the blunt dissection with this instrument has given the good results obtained.

The features recommending this new snare are as follows: 1. It is strong, heavy and will not get out of order. 2. It locks together, instead of having screws or fasteners. 3. It is easily kept clean. 4. It is easily and quickly threaded. 5. It has an entirely new device for fastening the wire; when once clamped the harder you pull the tighter it becomes.

Shreve Building.

DIFFUSE IDIOPATHIC HYPERTROPHY OF THE MAMMARY GLANDS OF THE FEMALE *

A REPORT OF A NEW CASE AND A CONSIDERATION OF THE
ETIOLOGY AND PATHOLOGY BASED ON DATA
OF RECORDED CASES

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REPORT OF CASES

The following clinical history of the case was furnished by Dr. H. Matthey of Davenport, Iowa:

Patient.—The patient, a girl 13 years of age, when examined August, 1903, was 5 feet and 5 inches tall, weighed 101 pounds and was found to be of a nervous temperament.

Fig. 1.—Patient with mammary hypertrophy; from photograph taken shortly before amputation of the left gland.

Family History.—The patient's parents were both living and well, her father being 39 years of age and her mother 36. She had one brother and one sister, both living. In none of these other members of the family was there any undue enlargement of the mammary glands.

Personal History.—The patient had had the usual diseases of childhood. Enlargement of the breasts began in the early part of June, 1903, and continued at such a rate that in August she was taken to a physician who estimated that each breast weighed about 8 pounds. Pressure applied by means of a bandage and maintained for several months was without benefit. In October when the patient first consulted me, the breasts weighed about 12 pounds each. Operation was advised, but refused. She now drifted into the hands of quacks who treated the condition in various way, without giving any relief. In July, 1904, she returned to me in poor general condition, feeble, anemic and emaciated. Her weight was 106 pounds, a little more than half of which was contributed by the breasts. Because of these facts, it was deemed advisable to remove only one breast at a time (Fig. 1). The first operation was undertaken July 14, 1904. The amputated left breast weighed 28 pounds. After being two weeks in the hospital, she was allowed to go home to recuperate for the

second operation. At this time her weight was 79 pounds. During the following two weeks she gained 13 pounds and returned for the operation, weighing at this time 92 pounds. The right breast was amputated Aug. 12, 1904. It weighed 26 pounds. Recovery was uneventful, healing being by primary intention. Patient remained in hospital two weeks and returned home in good general health and weighing 75 pounds. Six weeks after the second operation she menstruated for the first time and has been regular since. She was married in 1909 and has been delivered of a six-months developed child since. At present the general health of patient is good; weight, 115 pounds; height, 5 feet 9 inches.

PATHOLOGY OF SPECIMENS

This was essentially the same for the two glands.

Gross Pathology.—Shape: Both glands, which were rather spherical in shape and pendulous while attached to the body of the patient, became considerably flattened out between the skin surface and the base after their removal.

Size: The left gland, which was the larger, was, after removal from the body, 18 inches in diameter and 8 inches in thickness. Its greatest circumference was 58 inches and it

Fig. 2.—Base of left gland, showing lobulated and encapsulated appearance.

weighed 28 pounds. The right gland was 14 inches in diameter, $7\frac{1}{2}$ inches in thickness; its greatest circumference was 45 inches and weighed 26 pounds.

Surface Contour: The skin surface was smooth, being tightly stretched over the underlying gland substance. The nipple of each of the glands had become flattened out and the areola more diffuse, but less distinct than normally. The bases of the glands were distinctly lobulated; the lobulated areas varying from one to four inches in diameter (Fig. 2). The outlines of the glands at the base were so distinct as to be apparently well encapsulated.

Consistency: The glands were moderately soft in consistency. This was quite uniform throughout the gland mass, although on cut section certain areas were found to be much more firm in consistency than others. These were not distinct and circumscribed, but fused gradually with the more soft areas. A number of rather large ducts, some with a diameter of as much as $\frac{1}{8}$ of an inch were visible on the cut surface. The

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

subcutaneous adipose tissue had entirely disappeared. Only a small amount of fat was still noticeable about the base of the gland (Fig. 3).

