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## THE RELATION OF GYNECOLOGY TO THE GLANDS OF INTERNAL SECRETION\*

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**I**N the human body are a number of glands which do not possess ducts, but which are so intimately connected with the blood system that a current of blood circulates through them—hence the name of "blood glands" or "ductless glands," but it is only in quite recent times that any considerable knowledge has been gained of the physiology and pathology of these glands. It is in fact only since the last half of the nineteenth century that it has been known these glands secrete certain substances which are absorbed directly into the blood system, and for this reason the glands are sometimes called the "endocrine organs" (endo, within; krino, secrete), but more commonly they are known simply as the "glands of internal secretion."

These glands are situated in different parts of the body and are totally unlike in their structure. The internal secretions are peculiar to each individual gland, and play important but widely different roles in the human economy. As Cushing says, "A disturbance of each one of these glands, whether in the direction of over-activity or under-activity, doubtless will be found to possess its own characteristic clinical syndrome which differs from that of every other gland." The research work that has been done on the internal secretions up to the present time has established beyond doubt that these glands form a group which is so closely correlated that if one member of the group is injured by disease or removed at operation, changes soon occur in the other members of the group, thus showing that a circle has been broken and the physiological balance lost, with more or less disturbance ensuing to the

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system until the balance can be re-established. This disturbance may occasion alterations in one or possibly in all of the correlated glands during the compensating readjustment of the physiological processes, or the original exciting influence may have been the underlying cause for disturbance in several glands of the system at the same time, thus, in either case, producing a pluri-glandular syndrome. These changes vary with the particular gland affected and also with the age of the patient when the change occurs. In one instance it may appear as though a controlling force had been withdrawn, and in another case as though some stimulating influence had been lost.

The alteration of any one gland may excite it to greater activity, hence we speak of it as "hyper" functioning. The same gland may even seem at different times to possess both qualities, for over-activity, Mariel says, tends to a final stage of pathological gland sluggishness. A third prefix, "dys," is used to designate a disturbance of function in a gland whose component parts have different functions, and the clinical manifestations are not clearly of the hypo—or hyper—functioning type. The clinical experiments made by different workers along the lines of research are often contradictory, as the subject is so vast and the nature of the experiments difficult. I will try to give only the facts most generally accepted, to show in a very brief way the immense influence wielded by the glands of internal secretion in the general organism, and more especially in gynecology.

In the seventeenth century Descartes established the existence of the central nervous system in the regulation of the organic function of the component parts of the body and the inter-relation of function of the different parts. Messages are carried from the outside world by the centripetal nerves to the central nervous system, and from there the different activities of the body are regulated, controlled and co-ordinated. Up to the last half of the last century, scientists believed that the central nervous system was the sole agent

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by which the activities of the body were brought into co-ordination. The discovery of the circulation of the blood by Harvey proved the existence of a second channel of communication between the different parts of the body.

The first experimental proof of what we now call internal secretion was made by Berthold of Gottingen in 1849. In 1855 Claude Bernard, by clinical investigations upon the hepatic function, proved the existence of an internal secretion (Glycogen) in addition to the known external secretion (bile) of the liver. He stated that every organ of the body by a process of internal secretion whereby it yields the products up to the blood, determines the composition of the blood, and can, under certain conditions, modify and even change it, thus establishing a third mode of stimulation, viz., biochemical stimuli, or, as we now term these internal secretions, hormones (from *xzififfifi* to excite or arouse), since they pass through the blood and excite or arouse the activities of other glands of the body.

In the same year (1855) appeared Addison's classic monograph on diseases of the supra-renal capsules, describing a definite clinical syndrome ensuing after destructive alterations in these glands by disease, and in 1884 Pierre Marie demonstrated the condition "acromegaly" resulting from hyperactivity of the pituitary gland.

In 1869 Brown-Sequard further elaborated the conception of internal secretion, stating that all glands, with or without ducts, supply to the blood substances which are either useful or essential to the body, and the lack of which may produce pathological signs; but it was not until twenty years later (1889) that he was able to give experimental proof of his views and thus lay the foundation of the theory of internal secretions, and demonstrate the first practical application, thus affording a new method of treatment, which is now known as the Brown-Sequard method, or organo-therapy.

In this same year (1889) Rogowitch, by experimental studies, proved that lesions of one gland affect the structure and function of others. So the idea of organo-therapy has developed from the experimental studies of Brown-Sequard and Rogowitch, and we make use of it today (1) by feeding normal gland substance to an individual with a hypo-functionating gland of the same kind, or (2) by feeding normal gland substance to an individual

with a dissimilar and hyper-functionating gland when we have reason to believe the correlation of the two glands is close.

