Centenary Annual Meeting of Canadian Medical Association

[FROM A SPECIAL CORRESPONDENT]

The Canadian Medical Association celebrated its centenary by holding the 1967 Annual Meeting in Quebec City, the place of its founding in the year of Canadian Confederation, and in Montreal. As part of this meeting scientific sessions were held at the Château Frontenac Hotel, in Quebec. A report of some of these sessions is given below.

Triple-X Female

Dr. MURRAY BARR (London, Ontario) opened the scientific meeting with a discussion on the trisomy of chromosomes, with particular reference to that of the X chromosome. Dr. Barr—who during the course of the meeting was presented with the F. N. G. Starr Award by the Canadian Medical Association, as recognition of his contributions to the field of genetics—outlined the various genetic abnormalities that at present were identified with chromosomal non-disjunction. The latter was an error of mitosis, in which two similar chromosomes (instead of the usual one) were contributed to the daughter cell during germ cell maturation. This might occur with any of the 22 pairs of autosomes or with the sex chromosome.

Dr. Barr reminded his audience that each chromosome contained hundreds of genes, the number varying with the length of the chromosome. The deoxyribonucleic-acid-containing genes elaborated ribonucleic acid, both of a specific nature for each gene locus, and the ribonucleic acid in turn guided the production of specific cytoplasmic enzymes. When trisomy existed, each gene locus was present three times instead of twice, and consequently enzymes under control of the trisomic chromosome would theoretically be produced at 50% above their normal values. Enzymatic imbalances occurred and interfered with normal embryonic development. Dr. Barr observed that the longer the chromosome the greater the expected damage would be, and the details of the abnormalities produced would vary depending on which chromosome was trisomic.

When chromosomes were arranged as a conventional karyotype, the 44 autosomes could be divided into seven groups, A to G, on the basis of morphological similarity. Trisomy of autosomes in all seven groups was found in spontaneously aborted foetuses, while numerical chromosome abnormalities accounted for at least 20% of embryonic loss. Trisomy of autosomes was usually lethal during the first trimester, and with rare exceptions only three types of autosomal trisomy allowed the foetus to proceed to live birth—namely, trisomy 15, trisomy 18, and trisomy 21 (which caused mongolism or Langdon Down's syndrome).

Dr. Barr pointed out that, though the X chromosome was large, X chromosome trisomy did not result in death or in the production of serious physical defects as would be expected. The X chromosomes were about the same length as autosome 6, with a large number of gene loci, only a few of which were concerned directly with sex differentiation. Trisomy of the X chromosome did not interfere more drastically with the normal development of various systems and organs because of the phenomenon of X chromosome heteropyknosis—where one of the chromosomes of the female was tightly coiled, compact, and adherent to the inner surface of the nuclear membrane. This chromosome was relatively genetically inactive and ensured that there was not a great predominance of active genetic material from the female. Moreover, the X chromosome of paternal origin could take this inactive heteropyknotic role also, and the form of the X chromosome, paternal or maternal, was decided at the moment when the embryo underwent implantation.

This ability to form inactive X chromosomes gave the subject a protective mechanism not afforded in cases of autosomal trisomy, and gave a reasonable basis for explaining the lesser degrees of malformation found in triple-X trisomy. Dr. Barr presented accounts of six patients with X trisomy and noted that, though a clear clinical syndrome had not been established, certain features might be found in some cases—including club foot, subluxation of the elbow, flexion deformities of the fingers and other skeletal abnormalities, webbed fingers, hydrocephalus, spastic quadriplegia, optic atrophy, cataract, and corneal opacities. Nevertheless, triple X females were usually physically normal, but they ran a greater risk than average of some sort of defect, with no consistent pattern.

Concluding, Dr. Barr suggested that the incidence of X trisomy was 1 in 850 female babies, and noted that until mass chromosome analyses were done on all newborns chromosome abnormalities of this type would go undetected, lacking as they did a well-defined clinical picture.

Calcium Homoeostasis

Discussing the regulation of body calcium, Dr. D. H. COPP (Vancouver) emphasized that, though the body of a 60-kg. man contained over 1 kg. of calcium, less than 0.1% of this was extracellular and involved in important functions such as muscular contraction, neuromuscular excitability, membrane permeability, and enzyme activity.

