renal disease: the patient had proteinuria ≥ 1 g/24 hours (≥ 40 mg/hour/m²) or hypertension (mean blood pressure ≥ 105 mm Hg), or both, and GFR ≥ 60 ml/min/1.73 m².

State D—Renal insufficiency: the patient had GFR < 60 ml/min/1.73 m² or had died.

This classification has one difference from that in 1972: hypertension without proteinuria qualified for entry into State C. States A and B were considered to represent good outcomes and states C and D to represent poor outcomes.

The renal biopsy slides were all reviewed by observers unaware of the clinical classification of the patients and graded under the revised system evolved by the pathologists of the International Study of Kidney Disease in Children (ISKDC)*: grade I—minimal alterations; grade II—mesangial proliferation; grade III—(a) focal or (b) diffuse proliferation or sclerosis with $< 50\%$ crescents; grade IV—(a) focal or (b) diffuse mesangial proliferation or sclerosis with 50–75% crescents; grade V—(a) focal or (b) diffuse mesangial proliferation or sclerosis with $> 75\%$ crescents; grade VI—membranoproliferative-like lesion.

For this study we widened the definition of a crescent to include the smallest segmental proliferation of capsular epithelium, provided that it was accompanied by adhesion to the adjacent glomerular tuft, or loss of continuity of the capsular basement membrane. This definition therefore included what have been termed “capsular reactions” and “segmental crescents,” whereas in other papers we (and others) have discriminated between these relatively minor changes and “circumferential” crescents, in which extraglomerular proliferation surrounds, or nearly surrounds, the glomerulus.³

Results

The mean duration of follow-up (± 1 SD) was 9.9 ± 2.6 years (table I). Of the 88 patients 61 were normal, six had minor urinary abnormalities, nine had evidence of active renal disease, and 12 were in chronic renal failure or dead.

TABLE I—Duration of follow-up

Follow-up (years):	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
No of patients:	6	6	15	15	12	14	16	3	3	1				1	1	1

TABLE II—Prognosis from clinical state at two years in 76 patients

At 2 years		At $\geq 6\frac{1}{2}$ years			
State	No	A	B	C	D
A	36	33	0	3	0
B	25	14	5	4	2
C	11	3	0	2	6
D	4	0	0	0	4
Total	76	50	5	9	12

Information was available on the clinical state of 76 patients two years after onset and this is shown in table II in comparison with the later follow-up in the same patients. The number of patients in state D trebled from four at two years to 12, and their outcome is

*Protocol available from the offices of the ISKDC, Department of Paediatrics, Albert Einstein College of Medicine, Bronx, New York, NY, USA.

TABLE III—Details of patients in state D at six and a half years or more and their clinical stage two years after onset

Case No	Renal presentation	Histology	State at 2 years	At $\geq 6\frac{1}{2}$ years	
				Age (years)	Outcome
1	AN and proteinuria	IVb	C	15	Regular dialysis
2	AN and NS	IVb	C	11	GFR 3 ml/min
3	AN and NS	VI	C	4	Regular dialysis
4	AN and NS	IVa	B	9	GFR 50 ml/min
5	AN and NS	Vb	D		Died at 1 month
6	AN and NS	IVb	D		Died at 25 months
7	AN and NS	IIIb	D		Died at 4 months
8	AN and NS	II	C	14	GFR 29 ml/min
9	NS and haematuria	VI	D		Died at 9 months
10	Haematuria and proteinuria	Va	B	14	GFR 27 ml/min
11	Haematuria and proteinuria	IIIa	C	9	GFR 43 ml/min
12	Haematuria and proteinuria	Vb	C	5.8	Regular dialysis

AN = Acute nephritis. NS = Nephrotic syndrome.

shown in table III. Two-thirds of the children had no demonstrable abnormality compared with half after two years' follow-up. The abnormalities in the patients with active renal disease six and a half years or more after onset (state C) are shown in table IV in relation to their clinical state two years after onset.

