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D. Geraint James Lecture. The sarcoidosis saga: What insights from the past will guide us in the future

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Abstract. The sarcoidosis community in general and the World Association of Sarcoidosis and Other Granulomatous diseases (WASOG) in particular have led efforts to improve sarcoidosis diagnosis and care. Evidence based guidelines regarding the diagnosis and treatment have recently been published. In addition, several clinical trials examining existing and new treatments for sarcoidosis have been completed and published. In addition, WASOG has developed criteria and identified Centers of Excellence for sarcoidosis care around the world. In discussing what insights from the past will guide us in the future, this paper focuses on three specific topics: updating the diagnosis of sarcoidosis, using placebo-controlled trials to illuminate the natural course of pulmonary sarcoidosis; and exploring multidisciplinary sarcoidosis clinic care using Centers of Excellence. New approaches for diagnosis of sarcoidosis and steroid tapering are proposed based on current literature.

Key words: diagnosis, therapy centers of excellence, placebo, clinical trials

Introduction

I want to thank Dr. Natalia Riveria and the organizers for the opportunity to give this year's D. Geraint James lectureship at the WASOG meeting in Stockholm. I also wish to thank Drs. Daniel Culver and Athol Wells as presidents of WASOG for extending the invitation to give the lecture which is the basis of this paper. In discussing what insights from the past will guide us in the future, I will focus on three specific topics: updating the diagnosis of sarcoidosis, using placebo-controlled trials to illuminate the natural course of pulmonary sarcoidosis; and exploring multidisciplinary sarcoidosis clinic care using Centers of Excellence. The sarcoidosis clinic at University of Cincinnati has been co-directed by Dr. Elyse Lower and me since 1986. Over that time, we have seen over 3000 patients and published widely regarding the clinical presentation, outcome, and treatment of sarcoidosis. It is these shared experiences of Dr. Lower and myself that I base my comments.

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Updating the diagnosis of sarcoidosis

Sarcoidosis remains an elusive disease of unknown etiology and often a diagnosis is made by excluding other conditions. In 2020, the American Thoracic Society published a clinical practice guideline updating the information regarding diagnosis and detection of sarcoidosis (1). This evidence-based document provided specific recommendations regarding various aspects of the disease. Although the committee was unable to provide a specific evidence-based guide to diagnosis sarcoidosis, an algorithm was generated regarding diagnosis that utilized biopsy in patients with clinical presentation consistent with the diagnosis and in whom alternative conditions were excluded. Disappointing, this approach had not changed from the previous sarcoidosis statement published in 1999 (2).

While the concept of a "clinical presentation consistent with sarcoidosis" is widely cited by

researchers and clinicians, it has rarely been specified. One attempt to provide specific criteria for clinical presentation was the ACCESS organ assessment tool (3). That instrument provided specific criteria for individual organ involvement in a patient with biopsy confirmed sarcoidosis. In 2014, this organ assessment instrument was updated with consensus by an expert panel (4). Organ involvement could be classified as either "highly probable" or "at least probable". The WASOG organ assessment instrument has been used globally to compare organ involvement for various countries.

Sarcoidosis is a multi-organ disease and the more organ involvement detected, the more comfortable one can be regarding the diagnosis. In Cincinnati, we developed a Sarcoidosis Diagnostic Score (SDS) (5). For the individual patient, individual organ involvement due to sarcoidosis was scored based on whether one or more features were "highly probable" or "at least probable" for sarcoidosis. Figures 1 and 2 show examples of "highly probable" (Figure 1) or "at least probable" (Figure 2) involvement. The highest score for an individual organ is three. An **SDS clinical** score was calculated by summing all the scores for individual organ involvement. For **SDS biopsy**, the results were included from pathologic examination of tissue samples. For those with a biopsy demonstrating non caseating granuloma, five points were added to the SDS clinical score. For those with either a negative biopsy or no tissue, the SDS biopsy was the same as the SDS clinical.

Our original study examined nearly 1000 patients seen by Drs. Lower and myself over a six month period at our sarcoidosis clinical (5). Half of the patients had biopsy confirmed sarcoidosis. The study found a significant difference between those with and without sarcoidosis.

A validation study was performed on over 2000 patients seen at eight sites across the world (Figure 3). In this study, the control group included a significant number of patients with tuberculosis, malignancy, and non-infectious granulomatosis diseases (6). Once again, there was a significant difference between the groups. The higher the scores, the more likely one was dealing with sarcoidosis (Figure 4). However, there was overlap with the non-infectious granulomatous diseases. Patients with common variable immune deficiency, vasculitis, or chronic beryllium disease could have SDS clinical and SDS biopsy scores similar to that seen with sarcoidosis. These conditions can usually be detected by simple blood work (serum immunoglobulin levels and antineutrophilic cytoplastic antibody) and occupational exposure history. The study reported that an SDS clinical score of > nine was associated with sarcoidosis with a 99.8% sensitivity. However, that occurred in only 10% of the sarcoidosis patients studied. For those with a score of eight or less, a biopsy showing granulomas further enhanced the probability of sarcoidosis as the final diagnosis. However, the SDS clinical score can be useful even in those cases where a biopsy may not be possible. In the Jeny et al study (6),

