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Is cystic mastitis related to carcinoma of the breast?

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IS CYSTIC MASTITIS RELATED TO CARCINOMA OF THE BREAST

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INTRODUCTION

Carcinoma of the breast is second in rank among all Caucasian women suffering from cancer. First is cancer of the uterus. The mortality from carcinoma of the breast in the United States today is approximately 10 per-cent of mortality from all cancer reported.

The relationship of benign to malignant lesions of the breast is still one of the problems of present day surgery. There have been many thoughts and many things written on chronic cystic mastitis and its association with cancer of the breast. The purpose of this paper is to review what has been written on the subject and to try to point out some of the problems and discrepancies which have arisen among the many writers who have written on the subject.

By definition, cystic disease is a benign condition of the female breast in which there are one or more microscopic cysts which may have a thin epithelial lining or none at all, with only a fiberous shell, and occurring at or near menopause. Other names of this same condition include mammary dysplasia, fibroadenosis, cyclomastopathy, mastodynia, adenosis, fibrocystic disease, mazoplasia, and a host of other complex terms. The term "chronic cystic mastitis", according to Foot and Stewart (8), "conveys no indication of the

presence or absence of any histopathologic changes; moreover, it implies a common etiology for a variety of lesions, most of which are anything but basically inflammatory processes."

Incidence:

The incidence of chronic cystic mastitis is dependent to a large extent upon the clinical and pathological criteria used in making this diagnosis. Frantz and her colleagues (9) found evidence of chronic cystic disease in 53 per-cent of a group of women with so-called "normal breasts", based on an extensive study of a large number of postmortum cases. Arther Pudry Stout, as reported by Frantz (9), found evidence of chronic cystic disease in 74 per-cent of operative breast specimens sent to the surgical laboratory. Foote and Stewart (8) noted cystic or proliferative changes in 59 per-cent of 300 cancerous breasts and in 65 per-cent of 200 non-cancerous breasts. (Table I)

Table I

FREQUENCY OF CYSTIC AND PROLIFERATIVE LESIONS BY DECADES

Decade	Cancer cases		Non-cancer cases	
	One lesion	More than one lesion	One lesion	More than one lesion
30-40	58%	37%	60%	40%

Decade	Cancer cases		Non-cancer cases	
	One lesion	More than one lesion	One lesion	More than one lesion
40-50	63%	47%	82%	60%
50-60	50%	15%	57%	30%

Thus it can be seen that the incidence of chronic cystic mastitis is very high among women even though the statistics on the subject vary a great deal. It also can be seen that if there is some relation between this disease and carcinoma of the breast, it would be a very important finding in medical history.

Etiology:

Chronic cystic mastitis is neither a neoplastic nor an inflammatory process. It is generally felt by most authors on the subject that the condition is caused by an endocrine imbalance of the sex hormones. It appears fairly well established that the secretion of estrogen and progesterone from the ovary, as well as prolactin from the pituitary, are responsible for the normal changes that occur in the breast, and that an imbalance in this hormone control may result in pathologic changes consistent with chronic cystic mastitis.

According to Womack (20), chronic cystic mastitis does

not ordinarily appear before puberty and usually does not occur spontaneously after menopause. The most likely cause of the condition is excessive estrogen stimulation. This hyperestrinism may be, of course, the result of excessive estrogen secretion by the ovaries and adrenals, impairment of estrogen inactivation by the liver, or a decrease in the natural estrogen antagonists, such as progesterone, cortisone, or androgens.

With the development of anovulatory cycles toward the end of menstrual activity, adequate corpus luteum formation ceased before the cessation of considerable estrogen formation. The absence of progesterone inhibition leads to a considerable relative increase in estrogen levels. It is at this time that chronic cystic mastitis may develop.

The changes of chronic cystic mastitis and their relation to estrogens have been well documented in the mouse, rat, guinea pig, rabbit, goat, monkey, and in man.

