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.*).

To be published in full in the *Annals* (1972), 31, July issue

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*,

unless it is so loosely bound that it prefers to attach itself to the aggregated IgG that we used to absorb it.

DR. A. G. S. HILL (*Stoke Mandeville*) How much of the rheumatoid 19S is circulating in complex form?

DR. STANFORD Only in certain patients can one measure the 22S circulating antibodies which are thought to represent the binding of rheumatoid factor on to some of the 7S. I do not think this is taking place in the patient, it is purely in the methods that we are using to measure the antibody that the interference is taking place.

Aspects of Pathology in Rheumatoid Arthritis. By A. L. MACAFEE (*Orthopaedic Research Department, Musgrave Park Hospital, Balmoral, Belfast 9*).

In the 4 years between November, 1967, and October, 1971, a total of 631 total hip replacement operations have been carried out by the surgeons at the Withers Orthopaedic Centre, Musgrave Park Hospital. After each of these procedures the femoral head was retained for examination. A pilot study was aimed at investigating the clinical patterns of disease in cases of osteoarthritis and rheumatoid arthritis, by means of combining the clinical, radiological, and pathological changes.

Each specimen was fixed in formalin and stored in this state until examination. Colour photographs were taken at standard magnification of surface and cut sections. Haemotoxylin and eosin stained microscopical slides were prepared from paraffin blocks and for the purpose of this paper special views were taken.

The evidence suggests that there are differences in the tissue changes of osteoarthritis and rheumatoid arthritis. The main features may be summarized as follows:

Observation	Rheumatoid arthritis	Osteoarthritis
Sphericity of femoral head	Retention	Loss
Osteophytes	Nil	Present
Trabeculae	Thin with abundant marrow	Thick with cysts
Surface of femoral head	Absence of cartilage Pannus replacement Subchondral cysts not a feature	Retention of cartilage at non pressure area Thickening of subchondral bone with many small cysts

No conclusions have been drawn as to the long-term effects of these differences on the final outcome of surgery.

The macroscopic changes seen in the tissues of the knee joint in an early case and a late case of rheumatoid arthritis may be compared in the light of the current practice of synovectomy.

Discussion

PROF. D. L. GARDNER (*London*) How many cases have you examined and what selection does this presentation represent?

MR. MACAFEE We have performed approximately 600 total hip replacements and we are collecting the femoral heads. About fifty have been examined for this small pilot study.

MR. G. BENTLEY (*Oxford*) You showed osteoarthritis with tufts of cartilage. Did you imply that this was cartilage arising from original cartilage, or regenerative tissue from the subchondral marrow? One theory is that

subchondral cysts in osteoarthritis are areas of pressure necrosis, due to high loading, rather than areas of expulsion of synovial fluid from the joint.

MR. MACAFEE I do not know the origin of cartilage tufts. It has been suggested that some patients with osteoarthritis improve with rest in bed. In addition osteotomy with subsequent change in the pressure areas is said to result in 'regeneration' as evidenced radiologically. There is no doubt that many patients do improve and so perhaps there is regeneration of cartilage. It is with this in mind that the current study is progressing.

Natural History of Rheumatoid Cervical Subluxations. By P. H. SMITH, J. SHARP, and J. H. KELLGREN (*Rheumatism Research Centre, University of Manchester*).

Luxation of cervical vertebrae is a common feature of rheumatoid arthritis. This study attempts to define its natural history and the factors influencing its progression.

Of the 962 in-patients with classical or definite rheumatoid arthritis who had had routine lateral radiographs in extension and flexion between 1955 and 1964, 150 were noted to have vertebral luxations. In 1969-70, the ninety survivors (including six who had had cervical fusions) were reviewed clinically and radiologically. The average follow-up was 7.8 years (range 5 to 14). The gap between atlas and odontoid inflexion was recorded in millimetres. Below C2, subluxation was expressed as a fraction of the diameter of the lower vertebrae.

The initial degree and site of subluxation in radiographs of 150 cases are tabulated below.

Subluxation	Grade	Forward subluxation (mm.)	No of cases
At C 1/2	2	3.5-5.0*	50†
	3	5.5-7.5*	34†
	4	8.0 and > *	19†
Below C2	2	0.126-0.25‡	66
	3	0.26-0.32‡	22
	4	0.33 and > ‡	3

* Forwards only
† 10 cases of downward luxation omitted
‡ Forwards and backwards

The radiological progress in 84 survivors (ninety minus six cervical fusion cases) is demonstrated below.

Diagram A omits seven cases of forward luxation with finally developed downward luxation; also four cases in which there was downward luxation both initially and finally. Diagram B hides the fact that backward luxations progress more favourably than forward luxations (Figure, opposite).

Subluxations below C2 occurred more commonly and severely with advancing age. Downward luxations were found to be rare below the age of 60, and forward subluxations at C1/2 were less related to age and disease duration.

At follow-up, 62 patients had taken steroids and 22 had had none. The incidence of subluxations at C1/2 and below C2 were identical in both groups. At C1/2 subluxations progressed more favourably in those not taking steroids.

No beneficial effect on the progress of subluxations could be demonstrated from the use of collars. In the seven seronegative patients, no radiological deterioration was noted.