Color: The cut surface of the tumor was of a whitish-pinkish gray color. The pinkish tint was more marked in the firm than in the soft areas.

Microscopic Pathology.—Section from Firm Portion of Gland: The section consisted principally of full developed fibrous connective tissue with a fair number of capillary blood-vessels. The gland elements were found somewhat grouped in areas, corresponding to the lobules; the acini, however, were much more widely separated than in the normal gland. The acini which were of variable size, some quite large and many dilated, were lined by a single layer of a low columnar (almost cuboidal) gland epithelium, resting on a basement membrane consisting of flat cells. The lumen was free from

Fig. 3.—Cut surface of right gland, showing dark areas of glandular tissue, light areas of more pure connective tissue, and open spaces representing dilated ducts.

contents, except in a few in which debris, consisting of degenerated and desquamated cells, was found.

Section from Soft Light-Colored Portion of Gland: This section consisted almost entirely of fibrous connective tissue with only a very few gland elements. The connective tissue, which contained only a few widely separated nuclei, was somewhat edematous. There were numerous capillary blood-vessels and a number of fat cells.

Section through Skin, including a Portion of the Gland Substance of Medium Consistency: This section showed the connective tissue of the hypertrophied gland to be continuous with that of the subcutaneous tissue and the corium. Except for a few fat cells, the subcutaneous adipose tissue had entirely disappeared. The elastic fibers of the corium were fully as abundant as in the normal skin. I was unable to find any elastic fibers in the substance of the gland proper except, of course, in the larger blood-vessels.

Section from Base of Gland, Including the "Capsule": The "apparent" capsule of the gland was found to consist of condensed gland substance consisting of both gland and connective tissue elements. The glands were somewhat flattened.

Summary of Pathology.—The process was a diffuse hypertrophy affecting all parts of both glands rather uniformly and involving both the glandular and connective tissue elements, the increase affecting principally the latter. The gland acini were lined by a single layer of low columnar (almost cuboidal) epithelium, were larger than normal and more widely separated by intervening connective tissue, which was of the fully developed fibrous type. Capillary blood-vessels were numerous.

REVIEW OF CASES REPORTED

Diffuse idiopathic hypertrophy of the mammary glands is a rare condition. Several authors have collected data from a number of cases, but no attempt to collect all cases reported has been made for some time. In 1902 Kirchheim¹ collected most of the cases reported up to that time. I have reviewed the literature and have

Fig. 4.—Photomicrograph of dense glandular portion of right gland showing irregular variously shaped acini lined by a single layer of low columnar epithelium.

made an attempt to collect all cases reported to date and have summarized the essential data from these cases, so far as such has been available. In some instances I have not been able to secure the original report. In many more the data was very meager. In the majority of cases no description of the pathologic process was given, and I have little doubt but that I have included some cases that are not instances of "true" hypertrophy. I have purposely omitted a case of excessive adiposity of the mamma, diagnosed clinically as diffuse hypertrophy, of which I have the specimen, and another case concerning which I have been informed but of which no pathologic examination was made. I have not included in this paper the cases of mild degree of hypertrophy of the mammae of the male (gynecomastia), or of senile parenchymatous hypertrophy (Bloodgood²), partial or

1. Kirchheim: Arch. f. klin. Chir., 1902, lxxviii, 582.
2. Bloodgood: Surg., Gynec. and Obst., 1906, iii, 721.

localized hypertrophy, and the still more mild types of so-called hypertrophy occasionally seen associated with pulmonary tuberculosis.

Although I have summarized the principal data from the cases reported, I shall in this paper limit the consideration to the etiology and pathology of the condition.

Number of Cases Reported.—Aside from the one which I have just described, I have been able to collect reports of sixty-nine other cases of diffuse hypertrophy of the female mammae. Of these seventy cases sixty-two were bilateral and six unilateral, three affecting the right and three the left gland. In two instances I was unable to learn which glands were affected.

Age.—Although Bittner³ reported a case of hyperplasia (probably not true hypertrophy) of the mammary gland in a girl 6 months old, the age limit of the reported cases of true hypertrophy extends from 11 to 42 years, with practically every intervening year represented. The vast majority begin to develop about the time or soon after puberty or during gestation. Fifty-eight per cent. of the cases not associated with gestation developed between the ages of 11 and 16 and 40 per cent. during the fourteenth and fifteenth years of age.

