costeroids are unaffected by high dose dexamethasone and metyrapone.

In our patient, the adrenal function tests were so consistent with pituitary disease that the pulmonary lesion was initially thought to be coincidental. However, the resolution of hypercortisolism after excision of a tumour, known in adults³ to be associated with the ectopic adrenocorticotrophic hormone syndrome, and the finding of adrenocorticotrophic hormone and related peptides in the tumour, confirmed the diagnosis of ectopic adrenocorticotrophic hormone secretion.

Serum adrenocorticotrophic hormone concentrations in pituitary dependent and ectopic adrenocorticotrophic hormone dependent hypercortisolism overlap, and dexamethasone responsive bronchial carcinoids have been reported in adults.² Metyrapone in the dosage used produces a varying degree of block in patients with Cushing's syndrome. The block was incomplete in our patient. The very high values of cortisol derivatives found after the drug was given would usually be explained by the exaggerated pituitary adrenocorticotrophic hormone and cortisol response in patients with pituitary dependent disease resulting from a fall in circulating cortisol values in the first few hours of metyrapone administration.

Bronchial carcinoid tumours are rare in children,⁴ but as they may recur and metastasise a reliable tumour marker would be valuable. Although in this

patient the pattern of adrenocorticotrophic hormone related peptides in plasma did not indicate the source of secretion, recent studies of adrenocorticotrophic hormone and related peptides in plasma and tumour tissue suggest that this may eventually permit more accurate aetiological diagnosis of Cushing's syndrome and act as a tumour marker.⁵

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Arthritis in cystic fibrosis

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SUMMARY We have confirmed previous observations of a transient, non-disabling recurrent arthritis in patients with cystic fibrosis. This arthritis differs from classic rheumatoid arthritis, is frequently associated with skin arthritis lesions, and its occurrence is unrelated to the severity of lung disease.

The association of a transient arthritis with cystic fibrosis was first reported by Newman and Ansell in 1979.¹ We describe the clinical course and laboratory findings in 8 cystic fibrosis patients with acute arthritis not associated with pulmonary osteoarthropathy.

Patients

The group comprised 6 girls and two boys aged 3 to 29 years (mean 13.5 years). The diagnosis of cystic fibrosis had been made on the basis of clinical and radiological findings, and raised sweat electrolyte measurements. At the onset of joint disease, pulmonary disease was mild in five patients, moderate in two, and advanced in one. Six patients were taking pancreatic enzyme preparations; five had *Pseudomonas aeruginosa* in their sputum cultures; and 6 were taking oral antibiotics continuously, two on a sporadic basis. Clubbing of varying severity was present in all patients, however, none had long bone pain or radiological evidence of periosteal elevation.

None had pancreatitis, and only one had liver disease, manifested by hepatomegaly and abnormal liver function.

Results

Clinical and laboratory characteristics are summarised in the Table. Clinical manifestations consisted of recurrent episodes of joint swelling, pain, tenderness, and limitation of movement. Each episode lasted from 5 to 7 days and no patient had developed permanent joint deformities after 1 to 6 years of follow up. Arthritis was monoarticular in three patients and pauciarticular or polyarticular in five. The most commonly affected joints, in decreasing order of frequency, were the knees, ankles, wrists, proximal interphalangeal joints of the hands, shoulders, elbows, and hips. Seven patients had multiple (over three) episodes each year, usually occurring at three to 6 week intervals, and one had a single episode. Morning stiffness was reported by four patients. Arthritic exacerbations did not coincide with deterioration of pulmonary status and improved quickly with aspirin or other non-steroidal, anti-inflammatory drugs.

Skin lesions were seen in four girls. One had painful erythematous nodules over the anterior tibial area at the onset of arthritis. A biopsy showed vasculitis. Two other patients had purpura of the legs; recurrent, generalised erythematous, maculopapular rashes were also observed in one girl. There was no clear temporal relation between the onset of arthritis and that of rashes in these latter three patients.