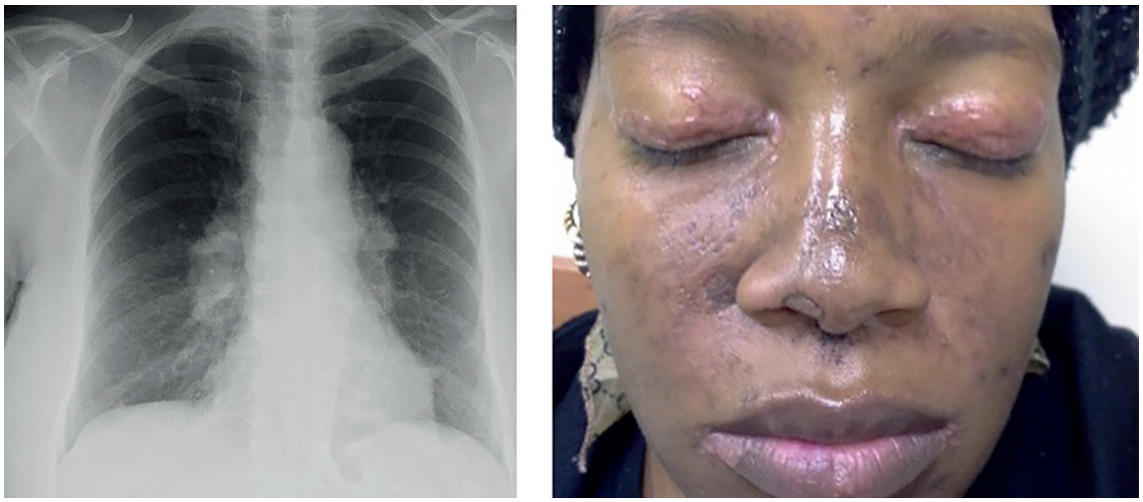

Figure 1. Two examples of highly probable organ involvement (4): bilateral hilar adenopathy in lungs (left) and lupus pernio of the skin (right). Presence of either of these would be scored as three points for individual organ involvement. Patient with lupus pernio provided written consent for publication of photograph of her facial lesion [From Jeny et al, 2023 (6), reprinted with permission of the American Thoracic Society. Copyright © 2023 American Thoracic Society. All rights reserved. Annals of the American Thoracic Society is an official journal of the American Thoracic Society].

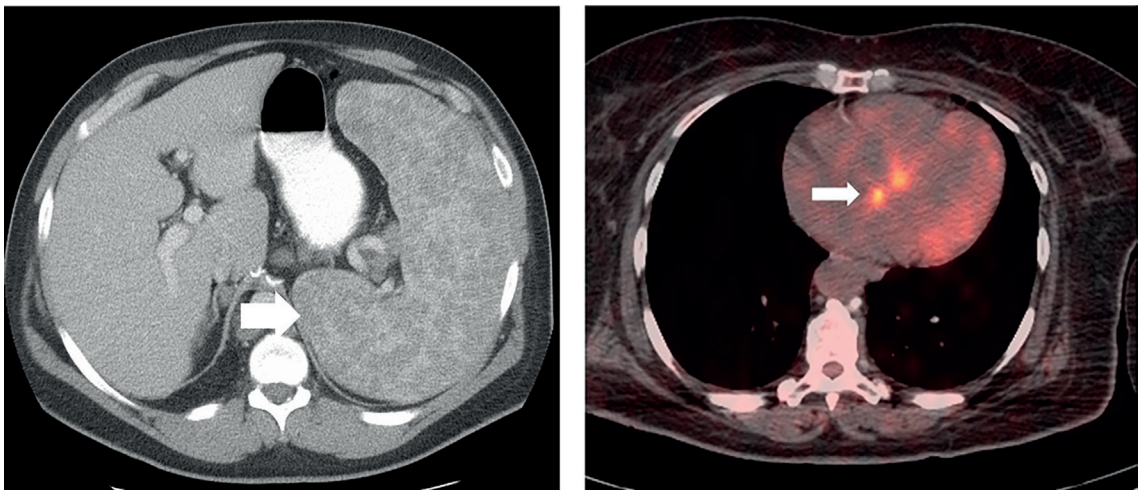

Figure 2. Two examples of at least probable organ involvement (4). On left is the CT image of the spleen showing infiltration by lower density areas (arrow). On right, increased FDG PET activity is seen in the septum of heart (arrow). Each of these would be worth two points for the SDS score.