Relation to clinical presentation—The main renal presentations were defined in the original paper.¹ Patients with a nephritic-nephrotic presentation fared worse (table V), but over 40% of this group were normal. In all the other groups significant renal disease was present, although most patients had recovered completely.

Outcome in relation to age—The proportion of patients with a poor outcome rose with the age at presentation, but the numbers at the extremes were too small for effective analysis (table VI). There was no apparent relation between the age at presentation and the clinical state at follow-up, and it was not possible to define an age under which the prognosis was invariably good or over which it was invariably poor.

TABLE IV—Details of patients in state C at six and a half years or more after onset

Case No	Clinical state at 2 years	Abnormality at $\geq 6\frac{1}{2}$ years
13	A	Proteinuria > 1 g/day (44 mg/h/m ²)
14	B	Proteinuria > 1 g/day (36 mg/h/m ²)
15	B	Blood pressure 130/90 mm Hg
16	B	Proteinuria > 1 g/day (62 mg/h/m ²)
17	A	Blood pressure 160/90 mm Hg
18	C	Blood pressure 125/100 mm Hg (on hypotensive drugs)
19	A	Blood pressure 155/90 mm Hg
20	B	Proteinuria > 1 g/day (108 mg/h/m ²)
21	C	Blood pressure 140/90 mm Hg

TABLE V—Relation between main renal presentation in 88 patients and outcome after six and a half years or more

Presenting features	No of patients	State at $\geq 6\frac{1}{2}$ years			
		A	B	C	D
Microscopic haematuria ..	5	4		1	
Proteinuria and haematuria ..	40	31	3	3	3
Nephrotic syndrome and haematuria ..	8	7			1
Proteinuria and acute nephritic syndrome ..	9	8			1
Nephrotic syndrome and acute nephritic syndrome ..	26	11	3	5	7
Total	88	61	6	9	12

TABLE VI—Relation between age at onset and outcome

Age (years):	< 6	6–11	≥ 12
State A ..	19	38	4
State B ..	2	4	0
State C ..	2	6	1
State D ..	1	9	2

Recurrence of rash—Six of the 21 patients whose rash recurred and 15 of the 67 patients without recurrence had a poor outcome.

Outcome in relation to renal morphology—All the patients with minimal alterations on renal biopsy were normal or nearly so at follow-up, while all the patients with over 75% crescents (grade V) had persisting renal disease or had died. More extensive histological changes were reflected by a poor prognosis (table VII), but grade VI histology was associated with complete recovery and also with death or renal insufficiency.

TABLE VII—Relation between renal morphology in 88 patients and outcome after six and a half years or more

Histological grade	No of patients	State at $\geq 6\frac{1}{2}$ years			
		A	B	C	D
I	6	5	1		
II	16	12		3	1
III	40	33	3	2	2
IV	17	9	1	3	4
V	4		1		3
VI	5	2		1	2
Total	88	61	6	9	12

Antistreptolysin O titre—The patients were separated into two groups for this analysis: those considered to have had evidence of preceding streptococcal infection (single ASO titres ≥ 250 or serial titres rising above 250), and those without such evidence (single ASO titres < 250 or serial titres not rising above 250). Outcome was assessed as good or poor. There was no difference in outcome between the two groups; 25 of the 34 patients with evidence of recent streptococcal infection and 25 of the 35 with no evidence of recent streptococcal infection had a good outcome.

Effect of treatment—The relation of treatment to outcome and renal morphology is shown in table VIII. Treatment consisted of corticosteroids alone, immunosuppressive agents alone, or steroids and immunosuppressive agents, and some of the patients received no treatment. When patients with any treatment were compared with those with no treatment and the outcome assessed as good or poor no significant difference was evident between the two groups (χ^2 with Yates's correction = 3.34). When the treatments or outcome grades were separated treatment was associated with a poorer outcome, but it was apparent that small numbers skewed the results. When the histological features were taken into account it was clear that the patients with the most extensive renal lesions were more likely to have been given active treatment.