Laboratory findings

Joint effusions and soft tissue swelling were evident on three of 8 radiographs. Synovial fluid for examination could not be obtained. The highest erythrocyte sedimentation rate detected was 30 mm in the first hour. Rheumatoid factor (by latex agglutination) at a titre higher than 1:20 was found in only one patient (case 8); a gradual rise in titres accompanied progressive lung involvement and reached a maximum of 1:2560. None of the patients had antinuclear antibodies (by immunofluorescence with Hep 2 cells); three of four tested had circulating immune complexes (by Cl_q binding fluid phase radio immunoassay), but their serum complement values (C_3 , C_4 , and total haemolytic complement) were normal. HLA typing (A and B phenotypes) in five patients did not identify a common haplotype.

In the 6 patients in whom they were measured, IgA and IgM concentrations were normal; IgG values were slightly raised in two patients as were IgE values in one (Table). Serum uric acid and amylase concentrations were normal in all patients and antistreptolysin O titres were negative.

Discussion

Rheumatoid factor-positive arthritis in cystic fibrosis and bronchiectasis of other aetiologies was first reported by Mathieu *et al.*² Sagransky *et al.*³ recently described one young woman with cystic fibrosis and classic, seropositive rheumatoid arthritis who required gold treatment. The patients described here, as well as those in Newman and Ansell's paper¹

Table Clinical and laboratory characteristics of 8 cystic fibrosis patients with arthritis

Case No	Sex	Age at onset of arthritis (years)	Lung involvement	Arthritis	Skin rash	Immunoglobulin values*	Cl_q binding (%)
1	F	11	Mild	Polyarticular (knees/wrists/proximal interphalangeal)	Maculopapular generalised	Normal	18.8
2	F	8½	Moderate	Monoarticular (hip)	None	Normal	20.4
3	F	6	Mild	Monoarticular (ankle)	Purpura	ND	ND
4	M	28	Mild	Polyarticular (knees/elbows/shoulders)	None	ND	ND
5	F	11	Mild	Pauciarticular (wrists/ankles)	Nodules (vasculitis)	Normal	ND
6	F	3½†	Moderate	Monoarticular (knee)	None	IgE, 64 IU	Normal
7	M	11	Mild	Polyarticular (knee/wrists/shoulders/ankles)	None	IgG 2200 mg/dl	ND
8	F	23‡	Advanced	Pauciarticular (knees)	Purpura and maculopapular generalised	IgG, 2500 mg/dl	24

*Normal range for age: IgG, 600–1800 mg/dl; IgE, up to 23 IU; Cl_q binding %, up to 13%.

†Died aged 4½ years.

‡Died aged 24 years.

ND=not done.

presented with seronegative joint disease. Rheumatoid factor was present in only one of our patients whose titres increased as her lung disease worsened, suggesting antigenic stimulation secondary to chronic pulmonary infection.

We did not detect a temporal or cause/effect relation between antibiotics and the onset of arthritis. At least two children who were not taking any antibiotics developed arthritis, the rest did so while taking oral tetracyclines, chloramphenicol or cephalixin, but none while receiving penicillins.

This clinical picture is reminiscent of the arthritis-dermatitis syndrome associated with jejuno-ileal bypass.⁴ This entity is characterised by polyarthritis, cutaneous vasculitis, and evidence of increased antigenic stimulation believed to originate in the blind bowel loop. The actual pathogenesis of this arthritis, however, has not yet been established. Similar lesions may be associated with pancreatitis,⁵ which our patients did not have.

Erythematous and purpuric rashes as well as erythema nodosum may be associated with arthritis in patients with cystic fibrosis.^{1,6} Hypergamma-globulinaemia and high serum complement have also been reported in association with these cutaneous lesions in cystic fibrosis^{6,7} and were seen in some of our patients as well. Whether these and other phenomena such as the presence of circulating immune complexes play a direct role in the pathogenesis of joint and skin lesions in cystic

fibrosis, or whether their association with these disorders is simply fortuitous, is currently a matter for speculation.

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