
Evaluation of a Simple Articular Index for Joint Tenderness in Rheumatoid Arthritis. By D. A. Ritchie, J. A. Boyle, J. M. McInnes, M. K. Jasani, T. G. Dalakos, P. Grievson, and W. W. Buchanan (Glasgow).—An index was described for the numerical measurement of joint tenderness in patients with rheumatoid arthritis. The index is based on the summation of a number of quantitative evaluations of the pain experienced by the patient when the joints were subjected to pressures when exerted over the articular margin or in some instances on movement of the joint.

A statistical analysis in experimentally controlled conditions was undertaken to test the validity and the errors of this simple clinical tool. There was a satisfactory degree of reproducibility when the assessment of joint tenderness using this index was made by one observer on different occasions. However, there was a far from acceptable degree of correlation between the results obtained by different observers.

That the index can record changes in the patient's joint tenderness in the practical clinical situation was shown by the fall in articular score of a group of patients treated in a formal double-blind cross-over study using aspirin, prednisolone and placebo. Clear differences were demonstrated not only for the major analgesic effect of prednisolone (compared with placebo), but also for the minor analgesic effect of aspirin (compared with placebo).

The limitations and advantages of this and other attempts to make a quantitative objective assessment of that most subjective phenomenon, pain, were discussed.

Discussion.—DR. S. GODFREY (London): We have studied observer error in pulmonary disease using both the standard deviation index and an experience agreement index which compared the most experienced with the less experienced observers. The results suggested the physical signs lay mid-way between completely random and completely reliable. Could you put your index in these terms?

DR. Buchanan. We did not analyse our data in these terms. We were surprised how big the differences were between observers. Indeed, a difference in score of 20 or less between two observers in any one patient was calculated not to be significant. Studies in other fields of medicine have also shown some high degrees of interobserver error. A clinician using an index or scoring system should assess inter- and intra-observer error as our laboratory colleagues do automatically when they estimate the standard error of a new laboratory technique.


Effect of Corticotrophin Therapy on Pituitary-adrenal Function. By Mary E. Carter and V. H. T. James (St. Mary's Hospital, London).—Patients receiving ACTH therapy were studied to assess the effect of this form of therapy on pituitary-adrenal function, using hypoglycaemia as a test stimulus. The results were compared with those found in steroid-treated patients, and the effect of previous steroid therapy was considered.

Discussion.—DR. A. B. MYLES (London): Dr. Jasani—how long after the dose of triamcinolone was the articular index calculated, and how long after the last dose was the plasma cortisol estimated?

DR. Jasani: For the measurement of diurnal rhythm as well as the assessment of the articular index the corticosteroid therapy was left unaltered. However, for determination of the plasma 11-OHCS responses to Synacthen, lysine8-vasopressin, and insulin-hypoglycaemia, in keeping with a previous study, corticosteroid therapy was discontinued 12 hours before the test in the patients given triamcinolone 4 mg. nightly.

DR. A. B. MYLES (London): In the patients who had the dose at night who had a low plasma cortisol in the morning, you do not know what happened at, for example, 2 p.m., because the night dose of steroids will suppress the early morning peak but the maximum rise may occur later. You also do not know what happened on the steroid-free days. You will get acute suppression by giving steroids at night but it would be surprising if you produced chronic suppression by giving such a small dose of triamcinolone for this period.

DR. Jasani: The schedule for the test procedures was designed to find out if we should obtain HPA axis suppression with such small doses of the corticosteroid given for 1 year. However, you have raised other interesting possibilities that need investigation.

DR. A. B. MYLES (London): You have shown some changes in the hypoglycaemia tests but all your results are within the normal range.

DR. Jasani: I agree that, with the exception of response to insulin hypoglycaemia in two out of six patients given triamcinolone 4 mg. nightly, the plasma 11-OHCS levels were not suppressed significantly. These findings probably reflect the use of a relatively smaller daily dose (5 mg. prednisolone equivalent) of triamcinolone. There might of course be a greater HPA axis suppression with administration of the corticosteroid using either regimen for a longer period.

DR. A. B. MYLES (London): The cortisol levels would have been influenced by the previous dose if taken on the night before.

DR. Jasani: The diurnal variation would be, and this is why it was not stopped. I accept your comment but I should add that the only compelling reason for adopting this practice was to conform to the design of study employed by Nichols, Nugent, and Taylor (1965). They measured the diurnal rhythm of cortisol during the 24 hours following a dose of dexamethasone at midnight and found it was completely abolished. In our study, the 10 p.m. dose of triamcinolone represents their nightly dose.

DR. A. B. MYLES (London): Why do you use triamcinolone which most other people do not use?
Dr. Jasani: Triamcinolone was selected because it had already been used in several similar studies.

Dr. O. Savage (London): How did the patients do clinically on the day they did not have the corticosteroid?