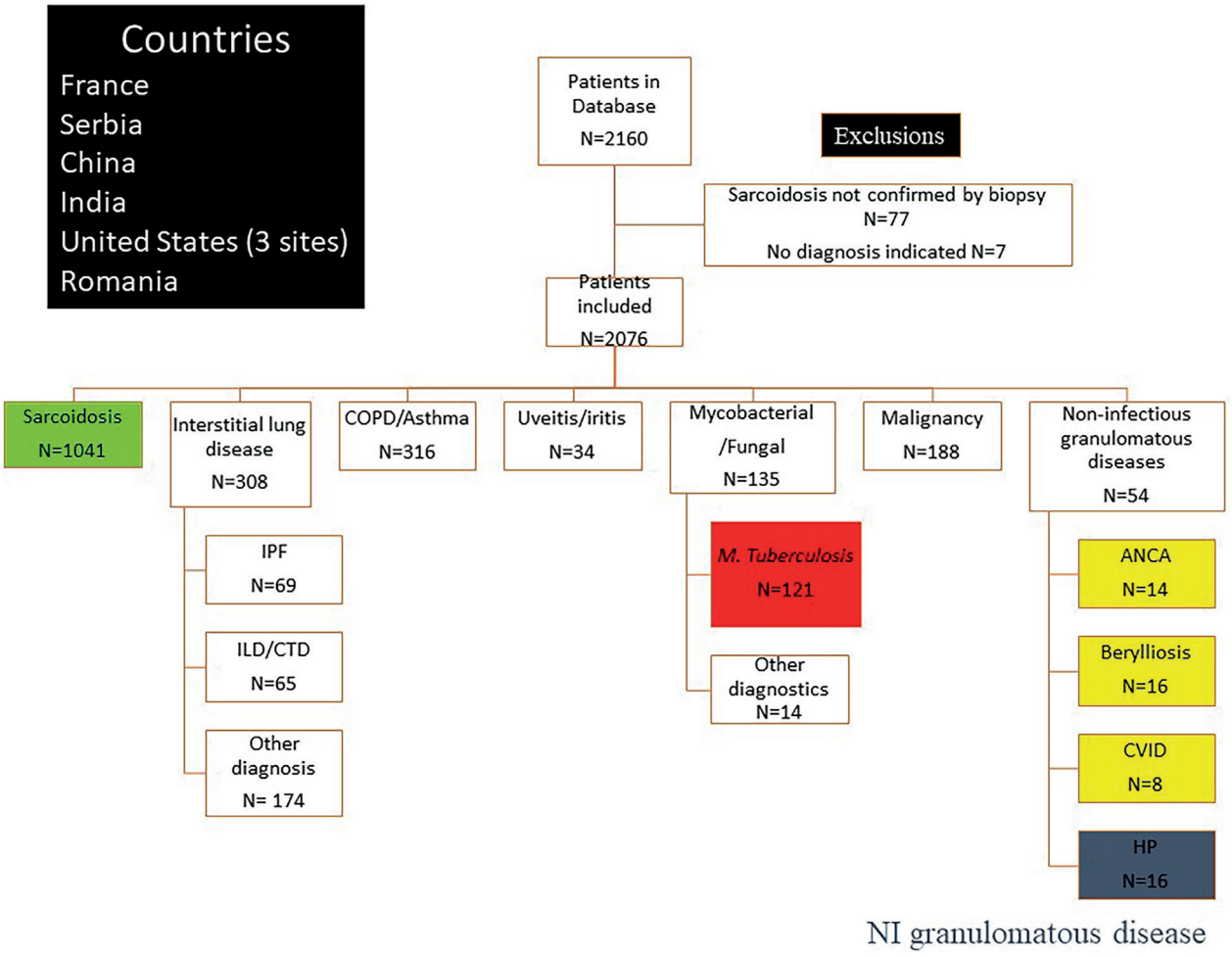

Figure 3. Flow diagram of patients in whom SDS clinical and SDS biopsy were calculated (6). Sarcoidosis patients were excluded from final analysis if no biopsy was available to confirm the diagnosis. The countries for each of the sites is noted. IPF: idiopathic pulmonary fibrosis; ILD/CTD: connective related lung disease; ANCA: ANCA related vasculitis; CVID: common variable immunodeficiency; HP: hypersensitivity pneumonitis.

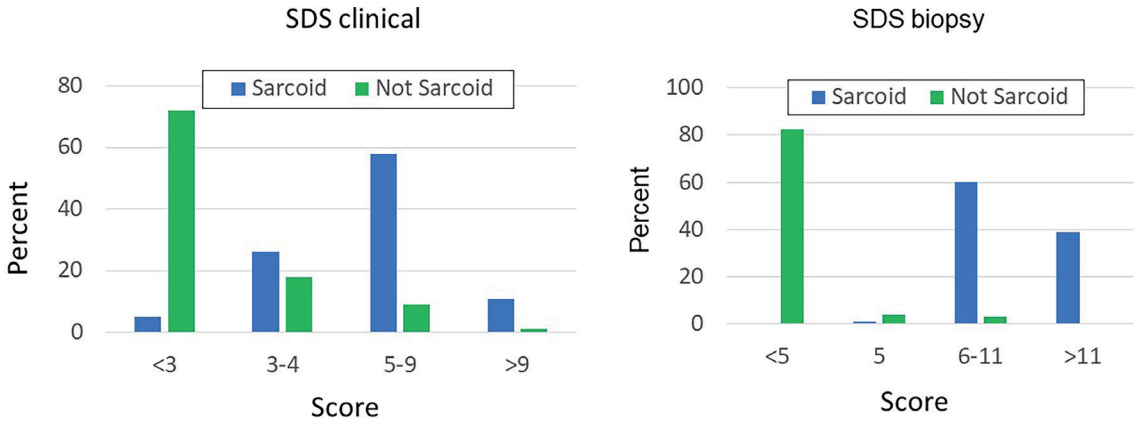

Figure 4. SDS clinical and SDS biopsy scores for patients with or without sarcoidosis from study reported by Jeny et al (6). Composition of patients in both groups shown in Figure 3. [From Jeny et al, 2023 (6), reprinted with permission of the American Thoracic Society. Copyright © 2023 American Thoracic Society. All rights reserved. Annals of the American Thoracic Society is an official journal of the American Thoracic Society].

71% of sarcoidosis patients had a SDS clinical score of 5 or greater. The likelihood ratio was 5.8 for a patient with an SDS clinical score of five or higher.

An important feature of the validation study was the inclusion of more than 120 patients with *M. tuberculosis*. The distinction between sarcoidosis and tuberculosis is important in many parts of the world, where tuberculosis is endemic (7). In general, the area under the curve for the receiver operator curves for SDS clinical was not significantly different for low versus high tuberculosis endemic centers. The SDS biopsy had a higher performance and there was no difference for tuberculosis endemic areas. The additional information from biopsy not only includes histologic confirmation of granulomas, but also tissue for culture and polymerase chain analysis (8). In patients with possible sarcoidosis, culture for mycobacteria and fungal infections adds to the diagnostic certainty of the final diagnosis.

