CHAPTER 1

Definition and history of sarcoidosis

O.P. Sharma

Correspondence: O.P. Sharma, Room 11-900, Los Angeles County-University of Southern California Medical Center, 1200 North State Street, Los Angeles, CA 90033, USA. Fax: 1 3232262738; E-mail: osharma@usc.edu

Sarcoidosis, a commonplace inflammatory disease, is characterised by the formation of noncaseating granulomas. The granuloma is a battle fought on a genetically vulnerable terrain between an unrecognised antigen(s) and a highly organised team of lymphocytes and macrophages. The disease occurs worldwide; no race, sex or age is immune from it. Its chameleon-like multisystemic presentation can involve any organ in the body. Owing to its diverse presentation, the disease easily crosses the artificial boundaries of medical specialities, and appears in the offices and clinics of practitioners of different disciplines. The fresh, innovative and individual approach of international investigators, scientists and specialists of different disciplines have constructed an engrossing historical saga of sarcoidosis (table 1).

Definition

It is hard to provide a concise definition of a disease whose cause is yet to be discovered. SCADDING and MITCHELL [3] recommended the following: "Sarcoidosis is a

Table 1. – Sarcoidosis milestones

	Event
1869	J. Hutchinson: first account of skin lesions
1888	E. Besnier: coined term lupus pernio
1892	M. Tenneson: defined histology
1897	C. Boeck: described a policeman with skin lesions
1902	R. Kienbock/K. Kreibich/O. Jungling: described bone changes
1906	Darier–Roussy syndrome: subcutaneous nodules described
1909–1910	H. Schumacher/Christian Heerfordt/F. Bering: recognised uveitis
1915	J. Schaumann: emphasised multisystemic disorder
1915	E. Kuznitsky: classified skin lesions
1915	A. Bittorf: described lung lesions
1937	W. Bruins-Slot/L-M. Pautrier/W.T. Longcope/J. Pierson/ J. Costa Waldenstrom: uveoparotid fever
1941	A. Kveim: introduced Kveim test S. Löfgren: described Löfgren's syndrome
1958	K. Wurm: first proposal for radiographic staging
1958	1st International Conference on Sarcoidosis: London, UK
1961	1st USA conference: Washington, DC, USA
1967–1981	H. Reynolds, G. Hunninghake, R Crystal: bronchoalveolar lavage
1976	Commemorative publication dedicated to L. Siltzbach: *Mount Sinai Journal of Medicine, New York* [1]
1984	G. Rizzato: starts journal *Sarcoidosis* (now called *Sarcoidosis, Vasculitis and Diffuse Lung Diseases*)
1987	G. Rizzato: founds World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG); D.G. James elected the first president
1987	Commemorative publication dedicated to D.G. James: *Sarcoidosis* [2]

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disease characterised by the formation in all of several affected tissues of epithelioid-cell tubercles without caseation though fibrinoid necrosis may be present at the centre of a few, proceeding either to resolution or to conversion into hyaline fibrous tissue". This definition emphasises only the histological features of the illness. Knowledge of the disease is now so expansive that not only the clinical but also the radiological, immunological, biochemical and genetic aspects of the illness need to be included. A brief definition of sarcoidosis is not possible because of ignorance of its cause. The following descriptive definition is provided in the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) statement on sarcoidosis of 1999 [4]: "Sarcoidosis is a multisystemic disorder of unknown cause. It commonly affects young and middle-aged adults and frequently presents with bilateral hilar adenopathy, pulmonary infiltration, ocular and skin lesions. The liver, spleen, lymph nodes, salivary glands, heart, nervous system, muscles, bones and other organs may also be involved. The diagnosis is established when clinico-radiographic findings are supported by histological evidence of noncaseating epithelioid cell granulomas. Granulomas of unknown causes and local sarcoid reactions must be excluded. Frequently observed immunological features are depression of cutaneous delayed type-hypersensitivity and a heightened Th-1 [T-helper cell type-1] immune response at sites of disease. Circulating immune-complexes along with signs of B-cell hyperactivity may also be found. The course and prognosis may correlate with the mode of the onset, and the extent of the disease. An acute onset with erythema nodosum or asymptomatic bilateral hilar adenopathy usually heralds a self-limiting course, whereas an insidious onset, especially with multiple extrapulmonary lesions, may be followed by relentless, progressive fibrosis of the lungs and other organs."

