

Paget's Disease of the Breast

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THE report by Sir James Paget¹⁴ in 1874 of cancer of the female breast preceded by or associated with eczematoid changes of the nipple remains a classic of clinical observation. Paget's description of this lesion of the nipple which was inevitably followed by the "formation of scirrhous cancer in the mammary gland" has not been improved upon. In Paget's patients the eruption in the nipple preceded the development of cancer and he postulated that the underlying cancer was stimulated or induced by the eczematoid changes. He was supported in this view by Butlin² who made the first microscopic studies and by Cheatle.³ Inglis⁸ postulated that the lesion begins in an intraductal carcinoma and spreads within the epithelium of the nipple. Most present-day pathologists support the view that the lesion of the nipple is an intraepithelial extension of an underlying intraductal carcinoma. Although the major pathologic features of this disease are agreed upon, its clinical course and treatment have been the subject of recent controversy. This review reports our experience with this disease and summarizes results of therapy.

Clinical Material

The records of all patients since 1948 with carcinoma of the breast at three New Orleans hospitals were reviewed. All cases

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with a history suggestive of Paget's disease (regardless of coded diagnosis) were studied, the pathologic reports reviewed, and the histologic sections re-examined. Patients with "Pagetoid" changes of the skin without nipple involvement were eliminated. These patients usually had far advanced lesions with later ulceration of the skin. Fifty-three patients, all female, with Paget's disease of the nipple comprise the basis of the report. Follow-up information was obtained on all patients (Fig. 1).

The patients are separable into two distinct clinical patterns: (1) Those with eczematoid changes of the nipple without a clinically discernible breast mass; (2) Those with nipple changes and breast masses (Fig. 2). Of the 53 patients, 32 (61%) had underlying breast masses, while 21 (39%) did not.

Incidence. At Charity Hospital, 2,447 patients have been treated for carcinoma of the breast since 1948. During this period there were 31 patients with Paget's disease, an incidence of 1.3%. This compares to the 0.7% reported by Dockerty and Harrington⁶ and the 3% reported by Lattes and Haagensen.¹⁰

Age. There appears to be no difference in age of onset between patients with masses and those without (Table 1). The peak decade of onset for both groups was 51 to 60 years. The average age at onset for patients with masses was 55.2 years and without 59 years. The average age of onset of all patients for carcinoma of the breast

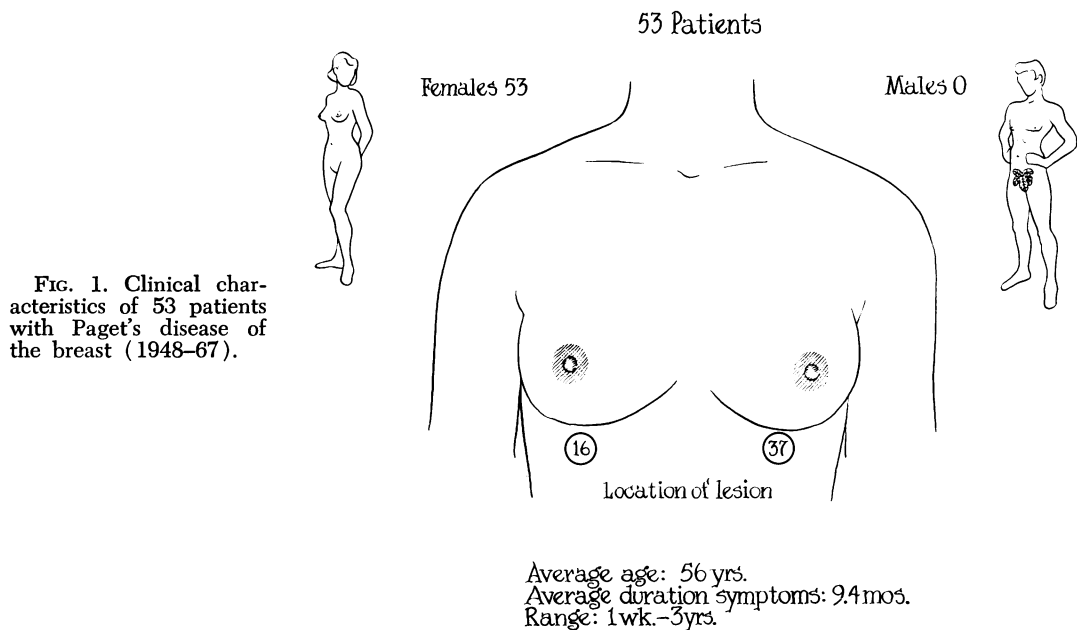
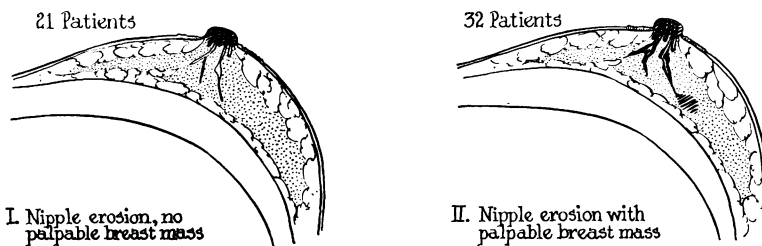