The use of EBUS to obtain tissue for pathologic examination has become a widely used method to evaluate possible sarcoidosis. The added value of the technique is that bronchial washings can be sent for culture. Mycobacterial cultures of bronchial washings have a high sensitivity for mycobacterial infection, even in those patients with no parenchymal lung disease on chest radiography (9). The combination of SDS and EBUS represents an excellent way to enhance certainty of diagnosis of sarcoidosis.

In the future, I think the incorporation of the SDS scores into the diagnostic algorithm can improve diagnostic accuracy in clinical practice and clinical trials (Figure 5). The SDS clinical scores can be an asset particularly when biopsy may not be possible. This includes conditions such as neurologic, cardiac, or ocular sarcoidosis.

Illuminating the natural course of pulmonary sarcoidosis using placebo-controlled trials

Prednisone remains the recommended initial treatment for symptomatic pulmonary sarcoidosis (10). However, this recommendation is based on limited trials, mostly performed on asymptomatic patients with persistent infiltrates on chest x-ray (11;12). Historically the sarcoid community has felt that symptomatic sarcoidosis patients with pulmonary infiltrates (Scadding stage 2, 3, or 4) should have therapy initiated and that these patients should not be randomized to placebo therapy. This attitude has hindered our understanding of the natural outcome of symptomatic pulmonary sarcoidosis.

Once patients initiate prednisone, several studies have reported that at least half of them will require treatment for years (13-15). Since long term prednisone and other glucocorticoid treatments have been associated with cumulative side effects (16), steroid-sparing alternatives have been recommended (10;17). These include non-biologic agents such as methotrexate, azathioprine, leflunomide, mycophenolate, and hydroxychloroquine. In addition, biologic agents are prescribed such as infliximab, adalimumab, rituximab, repository corticotropin injection (RCI), and Janus Kinase (JAK) inhibitors. These have been included in the ERS recommendations for treatment

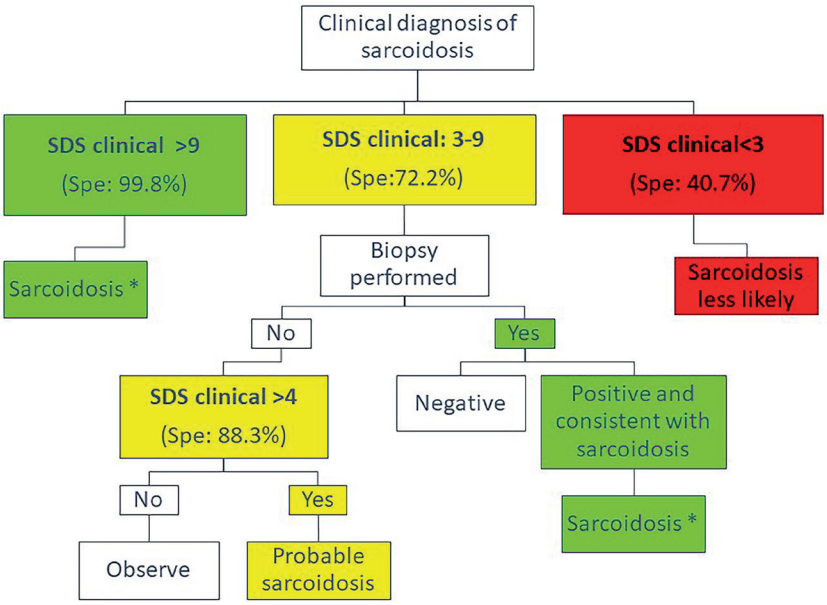

Figure 5. Use of the SDS clinical in an algorithm to diagnose sarcoidosis. *In patients with beryllium exposure, ANCA, or CVID, sarcoidosis can not be diagnosed by SDS clinical alone.
Adapted from Jeny et al, 2023 (6). ANCA: ANCA related vasculitis; CVID: common variable immunodeficiency. (Reprinted with permission of the American Thoracic Society. Copyright © 2023 American Thoracic Society. All rights reserved. Annals of the American Thoracic Society is an official journal of the American Thoracic Society).

of sarcoidosis (10). These guidelines contain few GRADE recommendations because of the limited number of placebo controlled clinical trials.

Over the past few years, placebo-controlled trials for chronic pulmonary sarcoidosis have been reported (18-26). Table 1 lists information from nine studies including 248 placebo-treated patients. These studies included patients who remained symptomatic despite receiving standard care for pulmonary sarcoidosis. The table lists what outcomes were measured in the placebo and active treatment arms. It does not comment on the effect of treatment on the outcome of the sarcoidosis. The table provides information regarding treatment at study entry. At initiation, not all patients were receiving specific sarcoidosis therapy. This data set of nearly 250 placebo treated chronic symptomatic pulmonary sarcoidosis patients educates us on the natural course of these patients.

In these studies, the most commonly reported parameter was the forced vital capacity (FVC). It has been recommended that the change in FVC % predicted be used as a measure of change in lung function (27). Seven of the studies reported the change in FVC % predicted while in an additional study (20), the change of FVC % predicted was calculated from published data. The results are shown in Figure 6 for a total of 224 patients. Only two studies reported a small, but clinically insignificant drop in FVC % predicted. In one study, the placebo treated patients had improvement in FVC % predicted of more than 2% at the end of the 48-week study. In total, these small changes in FVC for the placebo patients during prednisone withdrawal highlight the low sensitivity of FVC for identifying changes in pulmonary disease activity during treatment trials. Future studies should avoid using FVC as their sole end point and perhaps use changes in FVC only to identify whether patients are doing worse during a treatment regimen.