In the absence of estrogenic stimulation, the structural picture of chronic cystic mastitis has never been reported to occur, either in the human or in experimental animals. All women do not develop chronic cystic mastitis when subjected to excessive estrogens. This also is true of experimental animals. Therefore there must be factors in the formation of this lesion other than estrogen. In whatever

form they might exist, hereditary or other accessory factors would seem to be involved in the appearance of chronic cystic mastitis. What these other factors are remains speculative. It is possible that they serve as the initiating principle, and that estrogens act as the promoting or conditioning factor.

Histopathology:

The term "chronic cystic mastitis" is a broad term, and the histological criteria for making such a diagnosis varies a great deal with many different observers. This is one of the major reasons why statistics relating to this subject and also to its relationship to carcinoma vary so much.

According to Davis (5), the main theories of pathology which have developed in the past history of the disease can be listed as follows: 1) retention cysts, 2) chronic inflammation, 3) process of involution, 4) epithelial hyperplasia, 5) neoplastic process, and 6) sweat gland origin.

It generally is believed today that cystic disease of the breast is not a primary inflammatory process but basically is a condition of hyperplasia involving epithelium and connective tissue of the breast, often with the growth of cysts, sometimes progressing into a condition where marked

atypical epithelial hyperplasia occurs in the ducts. Probably there are two forms of the disease; a cystic type, in which the cysts are due to retention, and an adenocystic type, with multiple small cysts due to epithelial hyperplasia.

According to Foote and Stewart (8), most writers base their diagnosis of "chronic cystic mastitis", or a term of their own selection, on the presence of at least one or more of the following group of histologic findings (Table II):

Table II

CRITERIA FOR A DIAGNOSIS OF CHRONIC CYSTIC MASTITIS

1. A cyst or cysts
2. Duct papillomatosis
3. Blunt duct adenosis
4. Sclerosing adenosis
5. Apocrine epithelium
6. Stasis and distention of ducts
7. Periductal mastitis
8. Fat necrosis
9. Hyperplasia of duct epithelium
10. Fibro-adenoma
11. Tendency to fibro-adenoma

It is easy to see from the above list how the criteria for making the diagnosis of cystic disease varies with many writers. Such terms as "fibrosis", "hyalinized connective tissue", "cellular connective tissue", "lymphocytic infiltration", "desquamation", "atrophy", "epithelial hyperplasia",

and similar terms have been avoided.

Foote and Stewart (8) eliminated the last six in their list, stating that those lesions remaining could be summarized as "cystic and proliferative". The following histological descriptions of the lesions are summarized from their extensive study entitled "Comparative Studies of Cancerous Versus Non-Cancerous Breasts".

In order to classify a lesion as a cyst serial sections should be done to prove complete isolation and loss of communication with adjacent ducts or lobules. If one includes microscopic lesions as cystic, it is inevitable to confuse blunt end ducts, dilated ducts, or distended lobule components. Characteristically, cysts are accompanied by a group of what may be termed proliferative processes somewhat more numerous than the proliferative processes seen in a general average of breasts when these proliferative processes are enumerated with disregard of the presence of cysts.

Lesions described as ductal papillomatosis are included as stalked papillary adenomas. These usually are macroscopic lesions found in large and medium sized ducts. Also included here are cases with partial or complete epithelial plugging of the smaller stems of the duct system.

Blunt end adenosis is a term applied to ducts which

end abruptly and do not terminate in lobules. Blunt end ducts usually originate at the distal or near distal extremities of the duct system, and, since they begin at a point where periductal myoid tissue is absent or markedly attenuated, they typically lack this myoid investment and have a relatively poorly developed wall. The elastica in the walls of these ducts is quite variable in amount, but commonly one sees in the adjacent breast tissue an apparent condensation of extraductal elastica. The initial branch of a blunt end duct may not divide, but ordinarily one or often many subdivisions are encountered in serial sections. They are apt to end in an unusual cluster of closely, but irregularly spaced blind channels with no resemblance to usual lobule formation. The blunt end ducts often have relatively wide lumina which actually are wider than mammary ducts from which they sprouted. The epithelial lining of these ducts is not uniform and can vary from point to point in any given duct or its division. Sometimes there is a two-layered epithelial lining with a low or flat basal row and an outer row that varies from low to quite tall cylindrical. Blunt end ducts may have a single low or flat row of epithelium. The varable structure of blunt end ducts in all likelihood seems referable to whether the process is seen in an early or late

phase. The early lesions have relatively narrow lumina with taller lining cells, while the later lesions show broader lumina with shorter lining cells. In a single breast blunt end ducts of every phase may be found, as if the organ had responded to multiple periods of stimulation alternating with periods of quiescence. The degree of blunt duct adenosis ranges from an occasional focus to a level where almost all of a several centimeter mass of breast tissue may be made up principally of these structures.