FIG. 1. Clinical characteristics of 53 patients with Paget's disease of the breast (1948-67).



compiled in the tumor registry statistics of Charity Hospital is 56.5. Thus, patients with Paget's disease tend to be the same age as the average patient with mammary cancer. Maier and co-workers¹¹ reported that patients with Paget's disease averaged a decade older than patients with carcinoma of the breast.

Clinical Findings

The primary symptoms differed in the two groups. Eczema was the most common complaint of women who had no mass, while a lump was the most common presenting complaint of those patients with underlying breast masses. One patient who complained of a mass did not have one on physical examination and 13 who had underlying lumps on physical examination

were unaware of them. In patients with underlying breast masses, the left side was involved in 21, the right side in eight, and bilateral breast masses were palpated in one patient. In patients without a palpable mass the left breast was involved in 13 and the right breast in eight.

TABLE 1. Paget's Disease of the Breast
Age Distribution

Decade	Mass	No mass	Total
31-40	4	0	4
41-50	8	5	13
51-60	9	7	16
61-70	6	4	10
71-80	5	4	9
81-90	0	1	1
Totals	32	21	53

TABLE 2. *Symptoms of Patients with Paget's Disease of the Breast*

<i>Mass</i>			
	Primary Symptoms		Secondary Symptoms
Mass	13	Oozing	6
Eczema	10	Eczema	5
Bleeding	7	Pain	5
Pain	5	Mass	5
Oozing	4	Ulcer	4
Itching	2	Bleeding	3
Ulcer	1	Itching	2
Burning	1	Burning	1
<i>No Mass</i>			
	Primary Symptoms		Secondary Symptoms
Eczema	11	Eczema	3
Itching	6	Itching	2
Oozing	5	Bleeding	1
Pain	4	Pain	1
Bleeding	3	Erythema	11
Tenderness	1	Foul odor	1
Ulcer	1		
Mass	1		
No symptoms	2		

Duration of Symptoms. Prolonged symptoms are characteristic in Paget's disease. Almost 40% of patients had symptoms for a year or more. Delay in obtaining treatment has been reported by others.^{7, 11} Interestingly, delay in instituting definitive therapy had no apparent deleterious effect

on 5-year survival or on recurrence (Table 3).

Treatment. All patients *without* an underlying breast mass underwent what was intended as definitive therapy. Sixteen patients had radical mastectomies and five had simple mastectomies (Table 4). Some patients who had palpable masses had far advanced carcinomas. Eight underwent palliative simple mastectomies. Of the remaining 24 patients with masses, four had "definitive" simple mastectomies and 20 had radical mastectomies (Fig. 3). A few patients in both groups had postoperative irradiation of the axilla after simple mastectomies.

