An Address

ON

'CHRONIC MASTITIS' AS A TERM:
ITS FALLACY AND THE DANGER OF
ITS CLINICAL SIGNS.*

BY

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(With Special Plate.)

THE term "chronic mastitis" is fallacious because it does not allude, as its name implies, to an inflammation of the breast, and also because the clinical signs universally considered to be connected with it mask many and various states of breast hyperplasia. It is a dangerous diagnosis, because these clinical signs hide carcinoma in its earliest stages, advanced carcinoma in rarer examples, and many other states of epithelial hyperplasia.

I believe the want of a proper recognition of these facts has led to the present confusion of opinion as to whether so-called "chronic mastitis" is or is not a prelude to carcinoma. Instead of saying that it is a prelude to carcinoma, I would prefer, to-day, to put the matter thus: The clinical signs on which its diagnosis depends include early and, in rarer instances, late carcinoma, duct papillomata (with which carcinoma is so often associated), as well as many other states of hyperplasia. Hence the danger and inaccuracy that lurk behind these clinical signs.

As a result of my paper I may be accused of demonstrating errors of diagnosis instead of proving that the clinical signs which indicate "chronic mastitis" are applied to various and some dangerous pathological changes. The accusation would be wrong, for the whole profession, including myself, is being misled constantly by these clinical signs, which are totally insufficient to enable any of us to be sure what is happening in breasts that exhibit them. There can be no doubt that the issues are so important that we ought to know precisely what is occurring in these breasts. Let me go more fully into these points.

I have inferred that inflammation and hyperplasia are different processes—an inference that clearly demands that I should say what I mean by inflammation, and by chronic inflammation in particular. Pathologists agree that what is now called "chronic inflammation" is quite a different process from acute inflammation. My conception of acute inflammation is as follows:

Blood corpuscles are aggregated in the blood vessels. There is dilatation of the arteries (commonly preceded by a brief period of contraction), giving rise to more free flow through the capillaries. This arterial dilatation is a purely nervous act that has been proved by Dr. Ninian Bruce to be due to an axon reflex. Other changes are that red and white corpuscles are prone to stick to one another and to the blood vessel wall, and the circulation becomes slow. There is an exudation of plasma, and an exodus of blood corpuscles from the interior of the blood vessels into parts outside them. Also, there is loss of function in an inflamed part; for example, the loss of movements of the ciliae of ciliated epithelium (Lister). Lord Lister also stated that the lost movements of the granules in the pigment cells in the frog were another sign of lost function in the inflamed area. But our present knowledge renders pigmentation a much more complicated subject than it was in his time, and so much new work is in progress on this subject and that of acute inflammation that the pigmentary changes may prove, like the arteries, to be due to disturbed function and not lost function.

I have enumerated the changes that are classed together under the term "acute inflammation"; to them, when they last a long time and are less intense in degree, I assign the term "chronic inflammation." That is my conception of chronic inflammation, and I do not apply that term to any other tissue changes. The knowledge that has accumulated of growth, and of the effects of irritation applied directly to cells, has become so important that

Burdon-Sanderson's definition of inflammation (made in 1870) can no longer be accepted as true. He said: "Inflammation is the succession of changes which occur in a living tissue when it is injured, providing the injury is not of such a degree as to at once destroy its structure and vitality." That definition includes too much. In it there is no definition of injury, and there is no limitation of time, nor to the "succession of changes" that occur in tissues as a result of stimulation or irritation.

You may object and say that "Inflammation induces increased blood supply, which induces hyperplasia, and if that be so, therefore inflammation is at the bottom of hyperplasia." My reply would be that increase of blood may be essential to an increase of growth, but I do not admit for a moment that it can induce hyperplasia. I know that Hunter performed a classical experiment upon cocks, by which he intended to show that an increase of blood supply does induce an increase of growth. He transplanted their spurs into their combs, and an enormous growth of the spurs ensued.

In this experiment Hunter assumed many things, among which were that a cock's comb was a more vascular medium than the cock's leg, and that the subsequent excessive growth of the transplanted spur was due to the increase of blood supply it received.

I have repeated Hunter's experiment, and, in addition to transplanting spurs into combs, I placed them subcutaneously in the backs of the birds. The spurs seemed to me to grow equally big in both places. I had to cut short the lives of my birds because their vocal accomplishments disturbed the amenities of King's College and most of the inhabitants in the neighbouring Strand. I came to the following conclusions:

1. That the combs merely consist of a soft almost avascular gelatinous kind of substance that did not bleed at all on incision, and often there was smart haemorrhage during the removal of the spurs from the legs. The natural blood supply of the spurs seemed greater than that of the combs.

