Sarcoidosis

D. GERAINT JAMES
M.A., M.D., F.R.C.P.

Royal Northern Hospital, London N7

Descriptive definition

Sarcoidosis is one member of a large family of granulomatous disorders in which the common denominator is the histology of epithelioid cell granulomas. Like many other members of this loose-knit family, its aetiology is unknown.

It is a multisystem disorder which most commonly affects young adults, presenting with intrathoracic, skin and eye lesions. The diagnosis is most secure when clinico-radiographic findings are supported by histological evidence of widespread non-caseating epithelioid cell granulomas in more than one system. A positive Kveim-Siltzbach skin test and raised serum angiotensin-converting enzyme (SACE) levels both reflect activity of the disease. There is evidence of depression of delayed type hypersensitivity with impairment of thymus-mediated T cells in the peripheral blood but with evidence of increased numbers and activity of T helper cells in lungs, bronchoalveolar fluid and at other sites of activity away from the blood. There is simultaneous evidence of lympho-proliferation with overactivity of B cells, raised serum immunoglobulin levels, elevated lambda and kappa light chains, increased antiviral antibody titres and autoantibodies. Other common features are circulating immune complexes; and also hypercalciuria with or without hypercalcaemia.

The course and prognosis correlate with the mode of onset; an acute onset with erythema nodosum heralds a self-limiting course and spontaneous resolution, while an insidious onset may be followed by relentless progressive fibrosis (Table 1). Corticosteroids relieve symptoms, suppress inflammation and granuloma formation, suppress the Kveim-Siltzbach skin test and normalize raised SACE levels, thereby suggesting a direct action on the epithelioid granuloma.

Pathogenesis

The sarcoid granuloma is a battleground between the presumed antigen and the cellular and humoral defences of the body. Macrophages are stimulated by

the antigenic attack and eventually coalesce into giant cells and epithelioid cell granulomas. T helper cells are mobilized to this point of activity and cooperate with macrophages leading to B cell overactivity. The T cells provide various lymphokines and the B cells produce immunoglobulins and various antibodies. The enzymes secreted by the granuloma include angiotensin-converting enzyme, lysozyme, glucuronidase, and elastase. With ageing, the granulomas are infiltrated by fibroblasts and early fibrosis is recognized by increasing deposition of intracellular reticulin, which is gradually replaced by collagen, and this in turn is transformed into structureless eosinophilic hyaline material.

The activated macrophage within various sarcoid granulomas is now being finger-printed by a combination of immunofluorescent and histochemical techniques and by monoclonal antibodies directed against antigen-presenting macrophage subsets. This dynamic approach should lead towards a better understanding of the basic molecular biology and also some way towards the aetiology of sarcoidosis.

There are also certain background factors which contribute to granuloma formation in sarcoidosis. They include ethnic group; hormones; HLA types B8:A1, CW7, DR3; the interplay of OKT4:T8; and circulating immune complexes.

Epidemiology

Sarcoidosis has a worldwide distribution, but is more frequently recognized in sophisticated communities. Whenever tuberculosis or leprosy is rampant, sarcoidosis is in eclipse, but as they are brought under control so will sarcoidosis become more evident. It has a similar prevalence in the Western world and in Eastern Europe.

Sarcoidosis is 10 times more frequent in the American black than in the white population. It is a very common disorder in the black population of the Caribbean particularly when they migrate to London (from the British West Indies) or to Paris (from