Many health-related quality of life (HRQoL) instruments (28;29) were reported from the nine placebo-controlled trials. The most commonly used tool was the Saint George Respiratory Questionnaire (SGRQ) (30). Figure 7 demonstrates the change of SGRQ from four studies. In all four trials a > 4-point reduction in the SGRQ score was reported in the placebo treated patients. Since the minimal clinical important difference for SGRQ is 4 (30), this implies that the placebo effect is associated with improved quality of life in the majority of patients studied.

Table 1. Summary of Outcomes Assessed in Placebo Treatment for Chronic Sarcoidosis

	Number on Placebo	Background Therapy	Study Drug	Change in FVC% Predicted	Steroid Sparing	Change in HRQoL	Duration (weeks)
MTX: Methotrexate is steroid sparing in acute sarcoidosis: results of a double blind, randomized trial. (18)	6	Prednisone	Methotrexate	Yes	Yes	No	48
EFZO: Efzofitimod for the Treatment of Pulmonary Sarcoidosis. (19)	12	Prednisone plus Cytotoxic	Efzofitimod	Yes	Yes	KSQ, FAS, SAT	24
NICO: A Pilot Randomized Trial of Transdermal Nicotine for Pulmonary Sarcoidosis. (20)	26	Prednisone	Nicoderm	YES	No	SGRQ, FAS	26
PULSAR: Results From a Phase 4, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of Repository Corticotropin Injection for the Treatment of Pulmonary Sarcoidosis. (21)	28	Prednisone plus Cytotoxic	RCI	Yes	Yes	KSQ, FAS	48
CLEAR: Phase II Investigation of the Efficacy of Antimycobacterial Therapy in Chronic Pulmonary Sarcoidosis. (22)	48	Prednisone plus Cytotoxic plus Biologics	CLEAR	Yes	No	SGRQ	16
INFLIX: Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. (23)	45	Prednisone plus Cytotoxic	Infliximab	Yes	No	SGRQ	24
FLUTIC: Use of fluticasone in acute symptomatic pulmonary sarcoidosis. (24)	11	Prednisone	Fluticasone	Yes	Yes	SF-36	48
GOLIB: Safety and efficacy of ustekinumab or golimumab in patients with chronic sarcoidosis. (25)	58	Prednisone plus Cytotoxic	Golimumab or Ustekinumab	Yes	Yes	SGRQ, FAS, SAT, SF-36	28
PENTOX: Steroid sparing effects of pentoxifylline in pulmonary sarcoidosis. (26)	14	Prednisone	Pentoxifylline	NR	Yes	No	42

CLEAR: Concurrent levofloxacin, ethambutol, azithromycin, rifabutin; FAS: Fatigue Assessment Scale; KSQ: Kings Sarcoidosis Questionnaire; RCI: repository corticotropin injection; SAT: Sarcoidosis Assessment Tool; SF-36: Short Form-36; SGRQ: Saint George Respiratory Questionnaire;

Several of the trials evaluated steroid sparing. For the methotrexate study performed at one center with only two treating physicians, steroid withdrawal was fairly uniform (18). That study was able to demonstrate a difference in the prednisone dosage between the active and placebo treated groups. However, the rate of steroid withdrawal varied from center to center. For a multi-center trial, a standard guideline to steroid withdrawal seems reasonable.

A consensus schedule for steroid withdrawal was developed and reported in 2002 (24). Despite the consensus of investigators on the dosage and rate of withdrawal, compliance per visit was less than 80% in many cases. For five of the 22 patients in the study, compliance was fifty percent or less for steroid withdrawal at individual visits. Others noted that guidelines for steroid withdrawal may often be ignored based on specific clinical situations.

In addition to reducing overall prednisone dosage, steroid withdrawal may unmask patients who will relapse once glucocorticoids are withdrawn (13;15). Figure 9 shows the percent reduction of prednisone

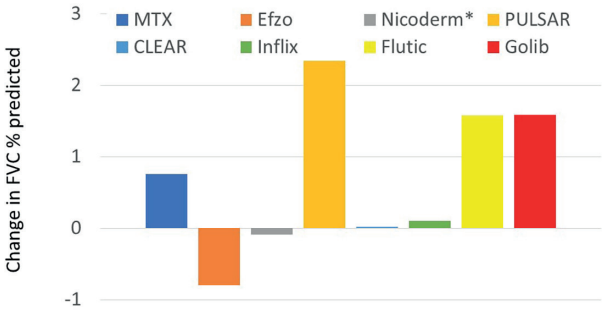

Figure 6. The change in FVC % predicted of placebo treated patients at the end of study visit for eight clinical trials (18-25). See Table 1 for details regarding individual trials. * The change in FVC % predicted for Nicoderm study was calculated from data presented in paper.

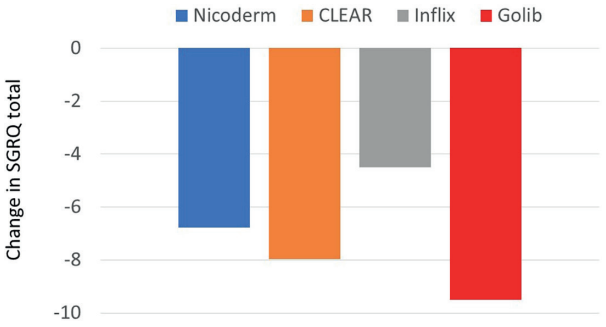

Figure 7. Change in Saint George Respiratory Questionnaire (SGRQ) total score for placebo treated patients in four clinical trials (20;22;23;25). The lower the score, the better the quality of life.

