

Trigeminal Neuropathy in Connective Tissue Diseases. By B. TAIT and B. ASHWORTH (*Rheumatism Research Centre and University Department of Neurology, Manchester Royal Infirmary*)

Six patients aged 33 to 66 years with various connective tissue diseases developed trigeminal neuropathy. They were not a homogenous group. Three had progressive systemic sclerosis (PSS), two had systemic lupus erythematosus (SLE) with features of PSS, and one had dermatomyositis. All noted numbness over the involved area of the face, and in some the tongue and buccal mucosa were affected. In some patients this was preceded by pain and in one pain was a feature for a year after the onset of the lesion. The onset was subacute and took up to one month to reach maximum development. Subsequently the signs have remained unchanged for periods of up to 6 years. The involvement varied in distribution but usually followed the divisions of the trigeminal nerve. In one case there was bilateral involvement, but in the remainder the involvement was largely unilateral, affecting one, two, or three divisions. The blink reflex was recorded in three patients: one showed a normal response, one showed an increase in latency, and in one there was virtual absence of the first component. There was a similar delay in response to supraorbital stimulation, suggesting that the delay is in nerve conduction. Evidence from these cases suggests that trigeminal neuropathy is a consequence of the connective tissue diseases but that the association is rare.

Discussion

DR. K. MUIRDEN (*Melbourne*) This is an important symptom to bring out, largely because in some cases there is a possibility of easing the pain of the trigeminal neuralgia. In two of our patients the pain was intermittent and it tends to be ignored because of the severity of the other symptoms. In these two patients we obtained improvement by the use of the drug Tegretol, and in one it was almost completely relieved. Have you had experience of this drug in this condition?

DR. TAIT No, we have not, but in our patients pain has never been a prominent feature, and three of the six had no pain at all. One had mild pain persisting for a year. This did not trouble her unduly and specific therapy was not given, although certainly one would expect Tegretol to help should pain be a problem.

DR. D. A. PITKEATHLY (*Manchester*) There was one patient (I think she was one of your series) who presented with trigeminal neuropathy as the sole manifestation of her disease, and later developed signs of systemic lupus erythematosus. I think this is a point to remember, that these conditions, particularly SLE, can actually present as cases of isolated trigeminal neuropathy.

DR. D. N. GOLDING (*Harlow*) I am most interested in this paper because, in 42 cases of peripheral neuropathy associated with rheumatoid arthritis, we had only one with cranial nerve involvement.

Amyloid Deposition in Cartilage. By E. G. L. BYWATERS and J. DORLING (*M.R.C. Rheumatism Unit, Canadian Red Cross Memorial Hospital, Taplow*) Published in full with the Discussion thereon in this issue of the *Annals* (1970), 29, 294.

Elasticity of Synovial Fluid. By A. J. PALFREY and D. V. DAVIES (*St. Thomas's Hospital Medical School, London*)

All fluids exhibit elastic properties which can be investigated using the Weissenberg Rheogoniometer as a cone and plate viscometer. The measurements required are those used in determining the viscosity of the fluid, but the calculations differ. In experiments in which the cone is subjected to a sinusoidal movement through small angles, the calculation is straightforward, but the curve is interrupted at the natural frequency of the torsion head. In experiments in which the cone rotates, the calculation uses measurements of the torque and of the normal force exerted by the fluid. The latter can be measured only at shear rates in excess of 100 sec.^{-1} and therefore it is possible to determine the elasticity only at those shear rates. The torque tracing exhibits a steady value preceded by an initial peak that corresponds to the immediate viscosity. Similarly, the normal force tracing shows an initial peak followed by a steady value. Four measures of the elasticity can thus be calculated at each shear rate.

These calculations are illustrated by data from fluids taken from the atlanto-axial, radio-carpal, and tibio-tarsal joints of healthy adult cattle, and compared with similar results from human fluids aspirated from patients with various types of arthritis. The role of elasticity in the functioning of synovial joints is assessed.