History

The London school

J. Hutchinson is a convenient starting point for tracing the history of sarcoidosis. Hutchinson was born on July 23, 1828 in Selby (UK) to a Quaker family. After graduating from St Bartholomew's Hospital (London, UK), he became the best known medical consultant in London because of his wide range of interests. He was dermatologist at the Blackfriars Hospital for Diseases of the Skin, ophthalmologist to the Royal London Ophthalmic Hospital, venereologist to the Lock Hospital, physician to the City of London Chest Hospital, and a general surgeon to the London and Metropolitan Hospitals (all London, UK). He became president of the Royal College of Surgeons (1889), the Pathological Society of London (1879), the Ophthalmological Society of the United Kingdom (1883), the Neurological Society (1887), the Medical Society of London (1892), the Royal Medical and Chirurgical Society (1894–1896), and the International Dermatology Congress (1896) (fig. 1).

In January 1869, a 58-yr-old coal-wharf worker, visited Hutchinson complaining of purple symmetrical skin plaques on his legs and hands that had developed gradually over the preceding 2 yrs. The lesions were neither tender nor painful. In 1877, HUTCHINSON [5] described the lesion as livid papillary psoriasis and considered that it was in some way related to the patient's gout. In a later publication, HUTCHINSON [6] described additional cases and described the lesion as a "form of skin disease which has – hitherto escaped special recognition". In Hutchinson's time, sarcoidosis was a dermatological curiosity. Hutchinson's contemporary, A.C. Doyle, the creator of Sherlock Holmes, made a skin disease, most probably cutaneous sarcoidosis, a basic ingredient of the plot of *The*

Fig. 1. – a) J. Hutchinson and b) his patient showing typical chronic sarcoidosis lesions.

Adventure of the Blanched Soldier [7]. Whether or not A.C. Doyle ever discussed patients with J. Hutchinson remains unclear, but it can be surmised that A.C. Doyle and J. Hutchinson must have met and exchanged ideas during one of the many London Medical Society meetings. J. Hutchinson was a member and regular discussant at the meetings, whereas A.C. Doyle practised at 2 Devonshire Street (London, UK), just a few steps away from 10 Chandos Street, home of the Medical Society of London.

From those early days, there have been other British pioneers of sarcoidosis, but none more influential and erudite than J.G. Scadding, who was stimulated to take up sarcoidosis by I. Snapper, Professor of Clinical Medicine at the University of Amsterdam (Amsterdam, The Netherlands). In the early 1940s, at the Hammersmith Hospital (London, UK), J.G. Scadding collaborated with S. Sherlock on a study of aspiration liver biopsy in sarcoidosis (fig. 2). This test became the most valuable tool for diagnosing sarcoidosis, and remained so for decades before being replaced by bronchoscopy. J.C. Scadding consolidated his vast personal experience of the disease, gathered at the Hammersmith Hospital and Brompton Chest Hospital, now the Royal Brompton (London, UK), in the widely acclaimed book *Sarcoidosis*, first published in 1967 by Eyre and Spottiswoode, London, UK. The credit for making sarcoidosis a household word, however, goes to the ebullient internist and medical historian D.G. James, who, in 1953, started the renowned sarcoidosis clinic in a small North London hospital. The clinic, in its heyday, attracted sarcoidologists from all over the world. The Royal Northern Sarcoidosis Clinic, as it was called, became a sarcoidosis Mecca. H. Israel, C. Johns, J.G. Scadding, S. Löfgren, Y. Hosoda, L. Sitzbach, L. Levinsky, E. Kendig, J. Chretien, N. Bethlem, T. Izumi, W. Jones Williams, R. Crystal, O.P. Sharma, G. Rizzato, S. Gupta,

Fig. 2. – D.G. James, S. Sherlock and S. Löfgren (from left to right, respectively).

D. Mitchell, U. Costabel, J. Costa Waldenstrom, F. Wegener, R. DeRemee, S. Sherlock, M. Turner-Warwick, O. Selroos, B. Djuric and many others lectured and actively participated in sarcoidosis meetings, conferences and group discussions at the Royal Northern Hospital. Neither the clinic nor the hospital exists any longer [8].

The 1st International Conference on Sarcoidosis, organised by D.G. James, was held in London in 1958, with a handful of physicians in attendance. The second international gathering on British soil was the 7th International Conference on Sarcoidosis, held in the historic city of Cardiff. W. Jones Williams was the host. R. Dubois staged the 15th WASOG Conference in London, UK, in 1995.