Apocrine epithelium, consisting of the very characteristic large, usually tall, cylindrical cells, have relatively small nuclei and abundant clear, bright, eosinophilic cytoplasm. Aggregates of this kind of epithelium can commonly be seen grossly as discrete, yellowish-brown, slightly elevated, glistening areas, usually 1 to 2 mm. in diameter, but occasionally of much larger dimension. The larger aggregates are almost invariably partly cystic structures or, less often they are seen in direct continuity with a mammary duct that is lined elsewhere by conventional epithelium. Complete isolation from the duct system is shown on occasion, and when this is true, cystic distention is the rule. Papillary hyperplasia of slight or moderate degree is rather common, appearing in about one-third of apocrine epithelial foci of

both cancerous and noncancerous breasts.

Sclerosing adenosis occurs in two forms: in the first a palpable tumor mass is present; in the second, minute focal areas are seen only on microscopic examination, and the lesions are 20 to 30 times as frequent as the discrete tumors and present no clinical problems. Microscopically, in the stage of sclerosis, the epithelium is "chocked" by fiberous or hyaline matrix. Epithelial columns become irregularily isolated.

Due to constrictive pressure, the shape of the epithelial cell is apt to be variable. The sum total yields an impression of pleomorphism plus invasiveness. Nuclear staining is irregular and mitosis is absent. Lobulation is grossly inconspicuous and the greatest degree of sclerosis occurs at the periphery of the lobulated portions. Eventually the entire lobulated area will become hyalinized. The occurence of cellular areas in the tumors is a further source of microscopic confusion. Florid and sclerosing areas may be present in the same tumor. During the florid phase, moderate cellular variability may be seen and mitoses are not infrequent. During the florid phase there is an extensive multiplication of duct-like structures. Both extralobular and intralobular members of the mammary parenchyma are seen to

participate, and the newly formed ducts often show papillary and solid epithelial plugging. Sometimes the proliferation is so diffuse that solid epithelial islands, small and large, are formed in which lumina are not visible, and again single microscopic fields can be found that individually would be indistinguishable from cancer. In purely florid areas connective tissue does not participate. Even in the florid phase of sclerosing adenosis there is a tendency to lobulation.

Benign Breast Disease and Cancer:

The relationship of chronic cystic mastitis to carcinoma of the breast has been a problem for many years. After reading the literature one is left extremely confused as to the rôle of so-called chronic cystic mastitis in mammary carcinoma. The coincidental occurrence of cancer and so-called chronic cystic mastitis is variously reported. (Table III)

Table III

COLLECTIVE REVIEW OF THE RELATIONSHIP
BETWEEN BENIGN BREAST DISEASE AND CANCER

Author	Year of Publication	Type of Diagnosis	Total N° of Cases	Percent Followed	Follow-up Period	Per-cent of cases Followed Developing Cancer	Remarks
Schimmelbusch	1890	Pathologic	43		None	7	Co-existence of cancer and benign breast disease
Speese (Personal)	1910	Pathologic	35		None	26	Co-existence of cancer and benign breast disease
Speese (Collected)	1910	Pathologic	295		None	15	Co-existence of cancer and benign breast disease
Greenough and Simmons	1914	Pathologic	102		1 - 17 years	4.8	58 patients out of 88 had a partial resection and 32 had a local excision. A 7 year average follow-up.
Bloodgood	1921	Pathologic	128			2.4	Follow-up period and number of patients not stated.
Johnson	1924-1925	Pathologic and clinical	107	61	1 - 20 years		Cystic disease alone considered.

