John Wynne Pugh: a medical saga

SIR HAROLD HIMSWORTH

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John Pugh died on 21 June 1976, 40 years, all but one month, after developing Addison's disease. Save for the first three years of this period, he lived a full life both socially and professionally. He developed his illness at a time when the treatment of this disease was in the research stage, so his history is something of a medical saga which his family feel should be put on record if only, as he himself would have wished, to encourage the others.

Early career

John Wynne Pugh (inadvertently named Jack, owing to an unfortunate slip of the tongue by his father at his christening) was born in London in 1902 into a closely knit family. He was educated at St Paul's School. From here he went to Oxford, where he graduated BA with honours in physiology in 1924. Then he came to University College Hospital, London, and in 1927 qualified as BM, BCh. After holding a succession of house appointments, including one in otorhinolaryngology, he was awarded the Radcliffe Travelling Fellowship of University College, Oxford, and spent 1930-2 working under Chevalier Jackson at the Presbyterian Hospital in New York, where the new technique of bronchoscopy was being developed. On returning to London he became registrar to the Royal Ear Hospital, which had recently been incorporated into University College Hospital, and it was practically a foregone conclusion that the next vacancy on the staff would fall to him.

Addison's disease

But in 1934, at a life insurance examination, pus cells were discovered in his urine and, on further investigation, tubercle bacilli were shown. As a result his right kidney was removed by Mr F J F Barrington and is now in the museum of his old hospital as the earliest example in its collection of tuberculosis of that organ. He made a good recovery, but two years later he began to notice, but did not report, that he was tiring very easily. Then in July 1936 he started to vomit and developed diarrhoea and it was obvious that he had Addison's disease.

At that time the first active extracts of adrenal cortex had just become available for clinical trial and, thanks to the generosity of Messrs Organon, some was supplied to him. His proved to be an exceptionally severe case. It was found impossible to reduce the dose of extract below 25 ml a day, despite his taking a daily supplement of 20 g of sodium chloride. After a stormy six months, however, his condition steadied, and he was sent on this regimen to Davos Platz. At the end of a year he came back and took a light job as an assistant in a sanatorium in North Wales. It became evident, however, that, exposed as he was in Britain to winter infections, his hold on life was precarious. At his suggestion, therefore, it was decided that he should go to South Africa, which he already knew and liked.

London

SIR HAROLD HIMSWORTH, MD, FRCP, FRS, former Secretary and Deputy Chairman, Medical Research Council

DOCA

But, before this, Ciba had produced the synthetic preparation desoxycorticosterone acetate (DOCA). At first this was given intramuscularly as a daily injection in oil, 4 ml of which seemed to be equivalent to 30 ml of the cortical extracts then available. For the first three weeks after receiving this preparation he felt much better. Then he began to fail, although his blood electrolytes remained at normal levels. So it was decided to revert to treatment with cortical extract and, on this regimen, he departed for Cape Town in November 1938, where he came under the care of Professor J F Brock.

Over the next year further experience was obtained with DOCA. As a result good reasons began to emerge for thinking that this drug, unlike cortical extract, did not contain all the principles required in Addison's disease.[1] But cortical extracts were very expensive and the amounts available limited. Furthermore, war was in the offing and it was feared that supplies might be cut off. Accordingly it was agreed, by correspondence, to put him on a regimen of 5 mg of DOCA and 25 ml of cortical extract on alternate days. On this his health became better than at any time previously. Tablets of DOCA for subcutaneous implantation then became available, and eventually it was found that by implanting four tablets of 50 mg each every four or five months he remained in excellent health, provided that he always took an additional 25 ml of cortical extract each week.

An active life

This was essentially the regimen on which he remained until cortisone became available in 1949-52. But, long before this, Pugh was in active work as an ear, nose, and throat surgeon at Durban, where he had become consultant to the King George V and Springfield hospitals. Further, he had married Lilla Brink, the widow of a brother of an old Oxford friend, and thereby acquired an unfailing source of support.

By this time I had gone to the Medical Research Council and my successor at University College Hospital, Max Rosenheim, took over as his UK contact. When John Pugh visited this country in 1953 he was taking 12·5 mg of oral cortisone daily, having implants of 300 mg DOCA every six months, and taking no extra salt. On this regimen he felt excellent and was no longer tired at the end of a long operating session. Pigmentation, always slight, had vanished and his blood pressure was 130/78 mm Hg. His condition was similar in 1956. By 1959, however, he had stopped the DOCA implants and was on a schedule of cortisone 12·5 mg, hydrocortisone 5 mg, and fluorohydrocortisone 0·1 mg daily. Throughout the rest of his life, this was the basis of his treatment. If tired or travelling he increased the doses but reduced them again when he felt better. Then, at a routine check in Durban in 1964, his systolic blood pressure was discovered to be 200 mm Hg, and he began to be troubled by lumbar spondylitis. Blood pressure was controlled by alseroxylon (Rauwiloid), and the spondylitis was relieved by butazolidine. When last seen in this country, in the summer of 1967, he had no symptoms of Addison's disease and his blood chemistry was normal. *X*-ray films showed slight calcification of his adrenals and, surprisingly, extensive calcification of his ear cartilages. His blood pressure was 150/85 mm Hg, but he was increasingly troubled by arthritis and had some oedema on the ankles and shortness of breath on exercise.

Thereafter, his arthritis steadily grew worse. In 1971 heart block developed and a pacemaker was inserted. A year later he

developed a severe hepatitis and never subsequently reverted to his previous good health. Nevertheless, he continued after his retirement to take three outpatient sessions a week until immediately before his death. Then, in June 1976, he contracted an "influenza-like" infection, was admitted to hospital but did not rally, and died three days later.