The Scandinavian school

In the summer of 1869, J. Hutchinson visited Christiania (now Oslo) University (Oslo, Norway), where W. Bidenkap showed him a collection of pathological drawings in the university museum. Among these was one of a patient of C.W. Boeck. The patient, a healthy Swedish sailor, had skin lesions similar to those of the 58-yr-old coal-wharf worker who had visited Hutchinson earlier, but did not suffer from gout. C.W. Boeck was an uncle of C. Boeck, who was later to make valuable contributions to the study of sarcoidosis. He coined the term "sarkoid" because the lesion resembled sarcoma, but was benign. Just before his death, C. Boeck published an extensive study of 24 cases of "benign miliary lupoids"; some of the cases showed involvement of the lungs, conjunctiva, bone, lymph nodes, spleen and nasal mucous membrane [9]. Thus, the malady that started as a curious skin ailment in London, UK, became a multisystemic disease in Oslo, Norway.

J. Schaumann was born in Soustad (Malmohus, Sweden) and studied medicine in nearby Lund, Sweden. He became a dermatologist at Saint Goran's Hospital and the Finsen Institute in Stockholm (Sweden). He provided a common pathological basis for diverse clinical aspects; he was the first to propose a clinico-pathological synthesis of multisystemic sarcoidosis. He called it lymphogranulomatosis benigna in order to distinguish it from Hodgkin's malignant granuloma. This he described in an admirable

Zambaco-prize-winning essay written in 1914. The article was not published until 1936 [10].

S. Löfgren was born in Stockholm, Sweden. He received his medical training there and married a Swedish physician. His medical life revolved around Saint Goran's Hospital, where he came under the scientific influence of A.V. Westergren and J. Schaumann. His elegant studies brought the mysterious disease of sarcoidosis out of the shadows and into the limelight as a common disorder with a good prognosis. Although erythema nodosum was first described by R. Willan (fig. 3) in his classic work *On Cutaneous Disorders* [11], published in parts between 1798 and 1808, it was S. Löfgren who, by obtaining tissue biopsy specimens, linked erythema nodosum and bilateral hilar adenopathy as manifestations of acute sarcoidosis [12, 13]. The combination of erythema nodosum and hilar adenopathy is now known as Löfgren's syndrome. When S. Löfgren attended the 1st International Conference on Sarcoidosis in London, UK, in 1958, he was strongly

Fig. 3. – R. Willan, known as the father of modern dermatology, is immortalised by his picture on every issue of the *British Journal of Dermatology*.

of the opinion that sarcoidosis was unlike and unrelated to tuberculosis and favoured a viral cause. At the London conference, he also described renal sarcoidosis, with kidney biopsy evidence of granulomas and associated abnormal calcium metabolism.

A. Kveim was born in Gjerstad, Norway, and became a dermatologist in the department of N. Danbolt at the Rikshospitalet in Oslo (Norway) during the period 1936–1945. He made the important observation that sarcoid lymph node tissue inoculated intradermally gave rise to papules of sarcoid tissue in l2 out of l3 of his sarcoidosis patients (fig. 4). Since the reaction did not occur in normal subjects or in one patient with lupus vulgaris, he concluded that the papule was the specific lesion caused by an unknown agent and that the test might serve to differentiate sarcoidosis from tuberculosis [14].

N. Svanborg, a prominent pulmonary physiologist, was born in Umeå, Sweden on February 5, 1920 and lived until the same month in 1997. He published the first and perhaps only authoritative monograph describing pulmonary function abnormalities in sarcoidosis in great detail [15].

C. Heerfordt, son of a local doctor, was born in Terndtrup, Denmark. He eventually became an ophthalmologist and drew attention to "febris uveoparotidea subchronica", a

