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MEETING REPORT: WORLD CONGRESS ON SARCOIDOSIS

Hot issues from the fifth WASOG Meeting Essen Germany, September 17–19 1997

G. Rizzato

The World Association for Sarcoidosis and Other Granulomatous Disorders (WASOG) was founded in Milan in 1987 during the XI World Congress of Sarcoidosis (President Founder: G. James, London). After Lisbon in 1989, Kyoto in 1991, Los Angeles in 1993 and London in 1995, the 1997 meeting has been the fifth, and probably the best meeting of the series, both for the scientific content and for the social programme. It is impossible here to describe all the excellent reports and posters heard and seen in Essen, for which we refer to the abstracts that are published in a supplement of the official journal of WASOG [1]. Two hundred and eighty participants from 38 countries attended this European Respiratory Society (ERS) sponsored meeting organized by U. Costabel.

Wednesday September 17. Workshop. Treatment of sarcoidosis

The congress started with a workshop on treatment (Chairpersons: R. Loddenkemper (Berlin) and O. Sharma (Los Angeles). J. Lynch (Ann Arbor, USA) presented a state-of-the-art lecture on the use of systemic corticosteroids. After reviewing the indications for therapy (chronic patients with stage II or III pattern on the chest radiograph, extrapulmonary involvement), he examined some controversial points. While there is no debate on the usefulness of corticosteroid therapy in the short-term, the long-term efficacy is less clear, with relapses occurring in 30–70% of cases after steroid withdrawal. Possible reasons for lack of success with steroids may include the inadequate dose or duration, noncompliance of the patient, irreversible fibrosis and intrinsic corticosteroid resistance. Lynch critically reviewed some of the published studies concerning the use of corticosteroid therapy in sarcoidosis. Eule *et al.* [2] found no effect in a long-term study over 9 yrs, but the selection of the patients was not appropriate. Lynch remarked that all the patients included in this study were free of sarcoidosis-related symptoms and had no significant functional impairment. Gottlieb *et al.* [3] showed a wide difference in relapses in patients with spontaneous remission (8% relapse) *versus* corticosteroid-induced remission (74% relapse), but their study was retrospective, and the results could be different in a prospective study.

Lynch suggested a protocol of prednisone, 40 mg daily for 4 weeks, then tapering, with some patients needing therapy indefinitely. In the discussion, Y. Kataria (Greenville, NC, USA) stated that it is not possible to establish fixed treatment protocols for a disease that is so variable. Doses and duration of therapy should be individualized for single patients.

The second topic of the workshop was corticosteroid therapy administered by inhalation, with two speakers: O. Selroos (Lund, Sweden; in favour) and N. Milman (Nasetved, Denmark; against). Selroos remarked that systemic corticosteroids are the drug of choice, but side-effects are frequent. Budesonide has no adverse effects, if minor throat irritation in 8% of patients is excluded. He presented some of the work of his group on this subject, and in particular the multicentre, double-blind, placebo-controlled study by Pietinalho *et al.* [4], with over 189 patients from 20 centres in Finland. After 3 months of prednisolone therapy (20 mg daily starting dose; or placebo), patients were shifted to inhaled budesonide, 800 μg *b.i.d.* for 15 months (or placebo). In 94 stage I patients, no difference was observed in the two groups. For 84 stage II patients active treatment resulted in significantly greater improvement in forced vital capacity (FVC) and transfer factor of the lung for carbon monoxide, but not in chest radiograph findings. Selroos concluded that inhaled budesonide is an effective alternative to oral steroids in the maintenance treatment of pulmonary stage II sarcoidosis.

Milman reported a study by his group [5] on a small group of patients who were given budesonide (*versus* placebo) at the dose of 1.2 mg·day^{-1} for 1 yr. No significant differences were observed in clinical parameters, lung function or angiotensin converting enzyme (ACE) course. In addition, taking into account a predominantly negative work by Alberts *et al.* [6], his conclusion was that no recognizable therapeutic effect on pulmonary sarcoidosis may be attributed to inhaled budesonide. However, he commented that some patients with sarcoid bronchitis might benefit, so a study, limited to patients with obstructive endobronchial sarcoidosis, should be performed.