Pathology. Typical Paget's disease of the breast was confirmed histologically in all patients. Essential criteria were the presence of tumor cells lying singly or in clusters within intact epidermis, showing no direct connection with an underlying carcinoma. There were a few cases reviewed in which there was extensive ulceration produced by a large mass of invasive carcinoma of the breast, with only a rare nest of intra-epithelial localization of tumor cells at the edge of the ulceration. These were considered ulcerative carcinomas and were excluded by the pathologist without knowledge of subsequent clinical courses.

TABLE 3. *Paget's Disease of the Breast Duration of Symptoms vs. Survival and Recurrence*

Duration symptoms	No. Cases	5 Year Survival	% 5 year Survival	Recurrence	Died of CA
Mass					
6 months	11	4 (11)*	36%	6 (11)	9
6 months-1 year	7	2 (7)	33%	5 (7)	4
1 year-2 years	9	5 (9)	55%	4 (9)	5
2 years or more	5	3 (5)	60%	4 (5)	3
Totals	32	13 (32)	40.6%	19 (32)	21
No Mass					
6 months	9	6 (8)*	85.7%	0	0
6 months	7	6 (6)	100%	0	0
1 year-2 years	2	1 (1)	100%	0	0
2 years or more	3	2 (2)	100%	0	0
Totals	21	16 (17)	94.1%	0	0

*Patients treated since 1964 excluded.

TABLE 4. Treatment and Survival of Patients with Paget's Disease of the Breast

Therapy	No. Cases	5-year Survival	% 5-year Survival	No. Died of Cancer
Mass				
Radical mastectomy	20	9 (20)*	45%	11
"Palliative" simple mastectomy	8	1 (8)	12%	8
"Definitive" simple mastectomy	4	3 (4)	75%	2
Totals	32	13 (32)	40.6%	21
No mass				
Radical mastectomy	16	11 (12)*	91%	0
Simple mastectomy	5	5 (5)	100%	0
Totals	21	16 (17)	94%	0

* Patients treated since 1964 excluded.

One listed as possible Paget's disease was reclassified as Bowen's disease, or intra-epithelial carcinoma of the skin and excluded.

In patients without a clinically palpable mass, the pathologist often had difficulty finding an underlying carcinoma. Such cases were characterized by small primary tumors found only after numerous sections of the surgical specimen. The most common underlying process was non-invasive intraductal carcinoma. In one patient no underlying primary could be found after extensive sections of the resected specimen. Only two patients without palpable masses were found to have invasive carcinoma (Fig. 4).

In contrast, 30 of 32 patients with palpable masses had underlying invasive carcinomas. Two with small palpable masses under the areola had non-invasive intraductal carcinomas. The underlying carci-

noma was always intraductal; no lobular carcinomas, colloid carcinomas, or medullary carcinomas with lymphoid stroma were encountered.

None of 16 patients without a mass, treated by radical mastectomy, had axillary metastases. The absence of axillary metastases in patients without a palpable mass is a prominent feature of all reports in which such data are given (Table 5), with only three patients having axillary metastases in a collected series of 70 patients. All three had large lesions with extensive skin involvement. All three died of metastases in spite of radical mastectomies.

Of the 20 patients with masses who were treated by radical mastectomies, nine had metastases to one or more lymph nodes in the axilla, nine had negative nodes, and in two patients the axillary contents were not reported. The incidence of axillary metas-

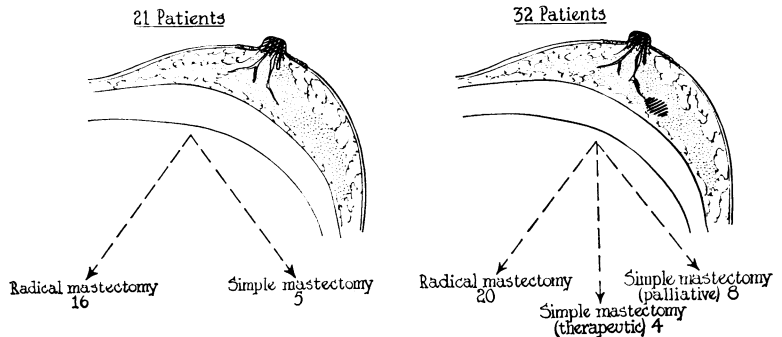


FIG. 3. Treatment of Paget's disease of the breast (1948-67).