TABLE 1. Features differentiating acute from chronic sarcoidosis

Sarcoidosis	Acute (transient)	Chronic (persistent)
Age (years)	<30	>40
Onset	Abrupt	Insidious
Chest X-ray	Bilateral hilar lymphadenopathy	Pulmonary infiltration/fibrosis
Eyes	Acute iritis, conjunctivitis, conjunctival nodules	Keratoconjunctivitis, chronic uveitis, glaucoma, cataract
Skin	Erythema nodosum, vesicles maculopapular rash	Lupus pernio, plaques, scars, keloids
Parotitis		
Lymphadenopathy	Usually transient	Rarely permanent
Splenomegaly		
Bell's palsy		
Bone cysts		
Histology	No Epithelioid and giant cells	Yes Hyaline fibrosis Interstitial pneumonitis
Acid phosphatase	Increased	Normal
Leucine aminopeptidase	Increased	Normal
Calcium metabolism	Hypercalcaemia, hypercalciuria	Nephrocalcinosis
Urinary hydroxyproline	Increased	Normal
Kveim-Siltzbach test	Positive	May be negative
Tuberculin test	Negative	±
K and NK cell	High	Unchanged
Gallium-67 uptake	High	Low
Macrophages in alveoli	High	Low
Angiotensin-converting enzyme	High	May be raised
Serum lysozyme	Increased	May be increased
Crystal's alveolitis	High intensity	Low intensity
Protein L1	Increased	Normal
Beta ₂ microglobulin	High	May be raised
Circulating immune process	++	±
T Helper: Suppressor ratio in:		
Lungs	10:5:1	1:4:1
Blood	0:8:1	1:0:1
Ia + T cells	Increased	Normal
Radioactive imipramine or propranolol reveal lung cell mass	Increased	Normal
Free light chains of immunoglobulins	Normal	Elevated
Lactoferrin	Increased	Normal
Serum collagenase	Elevated	Normal
Spontaneous remission	Frequent	Rare
Steroid therapy	Abortive effect	Symptomatic relief
Alternative drugs	Oxyphenbutazone	Chloroquine: Potaba methotrexate
Recurrence after steroid therapy	Rare	Frequent
Prognosis	Good	Poor

Martinique). Likewise it is common in Puerto Ricans living in New York. Is this due to genetic predisposition or environmental factors confronting susceptible individuals migrating from a rural to an urban community? Is the breeding ground for sarcoidosis in his native environment or in the sophisticated new world in which he adapts himself? It may be a bit of both worlds.

It is also becoming more evident in the black populations of Africa. It is likely that it will become

in the next 30 years a common disorder of the African either at home or particularly when he lives abroad.

Sarcoidosis is also frequently seen in the white population of Scandinavia, Ireland and throughout Europe. It is well-recognized in Japan because they have a special Commission on the look-out for it. It is extremely rare in the rest of Asia possibly because it is obscured by the presence of considerable tuberculosis.

TABLE 2. Features of sarcoidosis in the Royal Northern Hospital series compared with a worldwide survey

Sarcoidosis	Royal Northern Hospital		Worldwide	
	Number	(%)	Number	(%)
Total	818	100	3676	100
Female	500	61	2082	57
Presentation under 40 years	604	74	2504	68
Caucasian	728	89	—	—
West Indian	81	10	—	—
Intrathoracic	700	88	3224	87
Ocular	224	27	—	—
Erythema nodosum	251	34	640	17
Lupus pernio	35	4	—	—
Other skin lesions	113	14	324	9
Ocular lesions	224	27	539	15
Parotid enlargement	52	6	160	4
Nervous system	77	9	134	4
Bone	31	3	109	3
Lymph nodes and spleen	326	39	1031	28
Lymphadenopathy	225	27	—	—
Splenomegaly	101	12	—	—
Hepatomegaly	82	10	—	—
Heart	27	3	—	—
Lacrimal gland	22	3	—	—
Kidney	10	1	—	—
Upper respiratory tract	53	6	—	—
Systemic corticosteroid therapy	344	42	1738	47
Mortality due to				
sarcoidosis	25	3	84	2.2
other causes	23	3	54	1.4
Skin tests				
positive Kveim-Siltzbach	550/657	84	1714/2189	78
negative tuberculin test	488/702	70	2093/3268	64
Hyperglobulinaemia	161/526	31	808/1832	44
Hypercalcaemia	99/547	18	200/1760	11

Material

We have analyzed a series of 818 patients with clinical and histological evidence of sarcoidosis attending the Royal Northern Hospital, London. Five hundred (61%) were female, nine-tenths were Caucasian and one-tenth from the Caribbean. Seven hundred (88%) had radiographic evidence of intrathoracic sarcoidosis. Since sarcoidosis is a multisystem disorder, it was also evident in other systems, notably the skin (overall in 50% of the series), eyes (27%), reticulo-endothelial system (39%) and upper respiratory tract (6%).

