normal are between 20 and 50 mg./100 ml. serum. Quantitative determinations were made in cases of degenerative joint disease, inflammatory arthropathy (rheumatoid arthritis, psoriatic arthropathy, collagenoses, etc.) and during attacks of various other rheumatological diseases. The results, which are difficult to interpret at this stage, seem to indicate an increase in serum caeruleoplasmin, particularly in inflammatory arthropathies. This is not surprising in view of the alpha I glycoprotein changes.


It would be to the advantage of patients with rheumatic diseases if it were possible to treat them with corticotrophin and/or corticosteroids without causing impairment of hypothalamo-pituitary-adrenal function (HPA). We have made a series of studies aimed at finding such a regimen which is also clinically effective; only daily corticotrophin therapy, which has certain drawbacks, has so far satisfied these criteria.

There is scanty published work relating to attempts to preserve HPA function by giving steroids intermittently to patients with other chronic diseases such as nephrotic syndrome, asthma, sarcoidosis, ulcerative colitis, etc., and it has been claimed (Sadeghi-Nejad and Senior, 1969; Ackerman and Nolan, 1968) that a single dose of prednisone given once in every 48 hours results in less pituitary-adrenal suppression than daily divided doses.

It seems important to try to establish whether this method of steroid administration, especially as applied to the smaller maintenance doses usually employed in rheumatoid disease, would be a therapeutic proposition and would preserve stress responsiveness in these patients. We have therefore studied rheumatic patients on this regimen by serial testing of their responsiveness to the stress of insulin hypoglycaemia over prolonged treatment periods.

Our results so far show that patients converted from daily divided doses of prednisolone to a single equivalent dose taken once in every 48 hours gradually attain normal pituitary-adrenal responsiveness, but this may take as long as 40 weeks; as long, in fact, as it takes some patients to recover normal responsiveness after stopping steroid treatment, as shown by our own data. As usual in this field there is much patient variability. It is also apparent from our data that no firm deductions can be made from the results of single stress tests, and that it is necessary to repeat these tests over treatment periods of several months before any satisfactory conclusion can be reached.


A lowering of the complement level is one of the major immunological disturbances of rheumatoid synovitis.

The simultaneous quantitative determination of the total complement and its four primary components (C1, C4, C2, and C3) was performed on sixteen rheumatoid and nineteen non-rheumatoid synovial fluids. In the fluids of the rheumatoid group, a simultaneous lowering of C1, C4, and C2 was observed as well as a close and significant correlation between the level of C1 total and the level of C1 (0.01 < P < 0.02), C4 (P < × 10^-3), and C2 (0.001 < P < 0.01). These results would seem to indicate an immunological consumption of the synovial complement in rheumatoid polyarthritis. If this is the case there must be substances with anticomplementary action in rheumatoid synovial fluids.

The anticomplementary activity observed was on average quantitatively 4-5 times higher in rheumatoid synovial fluids than in non-rheumatoid synovial fluids. (P > 0.0001).

After fractioning strongly anticomplementary synovial fluids on a Sephadex G-200 column, the maximum anticomplementary activity appeared in the first fractions eluted. Analysis of these fractions to establish the nature of the proteins responsible for the anticomplementary activity is in progress.


Stimulatory tests of hypothalamo-pituitary-adrenal (HPA) axis function in patients receiving long-term oral corticosteroid therapy have suggested that suppression of the HPA axis occurs initially at the higher levels (Jasani, Boyle, Greig, Dalakos, Browning, Thompson, and Buchanan, 1967).

The response to insulin-induced hypoglycaemia and metyrapone tended to be abolished before the response to lysine 8-vasopressin, and the response to tetracosactrin was maintained the longest. Studies in which plasma 11-hydro xycorticosteroids (11-OHCS) were monitored during operation in patients who had received long-term corticosteroid therapy, and whose HPA axis had been assessed using the stimulatory tests mentioned above, showed that those patients who had a subnormal response to tetracosactrin had poor plasma 11-OHCS responses to the stress of surgery (Jasani, Freeman, Boyle, Reid, Diver, and Buchanan, 1968). There is, however, a relative paucity of information to guide clinicians as to the likely outcome of withdrawal of long-term corticosteroid therapy both in terms of the recovery of HPA axis function and in terms of the clinical response.

Thirty patients with rheumatoid arthritis who had received long-term oral corticosteroid therapy, and in whom the withdrawal of corticosteroid drugs was considered to be desirable for a variety of clinical reasons, were studied. A full clinical and HPA-axis assessment was carried out before and after the complete withdrawal of corticosteroid therapy. The clinical outcome and recovery of HPA-axis function are extremely variable. Some of these patients have been followed up for up to one year since the cessation of corticosteroid therapy, and some have undergone orthopaedic surgery without corticosteroid cover.
An attempt is made to correlate the clinical and endocrinological sequelae of corticosteroid withdrawal with details of preceding corticosteroid therapy and tests of HPA function.