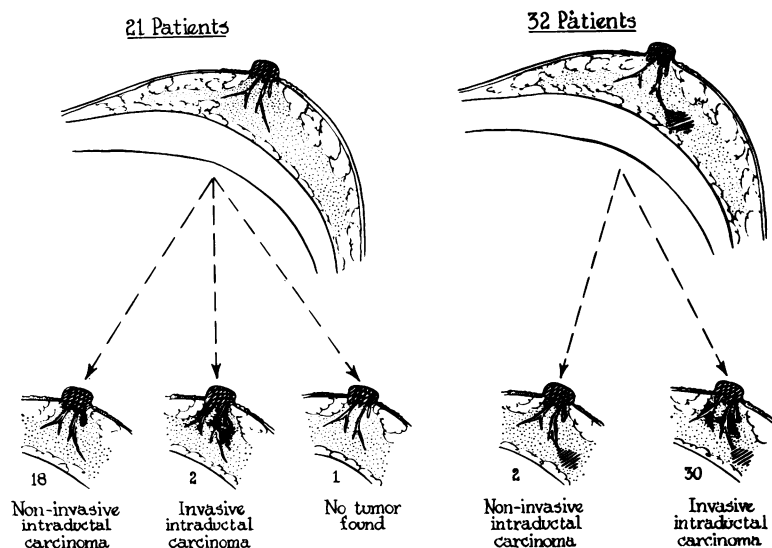


FIG. 4. Pathologic findings in 53 patients with Paget's disease of the breast. In patients *without* a mass only two were found to have invasive carcinoma.

tases in patients with masses is reported to be the same as in patients with carcinoma of the breast without Paget's disease.¹¹

Survival. Of 21 patients treated since 1948 for Paget's disease without a mass, 16 are living without evidence of recurrence (Fig. 5). The other five patients died of causes *other than cancer*, without recurrence and four survived more than 5 years. The 5-year survival rate for patients operated upon prior to 1964 was 94%.

In 32 patients with clinically palpable masses, 18 died of cancer of the breast in less than 5 years. Two died of cancer be-

yond 5 years and 3 died within 5 years of other diseases without evidence of recurrence. Nine patients survived 5 years without evidence of recurrence. The 5-year survival rate for all patients operated upon prior to 1964 was 36.6%. Of 20 patients with masses treated by radical mastectomies, nine (45%) survived for 5 years or longer. Three of four patients treated by "Definitive" simple mastectomies, survived 5 years. Only one of the eight patients who had "Palliative" simple mastectomy survived as long as 5 years. Five-year survival rate in patients with masses was

TABLE 5. Incidence of Axillary Metastases
Collected Series Treated by Radical Mastectomy

Authors	No Mass		Mass	
	No. Patients	No. with Axillary Metastases	No. Patients	No. with Axillary Metastases
McGregor and McGregor ¹²	5	0	5	0
Ridenhour <i>et al.</i> ¹⁴	8	0	12	8
West and Nickel ¹⁵	2	0	8	3
Kay ⁹	5	0	16	11
Helman and Kliman ⁷	4	1*	9	7
Culberson and Horn ⁵	11	1*	12	7
Lattes and Haagensen ¹⁰	19	1*	54	33
Nance <i>et al.</i>	16	0	18	9
Totals	70	3*	134	78

* All had extensive skin involvement.

