

importance, however, was the observation that diabetes was associated only in those cases where the islands of Langerhans were practically completely destroyed, and this was naturally most likely to occur in the interacinar type. The thought naturally occurred to Opie to make a systematic histological examination of the pancreas in a consecutive series of fatal diabetes cases. He found that in nearly every instance the islands were almost completely destroyed and had undergone a hyaline degeneration. Ssobolew, working independently, published in 1901 practically identical observations on the relationship between disease of the islands and diabetes. In view of the intimate relationship, in his series, between involvement of the islands and diabetes, Opie was led to conclude that there was a very intimate connection between them and carbohydrate metabolism. Laguesse and Schäfer had previously suggested that the islands furnish an internal secretion in the same manner that the thyroid and adrenals do. Owing to their minute size and the impossibility of isolating them from the rest of the gland substance, it has been practically impossible to produce experimental evidence supporting this view, although Ssobolew claims to have done so. Occurring as ductless glands, and being surrounded by a rich capillary network, it is extremely probable that these islands secrete some substance—call it a “glycolytic ferment” after Lépine if we will—which enters the circulating blood, and which is necessary for the proper combustion of carbohydrates in the system.

From what has been said it will be perfectly obvious to everyone *that* a careful microscopic examination of the pancreas is necessary before excluding it as a cause of diabetes. The gland on macroscopic examination may appear perfectly normal, while on microscopic study these small islands may be found completely degenerated, the remainder of the gland structures being perfectly intact. Opie's observations have been confirmed by numerous observers on this continent and abroad, but it must be pointed out that a number of instances have been recorded in which diabetes has occurred without any microscopic changes in the islands having been found. These negative results are subject to two interpretations. One inference is that all cases of diabetes are not actually of pancreatic origin, which is probably true. The other is that, although the islands show no microscopic change, they may be functionally inactive and fail to secrete their specific enzyme, just as we may have a functional inactivity of the oxyntic cells in the gastric mucosa with resultant acidity of the gastric juice.

Following closely upon these important researches. Otto Cohnheim, in 1903 and 1904, published results of experiments which seem destined to solve the problem of how the glucose of the circulating blood is ultimately burnt up in the body. This is the mystery which has puzzled