2. That the increased growth of the spurs was due to the want of wear and tear to which they are not subjected in their abnormal situations. In the days of cock-fighting spurs were protected by a kind of thimble which allowed them to grow into formidable weapons of offence; the thimble did not increase their blood supply—it only protected them from the wear and tear of life.

3. That there are other more recently acquired fundamental facts relating to growth that are also involved in this matter, but into which I need not enter.

The formation of keloids that occurs in the scars (and sometimes only in parts of scars) of only certain individuals is an obvious example of hyperplasia, with which the mysteries of growth are more concerned than those of inflammation, with which it is now classified. The healing of a wound is not a process of inflammation, but one of regulated and controlled hyperplasia.

Further, I have pointed out recently that the connective tissue around fibro-adenomata, in their early stages of growth, is in a state of a diffuse hyperplasia that is identical in structure with that of the tumour. The area of this diffuse hyperplasia resembles what is now assumed to be "chronic mastitis," but the altering tissues in the neighbourhood of the fibro-adenomata are really taking part in the formation of the tumours, and are not suffering from an inflammatory process. (See Figs. 1 and 2.)

The truth of the matter is that now we know the problems relating to growth are much more complicated than they were supposed to be in the times of Hunter, and later of Burdon-Sanderson. Although our knowledge of the problems concerning growth is elementary, yet it is great enough to impel us to consider all states of hyperplasia in terms of growth and not in terms of inflammation.

This conception is of immense practical importance when considering pathological changes of the breast in relation to their clinical signs. As an example of this point, I will show you later on a breast that was diagnosed as "chronic mastitis" by one of the ablest clinicians of our time. Besides containing many different states of hyperplasia and cysts (the existence of which he knew), it also contained, totally unsuspected, a fibro-adenoma, a duct papilloma, and carcinoma—all of which were discovered incidentally on

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making whole sections of this gland. With the exception of generalized nodularity and pain, there were no clinical signs to indicate the presence of any of these lesions. Discoveries such as this are not uncommon when breasts are examined by cutting whole sections for microscopic examination. Our knowledge of breasts cannot be accurate until their examination by means of whole microscopical sections is adopted universally.

I would go still further, and I would apply the term "hyperplasia" instead of "chronic inflammation" to other pathological states. Take, for example, the structure of a tubercle in tuberculosis. I would much prefer it were called a tuberculous hyperplasia and not "chronic inflammation." The lesion is one of pure hyperplasia. There is a giant cell surrounded by epithelioid cells, which are encompassed by an accumulation of lymphocytes, and an old tubercle is surrounded by newly formed fibrous tissue. You may say in surprise and indignation that surely lymphocytes are cells that belong essentially to "chronic inflammation." As a fact their presence is due to the laws that govern hyperplasia. You will remember that Carrel, in the famous address that he delivered before this Association, pointed out that lymphocytes and fibrous tissue cells respectively can grow and multiply *in vitro*.

There can be no doubt that acute inflammation and hyperplasia, different processes as they are, can occur at the same time. As an example, consider what is occurring in acute suppuration. Acute inflammation is present, and within the first hour it may be present alone. After two or three hours hyperplasia of tissue begins outside the centre of disease. Again, can there be a more wonderful state of hyperplasia than that which is occurring in the bone marrow, where the polynuclear leucocytes of suppuration are being manufactured in an enormous number? Nobody has suggested yet that the bone marrow is inflamed in this process.

You may tell me that tuberculous knees are hotter than normal joints, and that sign must always be one of the classical indications of inflammation. I agree it is, and chronic inflammation, as I have defined it, is also present when heat is manifest; but when proper physiological rest is applied to them the increased heat disappears, although tuberculous hyperplasia be still present. I may here point out that a breast suffering from what is now called "chronic mastitis" is usually of normal temperature.

Lastly, when I describe one of the types of desquamative hyperplasia of epithelium, it will be seen that colostrum corpuscles are being formed only in certain ducts of the breast, even when patients are virgins past their menstrual life. As the lesion is local and not affecting the whole breast, the result must be a combined effort of physiological and pathological processes that are operating locally. Hence much more complicated principles are concerned than merely those of inflammation.

I never use the term "chronic mastitis." I say the state is, as may be, either a local or a diffuse hyperplasia of the breast tissues respectively. Sir Humphry Rolleston, at my request, kindly suggested to me the term "mazoplasia."