Using sequential high calcium and low calcium perfusions of the parathyroid gland, Dr. Copp and his associates had observed a very rapid fall in plasma calcium during the high calcium perfusions, and the expected rise with low calcium perfusions—this presumably due to endogenous parathyroid hormone. Following the final perfusion, the test animals had had the thyroid and parathyroid glands removed. Instead of the expected fall in plasma calcium a marked and sustained rise had occurred, and it was suggested that the fall in calcium during high calcium perfusions was not due to suppressed parathyroid hormone production but to a humoral agent which actively lowered blood calcium. Hence they had concluded that a previously unrecognized hormone was involved. This was now accepted as calcitonin or thyrocalcitonin, derived from the "light cells" or "C" cells, which made up 2–4% of the mammalian thyroid.

Calcitonin was a straight-chain polypeptide, as was parathyroid hormone, but it was about one-half the size and lacked three amino-acids found in parathyroid hormone: isoleucine, trytophane, and cysteine. It was antigenic, with definite species differences, and was effective in man in doses of less than 0.1 mg.

Calcitonin had been found to be effective after nephrectomy and total evisceration, so that its action was not through either kidney or intestine. It was also effective in the parathyroidectomized animal, so that it was more than an inhibitor of parathyroid action. Experimental evidence suggested that, while parathyroid hormone increased osteolysis, calcitonin inhibited normal osteolysis, the osteolytic effect of parathyroid hormone, and also the osteolysis induced by vitamin A. Active remodelling of bone, stimulated by parathyroid hormone, was inhibited by calcitonin, with a reduction in the number of osteoclasts.

The control of serum calcium levels had two facets: firstly a fine control mechanism, and secondly a relatively crude control, which operated in the thyroparathyroidectomized animal. The former was the parathyroid-hormone–calcitonin system, in which each hormone could act independently of the other, and where the hormone output was controlled by the concentration of calcium ions in the blood. The latter depended on such factors as the labile calcium store in bone, the availability of calcium from the gut (favoured by the presence of vitamin D), the excretion of calcium, and the effect of calcium and phosphate in blood on the deposition of new bone mineral.

Dr. Copp emphasized that the clinical value of calcitonin had not been established. The great hope was that it might have a beneficial effect in cases of osteoporosis, but, discouragingly, calcitonin had been found to act much more effectively in the young animal in inhibiting osteolysis.

Gastrointestinal Polyps

Reviewing current concepts about polyps of the gastrointestinal tract, Dr. WALTER MACKENZIE (University of Alberta, Edmonton) decried the tendency for the terms polyp

and adenoma to be used interchangeably, and stated that this lack of precision, which was particularly noticeable in recent articles, had led to improper treatment.

In the diagnosis of benign tumour of the oesophagus, Dr. MacKenzie stressed the importance of careful *x*-ray examination, which revealed a smooth filling defect with normal mucosa overlying the tumour mass. He felt that gastric polyps were precarcinogenic, and he referred to a 12-year study of 20 patients with multiple gastric polyps, when three had developed proved malignancy. The use of gastroscopy had been invaluable in diagnosis, and could give an early indication of malignancy. Partial gastrectomy was the treatment of choice for multiple polyps, since this avoided the increased mortality and morbidity associated with total gastrectomy, and also the serious nutritional problems associated with the latter procedure.

The use of transillumination of the bowel in a dark-adapted operating-room was a useful procedure in visualizing small bowel tumours. The radiological examination of the small bowel was, Dr. MacKenzie stated, only as effective as the degree of awareness of the clinician and the degree of care taken by the radiologist.

In the colon a papillary or villous adenoma was potentially more dangerous than an adenomatous polyp, with an associated malignancy rate of 30–40 per cent. The relation of the adenomatous polyp to carcinoma remained one of the most controversial areas in the field of general surgery, though Dr. MacKenzie felt strongly that a significant positive correlation existed, pointing out that the frequency of carcinoma rose proportionately with the presence of multiple polyps. He supported the view that polyps might be the "flags" which signalled a carcinogenic stimulus. In congenital multiple polyposis of the colon possibly the carcinoma might be merely a manifestation of the large number of polyps and their potential to become malignant.

In the case of rectal polyps, it was generally agreed that removal of those within reach of the sigmoidoscope was indicated and was relatively simple. For those above this level he recommended colotomy and polypectomy for those which were clinically benign, and resection of the involved portion of the bowel for those which were not. He felt that the incidence of existing malignancy was greater with increased polyp size, but could see little justification for attempting to establish a so-called "critical" polyp size.

Industrial Rehabilitation

Mr. LAWRENCE PLEWES (Dunstable, Great Britain) outlined the services in the field of industrial rehabilitation available in England under the Disabled Persons Act. He pointed out that both the Ministry of Health and the Ministry of Labour were actively involved in this area, their activities being co-ordinated by a National Advisory Committee, composed of doctors, trade unionists, employers, and officials from both Ministries. At the local level there was the Disablement Advisory Committee with a similar composition, concentrating its efforts on local employment situations and individual disability problems.

