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 Cameron[5] 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 Association[7] 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 practitioner 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.

References

1 Meadow, S R, *et al*, *Quarterly Journal of Medicine*, 1972, **41**, 241.
2 Chantler, C, and Barratt, T M, *Archives of Disease in Childhood*, 1972, **47**, 613.
3 Brown, C B, *et al*, *Lancet*, 1974, **2**, 1166.
4 Levy, M, *et al*, *Actualités Nephrologiques de l'Hôpital Necker*, p 174. Paris, Flammarion, 1976.
5 Counahan, R, and Cameron, J S, in *Contributions to Nephrology. The Kidney in Systemic Disease*, ed S Massry. Basel, Karger. In press.
6 Kincaid-Smith, P, Saker, B M, and Fairley, K F, *Lancet*, 1968, **2**, 1360.
7 Schärer, K, *et al*, in *Proceedings of the European Dialysis and Transplant Association 13*, ed B H B Robinson, P Vereerstraeten, and P J B Hawkins, p 60. Tunbridge Wells, Pitman Medical, 1976.

(*Accepted 22 April 1977*)

Mycoplasma pneumoniae infection and arthritis in man

LUIS A HERNANDEZ, GEORGE E D URQUHART, W CARSON DICK

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 1966[6] 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-

Centre for Rheumatic Diseases, University Department of Medicine, Royal Infirmary, Glasgow
LUIS A HERNANDEZ, visiting research fellow
W CARSON DICK, MD, MRCP, consultant physician

Regional Virus Laboratory, Ruchill Hospital, Glasgow
GEORGE E D URQUHART, MRCPATH, consultant virologist

toms and signs. The patients were aged 6 to 43 years and 29 were female.

Thirty-eight of the 45 patients responded to the questionnaire and seven of these reported signs or symptoms of peripheral joint disease. All seven patients were contacted and each was comprehensively examined by LAH. A full personal and family history was taken and each patient was examined clinically. In addition a special examination of the musculoskeletal system was completed. The articular index of joint tenderness[11] and the duration of morning stiffness were assessed, and a radiological examination of hands, wrists, feet, knees, and cervical spine was completed in all patients. Rheumatoid factor was measured in all patients using the R_3-titration set based on the principle of latex floculation. Latex particles were coated with bovine γ-globulin (Denver Chemical Manufacturing Company, Stanford, USA). Serial measurements of serum complement concentration (C3, C4) and immunoglobulins were available for analysis in two patients. The three patients with a persistent articular problem were offered treatment with a single non-steroidal anti-inflammatory drug and all were followed to the conclusion of their illness. At the time of writing all the patients studied had been totally free of all symptoms for at least one year.

Results

The table summarises the clinical and laboratory details of each of the seven patients. All the patients had painful swollen peripheral joints during their acute illness. The progress was migratory in three and in all patients the middle-sized joints were affected (wrists, shoulders, ankles, knees). In one patient (case 5) the skin over the affected joint was red and inflamed. Each patient suffered considerable morning stiffness and pain. The articular manifestations appeared three to eight days after the onset of the initial illness, and in all except three patients, they had disappeared by eight weeks after their onset.

The course of the joint condition in the other three patients (cases 5-7) was rather different.

Case 5—The initial illness in this 35-year-old woman began in March 1974 with a respiratory infection followed by a polyarthritis one month later that affected particularly her ankles, hands, and wrists. On admission to hospital rheumatoid arthritis was diagnosed and she received treatment with phenylbutazone. Her condition did not improve and two months later she developed "septic arthritis" in the first metatarsophalangeal joint of the left foot. The joint was swollen, painful, and very tender and the overlying skin was red. She received lincomycin treatment and her condition improved but did not resolve completely. The patient complained of persistent pain in that joint and in other joints from time to time, particularly her hand and left ankle. She was negative for rheumatoid factor, but radiological examination showed a juxta-articular erosion in the left carpal bones which subsequently healed. After she had been asymptomatic for over a year all radiological and laboratory investigations gave normal results.

Case 6—This 41-year-old man's illness started in February 1974 when he suffered mycoplasma pneumonia. Shortly afterwards he developed pain in his knees and elbows. Physical examination showed tenderness of the affected joints. He was negative for rheumatoid factor and radiography showed no abnormalities. The patient received treatment with simple non-steroidal anti-inflammatory drugs for one year, and, at the time of writing, he was free of symptoms and had been receiving no treatment for one year. Tests for rheumatoid factor gave persistently negative results and serial *x*-ray examinations were normal.