My paper will be in vain if I cannot make you realize, when you are confronted by a breast which you now imagine to be one of "chronic mastitis," that you are in the presence of intricate problems of hyperplasia, that the clinical signs upon which you depend for the diagnosis of "chronic mastitis" do not convey an accurate conception of what is occurring in the breast before you, and that the life of the patient depends on the accuracy of your conclusions. In every breast that I examine clinically and microscopically my investigation is influenced absolutely by this dominating principle of hyperplasia and in what variety it may be present.

I proceed to give you examples of pathological changes that are included in this nebulous diagnosis of "chronic mastitis," and from them I trust you will see how inaccurate is the term, and how terribly anxious we ought to be when the only clinical signs to guide us are those of nodularity of the breasts and pain. I shall exclude all considerations of decided solitary tumours. The states of hyperplasia I shall describe occur, with some exceptions, mainly in the peripheral ducts, and also in some of the acini related to them.

The larger ducts may less commonly share in these processes, even as far as the nipple. This statement does not exclude the possibility of the hyperplasia occurring in the nipple itself, for it can be filled with secreting acini during lactation to such an extent that the ducts appear to be anatomically of minor importance. I will show that certain pathological changes are very often limited in site to the peripheral ducts and some acini connected with them. This limitation is common to various forms of epithelial and connective tissue hyperplasias, a fact that insists upon the consideration whether these processes are consecutive stages leading from one to the other should the action of the toxic agent be continued.

In order to make myself clear it is essential that I should draw your attention to the histological anatomy of the ducts and acini. Beneath the epithelial lining of the structures there is a layer of unstriated muscle fibres, which is separated from the elastica by a thin layer of a few bipolar cells loosely connected together by a delicate fibrillous tissue. The elastica is mainly limited to the ducts, and only occasionally surrounds acini; more rarely it surrounds a lobule. The delicate cellular fibrillous tissue that lies beneath the layer of unstriated muscle is continued around the acini, whether the elastica is continued around them or not. Outside the ducts and acini there is a layer of fibrous tissue that is in close contact with these structures. It is less dense in character than the supporting fibrous tissue of the breast, and forms the intralobular and pericanalicular fibrous tissue. This layer has almost a physiological connexion with the secreting elements. It often disappears in the breasts of virgins after about 35 years of age, so that the atrophied glandular elements are left in direct contact with the supporting fibrous tissue of the breast.

It is important to state that it is rare to find any type of connective tissue hyperplasia without a corresponding hyperplasia of the epithelium in the ducts or acini concerned; hence its presence may be assumed during the description of connective tissue hyperplasia. "Hyperplasia intra-elastica" is the term I apply to connective tissue hyperplasia that occurs internal to the elastica; "hyperplasia elastica" I apply to the enormous massive hyperplasia that sometimes occurs in the elastica itself; and when hyperplasia occurs in the pericanalicular and intralobular connective tissue, I term it "hyperplasia extra-elastica."

There is one more preliminary point. The best position in which to place a patient for the clinical examination of the breast is as follows: She should lie on a pillow that is placed immediately behind her chest. This position throws forward the breasts, the arms fall downwards with the elbows resting on the couch, and expose the axillae for clinical examination. The breasts and axillae should be examined, and the ampullae, ducts, and acini separately palpated.

I divide the pathological changes I am about to describe into three classes:

- I. Desquamative epithelial hyperplasia.
- II. Non-desquamative epithelial hyperplasia.
- III. In which the epithelial hyperplasia may be desquamative and non-desquamative in the same specimens, and in which the changes in the connective tissues appear to assume greater importance than the changes in the epithelium.

I must firmly impress upon the reader that the processes I describe often overlap each other to such an extent that I can show whole sections of breasts that contain in each respectively fibro-adenoma, duct papilloma, carcinoma, hyperplasia intra-elastica, hyperplasia elastica, hyperplasia extra-elastica, and cysts, as well as other types of epithelial hyperplasia.

CLASS I.—DESQUAMATIVE EPITHELIAL HYPERPLASIA.

This class consists of two types—A and B.

Type A.

Pathology.—In this type there is more commonly a generalized desquamative hyperplasia of epithelium, mainly in the peripheral ducts and also in some of the acini connected with them. It may, however, become

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FIG. 1.—A segment of breast removed from a girl aged 16 years. The fibro-adenoma D called for the operation, and irregularity of the breast between A and B was the only palpable clinical sign of a more generalized pathological state. This microscopical whole section of the parts removed shows a distinct macroscopical appearance of the breast between the letters A, B, and that part between the letters B, C, where the breast is normal. At E there is an unsuspected small fibro-adenoma. From F Fig. 2 is drawn. (Natural size.)