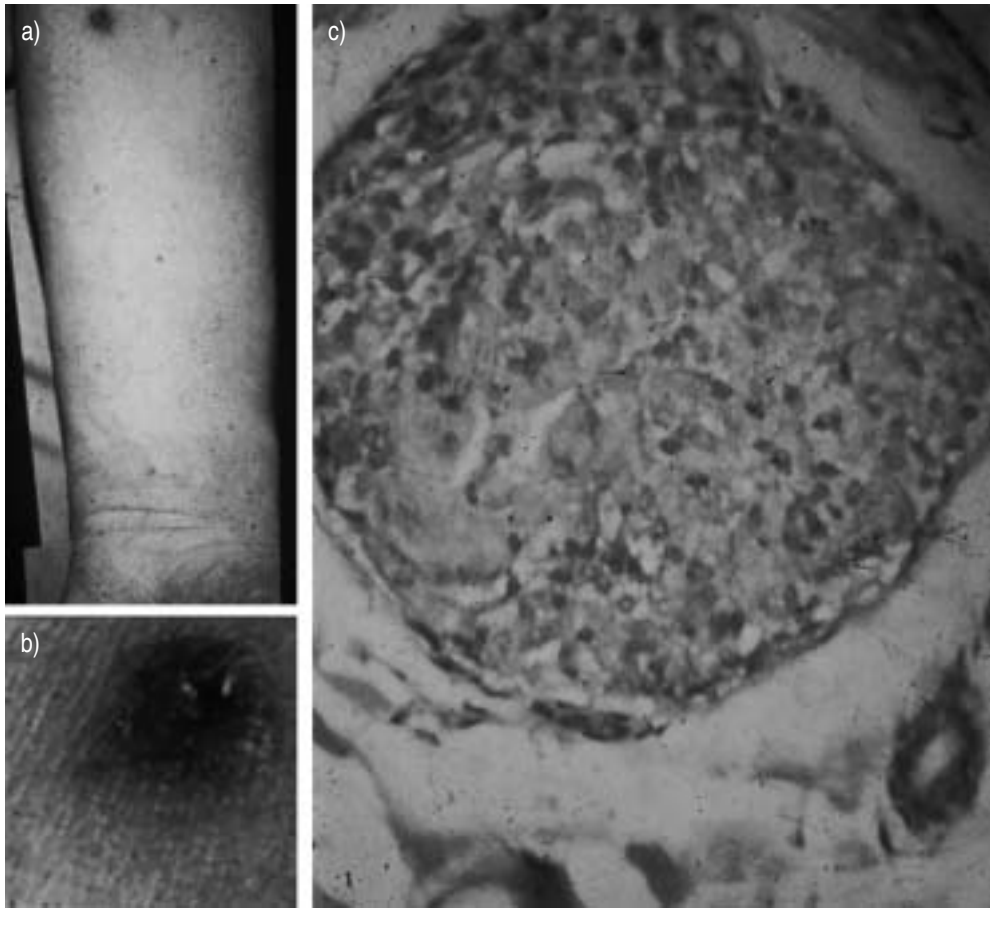

Fig. 4. – a) Kveim-Siltzbach test: a nodule appears at the site of inoculation in ~4–6 weeks and b) close up. c) The biopsy specimen shows a noncaseating granuloma.

combination of uveitis and enlargement of the parotid glands [16]. He noted that the condition was chronic and frequently complicated by cranial nerve palsies, especially of the seventh nerve, and pleocytosis of the cerebrospinal fluid. C. Heerfordt was keen to see Scandinavia and Europe form a single community and had written two books, *A New Europe I* and *II*, during the years 1924–1926.

A. Hanngren, Professor and Head of Thoracic Medicine at the Karolinska Institute (Stockholm, Sweden), was an ardent student of both tuberculosis and sarcoidosis. He regularly attended national as well as international sarcoidosis conferences. A. Hanngren enjoyed discussing the aetiology of sarcoidosis because he had definite views about the topic. He believed strongly that clinical medicine and experimental research should work together amicably. His philosophy helped to create excellent research opportunities for young Swedish doctors interested in chest disease.

Scandinavia had the distinct honour of holding the first WASOG Conference of the twenty-first century, held in June 2002 in Stockholm, Sweden. It was organised by O. Selroos, A. Eklund and J. Grunewald. The conference will be remembered for its in-depth exposition of the cytokine network leading to granuloma formation and discourse about the role of genetic make-up in predisposing to various phenotypes of sarcoidosis.

The French school

In 1889, E. Besnier described a patient with violaceous swellings of the nose, ears and fingers, for which he coined the term lupus pernio [17]. He referred to J. Hutchinson's patient (the 58-yr-old coal-wharf worker), but the distribution of the lesions was sufficiently dissimilar to justify his opinion that the two conditions were not identical [17]. In 1892, M. Tenneson reported another example of lupus pernio and described its essential histology of a "predominance of epithelioid cells and a variety of giant cells" in the skin lesions [18]. In the reports published by Besnier [17] and Tenneson [18], cases were not illustrated and wax models of the appearance of their patients were used instead to illustrate skin lesions.

