Studies on experimental diabetes mellitus, as produced by organic reagents

Oxine diabetes and dithizone diabetes

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Abstract

References

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Abstract

1. With the expectation that organic reagents, which react with zinc in the islets of Langerhans, may cause the destruction of the islet cells and produce diabetes, the six reagents were injected into rabbits.
2. By intravenous injection of 50 mg. per kilogram oxine, the three phases of blood sugar changes were observed. Initial hyperglycemia in one to four hours, followed by hypoglycemia in ten to twenty-four hours, and finally permanent diabetes after forty-eight hours were observed.
3. By injection of the same doses of oxine few rabbits showed transitory hyperglycemia which returned to normal value after twenty-four to forty-eight hours. Intravenous injection of 10 to 20 mg. per kilogram oxine caused only transitory hyperglycemia.
4. By intravenous injection of 50 to 200 mg. per kilogram dithizone in 0.2 to 0.5 per cent ammoniac solution, the three phases of blood sugar changes were observed, namely, initial hyperglycemia which reached its peak after one to two hours, followed by hypoglycemia in eight to twelve hours, and then gradual rise of blood sugar and permanent diabetes after twenty-four hours. Oral administration of 500 mg. per kilogram dithizone caused transitory hyperglycemia which continued for two to three days.
5. Quinaldinic acid, anthranilic acid, and 4-hydroxybenzthiazol caused no changes of blood sugar. After injection of diphenylthiocarbazide, a tendency to slight elevation of blood sugar was observed.
6. Histologic changes of the pancreas were observed by Gomori’s staining method at various intervals after intravenous injection of oxine and dithizone. In the initial hyperglycemic phase in six to twenty-four hours after injection of oxine, slight degenerative changes and necrosis were observed in the islets of Langerhans. The beta cells showed pyknotic or faintly stained nuclei and disappearance of granules in the cytoplasm, but alpha cells remained almost normal. In the hypoglycemic phase in eighteen to thirty-five hours, marked necrosis and disintegration of beta cells were observed. Centers of the islets became necrotic masses, but alpha cells at the periphery of the islets remained normal. In the final hyperglycemia after forty-eight hours and in permanent diabetes, degenerated beta cells were reduced and the islets were composed of alpha cells. In permanent diabetes of long duration, the islets were reduced in size and number and consisted of alpha cells.
7. In initial hyperglycemia two hours after intravenous injection of dithizone, islets showed necrosis of the nuclei and disappearance of granules and necrosis of beta cells. In the hypoglycemic phase in eight to twenty hours, beta cells in the centers of the islets showed marked necrosis and disintegration, forming necrotic homogenous masses with shadows of nuclei, whereas surrounding alpha cells remained almost normal. In the final hyperglycemia after twenty-four hours and in permanent diabetes, the islets were reduced, appearing small, and were composed chiefly of alpha cells with a few degenerated cells. In both kinds of diabetes, inflammatory reactions were not observed in the necrotic tissues of the islets.
8. Remarkable changes were not observed in other tissues in oxine and dithizone diabetes.
9. In the initial hyperglycemic phase of oxine and dithizone diabetes, histochemical zinc reactions in the islets were slightly reduced and were further reduced in the hypoglycemic phase. In the final hyperglycemic phase zinc was not found in the islets but was found slightly positive in permanent diabetes of long duration. These changes of zinc in the islets may be considered as changes of insulin content in the islets.

In the submaxillary gland, intestines, and prostate in which zinc is found in normal rabbits, zinc reactions generally were reduced. Much zinc was found in the submaxillary gland in permanent oxine diabetes of long duration.