in circumstances where stress and strain may be met with on recovery or where compensation for injury is hopefully, if subconsciously, anticipated.

The pains of anxiety states may well be due, in part, to muscle contraction and spasm—the somatic expression of the increased nervous tension which is occasioned by fear. Too often a depressive psychosis is overlooked as a cause of persistent psychogenic pain, though few would fail to appreciate the origin of the bizarre pains described with unrestrained verbal embellishments by the paranoidal valetudinarian and hypochondriac.

I have sought to show that the problems presented by the clinical analysis of pain can be solved only by those who look at the "whole" man. Those whose major field of medical practice is rheumatology must beware of the compartmental outlook, for their diagnostic field is general medicine. They must adopt the "synoptic" view and decide, if pain be the presenting symptom, whether it is dominantly physical or psychogenic. They must be prepared to spend time on taking the history and making a full examination, so that they can determine what accessory procedures, provided by x rays and clinical pathology, are necessary to reach a complete diagnosis, but they must not be bemused by the minor deviations from the normal which may be revealed by diagnostic machines, but which cannot possibly be related to the patient’s complaints.

I do not claim to have presented any novel thesis; nor, indeed, were I able to do so, would this occasion have been appropriate. I have sought to review the more recent advances in our knowledge of pain and the help they give to its clinical interpretation, so that yet another step may be taken towards fulfilling Hilton’s belief that "every pain has its distinct and pregnant signification if we will carefully search for it."

REFERENCES


HEBERDEN ROUND

The Heberden Round was conducted by Professor L. S. P. Davidson in the Edinburgh Royal Infirmary on May 10, 1951. Eight cases were shown in the East Medical Theatre. The first four cases illustrated that pigmentation of the skin due to excess production of melanin can occur in four entirely unrelated diseases.

Case 1, Mrs. E.B., aged 32, pregnant.—She presented the typical clinical features of Addison’s disease including pigmentation of the skin in the accepted situations. This was her second pregnancy, and the disease appeared to have followed immediately after the first pregnancy. She was treated with DOCA and salt. She was then put on to cortisone and at the time of the meeting was taking 15 mg. daily with DOCA twice
ANNALS OF THE RHEUMATIC DISEASES

weekly, and her health was excellent. Professor Davidson mentioned how rare it was for patients with Addison's disease to become pregnant, only some 44 having been reported to date in the world's literature.

Case 2, Mrs. E.S., aged 37.—She had been admitted to hospital with features highly suggestive of Addison's disease, namely asthenia, loss of weight, anaemia, vomiting, low blood pressure, and marked pigmentation of the skin and mucous membranes. Chemical tests for Addison's disease including blood sugar tests, insulin sensitivity tests, and the Kepler test were negative. Because the liver and spleen were enlarged the diagnosis was changed to chronic hepatitis (cirrhosis of the liver), a condition in which pigmentation may occur. This diagnosis was not sustained since every type of liver function test was normal and porphyrins were absent from the urine. It was then discovered that the patient was an ephedrine addict and had been taking 30 to 40 1/2-gr. tablets daily for many years. It was suggested that the pigmentation was due to increased amounts of dihydroxyphenylalanine (DOPA) being available for the synthesis of melanin because reduced amounts were required by the body for the formation of adrenaline.

Case 3, Mrs. J. F., aged 47.—She had had jaundice caused by infective hepatitis in 1947. In 1949 she experienced pains in the back, and increased adiposity with sciatric pains and oedema of the legs. Hepatic function tests were all strongly positive and her liver and spleen were enlarged. There was radiological evidence of oesophageal varices; her globulin/albunin ratio was 2:1. Since 1947 she had noted a progressive darkening of the skin. Biopsy of the skin showed a pigment which proved to be melanin. Her blood sugar curve was normal. She was thought to be a case of chronic hepatic cirrhosis with skin pigmentation.