Case 7—The illness of this 30-year-old woman started in July 1975, three weeks after she had suffered mycoplasma pneumonia. She developed polyarthralgia followed by definite symmetrical arthritis affecting the metacarpophalangeal joints and proximal interphalangeal joints of her hands with swelling at the articular margins and morning stiffness. She had rheumatoid factor with a titre of 1/32. Radiological examination was completely normal. Her arthritis settled after 10 months of symptoms and rheumatoid factor disappeared. Over 18 months' follow up it has not reappeared.

Discussion

These cases reflect some of the features recorded by other workers. Pronounced diathrodial joint symptoms with peripheral joint pain, stiffness, tenderness, and swelling is an uncommon feature of mycoplasma infection in man, whereas less well-defined arthralgias or myalgias are common. When articular disease is severe, the clinical presentation is that of an acute migratory arthritis of middle-sized joints, which may be accompanied by redness and heat in the overlying skin. The shoulders, knees, wrists, elbows, and ankles are more prominently affected than either the peripheral or central joints. Morning stiffness may be pronounced and may last up to four hours. "Gelling" with stiffness after inactivity may be recorded.

This pattern of arthritis does remit completely, although it took considerably longer to disappear in this series than in other reported series. In all our patients the arthritic features outlasted the other features of the illnesses. In one patient (case 6), who was seronegative for rheumatoid factor and who had no radiological signs of joint damage, the articular features did not disappear for over one year. His arthritis primarily affected his knees and elbows. Another patient (case 7) is of particular interest. Her arthritis was peripheral and symmetrical and her articular index reached 56 (range 0-78). She had clinical evidence of synovial hypertrophy in the metacarpophalangeal and proximate interphalangeal joints. She developed IgM rheumatoid factor during the course of her illness, which did not disappear until her symptoms settled 10 months after the onset of her disease. She initially presented with a pyrexial illness with articular symptoms throughout and no clinical signs in other systems. The skin overlying the inflamed ankle joint was itself red and warm. Serial measurements of serum C3 and C4 showed reduced concentrations of both during her illness, but concentrations returned to normal as her erythrocyte sedimentation rate and clinical state returned to normal. The combination of signs and symptoms is reminiscent of those encountered during "reactive" arthritis.[12]

The clinical pattern in case 5 of a "rheumatoid arthritis"-like polyarthritis after a respiratory illness was similar to that in the other cases. But this patient was given phenylbutazone, which is recognised to be the cause of iatrogenic mortality and morbidity[13] and would not now be given as the drug of first choice in reactive arthritis. The episode of "septic arthritis" that necessitated lincomycin treatment is reminiscent of the clinical picture seen in case 7, with redness and warmness of the skin overlying the joint. No organism was ever isolated. Today a "red hot joint" is diagnosed as being either crystal-induced arthropathy or joint sepsis.[14] Perhaps reactive arthritis should be added to form a differential diagnostic triad for the "red hot

Details of seven patients who developed arthritis after Mycoplasma pneumoniae infection

Case No	Sex	Age (years)	Joints affected	Duration of arthritis	Rheumatoid factor	Radiography
1	M	11	Both knees	2 weeks	Negative	Normal
2	F	15	Right shoulder and both ankles	2 months	Negative	Normal
3	F	6	Both elbows and both knees	6 weeks	Negative	Normal
4	M	37	Knees and shoulders	1 week	Negative	Normal
5	F	35	Ankles, hands, and wrists	1 year	Negative	Erosion
6	M	41	Knees and elbows	18 months	Negative	Normal
7	F	30	Metacarpophalangeal joints, proximal interphalangeal hand joints, ankles, shoulders, wrists, elbows	10 months	1/32	Normal

joint." It is of considerable interest that this patient developed an articular erosion in the carpal bones of the left hand, which has subsequently healed.

In conclusion, *Mycoplasma pneumoniae* infection may cause arthralgias or myalgias. Less commonly it may cause a migratory polyarthropathy affecting middle-sized joints. This condition may be severe, with joint swelling, morning stiffness, gelling, and considerable functional disability, and it may be the dominant clinical feature outlasting all other mainfestations of the disease, though remission can usually be expected within eight weeks.