In the discussion, the chairman (R. Loddenkemper) asked who in the audience was using inhaled steroids in pulmonary sarcoidosis. Just a few hands were raised; the great majority of the audience were not using inhaled steroids in sarcoidosis.

The following speaker, R. Baughman (Cincinnati, USA), presented his experience with methotrexate as a steroid sparing agent in sarcoidosis. The rationale for its use in sarcoidosis is derived from the fact that methotrexate is a well-established steroid sparing agent in rheumatoid arthritis. Its major effects are on macrophage function and on T-lymphocytes. A recent publication by his group

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[7] reported the safety and efficacy in 50 symptomatic patients who completed at least 2 yrs of therapy with methotrexate (although the drug was given for up to 7 yrs in some patients). The drug was used for a number of reasons: 27 patients wished to avoid prednisone; seven patients had no response to prednisone; seven had intolerable side-effects from prednisone. The dosage (5–10 mg administered once a week) was adjusted according to the patient's white blood cells count. The efficacy of the treatment was good, and the rarity of toxic effects clearly indicate that the drug has a place in the therapy of sarcoidosis. Liver biopsy was carried out in 41 patients after 2 yrs of therapy. In 19 patients it was normal, 16 patients showed sarcoid granuloma, and four showed liver toxicity that induced the physician to stop the therapy. In two other patients, a second liver biopsy carried out after 4 yrs of therapy showed liver toxicity that induced termination of therapy. Other reasons for withdrawing therapy were non-compliance in four patients and questionable efficacy in six. Thirty eight patients stopped therapy, 26 deteriorated after withdrawal, and 21 were restarted, all of whom had some further improvement during the second course. When administering methotrexate, monitoring should include haematological profile, liver enzymes and creatinine.

J. Müller-Quernheim (Borstel, Germany) discussed the use of chloroquine and azathioprine. Chloroquine (250 mg·day^{-1}) and hydroxychloroquine (200 mg·day^{-1}) appear to be equally effective, and their usefulness has been demonstrated, especially in sarcoidosis of the skin and in calcium metabolism abnormalities (hypercalcaemia and hypercalciuria). Their major action is probably to block the release of cytokines and 1-25(OH)2D3 by activated macrophages. Azathioprine is still an experimental drug in this disease, its rationale is based on the reduction of both CD4/CD8 ratio and tumour necrosis factor (TNF) production, but clinical experience is limited.

P. Zabel (Borstel, Germany) presented his experience with pentoxifylline (POF) [8].The rationale for it use lies in its capacity to inhibit the synthesis of TNF, both *in vitro* and *in vivo*. Eighteen patients with disease progression during the preceding 3 months were treated with POF, 25 mg·day^{-1} *per os*, and followed for 6 months of therapy. Eleven improved and seven remained stable. Zabel concluded that POF may improve therapeutic regimens in pulmonary sarcoidosis, either by sparing, or replacing corticosteroids. In the discussion, G. Rizzato (Milan, Italy) noted that one of the criteria of improvement was a 10% increase in the $T_{L,CO}$, a very small difference that could simply be due to chance fluctuation of this parameter. Moreover, more than 50% of patients were stage I or II, meaning that the improvement could be due to the natural remission of the disease especially when there is no control group.

C. Agostini (Padua, Italy) discussed the future immunological approaches with new immunomodulators offering considerable promise as adjuvant therapeutic agents for patients with sarcoidosis who do not respond to steroids or have severe corticosteroid-induced side-effects. At least 20 different cytokines have been related to the pathogenesis of sarcoidosis, and the redundance of cytokines released at sites of disease activity suggests that it is difficult to believe that a monotherapy with conventional immunosuppressants may modify the clinical course of sarcoidosis, which shows a high intrinsic variability. In theory, combination of two or more agents, acting at multiple levels, could offer the possibility of targetting different cytokines and effector cells, amplifying and prolonging the benefit of conventional therapies.

