Follow-up Studies on Synovectomy of the Knee in Rheumatoid Arthritis. By S. D. DEODHAR, W. W. DOWNIE, P. A. FREEMAN, W. C. DICK, G. NUKI, K. WHALEY, and W. W. BUCHANAN (*Glasgow*).

145 patients who had had unilateral synovectomy of the knee for rheumatoid arthritis were studied. The duration of follow-up after operation ranged from 6 months to 5 years. Before operation and at the time of follow-up each patient was assessed with regard to the status of the knee and to his general health. The assessment consisted of a subjective enquiry about knee and other general articular symptoms, an objective evaluation of the knee, and a general assessment based on examination of the other joints. 83 per cent. of subjects considered that the operation had been successful, and this subjective assessment was supported by a significant reduction in knee joint symptoms such as pain at rest and in motion, and stiffness, and a general improvement in functional grade. Objective corroboration of local improvement was found in the significant reduction of synovial hypertrophy, effusion, and knee joint tenderness on pressure, and generally by a marked reduction in the articular index of joint tenderness. In this group also there was a significant fall in the erythrocyte sedimentation rate. The remaining 17 per cent. who claimed that the operation had been unsuccessful showed no improvement in the knee symptoms, deterioration in functional capacity, and no change in the general articular index. There was significant improvement in the objective evaluation of the operated knee with reduction of synovial hypertrophy, effusion, and local tenderness, but this was much less than in the successful group, and in addition the erythrocyte sedimentation rate remained unchanged.

In view of these findings, the authors consider that the postoperative course of a synovectomized joint depends on the evolution of the rheumatoid disease in general, namely that a successful synovectomy is probably the result of spontaneous remission of the disease process. There is no evidence from the present study to support the suggestion that synovectomy *per se* can influence the course of rheumatoid process.

Painful Juxtameniscal Areas in Certain Arthropathies of the Knee and Their Treatment by Juxtameniscal Cortisone Infiltration. By M. LEQUESNE, M. BENSASSON, C. KEMMER, and J. AMOUROUX (*Paris*).

Painful juxtameniscal areas have been observed in three conditions:

- (1) Certain post-traumatic meniscal lesions;
- (2) Meniscal degeneration;
- (3) Certain cases of osteoarthritis of the knee.

The pain is often felt on the inner side of the knee, more rarely on the outer side. It is of a spontaneous nature and brought on especially by pressure on a specific site. This pain appears to be connected with a conjunctivo-vascular reaction, more or less congestive, and even inflammatory, that develops at one or more points of the peripheral edge of the meniscus and penetrates the external portion which has been injured by trauma or degeneration.

The authors studied thirty cases of this type, all of which had the following in common:

- (1) A predominantly lateral pain in the knee;
- (2) A point frankly painful to pressure on the antero-lateral portion or at the median pole of the meniscus;
- (3) Pain provoked by one of the McMurray manoeuvres, by external or internal rotation (this is precisely the pain reported by the patient).

After various experimental procedures on cadavers, in which the juxtameniscal area was infiltrated with a dye substance, followed by similar injections of an opaque substance on a living subject under radioscopic control, the authors regularly used juxtameniscal infiltration with 1 ml. of a cortisone derivative into the most tender point. In thirty cases they obtained more than 80 per cent. very good or good results; complete disappearance or a marked decrease in pain. Usually one to three juxtameniscal infiltrations of this type were sufficient. Radiographical study with a contrast substance showed there was no intra-articular penetration. Moreover, many of these patients had received several intra-articular cortisone infiltrations without relief.

The meniscus itself is not sensitive to pain, being an organ with neither blood vessels nor nerves. It is the peripheral wall of the meniscus and the juxtameniscal region which become painful because of a reactive vascular site. Such inflammatory islets have been observed by the authors in operated cases apart from the series discussed here. This doubtless explains the consistent success of the direct infiltration of the painful site. No complications have arisen.

Some successful results in patients about to undergo meniscectomy and in those suffering from osteoarthritis of the knee were dramatic.

The follow-up period varied from a few months to several years. The improvement or disappearance of the pain was usually permanent, but in some cases relapse made it necessary to repeat the juxtameniscal infiltration at intervals. In only one case in the series was it necessary to perform meniscectomy because of persistent pain.

A Study *in vivo* of the Stiffness of the Human Knee. By R. GODDARD, D. DOWSON, and V. WRIGHT (*Leeds*).

An apparatus has been devised which permits the study of joint stiffness of the human knee *in vivo* by direct, objective measurement. This 'Arthrograph' has been used to investigate the physical nature of joint stiffness in rheological terms.

Normal subjects and those whose joints were affected by rheumatoid arthritis or osteoarthritis were studied.

Physiological variations in stiffness were studied with relation to age, sex, and temperature (both intra- and extra-articular).

For the first time the phenomenon of 'articular gelling' associated with osteoarthritis has been demonstrated by objective measurement and its physical nature investigated. By similar techniques the nature of 'morning stiffness' associated with rheumatoid arthritis has also been studied.

Serum Caeruloplasmin in Rheumatology. By H. ROUX, R. AQUARON, R. GRANGIER, and A. M. RECORDIER (*Marseille*).

The authors carried out determinations of serum caeruloplasmin by the Ravin technique. The values considered

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 caeruloplasmin, particularly in inflammatory arthropathies. This is not surprising in view of the alpha I glycoprotein changes.

RAVIN, H. A. (1961) *J. Lab. clin. Med.*, **58**, 161.

Effect of Single-dose Alternate-day Corticosteroid Administration on Hypothalamo-pituitary-adrenal Function in Patients with Rheumatoid Disease. By M. E. CARTER, and V. H. T. JAMES (*St. Mary's Hospital, London*).

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.

ACKERMAN, G. L., AND NOLAN, C. M. (1968) *New Engl. J. Med.*, **278**, 405.

SADEGHI-NEJAD, A., AND SENIOR, B. (1969) *Pediatrics*, **43**, 277

Mechanism of the Fall in Complement Level in the Synovial Fluid in Cases of Rheumatoid Polyarthritis. By A. P. PELTIER and S. DE SÈZE (*Paris*).

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 < × 10⁻⁹), 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.

Observations on the Clinical Outcome and Recovery of Hypothalamo-Pituitary-Adrenal Axis Function after Complete withdrawal of Long-term Corticosteroid Therapy in Patients with Rheumatoid Arthritis. By G. NUKI, W. W. DOWNIE, K. WHALEY, W. C. DICK, P. A. FREEMAN, and W. W. BUCHANAN (*Glasgow*).

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.