Case 4, Mrs. K.D., aged 32.—She was admitted to hospital in 1948 with progressive and severe weakness, diarrhoea, and abdominal pain, with paraesthesiae and muscle cramps. She had been working in a munition works. She was extremely anaemic (haemoglobin 20 per cent.); the marrow biopsy showed a megaloblastic marrow. The history was obtained that between the ages of 8 and 21 she had had frequent attacks of vomiting and diarrhoea associated with the passing of pale bulky stools. Accordingly the diagnosis was made of coeliac disease continuing into adult life. This patient also had patchy pigmentation with areas of leucoderma. She had never grown fully, was only 4 ft. 9 in. tall and weighed 4 st. 13 oz. She made a dramatic improvement on folic acid. Liver extracts and vitamin B12 had failed to improve her anaemia. Later her condition worsened with return of tetany and weakness. Her blood pressure dropped. This was found to be associated with a low serum-sodium; the administration of sodium citrate raised the blood pressure and improved the asthma. The moral here was not to forget sodium deficiency in the malabsorption syndrome.

Case 5, Mrs. E.H., aged 60.—Hers was also a case of malabsorption syndrome associated with pigmentation. She was first admitted to hospital in 1940. She had lost 3 st. in weight and was passing eight sprue stools daily. She had spent 32 years in Ceylon and India but had never had diarrhoea there. She returned to the United Kingdom and remained well for 8 years before the onset of diarrhoea. Pigmentation was present on skin, nipples, and face. Cramps and tetany occurred from time to time. A microcytic anaemia passed through a dimorphic phase over the years to megaloblastic anaemia. Six times she had been admitted to hospital severely ill in relapse and suffering from diarrhoea and multiple deficiencies, and the prognosis appeared to be very bad indeed. At this time she was vaccinated against smallpox. At the sites of vaccination she developed a marked staphylococcal cellulitis with high fever, to be followed by suppurative parotitis which had to be surgically drained. From that time onwards she rapidly improved in health without any further treatment, so that she gained 4 st. in 4 months, and was able to eat anything she liked without precipitating diarrhoea. She has now been in perfect health for the last
7 years. It was suggested that this extraordinary cure might be due to a successful adaptation to a severe skin reaction which had stimulated the patient's output of cortisone. On this basis therefore trials of cortisone and ACTH were suggested for the sprue syndrome.

Case 6, J.A., a sailor, aged 43, who had since died.—He had developed the malabsorption syndrome due to intestinal obstruction secondary to tuberculosis. This patient then proceeded to develop signs of subacute combined degeneration of the spinal cord which were confirmed microscopically. The stomach was histologically normal.

Case 7, J.H., aged 55.—He complained of haemorrhages into the skin from the gums and elsewhere of 5 weeks' duration. He was found to have a palpable spleen; the white cells were normal but the platelets were reduced to 25,000 per c.mm. Marrow biopsy showed plenty of megakaryocytes. No aetiological agent was discovered. A diagnosis of idiopathic thrombocytopenic purpura was made. The severe bleeding was not controlled by local measures or blood transfusions given on three occasions. Accordingly, ACTH was given, and bleeding ceased within 12 hours, never to return. No change, however, was noticed in the bleeding time, capillary resistance, or platelet count to explain the cessation of bleeding. After 60 days all these features had returned to normal. Professor Davidson asked if this remarkable response was a spontaneous remission or therapeutically induced.

Case 8, Mrs. J.G., aged 21.—She had been given liver extract elsewhere for 11 years although she proved to be suffering from haemolytic anaemia (acholuric jaundice). She had become pregnant and during her pregnancy developed a severe megaloblastic anaemia. The marrow was returned to the normoblastic pattern by folic acid, 10 mg. three times daily, and she had a normal delivery of a normal child. Professor Davidson said that this was the only case of haemolytic anaemia which he had seen in 30 years which had developed a classical megaloblastic anaemia.

The President, Sir Henry Cohen, thanked Professor Davidson for his excellent demonstrations.

During the afternoon members visited the wards and ancillary departments at the Rheumatic Unit in the Northern General Hospital; demonstrations and cases of clinical interest were shown, and the following short communications were read:

Steroid Metabolism in the Chronic Rheumatic Diseases, by Professor G. F. Marrian.