There have been clinical trials with xenobiotics that affect T-cell activation at the level of interleukin (IL)-2 transcription factors (nuclear factor-activated T-cells (NF-AT)), including cyclosporine-A, but the majority of the data have been disappointing, partly because cyclo-sporine-A does not suppress the release of macrophage-derived cytokines which influence T-cell proliferation and recruitment at the sites of the sarcoid inflammatory process. Since the outcome of sarcoidosis is clearly related to the lung injury and the consequent development of lung fibrosis, an alternative approach could be to concentrate on the cytokines that cause the most long-term pulmonary damage. For instance, the use of antiTNF-α therapy with monoclonal antibodies or engineering antibody molecules are emerging as promising prospects in the control of events that favour the enhancement of local effector cell functions at sites of inflammation. Another approach may be to block specific effects of mediators that drive the process of fibrogenesis with specific antisense oligodeoxynucleotides or with agents competing for binding with cytokines, including TNF-receptor fusion proteins. Finally, research on counter-receptors that are needed to provide co-stimulatory signaling to lung T-cells (including CD40/CD154, CD80, CD86/CD28, CD152) leads us to expect that therapeutic agents could be designed to inhibit signal transduction pathways that drive T-cell activation in sarcoidosis. Nonetheless, the overall message is that the place of biological immunosuppressants in the therapy of chronic diseases, including sarcoidosis, is not clear. In particular, it is not yet known whether the benefit of treatment justifies the manufacturing costs of biological immunosuppressants in sarcoidosis.

ATS/ERS/WASOG statement on sarcoidosis

The guidelines for sarcoidosis have been in preparation for a year. The initiative was solicited by G. Rizzato, and thanks to the capacity of U. Costabel, and the initial drive of the American Thoracic Society (ATS), three scientific societies united their efforts in order to produce one document. Under the chairmanship of U. Costabel (Essen, Germany) and G. Hunninghake (Iowa City, USA), a panel of 15 members met in New York (December, 1996), in San Francisco (May, 1997), and in Essen (September 1997). The first presentation of the results to an open audience (Chairpersons: G. James, London and T. Izumi, Kyoto) was given on Wednesday September 17, at the Essen Congress. Epidemiology was presented by C. Rose (Denver, USA), Aetiology by S. Aguayo (Atlanta, USA), and Immunology by G. Semenzato (Padua, Italy). In the session on the clinical approach, three speakers illustrated the Clinical Presentation of Sarcoidosis (O. Sharma, Los Angeles, USA), Pathology (M. Kitaichi, Kyoto, Japan), and the Diagnostic Approaches and Staging (G. Rizzato, Milan, Italy). Prognosis and Natural History was presented by J. Lynch (Ann Arbor, USA) and Treatment and Follow-up by R. Baughman (Cincinnati, USA). There is no room here for even the main points of the guidelines;

however the full document will appear simultaneously in both the *American Journal of Respiratory and Critical Care Medicine and Sarcoidosis Vasculitis and Diffuse Lung Disease.*

Thursday September 18. Sarcoidosis

The whole day was devoted to sarcoidosis, with three Plenary Sessions.

Plenary Session I. Aetiology

Chaired by R. Dubois (London, UK) and R. Baughman (Cincinnati, USA), this session was opened by A. Teirstein (New York, USA) and C. Johns (Baltimore, USA), who presented the programme of a wide multicentre study from the National Heart, Lung and Blood Institute which had just begun. The name, ACCESS study, means A Case Control Etiologic Study of Sarcoidosis. Seven hundred and twenty patients over 18 yrs of age, all with tissue confirmation of their sarcoidosis in the last 6 months, and 720 matched controls were in the process of being recruited. There will be a follow up of at least 2 yrs. The major aim is to study the aetiology of sarcoidosis. A number of different investigations will be performed, including human lymphocyte antigen (HLA) typing, infective agents, deoxyribonucleic acid (DNA) polymerase chain reaction (PCR), cell wall deficient forms of mycobacteria, aetiologic antigen in Kveim reagent, pathogenic T-cells and immunogenetics. However, family history, socioeconomic status and psychological profile will also be objectives of the study. The results will probably be known at the beginning of the 21st century.

