

Sarcoidosis: A Mysterious Disease

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ABSTRACT

Ever since the description of sarcoidosis in 1877 by Jonathan Hutchinson and Caesar Boeck in 1899, sarcoidosis has fascinated the medical fraternity with its unique manifestations. Sarcoidosis is an inflammation, which produces small lumps of cells in different organs of the human body. It generally begins in the form of lymph nodes either in the chest cavity or the lungs and often affects skin, eyes, liver and rarely the kidneys, breast, thyroid gland. In India, sarcoidosis is often mistaken for tuberculosis. However, this disease has marked its beginning in our country. Sarcoidosis is not cancer and not even a contagious disease. More than half the patients experience weight loss, fatigue, night sweats, fever, anorexia or just an overall feeling of ill health in addition to pulmonary and extra pulmonary symptoms. Due to high incidence of tuberculosis in India and similarity of sarcoidosis with pulmonary tuberculosis, there is often diagnostic dilemma. Sarcoidosis is diagnosed by chest X-ray, pulmonary function test, blood test, ACE test, biopsy, gallium scanning and bronchoalveolar lavage. Corticosteroids mainly prednisone is the drug of choice for inflammation and granuloma formation. The present review article covers the symptoms, pathological features, diagnostic tests, pharmacotherapy and measures to prevent sarcoidosis.

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Background:

Originally Sarcoidosis was called Hutchinson's disease or Boeck's disease, as it was first identified in 1899 by two dermatologists, Dr. Jonathan Hutchinson in England and Dr. Caesar Boeck in Norway working independently. Sarcoidosis is a granulomatous disease of unknown etiology, which primarily affects the lungs and lymphatic systems of the body and is characterized by the formation of noncaseating small inflammatory nodules (lumps), called as granulomas. The word "non-caseating" means that the granuloma remain healthy, even while they are creating the inflammatory biochemicals (Cytokines) that are designed to help our immune systems and kill 'invading', 'foreign', organisms (viruses, bacteria and fungi). The term Sarcoidosis came from Greek word 'sark' and 'oid' meaning flesh like. The term describes the skin eruptions that are frequently caused by the illness. Sarcoidosis often affects other parts of the body, such as the eyes, skin and liver. It also includes spleen, heart, brain, nerves, salivary glands, tear glands, joints or bones which are less frequently affected. Kidneys, breast, thyroid gland or reproductive organs

may be affected but in rare cases. It generally involves two phases, active and non-active.

Active phase:

In this phase there is development of growth of granulomas due to still on-going T-cell and macrophage inflammation. Classical symptoms of Sarcoidosis may develop in this phase. There may be chances for scar tissue (fibrosis) to form granuloma.

Non-active phase:

This phase is characterized by decreases in inflammation and either stabilization or reduction in size of granulomas, which shows that the disease has come to rest and will probably not progress any further.

Hutchinson, who was an English physician, described a patient, whose hands and feet had multiple, raised, purplish cutaneous patches, which had developed over 2 years. Later Caesar Boeck, described a case of cutaneous lesions resembling Hutchinson's report, and he termed it "multiple benign sarkoid of the skin". Epithelioid cells and giant cells were noted on histologic examination. He used the term *sarkoid* (sarcoid → Sarcoidosis)

Key words :

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because he felt that the lesions resembled sarcoma, but were benign. The term *Sarcoidosis* stemmed from this report, however, it is now well established that sarcoidosis is not cancer but usually a self limiting disease, which subsides in 2-3 years.

Prevalence:

It is a common chronic illness that appears all over the world. Previously Sarcoidosis was considered a rare disease. Indeed, it is the most common of the scarring lung disorders and occurs often enough in the United States for Congress to have declared a national Sarcoidosis Awareness Day in 1990. Sarcoidosis occurs throughout the world in all races and in both the sexes with an average incidence of 16/100,000 in men and 19/100,000 in women (Hillerdal *et al.*, 1984). Anyone can get Sarcoidosis. Nevertheless, the risk is greater, if you are a young black adult, especially a black woman, or of Scandinavian, German, Irish, or Puerto Rican origin between the ages of twenty and forty. Severity of the disease may differ between people of different ethnicity. In the United States, Sarcoidosis is more common in people of African descent than Caucasians, with annual incidence reported as 35.5 and 10.9/100,000, respectively. Sarcoidosis is less commonly reported in South America, Spain, India, Canada, and Philippines. Incidence is highest for individuals younger than 40 years of age and peaks in the age-group from 20 to 29 years. A second peak is observed for women over 50 years. Sarcoidosis rarely develops before the age of 10 years or after the age of 60 years. The disease is most prevalent in Northern European countries, and the highest annual incidence of 60/100,000 is found in Sweden and Iceland. Manifestation appears to be slightly different according to race and sex. Erythema nodosum is far more common in women than in men. Studies have shown that Sarcoidosis is more likely to affect certain organs in specific populations. In Japan, Sarcoidosis of the eye and heart are more common. In Northern Europe, painful skin lumps on the legs happen more often. Sarcoidosis is one of the few pulmonary diseases with a higher prevalence in non smokers.

Causes of sarcoidosis:

Infective agents:

There are many infectious agents like *Propionibacterium acnes*, mycobacteria, viruses etc., which appear to be significantly associated with Sarcoidosis but none of the known associations is specific enough to suggest a direct causative role.

Non-infective agents:

Many non-infective causes of Sarcoidosis have been considered. There is development of granulomas on environmental exposure to beryllium, aluminum, and zirconium, which are similar to that of Sarcoidosis. Beryllium was proposed as a cause of sarcoid first by Gentry and associates in 1955 and by several investigators later. Pine pollen, hair sprays, peanut dust, eating clay, mineral oil, talc powder and the use of phenylbutazone, sulfonamides could also serve as causative agents.

Aberration in the immune system:

Local aberrations in immunological reactivity may initiate this disease. There is over stimulation of CD4+ T cells, which in turn promote the formation of granulomas. The development of a lymphocytic alveolitis is reflected by a lymphocytosis in the lavage. This is the feature, which differentiates Sarcoidosis from other interstitial lung disease, where polymorphonuclear cells predominate. Furthermore, the predominance of mononuclear cells in the interstitial infiltrates of Sarcoidosis is an important clue that immune mechanisms are involved. The most prominent cell types are macrophages and T lymphocytes. It was seen that the proportion of lymphocytes found in Sarcoidosis patients is 15-50% which is higher in comparison to normal volunteers containing 4-10% lymphocytes. The fact that no significant numbers of B lymphocytes appear either in lavage or in the tissues adds further weight to the concept that cell-mediated rather than antibody mediated mechanisms are at play, at least in the lung. Reports of raised circulating antibody levels and immune complexes in patients with Sarcoidosis may thus reflect secondary B cell stimulation, possibly of a polyclonal nature. The raised ratio of CD4+ T cells to CD8+ cells in sarcoid lavage is also seen in other chronic inflammatory disease such as rheumatoid arthritis. Here, the low number of CD8+ cells is taken as indicating dysfunction in immunoregulatory pathways. It is reported now that in the process of inflammation in Sarcoidosis activated pulmonary CD4+ T lymphocytes of the Th-1 type are essential and in granuloma formation production of IFN- α plays a crucial role. Recently it was found that T-effector cells are responsible for the formation of granulomas which are generated due to abnormal function of regulatory T cells (Grunewald and Eklund, 2007). It appears that regulatory T-lymphocytes in the periphery of sarcoid granulomas suppress IL-2 secretion which is hypothesized to cause the state of anergy by preventing antigen-specific memory responses.

Genetic associations:

Investigations of genetic susceptibility yielded many candidate genes but only a few were confirmed by further investigations and no reliable genetic markers are known. Currently most interesting candidate gene is BTNL2; several HLA-DR risk alleles are also investigated. In persistent Sarcoidosis the HLA haplotype HLA-B7-DR15 are either cooperating in disease or another gene between these two loci is associated. In non-persistent disease there is a strong genetic association with HLA DR3-DQ2.

Vitamin D dysregulation:

Dysregulation of vitamin D production was frequently caused in patients suffering from Sarcoidosis with an increase in extrarenal (outside the kidney) production. It is seen that there is an elevation in the level of hormone 1, 25-dihydroxyvitamin D in Sarcoidosis. This occurs due to macrophages specifically, which are present in the granulomas and are responsible for the conversion of vitamin D to its active form.

