Endocrine Exophthalmos

The severity of the systemic symptoms of hyperthyroidism in Graves’s disease often differs considerably from the severity of the ocular disturbances. The accumulation of clinical evidence, such as the occurrence of exophthalmos in association with pretilial myxoedema and the apparent increase in severity of exophthalmos after thyroideectomy, led to the concept of specific pituitary factors causing exophthalmos without stimulation of thyroid gland, but it was not until the development of biochemical, radioassay, bioassay, and immunoassay techniques that these clinical impressions began to receive support. Though the prime aetiological mechanism is still not clearly understood, recent work has gone some way towards clarifying the biochemical dysfunction in endocrine exophthalmos, and clinical assessment of the condition has become more accurate. Unfortunately drug treatment remains unsatisfactory. Though decomposition of the orbit is at times necessary, debate continues over the surgical technique that should be used.

Patients with exophthalmos which proves to be endocrine in origin may be clinically hyperthyroid or euthyroid. There is evidence that the eye symptoms of Graves’s disease such as stare, soreness, watering, lid retraction, lid lag, and delayed blinking are due to excessive activity of the thyroid hormone, whereas pure exophthalmos or the measured exophthalmos accompanying these symptoms is caused by pituitary factors. The separation between these factors becomes relevant because some authors have doubted whether true exophthalmos occurs in pure thyrotoxicosis. Certainly such patients rarely have a degree of exophthalmos which demands surgical decompression. A. N. Bowden and F. Clifford Rose, in reviewing 50 patients referred to a medical ophthalmology unit with the eye symptoms of “Graves’s disease,” noted exophthalmos in 46, but other symptoms such as lid lag and lid retraction in as many patients, a remarkably high incidence of these in view of the ophthalmological and neurological bias of the referrals. Twenty-four patients were euthyroid on the basis of the Wayne Clinical Index, though in six of these patients hyperthyroidism was detected on the basis of iodine-131 uptake or serum levels of protein-bound iodine-131. This substantiates the view that true endocrine exophthalmos occurs in the absence of clinical or biochemical evidence of hyperthyroidism.

Evidence suggests that the pathological changes in the orbital tissues found in endocrine exophthalmos are due to pituitary rather than thyroid factors. These include an exophthalmos-producing substance and thyroid-stimulating hormone.4 The triiodothyronine-suppression test, which measures the normal suppression of thyroid gland activity (radioiodine uptake) by the administration of a thyroid hormone (triiodothyronine) and which depends on inhibition of the production of thyroid-stimulating hormone by the pituitary, is used as a measure of autonomy of the pituitary in abnormal states. Many authors have found the triiodothyronine-suppression test to be abnormal in euthyroid patients with endocrine exophthalmos, thus lending support to the concept of these pituitary hormones being directly responsible for the exophthalmos. A third hormone, long-acting thyroid stimulator, has been thought to play some part in the production of endocrine exophthalmos, but the evidence for this is at present inconclusive and from several authors conflicting. Further support for the existence of a pituitary mechanism is obtained from the observations that, firstly, exophthalmos often begins after successful ablation of the thyroid gland, and, secondly, after iodine-131 treatment for thyrotoxicosis the exophthalmos tends to increase although the lessening of lid retraction may improve the ocular appearance.7 Rarely the exophthalmos attains “malignant” proportions, the increase in exophthalmos being greatest by the end of the first year after iodine-131 therapy. Thereafter the condition may remain static and later recede slowly.

The pathological changes within the orbit include inflammation and oedema of the connective tissue, fat, and muscles, and these are probably due to an increase in the mucopentosaccharides of the connective tissue ground-substance.8

The treatment of endocrine exophthalmos by drugs or thyroid surgery remains unsatisfactory. Total ablation of the thyroid by surgery or radioiodine has been suggested on theoretical grounds, but it does not relieve or halt visual deterioration. In these circumstances patients may be given a trial of corticosteroids in high dosage,9 10 but there is no way of predicting whether they will be effective. The natural history of the condition is very variable, and if deterioration in visual acuity has already occurred vision may be lost irretrievably while awaiting the effects of steroid therapy. To-day, therefore, it is wiser to consider orbital decompression as soon as any loss of vision occurs which is not relieved by lateral tarsorrhaphy. The decision has become easier with the development of the transantral operation.11-13 This has now largely replaced decompression by removal of the orbital roof through a frontal craniotomy.

In series reported so far, the complications have been few, and the transantral route appears to be the one of choice in the management of endocrine exophthalmos, to be employed early when loss of visual acuity occurs.

Pelvic Sepsis

Sepsis in the retroperitoneal tissues or in the pelvic bones in childhood is uncommon. In either condition the main presenting symptoms may be pain in the hip, pyrexia, and malaise. Osteomyelitis of the upper femoral metaphysis or septic arthritis of the hip may be suspected because of painful limitation of movement of the hip.

A. W. March, L. H. Riley, and R. A. Robinson describe the clinical findings in 14 children with retroperitoneal abscess and 20 patients with septic hip disease seen at the Johns Hopkins Hospital between 1946 and 1970. Though fever, hip pain, and limp were outstanding symptoms in both groups of patients, abdominal pain and back pain were more frequent symptoms in patients with retroperitoneal abscess. In retroperitoneal abscess the painful limitation of movement of the hip was greatest when the hip was abducted, extended, and medially rotated, the position in which the psoas and iliacus are put under tension.
Abdominal and rectal tenderness were more frequent in this condition, and a palpable mass in the loin or pelvis combined with absence of local swelling in the region of the hip indicated a diagnosis of retroperitoneal infection rather than a septic hip lesion. Radiological investigation often showed an abdominal or pelvic mass or widening of the psoas shadow.