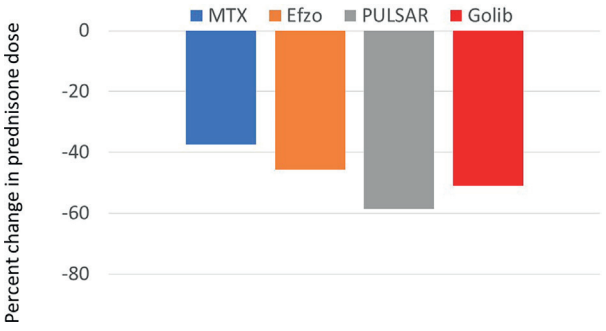

Figure 8. Percent reduction of prednisone dose for placebo treated patients in four studies (18,19,21,25).

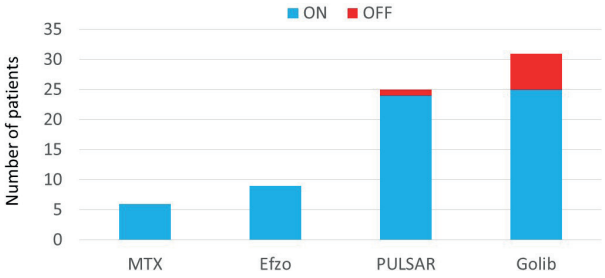

Figure 9. The number of patients who were still receiving prednisone (blue) versus those in whom prednisone had been withdrawn (red) is shown at the end of study for four clinical trials (18,19,21,25).

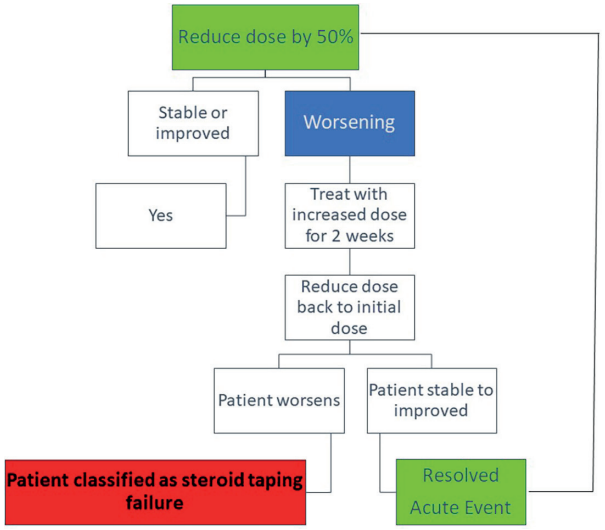

Figure 10. Proposed steroid tapering schedule. Patient on glucocorticoid therapy should be evaluated every four to six weeks. If the patient worsens, a short course of increased glucocorticoids should be instituted and dose reduced back to initial dose within two weeks. If patient requires more of longer increased treatment, then patient is classified as a steroid tapering failure.

dosage for the placebo treated patients in the four studies with available data. All four studies reported a reduction of prednisone dosage by at least 35%. In addition, about ten percent of placebo patients were able to totally withdraw from prednisone (Figure 10).

Prednisone tapering and withdrawal are commonly seen in the day-to-day management of sarcoidosis patients. In general, it is easier to withdraw prednisone than to keep the patient totally off treatment. In one study, 9 of 12 placebo treated patients flared with prednisone withdrawal (26). In several studies of chronic sarcoidosis, the relapse rate after treatment withdrawal is fifty percent (13-15). However, the relapse may not be immediately apparent. In one large study, only a third of relapses occurred within three months of drug withdrawal. Over two thirds of patients who relapsed did so within six months of prednisone withdrawal, but some relapses occurred two to three years after drug withdrawal (13).

Table 2. Summary of Outcome of Placebo Treated Patients*

Parameter Assessed	Number Studies	Number of Patients	Mean	Standard Error of Mean
Absolute change in FVC % predicted	8	224	0.59	0.785
Percent change in prednisone dose	4	71	-48.2	ND
SGRQ	4	168	-7.18	0.327

*Values were unweighted; FVC: Forced Vital Capacity; SGRQ: Saint George Respiratory Questionnaire

Several studies have employed a forced steroid tapering schedule (19;21;24). However, issues have occurred with implemented tapering. These include determining the initial steroid dose, agreeing to rate of withdrawal, assessing duration of follow-up once glucocorticoids are withdrawn, and distinguishing between an acute event requiring short course treatment versus a relapse of the underlying disease. In treating advanced pulmonary sarcoidosis, acute events are commonly encountered which respond to seven to ten days of increased prednisone with or without antibiotics (31). These are similar to the acute exacerbations seen in chronic bronchitis patients (32).

The development of a standard withdrawal protocol would be useful not only for clinical trials but in the day-to-day management of pulmonary sarcoidosis patients (27;29). Figure 6 is a proposed steroid withdrawal schedule. While the initial dose is not specified, the tapering of dosage by 50% every 4-6 weeks is consistent with previous publications.

Overall, the results of placebo treatment are important in understanding the natural history of pulmonary sarcoidosis. Placebo therapy provides a unique look at the disease variability while providing an estimate of what to expect during a clinical trial. Table 2 summarizes the outcome during placebo treatment for changes in FVC % predicted, prednisone dosage, and SGRQ. There was little change in FVC over time, like what has been noted in a large multi-center observation trial (33). Placebo treated patients may have clinically significant changes in both prednisone dosage and HRQoL. The changes seen during placebo treatment need to be considered in calculating the size of future trials. These studies reinforce the need for placebo control trials in sarcoidosis. For example, placebo treated patients had a nearly fifty percent reduction in their prednisone dose with minimal change in their forced vital capacity. Open label studies of new therapies being evaluated for steroid sparing need to be verified by placebo control studies.