Thyroid disease:

The association of Sarcoidosis and thyroid disease is significant for male patients but less marked in women. It has been found that women suffering from Sarcoidosis are at a greater risk for hypothyroidism, hyperthyroidism and thyroid autoimmunity and it appears that autoimmunity

is very important in the pathogenesis of thyroid disease in this population.

Hyperprolactinemia:

In Sarcoidosis, there is a frequent increase in prolactin level, that leads to amenorrhea, galactorrhea or nonpuerperal mastitis in women and it was reported in 3–32% cases. Generally elevation in Prolactin levels is associated with disease or may exacerbate symptoms in many autoimmune diseases. Medications causing reduction in prolactin has been proven beneficial in the management of Sarcoidosis.

Clinical features:

Sometimes no symptoms are experienced by people with this condition. It is a systemic disease and can affect any organ. It is discovered accidentally through chest X-ray actually taken for any other reason (Fig. 1).

Other organ involvement :

Other organs involvement in Sarcoidosis has been given in Table 1.

Special situations:**Sarcoidosis and pregnancy:**

Pregnancy usually doesn't affect the course of Sarcoidosis, and person can continue corticosteroid treatment throughout their pregnancy. None of the other

Table 1: Organs involvement in Sarcoidosis

Organ	Patients (%)
Mediastinal lymph nodes	95 to 98
Lungs (unrelenting dry cough, chest pain, fibrosis, progressive dyspnea, airflow limitation, bronchiectasis)	> 90
Liver (mild increase of hepatic enzymes usual, hepatic failure rare, pain in the right upper portion of abdomen underneath right ribs)	50 to 80
Spleen (splenomegaly, usually asymptomatic, reduction in platelet count)	40 to 80
Eyes (uveitis common, may lead to blindness)	20 to 50
Musculoskeletal system (joint pain usual, myopathy and bone cysts rare)	25 to 39
Peripheral lymph nodes (palpable, discrete, mobile, nontender; usually cervical, axillary, epitrochlear and inguinal)	30
Hematologic (anemia, leukopenia)	4 to 40
Skin (nonspecific lesions, erythema nodosum, lupus pernio)	15-25
Nervous system (cranial nerve palsies, space-occupying lesions, peripheral neuropathy, diabetes insipidus with pituitary involvement)	5-10
Heart (conduction abnormalities, infiltrative cardiomyopathy, sudden death) (more frequent in Japanese population, particularly in females > 50 years)	5
Hypercalcemia (may cause nephrocalcinosis, renal stones, and renal failure)	2 to 10
Parotid glands (unilateral or bilateral parotitis)	< 6
Gastrointestinal (usually stomach, also esophagus, appendix, rectum, pancreas)	< 1
Kidneys (interstitial nephritis, nephrocalcinosis)	Rare