Rarely a peripheral symmetrical polycarthritis indistinguishable from rheumatoid arthritis may occur. There may be synovial hypertrophy with a high articular index, and articular erosions or rheumatoid factor may be present. The overlying skin may be red and inflamed, which is not the case in uncomplicated rheumatoid arthritis. Serum complement concentrations may fall, but in our patient in whom this occurred all abnormalities reverted to normal and she was well two years later. In the two patients who developed polyarthritis resembling rheumatoid arthritis increases in *Mycoplasma pneumoniae* antibody titres were documented and there seems no reason to doubt that their illness was caused by mycoplasma arthritis. Clearly man can suffer mycoplasma infections and may respond with a clinical and laboratory picture very like that of classical rheumatoid arthritis. The most appropriate description of the illness suffered by these patients seems to be "reactive arthritis," and the prognosis seems to be favourable though the illness may be severe and prolonged. It would seem best to avoid the use of potentially toxic drug regimens in such patients.

Requests for reprints should be addressed to Dr W Carson Dick, Centre for Rheumatic Diseases, 35 Baird Street, Glasgow G4 0EH.

References

1 Sharp, J T, and Riggs, S, *Rheumatism*, 1976, **1**, 51.
2 Sharp, J T, *Arthritis and Rheumatism*, 1970, **13**, 263.
3 Sabin, A B, and Warren, J, *Journal of Bacteriology*, 1940, **40**, 823.
4 Jansson, E, Makisara, P, and Tuuri, S, *Scandinavian Journal of Rheumatology*, 1975, **4**, 165.
5 Mufson, M A, *et al*, *Journal of the American Medical Association*, 1961, **178**, 369.
6 George, R B, *et al*, *Annals of Internal Medicine*, 1966, **65**, 931.
7 Feizi, T, *et al*, *British Medical Journal*, 1967, **1**, 457.
8 Lambert, H P, *British Medical Journal*, 1968, **3**, 156.
9 Jones, M C, *Thorax*, 1970, **25**, 748.
10 Murray, H W, *et al*, *American Journal of Medicine*, 1975, **58**, 229.
11 Ritchie, D M, *et al*, *Quarterly Journal of Medicine*, 1968, **37**, 393.
12 Aho, K, *et al*, *Arthritis and Rheumatism*, 1974, **17**, 521.
13 Girwood, R H, *British Medical Journal*, 1974, **1**, 501.
14 Boyle, J A, and Buchanan, W W, *Clinical Rheumatology*. Edinburgh, Blackwell Scientific, 1971.

(*Accepted 22 April 1977*)

Spontaneous premature birth in twin pregnancy

A R L WEEKES, D N MENZIES, C R WEST

British Medical Journal, 1977, **2**, 16-18

Summary

Factors associated with spontaneous premature birth were investigated in 459 consecutive twin deliveries at this hospital. Low maternal age, low parity, and zygosity were significantly related to the incidence of this complication. The number of previous abortions, sex combinations and related birth order, and mode of presentation of the first twin were not related to the incidence of spontaneous premature delivery. We conclude that apart from low maternal age and low parity there are no obvious factors that would permit early identification of twin pregnancies at risk from spontaneous premature birth.

Introduction

Spontaneous premature birth is the main reason for the high perinatal mortality in twin pregnancy.[1 2] Since there are no satisfactory criteria for identifying twins at particular risk from premature birth, we decided to see whether there are any readily identifiable clinical features associated with spontaneous premature birth in twin pregnancy.

Liverpool Maternity Hospital, Liverpool L7 3BN
A R L WEEKES, FRCS, MRCOG, senior registrar
D N MENZIES, FRCS, FRCOG, consultant obstetrician and gynaecologist

Biostatistics Unit, University of Liverpool, Liverpool L69 3B5
C R WEST, MA, statistical assistant

Patients and methods

We reviewed the obstetric records of the 459 twin pregnancies documented at this hospital during 1964–73. Seventy-five patients were excluded from the final analysis because they aborted, required induction of labour for pregnancy complications, or were delivered by elective caesarean section. Of the remaining 384 patients, 95 (24·7%) went into spontaneous labour before the 36th week of gestation (premature delivery), and in 289 (75·3%) pregnancy continued until or beyond the 36th week. We compared the two groups with respect to maternal age, numbers of previous abortions, parity, zygosity and sex combinations of the twins, and mode of presentation of the first-born. Zygosity had been determined macroscopically, the generally accepted principles for examination of twin placentae being used.[3]

The significance of differences between the two groups was assessed with the χ^2 test. Partial correlation coefficient analysis was used to check that the results relating to maternal age were independent of parity. Weinberg's[4] differential method of estimating the proportion of monozygotic pairs to be expected in a given sample of twins was applied to verify the findings related to zygosity.

Results

There was a significant association between low maternal age and premature birth (table I; $P = 0{\cdot}0037$) particularly for age 20 or less ($P = 0{\cdot}000096$). This association was independent of parity (partial