Mr. Plewes felt strongly that traditional occupational therapy should be confined to diversional schemes for bed-ridden patients, and had no place in a modern rehabilitation service. All forms of passive physical therapy —such as heat, massage, diathermy, and ultrasonics—should be and had been replaced by exercises and machines and games. This change from the passive to the active form of therapy had not been easy, since it was difficult to persuade a patient, in a push-button age, that the best results would follow his own muscle contractions.

The usual pattern at a district general hospital was for limited rehabilitation services to cope with urgent short-stay patients. Regional centres with accommodation for in-patients catered for the more serious and long-term problems. The rehabilitation centre, such as the one at Luton, used a factory milieu to both mobilize and evaluate the recovery of the patient. Simple machines, which employed a conditioned reflex on the part of the operator, were generally used, and enabled the patient to do useful work, avoiding the boredom of simple exercise, and in addition fostering a feeling of accomplishment. Noise was purposefully present in a moderate degree, allowing for a gradual adjustment back to a noisy environment while the patient was under sedation. This was important in post head-injury cases, where sudden exposure to noise could be intolerable. Dr. Plewes stressed that this industrial method was used no matter what type of employment the patient had previously held, and it had been found effective.

In those patients who were unable to return to normal employment sheltered workshop accommodation should be available. Once a patient had progressed to a point satisfactory from the medical aspect, he could be either returned to his normal occupation or referred to the industrial rehabilitation unit. At the latter the disabled person was evaluated by a highly skilled staff, and was then given a trial at several different appropriate occupations or sent to a private industrial concern for highly specialized rehabilitation courses. In all cases rehabilitation was on industrial lines. The pace was graded, and vocational assessment was a continuing feature. If further training was necessary the patient was sent to a Government training centre or technical college.

Dr. Plewes felt that the involvement of trade unionists in these programmes was most important for their success. He estimated that a community of 230,000 should have an industrial rehabilitation centre for 50 persons at the hospital, another 50 places in local industry, and a sheltered workshop for 50 disabled persons, plus an additional 100 places for the mentally disabled, to meet adequately the demand for service.

Growth Hormone Deficiencies in Childhood

Professor DOUGLAS HUBBLE (Birmingham, Great Britain) delivered the Tisdall Lecture (established in memory of Dr. Frederick Tisdall, a great Canadian paediatrician and nutritionist), on defective growth in childhood. Detailing his experience with a group of twenty-one cases of growth hormon deficiency, he classified this into idiopathic, genetic, and secondary. Thirteen of his cases fell into the first category, and included perinatal injury. Two cases were classified as genetic, which would be either autosomal recessive or non-sexed linked. Under secondary causes Professor Hubble included cases of craniopharyngioma, chromophobe adenomas, healed tubercular meningitis, and trauma.

Only seven cases were isolated growth hormone deficiencies ; eleven cases also had thyroid-stimulating-hormone deficiency, as shown by low serum protein-bound iodine levels. Professor Hubble felt that in some cases there was some failure of the thyroid gland dependent on the growth hormone deficiency, though attempts to verify this hypothesis had been unsuccessful. Corticotrophin deficiency occurred in four of his patients. The clinical picture of patients with growth hormone deficiency was apparent immaturity, normal intelligence, truncal obesity, retarded skeletal maturation, marked growth retardation, and, in many cases, episodes of spontaneous hypoglycaemia. All the patients over 15 years of age had shown retardation of puberty.

A combination of the radioimmunoassay and the intravenous insulin-tolerance test had been used for diagnosis, in conjunction with the human growth hormone nitrogen-retention test. Although these involved considerable technical difficulties, these tests had enabled the diagnosis of growth hormone deficiency to be made with precision, and for it to be excluded in other cases.

In children with growth hormone deficiency the treatment was with growth hormone derived from human pituitaries, since preparations of animal growth hormone gave no response. The dosage varied from 6 mg. weekly to 18 mg. weekly, and produced a greatly accelerated velocity of growth in the first year of treatment. This initial spurt was called the "catch-up" period. Normal growth rates could be achieved by prolonged therapy, but the "catch-up" growth period by no means allowed the leeway which had occurred in the early years to be made up. Most of the 40 cm. of rapid growth in the first three years of life was irrecoverable. If hypothyroidism was present, thyroxine should be given concurrently, for the two hormones appeared to act synergistically, though thyroxine could not replace growth hormone.