Discussion.—PROF. E. G. L. BYWATERS (*Taplow*): Would Dr. Scott comment on the apparent decrease in turnover rate in one patient *after* allopurinol treatment: did he mean that this was during allopurinol treatment and that this decrease in turnover rates was due to allopurinol?

DR. SCOTT: The second study in the patient taking allopurinol was carried out while he was taking the drug—about 6 months after starting. Associated with the fall in plasma and urinary uric acid caused by xanthine oxidase inhibition there was a reduction in the exchangeable pool size and daily turn-over rate of uric acid. The pattern of decline in urinary specific activity now indicated the presence of a single-compartment rather than the two-compartment system before treatment.

Influence of Gold Salts on Adjuvant Arthritis in the Rat. By J. D. JESSOP and H. L. F. CURREY (*Departments of Physical Medicine and Rheumatology, The London Hospital*): This article and the discussion thereon is to be published in the next issue of the *Annals* (November, 1968).

Synovial Fluid and Serological Changes after Treatment in Arthritic Diseases. By N. WILLIAMSON and P. J. L. HOLT (*Rheumatism Research Wing, Department of Experimental Pathology, University of Birmingham*): 156 synovial fluid samples were collected from 48 patients suffering from various types of arthritic diseases, and 72 serum samples were also collected from thirty of these patients. These fluids and sera were examined and a comparison made of samples taken before and after treatment.

Indomethacin was used either alone or in combination with other drugs in 26 of the 48 patients; 24 received aspirin at some time during the study and because of its wide usage before admission to hospital the effects of this drug were difficult to assess. Systemic steroids were used in eight cases, intra-articular injection of steroids in five, phenylbutazone in two, and Biogastone in one.

Changes in synovial fluid cell cytology and in serology were observed after treatment. Neither synovial fluid cell count nor differential count showed any significant change with treatment; however, the staining reactions of cell smears showed marked differences. These differences were best seen with the PAS stain, there being marked diminution of staining following treatment. Similar results were obtained using enzyme histochemical techniques to demonstrate the lysosomal enzymes such as acid phosphatase and N-acetyl- β -glucosaminidase.

Serologically seven of thirty patients showed positive anti-nuclear factor, eighteen showed positive reticulin antibody, and five demonstrated a positive smooth muscle antibody. Changes in antinuclear factor staining were seen after treatment in three cases, and changes were seen in four out of five patients with a positive smooth muscle antibody. Little change was observed with the reticulin antibody.

Discussion.—DR. J. J. R. DUTHIE (*Edinburgh*): People should not be unwilling to have a joint aspirated two or three times, as long as you don't hurt them.

DR. D. N. GOLDING (*Harlow*): I was interested to hear the results of PAS staining in patients having indomethacin. This isn't a drug which everyone would agree has an important anti-inflammatory effect in rheumatoid disease. Have your figures concerning PAS-staining in indomethacin-treated patients been subjected to statistical analysis and, if so, are they significant?

DR. WILLIAMSON: No, they have not been subjected to statistical analysis. It may be necessary to increase the number of patients studied to reach a definite conclusion, but from the results so far, *i.e.* a decreased staining in twelve of twenty cases treated with indomethacin compared with none from ten cases treated with rest in bed, it will, I think, prove to be significant.

DR. J. BALL (*Manchester*): It is customary when discussing the PAS, as you must well know, to consider at least two controls, one for glycogen and another for oxidized lipid. I suppose that you have done these. Would you like, for the record, to tell us what the results were?

DR. WILLIAMSON: Control staining has been done. It does not appear to bear much relation to the changes observed. I do not feel that alterations in glycogen or oxidized lipid are related to the changes seen before and after treatment.

PROF. E. G. L. BYWATERS (*Taplow*): Might I perhaps ask if the authors studied the effect of indomethacin *in vitro* on synovial fluid cells or if they have any indication as to how early a detectable change comes in? I think all your figures referred to changes at 7 days only.

DR. WILLIAMSON: As far as changes are concerned we have no evidence that anything occurred earlier than one week. This was an arbitrary time chosen for the first synovial fluid aspiration. We have not studied the effects of indomethacin on synovial fluid cells *in vitro*. Dr. P. Weston, in our laboratory, has studied the effects of indomethacin *in vitro* on synovial hyaluronidase but has been unable to show any diminution in the activity of this enzyme on hyaluronic acid. We need to do more work on this aspect to establish whether treatment inhibits the action or production of the hyaluronidase *in vivo* to fit with the hypothesis I made earlier.

DR. W. R. M. ALEXANDER (*Edinburgh*): Is it possible that indomethacin, in some purely chemical way, interferes with the PAS-staining reaction without necessarily having any biological effect?

