twenty rheumatoid subjects with radiologically calcified synovium, we have not found crystals. This was the only instance of concurrence of the two diseases among our 87 cases of chondrocalcinosis.

DR. E. B. D. HAMILTON (London) Excluding our patients with haemochromatosis, we have seen about seventy cases of chondrocalcinosis in the last 5 years. This includes three patients with hyperparathyroidism and only one with clinical rheumatoid arthritis; although there were two others with positive tests for rheumatoid factor in low titre. More recently I have reviewed the x rays of 21 patients with hyperparathyroidism, seven of whom had chondrocalcinosis and two had co-existing rheumatoid arthritis.

Role of Cellular Immunity in the Pathogenesis of Amyloidosis. By E. S. CATHCART and A. S. COHEN (*Boston University Medical Center, Boston, Mass.*).

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Technical Difficulties in Interpreting Virus-specific IgM Antibodies in the Presence of Rheumatoid Factor. By P. V. SHIRODARIA, K. B. FRASER and C. F. STANFORD (*Belfast*).

Fluorescent antibody was used to detect virus-specific IgG and IgM in human sera. When four seropositive rheumatoid sera were tested, each produced IgM-specific staining of two or more virus antigens from the group measles, mumps, rubella, and herpes simplex. This effect corresponded to the presence of virus-specific IgG in the sera and was removed by the absorption of rheumatoid factor from the sera, using aggregated human IgG. Semi-purified rheumatoid factor, when added to four sera that each contained a different virus-specific IgG but no virus-specific IgM, caused IgM-specific staining of the virus to appear, but did not itself stain any virus antigen. In convalescent sera from 28 patients with virus infection (twenty patients under and eight over the age of 20 years), virus-specific IgM was found. In all but two patients this IgM staining was not removed by absorption of sera with aggregated human IgG. We conclude that there are two types of IgM staining: a *primary* staining that is caused by virus-specific IgM and a *secondary* staining that is caused by rheumatoid factor or like substances in some human sera.

Discussion

DR. P. D. FOWLER (Manchester) Did you obtain sera from children or adults following acute infections?

PROF. FRASER Mainly children.

Herpes Simplex Antibodies in Rheumatoid and Control Patients. By C. F. STANFORD, P. V. SHIRODARIA, and K. B. FRASER (*Belfast*).

A study of complement-fixing (CF) antibody in 45 rheumatoid patients and 45 age- and sex-matched controls showed that there was an inverse relationship between the titres of antibody to herpes simplex, measles, and mumps virus and the titre of rheumatoid factor. The mean antibody titres were higher in the controls than in the rheumatoid patients. After removal of rheumatoid factor with heat-aggregated human gamma globulin, the mean CF antibody titre for rheumatoid patients equalled that for

controls with mumps and became higher than that for controls with herpes simplex and measles (Stanford, C. F. *Ann. rheum. Dis.* (1972), 31, July issue).

Since IgM antibodies are frequently associated with recent infection, herpes simplex was selected, because of the above results, as the antigen to test the possibility of recent prolonged infection in rheumatoid patients. The effects of rheumatoid factor on the ability to stain virus-specific IgM by the indirect fluorescent method is discussed in the previous paper (Shirodaria, Fraser, and Stanford, submitted for publication in *Ann. rheum. Dis.*). In untreated sera, absorbed only with noninfected HEP2 cells, 37 of 45 rheumatoid patients showed strong IgM staining against herpes simplex infected HEP2 cells, while sixteen of 45 age- and sex-matched controls showed weak staining. After treatment of both rheumatoid and control sera with aggregated human gamma globulin, only seven of the rheumatoid and nine of the control sera showed IgM staining.

Thus, as might be expected from the well-known recurrence of herpes simplex in many patients, there is serological evidence of persistent or recent infection with this virus, but no great difference between rheumatoid and control patients [Further analysis of the data is to be published at a later date].

Discussion

DR. A. G. S. HILL (Stoke Mandeville) Is the final conclusion based only on herpes simplex or do you have corresponding figures for rubella?

PROF. FRASER Some years ago I did look for IgM staining with rubella virus. We got no more IgM staining with rubella virus in rheumatoid patients than in non-rheumatoid patients, but only six were involved, so that this result does not mean a great deal.

PROF. D. L. GARDNER (London) Have you any hypothesis to explain the mechanism by which this interference or blocking or removal mechanism takes effect, whether in the circulation or outside it?

DR. STANFORD I think that rheumatoid factor and complement compete for sites on the Fc fragment of the IgG molecule.

In the absence of rheumatoid factor any fluorescent staining indicates the presence of antiviral antibody in the IgG or IgM class (depending on which antiimmunoglobulin conjugates produce fluorescence). If rheumatoid factor is present it may attach to antiviral IgG and thus give the staining reaction for IgM. This is an artefact *in vitro*.

PROF. D. L. GARDNER (London) I always understood that rheumatoid factor circulated as 7S/19S (22S) complexes. If so, how can this interfere in the way suggested, and how do you account for the circulatory phenomena *in vivo*?

PROF. FRASER Our results indicate that rheumatoid factor is not bound to the antibodies that we are measuring *in vivo*, because we can separate it off from the patient's serum before we do the test, but if afterwards you add the antigen in a complement-fixation test, then it competes for attachment and interferes with the attachment of the complement. I think it is an indication that the rheumatoid factor that we are measuring is not bound to IgG *in vivo*,