We have compared this series followed in one London hospital with sarcoidosis seen in various centres throughout the world (Table 2).

Intrathoracic stages

It is customary to stage intrathoracic sarcoidosis according to the chest X-ray appearance on first presentation:

Stage 0—Normal.

Stage 1—Hilar lymphadenopathy.

Stage 2—Hilar lymphadenopathy and pulmonary infiltration.

Stage 3—Pulmonary infiltration without hilar adenopathy.

This is a crude classification with much overlapping. Lung biopsy may unexpectedly reveal sarcoid granulomas in Stages 0 and 1. Stage 3 may be an indivisible radiological mixture of irreversible fibrosis and reversible granulomas. But, allowing for many shortcomings, this staging is simple and, most important, it is recognized and understood throughout the world. Some centres make refinements, such as adding Stage 4; this suggests an even more advanced stage than 3, with more irreversible fibrosis and perhaps evidence of complicating cor pulmonale.

We have compared the chest X-ray changes on presentation and their fate in a homogeneous Royal Northern Hospital series with that observed in a heterogeneous worldwide survey (Table 3). The outcome in relation to steroid therapy has also been analyzed (Table 4).

TABLE 3. Chest X-ray appearances in the Royal Northern Hospital series compared with those in a worldwide survey

Stage†	Royal Northern Hospital series				Worldwide survey			
	Presentation		Resolution		Presentation		Resolution	
	Number	(%)	Number	(%)	Number	(%)	Number	(%)
0	118	14	—	—	277	8	—	—
1	458	65	268	59	1865	51	1217	65
2	150	22	59	39	1066	29	490	46
3	92	13	35	38	446	12	90	20
Total	818	100	362	52	3654	100	1797	49

†See text.

TABLE 4. Influence of steroid therapy on each stage of intrathoracic involvement in 362 patients achieving chest X-ray resolution

Stage†	Total number with chest X-ray changes	Without steroids		With steroids	
		Number	(%)	Number	(%)
1	458	175	65	93	35
2	150	31	53	28	47
3	92	25	71	10	29
Total	700	231	63	131	37

†See text.

Stage 1

Hilar adenopathy was bilateral in all but 20 patients, who presented with unilateral hilar adenopathy. There was eventual resolution in 268 of 458 (59%) patients (Table 3) but there were various courses before this was achieved. This resolution occurred directly in 210, but with infiltration in 92 instances. Steroid therapy did not seem to influence resolution for it was given to two-thirds of those who failed to resolve and only to one-third of those who did not attain chest X-ray resolution (Table 4). The chances of achieving a clear chest X-ray sooner or later is similar in London to that of other world centres.

Stage 2

One-hundred and fifty patients presented at this later stage and only 59 (39%) achieved a clear chest radiograph eventually. Once again steroid therapy did not seem to improve the incidence of resolution for it was used with equal frequency in those who did and did not achieve resolution (Table 4). Here again the incidence of resolution is similar to that in the worldwide survey.

Stage 3

This is a late stage of presentation and it spells

chronicity and pulmonary fibrosis, for resolution only occurred in 38%. Steroid therapy seemed to be singularly ineffective (Table 4).

