

The present study shows a positive correlation ($r = +0.75$) between peripheral venous renin activity and angiotensin pressor dose (Fig. 3). Similar results have recently been reported by Silah *et al.* (1967). So far as the group means are concerned the angiotensin infusion test corresponds closely to the renin determination. In individual cases, however, it is not a reliable gauge of renin activity. Renin activity indeed is not necessarily representative of true renin concentration (Pickens *et al.*, 1965).

The diagnostic value of both the angiotensin infusion test and the peripheral renin activity, when measured in the recumbent patient receiving a normal sodium intake, is limited by overlapping of values between diagnostic groups (Figs. 1 and 2). Using these two procedures we were unable to separate with certainty essential hypertensives from renovascular hypertensives. However, the diagnostic usefulness of the renin assay is greatly improved if determinations are done during sodium restriction and with the patient in the upright position. As we reported previously, both conditions cause a much higher renin increase in patients with renovascular hypotension than in essential hypertensives (Weidmann *et al.* 1967a). Similar observations have been published by Cohen *et al.* (1966), and a recent study by Kaneko *et al.* (1967) presents further evidence for the existence of an increased sensitivity of the renin-releasing mechanisms in renovascular hypertension. In their patients, as well as ours, excess renin was chiefly secreted by the stenotic kidney. If, therefore, the renin assay is used for detecting renovascular hypertension, determinations should be carried out on renal venous effluent and under the stated stimulatory conditions.

In cases with aldosteronism an increased resistance to the pressor effect of exogenous angiotensin makes Conn's syndrome highly improbable. Like other authors (Kaplan and Silah, 1964), we found a normal or increased angiotensin sensitivity and a low renin activity in such cases (Fig. 2). However, neither the angiotensin infusion test nor the renin assay makes it possible to differentiate with certainty between essential hypertension and Conn's syndrome.

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Syndrome with Joint Manifestations in Association with *Mycoplasma pneumoniae* Infection

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Summary: Three patients experienced a rheumatic-fever-like illness with painful limitation of joint movements. The illnesses were due to infection with *Mycoplasma pneumoniae*. Joint symptoms have not been previously described in cases of *M. pneumoniae* infection.

Introduction

Mycoplasma pneumoniae, formerly known as Eaton's agent, has in recent years become known as an important cause of

human respiratory disease. Most serious of the common manifestations of infection is a pneumonia which is sometimes accompanied by the development of cold agglutinins in the patient's serum. More commonly the patient has a mild lower respiratory tract illness, and infection may be subclinical and detectable only by changing titres of antibody against the organism (Chanock *et al.*, 1961). *M. pneumoniae* is occasionally associated with non-respiratory syndromes. Thus acute haemolytic anaemia with atypical pneumonia may be caused by *M. pneumoniae* infection, and a number of patients with Stevens-Johnson syndrome, or erythema multiforme minor, have shown evidence of infection with this organism.

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Meningoencephalitis, otitis media, bullous myringitis, acute pericarditis, and minor rashes have all been reported in patients with *M. pneumoniae* infection, but more work is needed to determine the frequency and significance of these associations (Chanock, 1965).

This report describes three patients who experienced a rheumatic-fever-like illness during the course of infection with *M. pneumoniae*. Results of complement fixation tests against *M. pneumoniae*, cold agglutinin, and antistreptolysin (A.S.O.) titres are shown in the Table; other results are given in the individual case reports.

Results of Tests

Case No.	Cold Agglutinin Titre	Complement Fixation Titre for <i>M. pneumoniae</i>			A.S.O. Titre
		On Admission	Later in Illness	After Recovery	
1	Not done	1,280	640	80	200
2	512	80	1,280	80	100
3	32	Not done	320	20	230

Case 1

A youth aged 17 became ill with fever, shivering, and abdominal pain. Though he had no cough, he was found to have evidence of consolidation at the left base, and this was confirmed by a chest radiograph. After two weeks of illness he began to improve, but in a few days his temperature rose again and he complained of pain and tenderness in both legs. His legs and thighs were tender and a small effusion was found in the right knee and later in the left. A few days later oedema of the left ankle was noticed. After the administration of prednisolone his general condition improved greatly and the swelling and tenderness of his knees subsided. A little oedema of the left ankle persisted for a time but his final recovery was complete.