The immense benefit derived in some instances from organo-therapy borders on the miraculous; in other cases there has been little or no improvement shown, but it does not seem too optimistic to hope for equally favorable results with other glands when further research work has been done along these lines.

### Brief Summary of the Most Important Characteristics of the Endocrinic Glands in Their Relation to Gynecology.

#### I. Varieties:

1. Sex Glands—(a) ovaries, (b) testes.
2. Hypophysis.
3. Thyroid.
4. Para Thyroid.
5. Adrenals.
6. Pineal.
7. Thymus.
8. Pancreas.
9. Mammary Gland.
10. Placenta.

#### II. Physiological and Pathological Characteristics:

##### 1. Ovaries.

- (a) Follicle apparatus
  - (1) Primordial follicle
  - (2) Ripening follicle
  - (3) Graafian follicle
- (b) Corpus Luteum
  - (1) of menstruation
  - (2) of pregnancy
- (c) Follicle Atresia
  - (1) obliterating
  - (2) cystic (cystic formation is the normal physiological process in the ovaries.
- (d) Interstitial Gland
 

This gland corresponds to the theca lutea cells of the atretic follicles.

Both clinical evidence and animal experimentation have shown that the follicle apparatus and the corpus luteum are glands of internal secretion, and it is probable the interstitial gland has also a similar secretion.

The follicle apparatus presides over the growth and nutrition of the genitalia and the corpus luteum over the cycle of menstruation. It prepares the endometrium for the possible embedding of the ovum and the corpus luteum of pregnancy, and

it is believed it maintains, certainly in the earliest weeks, the continuation of pregnancy. While the function of the interstitial gland is still in doubt, it seems probable that it has a role to play, together with the follicle apparatus in the development of the secondary sex characteristics, viz., female pelvis, the rounding of the form, breasts, increase of fat under the skin, length of hair, and its distribution, external genitalia, etc.; and it may continue to produce a secretion after the cessation of menstruation.

### III. Hypophysis (gland of feminism):

The correlation of the hypophysis with the genital glands is very close. The anterior lobe presides over the skeletal growth and genital development, the posterior lobe over tissue metabolism (sugar tolerance), and the activity of the renal and vascular system.

- (A) Hyperactivity of the anterior lobe before adolescence produces:
- (a) Gigantism,
  - (b) Eunuchoid,
  - (c) Hypodevelopment of the genitalia.

There is an overgrowth of the long bones with male type of pelvis, and absence or poor development of the secondary sex characteristics. The hands are large and square ("spade") with thick clubbed fingers. The teeth large and the upper incisors separated. Hirsutes is present, and dysmenorrhœa, amenorrhœa and sterility common.

- (B) Hyperactivity of the anterior lobe after adolescence produces:
- (a) Acromegaly,
  - (b) Secondary sex characteristics normal, as they are developed before puberty.

There is a thickening and coarsening of the skin of the hands and feet, and an infiltration of the tissues of the nose and lips, giving almost a negroid appearance at times.

Tandler and Gross, in 1908, first called attention to the similarity of the "facies of pregnancy" to the changes produced in acromegaly, and ascribed this to the increased physiologic activity of the gland during pregnancy. There is also a temporary thickening of the tissues of the hands and feet, an hypertrophy of the turbinates, an increase in stature, and a physiological glycosuria during pregnancy (Cushing).

Menstruation soon diminishes with the hyperactivity of the hypophysis, and sterility follows. The secondary sex characteristics are often lost.

- (C) Hyperactivity of the posterior lobe before adolescence produces:
- (a) Fat aplasia of the genitalia.
  - (b) Amenorrhœa, partial or complete.
- (D) Hyperactivity of the posterior lobe after adolescence produces:
- (a) Excessive fat, especially "girdle" fat.
  - (b) Adiposo genitalia.
  - (c) Amenorrhœa and sterility.
- (E) Hypoactivity of either lobe before adolescence produces aplasia of the genitalia.

Disturbance of both lobes before adolescence produces very definite conditions. The syndrome best described by Froehlich and known as "Type Froehlich" is not infrequently met in gynecology on account of the scanty or absent menstruation. The picture is one of undersized stature, maxillary prognathism, peculiar adiposity, aplasia of genitalia, sub-normal temperature and hypotrichosis of the male type. The hand is small, plump, with tapering fingers. In contrast to this is "Type Lorrain," or infantilism. The picture now is one of a weak, delicate, undersized girl with no secondary sex characteristics, and complete absence of menstruation. The hand is delicate, infantile and much pigmented.