Influence of steroid therapy on chest X-ray resolution

Oral steroids were given to 208 (45%) patients with Stage 1 involvement, 82 (55%) with Stage 2 changes and to 56 (61%) with Stage 3 disease. Of the 700 patients with a chest X-ray abnormality, complete radiological resolution was eventually achieved in 362 (52%) (Table 3); one-third achieved radiological resolution with and two-thirds without steroids (Table 4). Although there was no evidence that steroid therapy influenced the resolution of chest X-ray changes in pulmonary sarcoidosis, it is possible that without this therapy the number of patients with chronic persistent disease and its attendant morbidity might have been greater. Moreover, steroid therapy certainly provided symptomatic relief from disabling breathlessness, and overcame many manifestations of extrathoracic sarcoidosis.

Sarcoidosis of the upper respiratory tract (SURT)

It would seem natural to include sarcoidosis of the upper respiratory tract (SURT) in a discussion of respiratory tract sarcoidosis. In fact, sarcoidosis of the upper and lower respiratory tracts are strange bedfellows and bear little relationship to each other. SURT was noted in 53 of 818 (6%) patients in this series (Table 5). Women were affected twice as often as men; and 10 (19%) were from the West Indies. SURT is frequently associated with lupus pernio and other skin lesions, bone cysts, parotid gland enlargement and with chronic fibrotic pulmonary sarcoidosis. Sarcoid granulomas are found in the nasal mucosa, larynx and pharynx, and in nasal bone. There may be septal perforation because of submucosal resection to alleviate nasal obstruction.

There is a close association between nasal mucosal sarcoidosis and lupus pernio. It is tempting to postulate spread of the granulomatous process from

TABLE 5. A comparison of sarcoidosis of the upper respiratory tract (SURT) with sarcoidosis overall

Feature	Sarcoidosis overall		SURT	
	Number	(%)	Number	(%)
Total	818	100	53	100
Female	500	61	35	66
Presentation under 40 years	604	74	37	70
Caucasian	728	89	41	78
West Indian	81	10	10	19
Intrathoracic	700	88	48	90
Ocular	224	27	16	30
Erythema nodosum	251	31	13	25
Lupus pernio	35	4	15	30
Other skin lesions	117	14	21	40
Bone	31	3	7	11
Lymphadenopathy	225	27	8	15
Splenomegaly	101	12	4	7
Nervous system	77	9	3	6
Parotid	52	6	10	18
Lacrimal gland	22	3	2	4
Upper respiratory tract	53	6	53	100
Systemic corticosteroid therapy	344	42	40	75
Mortality due to:				
sarcoidosis	25	3	3	6
other causes	23	3	1	2

an initial focus in the nasal mucosa, through nasal bone, and then on to the overlying skin (We have noted a similar association between bone cysts and adjacent soft tissues in the hands and feet). Septal perforation may accelerate the development of lupus pernio of the overlying skin of the nose. In seven of these patients, lateral radiographs of the nasal bones showed abnormalities. The normal lateral film of the nasal bone represents the superimposed shadows of both alae. The bone texture is compact, the margins well-defined and there are linear translucencies due to suture lines. Sarcoid lesions appear as scattered punctate areas of porosis or frank destruction, later followed by a wide-meshed trabecular pattern. The suture lines may disappear. No periosteal reaction is evident.

Differential diagnosis

There are numerous conditions which mimic pulmonary sarcoidosis so it is essential to obtain histological confirmation of the diagnosis.

This is most easily obtained by fiberoptic bronchoscopy; flexible forceps biopsy is commendable for it yields both bronchial and lung tissue. A wide variety of techniques is available to suit the interests of all disciplines. They include biopsy of skin, lymph node, liver, muscle, minor salivary glands, conjunctiva, nasal mucosa, spleen, heart and by peritoneoscopy. The Kveim-Siltzbach skin test is yet another

alternative which is helpful because it is a measure of activity of sarcoidosis.