FIG. 2.—A low power magnification of the tissue changes occurring at F in Fig. 1. There is a marked extra-elastica hyperplasia, and it is a diffused state of the same changes that are occurring in a localized form in the two fibro-adenomata at D and E, Fig. 1.

FIG. 4.—A vertical whole section of a breast removed for cyst due to "chronic mastitis." At A, C, D, there are three foci of infiltrating carcinoma, and at B there is a multiradicular papilloma in a duct cyst. (Natural size.)

FIG. 5.—Horizontal whole section of breast. The shape is that of a normal breast. The structure of the breast is replaced by diffuse carcinoma. C, A, skin; B, subcutaneous tissue; D, remains of pectoralis major; and E points to one of the infiltrated ligamenta suspensoria of Sir Astley Cooper. (Natural size.)

FIG. 3.—A low power magnification of a peripheral duct in transverse section. The desquamative hyperplasia belongs to Type B of this article. The large colostrum-like cells A are distending the duct wall B at E, C, D; the constituents of the wall have been parted by the expanding pressure within the duct, and the cell contents are being pushed out into the surrounding tissues F.

FIG. 6.—A low power magnification of a peripheral duct cut in longitudinal section. C, elastica; A, carcinoma cells filling the duct; and at B carcinoma cells are forcing their ways from the inside to the outside of the duct.

W. A. H. MCKERROW: DORSO-LUMBAR DISLOCATION OF THE SPINE REDUCED BY OPERATION.

FIG. 1.—Before operation.

FIG. 2.—After operation.

J. G. WILLMORE AND M. DOUGLAS: SUPRARENAL TUMOUR, WITH DEGENERATION OF THE RETICULO-ENDOTHELIAL SYSTEM.

FIG. 1.

FIG. 2.

W. EVERETT: PERFORATION OF THE KIDNEY BY A LARGE BRANCHED CALCULUS.

more obvious clinically at one part or more than one part. All the affected structures are distended by this hyperplasia. The epithelium is proliferating universally from the surfaces of these structures. The cells thrown off are small, irregularly shaped, and desiccated, and are quite distinct in appearance from those thrown off by Type B. Hyperplasia extra-elastica is commonly in association, in which accumulations of lymphocytes are often present. The presence of lymphocytes is by no means an essential feature. Although this state affects most of the gland, there are parts which have not undergone these changes. This state of general epithelial hyperplasia is one of the early stages of cyst formation, Type B being the other. Also, slightly enlarged lymphatic glands sometimes occur in the axilla. Microscopical examination of these lymphatic glands reveals in their centres a diffuse hyperplasia of endothelium to which their enlargement is due. I have seen the same endothelial hyperplasia occurring in lymphatic glands that were secondary to carcinoma of the breast, and secondary to apparently aseptic operations upon animals.

Clinical Signs.—On palpation the whole breast is studded by multiple nodules which vary in size, but are seldom larger than a dried pea. The ducts are tortuous, and ampullae can often be felt enlarged. There is no discharge from the nipple. Occasionally the enlarged lymphatic gland may be felt in the axilla. This state attacks married and unmarried women from 30 years of age onwards. It may last for months or years. The general hyperplasia is painful, sometimes very painful. The pain may or may not be worse at the periods. Usually it has no relation to them. Pain is worse on palpation and when the breast is jarred. Pain is due to the distension of ducts and acini. The clinical signs appear local when the pathological changes are more advanced in one part than in other parts. When the changes appear to be local on clinical examination, the only way to be certain of the diagnosis between it and early carcinoma is to cut whole sections of the part removed for examination. How far is this practicable? This investigation is all the more essential when the affected parts are in the upper and outer segment of the breast, where the skin is often normally attached to the underlying breast.

Type B.

Pathology.—This type usually affects the peripheral parts of the ducts only, or acini only, or peripheral ducts and acini. It may affect mainly one part of a breast, or many quite isolated parts, or may complicate other states of hyperplasia. It attacks married and unmarried women from 30 onwards. As the processes in the ducts and acini are somewhat different, I will describe them separately.