The father of L-M. Pautrier was from Aix-en-Provence and his mother from Arles (both France); he was born in Marseilles (France) on August 2, 1876. He studied there and in Paris, France, where he became a dermatologist with L. Brocq at the Saint Louis Hospital. His doctorate was an imposing 350-page document on "Atypical cutaneous tuberculosis". During the First World War, he was in an artillery regiment and was awarded the French cross of the Legion of Honour, knight class. He became professor of dermatology at the University of Strasbourg (Strasbourg, France) and the University of Lausanne (Lausanne, Switzerland). In his 1939 textbook on sarcoidosis, he opposed the tuberculous theory and regarded the disease as a reticuloendotheliosis.

J. Turiaf was born in Martinique, into a family of seven brothers and sisters; their father was a French senator. Turiaf qualified in Paris in 1943 and eventually joined the Bichat Hospital (Paris) in 1954, where he remained for the remainder of his life. A chair of respiratory pathology was created for him. The 4th International Conference on Sarcoidosis was held on September 12–15, 1966, under the genial presidency of J. Turiaf. The proceedings contain voluminous information crammed into 782 pages.

J. Chretien was editor of the French Thoracic Society journal and elected an honorary fellow of the Royal College of Physicians (London, UK). Monoclonal antibodies first featured in sarcoidosis in the 1981 International Conference on Sarcoidosis organised by J. Chretien in Paris. F. Basset was the leading lady of the French sarcoidosis school. She also studied and wrote about eosinophilic granuloma, now called Langerhans' cell granulomatosis.

The Italian school

Italy has contributed more to the process of gathering information on sarcoidosis than any other country. G. Rizzato organised an International Conference on Sarcoidosis in Milan in 1987, and, at the same time, took the opportunity to found the WASOG. This infrastructure enables sarcoidologists worldwide to exchange information. In 1984, G. Rizzato founded a journal devoted to sarcoidosis; this is now a flourishing scientific document that appears four times each year under the editorship of G. Semenzato, an expert immunologist. The Italian sarcoidosis movement is also blessed with the contributions of A. Blasi, C. Grassi, C. Agostini, D. Olivieri, P. Rottoli, L. Allegra and other active members of the Italian school.

The USA school

In the last quarter of the nineteenth and earlier decades of the twentieth century, sarcoidosis was not a significant illness in the USA. Its existence was shrouded by tuberculosis. It was not uncommon for sarcoidosis patients to end up in tuberculosis sanatoria in the belief that they had pulmonary tuberculosis. Conversely, patients with sarcoid skin lesions were often incarcerated in leprosaria because the skin lesions of sarcoidosis were frequently misdiagnosed as lesions of lepromatous leprosy. Sarcoidosis did not appear in W. Osler's famous text, *The Principle and Practice of Medicine* [19]. Osler did not recognise the disease, but his 11-yr-old patient, who had bilateral parotid and lachrymal gland enlargement, splenomegaly, and a thickened and ulcerated nasal septum, was most probably the first example of sarcoidosis in a child [20].

W.T. Longcope was Professor of Medicine at Johns Hopkins Hospital, Baltimore, MD, from 1922–1946. He graduated from the medical school of Johns Hopkins University in 1901, was a student of W. Osler and a profound scholar of disease in the Oslerian tradition. His papers on sarcoidosis, which began to appear in 1936, did more than any other publications to create interest in the disease in the USA. He described all manifestations of the disease and established it as a distinct multisystemic clinical entity [21].

L. Siltzbach, M. Cummings, H. Israel and M. Sones were the four distinguished American sarcoidologists at the 1st International Conference on Sarcoidosis held in London, UK in June 1958. Later, to this list of adult sarcoidologists was added the name of E. Kendig Jr., who, from his home base in Richmond (VA, USA), spread the message that sarcoidosis effected, albeit rarely, children.

The London conference was followed by a second conference, held in Washington DC, USA, in June 1960. M. Cummings, who for a brief period believed that sarcoidosis was caused by pine pollens, masterminded it. The conferences became a model for all subsequent conferences. It was fruitful for it produced a working definition and exemplary proceedings. Participants also included the pioneers J. Chapman, C. Nelson and M. Michael Jr. During the 7th International Conference on Sarcoidosis, organised by L. Siltzbach, immunological aberrations associated with sarcoidosis were defined and serum angiotensin-converting enzyme was first recognised as a possible biochemical marker of active sarcoidosis. L. Siltzbach was a world leader in the sarcoidosis movement; he spread the sarcoidosis word around the world. L. Siltzbach popularised the Kveim test and affirmed its specificity in a large international study. The test is now called the Kveim–Siltzbach test. D.G. James edited a commemorative publication dedicated to L. Siltzbach while the latter was still alive, well and able to enjoy it [1].

