

PAGET'S DISEASE OF THE NIPPLE

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PAGET'S DISEASE of the nipple is not a common disease. Harrington,¹ in a review of 4,628 cases of carcinoma of the breasts, reports only 34 cases of Paget's disease, an incidence of 0.7 per cent. It is for this reason, perhaps, that the seriousness of an eczema of the nipple is not always appreciated.

In 1874, Sir James Paget² published an article titled: "On Disease of the Mammary Areola Preceding Cancer of the Mammary Gland." He stated that "certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus carcinoma of the mammary gland."

His classical description of the clinical features of the disease, in the 15 patients he had observed, is in part as follows: "The disease began as an eruption on the nipple and areola. In the majority it had the appearance of a florid, intensely red, raw surface, very finely granular, as if very nearly the whole thickness of the epidermis were removed; like the surface of a very acute diffuse eczema. From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish viscid exudation.

"It has happened in every case which I have been able to watch, cancer of the mammary gland has followed within, at the most, two years, and usually within one year. The formation of the cancer has not in any case taken place first in the diseased part of the skin. It has always been in the substance of the mammary gland, beneath or not far removed from the diseased skin, and always with a clear interval of apparently healthy tissue. In the cancers themselves, I have seen in these cases nothing peculiar. They have been various in form; some chronic, some acute, the majority following an average course, and all tending to the same end: recurring if removed, affecting lymph nodes and distant parts, showing nothing which might not be written in the ordinary history of cancer of the breast."

Because of the lack of a histopathologic description by Paget, there has been much confusion as to the true nature of the disease. Kilgore³ states that to-day a definite histologic picture is recognized, consisting of "epithelial hypertrophy, subepithelial round cell infiltration and Paget's cells." Paget cells, so-called, are large edematous cells in the epithelium, vacuolated, and with shrunken pyknotic nuclei. Muir^{4, 5} defines a Paget cell as a cancer cell growing within a healthy or at least nonneoplastic epithelium.

FIG. 1.

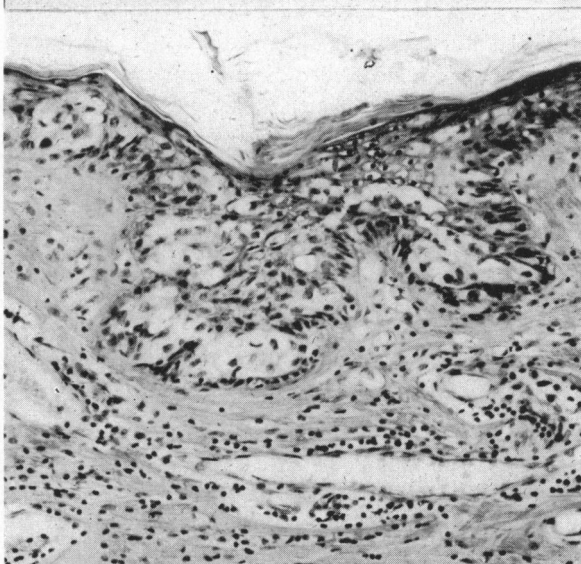


FIG. 2.

FIG. 1.—Case 1: Eczema of nipple and areola of two years' duration. Radical mastectomy. Nodes not involved. Well nine years.

FIG. 2.—Case 1: Section through nipple. Many Paget cells are seen in the epidermis. (X275)

According to Caylor⁶ there are at the present four chief opinions regarding Paget's disease: (1) That it is a dermatitis or eczema of the skin; (2) that it is a primary squamous cell epithelioma of the skin; (3) that it is a carcinoma developing from the lactiferous ducts in the nipple and the sudoriferous ducts of the skin, secondarily involving the skin and breast tissue; and (4) that it is a carcinoma beginning deep in the breast and growing up along the ducts of the nipple and finally invading the skin.

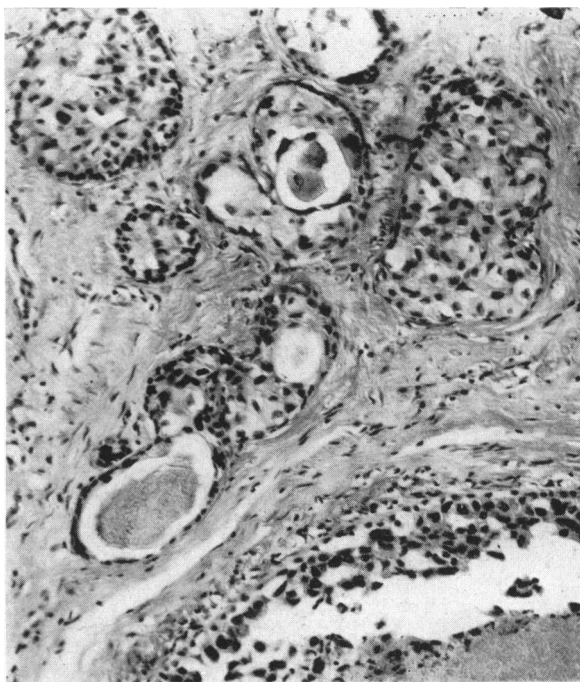


FIG. 3.—Case 1: Section through breast showing intraduct carcinoma. (X240)

Cheatle^{7, 8} feels that the classic signs that Paget described are caused by more than one condition and that it is not correct to limit the diagnosis of Paget's disease of the nipple to those states in which "Paget cells" are present.

