

"The 'Islets of Langerhans' of the Pancreas." By H. H. DALE, B.Ch., George Henry Lewes Student. Communicated by Professor STARLING, M.D., F.R.S. Received December 11, 1903,—Read January 28, 1904.

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(Abstract.)

These structures were first described by Langerhans in 1869. They have since been found by many observers in the pancreas of every species of mammal, bird, reptile, and amphibian in which they have been looked for. Kühne and Lea first recognised the peculiarly rich plexus of wide blood-capillaries in the islets. As regards their function, they have been regarded as connected with the nervous system, as lymphatic structures, as embryonic remnants, as patches of exhausted or degenerate pancreatic tissue, as furnishing a particular constituent of the pancreatic juice, and as internally secreting ductless glandular tissue, furnishing a substance necessary for normal carbohydrate metabolism, and quite unconnected with the externally secreting function of the pancreas. This last view has received support from many observations of the degeneration or absence of the islets in diabetes, and from the statement of several observers that, after occlusion of the pancreatic duct, the islets remain intact when the ordinary secretory tissue has disappeared.

Lewaschew, in 1885, first stated that activity of the pancreas led to an increase in the number of the islets, and that intermediate forms between the ordinary secretory tissue and the islets could be found, and were more abundant after activity.

This statement has been confirmed by Pischinger, Maximow, and Tschassownikow, and has also been repeatedly contradicted. Laguesse describes a perpetual change of secretory tissue into islets and *vice versa*, the islets being, in his view, pancreatic tissue in an internally secreting stage, and representing also the stage during which growth takes place.

My observations have been made on the pancreas of the dog, cat, rabbit, and toad. The pancreas was hardened in a mixture of corrosive sublimate and formaldehyde, sections cut in paraffin and stained with toluidine-blue and eosine. The islets appear, with a low magnification, as relatively unstained areas.

The pancreas was examined in conditions of "rest" (normal activity), of exhaustion produced by prolonged administration of secretin, and of starvation. Exhaustion was produced in the mammals (cat and dog) by repeated injections of secretin into the jugular vein during 6—12 hours, accompanied by bleeding towards the end of the

experiment, until the pancreas ceased or almost ceased to secrete. The animals were anaesthetised with morphia and A.C.E. mixture.

In the toad, secretin was injected into the dorsal lymph-sac by a hypodermic needle during 2—4 days. The effect of starvation was observed in a stray cat, picked up in an emaciated condition and killed immediately, and in toads which had been for several months in the laboratory tank.

In the resting glands of all the species the intermediate forms described by Lewaschew were observed, the islets being formed by an assimilation of the secreting epithelium to the centro-acinary cells and the epithelium of the ductules, with later rearrangement of the cells attended by formation of the wide tortuous blood-capillaries. In the toad evidence was also found of reconstruction of secreting alveoli from islets and of cell-multiplication in the islet stage.

The effect of exhaustion was in all cases the same—a very extensive conversion of the secretory tissue of the gland into large islets, of irregular outline, retaining obvious traces of their former alveolar structure, and containing numerous intermediate forms. Specimens have been obtained from a dog with the greater part of a lobule, and from a toad with the greater part of the whole pancreas thus converted.

The effect of prolonged starvation was, on the whole, very similar to that of exhaustion, but slighter in degree.

Experiments on the dog* and rabbit were also made to observe the effect of occluding the pancreatic duct. There resulted in all cases an interstitial fibrosis. The areas of pancreas not destroyed assumed the islet condition, but the preformed islets showed no special immunity from destruction.

The experiments leave the question of the function of the islets undecided, but the results of occlusion of the duct are in favour of Laguesse's view that they represent an internally secreting stage in the life of pancreatic tissue.

* On the dog only one experiment was made, in which the operation was performed for other purposes by Professor Starling.