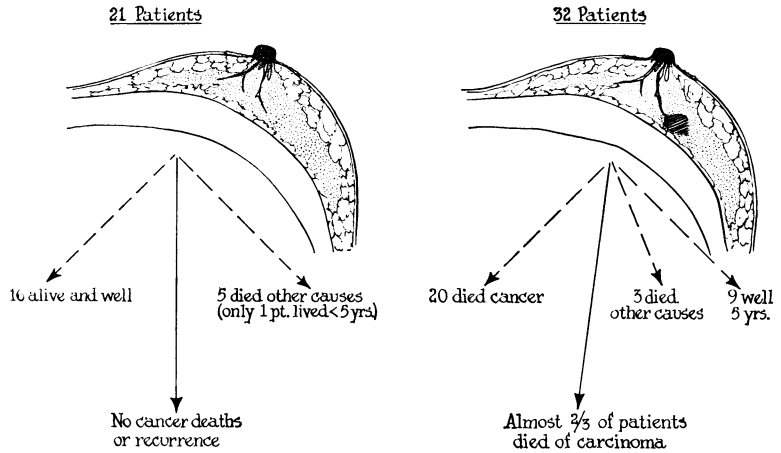


FIG. 5. Survival of patients treated for Paget's disease of the breast (1948-67).

lower than in an unselected population with mammary cancer, but if clinically incurable patients were excluded, the survival rate was no different than the survival of all patients with mammary cancer.⁷

Five-year survival for patients without a mass was high. None of 21 patients died of cancer and only one survived less than 5 years. None of Kay's⁹ seven patients died of cancer (two died of other causes). Only one of Culberson and Horn's⁵ 13 patients and one of Helman and Kliman's⁷ 15 patients died of cancer.

Discussion

Paget's disease of the breast with an incidence of 1 to 4% of all mammary cancers is important because it is frequently misdiagnosed and mistreated. The innocuous looking early lesion seldom prompts the patient to seek help. When she does, local therapy is frequently employed without biopsy. The end result is a delay of a year or more before definitive therapy is carried out. Any eczematoid lesion of the nipple which persists more than a few weeks should be viewed with suspicion and a biopsy should be obtained. Improvement and even temporary healing of the lesion sometimes occurs after local therapy, but always recurs. Few cancers give such a clear-cut warning of danger.

The pathologic diagnosis of Paget's disease of the breast ordinarily is not difficult,

but occasionally intra-epithelial carcinoma of the skin, and rarely superficial amelanotic melanoma may be confusing. In Paget's disease intra-epidermal tumor cells should not have visible direct connection to the underlying carcinoma. Any carcinoma of the breast may invade dermal lymphatics and in some instances extend directly into the epidermis. Extensive invasion may lead to breakdown of the epidermis with a few areas at the periphery containing intra-epidermal tumor cells or nests.

One of the striking findings of our study has been the clear-cut difference in clinical behavior of this disease depending on whether or not a mass is palpable in the breast. This difference may be sufficient to permit separation of therapeutic approaches. Two types of Paget's disease have been recognized. West and Nickel¹⁵ identified two clinical forms but divided their patients on the basis of complaints. The group of patients complaining of "tumor" did poorly following radical mastectomy. Those whose complaint was eczema did well. Eight of 13 patients with "eczema" had underlying breast masses. None of the patients without a mass died of carcinoma or had axillary metastases. West and Nickel, while recognizing the clinical difference between the two groups, recommended radical mastectomy for all patients with Paget's disease.

Colcock and Sommers⁴ separated pa-

tients into two groups on the basis of the presence or absence of a mass. They were struck by the poor prognosis of those with masses. Of eight, none survived 5 years. None of the patients without a mass had axillary metastases and none died of breast cancer. These authors recommend simple mastectomy for patients with Paget's disease without a palpable mass.

Lattes and Haagensen¹⁰ recognized three clinical types: patients with nipple erosion alone, breast mass alone, and nipple erosion with a breast mass. These authors advocate radical mastectomy for *all* instances of Paget's disease, but their data do not support their conclusion. Of 25 patients *without* a breast mass, 19 underwent radical mastectomies. Only one had axillary metastases and this patient had lymphedema. There were only two deaths from cancer in these patients: one had a previous mastectomy on the other side for invasive cancer; the other had extensive preoperative lymphedema of the breast. The remaining 18 patients had negative axillary nodes. One patient *with* axillary metastases was not cured by radical mastectomy.

