Treatment of rheumatoid polyarthritis with synthetic D-penicillamine 'Ho-Bay 950'. A. Santamaría, P. Barceló, M. Menchón, R. Ruiz de la torre, and M. Ripolls Gómez

Twenty patients affected with rheumatoid polyarthritis were treated from 6 to 14 months with synthetic D-penicillaminase (900 mg/d). Clinical improvement was evident, with the decrease of ESR beginning with the third month, thereby permitting the decrease and even the suspension in 7 cases of the dosage of steroids. The Cu and Fe decreased somewhat, but always within the normal physiological limits. Serological values decreased, attaining negativization in 10 cases. Similarly there was a decrease of IgG and IgM; serum C_1 and C_3 became normal. The 'R rosette' test showed an increase. Histological study of the synovial tissues showed favourable evolution of the inflammatory alterations. All of the changes became manifest beginning with the third or fourth month. The only side effects encountered were light proteinuria in one case, hypogeusia in 2, and skin rash with pruritus in another 2 which did not cause suspension of treatment.

Neutrophil chemotaxis in patients with rheumatoid arthritis: mechanisms responsible for impairment. A. G. Mowat (*Nuffield Orthopaedic Centre, Oxford*)

The polymorphonuclear leucocyte (PMN) is vital for the control of bacterial infection and plays a major role in wound healing. Most of the phases of PMN activity in the extracellular space, including phagocytosis and cell killing, are normal in patients with rheumatoid arthritis but chemotaxis is impaired (Mowat and Baum, 1971). The low mean chemotactic index $\pm$ 1 SD in patients with rheumatoid arthritis (369 ± 87) compared with controls (544 ± 78) has been confirmed. One suggested mechanism of prior ingestion of immune complexes has been supported by the demonstration of a significant correlation between the amount of soluble immune complexes in the serum and the chemotactic index in 21 unselected inpatients ($P < 0{\cdot}01$).

However, other mechanisms alter the chemotactic index. The mean index $\pm$ 1 SD in 21 patients with rheumatoid arthritis undergoing orthopaedic surgical treatment improved from a preoperative value of 369 ± 87 to 486 ± 98 on the second postoperative day, with a gradual fall to 433 ± 125 on day 6 and 372 ± 70 on day 14. Blood transfusion did not cause the improvement. Patients receiving corticosteroids showed a higher initial value with a smaller rise. Control subjects with osteoarthrosis showed no change over the period of an operation of similar magnitude. Although it seems likely that these changes are related to changes in blood cortisol levels, no alteration in the index can be produced by incubating the PMN with hydrocortisone *in vitro*. The results may explain the modest increase in incidence of bacterial infections during life and the relatively normal wound healing in these patients (Garner, Mowat, and Hazleman, 1973) despite all the factors which might be expected to seriously alter these findings. Further, the increased incidence of bacterial infection as a cause of death may reflect the failure of the PMN to recover normal chemotaxis at this point.

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Neutrophil immune complex interactions: possible contributions to rheumatoid inflammation. R. Turner, R. Collins, M. Parker, and L. De Chatelet

Previous studies have suggested that phagocytosis of immune complexes by neutrophils produces metabolic and functional alterations of these cells which may be important in the inflammatory process occurring in rheumatoid arthritis. Studies from our laboratories have described an *in vitro* system for the study of neutrophil phagocytosis of immunoglobulin G-rheumatoid factor (IgG–RF) complexes (Turner and others, 1973) and a system for measuring the uptake of chromium-51 tagged complexes has been utilized (Turner and others, 1974) to further study this phenomonon. These studies are extended here utilizing the chromium tagged immunoglobulin G system and the measurement of hexose monophosphate shunt activity by the conversion of glucose l-14 carbon CO_2 to study the interactions between soluble and insoluble complexes, rheumatoid factor, and neutrophils.

Results to date utilizing neutrophils incubated with various substances for 30 minutes at 37°C have shown: (1) neutrophil uptake of insoluble IgG complexes was not significantly affected by the addition of rheumatoid factor to the system (mean $\pm$ SEM uptake live-killed cells $n = 6$: IgG $= 19 \pm 3$, IgG–RF $= 20 \pm 7$). This addition also failed to significantly change the hexose monophosphate shunt activity of the neutrophils (phagocytosing-resting cpm $^{14}CO_2$: IgG = 16 131; IgG–RF = 18 125). (2) Soluble immunoglobulin G complexes in the same concentration as the insoluble complexes were not significantly taken up by the neutrophils and did not trigger an increase in shunt activity even in the presence of rheumatoid factor (phagocytosing-resting cpm $^{14}CO_2$: IgG = 126, IgG–RF = 296. (3) Rheumatoid factor added to soluble immunoglobulin G complexes produced precipitation of 77% of these complexes. Our studies therefore have shown that only insoluble IgG and/or IgG-RF are capable of being taken up by the neutrophils and of producing metabolic changes in these cells.

Additional studies are in progress to delineate further the interactions of complexes and neutrophils in the inflammatory process which may be occurring in the joints of patients with rheumatoid arthritis.

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A new associate spondyloarthritis. Does 'rheumatoid spondylo arthritis' exist? J. Rotés Querol, J. Tena, J. A. del Olmo Bru, J. Granados, J. Comulada Taberner, and J. Mitja Piferrer

We observed that all cases had clinical, radiological, and biological features common to both diseases but none were characteristic of one or the other. On the basis of these data we consider these cases not as mixed processes of AS and RA but rather as two different diseases. Fallet, on the basis of a simple coincidence of both diseases, estimated the frequency rate being between 1/500 and 1/2000 for AS and 1/100 for RA; the statistical possibility of encountering such a coincidence would range from 1/50000 to 1/200000.