After a number of very interesting free communications at a high scientific level, for which we refer to the abstracts, the session was closed with a keynote lecture on the issues of T-helper-1 and T-helper-2 (Th1, Th2) by G. Semenzato, (Padua, Italy). Taking advantage of the availability of pure recombinant cytokines and molecular probes for cytokines and their receptors, it has been possible to study in detail the involvement of several cytokines in the pathogenesis of sarcoidosis. Semenzato summarized the interactions between cytokines and their receptors, which define regulatory networks that ultimately contribute to the sarcoid granuloma formation and fibrosis development at sites of disease activity. The compartmentalization of different regulatory T-cells probably has distinct effects on the evolution of the granuloma. While CD4 positive cells predominate in the inner area of sarcoid granulomas, the few CD8 cells that are present predominate in the outer margin of the lymphocyte rim. However, there are data supporting the hypothesis that the different pattern of cytokine production by T-cells and, in particular, alteration in the Th1/Th2 balance may also influence the evolution of granulomatous lung inflammation. T-cells isolated from patients with active sarcoidosis show a dominant Th1 cytokine expression, with elevated messenger ribonucleic acid (mRNA) and protein levels of interferon-γ (IFN-γ), IL-2 but not IL-4. Furthermore, sarcoid alveolar macrophages (AMs) produce high amounts of IL-12, a cytokine that stimulates IFN-γ production, the proliferation of activated T-cells and is involved in the differentiation of Th0 cells into Th1 cells. There are also data indicating that macrophage-derived chemoattractant cytokines (including IL-8, IL-15, IL-16, IFN-γ inducible protein-10 (IP-10) monokine induced by IFN-γ (MIG) and regulated on activation, normal T-cell expressed and secreted (RANTES)) co-operate in the expansion of the intra-alveolar pool of CD4 memory cells within the inflamed areas. Once inside the sites of involvement, these freshly recruited cells contribute to the development of the newly forming granuloma structure.

Plenary Session II. Pathogenesis

Chaired by G. Semenzato and J. Müller-Quernheim, this session was opened by D. Moller (Baltimore, USA) with a lecture on Cells and Cytokines involved in the Granuloma Formation. He showed that IL-12 concentration is high in the bronchoalveolar lavage (BAL) fluid of sarcoid patients compared to controls or idiopathic pulmonary fibrosis patients. He hypothesized that dysregulated production of IL-12 from tissue macrophages, and probably dendritic cells, is critical to the initiation and maintenance of granuloma formation. Consistent with this hypothesis, enhanced production of transforming growth factor (TGF)-β, a potent inhibitor of IL-12, has been reported to be a predictor of spontaneous remission in sarcoidosis. He has found that pentoxifylline and thalidomide are potent inhibitors of IL-12 production, thereby providing a mechanism for the beneficial effects reported for these drugs in sarcoidosis.

J. Gauldie (Hamilton, Canada) in his keynote lecture provided an overview on the potential utility of studying transgenic and knock-out mice in the comprehension of the mechanisms leading to pulmonary fibrosis. Transfer of granulocyte/macrophage colony stimulating factor (GM-CSF) gene to rat lung induces eosinophilia, monocytosis and fibrotic reactions. GM-CSF overexpression did not enhance production of TNF-α in a significant manner, while the content of TGF-β1 was markedly induced in the lung. After GM-CSF gene transfer, AMs spontaneously released significant quantities of TGF-β *in vitro*, favouring the emergence of α-smooth muscle actin-rich myofibroblasts. Therefore, the hypothesis is that GM-CSF, which is actively released in sarcoid lung, may play a direct role in pulmonary fibrogenesis. It also appears that the GM-CSF transgenic lung model can be considered an ideal approach for testing cellular and molecular events involved in pulmonary fibrosis leading to the end-stage-lung of sarcoid patients.