Muir believes that Paget's disease occurs only when intraduct carcinoma is present in the upper portions of the ducts in the nipple, and is due to the spread of the cancer cells from ducts to the epidermis by the intra-epithelial route.

Weiner⁹ has published an excellent chronologic résumé of the more important literature on Paget's disease of the nipple. He was particularly interested in the extramammary form, and suggests that Paget's disease of the skin is the intra-epidermal metastasis from an underlying carcinoma of the apocrine sweat glands.

Ewing¹⁰ states that "Paget's disease is a specific, chronic, progressive disease of the mammary nipple and adjoining skin, which is closely related

to, and almost invariably followed by, carcinoma. It is probably to be interpreted as a precancerous affection at first, limited to the epidermis and the gland ducts, but later becomes true carcinoma. The writer's conclusions regarding the nature of Paget's disease are influenced by clinical characters as well as histologic studies, which indicate that there are two clinical varieties. One finds a typical group of cases in which there is no definite tumor of the breast but a slowly progressive eczematous lesion affecting the epidermis about the nipple, not extending deeply into the ducts but spreading widely over



FIG. 4.—Case 2: Eczema of nipple and surrounding skin of one year's duration. Radical mastectomy. Nodes not involved.

the skin, with a favorable prognosis under treatment. Contrasted with these cases are others in which, from the first, there is a carcinoma of ducts or parenchyma, a limited involvement of skin, a diffuse invasion of breast, an unfavorable prognosis, and often a rapid course. It is difficult to accept the conclusion that these two maladies are identical in nature, differing merely in grade of malignancy; but histologic studies show that the lesions are very similar."

It is not the object of this report to enter into the controversy concerning Paget's disease of the nipple. We wish to report our experience with the disease and to emphasize the observation of Paget, namely, that most cases of chronic eczema of the nipple are closely associated with a true carcinoma of the breast.

We have reviewed the records of 20 cases of Paget's disease of the nipple. Through the courtesy of the Surgical Department of St. Luke's

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Hospital we have been permitted to study 12 cases in their records. These patients were treated over a period of approximately 23 years (January, 1918–May, 1941), and eight were treated at the New York Hospital over a period of about nine years (September, 1932–May, 1941). The diagnosis in each case was based on the presence of an eczema or excoriation of the nipple which, on histologic section, showed epithelial hypertrophy, sub-epithelial round cell infiltration and Paget's cells.

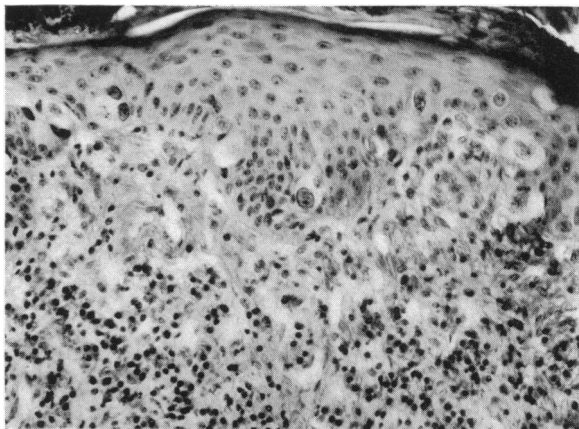


FIG. 5.—Case 2: Section through skin. Shows direct invasion of epidermis by carcinoma cells. Only a few Paget cells in this section. (X280)

As suggested by Ewing, these cases are readily divided into two clinical groups: In the first group (Table I) of 13 cases, all but two of whom were over 50 years of age, the chief complaint of each patient was an eczema of the nipple, usually of long duration. In only three instances was the lesion of the nipple present for less than one year. Section of the breasts, after removal, revealed a definite tumor in eight of the 13 cases, and in three of the eight there were axillary metastases. Of the three patients with axillary metastases, one died six months, and another four years, after operation; the