Dr. Jasani: The patients receiving 8 mg. of triamcinolone at 8 a.m. one day had a recrudescence of symptoms from about 2 p.m. the next day. Afterwards all patients had relatively greater relief of symptoms and did not mind having the steroid on alternate days.

Dr. O. Savage (London): They had a pretty unhappy time during part of the second day?

Dr. Jasani: In the beginning perhaps, but so did patients with the 4 mg. nightly dose, who experienced return of their symptoms between 2 and 6 p.m. on the following day.

Dr. O. Savage (London): Dr. Carter—you have shown that you can wake up a suppressed adrenal by giving ACTH. Have you any evidence that it stays awake? In the slides you showed, you had always put them back on systemic steroids.

Dr. Carter: No, not always. Pituitary-adrenal responsiveness is maintained whilst the patients receive ACTH, rapidly lost when they are converted to steroid therapy and regained if they revert to ACTH therapy. After ACTH had been discontinued the pituitary-adrenal responses remained normal.

Prof. J. J. R. Duthie (Edinburgh): Do these patients give themselves their injections?

Dr. Carter: Yes, mostly. One or two do not, either because they cannot calculate the dosage or because their hands are not agile enough.

Measurement of Synovial Blood Flow in Normal and Diseased Joints. By W. C. Dick, R. A. St. Onge, K. Whaley, F. Gillespie, J. A. Boyle, M. K. Jasani, and W. W. Buchanan (Glasgow).—Synovial blood flow has been calculated in normal and diseased knee joints using as a method the disappearance of radioactive Xenon from the knee. The mean value obtained from twelve normal knee joints was 2.78 ± 0.53, while for fourteen patients with osteoarthritis it was 3.97 ± 0.81 and for forty patients with rheumatoid arthritis it was 9.94 ± 0.69, all results being expressed as ml. per 100 g. synovial tissue per minute.

It has also been possible to demonstrate the anti-inflammatory effect of intra-articular injection of hydrocortisone in eleven rheumatoid patients, the mean blood flow before being 12.92 ± 1.65 and after the injection 8.87 ± 1.54 ml. per 100 g. synovial tissue per minute.

Discussion.—Prof. E. G. L. Bywaters (Taplow): I thought the Society might be interested to see two historical slides taken some 20 years ago, when I tried to measure synovial blood flow in the knee in man by using the joint as its own plethysmograph; we put in a needle on a three-way tap attached to a manometer, and then put on a venous cuff proximal to the joint, which was wrapped in a non-extensible bandage. This formed the plethysmograph box, and the rate of flow of saline out of the needle along the manometer gave an index of the amount of blood entering the joint. In several patients blood in-flow came up at something like 3 mm. per minute. Now our results were in terms of mm. per minute, which represented blood flow; you have used the term "ml. per g. tissue"—this must be a very difficult calculation to make unless you have weighed the tissue. Can you tell us how you got this?

Dr. Dick: Synovial blood flow is equal to the derived value from the exponential fall-off of radioactivity multiplied by Lambda, which is the partition coefficient of Xenon for synovial membrane with respect to blood. All radioactive methods of determining blood flow are based ultimately on three things, the Fick principle, the partition coefficient and the constant clearance, and all can be transposed mathematically quite acceptably into ml. per 100 g. per minute. This has been done for brain, for fat, and for muscle, by using this equation.

Prof. E. G. L. Bywaters (Taplow): This is a theoretical gramme rather than a measured gramme?

Dr. Dick: It is as practical as is any other measurement of a gramme in this field. I should not like to say more than that.

Dr. J. Ferguson (Glasgow): It struck me that one or two of your curves might be biexponential rather than monoexponential. Have you any explanation?

Dr. Dick: That is so. The fall off of radioactivity was in counts per minute against time. In many normal patients and in most patients with osteoarthritis we got a monoexponential curve, which was no problem. The mathematical expression was

\[ y = Ke^{-\lambda t} \]

With certain patients, however, at the beginning of the study we got curves with a rapid fall initially levelling off to a low level later, and by the method of Veall and Vetter these can be resolved into two components. We appeared to get these curves when we imposed more trauma on the patient. It appeared to correlate with pain initially; so we altered our technique and inserted a needle attached to a saline-loaded syringe into the joint cavity and left it absolutely still for 5 minutes. We then replaced the saline with Xenon and injected very carefully. With this technique we abolished the first component, so we concluded that this was an injection phenomenon, presumably because we were injecting practically straight into the blood vessels initially. In all subsequent investigations we got a monoexponential curve. The same has been noted in other fields by other workers.

Dr. M. I. V. Jayson (Bath): One of our problems has been that Xenon is particularly soluble in fat. Is this taken into account in your calculations?

Dr. Dick: The clearance from adipose tissue has been estimated by the same technique to be 2.86 ml. per 100 g. per minute; that is, a normal synovial level, so this can hardly account for the difference. Furthermore by directly measuring the partition coefficient of Xenon for synovial tissue with respect to blood, I think we have obviated this problem.
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M E Carter and V H James

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