Paget's Disease in Population Samples. By J. S. LAWRENCE (*Manchester*).

The prevalence of Paget's disease was determined radiologically in three Caucasian population samples in the United Kingdom, in three American Indian populations in the United States and Canada, and in one Negro population in Jamaica.

No significant difference was found between the Caucasian and Negro populations, but the American Indians had significantly less, no Paget's disease being observed in the 568 Indians over the age of 54 years in whom routine pelvic *x* rays were taken.

In the United Kingdom populations the disease was not seen below the age of 45 years. Thereafter the prevalence increased exponentially up to age 74.

The data are consistent with the hypothesis that the disease is initiated by one or more somatic mutations. An osteoclast precursor is suggested as the cell undergoing mutation, and the regulator gene controlling the synthesis of proteolytic enzyme as the affected locus.

Discussion

DR. V. WRIGHT (*Leeds*) Two questions, quite unrelated: What is your inter- and intra-observer error?, and what do you mean by somatic mutation?

DR. LAWRENCE I have not made an assessment of the inter-observer error, but these *x* rays from various surveys were mixed together and read blind by one observer, so only intra-observer error is involved. The correlation coefficient for two readings by this observer was $r = +0.83$, so it is unlikely that observer error played an important part.

By somatic mutation I mean an error in replication of the DNA molecule occurring during division of a somatic cell. This might be a gross error, such as a deletion or duplication of part of a chromosome, or it might be limited to one nucleotide pair. In either event it gives rise to a clone of abnormal cells if the mutated cell is viable.

DR. J. H. GLYN (*London*) I did not know until recently that Paget's disease could be familial, but I have come across a family in which three sisters definitely suffered from it, and a brother was reputed to be affected. I would therefore like to ask how common is this familial aggregation and how it affects your interpretation of data from population surveys?

DR. LAWRENCE There have been very few reports of family studies and there have been no formal surveys of Paget's disease in families, but there are some very striking family reports. I think my findings of the difference between American Indians and Caucasians suggests that there is a racial difference in predisposition and that would fit in with a genetic hypothesis. A genetic influence on somatic mutation has been postulated though not proved.

DR. A. ST. J. DIXON (*Bath*) Dr. Lawrence has outlined some of the fascinating aspects of the natural history of Paget's disease, such as the sharp demarcation line which is sometimes seen between advancing Paget's and normal bone, and its inability to cross the joint. There is one crucial experiment to which perhaps mem-

bers of the Society might be in a position to persuade some of their more co-operative patients to submit, *i.e.* cross-grafting segments of fibula between an affected and a normal side. The fibula after all is one of the few disposable bones we have. If we were able to cross-graft a bit of 'Pagety' fibula from one side and put the normal piece in the gap on the other side, one of three things might happen (supposing the graft actually took). The normal bone would begin to colonize the Pagety bone, or the Pagety bone would begin to colonize the normal bone, or they might both just stay as they were. Whatever happened, the answer would be very interesting.

PROF. J. J. R. DUTHIE (*Edinburgh*) How does Dr. Lawrence explain the action of calcitonin on his theory?

DR. LAWRENCE I should think that the action of calcitonin (which reduces the serum alkaline phosphatase) is to inhibit bone resorption and so reduce the need for new bone formation. Alkaline phosphatase is concerned with bone construction rather than with bone destruction.

Physician's Assessment of Functional Overlay. By E. N. COOMES (*St. Mary Abbots Hospital, Kensington, London*)

In hospital practice it is always difficult for the doctor to assess the degree of functional overlay in his patients; the usual criteria used are imprecise and often seem strangely anachronistic. The purpose of this study was to determine the correlation between two physicians' ratings of functional overlay and certain psychological test scores, and also the types of complaint most likely to lead the physician to make a diagnosis of functional overlay.

143 consecutive patients were assessed and the physician's estimate of the degree of overlay was rated at 25, 50, 75, and 100 per cent. Before history taking and examination, each patient completed an Eysenck Personality Inventory questionnaire and a Cornell Medical Index. There was a good correlation for neuroticism between the two forms, but the physicians' assessment differed considerably. We also analysed the type of patient which each of us picked out as showing functional overlay; certain differences were found between the two observers.

Discussion

DR. V. WRIGHT (*Leeds*) We have been studying periarthritis of the shoulder using these indices to quantitate the 'periarthritis personality', but one of the hardest problems is to find a 'normal' group. Another experiment that we have been meaning to do but have not yet done (and I wonder if you have) is to repeat the inventory at a later date, especially after the patient has improved. Do follow-up studies show an alteration? In other words, are we measuring something which is a result of the disease rather than something which is the background to it? And a third point, do you make provision for finding out the liars? I wonder how many of those you have.

