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**PHYSIOLOGY OF THE DUCTLESS GLANDS IN THEIR
RELATIONS TO OBSTETRICS.***

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"THE physiology of the internal secretions in twenty minutes" about represents the instructions received from your secretary when he requested me to prepare this paper. Such a feat might have been accomplished ten years ago when it almost meant danger to one's reputation and well-being to carry on researches on the ductless glands. But things have changed, and the field has become so vast that about all I shall be able to do in the time available will be to refer briefly to those features of the general subject which bear a direct connection with your special line of work.

"In Southern Italy it has long been the custom for the parent to measure the circumference of the daughter's neck before and after marriage, an increase in size being considered as an evidence of conception," as stated by Richardson. The clinical observations of Nicholson, Lange, and others, have fully confirmed the existence of a functional relationship between the reproductive organs and the thyroid. Moreover experiments upon pregnant and nonpregnant animals have shown that the pregnant animals require much more thyroid than those which were not pregnant. While the latter could exist normally with but one-fifth of the organ, if they became pregnant they speedily suffered from convulsions. Conversely, as Lanz and others have shown, even in herbivora, goats for example, which do not need

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- the thyroid as much as the carnivora, since they can live a long time after removal of the thyroid, the sexual and reproductive capacity is greatly impaired after this operative procedure. They either do not become pregnant or they abort. These and many other facts which could be adduced, bearing upon puberty, menstruation, lactation, menopause, etc., indicate clearly that during pregnancy the former takes part in the active process of fetal development.

What is the physiological rôle of the thyroid apparatus in this connection? It is one of such importance that if it were more generally known by the profession at large, and the therapeutic suggestions it offers more frequently heeded, puerperal complications could be prevented in many cases which at present only too often are lost.

What has been termed the "detoxicatory" functions of the thyroid apparatus has been before us many years. The theories which restricted the antitoxic process to the gland proper, this organ being supposed to detoxicate the blood coursing through it, have had their day; The only view which has survived the test of experimental inquiry is that based on Schiff's original idea that the thyroid supplies a secretion to the blood. Since his time, one of its rôles has been found to be the destruction of poisons in the blood—the all-important function referred to above. My own labors then suggested that the thyroid and parathyroids were directly connected with the production of antibodies and opsonins in the blood-stream, a view since confirmed by Fassin, Stepanoff and Marbé, the latter two observers working at the Pasteur Institute.

The rôle of the thyroid apparatus—by which I mean the thyroid and parathyroids—in pregnancy, thus becomes clear. During this physiological state, maternal wastes are not alone to be dealt with, but also those of the fetus. Hence the need of supplementary resources to convert them into eliminable end-products. The thyroparathyroid secretion taking part (with other antibodies let me add) in this process, the thyroid assumes greater activity and thereby serves to protect the maternal organism against harm. When this source of help fails, the antitoxic process is not completed and toxic intermediate wastes, which are extremely irritating to the kidney, are formed, giving rise to albuminuria, edema and other complications dreaded by obstetricians, and favoring the development of puerperal eclampsia. That we have in thyroid gland used

therapeutically, a potent aid in this connection has been sustained clinically.

The beneficial influence of thyroid preparations on lactation, pointed out by Hertoghe, Chéron and others, who found that in some cases of agalactia the secretion of milk was free as long as thyroid was taken and failed when it was neglected, is explained by the well-known influence of the gland on general metabolism, which it greatly enhances. The secreting elements of the mammary gland are simply rendered more active because cellular interchanges or vital activity in them is greatly activated. Besides the inherent help that small doses of thyroid afford, is the very important fact that the maternal milk serves not only to nourish the infant, but also to protect it against infection, while its own autoprotective organs are not sufficiently developed to defend it adequately. So marked is this defensive property of maternal milk that in 1870 during the siege of Paris, the mortality was lowered 40 per cent. because mothers were driven to nurse their babies for lack of cow's milk, although in the same period the general mortality in the city was doubled (Winters). As far back as 1892 Ehrlich and Brieger showed that when mice had been immunized against the action of tetanus toxin, their milk conferred the same immunity upon the mice they suckled. These and many other facts which could be adduced indicate not only that thyroid products increase the flow of milk, but also, through this fact, protect the infant if need be against infection.