Semb	1928	Pathologic	144		None	17	Frequency of cancer in pathologic examination of primary fibroadenomatosis.
Oliver and Major	1934		106		5+ years	1	
Campbell	1934		190	62	5+ years	0.5	Simple cystic disease
Campbell	1934		42	52	5+ years	0	Adenocystic disease
Klingenstein	1935	Pathologic	226	24	2-11 years	3.7	Patients upon whom only partial breast excision was done
Warren I	1940	Pathologic	1206		Average 9 years	3.5	Aggregate cases including chronic mastitis, cystadenomas, adenomas, in all cases.
Warren II	1940	Pathologic	604	67	Average 9+ years	4.9	Massachusetts cases alone: chronic mastitis - 173; chronic cystic mastitis - 340; cystadenomas - 21; Adenomas - 70; Cancer - 30
Warren III	1940	Pathologic	602		5+ years in 2/3 of cases		Toronto cases alone: Chronic mastitis - 128; chronic cystic mastitis - 403; Duct papilloma - 71; cancer - 12
McKinley	1943	Pathologic	60	47	1-10 years	0	Average follow-up period only 3 years

Clagett et al.	1944	Pathologic	442	86	5 - 6 years	1.8	Short time follow-up from Mayo Clinic.
Geschickter	1948	Pathologic and Clinical	793		5 - 30 years; Average 10+ years	1.3	Mastodynia 231; cancer in 0. Adenosis 185; cancer in 6. Cystic disease 378; cancer in 4.
Atkins	1950	Pathologic and Clinical	328	78	1 - 14 years	0.8	Material from Mastitis Clinic of Guy's Hospital. All cases called fibroadenosis.
Lewison and Lyons	1953	Pathologic	451	85	1 - 25 years	1.8	Average follow-up period of 13.6 years with 75 per-cent of all patients being followed from 10 to 25 years.

The numerous writings on the subject have been reported in various ways: 1) evidence of unsuspected carcinomatosis changes in breast tissue removed for chronic cystic mastitis, 2) evidence of changes of chronic cystic mastitis in breasts removed for carcinoma, 3) the number of cases of chronic cystic mastitis which later developed carcinoma as evidenced by case follow-ups, 4) animal experiments, and 5) histologic investigation showing the transitional stages between the two conditions.

The co-existence of chronic cystic mastitis and cancer based upon clinical findings:

Mammary dysplasia and cancer in the same patient should occur coincidentally in a certain percentage of the population, even if the diseases are etiologically unrelated, since they both have their maximum incidence in women between the ages of 35 and 50 years.

It is extremely rare to find grossly evident cystic disease and carcinoma at exploration of a breast lesion; in most of the cases one finds either one or the other. Bloodgood (1) stated that "in more than 500 cases in which the breast was the seat of one or more blue-domed cysts, a cancer had been proved in only five." Bloodgood's statis-

tics were based upon grossly evident cysts and not upon microscopic examination.

Semb, as reported by Lewison (15), carried out a study of the co-existence of cystic disease and carcinoma in breasts removed for carcinoma. He found, in a total of 122 cancerous breasts, evidence of microscopic cystic disease in 77 per-cent.

Similar statistics were pointed out by Davis (5) in his extensive review of the literature which he reported on at the Fiftienth Annual Meeting of the Western Surgical Association in 1940. Tables IV and V were taken from this work.

Table IV

UNSUSPECTED CARCINOMA IN BREAST TISSUE

REMOVED FOR CHRONIC CYSTIC MASTITIS

Author	Year	Cases	Carcinoma	Per-cent
Schimmelbusch	1892	43	3	7
Sosse	1897	9	2	22
Greenough and Hartwell	1903	30	3	10
Roloff	1900	11	4	36.3
J. C. Warren	1905	115	15	13
Theile	1909	19	3	15.8

Speese	1910	35	9	25.7
Semb	1928	100	24	24
Kazhevnikoff	1930	80	6	7.5
		442	69	7.5

