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## THE SOURCE OF THE CHROMAFFIN CELLS OF THE ADRENALS OF THE PIG.

MILDRED YULE.

That the adrenals of mammals consist of cortical and medullary portions is well known, but there has been considerable diversity of views as to the source of these, especially as to the source of the medullary portion or the chromaffin substance.

It is generally conceded that the anlagen of the adrenals arise in mammalian embryos as buds of cells which proliferate from the peritoneal epithelium. These push dorsally between the aorta and the wolffian bodies to the position finally occupied by the mature gland.

Early observers disagreed in their conclusions as to the source of the chromaffin substance. As early as 1878 Balfour, working upon fishes, stated that its origin was from the sympathetic ganglia of the region. During the intervening time until 1901 its origin was variously ascribed to the mesenchyme, to the peritoneal epithelium, and to the epithelium of the pronephros. Later observers agree more closely. Wiesel ('01) working upon embryos of the pig too old to show the beginning of the adrenals concludes that the chromaffin substance is derived from the sympathetic plexuses. Whitehead ('03) agrees with this conclusion, his observations having been made upon younger embryos of the pig. Poll ('06) sums up the evidence in all classes of vertebrata as favoring the view that cells separated from the sympathetic nervous system give rise to the chromaffin substance of the adrenals. The work of Kuntz ('12) shows conclusively that in the turtle there can be no doubt as to the origin of the chromaffin substance from the sympathetic system.

The following observations upon embryos of the pig were made by the writer during the past year.

No cells destined to become chromaffin cells were seen in the adrenal buds until after the sympathetic matter had pushed ventrally below the level of the aorta, which position is also ventromesial and in close proximity to the adrenals. Embryos 6 mm in length show no sympathetic cells ventral to the middle level of the aorta while the adrenal buds are well formed. Small groups of sympathetic cells are seen dorso-laterally to the aorta, evidently moving toward the adrenal region. In embryos 12 mm. in length sympathetic cells have formed loose lines near the mesial surface of the wolffian bodies directed ventrally to the level of the adrenal buds where they swing mesially and meet ventral to the aorta. The sympathetic matter in the region of the coeliac plexus in embryos 19 and 20 mm. in length has increased greatly in the number of cells and shows distinct fibres in the central region. Almost the entire mesial surface of the bud lies in contact with aggregates of sympathetic cells. Some of these cells have migrated laterally and envelop the

adrenal bud within the thin mesodermic capsule. These cells are cells of an indifferent character, viz., the "indifferent" cells of Schaper and are destined to become the chromaffin substance.

Older embryos, 25-35 mm. in length, show inward migration of these indifferent cells. Cords and masses of them push in between the aggregates of cortical cells into which the bud is now broken. The cortical cells are characterized by larger size and by a difference in their staining properties. These migrating cells continue to displace the cortical matter until in embryos 80 mm. in length indifferent or chromaffin masses predominate in the central region, while in the embryo 180 mm. in length little but chromaffin material is left in the medullary portion.

While surrounding the bud and early in the migration, the cells from the sympathetic masses are similar in size and stain to those of the adjacent sympathetic aggregates. The beginning of differentiation of these indifferent sympathetic cells into chromaffin cells is coincident with migration.

After the embryos have attained about 40 mm. in length the capsule closes around the gland except along the mesial surface. This portion thickens and the capsule is entire in embryos 90 mm. in length which suggests that further entrance of migratory cells is prohibited. This would leave the above described entrance probably the only one for such cells and since only cells of sympathetic origin enter in this manner we are forced to the conclusion that the chromaffin substance of the adrenals is derived from the sympathetic system.