Case 2

An 11-year-old boy had sore throats from time to time, the last a week before his admission to hospital. After this he was well for a few days, but during the three days before admission he had been ill with fever, malaise, and pain in the right knee and right ankle. There were no chest symptoms. His temperature was 101.6° F. (38.7° C.), and the pharynx was red, but there were no abnormal signs elsewhere. The right knee and right ankle were painful on movement but there were no abnormal signs in or around the joints. He developed a slight dry cough for a few days after admission. Radiography showed consolidation of the left lower lobe with a small left pleural effusion; the changes had regressed a week later and had resolved almost completely after 17 days. Haemoglobin was 13.0 g./100 ml. (89%) and W.B.C. 4,000/cu. mm., with normal differential count. Throat swab grew no pathogens, clean specimen of urine showed no abnormality on microscopy or culture, virus was not isolated in tissue culture from throat swab or stool, and complement fixation tests against influenza A, B, C, and adenovirus showed titres of less than 1:8. The joint pains resolved within a few days of admission, and during this time he developed signs of left lower lobe consolidation. His temperature returned to normal within three days.

Case 3

A boy aged 14 had a sore throat for a few days three weeks before admission. Sixteen days before admission he developed pain in both feet, then in the knees, shoulders, and fingers. The joints were painful for about two weeks, but the pain had subsided by the time he came into hospital. He had also suffered from headache and a dry cough. There was no history of chest illness.

On examination his temperature was 100° F. (37.8° C.) and there was impaired percussion with diminished breath sounds and crepitations at the right lung base. The spleen was palpable. There were no objective abnormalities in the joints, and no other abnormal signs. Radiography of the chest showed enlarged right hilar glands

and minor shadowing in the right lower lobe; these changes had resolved in a film taken 13 days later. Haemoglobin was 13.0 g./100 ml. (89%), W.B.C. 11,000/cu. mm., with normal differential, E.S.R. 36 mm./hour, throat swab grew no pathogens, serum proteins were normal, Wassermann, Kahn, and Widal reactions were negative, Mantoux positive 1:10 (B.C.G. given in infancy). Complement fixation tests for influenza, psittacosis, Q fever, and adenovirus all gave titres of less than 1 in 8.

His clinical recovery was rapid, the E.S.R. returning to normal after a week. Three weeks after admission, however, rales could still be heard at the right base. After a period of convalescence he returned to the clinic. He was then and on subsequent visits in normal health. It was thought possible that he had suffered a mild attack of rheumatic fever, and oral penicillin was given for several months, until the results of serial complement fixation tests for *M. pneumoniae* made it likely that this organism was the cause of his illness.

Discussion

Joint symptoms have not previously been described in *M. pneumoniae* infection, though George *et al.* (1966), in describing a large number of cases of mycoplasma pneumoniae at a U.S. Air Force base, mention a girl of 16, the daughter of an instructor on the base, who developed acute arthritis of the knee in association with a rise in serum cold agglutinins. Her serum was not tested for antibody to *M. pneumoniae*.

All three patients reported above suffered illnesses in which joint symptoms were prominent, and in two of them a provisional diagnosis of rheumatic fever was made. One had objective arthritis, the other two subjective joint symptoms only, albeit severe ones with painful limitation of joint movements. No other explanation for the arthralgia or arthritis was forthcoming, and antistreptolysin titres on all three patients were low. Drug sensitivity could be entertained as a possible factor in the first patient, who had received several antibiotics before the arthritis appeared, but no other signs of a drug reaction appeared. Drugs could not be invoked as a cause for arthralgia in the other two patients.

Joint symptoms in *M. pneumoniae* infection must be very uncommon, as they have not been described in many reports of large numbers of patients infected by this organism. On the other hand, acute febrile arthralgia often provides a difficult diagnostic problem, especially in children and young adults. If no unequivocal evidence of acute rheumatic fever is found the diagnosis, and so also the desirability of long-term prophylaxis against streptococcal infection, remains in doubt. It would be reasonable to include tests for *M. pneumoniae* infection in the investigation of such patients.

A different problem is the possible association of mycoplasmas with chronic joint disease. Polyarthritides is a feature of some animal mycoplasma infections (Sharp, 1964). Various *Mycoplasma* species, other than *M. pneumoniae*, have been isolated from the joint fluids and synovial membranes of patients with rheumatoid arthritis, systemic lupus erythematosus, Reiter's syndrome, and occasionally other joint diseases. The significance of these findings, which have recently been reviewed by Marmion (1967), remains a matter of controversy.

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