Discussion

The series is biased towards children who presented with serious renal disease. Early in the course of this study several children who had only minor urinary abnormalities underwent renal biopsy. The high incidence of minor histological changes, however, persuaded us to adopt a more selective policy for renal biopsy, so that later only patients with nitrogen retention, hypertension, heavy proteinuria, nephrotic syndrome, or mixed nephritic-nephrotic syndrome underwent biopsy.

When Meadow *et al*¹ first reviewed these patients a poor prognosis was associated with (a) a presentation that included both nephritic and nephrotic features, (b) the presence of a high proportion of crescents in the renal biopsy specimen, and (c) an age at onset greater than 6 years. It was also considered

that deterioration rarely occurred more than two years after presentation. At that time only 62 of the 88 patients had been followed for two years or more. We have reported here follow-up information on all the patients six and a half years or more (mean 9.9 years) after presentation and have also compared the clinical state at two years of 76 patients with their state after follow-up for six and a half years or longer.

About 24% of the patients had active renal disease, renal impairment, or had died (states C and D) after six and a half years compared with 20% at two years. Clearly both deterioration and full recovery have occurred since two years from onset (see table II). The proportion of patients with minor urinary abnormalities (state B) decreased with longer follow-up, while that of patients with active renal disease without renal impairment (state C) was much the same. Excluding state D, both recovery and deterioration were seen in patients in all clinical states, but deterioration was most significant from state C: six of the 11 patients in this state at two years subsequently developed renal insufficiency. The most important change was the trebling of the numbers of patients who had chronic renal insufficiency or had died (state D).

We have confirmed that presentation with a nephritic and nephrotic syndrome combined and an increased proportion of crescents on renal biopsy were associated with a poor prognosis, but neither the clinical presentations nor the renal morphology were clear discriminants of outcome. Half the patients with a nephritic-nephrotic presentation recovered fully, and a significant minority of those with milder presentations had a poor outcome (see table V). The histological grading emphasises the proportion of crescents as the main index of severity. Grade V histology was never associated with complete recovery, but only four patients were in this grade. In both grade VI and in the other grades complete recovery has occurred (table VII). The significance of grade VI histology is not clear, and Levy *et al*⁴ have also reported both full recovery and progression to death in this grade. Even when clinical presentation and morphological grading were combined it was not possible to predict the outcome accurately. For example, 54% of the nephritic-nephrotic group recovered fully or had minor abnormality. Even when only patients in that group with grade III to V histology were considered a good prognosis was observed in 58%. If only grades IV and V were considered (14 patients) a good outcome was still evident in half of them. Inclusion of grade VI patients did not affect these figures. The new system of histological grading is still imprecise and the problem of defining a crescent remains. What different histologists call "crescents" varies, so the conclusions drawn about the clinical or prognostic significance will also vary.

We have purposely listed the individual reasons for classifying patients as having active renal disease (state C; table IV) because hypertension alone was one of the criteria and it was borderline in some. This is obviously a controversial point, but we consider that these relatively minor changes should be noted because of the unknown contribution of renal disease in childhood to hypertension in later life. A disturbing finding was the progression of three patients from State A at two years to state C later. Two of these patients had hypertension with normal urine and one had heavy proteinuria.

The outcome was not strongly related to age at presentation, previous streptococcal infection, or recurrences of the rash, and no form of treatment could be shown to be of value. Levy *et al*⁴

TABLE VIII—Relation between treatment and outcome

Treatment	Outcome at $\geq 6\frac{1}{2}$ years				Histology grade					
	A	B	C	D	I	II	III	IV	V	VI
No treatment	30	3	3	2	3	7	22	2	1	2
Corticosteroids	15	2	2	2	3	7	10	2	0	0
Immunosuppressives	4	0	3	3	0	1	2	3	2	2
Steroids and immunosuppressives	12	1	1	5	0	1	6	10	1	1

thought that treatment had a marginal advantage, but no controlled trials have been carried out. One is currently being conducted by the ISKDC. Counahan and Cameron⁵ have reported equivocal results of treatment in six patients with severe Henoch-Schönlein nephritis with combined immunosuppression and anticoagulation, though success in some patients was striking.