TABLE I

GROUP I—PAGET'S DISEASE OF THE NIPPLE—CHIEF COMPLAINT: ECZEMA OF NIPPLE

Case No.	Age	Duration of Eczema	Breast Tumor	Mastectomy	Node Involvement	Result
1.	74	6 yrs.	No	Simple	Not removed	Well—2 mos.
2.	59	5 yrs.	Yes	Radical	Yes	Died—4 yrs.
3.	60	4 yrs.	No	Radical	No	Well—17 yrs.
4.	55	4 yrs.	Yes	Radical	Yes	Died—6 mos.
5.	62	2 yrs.	Yes	Radical	No	Well—9 yrs.
6.	57	18 mos.	No	Simple	Not removed	Well—15 yrs.
7.	60	15 mos.	Yes	Radical	No	Well—3 yrs.
8.	50	1 yr.	Yes	Radical	No	Well—1 mo.
9.	67	1 yr.	No	Radical	No	Well—2 yrs.
10.	64	1 yr.	Yes	Radical	Yes	Well—1 yr.
11.	52	8 mos.	Yes	Radical	No	Well—10 yrs.
12.	41	3 mos.	No	Simple	Not removed	Well—4 yrs.
13.	47	2 mos.	Yes	Radical	No	Well—3 yrs.

third was subjected to operation only one year ago, and is alive and well, without evidence of recurrence. The remaining ten patients are alive and well, two, for more than 15 years, one, ten years, one, nine years, three for three years, and three operated upon within the past year.

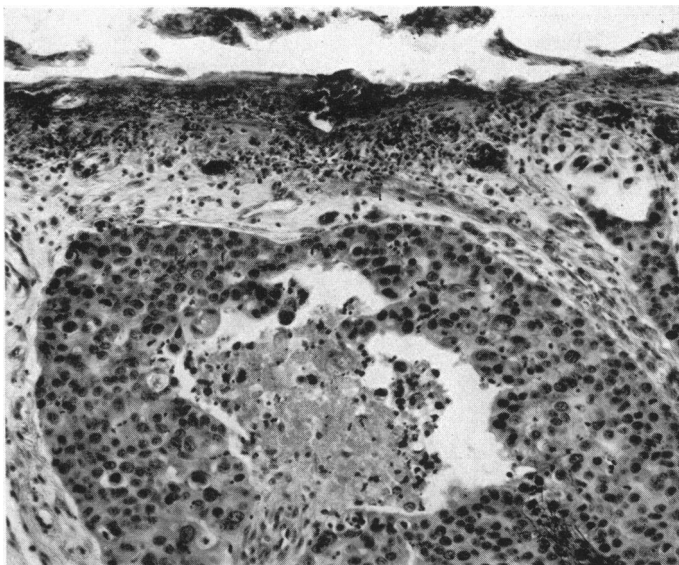


FIG. 6.—Case 2: Section through breast. Shows a duct cell-type carcinoma.

This group of 13 cases emphasizes the close relationship between chronic lesions of the nipple and carcinoma of the breast. It also suggests that carcinoma of nipple origin is slow to metastasize to the axillary lymph nodes and, therefore, forms a favorable group with proper treatment. We agree with Cohn¹¹ that all lesions of the nipple which do not quickly respond to simple treatment should be subjected to a biopsy which includes a good section of the underlying breast tissue, and if the histologic picture is that of Paget's disease a radical mastectomy should be performed.

In the second group of seven cases (Table II) all the patients were aware of a tumor of the breast at the time they sought medical advice, and only two complained of an associated eczema of the nipple. In fact the nipple lesions were so inconspicuous that in not a single instance was the clinical diagnosis of Paget's disease made. Histologic studies of the nipples, however, revealed changes similar to those of the first group. The second group is also distinct from the first in that the symptoms were of relatively short duration, the average being four months. Four of these patients are known to have died of their carcinomata within three years after operation, one has been alive for one year but has a local recurrence, and the result in the other two is not known.

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TABLE II

GROUP II—PAGET'S DISEASE OF THE NIPPLE—CHIEF COMPLAINT: BREAST TUMOR

Case No.	Age	Duration of Tumor	Secondary Nipple Changes	Mastectomy	Node Involvement	Result
1.	46	9 mos.	Yes	Radical	No	Died—3 yrs.
2.	44	6 mos.	Yes	Radical	No	Unknown
3.	50	6 mos.	Yes	Radical	Yes	Died—6 mos.
4.	38	3 mos.	Yes	Radical	Yes	Died—2 yrs.
5.	40	2 mos.	Yes	Radical	Yes	Died—2 yrs.
6.	50	1 mo.	Yes	Radical	Yes	Recurrence—1 yr.
7.	62	1 mo.	Yes	Radical	Yes	Unknown

CONCLUSIONS

From the clinical point of view there appear to be two groups of cases in which nipple changes characteristic of Paget's disease are noted: (1) Those presenting an eczema of long standing, which may or may not be associated with a definite tumor in the breast, and in whom the prognosis is good with early surgical treatment; (2) those who, from the first, apparently have a carcinoma of the breast with secondary invasion of the nipple and in whom the prognosis is poor. Metastasis occurs in both groups, more frequently in the second than in the first.

The close relationship between chronic eczematoid lesions of the nipple and carcinoma of the breast makes it imperative that early and adequate biopsy be made of every chronic nipple lesion. If a diagnosis of Paget's disease is made, regardless of whether or not a definite tumor can be demonstrated in the breast, the patient should be subjected to a radical mastectomy.

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