

## Juvenile Spondylarthritis

The condition known as juvenile spondylarthritis or "discitis" is a disorder of early childhood. It is characterized by sudden onset of pain in the back and narrowing of an intervertebral disc space with or without vertebral erosion. Systemic upset is slight, and the condition runs a short course with a good prognosis for general health and spinal function.

Formerly the disease was thought to be infective in origin, as the radiological features closely resemble those of known infective conditions. But nine years ago R. C. Jamison and colleagues<sup>1</sup> did not accept this view, and now C. J. Alexander,<sup>2</sup> from New Zealand, adds his dissenting voice to theirs. He reviews 120 cases and compares them with 131 cases of infectious spondylitis in adults reported over the same period. The infected cases had destruction of vertebral bodies, often severe and usually affecting both vertebrae, whereas the cases of juvenile spondylarthritis (or discitis) were never severe, and erosion was usually confined to one vertebra or was absent. The neural arch was sometimes destroyed in infectious spondylitis, never in juvenile spondylarthritis. Ankylosis was common in the former (70%), rare in the latter (about 5%), and the disc was usually destroyed in infectious spondylitis but in only three of the cases of juvenile spondylarthritis.

That this was not due to suppression of infection by antibiotics is shown by the fact that in half the cases antibiotics were not given, usually because the patients responded promptly to bed rest alone. Six patients with infectious spondylitis died of the disease, but none with spondylarthritis did so. The duration of juvenile spondylarthritis was usually shorter, commonly two to five weeks and occasionally up to 12.

A history of trauma was given by only three of the patients with infective disease but by 24 with juvenile spondylarthritis. Only three of the cases of spondylarthritis showed eventual abscess formation. Alexander considers that a non-infective cause should be sought, because in the large majority of cases no evidence of an infection appears. He suggests that partial dislocation of the epiphysis occurs during the vulnerable phase before the development of protective metaphyseal changes, which start about the age of 7 or 8 years, and that this dislocation, and not an infective process, is the cause. The common site—the third to fifth lumbar vertebrae—is, he states, the site of maximum stress on forward flexion and of maximal mobility on lateral flexion. The condition is rare above the tenth dorsal vertebra, a level above which the range of lateral flexion is much less. The hypothesis is relevant to treatment, because though rest would seem to be reasonable the use of antibiotics is more debatable in the absence of proof of an infective process.

R. F. Smith and T. K. F. Taylor<sup>3</sup> reviewed 20 cases of lesions of the intervertebral discs in children which were considered to be inflammatory in origin. Several radiographs showed a consistent pattern of vertebral disease with later a partial restoration of the disc's normal thickness. Persistent cavitation in vertebrae was seen and varying degrees of vertebral overgrowth. The average age of their patients was four years, and all but two were under six. Their presenting symptoms were refusal to walk and pains in the back, hips, or thighs. The lesions were at one disc level in 18 cases and two disc levels in two. The discs of the first, fourth, and fifth lumbar vertebrae were the most commonly affected.

The authors found little to indicate that antibiotics helped greatly, though application of a plaster spica in their opinion did so.

The satisfactory outcome, mild nature of the disorder, and inadequate proof of infection make a non-infective aetiology seem most likely in these cases. Here the matter rests until more pathological and bacteriological evidence is forthcoming. In a benign disorder of this nature such evidence is not easy to find.

## Antiserum Against Smallpox

Smallpox antiserum or gammaglobulin has been used for the treatment and prophylaxis of smallpox and of the complications of vaccination. Its value in the treatment of smallpox is debatable,<sup>1 2</sup> though E. A. Boulter and colleagues<sup>3</sup> showed in a rabbitpox model that serum therapy could be effective after overt disease had developed and that it had a beneficial effect even when given on the third day of pyrexia. There are encouraging reports<sup>4 5</sup> of the successful use of gammaglobulin in the prophylaxis or amelioration of smallpox in contacts.

C. H. Kempe<sup>5</sup> has reviewed the use of gammaglobulin in the complications of vaccination. In 62 cases of generalized vaccinia the response was generally prompt and no further lesions appeared, though 4 patients required a second administration of gammaglobulin because of the recrudescence of lesions; in 132 cases of eczema vaccinatum the mortality was reduced to 7% from the usual level of 30-40%; in 23 cases of the uniformly fatal vaccinia necrosum only 30% of treated patients died. Gammaglobulin had no effect in 12 cases of vaccinia encephalitis. In a series of 239 cases with complications of vaccination S. Sussman and M. Grossman reported similar results.<sup>6</sup> There is thus no doubt about the value of smallpox gammaglobulin, at least in the treatment and prevention of many of the complications of vaccination.