Ducts.—In the early stages, what is seen is this: At four or five different spots in the circumference of the ducts the epithelial cells become long and feathery, undergo proliferation, and throw off large and swollen cells, and stain badly with a small degenerated nucleus. In other cells of the same type the protoplasm may stain badly, but the nucleus stains well. The various stages in the development of these large cells from the feathery cells can be demonstrated with certainty. In the later stages the duct is distended by these large desquamated cells and no surface feathery cells can be seen. One type of cysts arises from this type of epithelial proliferation in the ducts. I will show you in a transverse section of a duct what may happen when it becomes overdistended by this type of hyperplasia. You will see that mechanical rupture of its wall has occurred, and the big swollen cells are being pushed into the parts surrounding it (Fig. 3). In another specimen I saw a large collection of these particular cells lying loose, as it were, in the supporting fibrous tissue of the breast, and I wondered how they had got there. The explanation lies in this very interesting little discovery.

Before passing on to describe the changes in the acini, I would like to say this: The large swollen desquamated cells of this type resemble colostrum corpuscles. I am confident they are colostrum corpuscles. If so, the origin of the latter in breasts of all ages and stages is clearly from the walls of the ducts and not from the acini, for in all my specimens these cells can be traced in all stages of formation as they arise direct from the duct cells.

Acini.—The epithelial cells lining the acini become long and feathery, but I have not seen among them the large colostrum cells that occur in the ducts. Eventually the cells lose their feathery type and become more cubical and spheroidal, and sometimes form columns consisting of four or five cells that grow into the interior of the dilated acinus. Often small, intracystic papillomata of delicate structure are formed. Acinous cysts thus formed may reach a large size.

I consider that the pathological changes in Types A and B are proemial and are preparing the way for many sequences—for example, cysts, stagnation of contents in cysts, papillomata, and even carcinoma.

Cystic Breasts.

Pathology.—The multiple cysts are a result of the changes described above in Types A and B. Cysts may be general throughout the breast, or more or less local. The smallest cysts, which are microscopical, still exhibit desquamative hyperplasia of epithelium of the type to which they belong. The larger cysts are lined by a layer, sometimes more than one layer, of more or less degenerated epithelium. Whole microscopical sections of these glands form an instructive object of study. I will give five examples. In the first, the breast is riddled with cysts of various sizes. There is no evidence of any intracystic growth. There are points in it where hyperplasia extra-elastica has become so marked as to form small fibro-adenomata. The second contains many cysts, in only one of which I was able to discover a papilloma, which happened to be of the rare uniradicular type. The cyst containing this papilloma was a small dilated duct. The third multiple cystic state (Fig. 4) exhibits one small cyst in which there is a duct papilloma of the multiradicular type. In three separate parts of the breast there are foci of carcinoma in which epithelial cells are infiltrating the fibrous tissue of the gland and fat in their immediate neighbourhood. There were no clinical signs to indicate the presence of these complications, which were only incidentally discovered on microscopical examination of whole sections. The breast was removed upon a diagnosis of "cysts due to 'chronic mastitis.'" Fourth, there are other cystic breasts in which papillomata commonly originate. There is a fifth and more rare state in which carcinoma is incidentally discovered in large cysts when whole sections have been made.

I have the breasts of five separate patients which show remarkable and surprising pathological changes. On making whole sections of these breasts I found totally unsuspected carcinoma within large cysts. The cysts contained clear fluid and their walls were soft. What makes these observations so important is that medical men are apt to conclude that large cysts are never dangerous. Moreover, when they tap these cysts, they are content to regard them as simple when they extract a clear fluid and discover that their walls and surrounding parts of the breast are soft. Although I agree that large cysts, as a rule, are not dangerous, I do not consider that the clearness of the fluid, and the softness of surrounding tissue, are indications of complete safety. I am convinced that small cysts are liable to be dangerous and that carcinoma commonly may begin either in them or by a malignant small cyst formation, which I will describe later on.

Clinical Signs.—Over the whole breast multiple nodules occur, and vary from the size of a pea to that of an ordinary hen's egg. The larger nodules fluctuate definitely. Smaller ones are so decidedly elastic that no doubt could be entertained of their fluid contents. It is impossible to declare on clinical signs alone that there are no intracystic growths present. The fluid nature of their contents obscures the presence of internal growth. As a rule, on the formation of cysts pain disappears and is substituted by a feeling of general discomfort. Generally there is no discharge from the nipple, though gentle pressure on the breast may induce a clear or greenish discharge from the nipple. Lymphatic glands are not as a rule enlarged. When present, they exhibit endothelial hyperplasia, unless one of the cysts contains a carcinoma, when the gland might contain epithelial cells. Hence in doubtful states it would be well to remove the enlarged lymphatic gland and determine its contents by microscopical examination.

CLASS II.—NON-DESQUAMATIVE EPITHELIAL HYPERPLASIA.

A. Diffuse Carcinoma.

Pathology.—One would consider that advanced diffuse carcinoma could never be diagnosed as "chronic mastitis," but such is the fact. I will describe a breast of one patient, and the breasts of another.