Exploring multidisciplinary sarcoidosis care with centers of excellence

Sarcoidosis care has evolved from single clinics to multispecialty clinics to comprehensive care programs leading to Sarcoidosis Centers of Excellence. Sarcoidosis clinics were first established by physicians interested in providing care for both pulmonary and extra-pulmonary disease manifestations. The original international giants included Drs. D. Geraint James in London, Gianfranco Rizzato in Milan, Carol Johns in Baltimore, Louis Siltzback and Al Teirstein in New York, Om Sharma of Los Angeles, and Takateru Izumi and Sonoko Nagai in Kyoto. These global clinics and their founders eventually formed the backbone of the World Association of Sarcoidosis and Other Granulomatous diseases. Although all of these physician directors were trained pulmonologists, the leaders of the clinic recognized the multi-organ facets of the disease.

In Cincinnati, we established a multidisciplinary clinic for sarcoidosis in 1986. Staffed by a pulmonologist (RPB) and hematologist/oncologist (EEL), we have jointly seen thousands of sarcoidosis patients over the years. The initial inclusion of a hematologist/oncologist was to safely guide the administration of steroid-sparing drugs such as methotrexate and other treatments which may have hematologic consequences. Over the years, we developed treatment regimens for methotrexate (18;34-36), leflunomide (37), thalidomide (38), infliximab (39;40), rituximab (41), and other treatments for sarcoidosis (41;42). The addition of another specialist in the care of sarcoidosis patients also spurred interest in areas not usually investigated by pulmonologists. Dr. Lower's hematologist/oncologist expertise was useful in studying the hematologic aspects of sarcoidosis (43) and in evaluating breast sarcoidosis versus breast cancer (44). In addition, some of the very troublesome parasarcoidosis symptoms such as

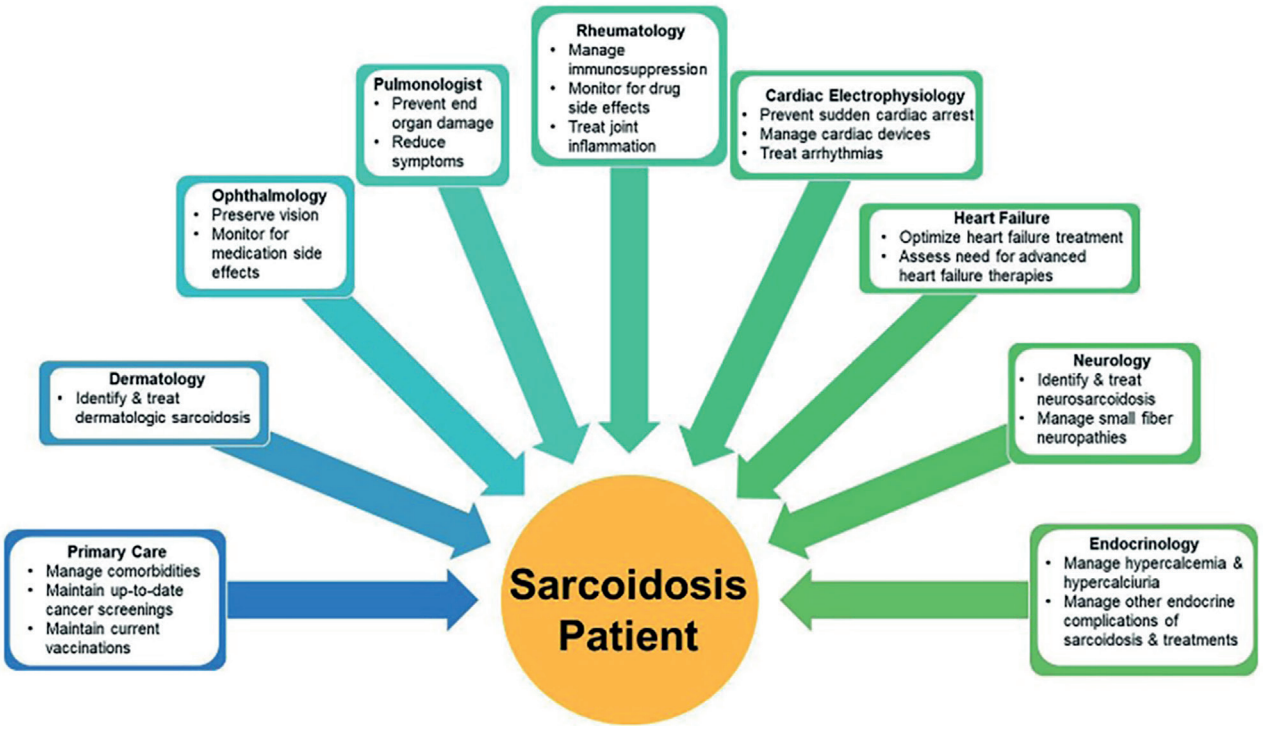

Figure 11. A multidisciplinary approach to sarcoidosis centers which includes specialists in multiple areas either physically in the clinic or available for consultation. From Kron et al (59).

fatigue and small fiber neuropathy have been encountered in cancer care. This led to observational and clinical trials for these important features of sarcoidosis which do not usually respond to anti-inflammatory therapy (45-47).

Like many current day sarcoidosis clinics, we have collaborated with specific experts dealing with other manifestations of sarcoidosis. Over the years we have completed trials for several of these manifestations of sarcoidosis including ocular disease with Dr. Adam Kaufman (48-50), sarcoidosis associated pulmonary hypertension with Dr. Peter Engel (51-53), hepatic disease with Dr. Frederick Weber (54), and cardiac disease with Dr. Alexadru Costea (55;56).