Table V

EVIDENCE OF CHRONIC CYSTIC MASTITIS

IN BREASTS REMOVED FOR CARCINOMA

Author	Year	Carcinoma	Cystic Disease	Per-cent
J. C. Warren	1905	307	15	3
Deaver and McFarland	1917	335	23	6.8
Fischer	1925	151	21	14
Semb	1928	140	112	80
McGlannen	1930	100	8	8
Morpurgo	1930	196	47	24
Lewis and Geschickter	1938	2675	29	1.1

Berehardt and Jaffe, Franzas, Walchshofer, Lindgren, and Geschickter, as summarized by Haagensen (12), studied the incidence of microscopic cystic disease in so-called normal breasts of women coming to autopsy, and the incidence of microscopic changes of chronic cystic mastitis was found to be high.

Geschickter (10) states that, "if one considers the frequency of microscopic changes resembling chronic cystic mastitis in the so-called normal adult breast and the relatively low incidence of mammary carcinoma, such atypical involutional changes must be considered relatively innocent and without special significance in the etiology of mammary carcinoma."

The relation of Chronic Cystic Mastitis to Cancer as Determined by Follow-up Reports:

Lewison (14) stated, "Seasoned statistics are the scaffold of experience upon which to build some clinical judgement." He believed that the most reliable method of determining the relationship between cancer and benign breast disease is the long term follow-up of a substantial group of patients.

The following chart compiled from Davis and others will show some of the confusion which has been associated with this method of study.

Table VI

Author	Year	Cases	Carcinoma	Per-cent
Greenough and Simmons	1914	83	4	4.8

Bloodgood	1921	128	3	2.3
Peck and White	1922	63	0	0
Johnson	1925	107	2	1.9
Campbell	1934	233	1	0.4
Klingenstein	1935	54	2	3.7
Lewis and Geschickter	1938	250	1	0.4
S. Warren	1940	340	14	4.1
McKinley	1943	60	0	0
Clagett et al.	1944	183	-	3.3
Atkins	1950	385	7	1.8

Satisfactory data compiled on the incidence of carcinoma of the breast following the demonstration of gross cysts should meet several requirements according to Haagensen (12), the following of which he believed to be the most important:

1) The data should be obtained from adequate clinical histories and careful pathological study.

2) Cystic disease should be defined as the complex, including grossly visible cysts, as well as the microscopic cysts and the various types of epithelial proliferation and metaplasia, and duct and acinal multiplication, usually associated with them. Other benign diseases of the breasts -- adenofibroma, adenosis, fibrous disease, intraductal

papilloma, and ectasia of the ducts -- should not be included.

3) The total number of patients with cystic disease, proved pathologically, should be stated, as well as the type of operation preformed.

4) The number of patients successfully followed after operation should be stated. The proportion of patients followed probably has an important bearing on the reported incidence of carcinoma, since those patients who are cured will probably not return to the clinics.

5) The length of follow-up should be stated in detail. The data should include at least a 10 year follow-up with a significant number of patients, a hundred or more.

6) For each patient who develops carcinoma of the breast, at least the bare essentials of a case history should be presented.

It is the opinion of the author that if the above standards were followed by the various writers on the subject, much of the confusion on the subject would be cleared up.

Animal Experiments:

In recent years it has been possible to produce breast cancer in mice and rats by intensive and prolonged

estrogenic stimulation. If large doses of estrogen in oil are injected at repeated intervals, cystic changes accompanied by various degrees of epithelial hyperplasia precede the formation of cancer by several weeks or months.

Goormatigh and Amerlinck, Lacassagne, Geschickter, Pullinger, Cheatle and Cutler, and others, as reported by Lewison (14), all have worked with this subject and all agree that estrogen stimulation produces changes characteristic of benign breast disease; but, they are not in agreement as to whether this is an actual precursor of cancer.

Most of the experimental work has one serious defect in common: all conclusions are based upon experimental research with small animals. Perhaps, as suggested by Foote and Stewart (8), "the physiologic gap between two species is too wide for mutual transposition of morphologic observations."

A systematic clinical study by the members of the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association (18) concerning the effects of massive and prolonged estrogen therapy in patients with advanced or metastatic breast cancer has revealed neither the induction of benign breast disease or secondary breast cancer in post-menopausal women in excess

of what might be expected.

