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Pancreatic islet lesions of autoimmune origin, and ICA and ICSA.

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Abstract

CHBB male rats, 120-150 g in weight, were used both as animals to be sensitized and as donors of homologous islets as antigen. At no time did sensitized animals give a positive reaction for islet-cell antibodies or islet-cell surface bound antibodies at any of the dilutions tested. None of the frozen sections of the pancreas were positive for fluorescence specific for IgG or C3. Marked fibrosis and cell infiltration of pancreatic islets, a high degree of pyknosis of parenchymatous cells of islets, phagocytosis of fragmented islet cell nuclei by histiocytes, and a marked reduction in the number of beta cells were noted.

KEYWORDS: islet autoimmune lesions, anti-islet cell antibodies, islet cell surface bound antibodies

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— BRIEF NOTE —

**PANCREATIC ISLET LESIONS OF AUTOIMMUNE ORIGIN,
AND ICA AND ICSA**

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Abstract. CHBB male rats, 120-150 g in weight, were used both as animals to be sensitized and as donors of homologous islets as antigen. At no time did sensitized animals give a positive reaction for islet-cell antibodies or islet-cell surface bound antibodies at any of the dilutions tested. None of the frozen sections of the pancreas were positive for fluorescence specific for IgG or C₃. Marked fibrosis and cell infiltration of pancreatic islets, a high degree of pyknosis of parenchymatous cells of islets, phagocytosis of fragmented islet cell nuclei by histiocytes, and a marked reduction in the number of beta cells were noted.

Key words : islet autoimmune lesions, anti-islet cell antibodies, islet cell surface bound antibodies

Shortly after the discovery of organ-specific autoimmunity, an association between juvenile diabetes and diseases of putative autoimmune origin was reported (1). A high incidence of specific antibodies to pancreatic islets has been shown in patients during the early stages of the onset of juvenile diabetes (2).

Lacy and co-worker (3) recognized fibrosis and structural changes in pancreatic islets as well as slight lymphocytic infiltration and hemosiderin deposits in peri-insular tissues in rats sensitized by repeatedly injecting homologous islet homogenate. They suggested that these unusual changes in islets were the result of an antigen-antibody reaction occurring in the islets.

Anti-islet cell antibodies (ICA) and islet cell surface bound antibodies (ICSA) are probably involved in the antigen-antibody reaction taking place in pancreatic islets. If so, the relevant antibodies must be present in peripheral blood during the development of immunity in animals treated by the methods of sensitization described by these authors; furthermore, deposits of IgG and C₃ ought to exist in the involved islets.

CHBB male rats, 120-150 g in weight, were used both as animals to be sensitized and as donors of homologous islets as antigen. Pancreatic islets were

This work was previously presented at the 17th Meeting of the European Association for the Study of Diabetes, Amsterdam, 15-18 September 1981 and published in abstract form in *Diabetologia* 21, 310 (1981).

obtained by digestion of the exocrine portion of the pancreas with collagenase according to the method of Lacy *et al.* Islets, contained in a solution of salts at a concentration of 50 per ml, were crushed with a glass homogenizer; the resulting suspension was mixed with an equal volume of complete Freund's adjuvant to prepare an emulsion. The emulsion was injected subcutaneously at four different sites on the back biweekly for a total of 12 times. During the course of this sensitizing procedure, blood was taken from the tail vein twice a week for a total of 12 times. The sera obtained were kept frozen at -20°C until use.

Rabbit IgG anti-rat IgG fluorescein isothiocyanate (FITC) conjugate (Byk-Mallinckrodt, West Germany) and rabbit IgG anti-rat C_3 FITC conjugate (Byk-Mallinckrodt, West Germany) were employed as labels for the detection of antibodies by immunofluorescence.

In order to detect ICA, frozen sections of the pancreas from healthy male rats of the same strain were allowed to react first with test sera in 1 to 128-fold dilutions for 30 min at room temperature, then with IgG in a 1: 15 dilution as the label for another 30 min at room temperature. For the detection of ICSA, islets cells from normal male rats of the same strain were obtained by the method of Lernmark (4) and were incubated with test sera in 1 to 128-fold dilutions for 60 min at 37°C . In either case the reaction mixture in suspension was placed in a Cunningham chamber to be examined under a fluorescence microscope with an epifluorescence condenser.