Classification of Cases.—Cases of idiopathic hypertrophy may be classified into (1) those associated with gestation and (2) those not associated with gestation, most of which are closely related to puberty.

1. *Gestation Idiopathic Hypertrophy.*—Of the seventy cases eighteen were of this type. Fourteen of these were bilateral and four unilateral. The relation to gestation is clearly indicated by the fact that, after the termination of pregnancy, the condition subsides, although it does not return completely to the normal, and that it frequently reappears during subsequent pregnancies. The enlargement usually begins during the first pregnancy. Sometimes, however, it occurs for the first time during the second or third. In one instance it did not develop until the eighth pregnancy.

2. *Cases Not Associated with Gestation.*—The relation of puberty to cases of hypertrophy is suggested by the fact that 58 per cent. of the cases not associated with gestation developed between the ages of 11 and 16, the period during which puberty ordinarily occurs, and that in a large number of cases menstruation did not set in until after the enlarged glands were removed. In many cases, however, there seems to be no association with either puberty or gestation.

Etiology.—The real cause of this condition is unknown. Such factors as heredity, traumatism, undue sexual activity, general malnutrition, etc., which have been mentioned in connection with the process, seem to have nothing to do with it. Pathologically the process appears to be simply an excessive development of the normal enlargement as seen especially at puberty and during gestation. Presumably the causes which produce the normal enlargement are also at work on this pathologic form, the latter being produced either because of a large amount (or undue activity) of the same cause, or a lack of the inhibitory influences which, under normal conditions, limit the extent of the enlargement.

Recent experimental work has shown that the normal enlargement of the glands is not always due to the same cause. The work of Lane-Clayton and Starling⁴ in producing an increase in the size of the mammary gland of

virgin rabbits by the injection of extracts from the body of rabbit fetuses has shown very conclusively that the enlargement of the mammae during gestation is through the action of a hormone produced in the fetus. That this may also be the cause of the idiopathic gestation hypertrophy is very probable, especially inasmuch as that condition subsides after the termination of the pregnant state.

The cause of the normal enlargement of the glands at puberty is not so well understood. The evidence at hand seems to indicate that a hormone in the ovaries is the principal factor responsible for the development of the mammary glands outside of pregnancy. If this proves to be the case it would seem that removal of portions of the ovaries would be indicated in the treatment of the condition. Up to the present time the only treatment that has been of value is amputation of the glands. Removal of portions of the ovaries has not been tried, so far as I know.

It is very doubtful whether or not the cessation or irregularity of the menses, noticed shortly before and during the hypertrophy in many of the cases not associated with gestation, is of etiologic significance. This may simply be a symptom of the condition, as it is a symptom of other diseases in which the vitality is lowered. On the other hand is to be noted the fact that the general health is usually not affected until after the disease is well advanced, whereas the cessation of the menses is frequently of sudden occurrence several months before the glands begin to enlarge.

Gross Pathologic Morphology.—Shape: The enlarged glands stand out prominently from the chest wall for some time. Later their weight causes them to become pendent and often pedunculated, the gland substance assuming a rather spherical mass, drawn away from the muscles of the chest and hanging over the front of the abdomen, sometimes as far down as the knees. Their large size frequently causes the patient much discomfort and sometimes necessitates the patient remaining in a recumbent position.

Size: The size of the different glands may be compared (1) by their greatest circumference and (2) by their weight.

1. The greatest circumference of the individual glands for which figures are available varies from 20½ inches to 51½ inches, the average being 31½ inches. The average circumference of the hypertrophied left glands is one inch more than the right.

2. The weight of individual glands varies from 1½ pounds to 64 pounds with an average per gland (of all cases) of seventeen pounds. The weight of the combined glands of cases of bilateral hypertrophy varies from three pounds to 124 pounds (Durstons' case) with an average of 37 pounds. In most cases and on a general average, the left gland weighed a little more than the right. The average weight of the gland in the cases of unilateral hypertrophy is 15 pounds. In the cases reported by Durston⁵ and myself the weight of the two glands exceeded the weight of the remainder of the body.