Articular Gelling in Osteoarthritis—A Bioengineering Study. By V. WRIGHT, R. GODDARD, D. DAWSON, and M. D. LONGFIELD (*Rheumatism Research Unit and Institute of Tribology, University of Leeds*)

An arthrograph has been devised and constructed for the measurement of stiffness at the knee joint. A sinusoidal motion is imposed upon the knee passively, and the resisting torque, recorded from strain gauge plates bonded on to a lever, is plotted against angular displacement.

Normal subjects and osteoarthrotic patients have sat in one position for varying periods and torque/displacement records have been taken. In normal subjects there was no increase in stiffness, but in many patients with osteoarthritis there was a marked increase. The stiffness of the normal joint averaged about 20 kg./cm., but for articular gelling figures as high as 102 kg./cm. were found. Analysis of the records demonstrated that there was an increase in elastic stiffness and an increase in dissipatory forces, but that the former far outweighed the latter. This suggests that the phenomenon is not due to a gelling of synovial fluid but to a change in the periarticular structures.

Preliminary Studies on the Development of a Synthetic Polymer with Flow Characteristics of Normal Synovial Fluid. By G. NUKI, J. FERGUSON, K. BODDY, and M. POND (*Centre for Rheumatic Diseases and University Department of Medicine, Royal Infirmary, Glasgow; Fibre Science Department, University of Strathclyde; Scottish Research Reactor Centre, East Kilbride; and University Department of Veterinary Surgery, Glasgow*)

There is at present considerable interest in the possibility of treating joint diseases by the intra-articular injection of synthetic lubricants.

Normal synovial fluid is highly viscous, non-Newtonian, thixotropic, and elastic, but these remarkable flow properties are lost in patients with rheumatoid arthritis.

The laboratory synthesis of a polymer of polyvinylpyrrolidone (PVP), the rheological characteristics of which closely resemble those of normal synovial fluid, is described together with the results of preliminary studies after its injection into the joints of pigs.

Discussion (of the three foregoing papers)

DR. V. WRIGHT I was very much interested in both the first and the last paper (and the middle one, for that matter). There are one or two questions I should like to ask Dr. Palfrey. What does he think to be the significance of the variation of modulus in different joints, and does he think that elasticity is anything more than an interesting by-product phenomenon? Its value is really so low that one would doubt that it could be operative in the mechanisms of lubrication of the human joint. Vos and Theyse (1969) have suggested that elasticity may be of more diagnostic significance than viscosity, but I have seen little evidence for that. My other comment is that I wonder whether at this stage we are getting past the point where we are interested merely in the properties of what I call 'bulk' synovial fluid. We have increasing evidence that the synovial fluid is altered during joint movement and I wonder if the properties of the gels that form on the surface are more important?

My question to Dr. Nuki concerns the artificial lubricant. At a meeting of the Biological Engineering Society held in Leeds we set out properties that we felt were desirable for a potential artificial lubricant, and there is no doubt that PVP fulfils quite a number of them. We have hesitated to use it because of the data showing that by subcutaneous injection into animals it causes sarcoma, and I wonder if Dr. Nuki would like to comment on that? The other information that we shall await with interest is how it degrades mechanically. I am a little hesitant when I learn that the Duff-Barclay simulator is being used, because, as Dr. Nuki probably knows, this does not simulate the load cycle in a human joint. The loads go down to zero and then come up to three or four times body weight at heel strike and toe off. The Duff-Barclay simulator produces much valuable information in testing prostheses, but is not the best type of simulator to use for testing artificial lubricants.

DR. PALFREY It seems difficult to assess the significance of the differences between the fluids from different joints. Perhaps the best way to tackle this problem is to measure as many parameters for the fluid as one can, and then to relate these to known rates of angular movement and to the curvature of the joint surface in order to estimate the shear rate. I agree that our values for elasticity are low, but I think this bears reporting. In our understanding of the behaviour of synovial joints, particularly on the basis of the results of scanning electron microscopy, we are approaching molecular levels. You can establish a basis for speculation at the molecular

level only if you describe the fluid under conditions in which its properties can be measured.