Turning to the first, the breast appears of normal shape and size (Fig. 5). Curiously enough, there is no sign of breast tissue to be seen. The site of the normal breast is entirely occupied by a diffuse carcinoma. Epithelial cells have an alveolar arrangement. They completely fill spaces divided from each other by a thin network of fibrous tissue. The spaces vary in size, and are irregular in shape. There is no solitary lump. At many points the bases of the ligamenta suspensoria are attacked by carcinoma. Their attachment to the skin gave rise to the general nodularity which led to the diagnosis of "chronic mastitis." Lymphatic glands in the axilla contained carcinoma, although clinically they could not be distinguished.

In the second patient both breasts were affected by diffuse carcinoma. There were no solitary lumps. Carcinoma had invaded the bases of the ligamenta suspensoria, which gave rise to the general nodularity of the breasts. The pathological states of these breasts were the same and in no way resembled the remarkable appearances seen in the breast of the first patient. There was a primary carcinoma in each breast, which had spread in the usual method. Parts of the gland could be easily demonstrated in different parts of these breasts. Lymphatic glands in the axillae contained carcinoma, although they could not be distinguished clinically.

Clinical Signs.—The shape and the size of breasts belonging to this type remain unaltered. Careful palpation reveals diffuse puckering of the skin, general nodularity, and the absence of a decided solitary tumour. The breast may move freely over the pectoral fascia, or become fixed to it. Lymphatic glands in the axillae contain carcinoma, although their detection may not be possible clinically. The diagnosis is often rendered difficult by the fact that the patients may be fat. The two patients to whom I have referred were under the care of highly experienced observers, who, although they were always worried about these women, kept them under observation for eight months and eighteen months respectively. Doctors and patients were convinced that the states of the glands had not altered during these times.

B. Local Carcinoma.

Pathology.—I am about to describe what I believe to be a common method by which carcinoma begins. A localized collection of peripheral ducts and acini are distended by well stained malignant-looking cells. After careful search made of whole sections of a breast, small definite areas can be seen in which epithelial cells of precisely the same appearances have invaded the surrounding tissue. The distended ducts and acini in parts are more or less cystic and contain a clear fluid. The duct cysts may contain multiradicular papillomata. The acinous cysts may contain sessile growths, which project into the interior. I have not yet seen an early stage of carcinoma in which the peripheral duct or ducts were not implicated in the process. The epithelium of these cysts is identical in appearance with those that have invaded the surrounding tissue. It may be that the epithelial cells which have undergone hyperplasia may exist within the ducts and acini for a considerable period before the invasion of the surrounding parts occurs. I am led to believe, by what I have shown you in ducts and other breasts, that the invasion may be the result of accidental rupture of the walls of the small ducts or acini, and because the cells are malignant and capable of proliferation they continue to grow and spread to other parts of the body. Should the epithelial invasion of surrounding breast structures occur in the middle of the lesion, the ligamenta suspensoria are not affected and enable the diseased area to be pushed about without puckering the skin. The tumour may reach a large size before puckering of the skin can be demonstrated. I am sorry to say that breasts containing the early stages of this type are nearly always diagnosed as "chronic mastitis." Carcinoma may begin and spread also in a pre-existing cyst small in size.

Clinical Signs.—There is usually a history of pain, yet pain may be absent at the time of examination. When present it is made worse on palpation. There is nodularity of the affected area. There is no puckering of the skin in the early stages. It is certain to appear later, but the disease may be advanced beforehand. Enlargement of

carcinomatous lymphatic glands is usual except in the earliest stages of carcinoma, when it is limited within ducts and acini.

C. A Diffuse Non-desquamative Hyperplasia of Epithelium.

Pathology.—There is a type of non-desquamative hyperplasia of epithelium which can affect only one peripheral duct and some of its acini and sometimes none of its acini. In other patients a non-desquamative hyperplasia of epithelium somewhat akin to this state can affect whole lengths of ducts secondary to Paget's disease of the nipple and to other forms of carcinoma of the breast. In those breasts in which only one peripheral duct and some of the acini are affected these structures are full of epithelial cells whose nuclei and protoplasm stain well, with no appearance of desiccated cells, nor of the large, swollen, colostrum-like cells, and look decidedly malignant. The appearances seen in these ducts lead me to believe that carcinoma in an early stage can exist for long periods in ducts which do not show epithelial transgression of their walls. Epithelial cells in the earliest stages of carcinoma are heaped up in ducts and acini, and distend them as if they were waiting for the final accident of rupture, through which they can escape into the surrounding tissue. Precisely similar changes are seen in the early stages of tar cancer in mice. This observation is supported by the appearances noted in a duct whose epithelial hyperplasia belongs to this type (Fig. 6). This duct is distended by non-desquamative epithelial cells; at one part of it there is a solution of its continuity, and through which non-desquamative epithelial cells are pouring into the connective tissue, and carcinoma is undoubtedly present. It is most instructive and interesting to compare this ruptured carcinomatous duct with that duct in which the rupture occurred from overdistension, by the heaping up within its interior of large desquamated cells of colostrum type (see Fig. 3).