The pancreas of each treated animal was fixed in Bouin's fluid, sectioned and stained with hematoxylin-eosin, chrome-hematoxylin-phloxine, azan and aldehyde-fuchsin for microscopic examination.

Frozen sections were prepared from part of the removed pancreas, incubated with the two labels mentioned above, i.e., IgG and C_3 in 1: 10 dilution, for 30 min at room temperature, then examined under a fluorescence microscope. At no time was ICA or ICSA demonstrated in sensitized animals at any of the dilutions tested.

Histologically, besides alterations in architecture, marked fibrosis and cell infiltration of pancreatic islets, a high degree of pyknosis of parenchymatous cells of islets (Fig. 1.), phagocytosis of fragmented islet cell nuclei by histiocytes (Fig. 2.) and marked decrease in the number of beta cells were noted.

None of the frozen sections was positive for fluorescence specific for IgG and C_3 . These results indicate that ICA and ICSA do not play an etiologic role, in terms of typical type III allergic reaction, in the production of lesions of pancreatic islets. More sensitive methods for demonstration of these antibodies ought to reveal participation of type II allergic reaction involving antibody dependent cell-mediated cytotoxicity, because, at the present time, ICA and ICSA can be demonstrated only by the indirect immunofluorescence method.

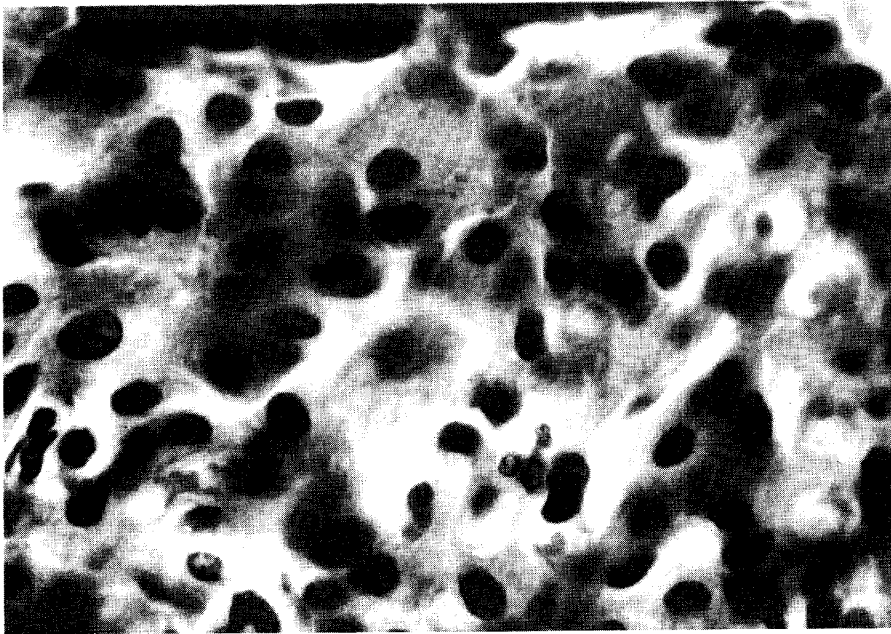


Fig. 1. A high degree of pyknosis of islet cells. Chrome-hematoxylin-phloxine stain; $\times 1,000$

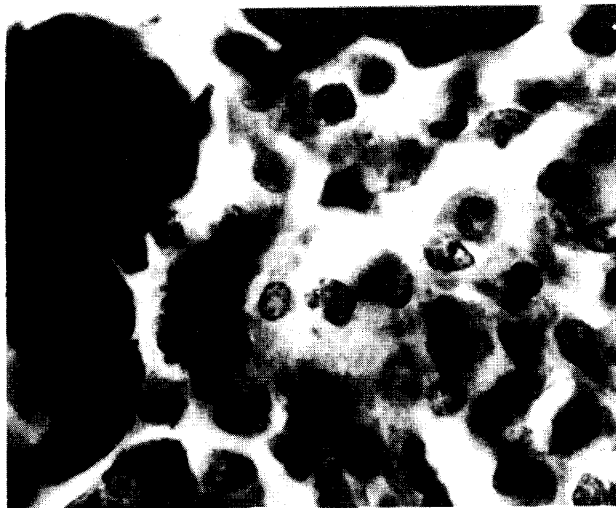


Fig. 2. Fragmented islet cell nuclei are phagocytized by a histiocyte. Chrome-hematoxylin-phloxine stain; $\times 1,000$

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