Similar diagnostic problems may arise in acute osteomyelitis of the pelvis. A. Morgan and A. K. Yates drew attention to the fact that patients with osteomyelitis of the pelvis may present with symptoms and signs in the hip, but, as in retroperitoneal abscess, there is differential limitation of hip extension and medial rotation. In some patients the lesion presented as an abdominal syndrome with clinical features simulating acute appendicitis on the right side and paracolic abscess on the left. Laparotomy, with removal of a normal appendix, was recorded on a number of occasions. Other patients with osteomyelitis of the pelvis may present with pain in the buttock or sciatica. Radiographic findings are late in appearing, and the infection may be well established and involve a large area of bone before any changes are recognizable. Even when the whole clinical picture indicates the presence of a large abscess, it may be difficult to discover where it is and even more difficult to drain it surgically.

In contrast, septic arthritis of the hip presents with painful limitation of hip movement in all directions and with local swelling and tenderness over the joint only. Osteomyelitis of the pelvis involving the innominate aspect of the joint may simulate almost completely the signs of septic arthritis. But critical examination should allow the true source of sepsis that may be masquerading as a lesion of the hip to be discovered.


Cancer Research: Preparing for a Long Haul

During the last few years the aura of ballyhoo surrounding cancer research in Britain has faded. Talk of finding "the answer" to what was wrongly presumed to be but a single question is far less in evidence, and words like "breakthrough" are heard less often. Several factors have helped to bring about these welcome changes, and one of them is the reorganization and modernization of the Cancer Research Campaign. The 49th Annual Report of the Campaign covering the year 1971, published this week, is in the new form adopted for the first time last year. Two-thirds of the 143-page report is taken up by lists of titles of research projects and of publications by research workers supported by the Campaign. Much of the remainder is necessarily concerned with financial matters and a report of the opening on 18 November 1971 of the Gray Laboratory at Mount Vernon Hospital, Middlesex, by Mr. Jack Hawkins. The laboratory is in reality an extension of the research unit in radiobiology which was opened in 1957 and whose first director was Dr. L. H. Gray. Research in the enlarged laboratory will not, however, be restricted to radiobiological studies.

Included in the report are general reviews of three aspects of cancer research. The first of these is by Sir Richard Doll and Dr. L. J. Kinlen and is concerned with epidemiology as an aid to determining the causes of cancers. Much of the content is well known, but snippets of information scattered here and there make it necessary and worthwhile to read the whole. Thus not everyone will know that the skin cancers which the early radiobiologists developed were mainly on the backs of the hands, that the risk of cancer from asbestos began 100 years ago with the discovery of deposits of chrysotile in Canada and Russia, that "Chatta cancer" of the palate in Vizagapatam is attributable to the local habit of smoking cigars with the lighted end inside the mouth, or that a rapid rise in the incidence of oesophageal cancer in parts of eastern and central Africa seems to be associated with the recent introduction into those areas of a method of preparing beer by the fermentation of maize. But perhaps the most important development mentioned in this article is the starting, with the support of the Campaign, of a prospective epidemiological survey of patients receiving immunosuppressant drugs for the prevention of graft rejection after transplantation surgery or for other reasons. There is already evidence that recipients of kidney grafts are more likely to develop lymphomas, reticulum-cell sarcomas, and a variety of other neoplasms than persons of comparable ages in the general population. However, it is not certain whether the increased risk is attributable solely to the prolonged exposure of the recipients of tissue grafts to immunosuppressant drugs or whether the presence of foreign proteins (antigens) for long periods is itself a factor that favours the development of cancer. Some evidence from experiments on laboratory animals suggests that continued antigenic stimulus may predispose to the development of neoplasms. The possibility that neoplasms result from activation of oncogenic viruses where there is both antigenic stimulation and immunosuppression has recently been discussed.

In the 1972 Walker prize lecture at the Royal College of Surgeons Mr. Denis Burkitt propounded a theory that the low-roughage diets consumed by Europeans and North Americans predispose to constipation, diverticulitis, and cancer of the lower bowel. The prolonged residence of material in the gut might, he thought, permit carcinogens to be formed by the bacterial degradations of bile salts and give such carcinogens time to act on the cells lining the gut.

Professor R. E. O. Williams and his colleagues at St. Mary's Hospital, London, recently reported different concentrations of steroids and differences in gut flora between persons living in communities where colon cancer is common and persons living in communities where it is rare. There is a natural aversion among research workers to studying faecal matter, and methods for studying gut bacteria are poorly developed. Nevertheless, the fact that more enzymic activity takes place within the gut and the gut wall than in the liver should long ago have directed the attention of cancer biochemists to the urgent need for more factual information about the contents of the intestines.

In their up-to-date review of the chemical causes of cancer Professor P. N. Magee and Dr. A. E. Pegg look again at Walter Burdette's conclusion, written in 1955, that "a general correlation between mutagenicity and carcinogenicity cannot be proposed from present evidence." As Burdette himself realized, the failure of carcinogenic chemicals to induce mutation in higher organisms may be due to a failure of the administered substance or its active metabolite to reach the germ cells. Similarly the failure of a mutagen to induce cancer may mean no more than that the administered substance or its active metabolite did not reach a carcinogen-sensitive target. Magee and Pegg stress the im-