While only a few patients with Henoch-Schönlein nephritis develop permanent renal damage or renal failure, it is difficult to identify these patients early in the course of the disease, when treatment might alter its course. The combination of immunosuppressives, steroids, and anticoagulants has been used with apparent success in some aggressive forms of glomerulonephritis,^{3 6} and it is clearly desirable to identify patients who might benefit before the disease has become unalterably established, as well as excluding from such potentially dangerous treatment those patients in whom it is unnecessary.

We have shown in this study that significant changes in outcome occurred more than two years after presentation. Most patients improved, but a significant number deteriorated. The European Dialysis and Transplant Association⁷ have reported an increase in the proportion of children with end-stage renal failure due to Henoch-Schönlein nephritis; we have shown that early recognition of some of these children is difficult. Prolonged follow-up of asymptomatic children may induce unnecessary anxiety. We nevertheless suggest that an annual blood pressure check and urine test for protein and blood by the general prac-

titioner would be an effective way of observing those patients for whom specialist follow-up was unnecessary. Our findings suggest that all patients should be followed for at least five years.

The efficiency of the staff of the National Health Service Central Register, in particular Mrs E A Evans, in helping us to locate many of the patients was remarkable. We thank the many general practitioners for their help in finding some patients, for their courtesy in allowing us to examine them, and examining some patients on our behalf. We were also helped by many family practitioner committees, paediatricians, the Sussex and Cheshire Police, and the Australian High Commission. Dr D R Turner gave us valuable advice on interpreting the renal morphology.

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(Accepted 22 April 1977)

Mycoplasma pneumoniae infection and arthritis in man

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British Medical Journal, 1977, **2**, 14-16

Summary

Seven patients developed arthritis after *Mycoplasma pneumoniae* infection. Their joint symptoms persisted for up to one year. One patient developed an articular erosion and in another rheumatoid factor was present in serum transiently. *Mycoplasma* infection often causes ill-defined arthralgias and myalgias, but the migratory polyarthropathy of middle-sized joints that occurred in these patients is much less common. The prognosis seems to be good.

Introduction

That mycoplasma infection may produce chronic inflammatory joint disease in animals is not in doubt.^{1 2} Indeed, laboratory models of mycoplasma arthritis have been used to study the

effects of proposed new antirheumatic drugs.³ But the role of this organism in producing chronic arthritis in man is less well established. Jansson *et al*⁴ found mycoplasma antibody titres of 16 or higher in patients with definite rheumatoid arthritis.

Non-specific "arthralgias" or "myalgias" are a frequent accompaniment of human *Mycoplasma pneumoniae* infection.⁵⁻⁷ Nevertheless, diarthrodial joint involvement in human mycoplasma infection was not even recorded until 1966⁶ and has been reported only rarely since.⁸⁻¹⁰ One major study claimed that only eight cases had been recorded,¹⁰ and in all cases reported to date joint disease has been transient and recovery complete within the time course of the acute illness. The pattern of disease was migratory and polyarticular, the larger joints being affected more often than smaller ones. Subcutaneous nodule formation was recorded in one patient, and some patients had clinical signs of synovial effusions.

We report here a group of patients who had suffered from mycoplasma infection and who were carefully followed up to see whether they would develop diarthrodial joint disease.

Patients and methods

A standardised questionnaire, which included direct questions about peripheral joint pain, tenderness, swelling, or stiffness, was sent to 45 patients who had been admitted to Ruchill Hospital in the previous 12 months (1974-5) with clearly documented *Mycoplasma pneumoniae* infection. Patients who had had a less than fourfold increase or antibody titres less than 256 by complement fixation to *Mycoplasma pneumoniae* during their hospital admission were not included. The case records of each patient were examined and showed that all had suffered an acute febrile illness with primarily respiratory tract symp-

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