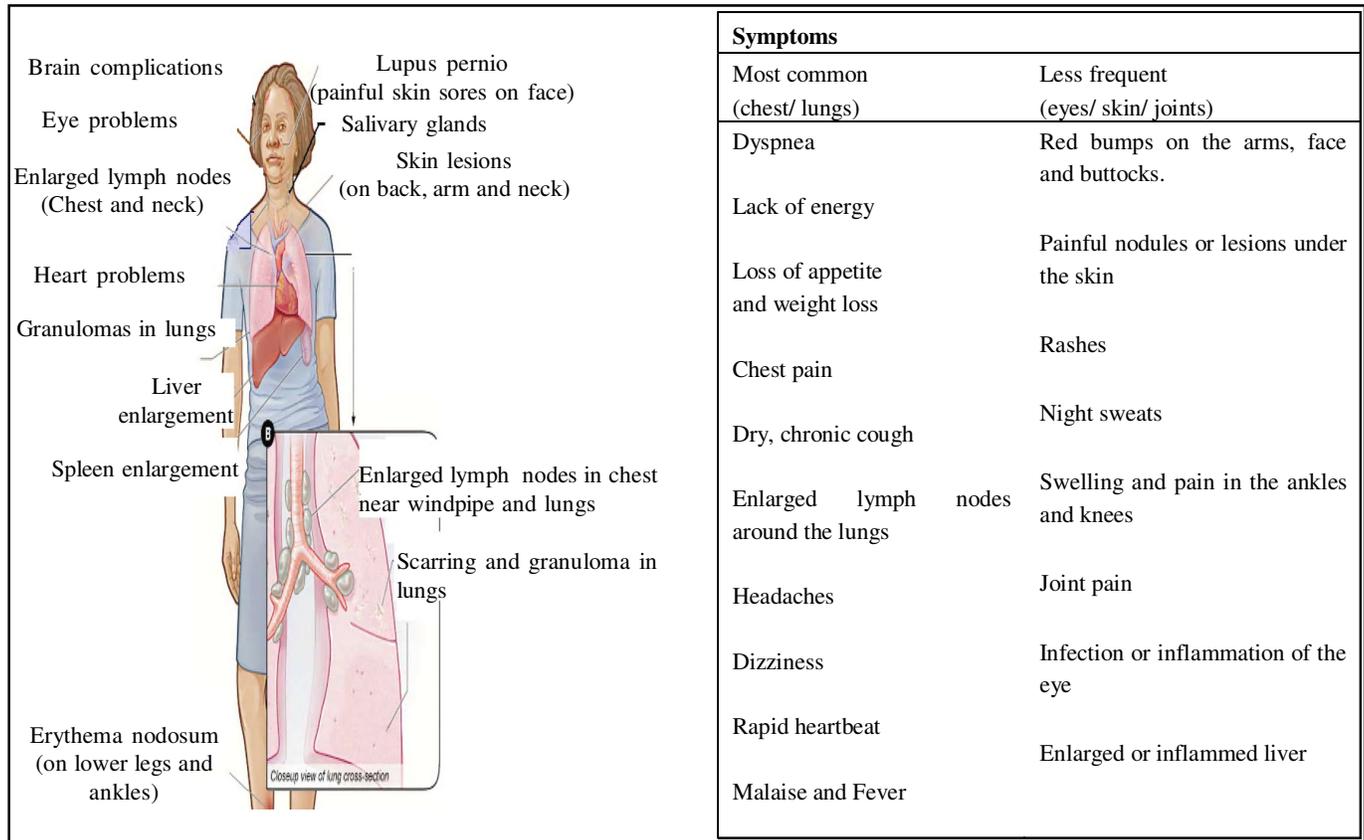


Fig. 1: Signs and symptoms of sarcoidosis education in pregnant study subjects

drugs are recommended for use during pregnancy. Pregnancy should be avoided when treatments other than corticosteroids are necessary because of potential foetal toxicity or teratogenicity. It is also contra-indicated in case of severe visceral involvement, particularly advanced respiratory insufficiency.

Sarcoidosis in children:

Sarcoidosis is rare before the age of 15 and exceptional before age 4. The disease of children resembles that of adults with respect to the distribution of organs involved. In old literature, Sarcoidosis with an onset in children under the age of 4 has been reported to have an original presentation characterized by the combination of polyarthritis, uveitis and skin rash. It is likely that most of reported cases had actually Blau syndrome.

Diagnostic tests:

The preliminary diagnosis of Sarcoidosis is based on the patient's medical history, routine tests, physical examination and a chest X-ray. Precise diagnosis of Sarcoidosis is not easy and often a matter of exclusion. Sarcoidosis is confirmed by eliminating other diseases with

similar features such as Tuberculosis, farmer's lung disease, rheumatoid arthritis, rheumatoid fever, fungal infections, cancer of lymph nodes (lymphoma) and berylliosis. Tuberculosis shows several similar clinical and pathological features resembling Sarcoidosis. Therefore,

Table 2: Recommended tests for evaluation of sarcoidosis

History (occupational and environmental exposure, systems, family background)
Physical examination
Posteroanterior chest radiography
Pulmonary function tests: spirometry and carbon monoxide diffusion capacity
Blood test : white blood cells, red blood cells, platelets; ACE test
Serum chemistry: calcium, liver enzymes, creatinine, blood urea nitrogen
Urine analysis
Routine ophthalmologic examination
Electrocardiography
Tuberculin skin test (Exclusion test)
ANCA test (Anti-Neutrophil Cytoplasmic Antibody test) (Exclusion test)

physicians carry out a tuberculin skin test, which rules out tuberculosis. Patient's medical history gives information about his job profile, family history of Sarcoidosis or if he had a disease resulting from exposure to beryllium metal called as berylliosis. Physical examination includes symptoms like swollen lymph nodes, red bumps on the skin, enlarged liver or spleen, and redness in the eyes. There is no single specific test for diagnosis of Sarcoidosis, therefore, a battery of tests as described below need to be performed (Table 2).