Ocular involvement

Slit-lamp examination of the eyes should be routine. Lesions include acute and chronic iridocyclitis, choroidoretinitis, papilloedema, kerato-conjunctivitis, conjunctival follicles and the late complications of cataract and secondary glaucoma. Ocular involvement is one manifestation of a multisystem disorder in which there are many clinical associations often interwoven into well-defined patterns of disease. Acute iritis, erythema nodosum and hilar adenopathy have a benign self-limiting course and a satisfactory outcome. Lupus pernio is associated with chronic uveitis, pulmonary fibrosis and bone cysts; the course is persistent and troublesome. Keratoconjunctivitis sicca, with or without parotid and lacrimal gland enlargement mimics Sjogren's syndrome. Parotid gland enlargement, anterior uveitis and facial palsy constitute Heerfordt's syndrome.

Neurosarcoidosis

This occurs in about 4-7% of patients with sarcoidosis. Facial palsy is the most frequent presentation either alone or with other cranial nerve palsies or with papilloedema. Other features include peripheral neuropathy, myopathy, meningitis, space-occupying brain lesions, epilepsy, cerebellar ataxia, hypopituitarism and diabetes insipidus. Neurosarcoidosis

has a mortality of 10%, which is twice the overall mortality of sarcoidosis. The response to corticosteroids is more likely to occur in younger patients with an explosive onset of meningitis with erythema nodosum than in those with a space-occupying intracranial mass, chronic skin lesions, chronic uveitis or pulmonary fibrosis.

Skin lesions

Erythema nodosum. This is associated with bilateral hilar lymphadenopathy, polyarthralgia, and occasionally acute iritis. It predominates in women of the child-bearing years and is often associated with pregnancy or lactation, suggesting a hormonal factor in its genesis. Transient circulating immune complexes may be detectable in this phase of sarcoidosis.

Lupus pernio. This is a chronic persistent violaceous lesion with a predilection for nose, cheeks and ears. It reflects chronic fibrotic sarcoidosis. It develops insidiously and progresses indolently over the years.

Other skin lesions. These include persistent plaques, maculopapular eruptions, scars and keloids. These keloids may be found at the sites of surgery, earpiercing, tattooing, repeated venesection in the antecubital fossa or even where tuberculin and other skin tests have been performed.

The heart

Myocardial sarcoidosis is difficult to recognise clinically. It should be considered if a patient with florid multisystem sarcoidosis develops bundle branch block, arrhythmias, congestive cardiac failure, pericarditis or clinical evidence of cardiomyopathy. Sudden death without previous evidence of a heart lesion may occur, particularly in patients over 40 years of age. Macroscopic changes are most evident in the posterior part of the ventricular septum. Microscopy discloses granulomas or fibrous tissue or an admixture.

Lymphoreticular

The lymph nodes and spleen were enlarged in 39% of the London series and in 28% worldwide.

Hepatomegaly was noted in 82 (10%) and hepatosplenomegaly in 43 (5%).

Locomotor

Bone sarcoidosis. A hallmark of chronic fibrotic sarcoidosis, was noted in 31 (4%) patients in the London series and in 109 (3%) worldwide. It is most frequent in hands and feet but rarely it involves temporal or frontal bone, the hard palate and nasal cartilage. It is associated with soft tissue swelling, joint stiffness and pain. There is no correlation

between bone involvement and abnormal calcium metabolism. There are three radiological types of bone lesions:

Permeative. There is progressive cortical 'tunnelling' with remodelling of trabecular and cortical architecture.

Lytic. These punched-out cysts are associated with pressure narrowing of the shaft, pathological fractures and residual cavities.

Destructive. Rapid destructive change may cause secondary joint surface involvement and this may be followed by a periosteal reaction.

Muscle disease. This runs an independent course from bone disease but may be just as troublesome. It comprises acute polymyositis, chronic myopathy, muscle nodules, contractures and atrophy.