Were the adrenals also situated under the skin, they could likewise be seen to enlarge during pregnancy. They are the seat of active hyperemia, their whole vascular supply being erethic, while their cellular elements show every evidence of abnormal activity. Neu has recently shown that the epinephrin in the blood corresponded quantitatively with the activity of the gestative process, including pregnancy, labor and the puerperal period. The prevailing conception of the action of the adrenal secretion that it serves to sustain the vasomotor tone through its action on the cardiovascular system, while perfectly correct, fails to account for this striking development of functional activity. But such is not the case with my own view that the adrenals sustain oxidation and metabolism. There is not only the normal maternal metabolism to subserve, but also that of the developing fetus and the vast up-building of tissue this process entails, the increase in size of the uterine walls, the de-

velopment of the placenta, etc. This relationship between the adrenals and parturition constitutes a new field for study. I may add for the benefit of those who might wish to take it up, that so eminent an author as Prof. Schäfer, also expressed the opinion, since I did so, that the adrenals were related to metabolic changes—the keynote, as I view it, of their connection with parturition.

The adrenals in the new-born merit even more than those of the mother—as far as present knowledge warrants—the attention of the obstetrician, for the destruction of these organs through local hemorrhage is a frequent—and let me say often unrecognized—cause of death in the nursling during the first few weeks of life. So common is adrenal hemorrhage in infants, in fact, that Loeper and Oppenheim found it in 45 per cent. of 250 nurslings examined postmortem. How is it produced?

Various toxic substances, pneumobacillus cultures, diphtheria and other toxins, vegetable poisons, etc., have been shown to cause when injected experimentally, congestion of the adrenals—so marked in some instances as to provoke rupture of their vessels. All the investigators who have reported these observations agree that the organs give the typical signs of marked activity in addition to the vascular engorgement. Whatever the purpose of this activity is, whether to sustain the cardiovascular tonus, or whether, as I believe, to sustain metabolism or carry on both these functions—which is probably the truth—the fact remains that the two salient points to remember are that while overactive adrenals raise the blood-pressure in proportion, the adrenals of the infant are relatively very large while their parenchyma is extremely friable. The meaning of high blood-pressure under these conditions is self-evident: the contracted arteries of the body at large so increase the pressure in the delicate adrenal vessels—which are in reality but sinusoidal capillaries—that they rupture, thus constituting adrenal hemorrhage.

But through what agency are the poisons which cause adrenal hemorrhage produced in the new-born? Barring the occasional cases of this condition due to trauma or pressure during birth, we are brought to the protective influence of the mother over her infant. A child borne with toxic wastes in its blood, because its mother through inadequate autoprotective functions has not kept its, and her blood, free of them, is a candidate for adrenal hemorrhage. In many instances even the maternal milk, through its antitoxic properties, fails to save the infant; but what is the prognosis of such infants when artificially fed? Ample evidence

is available to show the evil influence of the latter. The moral of all these facts is plain: By the judicious use of thyroid gland during parturition, when indications for it are present, you can not only protect the mother, but also her child, both while it is *in utero*, and through her milk after birth.

Concerning the other organs which have been classified as ductless glands that have proven of interest to obstetricians, the pituitary body, ovaries and Graafian follicles, I am brought, through the fact that I am restricted to the physiology of these organs as ductless glands, to state that I am still to be convinced that they produce *bona fide* internal secretions. It has long been my opinion, though quite prepared to yield to substantial proof to the contrary, that true internal secretions are by no means as numerous in the body as they are thought to be, and that the effects obtained from many organic extracts do not represent those of any internal secretion whatsoever. They are from my viewpoint mere tissue extracts, whose effects, therefore, are all very similar, the variations observed being due to the differences in the composition of these tissues. The posterior portion of the pituitary body, for example, is known to be rich in nerve-cells, while the ovaries and Graafian follicles are rich in nucleins. Yet all these tissues give the chromaffin test, showing that all are rich in adrenal substance though closely bound up in organic combination with the specific tissues of each organ. Under these conditions, we should obtain the effects of the adrenal extractives from all these organs; this is precisely what we do get: all are oxidizing agents, raise the blood-pressure, slow the heart beat, and enhance metabolism. This applies also to kidney and testicular extracts. They all belong also to what has been termed the chromaffin system and are closely related to one another through the sympathetic system which plays an important part in the many functional relationships they so plainly show. We obtain a sudden rise of blood-pressure from pure adrenal extractives and a rapid fall from extracts of the other organs; the rise of blood-pressure is of longer duration because the adrenal extractives here are in combination with other organic substances which, to a material degree, prolong and modify its action. All this does not impair in the least the therapeutic and special value of each of these different extracts; it only deprives them of what appear to me as fictitious functions, that is to say, functions which on insufficient grounds have been compared to those of a *bona fide* internal secretion, that of the adrenals for example.

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