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## A BRIEF REVIEW OF THE PHYSIOLOGICAL AND EMBRYOLOGICAL GENESIS OF PSEUDOHERMAPHRODITISM, WITH REPORT OF A CASE\*

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**P**SEUDOHERMAPHRODITISM, while apparently rare in the human, is possibly more frequent in lower animals, cases having been reported in cladocera,<sup>1</sup> crustacia,<sup>2</sup> birds and cattle.<sup>3</sup>

Cattle often deliver themselves of twins. It frequently happens that the female co-twin, the other being a male, is usually sterile and has a modified genital tract resembling the pseudohermaphrodite of the human. These animals are known as free martins and their gonads as free martin gonads.

The structure of a free martin gonad according to Willier,<sup>4</sup> may be any degree of transformation of the ovary into the testicle. This transformation is due to the hormone action of the testes of the male co-twin, when there is a common embryonic or extra-embryonic circulation in utero. These gonads having a varying structure, may show sexual cords exhibiting a series of gradations between medullary cords

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and seminiferous tubules, increase in interstitial cells, transformation of rete in the male direction, by developing connecting tubules between the rete tubules and the seminiferous tubules, arrangement of blood supply form a typical ovarian, to a typical testicular type and lastly they may even develop an epididymis. This in the complete form resembles the testes morphologically, yet is functionally inactive as far as the production of the germ cells is concerned.

A modification of the reproductive system can be produced in chick

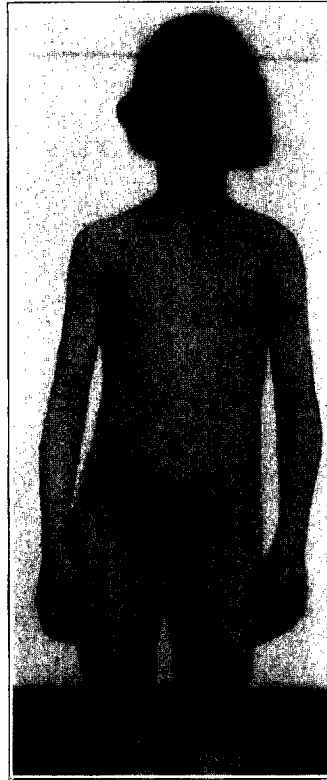


Fig. 1.—Shows male habitus and normal vulva. Picture taken after clitoridectomy was performed.

embryos, by transplanting opposite gonads,<sup>5</sup> showing that the sex hormones play a very important part in the development of this system. In free martin cattle it is the testicular hormone of the male co-twin that influences the gonad development, and it is the internal secretion of this modified gonad that results in the development of an atypical genital tract in the female co-twin. Atypical gonad development in the human pseudohermaphrodite cannot be explained on the basis of the hormone action of a male co-twin, but knowing that sex determination is transmitted through the primary germ cell, is it not possible that this sex determination for some unknown reason is perverted, and that this perversion is inherited?

This inheritance is very suggestive in my case, which is as follows:

E. P., age fourteen, born in the United States. Chief complaint: Headaches and weakness for nine weeks. Masturbation since infancy. Family history: Father living and well. Mother has tuberculosis. *Two aunts on the father's side are known never to have menstruated or borne children and had no mammary development.* Past history: Measles in infancy; no other illness or operations. Personal history: Mental development is retarded; is only in the sixth school grade. Menstrual history: Has never menstruated. Present illness: As long as patient can recollect, she has had headache daily, usually starts on awakening and lasts for a good part of the day; is throbbing in character and is associated with nausea and vertigo. Has had two convulsions in the last month during which she was unconscious for three minutes. Has lost 10 pounds in nine weeks. Physical, general: Underdeveloped child; no mammary development; harsh voice; male habitus. (Fig.

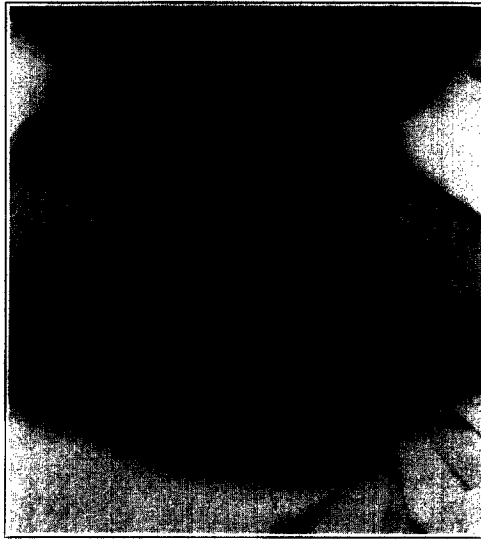


Fig. 2.—Shows large mass at site of clitoris—and prominence of right labium majus, due to presence of gonad.