John Pugh was thus probably the first person to have shown unequivocally that, with modern treatment, even severe Addison's disease is compatible with a lifetime of normal activity. He was lucky in that he did not develop the disease before effective drugs were beginning to be devised. Had he done so he could hardly have survived for six months. But the major credit for the outcome belongs to him. By using his common sense (with which he was exceptionally well endowed) he adjusted his regimen to his needs. Thereby he was enabled to live a full life in every sense of the word. But, as every doctor knows, success or failure in treating a condition that poses a continuing threat of disaster depends largely on the patient's attitude. And behind all John Pugh's humour, good fellowship, and panache lay an ability to face facts without flinching and to take adversity in his stride. It was this more than anything else that enabled him to triumph over his circumstances and preserve his personality intact.

Reference

1 Himsworth, H P, *Proceedings of the Royal Society of Medicine*, 1939, **32**, 702.

SHORT REPORTS

^{125}I-fibrinogen uptake test

The development of research into postoperative venous thrombosis owes much to the ^{125}I-fibrinogen uptake test. Its accuracy in detecting thrombi compares well with that of venography, the correlation being over 90% when applied to "major" general surgical cases (though patients undergoing leg surgery were excluded).[1] More recently, the ^{125}I-fibrinogen test has been used in detecting deep vein thrombosis after leg surgery, and high positive rates of between 37%[2] and 75%[3] have been shown after hip surgery (excluding the operative zone, which itself produces false-positives). Although many studies have also included venography, little has been published on a direct comparison between the ^{125}I-fibrinogen test and venography after leg operations. Barrie *et al*, however, found confirmatory venographic evidence of thrombosis in only 53% of limbs with a positive ^{125}I-fibrinogen uptake after hip fracture.[4]

Patients, methods, and results

In a study of 40 patients who had undergone total hip replacement in Gartnavel General Hospital, Glasgow 77 limbs were examined using both ^{125}I-fibrinogen and venography. ^{125}I-fibrinogen 100 μCi was injected on the day of operation. The Pitman 235 Ratemeter was used to take readings of the counts (%) at seven points on each leg, ankle to mid-thigh. The counts were taken one, two, three, five, seven, and nine days after operation with the bed-end raised. A positive result occurred when the count rose 20% above the praecordial count for two days on the same spot or 20% above the count on the corresponding spot on the other leg. Bilateral ascending venography was carried out between days 6 and 9, radiological interpretation of the venogram being carried out in ignorance of the result of the ^{125}fibrinogen test.

Of the 77 limbs, 40 had a negative fibrinogen test result, and all showed a normal venogram. Of the 37 limbs positive on the fibrinogen test only 24 had confirmatory venographic evidence of thrombosis.

Comment

Among the 13 limbs in which venographic and fibrinogen results did not agree only five were on the operation side. This would suggest that the operation by itself was not a major cause of the discrepancy. Furthermore, the discrepancy did not occur only over the calf veins, where venography may be less accurate; in six cases the uptake test gave a positive finding above the knee. While the ^{125}I-fibrinogen uptake test may indeed have been detecting thrombosis in the smaller venous tributaries of the thigh, no thrombi were ever seen in the popliteal or superficial femoral veins, or in the mouths of the profunda veins. Interpretation of such a venogram would surely not encourage the clinician to offer any treatment.

This means either that the ^{125}I-fibrinogen is too sensitive or that the venogram is too insensitive. We are tempted to suggest, however, that a thrombus that cannot be seen on venography is not worth preventing or treating, as it is either very small or confined to a calf vein. It would be interesting to know if this pattern is confirmed by others. If it is, the ^{125}I-fibrinogen test is really being used as a screening procedure for venography. Certainly, with such a high "false-positive" rate, estimates of venous thrombosis after hip surgery cannot be made by using the ^{125}I-fibrinogen uptake test, and confirmatory evidence by venography should always be sought. On the other hand a negative fibrinogen test result alone would seem to be strong evidence that thrombosis has not occurred.

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3 Field, E S, *et al*, *British Journal of Surgery*, 1972, **59**, 377.
4 Barrie, W W, *et al*, *British Medical Journal*, 1972, **4**, 130.

Gartnavel General Hospital, Glasgow
J R LOUDON, FRCS GLAS, senior registrar in orthopaedics (present address: Royal Hospital for Sick Children, Glasgow G3 8SJ)

Malignant phaeochromocytoma with severe constipation and myocardial necrosis

Phaeochromocytoma accounts for under 1% of all cases of hypertension.[1] The quoted incidence of malignancy varies according to the diagnostic criteria but is probably about 3% of all phaeochromocytomas.[1] We describe here a patient who presented with skeletal metastases and the unusual feature of obstinate constipation.

Case report

A 54-year-old woman complained of pains in the back, chest, limbs, severe constipation, anorexia, and weight loss, with a tendency to excessive sweating. Examination showed a sinus tachycardia; blood pressure 240/130 mm Hg; tenderness over the thoracic spine and ribs; and a rectum loaded with hard faeces.

The erythrocyte sedimentation rate was 76 mm in 1 h, and serum calcium concentration was 2·8 mmol/l (11·2 mg/100 ml). Albuminuria but no glycosuria was present. Radiographs showed a translucent area in ribs and thoracolumbar spine; intravenous pyelograms, initially thought to be normal, in retrospect suggested a lesion distorting the right renal pelvis from