Plenary Session III. Diagnosis and treatment

Chaired by N. Konietzko (Essen, Germany) and G. Rizzato (Milan, Italy), this session was opened with a lecture by A. Wells (Auckland, New Zealand) on CT imaging in sarcoidosis and diffuse lung disease. He mainly discussed the potential role of computed tomography (CT) in defining reversible disease. A nodular pattern is almost invariably reversible, reticular abnormalities and anatomical distorsion denote a fibrotic histological picture, ground-glass opacification may be indicative of alveolitis or fine fibrosis. However, in clinical practice, use of CT influences therapeutic decisions in a minority of cases. The greatest diagnostic utility of CT lies in difficult cases of

diffuse lung disease with wide differential diagnosis; sarcoidosis can sometimes be diagnosed confidently, and can often be excluded when CT appearances are pathognomonic of an alternative disease such as extrinsic allergic alveolitis, lymphangitic carcinomatosis or fibrosing alveolitis.

Another keynote lecture was given by L. Newman (Denver, CO, USA) who compared sarcoidosis and berylliosis. Clinically, these two granulomatous disorders are very similar, but sarcoidosis tends to present more often with hilar lymphadenopathy, and more often affects extrapulmonary organs. On histopathology, the two conditions are indistinguishable. The immunological responses, as well as the history of beryllium exposure, are most useful in differentiating between these diseases. In berylliosis, lymphocytes from blood or BAL fluid proliferate in re-sponse to *in vitro* stimulation with beryllium sulphate, whereas sarcoidosis cells do not. Similarly, patients with berylliosis demonstrate a delayed-type hypersensitivity skin response to beryllium salts. Both disorders are associated with a lymphocytic alveolitis, CD4+ T-cell clones that express a limited set of T-cell antigen receptors, and which produce Th1-type cytokines. Both conditions have been associated with allelic differences in major histocompatibility loci. Macrophages in both disorders produce high levels of cytokines and growth factors that promote nonspecific inflammatory responses.

G. Rizzato (Milan, Italy) presented the changing strategies of lung biopsy in diffuse lung disease in Italy. Videothoracoscopic lung biopsy (VTLB) has now replaced open lung biopsy (OLB) when transbronchial biopsy is negative. A series of 65 VTLB procedures was compared to a previous series of 68 OLBs. VTLB compares favourably to OLB for lower need for analgesia, lower blood loss in the first postoperative day and shorter postoperative stay. VTLB is, at present, the clue to diagnosis in 17% of sarcoid patients in Italy. A. Teirstein (New York, USA) remarked that the higher cost of VTLB due to disposable materials should be a reason to prefer OLB. G. Rizzato replied that his analysis was not aimed at an evaluation of costs, although a similar comparative study from the UK [9] disclosed that reduced postoperative disability in the VATS group decreased hospital stay, offsetting the increased cost in disposables. Furthermore, L. Newman (Denver, USA) argued that the lower pain should also be taken into consideration when evaluating the global cost of the two procedures.

R. Loddenkemper and N. Schönfeld (Berlin, Germany) presented a prospective multicentre German study aimed at establishing indications, modalities and duration of a systemic corticosteroid therapy. Patients were randomized to receive either 6 or 24 months of therapy. Both groups showed a slight increase in vital capacity without differing significantly from each other. The conclusion was that a systemic steroid treatment should be initially planned for no longer than 6 months. A prolonged treatment based on the individual course of the disease is needed only in a minority of patients.