C.J. Johns, an internationally recognised clinician and teacher, organised the 10th International Conference on Sarcoidosis in Baltimore in 1984. V. McKusick delivered a memorable opening lecture, "Sarcoidosis: a case study in nosology" [22]. The concept of

activity of sarcoidosis was extensively discussed in the context of the then recently developed techniques of gallium scanning and bronchoalveolar lavage fluid analysis. The proceedings of this highly scientific conference were edited by C.J. Johns and published in a massive 750-page document. C.J. Johns was an untiring advocate of the women's cause and was elected to the Johns Hopkins Women's Medical Alumnae Association's Hall of Fame.

H. Israel was a popular clinician and teacher. He diagnosed, treated, taught and wrote about a number of illnesses, including tuberculosis, Wegener's granulomatosis, pulmonary embolism, histoplasmosis, aspergillosis and, of course, sarcoidosis. In 1951, he recommended corticosteroids for the treatment of sarcoidosis.

E.L. Kendig Jr. was Professor of Paediatrics at the University of Virginia, Richmond (VA, USA). He wrote extensively about childhood sarcoidosis. He was the only member of the WASOG who was recognised for his expertise in the field of childhood sarcoidosis.

The Japanese school

Japan has been a prolific contributor on granulomatous disorders, with significant contributions on clinical features, epidemiology, microbiology and immunology. It has hosted three International/WASOG Conferences on Sarcoidosis and has a splendid Japanese Sarcoidosis Association. Y. Hosoda is its worldwide ambassador, and has made important contributions as a general chest physician, an occupational/environmental expert and an epidemiologist. Y. Hosoda organised the 6th International Conference on Sarcoidosis in 1972 in Tokyo, with 300 delegates representing 22 countries. Recently, in order to understand the relationship between sarcoidosis and tuberculosis, HOSODA *et al.* [23] analysed a series of health surveillance data in a Japanese work population of 460,000 employees. This population underwent annual radiography and tuberculin testing. The authors found no causal relationship between tuberculosis and sarcoidosis. This study represents a landmark in the curious history of tuberculosis and sarcoidosis. The Japanese school has been a leader in investigating the role of *Propionibacterium acnes* in the causation and pathogenesis of sarcoidosis.

T. Izumi, Professor of Medicine at Kyoto University (Kyoto, Japan), organised, together with S. Nagai, the 1991 WASOG Conference in Kyoto jointly with the XI Annual Meeting of the Japan Society of Sarcoidosis. He edited the 681-page proceedings as a special issue of the journal *Sarcoidosis*. M. Ando hosted the 7th WASOG Conference in Kumamoto in 1999.

Germany

The German pioneers in the field include A. Bittorf, E. Kuznitsky, P. Langerhans, T. Langhans, E. Uehlinger, F. Wegener, H. Eule, J. Meier-Sydow and K. Wurm. In 1958, K. Wurm developed the radiological staging of pulmonary sarcoidosis that was adopted by clinical investigators all over the world. In 1997, U. Costabel hosted a superb and memorable conference in Essen (Germany).

Czechoslovakia

K. Kreibich was born on May 20, 1869 in Prague (Czechoslovakia) and graduated in 1894 in the German Medical Faculty in Prague. His extensive postgraduate training in Vienna (Austria) included 6 yrs with M. Kaposi in the Dermatology Department. In 1909, he succeeded F.J. Pick as Professor of Dermatology and later became Dean (1913) and Rector (1923) of the German University in Prague. He died in Prague on

December 30, 1932. Three of his 200 scientific papers were on lupus pernio. In one of his patients, he noted lattice-like rarefactions of the terminal phalanges; this was the first description of bone cysts in sarcoidosis [24].

L. Levinsky, recently deceased, was a retired chest physician in Prague. Delegates from 37 countries attended his International Conference on Sarcoidosis (1969), from which he produced a wide-ranging 653-page transaction. Recently, under the leadership of V. Kolek, the nerve centre of Czech sarcoidosis activity has shifted to Olomouc (Czech Republic).

