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


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 antitibody in the IgG or IgM class (depending on which antiglobulin 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.
MACAFFEE (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 Ortho-
paedic 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 osteoarthrosis 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 osteoarthrosis and rheumatoid arthritis.
The main features may be summarized as follows:

<table>
<thead>
<tr>
<th>Observation</th>
<th>Rheumatoid arthritis</th>
<th>Osteoarthrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sphericity of femoral head</td>
<td>Retention</td>
<td>Loss</td>
</tr>
<tr>
<td>Osteophytes</td>
<td>Nil</td>
<td>Present</td>
</tr>
<tr>
<td>Trabeculae</td>
<td>Thin with abundant marrow</td>
<td>Thick with cysts</td>
</tr>
<tr>
<td>Surface of femoral head</td>
<td>Absence of cartilage</td>
<td>Retention of cartilage at non pressure area</td>
</tr>
<tr>
<td></td>
<td>Panus replacement</td>
<td>Thickening of subchondral bone with many small cysts</td>
</tr>
<tr>
<td></td>
<td>Subchondral cysts not a feature</td>
<td></td>
</tr>
</tbody>
</table>

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. MACAFFEE 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 osteoarthrosis
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 osteoarthrosis are areas of pressure
necrosis, due to high loading, rather than areas of expulsion
of synovial fluid from the joint.

MR. MACAFFEE I do not know the origin of cartilage
tufts. It has been suggested that some patients with osteo-
arthritis 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 rheuma-
toid 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.

<table>
<thead>
<tr>
<th>Subluxation</th>
<th>Grade</th>
<th>Forward subluxation (mm.)</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>At C 1/2</td>
<td>2</td>
<td>0-126-0.25†</td>
<td>50†</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0-26-0.32†</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0-33 and &gt; †</td>
<td>3</td>
</tr>
<tr>
<td>Below C2</td>
<td>2</td>
<td>0-126-0.25†</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0-26-0.32†</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0-33 and &gt; †</td>
<td>3</td>
</tr>
</tbody>
</table>

† 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 sub-
luxations 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 sub-
luxations 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.