Pulmonary manifestations:

Chest X-ray:

It gives a picture of lungs, heart as well as surrounding tissue containing lymph nodes (where infection-fighting white blood cells form) and gives the first indication of Sarcoidosis. For example, a swelling of the lymph glands between the two lungs can show up on an X-ray. An X-ray can also show, which areas of the lung are affected. It involves a staging system of 0-4. Approximately 95% of persons with Sarcoidosis have an abnormal chest X-ray. The staging system used by clinicians is as under:

Stage 0: Normal Chest X-Ray

Stage 1: Chest X-Ray shows enlarged lymph nodes, but otherwise clear lungs

Stage 2: Chest X-Ray shows enlarged lymph nodes and shadows in the lungs

Stage 3: Chest X-Ray shows shadows in the lungs, but no enlarged lymph nodes

Stage 4: Chest X-Ray shows scars in the lung tissue

This staging system indicates the worsening of the lung function and the advancement of the disease.

Pulmonary function test (PFT):

It is done to check the expanding capacity of lungs and oxygen and carbon dioxide exchange efficiency with the blood. It is a restrictive disease of the lungs, causing decrease in lung volume and decreased compliance (ability to stretch) due to granulomas and fibrosis of lung tissue. There is impaired exchange of gases between the lungs and blood. Spirometer, a mechanical device, that records changes in the lung size as air is inhaled and exhaled, as well as the time it takes the patient to do this, is used for PFT procedure.

Exercise pulse oximetry:

Pulse Oximetry involves attaching a small clip to the patient's finger which can show the oxygen level in his blood. Pulse Oximetry is often normal, when measured

at rest but may show effort desaturation with more extensive lung involvement. Arterial blood gas (ABG) analysis at rest and during exercise is more sensitive than pulse oximetry.

Biopsy:

Microscopic examination of specimens of lung tissue obtained with a bronchoscope, or of specimens of other tissues, can tell a doctor where granulomas have formed in the body and help in ultimate diagnosis.

Chest high resolution computed tomography (HRCT):

The images obtained by HRCT provide more detailed information and has better diagnosis accuracy than chest X-ray. The images can give a doctor more information about how a person's lung has been affected by Sarcoidosis, or even detect Sarcoidosis in the liver. The hallmark of pulmonary Sarcoidosis is widespread micronodules with a typical perilymphangitic distribution and predominance for the middle and upper parts of the lungs. HRCT is particularly useful in cases which do not respond to conventional treatment. In complications of the lung disease and tricky cases HRCT makes compelling diagnostic contributions.

Magnetic resonance scan testing:

This test can provide images of organs that one does not wish to risk performing a biopsy on; *e.g.* brain/ heart/ spinal cord.

Screening tests recommended for extrapulmonary disease:

Slit-lamp ophthalmologic examination:

An instrument called a slit lamp, which permits examination of the inside of the eye, can be used to detect silent damage from Sarcoidosis.

Laboratory testing:

Routine blood tests to evaluate renal and hepatic function:

Laboratory testing plays an adjunctive role in establishing the diagnosis and extent of organ involvement. Complete blood count (CBC) may show anemia, eosinophilia, or leucopenia. Renal and hepatic Sarcoidosis may be shown by elevation in blood urea nitrogen, creatinine, and liver function test. Elevated Erythrocyte Sedimentation Rate is common but nonspecific. Blood analyses may reveal the number and types of blood cells in the body and how well the cells are functioning. They can also measure the levels of various blood proteins known to be involved in immunological activities. Due to

hypergammaglobulinemia there may be increase in total proteins.