Surface Contour: The surface of the glands is quite smooth, and skin tightly drawn. The stretching of the skin usually causes the nipples to be flattened out. In one instance they were reported as being retracted; in two, as having become enlarged—in Delfis' case, as large as a hen's egg. The pigmented areas also become less definite and distinct as the skin becomes stretched. The

3. Bittner, W.: Fall von Hyperplasie beider Mammæ bei einem 6 Monate alten Mädchen, *Prag. med. Wchnschr.*, 1895, xx, 492.

4. Lane-Clayton and Starling: An Experimental Enquiry into the Factors Which Determine the Growth and Activity of the Mammary Glands, *Proc. Roy. Soc., London*, 1906, lxxvii, B, 505-522.

5. Durston: *Phil. Tr. Roy. Soc., London*, 1069.

6. Delfis: *Jour. de physiol. exper. de Magendie*, 1825.

skin remains quite freely movable over the underlying gland, even though the subcutaneous fat tends to disappear and the connective tissue of the skin gradually fuses with that of the gland. In the later stages, the skin may become thick and hard. In many instances the superficial veins become very large and stand out prominently as blue streaks.

Consistency: During the early stages the hypertrophic glands are firm and elastic, as they are during the normal enlargement at puberty or during the early part of gestation. Later, when they become larger and pendent, they also become flaccid. At first the glands usually feel somewhat nodular; later, however, these tend to disappear. Even when the process feels quite diffusely uniform through the skin, the cut surface may show areas considerably more firm in consistency than others. Such areas diffuse into one another gradually.

Color: The color of the cut surface of the hypertrophic gland in the few cases in which it has been noted, is apparently the same as under normal conditions.

Microscopic Pathologic Morphology.—Unfortunately, microscopic examinations of the specimens were made in only about twenty of the cases. In all of the cases not associated with gestation, it is recorded that there is an increase of both the glandular and the connective tissue elements. In most instances the connective tissue is reported as being principally increased, although in four cases special mention is made of the marked glandular increase. The gland acini are usually described as being larger than normal, more widely separated and sometimes found to be lined with several layers of gland epithelium. I am inclined to think that this last-mentioned phenomenon is due principally to the thickness of the section and the cutting of the acini in an oblique manner. In many instances the glands are considerably dilated and contain granular degenerated material. Such changes in the glands have been likened to the changes that occur in the glands during the early stages of pregnancy. The fibrous connective tissue is usually described as being of the fully developed type with, as a rule, very few nuclei, although some are mentioned as being quite cellular—which may, of course, have been due to an associated inflammation. In the three cases of idiopathic gestation hypertrophy in which a microscopic examination was recorded, the microscopic findings were like those of the mammary gland during pregnancy. Such findings, indeed, may reasonably be expected.

Pathological Physiology.—Gestation hypertrophic glands usually functionate as do the normal ones, although it is often difficult to nurse the infant because of the flattening out of the nipple. Those not associated with hypertrophy are functionless during non-pregnant conditions, although it has been possible to squeeze colostrum-like fluid from the ducts in some cases. Usually, also there is no lactation after the birth of a full-term child. In several instances, however, there was normal lactation in the glands that had been enlarged before the pregnant state. In one case associated with gestation, there was marked galactorrhea of eight months' duration.

Nature of Pathologic Condition.—Idiopathic hypertrophy has been regarded variously by different authors as a circulatory (edema), an inflammatory, a neoplastic or as a simple hypertrophic process.

In favor of its being an edematous process is the rather sudden onset that has been reported in several cases. In the cases of Durston⁸ and Delbet,⁷ for in-

stance, the patients retired in the evening, slept quietly as usual and in the morning on awaking found themselves scarcely able to turn around. When they tried to get up, the weight of the suddenly enlarged glands caused them to sink back. Usually, however, the onset is very gradual.

Opposed to its being a circulatory process is the fact that there was no mention made of pitting on pressure in the cases reported, nor has the tissue of the glands removed been reported as edematous. For a long time the enlarged glands are firm and elastic and stand out prominently from the body; this would not be the case in edema. The increase in connective tissue following edema is in the nature of a fibrosis rather than an increase of all of the tissue elements. The slight edema which I found in my specimens and which accounts in part for their great shrinkage when placed in formaldehyde solution may readily be explained by the interference with circulation caused by the pendant glands.