Clinical Signs.—The distended ducts and acini give rise to marked local nodularity. Pain is associated with the state and is referred to the site of nodularity, and is made worse on palpation. There is no discharge from the nipple, and lymphatic glands may be enlarged in those examples where the epithelial cells have passed their natural boundaries. This is one of the types that are so important to remove at the earliest possible moment. As a rule it comes for operation after it has passed through the usual period of diagnosis of "chronic mastitis."

D. Papillomata.

Pathology.—Although one papilloma may exist in a breast, it is uncommon, and as a general rule it contains many papillomata. Where one papilloma exists, it is situated generally in an ampulla. Where many exist, one of them is usually found in the ampulla and the rest are scattered diffusely throughout one duct or more than one duct. I have whole sections of a breast in my possession that contain two ducts and their ampullae full of papillomata. Altogether over 170 can be counted in one of the sections. The papillomata belonging to this class are multiradicular as a rule—that is to say, each papilloma may arise from many points in the wall of the duct. The epithelium in the tops of these papillomata coalesce. Sometimes the epithelial cells form columns which unite at their tops, also masses of epithelial hyperplasia arise directly from the lining of the duct and give rise to sessile tumours. The connective tissue in papillomata may be one of three types. It may consist purely of intra-elastica connective tissue; it may contain stalks of extra-elastica tissue, and hence contain the elastica in the centre of the stalk; and thirdly, the latter type may also contain an intra-elastica hyperplasia. It is a very interesting fact that papillomata are frequently present in the parts of those ducts which lead directly into the mass of spreading carcinoma. Papillomata often show evidence of past haemorrhage into their structure and into their ducts. I have no time to discuss the problem as to whether papillomata can become malignant. They may grow to enormous proportions. A uniradicular papilloma is a rare occurrence.

Clinical Signs.—The general appearance of a breast is normal when the papillomata are small. When they become large they may deform the breast and even protrude from a duct orifice on the surface of the nipple. There is often a history of pain, not of a severe character. Sometimes there is a history of discharge of blood or serum from the nipple. I possess a specimen the clinical signs of which had lasted eight years and a blood discharge from the nipple was only noticed once, and that was in the middle of its history. When haemorrhage from the nipple occurs, it is a classical sign of papillomata or carcinoma of a duct. Papillomata can exist, however, without inducing haemorrhage from the nipple. On palpation one ampulla or more than one ampulla may be felt enlarged, palpation of which may induce pain and haemorrhage, or a discharge of serum. When the duct is full of papillomata an enlarged ampulla can be felt, and its ducts and branches can be distinguished tortuous and enlarged right down to the periphery. The general sensation on palpation is one of nodularity, and more than one duct may be affected.

CLASS III.—IN WHICH EPITHELIAL HYPERPLASIA APPEARS TO BE, HISTOLOGICALLY, OF LESS IMPORTANCE THAN THE HYPERPLASIA OF THE CONNECTIVE TISSUE.

A. *Hyperplasia Elastica.*

Pathology.—In this state there is a universal massive hyperplasia elastica throughout the whole lengths of all the ducts and those acini that happen to be surrounded by elastica. It is of enormous and surprising proportions and density. Hyperplasia elastica is accompanied by a loose hyperplasia extra-elastica. One never extends beyond the limits of the other, and their limit is the general supporting connective tissue of the breast. The state I discovered incidentally, on making whole microscopical sections of carcinomatous breasts, and of non-desquamative hyperplasia of epithelium (Type C). In one of the carcinomatous patients primary malignant disease and massive hyperplasia elastica were present in both breasts. Less marked hyperplasia elastica occurs in ducts that contain carcinoma and in ducts that contain a highly suspicious type of non-desquamative epithelial hyperplasia.

Clinical Signs.—Massive hyperplasia elastica gives rise to multiple solid nodules over the whole breast, which are due to tortuous, thickened ducts and the affected acini. The condition is painless, and I do not know how it can be diagnosed by clinical examination.