DR. NUKI To answer the first points that Dr. Wright raised. As regards the production of sarcomas in mice, I know of only one paper in which this was suggested and the author later withdrew the suggestion (Heuper, 1959, 1961), considering that the sarcomas which had been produced were due to impurities in the PVP preparation. Our own reluctance to go ahead with any human experiments is due to the fact that we are unfortunately forced at present to use our own synthesized PVP and not the pharmaceutical grade, and we therefore feel we must be very much more certain than we can be from animal experiments. We have not the resources that pharmaceutical companies have at their disposal, but we hope perhaps to enlist some of these.

To answer Dr. Wright's second question, why we are proposing to use the Duff-Barclay simulator, my answer is that it is the best one available to us.

DR. M. I. V. JAYSON (*Bath*) We have reported to the Society a study of patients with severe arthralgia in whom the clinical or radiological evidence of arthritis was very slight or absent, but in whom we were able to demonstrate increased joint elastance, by which we meant increased pressure change for a unit volume of simulated effusion. It seems to me that this type of elastance is similar to the elasticity described by Dr. Wright. I should like to ask if he was able to relate the changes to the patients' symptoms, and particularly whether there was any difference between the elastic stiffness as measured by his technique in patients with the radiological changes of osteoarthritis, but with and without symptoms?

DR. WRIGHT No sir, we have not yet evaluated our data from that point of view, though this study is in progress. We have found that the patients with no radiological change, that is normal folk, have a stiffness which is within the normal range and do not show this phenomenon of articular gelling measured objectively. We find that many of our patients with osteoarthritis show an increased stiffness and many show this articular gelling so measured, but the radiographic correlation has not yet been done.

PROF. BYWATERS (*Taplow*) Two questions. First, Dr. Wright, is there any correlation between the duration of immobilization and the degree of stiffness which develops in these osteoarthritic patients? Second, Dr. Nuki, does it matter how you remove the glass load before freeze drying, and in fact how do you do it?

DR. WRIGHT Our figures have come down from about 130 to about 40 kg./cm. As to time, we usually immobilize the patients for 30 minutes, but we find that many of them develop this stiffness within 10 minutes.

PROF. BYWATERS (*Taplow*) It doesn't increase?

DR. WRIGHT No, it doesn't increase.

DR. NUKI The load was in fact a glass slide on which simple weights were placed and then removed. We have tried removing the slide in different ways, either by simply taking it off or by putting the specimen into the liquid nitrogen before removing the slide, and we find that the appearances are not appreciably affected. This has added to our feeling that these are, in fact, drying appearances

on the surface of the cartilage and have no particular significance as regards the molecular configuration *in vivo*.

DR. P. J. L. HOLT (*London*) Dr. Wright has looked at the question of immobilizing these patients when they develop stiffness. Has anyone looked at the reverse situation? Are patients who do not develop stiffness prone to be jumpy and fidgety? It seems to me that one aspect of rheumatoid disease or arthritis that no one has studied is the question of movement. Some patients may move more than others, some may just sit still and literally seize up. Can the amount of movement be used as a method of assessing anti-inflammatory activity of drugs? We have had little success with this problem so far.

DR. WRIGHT That is a very interesting question. We have studied it from the point of view of morning stiffness, and with great dedication have got up at 5.00 a.m. to be in the hospital for 6.00 a.m. We have got the patients up and moved them and exercised their hands, and we have found that movement of this type alters the circadian rhythm of grip strength and alters the stiffness that patients experience first thing in the morning. But this is as far as we have gone.