The closing lecture was given by G. James (London, UK) on Life-threatening Situations in Sarcoidosis. Lung, heart, kidney, liver and brain are the key organs where damage could cause death, and the management of each situation has been adequately discussed. Moreover, although not life-threatening, the quality of life may be grossly affected, and this may lead to a shorter life expectancy, due to conditions such as uveitis, blindness and adverse effects of corticosteroid therapy. One poster of remarkable interest on this subject was presented by D. Winget (from Baughman's group, Cincinnati, OH, USA), on Liver Function Abnormalities in Sarcoidosis. He observed liver function abnormalities in 18% of 652 sarcoid patients. Five had variceal bleeding at presentation, and two died of hepatic failure. Moreover, obstructive jaundice due to lymph node compression was seen in one patient. The most frequently impaired liver test was alkaline phosphatase; its serum level was moderately elevated in 54 patients and severely elevated in 20.

Friday September 19. Other granulomatous and interstitial lung diseases

There were also three Plenary Sessions on Friday.

Plenary Session IV. ANCA-associated vasculitis

Chaired by W. Gross (Bad Bramstedt, Germany) and R. De Remee (Rochester, USA), this session was opened with a keynote lecture by E. Csernok on Pathogenesis of Wegener's Disease. Wegener granulomatosis (WG) is a single disease but displays a set of clinical manifestations each with a different immunopathogenesis. The different clinical manifestations are characterized by multiple immune abnormalities that culminate in the overproduction of autoantibodies directed against proteinase 3 (PR-3), an important neutrophil protease (PR3-antineutrophil cytoplasmic antibody (ANCA)). There are a number of observations that suggest potential mechanisms by which the production of ANCA could result in neutrophil-mediated vascular injury. The most common postulated scenario for ANCA-mediated vasculitis involves neutrophil and monocyte adhesion to and penetration of vessel walls, *via* cell adhesion molecule interaction, with release of lytic enzymes and toxic oxygen radicals. The proposed initiating pathway is ANCA-induced leucocyte activation. Cell-derived mediators are intimately involved in these events. The result is necrotizing inflammation of vessel walls. However, the pathological hallmark of WG is the coexistence of vasculitis and granuloma. The causative agent leading to granuloma formation is still unknown, but the presence of granulomatous inflammation indicates T-cell hyperactivity. Immunohistochemical studies have shown that the cellular infiltrations in renal and pulmonary lesions contain primarily macrophages and CD4+ T-cells. It has recently been demonstrated that CD4+ T-cells from granulomatous lesions in the nose and from BAL fluid predominantly express the Th1 cytokine IFN-γ, which predominantly stimulates cell-mediated immune responses. This supports the hypothesis that due to the two-phase course of WG, a polarization of T-cell subpopulations (Th1 *versus* Th2 type) occurs, which may explain the transition from the initial granulomatous phase to the generalized systemic vasculitis phase.

Another keynote lecture was given by U. Specks (Rochester, USA) on diagnosis and treatment of ANCA-related disorders. Despite ANCA-testing, the diagnosis

remains a clinicopathological one. Immunosuppressive therapy including oral cyclophosphamide continues to be the most effective treatment approach. The suggested dose is 2 $mg \cdot kg^{-1} \cdot day^{-1}$ for at least 1 yr before tapering, but in some cases doses up to 5 mg are needed. Side-effects are frequent: cystitis occurs in 43% of patients, 2.8% develop bladder cancer, 2% develop myelodysplasia and lung fibrosis is less frequent. In order to reduce side-effects, it is better to give the drug in the morning. Moreover, some alternatives like cotrimoxazole or low dose (20–25 $mg \cdot week^{-1}$) methotrexate (MTX) (plus folic acid) are being evaluated and appear to be good choices during remissions. Prednisone (1 $mg \cdot kg^{-1} \cdot day^{-1}$) is given together with MTX. Lifelong therapy with cotrimoxazole is well tolerated. Stent placement for airway involvement and renal transplantation in patients with end-stage renal disease have shown promising results.