These complications can of course be reduced by careful attention to the contraindications to vaccination, by special precautions when vaccination has to be done on individuals with contraindications, by careful selection of the virus used for producing the vaccine,<sup>7 8</sup> and by the use of gammaglobulin at the time of vaccination.<sup>5</sup> Now that thiosemicarbazones are available, their use needs to be studied whether they are given alone or in combination with gammaglobulin in the various roles for which the latter has been used. Methyilsatin  $\beta$ -thiosemicarbazone appears to be of value in the prophylaxis of smallpox in contacts, in the treatment of eczema vaccinatum and vaccinia gangrenosa,<sup>9</sup> and in the vaccination of children with contraindications.<sup>10</sup>

E. A. Boulter<sup>11</sup> showed clearly the great importance of

<sup>1</sup> Patel, T. B., and Naidu, B. P. B., *Indian Medical Gazette*, 1940, 75, 730.

<sup>2</sup> Couzi, G., and Kircher, J. P., *Bulletin de l'Institut d'Hygiene du Maroc*, 1941, 1, 59.

<sup>3</sup> Boulter, E. A., Westwood, J. C. N., and Maber, H. B., *Lancet*, 1961, 2, 1012.

<sup>4</sup> Peirce, E. R., Melville, F. S., Downie, A. W., and Duckworth, M. J., *Lancet*, 1958, 2, 635.

<sup>5</sup> Kempe, C. H., *Pediatrics*, 1960, 26, 176.

<sup>6</sup> Sussman, S., and Grossman, M., *Journal of Pediatrics*, 1965, 67, 1168.

<sup>7</sup> Kaplan, C., *British Medical Bulletin*, 1969, 25, 131.

<sup>8</sup> Polak, M. F., Brans, L. M., Beunders, B. J. W., and Van Der Werff, A. R., *Bulletin of the World Health Organization*, 1962, 27, 311.

<sup>9</sup> Bauer, D. J., *Annals of the New York Acad. of Sciences*, 1965, 130, 110.

<sup>10</sup> Jarosynska-Weinberger, B., and Mészáros, J., *Lancet*, 1966, 1, 948.

<sup>11</sup> Boulter, E. A., *Proceedings of the Royal Society of Medicine*, 1969, 62, 295.

<sup>12</sup> Anderson, S. G., and Skegg, J., *Bulletin of the World Health Organization*, 1970, 42, 515.

<sup>1</sup> Jamison, R. C., Heimlich, M. D., Meithke, J. C., and O'Loughlin, B. J., *Radiology*, 1961, 77, 355.

<sup>2</sup> Alexander, C. J., *Clinical Radiology*, 1970, 21, 178.

<sup>3</sup> Smith, R. F., and Taylor, T. K. F., *Journal of Bone and Joint Surgery*, 1967, 49A, 1508.

the quality of the antibody necessary for therapeutic or prophylactic efficacy. He found that, while antibody formed in response to an active infection with vaccinia virus was highly active when used passively for treatment or prophylaxis, antibody with a similar neutralizing titre but formed in response to inactivated virus was lacking in therapeutic or prophylactic properties. The active antibody is apparently a response to the outermost layer of the vaccinia virus. This is present only on virus naturally excreted by cells. The tests described in connexion with the International Standard<sup>12</sup> would not specifically detect this essential property of gammaglobulin for therapy or prophylaxis. While there is no doubt that the International Standard (composed of serum collected from people convalescent from smallpox, most of whom had been previously vaccinated) would contain the desired type of antibody, the comparative tests reported with it would give evidence only of its quality in terms of neutralizing antibody, not of its potential therapeutic activity. An adequate test for that activity necessitates the use of virus naturally excreted from infected cells.

## Hidden Hyperthyroidism

Diagnosis of thyrotoxicosis in the hyperkinetic patient with exophthalmos, intolerance of heat, bounding pulse, fine tremor, increased appetite, and bowel frequency presents little problem, but the disease often appears in an atypical manner.