The concept of a multi-disciplinary conference has proved useful in the management of interstitial lung diseases (57). In the past few years, multi-disciplinary sarcoidosis clinics have been established in London by Drs. Athol Wells and Vasilis Kouranos and in Cleveland by Drs. Daniel Culver and Manuel Ribeiro (58). These conferences have proved useful, and other centers across the world have established similar venues to facilitate comprehensive patient management and education.

In establishing a sarcoidosis clinic, Dr. Jordana Kron proposed a model which highlights the need for input from various specialties in the field of medicine (Figure 11) (59). Patient support is necessary from other sources such as social services, physical therapy, and nutrition. While many of these specialties are unlikely to physically see all patients in the same clinic at the same time, they can be involved in a multi-disciplinary conference. Drs. Jan Grutters and Marcel Veltkamp have established such a conference in Nieuwegein.

Contemporary sarcoidosis clinical care requires multispecialty input from various experts in the fields of cardiology, ophthalmology, and neurology. Along with allied health support including physical medicine, nutrition, social work, financial counseling, and integrative health. Although ideally these comprehensive services could be provided in one setting this is impractical for al most all centers. Luckily today, these needs can often be provided to both physicians and patients via remote formats.

It is important that the WASOG provides a structure to evaluate clinical sarcoidosis care. The WASOG Centers of Excellence project started in 2016, and the first centers were chosen in 2019 (60). The most recent centers are listed at https://www.wasog.org/about/wasog-centers-of-excellence.html. The criteria to be a Center of Excellence includes an established leader interested in sarcoidosis who has identified collaborators in various specialties. As in other accreditation agencies, the criteria for a Center of Excellence will continue to evolve. In the future, we predict that the multi-disciplinary aspects of sarcoidosis will need to incorporate clinical investigation as an integral component for Center of Excellence awarding.

Conclusion

The lack of absolute certainty persists in the diagnosis of sarcoidosis. However, as one applies more standard criteria for clinical manifestations, one can be more confident in the diagnosis. Enhanced diagnostic certainly will facilitate more standard patient selection for clinical trials. For those in whom biopsy confirmation may be difficult, such as neurologic or cardiac disease, standard clinical criteria may be applied to allow for future studies.

Future clinical trials for pulmonary, extrapulmonary, and parasarcoidosis manifestations including fatigue and small fiber neuropathy need to include placebo treated groups. Data from the relatively large number of placebo treated pulmonary patients illuminates the natural course of chronic pulmonary sarcoidosis. Additionally, this education will aid in the design of future intervention trials. Although the primary end point of a pulmonary clinical trial remains debatable, the reliance on FVC is unreasonable as the only study end point.

As we have discussed many questions remain regarding sarcoidosis diagnosis, phenotyping, and treatment for all stages and manifestations. Sarcoidosis Centers of Excellence will prove a useful resource for management of sarcoidosis. Vetting of these Centers of Excellence will help to assure that the most up to date information is provided to patients. Clinical investigation and basic research are the drivers of future sarcoidosis discovery.

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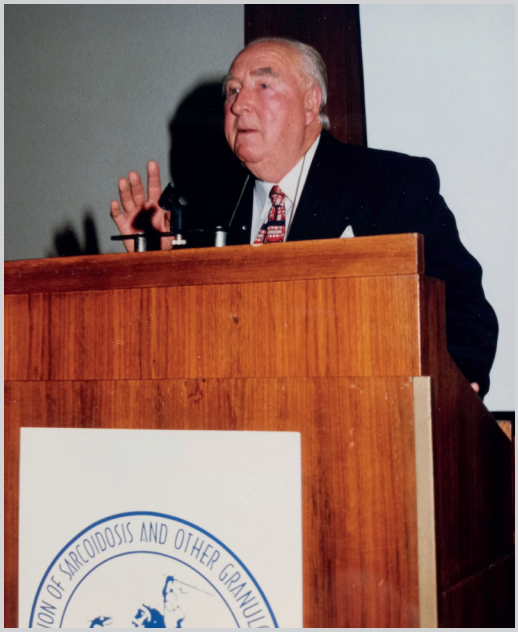
D. Geraint James



Professor James lecturing at the 5th WASOG Congress, in 1997, in Essen. Courtesy of Ulrich Costabel, MD.

David Geraint (Gerry) James (1922-2010) was a Welsh physician whose legacy embodies the best features of our work today. After serving in World War II, he studied with both John Scadding and Louis Siltzbach, and became fascinated with sarcoidosis. In 1958, he organized the first international conference on sarcoidosis at the Brompton Hospital, with 28 delegates representing eight countries. In 1959, he founded a renowned sarcoidosis clinic at the Royal Northern Hospital in London. The clinic was remarkable for its multidisciplinary approach and for training myriad specialists from around the world.

In 1987, Professor James and a small group of international colleagues founded the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) in Milan. He served as its first president. Around the same time, along with Gianfranco Rizzato, he established the journal Sarcoidosis as the official journal of WASOG. Today, the journal is known as Sarcoidosis, Vasculitis and Diffuse Lung Disease.

Besides cultivating a generation of physicians and researchers interested in sarcoidosis, Gerry James was an avid medical historian and a prolific writer. He authored approximately 1000 papers. He was known as a skillful orator and an excellent writer. His relentless passion was to improve the care and study of patients with all forms of sarcoidosis. Interestingly, his wife of 50 years, Dame Sheila Sherlock, was herself an accomplished physician who was the central individual responsible for developing the field of hepatology.

The D. Geraint James Lecture was established by the Executive Committee of WASOG to recognize an individual whose body of work exemplifies the standards exhibited by Gerry James. These include excellence in clinical care, the study and dissemination of knowledge, development of new physicians and researchers, and promotion of the worldwide sarcoidosis community.

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