There is really no evidence in favor of its being an inflammatory process. The pain sometimes noticed may readily be accounted for on the basis of pressure and a stretching of the nerves.

The neoplastic theory has several supporters. In Porter's⁸ case, in which the glands weighed 17 and 43 pounds respectively, the diagnosis made was intracanalicular fibroma. Kirchheim¹ regards it as a diffuse fibroma. It is true that a section of the hypertrophic gland may be like one from a case of adenofibroma, but a tumor is usually thought of as a more localized and circumscribed process, especially if it is benign. The idiopathic hypertrophy, however, which pathologically is benign, is a diffuse process involving all parts of the gland. The fact that it may begin as a rather localized process, limited to a certain part of the gland, simply means that such represents the beginning point, probably the most susceptible tissue, just as one gland sometimes becomes involved before the other.

Considered from all standpoints, it must be regarded as a simple hypertrophic process involving all of the elements of the gland, but especially the part which at the time, is the most actively growing tissue, namely, the glandular tissue during gestation and the connective tissue at other times, especially during puberty.

The question has been raised as to whether or not cases of unilateral enlargements are cases of true hypertrophy. With a clinical history like those of bilateral hypertrophy, with the same pathologic condition, so far as we know, and an average weight of 15 pounds as against 17 pounds in case of the bilateral type, there is no reason, it seems to me, why they should not be regarded as identical. Indeed, in Van Swieten's⁹ case, the unusual enlargement of one breast which occurred during pregnancy subsided after the termination of gestation. During the second pregnancy it again enlarged.

Associated Pathologic Conditions.—When the glands become of large size, the friction of the glands against a bracing bandage or supporting clothing frequently causes an excoriation of the epidermis chiefly at the most dependent portion. Such friction is apt to be followed by inflammation, abscess and fistula formation, eczema, erysipelas and gangrene. In one case, there was a hernial protrusion of gland-substance through an excoriated opening. Although Billroth¹⁰ reported a case

8. Porter: Boston Med. and Surg. Jour., March 3, 1892.

9. Van Swieten: Commentaria in H. Boerhaave Aphorism de cognoscendis et curandis morbis, Leyden, 1704, A iv.

10. Billroth: Krankheiten der Brustdrüsen, Deutsche Chirurgie, 1880, Instalment xii, 69.

7. Delbet: Traité de Chirurgie (Duplay Reclus), v.

of sarcoma and Bloodgood² a case of carcinoma in a gland idiopathically hypertrophied, such glands do not appear to be any more prone to malignant tumor formation than under other conditions. In several cases the axillary lymph-nodes were found to be enlarged. In the majority of these cases, there was some acute inflammation of the mammae which readily accounted for the involvement of the lymph-nodes. In several, however, there was no recognizable acute inflammation of the mammae. Even in such cases, the lymph-node enlargement was of a fibrous (chronic inflammatory) character. In no case has there been any metastatic formation of the hypertrophic mammae.

GENERAL SUMMARY

1. Of the seventy reported cases of diffuse hypertrophy of the female mammae, in eighteen the enlargement occurred during gestation; most of the others occurred about the time of or soon after puberty.

2. Of the seventy cases, sixty-two were bilateral.

3. Fifty-eight per cent. of the cases not associated with gestation developed between the ages of 11 and 16 and 40 per cent. during the ages of 14 and 15.

4. The etiology of the condition is obscure. It is very probably due to the action of the same hormones that produce the physiologic enlargements.

5. Pathologically, the condition is a simple diffuse hypertrophy, involving both glands and connective elements. The increase in the gland elements occurs principally in the cases occurring during gestation, whereas the connective tissue increase usually predominates in those not associated with that condition. The process appears to be essentially an exaggeration or continuation of the enlargements that affect the gland normally at puberty and during gestation.

6. The weight of the glands varies from $1\frac{1}{3}$ to 64 pounds, the average per gland of all cases being 17 pounds. In one instance, one of the glands weighed 64 pounds and both glands, 124 pounds. In two instances the combined weight of the two glands exceeded the weight of the remainder of the body.