ACE test:

Measuring levels of Angiotensin converting enzyme (ACE) in blood can help doctors in diagnosis or assessing its severity. Because the cells that make up granulomas secrete large amounts of ACE. The ACE levels are often high in patients with Sarcoidosis. Initially it was thought that an elevated ACE/ sACE (Serum angiotensin converting enzyme) was diagnostic of Sarcoidosis but it is neither sensitive nor specific enough to be diagnostic for the disease.

Serum soluble interleukin-2 receptor

Serum sIL-2R is other frequently used blood test. It is especially useful in evaluation of pulmonary Sarcoidosis. When high levels of serum sIL-2R are found in patients along with slight involvement of lung, it gives the indication of extrapulmonary organ involvement.

CC chemokine ligand 18 (CCL18) and chitotriosidase:

A study on CC chemokine ligand 18 (CCL18) suggested that this marker could be a novel test for the pulmonary fibrotic response in Sarcoidosis. Some other studies have suggested that measurement of chitotriosidase (a chitinase produced by activated macrophages) might be a new marker. Nevertheless, both markers will need further validation before they should be used in routine clinical practice.

Electrocardiogram (EKG) and Serum Ca levels:

It is done to examine whether heart has been affected by Sarcoidosis or not. Serum Ca may be elevated because of production of vitamin D analogs by activated macrophages.

Other adjunctive test:

BAL (Bronchoalveolar lavage):

BAL is used to help exclude other forms of interstitial lung disease, if the diagnosis of Sarcoidosis is in doubt and to rule out infection. In this bronchoscope is used for airway examination and to lavage cells and other materials from inside the lungs. The fluid and cells are then examined for signs of inflammation and immune activity in the lungs. A high number of white blood cells in this fluid usually indicate an inflammation in the lungs. In 90% of cases, in broncho-alveolar lavage (BAL), lymphocytosis is observed and it was found that in 50% of cases CD4+/CD8+ T lymphocyte ratio was greater than 3.5.

Gallium scanning:

Whole-body gallium scanning may provide useful supportive evidence in the absence of tissue confirmation. Symmetric increased uptake in mediastinal and hilar nodes (lambda sign) and in lacrimal, parotid, and salivary glands (panda sign) are patterns highly suggestive of Sarcoidosis. After the injection, the body is scanned for radioactivity. Increases in gallium uptake at any site in the body gives the indication of development of inflammatory activity at the site and give an idea of which tissue, and how much tissue, has been affected. Radioactive Thallium can also be used in place of gallium.

Positron Emission Tomography (PET) scan testing:

PET is one of the novel imaging techniques, which have been explored in Sarcoidosis. In this L-[3-¹⁸F]- α -methyltyrosine is used, which is more specific for malignancy than ¹⁸F-fluorodeoxyglucose positron emission tomography. The combined modality of L-[3-¹⁸F]- α -methyltyrosine-positron emission tomography with fluorodeoxyglucose-positron emission tomography could successfully discriminate Sarcoidosis from malignancy. It is another test that uses radioactive injections.

Kveim test:

An old diagnostic test for Sarcoidosis is the Kveim test, which is unfortunately not very sensitive. Therefore, the Kveim test is not a standard diagnostic test for Sarcoidosis.

ANCA test (Exclusion test):

Anti-neutrophil cytoplasmic antibodies (ANCAs) are a group of autoantibodies, mainly of the IgG type, are detected as a blood test in a number of autoimmune disorders, but are particularly associated with systemic vasculitis, so called ANCA-associated vasculitides. ANCA is divided into two categories: c-ANCA and p-ANCA, based on the pattern of staining on ethanol-fixed neutrophils and the main target antigen. P-ANCA is used to diagnose Churg-Strauss syndrome, and primary sclerosing cholangitis and sometimes polyarteritis nodosa. c-ANCA is associated with Wegener's granulomatosis. Mainly this test is used to rule out these specified autoimmune diseases.