A similar observation may be made of Culberson and Horn's⁵ conclusions. These authors reported 25 cases of Paget's disease. Thirteen patients had no mass and the only one who had axillary metastases was a patient with extensive superficial skin involvement. Only the patient with extensive skin changes died. She was not helped by radical mastectomy. The remainder of the patients with no mass were living and free of disease at the time of the report. By contrast, seven of twelve patients with masses had axillary metastases; five had died. Despite the difference between the two groups these authors recommended radical mastectomy "since there are cases, however few, in which axillary lymph node metastases occur in the absence of a palpable breast tumor."

Helman and Kliman⁷ recognized two clinical types of disease. Of 15 patients without a mass, only one died of cancer

(again a patient with a large area of breast skin involved). The patient who died had been treated by radical mastectomy. Eleven others were treated by local excision and x-ray, or by simple mastectomies. In contrast, 12 patients with masses had been treated, nine radical mastectomies and the remainder by palliative operations. Ten of the 12 patients died with cancer. These authors concluded that simple mastectomy and irradiation were as effective as radical mastectomy in patients who had no breast mass.

Kay's⁹ report in 1966 of 23 patients with Paget's disease strongly advocated simple mastectomy alone as treatment for Paget's disease without a mass. Of six patients without a mass, none had axillary metastases and none died of cancer. Only three of 16 patients with masses survived 5 years.

Maier *et al.*¹¹ reviewed 137 cases of Paget's disease treated in Philadelphia County from 1951 to 1964. Fifty-six patients had no mass. Axillary node metastases were reported in eight of these and on this basis the authors recommended radical mastectomy for all patients with Paget's disease. Unfortunately, survival figures do not permit determination of cause of death and it is not possible to determine which of the "no mass" group died of cancer. In their study also only sixty histologic specimens were reviewed by the authors. This is the only report which failed to note a clear-cut difference between the two types of Paget's disease.

The experience of 11 authors with a total of 279 cases of Paget's disease is given in Table 6. The data are remarkably consistent. Patients with masses had a high incidence of axillary metastases (when such data were given) and 5-year survival for the group was only 29%. In the patients without a mass, axillary nodes were reported in only three of 125 patients (each of the three patients had large lesions with extensive skin involvement). These patients all died even though treated by radical mastectomies. Only one patient in the

TABLE 6. *Survival from Paget's Disease of the Breast Collected Series*

First Author	Year	No Mass					Mass				
		No. Patients	No. Patients	Lived 5 Years	Axillary Nodes	Died CA	No. Patients	Lived 5 Years	Axillary Nodes	Died CA	
Nance	1970	53	21	(16) (17)	0 (16)	0	32	13 (32)	9 (18)	21	
Ridenhour ¹⁴	1969	20	8	6 (8)	0 (8)	0	12	3 (12)	8 (12)	9	
Bernhard ¹	1966	3	2	2 (2)	—	0	1	0 (1)	1 (1)	1	
Kay ⁹	1966	23	7	5 (6)	0 (5)	0	16	3 (16)	11 (16)	13	
McGregor ¹²	1959	21	14	6 (6)	0 (5)	0	7	2 (4)	—	2	
Culberson ⁵	1956	25	13	4 (5)	1 (11)	1	12	3 (8)	7 (12)	5	
Helman ⁷	1956	27	15	5 (6)	1 (4)	1	12	1 (10)	7 (9)	10	
Lattes ¹⁰	1954	64	25	5 (7)	1 (19)	2	39	10 (24)	21 (39)	14	
Colcock ⁴	1954	23	15	6 (6)	—	0	8	0 (8)	7 (8)	8	
West ¹⁸	1942	20	5	2 (2)	0	0	15	2 (15)	7 (15)	7	
Totals		279	125	54 (65)	3 (70)	4	154	37 (130)	78 (130)	87	

series without a mass died and she had a previous radical mastectomy for carcinoma of the opposite breast.