7. In cases associated with gestation, lactation is, as a rule, normal. In those hypertrophies not associated with gestation the glands seldom functionate, even after pregnancy.

Dubuque and Jefferson Streets.

ABSTRACT OF DISCUSSION

DR. A. S. WARTHIN, Ann Arbor, Mich.: I should like to ask Dr. Albert whether this woman was able to throw her mammary glands over her shoulder; a similar hypertrophy of the mammary gland is often seen in Hottentot women, who are able to throw their breasts over their shoulders and suckle their children, who are carried in slings on their backs. I should also like to know to what type of man this woman corresponded. Did she have any features that go with the Australoid type or Negroid type? Would there be any anthropologic interest in this case as an instance of reversion?

DR. JAMES J. TERRILL, Galveston: Was there any pain associated with the condition? I remember seeing specimens from a somewhat similar case in the early part of this year. The patient, a girl aged about eighteen, had what was diagnosed as diffuse virginal hypertrophy of the breast. Both breasts enlarged but did not weigh more than two pounds each. One breast had to be removed, however, on account of excessive pain, the cause of which was never discovered; but on removal of the first breast, the pain disappeared and the other breast gradually grew smaller in size. Sections pre-

sented an appearance practically identical with that of the sections in Dr. Albert's case.

DR. GREER BAUGHMAN, Richmond, Va.: I saw a case in November, 1903, with Dr. George B. Johnson, in a young white woman. The left breast weighed $10\frac{1}{4}$ pounds; the right $7\frac{3}{4}$. The microscopic findings were almost the same as those in Dr. Albert's case—a true hypertrophy of the mamma—non-functionating, except that there was not so much dilatation of the acini and very little fat.

DR. HENRY ALBERT, Iowa City, Iowa: The patient was not able to throw her breasts over her shoulders. I did not see the patient; but I made careful inquiry of the clinician as to any peculiarities suggestive of reversion and was informed that there were none; nor did her parents present any unusual appearance. There was no pain except that which may be readily explained by the enlarged size of the breast. In the reported cases, however, there are a number associated with severe pain, and in a few instances pain was present from the beginning of the process.

A patient whom I saw three or four weeks ago presented considerable enlargement of the mammary glands. A diagnosis of diffuse hypertrophy was made. The process began about a year ago, but it was only during the last three months that the pain had become extreme. On examining the glands microscopically after removal we found nothing but fatty and a little fibrous connective tissue. One of the cases in the literature contains a reference to the fact that the hypertrophy was not due to glandular, but to fatty increase.

A STUDY OF MISTAKEN DIAGNOSES

BASED ON THE ANALYSIS OF 1,000 AUTOPSIES AND A COMPARISON WITH THE CLINICAL FINDINGS *

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The subject of this paper was suggested by my experiences in a weekly conference with senior medical students at the Harvard Medical School. At this conference the organs obtained from all the autopsies performed at the Massachusetts General Hospital during the week preceding are brought before the class. Before the demonstration of each set of organs I discuss with the students a typewritten summary of the clinical findings in the corresponding patient, including the history, the physical examinations, the reports on blood, urine, stomach contents and feces, the x-ray plates and all other data on which diagnosis was based during life. I never let anyone inform me beforehand of the autopsy findings. After we have committed ourselves definitely regarding the pathologic changes which we expect to find the hospital pathologist, Dr. Oscar Richardson, reads the autopsy protocol and demonstrates the organs.

In this exercise I have been forced once a week for three years to compare my diagnoses with post-mortem findings. It has proved so salutary and instructive, especially when I have been mistaken, that it has seemed to me well to summarize the results of a large series of comparisons between the judgments arrived at by a careful study of clinical data and the anatomic conditions revealed post mortem.

I. METHODS USED IN THE STUDY

I must first explain, as nearly as I can, the plan followed. It is not a simple matter to collate ante-mortem

* Oration in Medicine read before the Section on Practice of Medicine of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

* Because of the space required, the article is slightly abbreviated in THE JOURNAL. It appears in full in the Transactions of the Section and in the author's reprints.