DIABETES MELLITUS AND CARCINOMA OF THE PANCREAS.

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SOME time ago we saw a patient who developed diabetes mellitus with classical symptoms and a strong family history of the disease. Shortly thereafter he developed obstructive jaundice, and at laparotomy was found to have a small carcinoma localised to the head of the pancreas and obstructing the common bile duct. A partial pancreatectomy was performed and the patient survived the operation successfully for five years. This case raised some queries in our minds regarding the character and behaviour of diabetes as a manifestation of a pancreatic tumour and its value in differential diagnosis. (We include some data on this patient later.) An unusually interesting and somewhat similar case was reported by Hennessey. At the same time we set about investigating some 66 cases of pancreatic carcinoma seen at the Royal Victoria Hospital, Montreal, over the period 1944-54. A small number of these patients were seen by the author in life, the majority were not. Autopsies were performed on all but a few cases. It seemed that there were many questions raised at the bedside regarding the association of these two conditions, the answers to which were not too clear. The purpose of this paper is to attempt to clarify a number of these queries with clinical and pathological data.

The following facts are well known and generally accepted: (1) Diabetes occurs fairly often from carcinoma of the pancreas, the frequency varying somewhat, depending on how carefully it is sought. Up to one-third of the patients in some series showed either glycosuria or abnormal blood sugar levels, while in cases studied by glucose tolerance curves a much higher percentage reveal significant abnormalities. Berk reports on 34 cases: 9 had tolerance curves and 7 were abnormal. Arkin and Weisberg in a review of 75 cases found abnormal glucose tolerance curves in all of 19 so tested, and in the cases of Dalshiel and Palmer the figures were 18 abnormal curves in 21 cases. (2) The diabetes is usually of mild degree and easily controlled by less than 40 units of insulin per day. (3) Ketosis is a rare complication.

Grauer, discussing some of the pathological features of the condition, drew attention to the fact that frequently the acini are destroyed by back pressure from obstruction to the pancreatic duct, whereas islet tissue is seen intact. He found the blood sugar elevated significantly in 8 of 14 cases and was unable to correlate the impaired carbohydrate tolerance with enlargement of or metastases to the liver. Best carmine stains for glycoegen granules revealed these to be decreased and confined to the periphery of the lobule. He concluded that diabetes resulted mainly from massive invasion of the gland by tumour. On the other hand, Schredorf and Orr found no case of diabetes in 52 cases. Joslin concluded an article on the subject by saying that roughly 95 per cent. of the pancreas has to be destroyed before a deficiency of insulin sufficient to cause diabetes will result. The survival of islet tissue in the
tail, having an independent blood supply, may account for some apparent discrepancies among the various reports. Pygott and Osborn have reported a case of cancer of the tail causing diabetes with classical symptoms that is of interest in this respect.

Many have noted the striking weight loss in the disease and cite this as a possible ameliorating factor in the diabetes. They have found that the diabetes becomes less severe as the underlying lesion advances. However, a poor food intake, through its effect on the liver, can act to aggravate rather than to reduce the severity of diabetes. Furthermore, as pointed out by Marble, glucose tolerance curves are abnormal in a high percentage of carcinomas occurring anywhere. The factors involved include poor food intake, hepatic metastases and biliary obstruction. In these cases the fasting sugar level may be normal, whereas the post cibum values are high. Marble reported a case of biliary obstruction in which the glucose tolerance returned to normal after anastomosis of the gallbladder to the stomach. It would be of interest to know if this may also occur spontaneously in the remission of cholangiolitic hepatitis, as the differential diagnosis of this condition from a tumour in the head of the pancreas is often extremely difficult. Moreover, a few cases of improvement of diabetes after pancreatectomy have been reported possibly due to removal of glucagon (hyperglycaemic factor of alpha cells).

Statistically, the incidence of carcinoma of the pancreas developing among old-standing diabetics is significantly greater than in a normal population of comparable age group. Marble discusses this question of cancer in general among diabetic patients. Some of his findings are interesting and worthy of comment here. In reviewing 10,000 diabetic cases seen at Joslin Clinic, he found 256 malignancies, giving an incidence of 2.6 per cent. Cancer of the pancreas was the commonest single tumour encountered (33 cases, 13 per cent. of the total). This is in marked contrast to the frequency of pancreatic cancer among tumours in general. For every 100 persons dying of cancer in the ordinary population, only 3 will have a pancreatic tumour. Thus it seems that patients with diabetes are unusually prone to develop pancreatic malignancy. He does not comment on the effect of the tumour supervening on old-standing diabetes. Among his series, Marble found the average duration of diabetes in patients with cancer of the pancreas to be 3-4 years and the average duration of the symptoms of the cancer one year. He comments that this is the shortest duration of diabetes of any group of diabetics under observation, and implies that in some of these cases the diabetes may have been directly due to the tumour and presented as a very early manifestation of the malignancy. (See Case No. 53.)

Marble also commented on carbohydrate tolerance in non-diabetic patients with cancer. This is apt to be impaired from poor nutrition and hepatic metastases, among other things. He concluded that the glucose tolerance curve is often abnormal in cancer patients, due to the fact that the sugar given may overload the cachectic patient and that no true defect in carbohydrate tolerance exists. Actual diabetes is rare.

Finally, Marble found that the diabetic state in his patients, regardless of the location of the tumour, seemed to be ameliorated as the malignant process progressed. This was associated with a greater proneness to