Chétivisme is the term employed by the French to describe the arrest of development with conservation of the relative adult proportions of the body, and "Uanism Complet" is the superlative of Chétivisme when certain morphological characteristics of infancy are retained.

### IV. Thyroid.

- (1) Absence of thyroid produces cretinism.
- (2) Hypothyroid produces myxoedema.
- (3) Hyperthyroid produces Graves' Disease.

Physiological enlargement of the gland occurs during menstruation, and pregnancy. Amenorrhœa occurs in cretinism and myxoedema; and menorrhagia and metrorrhagia, dysmenorrhœa, sterility, miscarriages in hyperthyroidism; nervous excitability in the menstrual epochs, and menstrual depression. In hyperfunction

of the gland the skin is usually fair, teeth regular and enamel glistening white, hair thin or deficient. In hypoactivity the skin is dull, scaly and acne often seen. Hyperactivity before development means prematurely old (Liliputian) and senile. Guder-natch fed tadpoles (1) with thyroid and obtained fully developed tiny frogs ("petit vieux"), (2) with thymus and obtained enormous tadpoles ("grands enfants").

#### V. Para Thyroid.

Hyperactivity is evidenced in pregnancy by the tetany of pregnancy.

#### VI. Adrenals (the gland of masculinism).

- (1) Cortex.
- (2) Medulla.

There is evidence that both are hypertrophied during pregnancy and probably at time of menstruation.

Hyperactivity of the gland is characterized by pigmentation of the skin in freckles or moles, and by pigmentation of labia minora and vaginal mucosa. Hirsutes and stained or spotted teeth are common. Physiological activity of the gland is shown during pregnancy by the pigmentation of the nipples (aureola) and face in the so-called "mask of pregnancy."

Amenorrhœa and sterility are frequent occurrences when Addison's Disease is established, and often a very early symptom.

#### VII. Pineal Gland.

Activity of the gland causes precocity, both corporeal and sexual

#### VIII. Thymus.

This gland usually disappears at puberty, and its persistence means delayed gonadal gland development and resultant "juvenilism."

#### IX. Pancreas.

Its activity is manifested during pregnancy by the physiological glycosuria of pregnancy.

#### X. Mammary Gland.

The relation to menstruation is shown by the swelling and painful sensation which frequently precede the onset of menstruation. The physiological action is demonstrated in the tonic effect on the muscle of the uterus after labor by the stimuli of nursing.

#### XI. Placenta.

This gland is responsible for the hyperplasia of the breast during pregnancy, and institutes secretion of the mammary gland.

Causes of alterations of the glands of internal secretion:

- (1) Inheritance.
- (2) Developmental defects.
- (3) Trauma (gun-shot wounds).
- (4) Physiological.  
The epochs of life—i. e., puberty, pregnancy, menopause.
- (5) Infectious diseases.
- (6) Operations (castration).

#### XII. Organotherapy.

- (1) Glandular extracts.
- (2) Glandular residue.
- (3) Whole gland.
- (4) Gland transplantation (whole or in part) in the body.

#### Conclusion

We have seen how closely related are the glands of internal secretion to the generative glands. In many instances the first symptom of disturbance in one gland is manifested by alteration in the menstrual cycle. During the child-bearing and menstrual period of life Graves says, "The ovaries not only exercise a distinct and trophic influence over the uterus and external genitals, but they seem to play a certain more or less important part in the general chemistry of the organism." The influence of the internal secretion of the ovary is seen before puberty, though; for it is through this internal secretion that the physical characteristics of the child change into those of the young girl, and again in the lack of influence seen in the artificial menopause produced by removal of the ovaries, when the pathological manifestations often transcend those of the natural menopause. The ovary acts as a central gland, gathering up the stimuli of the other glands in the system to transmit messages anew. As Virchow stated, the generative glands are not for the production only of ova, but they possess an internal secretion which is a great controlling force for good or ill throughout the body. Just as it checks the activity of other glands, so is its influence held in abeyance by the other members of the group. The relation of gynecology to the glands of internal secretion would seem then to be closer than between any other two glands of the system. As Loeb says, "We must consider the possibility that the relation between uterus and ovaries represents a chain of connected phenomena of which the first and last members are uterus and ovaries, and the intermediate links are formed by other glands of internal secretion or certain nervous structures."