Biochemistry

We have done numerous biochemical investigations in our series (Table 6). The serum globulin levels are abnormal in about one-third because of overactive B cells. The serum alkaline phosphatase level is elevated in one-quarter of patients; this is due to space-occupying hepatic granulomas rather than due to bone cysts. Hypercalcaemia is a feature in one-fifth of patients, and transient hypercalciuria is even more frequent. Elevated serum uric acid levels reflect renal involvement at a stage of late chronic fibrotic sarcoidosis.

TABLE 6. Blood biochemical abnormalities in a series of 818 patients with sarcoidosis

	Number tested	Number abnormal (%)*
Albumin	526	82(16)
Globulin	526	161(31)
Calcium	547	99(18)
Phosphate	343	47(13)
Alkaline phosphatase	252	58(23)
Urea	213	42(20)
Uric acid (urate)	50	9(18)
Bilirubin	164	12(7)

*Outside the normal range of values in our laboratory

Criteria of activity

During the previous hundred years very few markers of activity of sarcoidosis have been recognized. During the last 10 years we have been inundated with too many, so it is becoming increasingly difficult to choose the most helpful. We have grouped them into the following categories (Table 7):

- Clinical features which indicate activity and also bedside techniques which proclaim activity.
- Biochemical.
- Immunological.

In clinical practice, we would prefer to choose a

TABLE 7. Markers of activity of sarcoidosis

Clinical	Biochemical	Immunological	Other findings
Erythema nodosum	Hypercalcaemia	B2 microglobulins	Changing chest X-ray
Uveitis	Hypercalciuria	TM helper cells in BAL	Transfer factor
Maculopapular rash	SACE	Increased OKT4:OKT8 ratio (in BAL)	Exercise KCO
Dactylitis	SACE		Fluorescein angiography
Polyarthralgia	serum lysozyme	Decreased OKT4:OKT8 ratio (in blood)	Tuberculin skin test
Myopathy	serum collagenase	Kappa and lamda light chains (by radio-immunoassay)	Kveim-Siltzbach skin test
Neuropathy	Urinary hydroxyproline		Biopsies
Granulomatous scars	Glucuronidase	Circulating immune complexes	Radioactive gallium scan
Splenomegaly			Thallium-201 myocardial scan
Lymphadenopathy			24-hr ECG tape
Salivary and lacrimal gland enlargement			Bronchoalveolar lavage
Cardiac arrhythmia			

measure which is specific and reliable, reproducible around the world, preferably cheap, and sufficiently easy to permit serial measurements to monitor progress. Each of the methods to be discussed has some defect which prevents it from being the perfect bedside tool.

Serum angiotensin-converting enzyme (SACE)

SACE is elevated in about 60% of patients with active sarcoidosis but it is also associated with a false-positive rate of about 10%; thus it is not a good diagnostic test. Its true value is to monitor progress of known sarcoidosis. In this respect it is a more sensitive index of activity of epithelioid cell granulomas than the chest radiograph. Its introduction should halve the number of chest radiographs done, particularly since many are unnecessary. It is an invaluable monitor in pregnancy.

The Japanese have just introduced a do-it-yourself bedside kit which should be as helpful as bedside blood glucose sticks for diabetes mellitus.

Radioactive gallium-scanning

The activated macrophages in granulomas avidly accumulate gallium and delineate the extent of granulomatous involvement in lungs and hilar lymph nodes. It is taken up by liver, spleen and bone in the normal person, so it is not helpful in detecting granulomas in the abdominal viscera or in the central nervous system. Lung uptake is crudely measured by comparison with the density of liver uptake. Radioactive gallium is also taken up by protein of inflammatory exudates so it is not specific for sarcoidosis. Positive scans are found in asbestosis, silicosis, fibrosing alveolitis, cancer, bleomycin lung and in lymphomas. Its value, like SACE, is as a

monitor of progress. Its other defect is its cost, which would be prohibitive in many centres.