Chinese physicians in the seventh and eighth centuries<sup>1</sup> recognized the association of emotional disturbances with goitres. But it was not until 44 years after the first Western description of hyperthyroidism by C. H. Parry in 1825<sup>2</sup> that F. Chvostek<sup>3</sup> drew attention to some pitfalls in diagnosis. He pointed out that the condition may affect one particular system of the body to such an extent that the attention of both the patient and the physician may be directed towards a primary disorder of that system and away from the possibility of thyroid disease. Such masked or hidden hyperthyroidism most commonly affects the heart, producing otherwise unexplained heart failure or atrial fibrillation, particularly in the elderly. The disease may also present as loss of weight, or it may affect the gastrointestinal tract, producing malabsorption or diarrhoea, or the neuromuscular system, causing acute or chronic muscle weakness, fits, and encephalopathic or choreiform syndromes. Abnormal psychiatric states may be seen with few other obvious symptoms of hyperthyroidism.

One variety of the disease was called "apathetic hyperthyroidism" by F. H. Lahey,<sup>4</sup> and a timely reminder of its importance has come with the recent description by F. B. Thomas and his colleagues<sup>5</sup> of nine cases seen in a year in one department of medicine. In each of their cases apathy was the cardinal clinical feature apart from the congestive

cardiac failure with which the patients were admitted. No patient was initially suspected of suffering from thyrotoxicosis, and indeed in two of them myxoedema had been thought of as a possible diagnosis. The discovery by a routine test of a raised protein-bound iodine pointed to the true diagnosis. A full laboratory investigation and the satisfactory response to antithyroid treatment confirmed it. Since studies of thyroid function are rarely performed in Great Britain as a routine without clinical suspicion of thyroid disorder, the possibility of a diagnosis of apathetic hyperthyroidism must be remembered.

Though the patient is usually past middle age, the apathetic type of the disease has been recorded in childhood.<sup>6</sup> In addition to apathy the clinical features include depression and lethargy, heart failure with atrial dysrhythmias, loss of weight, and muscle wasting, but only rarely are the usual eye signs prominent. On the contrary Thomas and his co-authors point out that ptosis is frequently found. Since the laboratory indices of thyroid function usually suggest thyrotoxicosis once it is suspected, the diagnosis is easily confirmed, and conventional treatment is rewarding.

The key therefore to correct diagnosis in hidden hyperthyroidism is to maintain a high index of suspicion and not necessarily to expect other clinical features of thyrotoxicosis. The apathetic thyrotoxic person may pass suddenly into a more typical agitated state, but Lahey observed in 1931 that these quiet, disinterested patients, who look old for their age but do not look extremely ill, may "quietly and peacefully sink into apathy, from that into coma, and die an absolutely relaxed death and without activation." This should be a warning to us that the condition may remain atypical throughout its course.

## Enterprise at Edinburgh

This week and next the *B.M.J.* is publishing shortened versions of the papers given at a recent conference in Edinburgh on "Immunological Aspects of Cancer." We have printed these at length because of the quality of the contributions themselves and the rapid progress in this field, and because comparatively little has appeared about it so far in non-specialist journals.

The symposium was organized by the Royal Medical Society of Edinburgh, and both it and the symposium convenor, Mr. Ian Smith, are to be congratulated on their enterprise in arranging this conference, which all attending agreed to be outstanding. The Society is a student one, and dates from the year 1737, when ten medical students agreed to meet weekly in a tavern to hear one of their number read a dissertation on some medical subject. It is the oldest medical students' society in Great Britain, and the only one to hold a Royal Charter (which was granted by King George III in 1779). The Society has a long and distinguished tradition; among its past members are Lister, Simpson, Joseph Bell, Charles Darwin, and Andrew Duncan.

As one of the distinguished contributors to the symposium, Professor Georges Mathé, commented, if only students all over Europe would abandon hurling paving stones at the authorities and adopt the constructive approach shown at Edinburgh, our universities might be much happier places.

<sup>1</sup> Needham, J., and Lu Gwei-Djen, *Japanese Studies in the History of Science*, 1966, 5, 150.

<sup>2</sup> Parry, C. H., *Collections from the Unpublished Writings of the Late Caleb Hillier Parry*, 2, p. 111. London, Underwood, 1825.

<sup>3</sup> Chvostek, F., *Wiener medizinische Presse*, 1869, 10, 434.

<sup>4</sup> Lahey, F. H., *New England Journal of Medicine*, 1931, 204, 747.

<sup>5</sup> Thomas, F. B., Mazzaferri, E. L., and Skillman, T. G., *Annals of Internal Medicine*, 1970, 72, 679.

<sup>6</sup> Grossman, A., and Waldstein, S. S., *Pediatrics*, 1961, 28, 447.