A brief account was given of the work carried out in collaboration with Dr. Duthie and Dr. Sinclair in the metabolism of administered progesterone in rheumatoid arthritis. In severe cases clear evidence has been obtained of an abnormality in the metabolism of this hormone, but the exact significance of this finding is as yet obscure.

An outline was also given of recent work carried out on the quantitative determination in urine of metabolites of the adrenocortical hormones. It was stressed that by existing methods only a small fraction of these urinary metabolites are actually determined.

Clinical Trials of ACTH and Cortisone, by Dr. W. R. M. Alexander.

The methods used in the clinical assessment of two cases of rheumatoid arthritis and one case of gout were described, and differences in certain effects of the two hormones in the same patient were discussed.

C-Reactive Protein in Rheumatic Diseases, by Dr. Alan G. S. Hill.

Results were presented of tests for C-reactive protein in serum from examples of various types of rheumatic disease. Positive results were obtained in all active cases of rheumatic fever, in most active cases of rheumatoid arthritis, and in gout during acute episodes. C-reactive protein was absent in osteo-arthritis, in a small group of cases of acute disseminated lupus erythematosus (except during incidents of superadded bacterial
infection), in dermatomyositis, and in scleroderma. In cases of rheumatoid arthritis treated with ACTH or cortisone, C-reactive protein rapidly disappeared. It was suggested that the test might be profitably used in assessing the response to other therapeutic agents with possible anti-rheumatic activity.

**Radiotherapy in Ankylosing Spondylitis**, by Dr. J. L. Potter.

An investigation of the clinical, haematological, and biochemical effects of radiotherapy in ten cases of ankylosing spondylitis and one case of spinal osteo-arthritis were described, and the results reported. It was suggested that the early clinical improvement observed may be mediated partly by an increased adreno-cortical activity, and further experiments to confirm this hypothesis were discussed.

**The Sterno-Manubrial Joint in Rheumatoid Arthritis and Ankylosing Spondylitis**, by Dr. Bruce Cruickshank.

The histological changes which occur in the manubrio-sternal joint and in symphysis pubis in ankylosing spondylitis were discussed, illustrated, and correlated with the radiological appearances. It was suggested that the pathological process in these cartilaginous joints is analogous to that seen in synovial joints in the disease.

**Clinical and Metabolic Effects of Glutathione in Rheumatoid Arthritis**, by Dr. A. P. Meiklejohn.

The clinical effect obtained by the intravenous administration of glutathione to a case of rheumatoid arthritis was described, but it was reported that attempts to repeat this effect had met with failure. The theoretical implications were discussed with special reference to the utilization of vitamin C in rheumatoid arthritis.

**A Method of Demonstrating the Union of Antibody and Antigen in Tissues**, by Dr. Alan G. S. Hill.

The use of fluorescein-tagged antibody as a specific cytochemical reagent for the detection of antigenic material in tissues was described. Illustrations were shown of results obtained in a study of the localization of an injected bacterial polysaccharide in animal tissues. The possibility of applying the method to a study of the rheumatic diseases was discussed.

---

**CLINICAL MEETING**

The Heberden Society met at the Ciba Foundation, 41 Portland Place, London, W.1, on July 27, 1951. The President, Professor Sir Henry Cohen, was in the Chair.

**Dr. W. H. Bradley** gave a paper on *The Antagonism between Jaundice and Rheumatism.* He said that intermittent and spontaneous recovery was an unpredictable feature of the chronic rheumatic diseases, but that there was a persistent claim that certain acute infections, pregnancy, and jaundice antagonized rheumatism. The first important contribution to this subject had been made in 1933 by Hench, who by 1940 had collected 72 cases in which jaundice appeared to ameliorate rheumatism and wrote that:

Within the bodies of patients who have even the severest arthritis powerful forces lie dormant which merely await proper stimulation.

Light on the subject had since come from:

(a) experimental induction of hyperbilirubinuria.

(b) jaundice incidental to therapy with synthetic analgesic drugs: Lactophen, Atophan, Nirvanol, and, in a special class, gold.