DR. F. DUDLEY HART (*London*) We did try an instrument some years ago which we called an 'agitometer', to record the amount of movement in a limb and to see how much, more or less, a limb was moved on treatment—for instance the arm in rheumatoid arthritis. The device proved unsatisfactory as it did not record movements in all planes, being based essentially on the self-winding wrist-watch. We have not overcome these difficulties even yet. I should be glad to hear of other people's experiences.

DR. R. GRAHAME (*London*) Has Dr. Wright performed any of his estimations with his subjects under general anaesthesia to abolish muscular tone?

DR. WRIGHT The answer is no, sir.

DR. J. H. GLYN (*London*) If, as I understand it, Dr. Wright's work tends to exonerate the joint structures themselves as the cause of gelling, and he postulates a periarticular pathology, could he give us any idea of what type of periarticular pathology he is postulating to explain these phenomena?

DR. WRIGHT My hunch, with little evidence, is that it is a vascular phenomenon. My evidence is that we have occluded the blood supply in the arm for certain periods, and have found that by absolute occlusion or diminution of the blood supply stiffness is increased. Whether this is the mechanism which is operating I do not know.

DR. D. N. GOLDING (*Harlow*) Could any of the speakers explain the efficacy of silicone oil if in fact it is effective? I know that the trial of Helal and Karadi (1968) was not controlled, but I think a few people are

using silicone oil in experimental clinical trials and it seems that it may be clinically effective. Is there a theoretical explanation for this, in view of the fact that silicone oil behaves in a Newtonian manner?

DR. WRIGHT Yes, we have also been using silicone oil, not because we believe in it but because it has been used and therefore we think it ought to be tested. Theoretically it shouldn't work; that is the first thing to say because, unlike the careful studies of Dr. Nuki, it in no way mimicks synovial fluid. You are just putting 'goo' in between the joint surfaces, and if it works by altering the lubrication mechanism, it must be because the goo separates the joint surfaces. But it may be possible that it works (and that's not proven yet) by another mechanism. It certainly does not work by mimicking the normal mechanism of joint lubrication.

DR. A. G. WHITE (*London*) There have recently been reports of the dissolution of the terminal phalanges and of the development of sacroiliitis in workers in the polymer industry. Can Dr. Nuki tell us if there is any evidence of the safety of the polymers he has been using when they are present in the body over a long period?

DR. NUKI I think you are referring to workers with polyvinylchloride (PVC). This really has no bearing on polyvinylpyrrolidone. There is no polymer which has been used more in the body and over a greater number of years with no reports of hazard, apart from that mentioned by Dr. Wright which as far as I know was later denied. Just to comment on the question of why silicone fluid might work, I think there are many substances which have symptomatic value if injected into the joints in uncontrolled trials. Clearly, as Dr. Wright says, if you separate the surfaces by putting in a large amount of fluid (Helal puts in up to 20 ml.), you will diminish abrasion within the joint. This has been demonstrated by measuring crepitus and showing it to be decreased. There is one other feature of silicone fluids, apart from the fact that they behave in a Newtonian manner, which is very different from the sort of polymer we have been using, namely that silicone is immiscible with water and body fluids. Whatever else you can conclude from the surface characteristics of PVP in the scanning electron microscope, the pictures make it clear that silicone forms some kind of homogeneous complex with the synovial fluid in the natural state.

DR. J. BALL (*Manchester*) It may be worth mentioning that lymph flow is increased in exercise. If the contrary is true, the stiffness may perhaps be related to changes in the extravascular extracellular fluid in the joint capsule consequent on immobilization.

References

- HELAL, B., AND KARADI, B. S. (1968) *Ann. phys. Med.*, 9, 334.
 HUEPER, W. C. (1959) *Arch. Path.*, 67, 589.
 — (1961) *J. nat. Cancer Inst.*, 26, 229.
 VOS, R., AND THEYSE, F. (1969) "Lubricating properties of synovial fluid in human and animal joints", in "Lubrication and Wear in Joints", ed. V. Wright, pp. 29-34. Sector, London.