**Rheumatoid Rosettes (Significance of the Phenomenon).** By F. Delrieu, F. Delbarre, and J. F. Bach (Paris).

When the lymphocytes of a patient suffering from rheumatoid arthritis and human group O, Rh negative, red blood corpuscles sensitized with rabbit immunoglobulin react with each other, the phenomenon of the rheumatoid rosette is observed microscopically.

Some of the lymphocytes are surrounded by a ring of more than four red blood corpuscles attached to them; the number of 'rosettes' in proportion to the total number of lymphocytes in the preparation is in excess of 6 per 1,000.

This phenomenon is the application to rheumatoid arthritis of a general phenomenon used to detect antibodies present on the surface of the lymphocytes (Biozzi). The technique is simple and takes only a few hours.

Theoretically, the fact that the rosette phenomenon is positive in 80 per cent. of cases of rheumatoid arthritis, but nearly always negative in other conditions, including osteoarthrosis, ankylosing spondylitis, and psoriatic arthropathy, is of great interest. There is an excellent correlation between the results of the Waaler-Rose test and the rosette test; for example, the test is also positive in certain related conditions and in non-rheumatological conditions with positive Waaler-Rose tests (cirrhosis, renal transplant).

There is, however, one important exception. In some slowly evolving polyarthritides, a positive rosette test at a stage when the Waaler-Rose is negative establishes the diagnosis of rheumatoid arthritis and assists the differentiation of cases which are clinically similar but in which basic biological tests give different results.

The rheumatoid rosette test becomes positive earlier than the Waaler-Rose test since the results are less closely related to the duration of the rheumatism. The results do not seem to be influenced by sex, or severity of disease.

Lastly, the phenomenon of rheumatoid rosettes appears to confirm that rheumatoid factor is secreted by the lymphocytes.

**Sympathetic Control of Synovial Blood Vessels.** By W. C. Dick, B. Porter, K. Whalley, G. Nuki, W. W. Downie, and W. W. Buchanan (Glasgow).

A method of continuous monitoring of $^{133}$Xe clearance from the animal joint, femoral venous flow rate, and femoral venous count rate has been devised.

It was established by this method that over 90 per cent. of the isotope cleared from the joint could be accounted for in the femoral vein. By measuring the diffusion and partition coefficients of $^{133}$Xe it was then possible to derive an indirect measure of synovial blood flow.

Isoprenaline was then injected intra-articularly, and the clearance rate, femoral venous flow rate, and femoral venous count rate all increased. Conversely, when noradrenaline was administered by the same route, all three rates fell. Neither of these responses was obtained after first administering the appropriate blocking agent. Thus, both alpha and beta receptors are present in synovial blood vessels.

The effect of these drugs when administered intravenously was also studied.

Finally, the effects of isoprenaline and noradrenaline on the human joint were studied by the $^{133}$Xe clearance technique. Each drug was administered first alone, and then after the administration of its respective blocking agent to normal subjects, to osteoarthritics, and to rheumatoid arthritics.


This histological review covers seventy surgical excisions carried out in the past 6 years. It includes 35 hygromata proper (knee 29; elbow 14; other sites 2) and compared with 35 cysts or synovial pseudocysts (popliteal space 13; wrist 11; back of the foot 11).

In benign attacks of bursitis, the structure and basic lesions resemble those of the articular synovium.

More severe cases show evidence of traumatic changes in the connective tissue and resulting inflammatory reactions, such as fibrinoid necrosis, vascular hyperplasia, and various types of extensive sclerosis.

**The Technetium Scintigram as an Indicator of Synovial Vascularity in Rheumatoid Arthritis: its Comparison with the Results of Temperature Measurement.** By J. A. Cosh, D. J. Lindsay, E. Rhys Davies, and F. J. Ring (Bath).

Scintigrams were made by scanning knee joints with a scintillation counter 30 min. after the intravenous injection of Technetium $^{99}$M. In the presence of active rheumatoid arthritis, greatly increased radioactivity was found in the synovium, indicating an increase in local blood volume. A small proportion of radioactivity was shown to be derived from the concentration of isotope in synovial fluid. After the intra-articular injection of steroid repeat scans 7 and 14 days later showed the synovial radioactivity to be greatly reduced.

Parallel studies of the temperature of the knee joint were made by thermistors, radiometers, and thermography. They showed a corresponding reduction in temperature after steroid injection. This can be attributed to reduction in synovial blood flow, the flow being increased in the presence of inflammation.

The techniques of scintigraphy and of temperature measurement thus give similar information in rheumatoid arthritis, the former being derived from synovial blood volume and the latter from synovial blood flow. Temperature measurement is simpler and lends itself more readily to quantitation.


Narrowing of the lumbar spinal canal may cause compression of the roots of the cauda equina.

G Nuki, W W Downie, K Whaley, W C Dick, P A Freeman and W W Buchanan

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