B. *Hyperplasia Intra-elastica.*

Pathology.—Hyperplasia intra-elastica affects mainly peripheral ducts and acini, sometimes picking out a terminal duct and its lobule. Its presence is very marked and always local. I have never seen it generalized. In the early stages the loose, delicate, cellular, fibrillous tissue inside the elastica undergoes diffuse hyperplasia. It may be evenly distributed, or it may be more marked at one place than another. The fibrillous matrix supports isolated bipolar or stellate cells. Here and there the layer shows a marked tendency to grow larger and give rise to a small intra-elastica fibro-adenoma, an intra-elastica papilloma, or only an irregularity of its surface. It usually undergoes degeneration, when only an occasional cell can be stained to prove its cellular origin. It is not a common state, and it is often associated with carcinomatous breasts. Certain types of fibro-adenomata are derived from this tissue.

Clinical Signs.—Hyperplasia intra-elastica generally occurs in women over 35 years of age. Enlarged ducts and acini give rise to local nodularity of the breast. The breasts are nodular, but there are no special clinical signs by which the state can be diagnosed. I have discovered it only on making large microscopical sections and during their examination for other diseases.

C. *Hyperplasia Extra-elastica.*

Pathology.—This type is found distributed generally throughout the gland, or only in association with the formation of the extra-elastica type of fibro-adenoma; it is an essential part in the formation of this tumour. It

is unnecessary to do more than allude to the general state of hyperplasia extra-elastica. I will deal only with the local state in connexion with the formation of fibro-adenoma. On cutting the breast in half, so that the incision passes through the affected and normal parts of the breast, a difference in the structure between these parts is at once evident macroscopically. The normal part of the breast appears white, the affected part appears lightish grey. The affected part usually occurs in the smaller ducts and acini at the periphery of the gland, and macroscopically looks definitely limited. Microscopically the limitation is not so definite. On cutting whole sections of these breasts for microscopical examination three things may be seen in the affected part: First, the fibro-adenoma, which attracts attention to the breast, is quite obvious. Secondly, a small, definite, unsuspected fibro-adenoma may be discovered in juxtaposition to it, or separated from it by a small area of breast tissue. Thirdly, the parts that appear lightish grey on macroscopical examination show marked hyperplasia extra-elastica, which is an essential part in the growth of this tumour. The parts of the breast that appear white are normal on microscopical examination.

Clinical Signs.—The fibro-adenomata are seen mainly in young people from 15 to 25 years of age, but may occur in breasts of much older people. Attention is drawn to the breast by the fibro-adenoma. On palpation the surrounding parts are nodular; the nodules are about the size of small shot. There is very little pain connected with this type, and it is usually localized to one segment of the breast.

I have not dealt with the management and treatment of these diseases, for these reasons—namely, that the correct management and treatment frequently depend absolutely on the most careful judgement and laborious and precise preliminary microscopical examination. The detailed description would take me so long that I must reserve this part of my subject for another time.

Finally, I hope I have said enough to show you that the term "chronic mastitis" is a misnomer, and does not correctly indicate the states to which it is universally applied; that the clinical signs on which its diagnosis now depends can only indicate the possibility of many, without specifying one, of the various lesions they hide, and that these lesions may include carcinoma in its earliest as well as in its late stages.

PSICAINE: A NEW LOCAL ANAESTHETIC.*

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THIS cocaine substitute is an optically active isomer of ordinary cocaine prepared by Willstätter in collaboration with the firm of E. Merck of Darmstadt.

Cocaine is formed from the combination of l-ecgonine with methyl alcohol and benzoic acid. L-ecgonine contains four asymmetric carbon atoms, so that sixteen optical isomers are possible, eight of which are the mirror images of the other eight. One isomer of l-ecgonine is d-ψ-ecgonine, which differs from the former in the arrangement in space of the H and OH groups. D-ψ-cocaine is built up from this in exactly the same way as cocaine is built up from l-ecgonine, and the acid tartrate of this substance is known as "psicaine."

In Germany psicaine is approximately twice as expensive as cocaine, but it is said to have double the anaesthetic power, half the toxicity, and to be free from addiction properties. Psicaine is freely soluble in cold water up to 25 per cent., and is not precipitated by saline solution, Ringer, nor by proteins.

On the cornea psicaine in my experiments has approximately one-sixteenth the anaesthetic power of cocaine. The minimal effective concentrations to give complete anaesthesia after instillations lasting one minute are—for cocaine 0.25 per cent., and for psicaine 2.5 per cent.; on the other

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