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EXPERIMENTAL DIABETES RESEARCH IN FISH

On the Morphology and Physiology of the Endocrine Pancreatic Tissue of the Marine Teleost Cottus scorpius with Special Reference to the Role of Glutathione in the Mechanism of Alloxan Diabetes Using a Modified Nitroprusside Method

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GENERAL INTRODUCTION

Pathological and clinical studies in man as well as experimental investigations on animals have not yet been able to elucidate the etiology and pathogenesis of diabetes mellitus. This is one reason why there has been a growing interest during the last few years in using other experimental animals in diabetes research than the conventional laboratory mammals. This tendency may be exemplified by recent investigations performed on birds (Beekman 1956; Runge et al. 1956; Ferner et al. 1957; Mialhe 1958; Mirsky & Gitelson 1958), lizards (Miller & Wurster 1956, 1958, 1959; Miller 1960), snakes (Prado 1947; Houssay & Penhos 1960), turtles (Foglia et al. 1955; Lopes 1955; Marques 1955; Cardeza 1957; Corrêa et al. 1960), frogs (Seiden 1945; Wright 1959), and bony fishes (Doerr 1950; Mialhe 1952; Nace 1955, 1960; Cooperstein et al. 1956; Fodden 1956; Maske et al. 1956; Mosca 1951, 1959; Murrell & Nace 1958, 1959; Nace et al. 1958, 1959; Davidson 1958, 1959).

The bony fishes are of particular interest in experimental diabetes research as their endocrine pancreatic tissue may be concentrated into one or a few grossly visible structures in the abdominal cavity, the so-called “principal islets” (Rennie 1905) (“Brockmannische Körperchen”, “dorsale Pankreaskörperchen”, cf. Baron 1934, Bargmann 1939). It was owing to this unique anatomical feature that it was possible in the 1920's to prove ultimately that insulin is produced by the islet tissue of the pancreas and not by the acinar parenchyma (Macleod 1922; Vincent et al. 1924, 1925). Bony fishes thus offer unequalled possibilities for chemical and metabolic studies of pure islet tissue (Lazarow & Cooperstein 1951; Maske et al. 1956; Lazarow et al. 1957, 1959; Davidson 1958, 1959; Wright 1958). Moreover, it is possible to extirpate the islet tissue selectively without damaging the exocrine pancreatic tissue (McCormick & Macleod 1925; Macleod 1927). The teleostean principal islets contain a type of insulin which neither differs from ordinary mammalian insulin in its effect on man nor in its other hormonal and antigenic properties (McCormick & Noble 1924; Jensen et al. 1929; Scott 1931; Yamamoto et al. 1960). It has been used therapeutically (Zeile et al. 1948; Yamamoto et al. 1960) and in industrial insulin production (Tohyama et al. 1941; Zeile et al. 1948; Planas Mestres 1957 a). This analogy between teleostean and mammalian insulin suggests that it may be possible to draw conclusions about the conditions in human islet tissue from experimental results obtained from these poikilotherm animals to as great an extent as in the case for the homotherm laboratory animals.

The principal islets of most bony fishes, however, are not free from admixture
of exocrine pancreatic tissue (Diamare 1899, 1905; Rennie 1905; Bargmann 1939). This is the reason why the principal islets of different strains of bony fishes in the 1920’s were found to show great variations in the content of insulin per gram tissue. The strains with the most “pure” islets (i.e., no or only slight admixture of acinar pancreatic tissue) had the greatest insulin concentrations in their principal islets (cf. Macleod 1927). The highest yield of insulin was obtained from the principal islets of Lophius piscatorius and Cottus scorpius and some other Cottus strains (McCormick & Noble 1924; Vincent et al. 1925; cf. Bargmann 1939).

In spite of the fact that during the last few years bony fishes have been used to some extent as experimental animals in diabetes research, the fundamental facts concerning the morphology and physiology of the pancreatic islet tissue are rather incompletely known. Thus, the morphology of the principal islets has not been studied systematically with modern histological and histochemical methods; and knowledge of the blood sugar regulation, including the reactions to alloxan administration, lags behind that of mammals.

The present investigation was performed in order to elucidate these subjects in Cottus scorpius L. (the daddy or short-horn sculpin). It is a marine teleost which is very common in arctic and boreal seas on both sides of the Atlantic (Lilljeborg 1891; McCormick & Macleod 1925; Kyle & Ehrenbaum 1929). It can easily be obtained in fairly large numbers and is also suitable in other respects for experimental research. It is thus very hardy in aquaria, it feeds readily and does not seem to get lethal “laboratory diuresis” (Smith 1953; Forster 1953). Moreover, it is easy to handle and the sensitivity to pain is apparently very low (Lilljeborg 1891). It is possible to make intravenous injections and blood sampling as well as catheterization of the urinary bladder (Forster 1953).

This report concerns the following points:

1. Light microscopical investigations of the histology and histochemistry of the islet tissue together with an estimate of the quantitative distribution of the different kinds of cells in the principal islets.

2. Some experiments on the blood sugar regulation including the effects of the usual hyper- and hypoglycemic agents and procedures.

3. Studies on the reaction to alloxan administration including mortality at different doses, type of blood sugar fluctuations, frequency of glycosuria and histological changes in the principal islets, kidneys and liver.

4. An attempt to make use of the unique anatomical features of teleostean pancreatic islet tissue in an experimental examination of Lazarow’s (1946, 1949) theory concerning the role of glutathione in the mechanism of alloxan diabetes. Here the nitroprusside method for glutathione determination has been slightly modified, and its sources of error have been scrutinized.