Bronchoalveolar lavage (BAL)

Bronchopulmonary lavage with about 100–300 ml of fluid provides specimens which can be measured for alveolar macrophages, lymphocytes, T and B cells, angiotensin-converting enzyme, lysozyme, protein complement and immunoglobulins. The more active the pulmonary disorder, the richer the yield and the more interesting the differential diagnosis. Findings differ in various interstitial lung disorders.

Lung function tests

Sarcoidosis is a restrictive lung disease with abnormal gas exchange; its pathophysiology is similar to that of other interstitial lung diseases, with decreased lung compliance, decreased lung volumes and capacities as the main features. There is diminished carbon monoxide diffusing capacity and increased alveolar-arterial oxygen gradient. The latter may cause hypoxaemia at rest and this worsens with exercise. These tests are helpful in defining the functional impairment and in monitoring progress. However, quite often they do not correlate with the symptoms or signs, with the stage of chest X-ray abnormality, or with the immunological upset.

Aetiology

The cause remains unknown despite an extensive search to uncover an infective agent, an immunological upset, an allergic mechanism, or a specific diathesis.

Is it an infection?

It was traditional to regard it as an odd form of tuberculosis and the two diseases have certainly been confused with each other throughout this century but there are crucial differences. Attempts have been made to detect granulomagenic components of various mycobacteria in sarcoid tissue. The presence of mycolic acid esters aroused interest but they are also found in normal tissue. Muramyl dipeptide and bacterial lipopolysaccharides are granulomagenic at injection sites but they do not produce multisystem granulomas.

Many claims have been made for infection due to fungi, viruses and bacteria but their occasional presence seems coincidental rather than causal.

Is it an immunological aberration?

Sarcoidosis is a lymphoproliferative disorder with evidence of depression of delayed-type hypersensitivity, imbalance of OKT4:T8 subsets, hyper-reactive B cells and frequent circulating immune complexes. Could this be a background factor providing an infective agent or other antigenic insult with a salubrious soil?

Is it due to hypersensitivity?

Claims have been made for such diverse regional contributory factors as pine pollen, peanut dust, clay-eating and chewing pine pitch. Beryllium and zirconium are known to produce sarcoid granulomas in sensitized individuals.

Is there a predisposition?

Hormonal factors play some part for erythema nodosum due to sarcoidosis commonly occurs in women of the child-bearing years of life, during early pregnancy, and also in women taking the oral contraceptive pill.

Sarcoid arthritis and erythema nodosum are most likely to occur in women who are HLA-B8, A1, CW7, DR3. This predisposition is associated with a

short course and good prognosis, whereas HLA-B13 is more likely to be associated with chronicity of the disease.

Treatment*Steroids*

Corticosteroid therapy constitutes a mainstay of treatment around the world. It is particularly indicated for ocular involvement; an abnormal chest radiograph associated with a significant elevation of SACE, a positive gallium scan, or abnormal bronchoalveolar fluid; troublesome breathlessness; persistent hypercalciuria; disfiguring skin lesions; or involvement of myocardium, nervous system or lacrimal and salivary glands. It may be needed on a long-term basis for troublesome involvement of the upper respiratory tract or pain, swelling and deformity associated with bone cysts.

Alternative regimens

Steroid therapy may be contraindicated or needs reinforcement. Alternative drugs include indomethacin and oxyphenbutazone for acute exudative disease; methotrexate and chloroquine for chronic fibrotic persistent sarcoidosis.

Cyclosporin A is a fungal metabolite with interesting immunosuppressant properties. It acts selectively on T helper cells interfering with leukotriene production and thereby preventing organ rejection. It exerts profound effects on experimental epithelioid cell granulomas produced in rats by injections of various mycobacteria and then given oral cyclosporin in a dose of 20 mg/kg. It prevents the formation of epithelioid cell granulomas or the development of caseous necrosis. Its value in the human disease has not yet been assessed.

Further reading

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