Pharmacotherapy of sarcoidosis:

Systemic corticosteroids:

Fortunately, treatment is not required in 30-70% of the patients. During recommendation of therapy, the main goal is to keep the lungs and other affected body organs working and to relieve symptoms. Once the symptoms

Table 3: Side effects of prednisone

*Difficulty in sleeping	*Heartburn
*Acne	*Glaucoma
*Cataracts	*Weight gain
*Diabetes	*High blood pressure
*Mood swings	*Depression
*Osteoporosis	*Adrenal gland insufficiency

fade the disease is considered inactive. Corticosteroid therapy remains the standard treatment usually in the form

of 'Prednisone'. Prednisone is an anti-inflammatory medication which is sometimes used in conjunction with other medications, even other corticosteroids. Prednisone nearly always relieves inflammation, and is usually prescribed for several months or for a year or more. At lower doses, Prednisone can relieve symptoms of Sarcoidosis without major side effects. Current treatment protocols indicate the use of 30 to 40 mg of prednisone daily for 8 to 12 weeks, with gradual tapering of the dose to 10 to 20 mg every other day over a period of 6 to 12 months.

Table 4 : Commonly used medicines for Sarcoidosis

Medicines	Usual dosage	Adverse effects	Remarks
Corticosteroids (prednisone, prednisolone)	Initial: 20 to 40 mg daily Maintenance: 5 to 10 mg daily on alternate days	Diabetes, hypertension, osteoporosis, insomnia, increased risk of infection	Highly recommended medicine for Sarcoidosis
Cytotoxic agents (In all cytotoxic agents dosage may be adjusted to prevent toxicity)			
Methotrexate (Rheumatrex)	10 to 20 mg per week	Nausea, neutropenia, hepatotoxicity	Useful for chronic Sarcoidosis; takes up to six months to become effective
Azathioprine (Imuran)	50 to 150 mg daily	Nausea, neutropenia	Not as widely studied as methotrexate.
Cyclophosphamide (Cytoxan)	Oral: 50 to 150 mg per day IV pulse: 500 to 1,500 mg every two to four weeks	Neutropenia, nausea, cystitis, carcinogenicity	Effective, but toxicity limits its use to refractory cases
Immunomodulators (In all immunosuppressants dosage may be adjusted to prevent toxicity)			
Pentoxifylline (Trental)	400 to 1,200 mg daily	Nausea	May be useful in acute disease only
Thalidomide (Thalomid)	50 to 200 mg daily	Somnolence, teratogenicity, constipation, peripheral neuropathy	Most useful for skin disease; not as effective for pulmonary disease
Cyclosporine (Neoral)	25 to 200 mg daily	Increased risk of infection, renal failure, hypertension, carcinogenicity	May be useful for treatment of neurosarcoidosis. Efficacy doubtful
Infliximab (Remicade)	5 mg per kg IV at weeks 0,2,6,12, 18 and 24 and followed upto week 52	Increased rate of infection, especially TB; allergic reaction to infusion; cannot given to patients with CHF; possibly carcinogenic	Not much data available
Antimalarial agents			
Chloroquine (Aralen)	500 mg daily	Nausea	Useful for skin disease and hypercalcemia
Hydroxychloroquine (Plaquenil)	200 to 400 mg per day	Ocular toxicity	—

Inhaled corticosteroids:

In special situations where Sarcoidosis involves the airways and the patient is being treated with prednisone, inhaled corticosteroid therapy may be utilized as a means of decreasing the dose of the prednisone. Corticosteroids have many recognized dose- and duration-related side effects (which can be reduced through the use of alternate-day dosing for those on chronic prednisone therapy), and their use is generally limited to severe, progressive, or organ-threatening disease. There are; however, some side-effects of Prednisone that persons taking it have reported (Table 3).

A pulmonary rehabilitation program should also supplement the oxygen program. Exercise is very useful in improving the condition of the patient and the efficiency of the muscles is maintained well by regular exercise, which strengthens the deteriorating lungs. The rehabilitation program is useful because an individual can be pushed to a higher level of exertion in a protected environment. The exercise schedule (*e.g.*, 30 to 45 minutes of daily walking) can be continued on a home basis after the controlled, supervised program. There are other medications which can be taken to treat Sarcoidosis, and your doctor may prescribe them if you can no longer tolerate Prednisone, or if you get worse while taking it. The majority of these medications are immune suppressants which prevent your immune system from fighting viruses and bacteria, increasing the risk that you will get an infection. They are summarized below in Table 4. These medications may increase your risk of getting cancer, and may have serious side effects. Some of the medications are oral ones, while others are applied locally. Medications that can be used in local treatment come in the form of skin creams, eye drops and medications that are inhaled. In some situations, the scarring process may progress. In these situations if the scarring is combined with a decreased oxygen value, supplemental oxygen can be beneficial. The heart has to work harder because of the increased pressure in the lungs from the fibrosis and soon fails. Oxygen has a direct benefit for the heart (Coker, 2009).