1) Local physical: At the site of the clitoris there is a large mass (Fig. 2) consisting of two corpora spongiosa and glans covered by foreskin. Rest of vulva normal; vaginal cavity ends blindly. Uterus, tubes and ovaries could not be felt by recto-abdominal examination under anesthesia. In right labium majus is a small oval mass the size of a lima bean, presumably a testicle. (See prominence of right labium in Fig. 2.) Diagnosis: Pseudohermaphroditism, complicated by epilepsy. Operation: Separation of foreskin was attempted but was not feasible and a clitoridectomy was performed by Dr. S. Wiener. Postoperative course: The wound healed per primum, and the vulva resembled that of the normal (Fig. 1). Patient was transferred to the Neurological service for the treatment of her epilepsy. Laboratory findings: Wassermann negative. Surgical pathology: tissue removed consists of erectile and fibrous tissue containing nerves, covered by normal squamous epithelium.

In identifying my case I have followed Neugebauer's classification which is as follows:

- I—Hermaphroditismus verus (truly bisexual, very rare)
- II—Pseudohermaphroditismus (sex organs of one type associated  
with sex organs of the opposite type)
  - a—Internus (Masculinus)  
(Feminus ) Int. organs opposite
  - b—Externus (Masculinus)  
(Feminus ) Ext. organs opposite

My case can be classified as one of *pseudohermaphroditismus feminus externus*, as the external female organs are present and normal except for an overdevelopment of the clitoris. Internally there is a gonad in the right labium majus presumably a rudimentary testis, possibly to be classified as similar to a free martin gonad of cattle. The uterus, tubes and ovaries are apparently absent.

According to Neugebauer,<sup>6</sup> who collected 910 cases of hermaphroditism, there were 722 of the male variety and 188 of the female. Six hundred thirteen of the whole series were of the pseudohermaphroditismus masculinus externus type, that is they had external male genitals, with internal female sex organs. Most of these cases had ovaries, uteri or tubes in a hernial sac.

Embryologically the anomalies of the genital tract can be explained by a brief review of the development of this tract. During the period of mesonephric development, the human embryo is bisexual, containing all structures necessary for the development of both sexes. About this time there develops a ridge along the border of both mesonephra which gives rise to the müllerian ducts.<sup>7</sup> The primitive urogenital or wolffian ducts lie external to these but both empty together into the urogenital sinus. As sex differentiation takes place when the embryo is about 4 cm. long, corresponding with the beginning differentiation of ovaries or testes, these tubular structures become differentiated as follows:

The wolffian ducts disintegrate leaving only a small portion, which in the male forms the epididymis, seminal vesicles, conivasculosi, the vasa efferentia and ejaculatory duct. In the female it forms the paroophoron, the duct of Gärtner and the parovarian or organ of Rosenmüller. The müllerian ducts in the male involute in the eighth week, the rudiments remaining as utriculus masculinus and hydatid of the epididymis. In the female they continue to develop, fuse anteriorly to form the tubes, posteriorly to form the uterus and vagina. Incidentally it is this posterior fusion which when incomplete or absent gives rise to uterus bicornis, didelphus, septate or double vagina.

In our case during embryonal life, an atypical male gonad developed in all probability and descended through the inguinal canal into the labium majus. A posterior fusion of the very lowest or caudal ends of the müllerian ducts gave rise to a vagina. Whether or not the wolffian

ducts developed an epididymis and vas deferens cannot be stated definitely.

From the urogenital sinus dates the development of the vulva, bladder and urethra.<sup>8</sup> In the indifferent embryo there develops a genital tubercle, a ridge and two grooves from this sinus. The tubercle is the *anlage* for the clitoris or penis. The ridge forms the labia minora or the anterior urethra in the male. The urethra of the female comes directly from the sinus which is the posterior urethra in the male. The grooves grow towards each other fusing in the male to become the scrotum and in the female remain unfused as the labia majora. The clitoris *anlage* grows very slowly and droops caudad while the rest of the vulva grows rapidly, giving eventually a relatively small organ covered by a reflection from the labia minora. The penis *anlage*, however, develops faster in an anterior direction.<sup>9</sup>

In this case there was a normal development of the urethra and vulva but an overdevelopment of the clitoris *anlage* in an anterior direction as occurs in the male.

The reason for the atypical development of the genital tract in my case is possibly due to the hormone action of an atypical gonad, whether or not this gonad would resemble a free martin gonad as described I am unable to state as we did not obtain permission for its removal and consequently it could not be studied.

#### CONCLUSIONS

1. Pseudohermaphroditism can be experimentally produced and explained in animals.
2. Some animal pseudohermaphrodites have free martin gonads.
3. Sex hormones probably determine the development of the genital tract.
4. Something transmitted through the primary germ cell determines the development of the normal gonad.
5. This influence may be perverted and as in my case this perversion may possibly be inherited.
6. The gonads in human pseudohermaphrodites are possibly free martin gonads.

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