EFFECTS OF CYCLOSPORIN A
ON THE ENDOCRINE PANCREAS OF THE RAT.
MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDIES

REGINA JABLENSKA, VESKA OGENA, PETKO PETKOV

Katedra po Anatomia, Histologia i Embryologia, Medicinska Akademia, Sofia, Bulgaria

Cyclosporin A, a cyclic undecapeptide isolated from the fungus Tolypocladium inflatum Gams, is one of the most powerful agents used in the last decade for suppressing the humoral and cell-mediated immune responses. The observation that cyclosporin A (CsA) prevents the onset of diabetes in diabetes-prone BB rats, and the hypothesis that IDDM is an autoimmune disorder, have prompted work aimed at assessing the effects of immunosuppressive therapy with CsA in diabetic patients. However, even the application of CsA in therapeutic doses leads to an inhibitory effect on insulin secretion.

CsA is now widely used as an immunosuppressant in organ transplantation; it suppresses the immune response when applied in very low concentrations, with minimal side effects.

However, there are data suggesting that it may accumulate in some organs even at the low doses normally used in clinical medicine. An increasing flow of data has been reported on the risks of CsA treatment: it may affect the kidney, the liver, and the islet cells of the pancreas. Damaging effects on Langerhans' islet cells have been described, and this observation has led to mainly biochemical studies, leaving a gap in the study of the morphological correlates.

The present paper reports on morphological changes observed in the endocrine pancreas of the rat following in vivo treatment with CsA.

MATERIALS AND METHODS

Ten normal male Wistar rats weighing 120 to 150 g were investigated, and another series of 5 rats was used as controls. The animals were treated daily

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for 2 weeks with a 5% solution of CsA (Sandimmun/Sandoz) in olive oil, at an oral dose of 50 mg/body weight. On day 14 the experimental animals and controls were sacrificed (by decapitation), the pancreas was removed immediately, and small portions were fixated in: (a) Bouin solution for immunocytochemistry and light microscopy; and (b) glutaraldehyde with OsO4 postfixation for electron microscopy. Haematoxyline-eosin (HE), paraaldehyde fuchsin