From the study of our cases we think that the process does not seem to be a coincidence of both diseases but rather of the action of the X factor or factors of RA upon the domain of AS which would result in a variant of associate AS. This would be the true 'rheumatoid spondyloarthritis'. Its rate of frequency, since the predominance of AS marked by HL-A 27 is 6% in our country, would be somewhat higher than that reported by Fallet, if our hypothesis proves to be correct. Evidently it would not reach the ratio of 1/1600 which is the ratio to be expected if every factor of RA, by incidence of the HL-A 27, would cause this mixed picture.

Ankylosing spondylitis and epidemic Reiter's syndrome: genetics and environment. A. Calin and J. F. Fries

The greatly increased frequency of HL-A 27 in both ankylosing spondylitis (AS) and Reiter's syndrome (RS) has been well recognized. Both environmental and genetic factors appear to contribute. To elucidate this interplay, two parallel studies were performed.

(1) Evaluation of 78 presumed 'healthy' HL-A 27 positive blood donors (30 males, 48 females) yielded 14 cases (20% and 16·7% respectively) of definite AS, the New York criteria being used as a minimum standard. 122 race, sex, and age-matched HL-A 27 negative controls failed to yield a single case. Using published disease frequencies, the expected prevalence of AS among HL-A 27 positive individuals should be 2% and 0·2% for males and females, respectively. In contrast, this study strongly suggests that at least 20% of subjects with HL-A 27 are likely to develop AS, and that the frequency is comparable in both sexes. (2) An attempt was made to locate and HL-A type the 9 men who developed RS after the 1963 epidemic of proven shigellosis in 602 individuals on a U.S. naval ship. To date, 5 have been traced and 4 of these are HL-A 27. Given the racial make-up of the U.S. navy, about 36 of those who developed dysentery would have been HL-A 27 positive, suggesting that between 12% and 25% of those at genetic risk developed RS after this single environmental insult.

It thus appears that in both AS and epidemic RS some 12% to 25% of those with HL-A 27 may develop the disease. In the case of RS this may follow shigellosis; in AS some unknown environmental insult may be implicated; in both there may be interplay with other unidentified genetic factors. The presence of typical clinical findings in the occasional HL-A 27 negative individual suggests either such additional operative genetic factors or 'environmental over-ride'. Preliminary data showing that there is an increased proportion of HL-A 27 negative spondylitic patients with shigella dysentery or inflammatory bowel disease compared with idiopathic AS subjects, indicates that a sufficient environmental insult can result in the expression of disease even in a genetically 'nonsusceptible' individual.

Histocompatibility antigens in polyarthrosis in the hand. J. Múñoz Gómez, M. A. Brancos Cunilla, and G. Ercilla Goncáles

In 1958 Kellgren and Lawrence described a pattern of arthrosis in the hand, appearing mostly in women. It has been shown that when there are more than five arthritic joints in the hand, there is a significant correlation ($P < 0.01$) with the existence of a pseudospondylolysthesis secondary to arthrosis in the posterior interapophyseal joints. This arthrotic pattern seems to be genetically determined. For this reason we attempted to study the histocompatibility antigens in these cases. There seems to be no significant statistical differences when comparing the frequency rates of the diverse antigens in the arthritic group studied and in the controls.

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HL-A frequencies in less common arthropathies. A. Robitaille, C. Cockburn, D. C. O. James, and B. M. Ansell (*MRC Rheumatism Research Unit, Taplow, and Tissue Typing Laboratories, Westminster Hospital*)

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Study of diagnostic importance of a group of immunological parameters in 212 rheumatic patients, with special reference to rheumatoid arthritis. E. Noguera Hernando, A. Larrea Gayarre, E. Fernández Cruz, M. Kreisler, and A. Bootello

(1) The most frequent associations, referring to immunological alterations, are rheumatoid factor, ANA, and polyclonal increase of immunoglobulins, all of which are basically visible in RA. (2) The increase in immunoglobulin levels was observed in a great number of rheumatic processes, and does not seem to be specific, constituting an index of the disease activity. (3) With the exception of RA, rheumatoid factor appeared in a low proportion in other processes, 1 out of 5 in DEL, in 1 out of 2 in scleroderma, and in 4 out of 14 in nonspecific polyarthritis, in our series. (4) ANA was present in 39·5% of seropositive RA, among other processes. Titration and staining pattern are of main importance for the diagnosis, as it allows differentiation of two entities which at certain evolutive stages may display great clinical similarity, as with DEL and RA. (5) Low values of serum complement were observed in RA (13·9%) and in other processes of the so-called autoimmune diseases such as SLE and scleroderma. (6) The presence of AAML is of specific diagnostic importance as in the case of some chronic hepatopathies, its incidence being low in RA (10%). AAML showed more specificity for primary biliary cirrhosis. We could only find it in one case of seropositive RA (1·6%). Evidence of both in RS would reflect the existence of one more autoimmunity phenomenon.

Naproxen in treatment of ankylosing spondylitis. H. F. H. Hill and A. G. S. Hill (*Oxford Regional Rheumatic Diseases Research Centre, Aylesbury, Bucks.*)

Thirty-six patients with ankylosing spondylitis have been treated with a daily dose of 500 mg naproxen for 1–30 months. Diagnosis was based on radiographic evidence of sacroiliitis and characteristic symptoms started before the age of 30. Patients with sacroiliitis associated with psoriasis, ulcerative colitis, regional ileitis, Reiter's and Behçet's disease were excluded. At the end of the first month of treatment 35 of 36 patients assessed naproxen as being equal to or better than previous therapy. At 12 months, 3 had gone into remission and