Preventive measures:

- Quit smoking
- Stay active but do not over-exert yourself to exhaustion. Exercise at least three times per week and otherwise daily
- Avoid sun exposure as much as you can
- Avoid dust and chemical agents that can irritate your lungs
- Consume healthy diet.

- Eat proper whole foods like vegetables, fruits, nuts and seeds. Animal protein like eggs, turkey, chicken, etc are beneficial. Fish should be (preferably) fresh and free from mercury as far as possible.

- Avoid fast foods or junk foods. Eliminate, or significantly reduce, refined, processed, packaged and sugary foods.

- Eliminate fructose and high fructose corn syrup.

- Use healthy oils such as olive oil, coconut oil, cold-pressed grapeseed oil, avocado oil, ghee (clarified butter), and even organic butter. Oils like coconut and avocado are best to cook with as they have a high “smoke point”. Otherwise, cook your foods and drizzle the oil for complete removal afterwards.

- Drink at least 6 – 8 glasses of purified, alkaline water each day.

- Decrease caffeine usage.

Doctors opine that Sarcoidosis is not a crippling condition and does settle down within 24 to 36 months. Even if it takes longer, patients need not panic and can carry on with their lives normally.

Celebrities who became victims of Sarcoidosis:

Bernie Mac	: Comedian and actor
Karen Duffy	: Former MTV V jay and Revlon Model
Bill Russell	: Basketball legend
Reggie White	: Great Football player
Van Ludwig	: Music composer
Beethoven	
Tisha	: Actress
Campbell-Martin	
Angie Stone	: Singer
Travis Michael Holder	: Actor, playwright and reviewer in the LA theatre scene

Concluding remarks:

Researchers supported by the National Heart, Lung, and Blood Institute are trying to solve some of these mysteries. Some unanswered questions about Sarcoidosis are as under :

- Does Sarcoidosis have many causes, or is it produced by a single agent?
- In which body organ does Sarcoidosis actually start?
- How does Sarcoidosis spread from one part of the body to another?
- Do heredity, environment, and lifestyle play any role in the appearance, severity, or length of the disease?
- Is the abnormal immune response seen in patients

a cause or an effect of the disease?

Sarcoidosis is not a cancer. It is not even a contagious disease, your friends and family members will not catch it from you. Although it can occur in families, there is no direct evidence that Sarcoidosis is passed from parents to children. Elementary and secondary school teachers and firefighters, non-smokers, healthcare workers, and persons who have been exposed to agricultural insecticides, dust, pesticides or molds are at greater risk. Sarcoidosis is believed to be one of the autoimmune diseases, where the body attacks itself. The prognosis for most people with Sarcoidosis is good. Only 5% develop severe lung problems and about 15% of those with Sarcoidosis have symptoms that get worse. Our main aim is to improve the quality of life for Sarcoidosis patients, no matter what the level of severity. By taking proper diet and healthy nutrients to the cells, it is important to decrease the toxic burden on the body, which may help in reduction of inflammation and improve their surveillance. There is no great fund of money for research into its causes and potential treatments or cures, since Sarcoidosis is relatively rare. There is some work ongoing, in the U.S. and world-wide, mostly at very low levels such as cellular physiology, immunology, and genetics. For example, one recent publication had an article from a group in Japan that has discovered what may be a marker for a genetic risk factor for Sarcoidosis. Whether work at this level will lead to anything of clinical use remains to be seen, but these published results are small steps along the path to understanding of this disease. Research specifically into Sarcoidosis may not be “high profile” or

widespread, but work in other areas may also lead to hope for Sarcoidosis patients. The use of thalidomide for neurosarcoidosis directly stems from the clinical work with this drug and rheumatoid arthritis. Also, work with various drugs for asthma and cystic fibrosis may help the patient with chronic pulmonary Sarcoidosis, at least symptomatically. It is impossible to predict the direction, from which a major breakthrough would come, but there is hope.

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