DR. COOMES In answer to the first question: how to find a normal group? Eysenck has gone into this on a

large scale; his book details various groups of occupations running into several thousands of people, and his 9.1 mean is, I believe, fair. Of course, there is variation between different occupational groups.

The next question is very important: these tests are not as precise as a haemoglobin estimation. If a patient's haemoglobin is 10 g. per cent. you have an accurate estimation, but a score of 12 on the Cornell Index is not in the same category; one should use these tests on groups rather than individuals. The last question was about 'the liars'. We did incorporate a 'lie scale' on the Eysenck Inventory but I was limited by time in discussing it. I have the data and can let you see it.

DR. K. D. MUIRDEN (*Melbourne*) I should like to follow up Dr. Wright's remark. We studied a group of 76 rheumatoid arthritics with the Eysenck Personality Inventory, and we found that the level of neuroticism was much higher than that of the published controls, being about 13, which is quite significant. At the same time our unit engaged in a similar study with patients with angina and a similar high level was found. We wondered whether in fact this level of neuroticism was not an acquired trait, secondary to the common factors in these two diseases, presumably pain and fear. I think this is different from what the psychologists say about the inventory?

DR. COOMES I quite agree with you. I think this is very fair comment on these tests.

DR. M. I. V. JAYSON (*Bath*) The relationship between mind and body is fascinating. It has been shown that psychological changes can effect the course of disease; for example it has been shown that psychologically you can suppress the tuberculin response in a Mantoux test, or you can suppress skin responses to substances to which the patient is allergic. Have you observed whether the mind affects the inflammatory process in rheumatoid arthritis?

DR. COOMES I can not answer that I'm afraid.

DR. P. J. L. HOLT (*London*) Can you completely rule out the use of drugs? Cortisone, admittedly in larger doses than you are using, can affect the mood, as can indomethacin and to a certain extent aspirin if taken in large enough doses.

DR. COOMES These Eysenck Inventories were filled in before the patients had had any treatment with cortisone, indomethacin, or aspirin.

Observations on Connective Tissue Tensile Strength in the Chick Embryo. By S. D. ORLOFF (*Rheumatology Laboratory, Brussels Medical School*).

In studying the effect of lathyrism in chick embryos, the following observations were made:

- (1) The tensile strength of connective tissue in normal embryos is predictable as a function of age and weight.
- (2) The total collagen content in normal embryos and their tensile strength run on parallel evolutions in time between Days 5 and 18 of incubation.
- (3) In lathyratic embryos collagen extractability and tensile strength are closely related and have a parallel evolution in time.

(4) The collagen extractability in lathyratic embryos is dosage dependent.

(5) Lathyrism pulls embryos down the time scale in respect of the tensile strength of connective tissue.

Discussion

DR. V. WRIGHT (*Leeds*) I am a little concerned about your method of finding the tensile strength. I wonder if you would not do better to use an impact load, because inevitably with your method you will obtain time-dependent effects. With an impact load you will have a better reflection of the true elastic properties, whereas with your method the visco-elastic properties of the material will presumably play a part. The alternative would be to plot a stress/strain curve which would give you a good deal of information. I was not clear how you calculated the tensile strength from the hydroxyproline content, and I wonder if you could please clarify that.

DR. ORLOFF To answer the first question, about time-dependence. We made studies using different flow rates and found that the weight of our basket was the most reliable parameter; we had much better correlation within our different experiments using the weight as a parameter.

To answer the second question, perhaps I did not make the point clearly enough: I meant that at the molecular level collagen extractability reflected alteration of the collagen molecule; on the other hand the macroscopic expression of this alteration was increased fragility.

Ochronotic Densification. By E. G. L. BYWATERS, J. DORLING, and J. SUTOR (*Taplow*).

The characteristic radiological opacity of the intervertebral regions in ochronosis has been attributed to bony sclerosis following break-up and loss of cartilage. Histological and crystallographical study of the discs from a Birmingham patient (of Dr. Clifford Hawkins) has shown the presence of hydroxyapatite in the degenerating disc material and in that protruded when degeneration is complete. By contrast, synovial membrane contains calcium pyrophosphate crystals. This identification has been confirmed by x-ray diffraction study.

Discussion

DR. E. N. GLICK (*London*) Do you know whether any of these patients had had attacks of pseudo-gout in the spine or in the peripheral joints in view of the calcium deposits?

PROF. BYWATERS The two patients whom we have seen at Taplow have not had attacks of pseudo-gout.

DR. N. WILLIAMS (*Birmingham*) The Birmingham patient with ochronosis did in fact have calcium pyrophosphate crystals in the synovial fluid and these had been present for some 4 years. But there was never a severe infiltration with inflammatory cells. Usually the cell count was about 600 and these were mainly large mononuclear cells, so that it seems to have been a chronic process rather than an acute arthritis caused by the crystals.