Histologic investigations:

Many observers have considered the microscopic changes of mammary dysplasia significant in the etiology of breast cancer and have tried to trace the histologic beginnings of the disease to such a starting point. Although Foote and Stewart (8) have no precise figures, they state, "We can confidently say that we have seen cancer begin in duct papillomatosis, solitary and multiple cysts, apocrine epithelium, and blunt duct adenosis."

Campbell (2), after reviewing the literature, states, "if such a theory were indeed a fact, the maximum incidence of adenocystic forms would be found in a higher age group than that of simple cystic disease. Such is not the case, however, for the maximum incidence of adenocystic disease is between the ages of 30 and 40, cystic dysease between the ages of 40 and 45."

Cheatle and Cutler (3) describe "desquamative epithelial hyperplasia", wherein cysts are formed which may pass gradually from benign to malignant hyperplasia or neoplasia.

Perhaps some of the most recent work on this subject

was done by Davis, Simons, and Davis (7). In a series of 282 cases of chronic cystic mastitis, each lesion was classified according to Foote and Stewart's classification (see Table II). In this series 35 cases, or 12.4 per-cent, showed microscopic evidence of intraductal hyperplasia of varying degree. Of these 35 cases, one, or 2.8 per-cent, developed invasive carcinoma of the breast. Papillomatosis, intraductal connective tissue stalks covered with epithelium, was noted in 83 cases, or 29.4 per-cent, with one, or 1.39 per-cent, of these developing invasive carcinoma. The remainder of the 185 patients without intraductal hyperplasia remained relatively symptom-free with no future cystic disease, and only one, or 0.6 per-cent, developed invasive carcinoma. From these statistics it can be seen that 34.4 per-cent showed intraductal epithelial hyperplasia, and cystic disease and hyperplasia was seen in 65.6 per-cent. Of the 282 patients studied, 266 were followed. Invasive carcinoma developed in three of the follow-up patients for an incidence of 1.1 per-cent. This is 1.2 times the expected incidence of carcinoma in the female population where an incidence of 64 per 100,000 was reported by Gerhardt, Goldberg, and Leven, as quoted by Davis, Simons, and Davis (7). The incidence of the development of carnin-

oma was found to be much higher than the average for these with hyperplasia or papillomatosis, and lower in the 173 patients followed with no epithelial hyperplasia.

Davis, Simons, and Davis (7) next stated the incidence of cystic disease in 327 patients studied with carcinoma. Cystic disease was associated in 128 patients, of which 90, or 27.4 per-cent, were found to be simple cysts with epithelial hyperplasia, and 82, or 25 per-cent, were found to have intraductal epithelial hyperplasia.

Davis, Simons, and Davis (7) next studied the three most common types of carcinoma to determine the frequency of associated benigh intraductal epithelial hyperplasia. The following chart is taken from the results:

TABLE VII

THREE MAIN TYPES OF CARCINOMA

IN 327 CASES STUDIED

Type	N° of Cases	Per-cent	Associated Intraductal Hyperplasia	Per-cent
Scirrhous	143	43.7	6	4.2
Comedo	104	31.8	21	20
Papillary	44	13.4	13	29

From this one could say that pure scirrhous carcinoma is rarely associated with carcinoma, and comedo and papillary carcinoma is more often associated with carcinoma.

In a study of the age incidence of the three types of carcinoma, Davis, Simons, and Davis (7) found a positive relationship between cystic disease and age, since the peak was noted from 44 to 49 years. The age relationship was not as definite in the scirrhous and papillary carcinoma series.

Davis, Simons, and Davis (7) thus concluded that there is a high relationship between the incidence of carcinoma of the breast and papillomatosis and hyperplasia, and that this incidence is especially high in comedo and possibly in papillary carcinoma.

SUMMARY

It can be seen from this paper that the disease "chronic cystic mastitis" has been a curious entity for many years. The term itself denotes a benign condition of the breast; however, its relationship to cancer of the breast has been a subject of controversy for many years.