Plenary Session V. Extrinsic allergic alveolitis

Chaired by P. Haslam (London, UK) and J. Grunewald (Stockholm, Sweden), this session was opened with a lecture by M. Ando (Kumamoto, Japan) reviewing the broad range of organic dusts and microbial and inorganic antigens known to cause extrinsic allergic alveolitis. Immunological studies are sometimes necessary to determine the causative agent, and inhalation provocation with the suspected antigen is the only reliable test to determine the causative agent. In a further lecture C. Vogelmeier (Munich, Germany) reviewed some basic mechanisms of this disease.

Plenary Session VI. Other granulomatous and interstitial lung disease

Chaired by D. Kirsten (Grosshansdorf, Germany) and J.F. Cordier (Lyon, France), this session was opened with a lecture by F. Erkan (Istanbul, Turkey) on Behçet's disease. She discussed the major complications of pulmonary vasculitis, leading to aneurysm formation with adjacent bronchial erosion and possible rupture into a bronchial lumen leading to haemoptysis, which may be fatal. Pulmonary vasculitis may also result in arterial or venous thrombosis, with infarct areas of various sizes. The new techniques, such as spiral CT or magnetic resonance (MR) are very useful for the study of such aneurysms. A combination therapy with high dose cyclophosphamide and prednisone has proved useful in obtaining regression or disappearance of aneurysms in nine cases. Two patients, however, ultimately died, although their aneurysms had showed a 25–50% radiological regression.

J.F. Cordier (Lyon, France) has discussed the topic "Nonspecific Interstitial Pneumonia (NSIP): Really a New Entity?". He reviewed 12 cases with this diagnosis given on the basis of an open lung biopsy. Most patients presented with dyspnoea and cough, accompanied by crackles on auscultation. All had diffuse infiltrative opacities on chest radiography, and a reduced value of $T_{L,CO}$. BAL fluid examination showed alveolitis in all patients, with a high-intensity lymphocytosis (>28%) in eight of 12 patients, and a neutrophilic or mixed pattern in the others. CT showed ground glass and alveolar opacities, and thickening of septa. Histologically, varying proportions of inflammation and fibrosis were seen. Marked improvement was obtained in 10 out of 12 patients with corticosteroids, associated in some with immunosuppressants. The response to therapy appeared much better than in usual interstitial pneumonia. Cordier concluded that, after exclusion of extrinsic allergic alveolitis, drug toxicity and collagen vascular diseases, idiopathic NSIP merits status as a clinicopathologic entity.

The last lecture of the session was given by T. Izumi (Kyoto, Japan) on lymphangioleiomyomatosis (LAM). He presented 64 LAM cases from 41 Japanese hospitals. Major symptoms were dyspnoea (57%) and cough (33%). Pneumothorax occurred in 52% of patients. Several modalities of hormone therapy were evaluated, but improvement was observed in only one patient. In comparison to European and American patients, clinical features appeared less pronounced and the rate of survival appeared higher in Japanese patients. These differences might be due to earlier detection enabled by the easy access to medical facilities in Japan. In the discussion, O. Sharma (Los Angeles, CA, USA) observed that LAM may return in the transplanted lung.

It is regrettable that many other interesting communications and posters cannot be taken into account in this report, but at least one other poster should be mentioned; this is again from Cincinnati (Lower and Baughman: Breast Disease in Sarcoidosis). Of 649 patients seen in the Cincinnati Sarcoid Clinic, 449 were females. Six presented with a breast mass, and neither physical examination, nor mammography was useful in distinguishing between sarcoidosis and cancer. In all six cases, biopsy was performed to rule out cancer.

Conclusion

This was a very satisfactory congress. The organization, in the sure hands of U. Costabel, was perfect and the social programme and setting were very agreeable (fig. 1).

Fig. 1. – Hugenport Castle, near Essen, where the invited speakers' dinner was held.

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