Our data supports the conclusions of Kay,⁹ Colcock and Sommers,⁴ and Helman and Kliman.⁷ Paget's disease with a palpable mass behaves little differently from ordinary cancer of the breast and should be treated in the same manner. The prognosis in these patients differs only slightly from that of all patients with carcinoma of the breast. Our 5-year survival in these patients was 40.6%. Others consider the presence of a mass an indication of poor prognosis. The difference between our experience and others may be that we have *not* included patients who have intra-epidermal tumor nests adjacent to ulcerated skin over a bulky tumor. Most of these patients have far advanced lesions and contribute to an overall poor prognosis in any series. We do not consider this lesion true Paget's disease unless invasion of the epithelium of nipple ducts is present.

We would caution against local excision of the nipple as definitive therapy. We have noted in our own material that residual intraductal carcinoma is frequently present in resected breast specimens after prior nipple excision. Others have made similar observations and there have been

reports of recurrence and death from such inadequately excised lesions.

The following conclusions about therapy seem warranted: 1) No excoriation or eczematous lesion of the nipple should be treated longer than 2 weeks without biopsy. Any unilateral lesion should be considered Paget's disease until proven otherwise by biopsy. 2) Paget's disease associated with a palpable mass usually means underlying invasive carcinoma. Biopsy of the mass and radical mastectomy is appropriate if the lesion is confined to the regional nodes. 3) If no tumor can be detected in the breast of a patient with Paget's disease of the nipple, and the nipple erosion has not extended beyond the areola, simple mastectomy should be considered definitive therapy, particularly in poor-risk patients. Although this study was based solely on *palpatory* findings, mammography might give further assurance that no underlying tumor is present. Most patients do not have invasive lesions and virtually all survive free from cancer.

Summary

1. A review of 53 patients with Paget's disease of the breast seen at three New Orleans Hospitals from 1948 to 1969 has been made. Two clearly definable forms of the disease have been identified depending on

whether or not a breast tumor was palpable at the time of treatment.

2. Patients with Paget's disease of the breast *with* an associated underlying tumor had a lesion which behaved much like ordinary carcinoma of the breast. Axillary metastases were present in 50% and the overall 5-year survival was 40.6%. Radical mastectomy seems to be appropriate therapy for these lesions.

3. Patients with Paget's disease of the breast *without* an underlying breast tumor did not have axillary metastases. Invasive cancer was present in only a small percentage. All patients in our series survived free from cancer. In patients in whom careful palpation excludes a mass and whose lesions are limited to the nipple and areola, simple mastectomy should be considered definitive therapy.

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DISCUSSION

DR. HOWARD A. PATTERSON (New York): This report is concerned with a field in which surgeons, young and old, find a high proportion of their tragic results. The fact that many of the victims are young makes this even worse. The pendulum swings back and forth, and it is no wonder that our young surgeons and our students are bewildered by what they hear and what they read.

We all agree that the aggressiveness of the tumor has more to do with the outcome than the aggressiveness of the surgeon. We also see patients with an apparently early and favorable lesion die rapidly, and some with advanced lesions live out a full life span. This is likely to make young surgeons fatalists, believing that treatment does not really matter. We must teach them otherwise, and George Finney has proved to us in his excellent report that it *does* matter, very much indeed.

A discussor should disagree and stimulate further argument, but I can find nothing in this report with which I can really disagree. The hot

arguments about the management of breast cancer are not as hot now as they used to be. You have heard Willy Meyer's name mentioned in this paper as one of the two pioneer advocates of radical mastectomy. I was present at a meeting of the New York Surgical Society 40 years ago when he dropped dead on the platform defending routine radical mastectomy.

As the pendulum swings, we hear a famous surgeon say that a surgeon who does not divide the clavicle routinely and add neck dissection to radical mastectomy is like a bird-dog who refused to go through a barbed wire fence to retrieve a bird that fell on the other side—this in spite of the fact that the involvement of neck nodes always comes up from the mediastinum, and not the axilla.

We also see various diagrams urging removal of large parts of the bony thoracic wall. On the other end of the pendulum swing we hear that the nodes are helpful and that the less surgery the better.

The one point I wish to stress is that the prin-