By definition the term cystic disease is a benign condition of the female breast in which there are one or more microscopic cysts which may have a thin epithelial lining or none at all, with only a fiberous shell, and occurring at or near menopause.

The incidence appears to be between 50 and 75 per-cent of the women with non-cancerous breasts in the age group of 35 to 50 years. This is approximately the same age group that cancer of the breast has its highest incidence.

The etiology is believed by most authors to be an endocrine imbalance of sex hormones. Excessive estrogen, from whatever cause, was believed to produce the condition, since this was proved in experimental animals. Hyperestrinism does not produce chronic cystic mastitis in all women, and therefore it is believed that there must be an additional factor or factors in the formation of the lesion.

In a study of the histopathology one notes a large amount of confusion and discrepancy. Foote and Stewart (8) believe the main findings necessary in making a diagnosis of chronic cystic mastitis are 1) cystitis, 2) duct papillomatosis, 3) blunt duct adenosis, 4) sclerosing adenosis, 5) apocrine epithelium, and 6) stasis and distension of ducts. These men feel that one or more must be present before making the diagnosis of chronic cystic mastitis. Many writers also have included such things as "periductal mastitis", "fat necrosis", "fibroadenoma", "hyaline connective tissue", et cetera.

There have been various methods of studying the relationship of cystic mastitis to carcinoma of the breast. These were discussed in this paper under the following headings: 1) evidence of unsuspected carcinomotosis in breast tissue removed for chronic cystic mastitis, 2) evidence of changes of chronic cystic mastitis in breasts removed for carcinoma, 3) the number of cases of chronic cystic mastitis which later developed carcinoma as evidenced by case follow-up studies, 4) animal experiments, and 5) histologic investigations showing the transitional stages between the two conditions.

Many observers believe that the histologic changes

noted in mammary dysplasia have a definite relationship to breast cancer and have tried to trace the histologic beginnings of the disease to its starting point. Foote and Stewart (8) state that they have seen cancer begin in duct papillamotosis, solitary and multiple cysts, apocrine epithelium, and blunt duct adenosis. Cheatle and Cutler (3) also believe that there is a type of cyst which may pass gradually from a benign to a malignant state. Davis, Simons, and Davis (7) in their series concluded that the incidence of breast cancer in those women with papillomatosis and hyperplasia appears to be higher than in those without these conditions. They also found that those women with hyperplastic breast lesions have a high incidence of developing comedo and possibly papillary types of carcinoma.

CONCLUSION

A review of the literature has left the author with the feeling that the research on the relationship between cystic mastitis and breast carcinoma has failed to lessen the confussion on the subject. There are still many facts which must be uncovered in the realm of breast cancer, as well as the part, if any, that is played by cystic mastitis in the etiology of breast cancer.

A question which arises is why is there so much variation and confussion in the literature on the subject under discussion. Some of the reasons may be summarized as follows: 1) many of the reports are scanty, 2) many are written without any definite objective, 3) many studies are made on statistical basis alone without any attempt to establish a histologic relationship, 4) in many series a large number of patients were lost to follow-up statistics, 5) many of the follow-up studies were made for only a short period of time, 6) many studies were made on animal experiments alone, 7) in many series the validity of the diagnosis, clinical or pathological, is questionable, and 8) probably the most important is the difference of opinion as to the actual definition of chronic cystic mastitis.

The weight of evidence points to the fact that cystic disease is a pre-cancerous lesion; however, there are many who still believe the contrary. Although anatomic and scientific studies cannot definitely say that cystic-disease is related to breast cancer, the frequent association between the two diseases noted in this paper would seem to indicate that a relation does exist.

Despite the lack of evidence, it is the belief of the author that the proliferative lesions of chronic cystic mastitis predispose towards a slightly higher indicence of cancer. With a concerted effort on the part of the many workers interested in this subject, along with some basic ground rules which may be followed, sound conclusions should be reached in the near future.

Since there is some strong indication that chronic cystic mastitis is predisposing to cancer of the breast, it would seem that the best treatment is that used for any precancerous lesion: excisional biopsy of the area in question with close follow-up examinations. If carcinoma does develop, it can be detected in an early stage, and prompt treatment may be administered.

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