DR. WILLIAMSON: This is a possibility, but against this we have obtained similar results with both aspirin and intra-articular steroids. Also four of the twenty cases on indomethacin showed an increase in staining after therapy, which would not be expected if the action was purely chemical. Perhaps the main factor in support of a biological effect is that the patients who showed diminished staining were the ones who responded well to therapy, whereas the patients showing increased staining all demonstrated some worsening of their condition.

DR. T. M. CHALMERS (*Manchester*): I should like to ask whether you had any evidence of quantitative changes in enzyme activity in synovial fluid before and after treatment?

DR. WILLIAMSON: We attempted to estimate both acid phosphatase and N-acetyl- β -glucosaminidase in synovial

fluid cell extracts. The results were not very conclusive, but there appeared to be an increase of enzyme in the extracts of cells which had shown diminished PAS staining. But we are reluctant to put much reliance on these results as in many cases we were dealing with very small quantities of cells.

Prevalence of Ulcerative Colitis in Ankylosing Spondylitis. By M. I. V. JAYSON, I. A. D. BOUCHIER, and P. R. SALMON (*Bath*).

This paper was published in full in the May issue of the *Annals* (1968, 27, 219).

Discussion.—DR. J. J. R. DUTHIE (*Edinburgh*): Did you find any sign of regional ileitis?

DR. JAYSON: We have not looked specifically for this but it would be well worth doing.

DR. H. L. F. CURREY (*London*): Can you tell me how many patients refused examination? Secondly, how did these patients present? Were they collected from a rheumatism clinic or from the general hospital records, and how many of them had in fact first presented with ulcerative colitis, or colitic symptoms, and later on had their ankylosing spondylitis recognized? Could there be any bias because of an interest in colitic symptoms? Thirdly, has any group, either rheumatic or non-rheumatic, had this sort of survey carried out on it previously? Have we any figures for the normal population or any other rheumatic group having this sort of investigation carried out?

DR. JAYSON: We traced all patients who had a diagnosis of ankylosing spondylitis recorded in the hospital records and wrote and asked them to attend a special clinic at which a gastroenterologist and myself were present. 107 patients were asked in all and 58 agreed to undergo investigations. Some of these patients were rejected because they did not fit the criteria for ankylosing spondylitis. Discounting to the maximum the bias due to patients with symptoms being more likely to volunteer for this type of investigation, we are left with a prevalence of 15 per cent. To my knowledge there have been no other studies using these criteria for the presence of ulcerative colitis in a rheumatic population.

DR. J. A. MATHEWS (*London*): Does any one of your investigations account for the majority of the extra percentage of patients diagnosed with colitis above the other series?

DR. JAYSON: The investigation which recorded most positives was the barium enema but the chief thing is that these changes may be present in patients who would not otherwise have been investigated. From the point of

view of severity of symptoms probably only three would have been investigated because of diarrhoea, the one who had had the severe colitis in the first place, and the other two who had passed blood per rectum. Two other patients had diarrhoea, which was surprisingly mild in view of the x-ray changes.

PROF. E. G. L. BYWATERS (*Taplow*): Was the sex ratio the same in spondylitics with colitis as in those without?

DR. JAYSON: All the patients with colitis were male as against 85 per cent. of those with normal bowels. This was not a significant difference.

DR. V. WRIGHT (*Leeds*): This is a very interesting and important piece of work, and I find the results very surprising. All of us appreciate that ulcerative colitis may become worse without symptoms, and it is important to know whether it can be present without symptoms. We have been very interested in this matter and have performed barium enemas on several spondylitic patients without symptoms of ulcerative colitis, but our incidence is not nearly as high as this. We have not analysed yet our figures in detail, but the only patient that comes to mind is one who previously had an operation for obstruction, and proved to have had regional ileitis. How extensive were the changes on barium enema examination, and do you regard procto-colitis as a type of ulcerative colitis or not?

DR. JAYSON: The one patient who underwent colectomy had very extensive and severe ulcerative colitis. In the remaining seven with radiological evidence, the changes were moderately severe in four and mild in three, the last being shown in the first x ray. We do consider procto-colitis to be a variant of ulcerative colitis.

DR. D. N. GOLDING (*Harlow*): Was there any relationship between the extent of radiological involvement of the spine and the presence of ulcerative colitis? I am asking this because one might have expected less tendency to involvement of the spine above the sacro-iliac joints when ulcerative colitis was found, since patients with this condition usually have only sacro-iliitis.

DR. JAYSON: We analysed the incidence of fusion of sacro-iliac joints in colitic and non-colitic patients, and found no significant difference.

PROF. E. G. L. BYWATERS (*Taplow*): Might I ask if Dr. Jayson studied the involvement of particular peripheral joints? I remember well that we have sometimes been able to detect ulcerative colitis in patients with chronic sero-negative polyarthritis but without symptoms of colitis by the involvement of the small joints of the toes, which seem to me to be particularly liable to involvement in this disease.

DR. JAYSON: We have not analysed our patients from that point of view.