Portugal

T.G. Villar was a man of Lisbon (Portugal). He was born, educated, practised medicine and died there. After postgraduate studies in Jersey City (NJ, USA), he returned to Lisbon, where he became Professor of Lung Disease and president of Portugal's Respiratory Pathology Society in 1974. He was truly international, being elected honorary fellow of the British Thoracic Society in 1977 and representing the American College of Chest Physicians as Fellow (1973), Governor (1974) and Regent (1978). He funded two Portuguese medical reviews, *Pneumologia* and *Medicina Thoracalis*; became vice-president of the International Association of Bronchopneumology in 1973; and pursued active research on hypersensitivity pneumonitis, particularly suberosis. In 1976, he co-authored, with R. Avila, an international text on pulmonary granulomatoses due to inhaled particles. M. Freitas e Costa was Professor of Respiratory Disease at the University Medical School, Lisbon. In 1989, he organised a sarcoidosis conference that attracted 322 delegates; there were 76 oral presentations and 76 posters. The transactions formed a special issue of the journal *Sarcoidosis*.

Yugoslavia

For almost 30 yrs, O. and B. Djuric (a brother and sister team) kept the sarcoidosis candle burning by conducting clinical research and participating in various international conferences. In 2000, V. Vucinic formed the Yugoslav Association of Sarcoidosis, which now holds a sarcoidosis conference every year.

India

Although a short review of sarcoidosis with a case report was published as early as 1957 in the *Indian Journal of Dermatology* [25], the disease remained hidden under the menace of widespread tuberculosis for a long time. The late S. Gupta shared his experience on clinical aspects of sarcoidosis in India at various national and international conferences. In his hometown, Kolkata (previously known as Calcutta), India, on February 22, 2003, the Indian Association of Sarcoidosis and other Granulomatous Disorders (IASOG) was inaugurated. The first annual meeting of the IASOG was held on January 12, 2004 and was organised by A. Shah. The events came too late for S. Gupta, a pioneer in sarcoidosis and tuberculosis, who had passed away earlier on September 9, 2002.

Brazil

N. Bethlem was Titular Professor of Physiology and Pneumology at the Federal University of Rio de Janeiro (Rio de Janeiro, Brazil) from 1964–1986. He taught about

sarcoidosis, wrote about it, and was a frequent participant at various national and international meetings. After his death in 1998, his son E.P. Bethlem inherited his father's love for and dedication to sarcoidosis. He continues to be WASOG ambassador in South America.

The future

The cause of sarcoidosis and related symptoms remains a mystery [26, 27]. The most recent WASOG Conference was held in 2005 (June 12–15) in Denver (CO, USA), under the leadership of R. Baughman and L. Newman. More than 400 delegates from all over the world were in attendance. Once again, there was intense scrutiny and research concentrated on finding out the cause and genetic predisposition of sarcoidosis. Moreover, young investigators were challenged to try to explore the many remaining questions.

Key points

1. Sarcoidosis, a multisystemic granulomatous disease, has a long and distinguished medical history that stretches over all the continents and covers the last 150 yrs.
2. Since the 1950s, there has been rapid progress in the understanding of the clinical, radiological, physiological, biochemical and immunological aspects of the granulomatous process.
3. Advances in the field of medical genomics and proteomics may hold the key to the aetiology of sarcoidosis.

Summary

More than a century ago, J. Hutchinson, a surgeon-dermatologist, identified the first case of sarcoidosis at King's College Hospital (London, UK). In the decades before and following the turn of the nineteenth century, several publications independently drew attention to what is now regarded as sarcoidosis. This trend gained a significant momentum in the latter part of the twentieth century and has continued relentlessly into the nascent years of the twenty-first century. This brief account provides a working definition of the disease and outlines the countries, institutions and individuals that have participated in the historical journey of sarcoidosis to the present.

Keywords: Granuloma, J. Hutchinson, Kveim test, Löfgren's syndrome, sarcoidosis, World Association of Sarcoidosis and Other Granulomatous Disorders.

Editor's note. O. Sharma, the author of this chapter and current World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) president, is himself a distinguished member of the USA school. As a master clinician in the field, he has made significant contributions to the management of extrathoracic manifestations of sarcoidosis and the mechanism leading to hypercalcaemia. In 1993, he was a perfect host of the memorable 3rd WASOG meeting in Los Angeles (CA, USA) and edited the 474-page proceedings as a special issue of the journal *Sarcoidosis*.

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