

The present state of our knowledge respecting the connection between eczema and an affection resembling eczema of the nipple, and a malignant disease of the breast / by Walter F. Atlee.

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ARTICLE XVII.

THE PRESENT STATE OF OUR KNOWLEDGE RESPECTING THE CONNECTION BETWEEN ECZEMA AND AN AFFECTION RESEMBLING ECZEMA OF THE NIPPLE, AND A MALIGNANT DISEASE OF THE BREAST. By WALTER F. ATLEE, A.M., M.D., of Philadelphia.

IN the *St. Bartholomew's Hospital Reports*, for 1874, is the often referred to paper of Sir James Paget, entitled "On Disease of the Mammary Areola preceding Cancer of the Mammary Gland." The whole paper is very little over two pages in length. He says:—

"I believe it has not yet been published that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus cancer in the mammary gland. I have seen about fifteen cases in which this has happened, and the events were in all of them so similar that one description may suffice.

"The patients were all women, varying in age from forty to sixty or more years, having in common nothing remarkable but their disease. In all of them 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 nearly the whole thickness of the epidermis were removed; like the surface of very acute diffuse eczema, or like that of an acute balanitis.

"From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish, viscid exudation. The sensations were commonly tingling, itching, and burning, but the malady was never attended by disturbance of the general health. I have not seen this form of eruption extend beyond the areola, and only once have seen it pass into a deeper ulceration of the skin after the manner of a rodent ulcer.

"In some of the cases the eruption has presented the characters of an ordinary chronic eczema, with minute vesications, succeeded by soft, moist, yellowish scabs or scales, and constant viscid exudation. In some it has been like psoriasis, dry, with a few white scales slowly desquamating; and in both these forms, especially in the psoriasis, I have seen the eruption spreading beyond the areola in widening circles, or, with scattered blotches of redness, covering nearly the whole breast.

"I am not aware that in any of the cases which I have seen the eruption was different from what may be described as long persistent eczema, or psoriasis, or by some other name, in treatises on diseases of the skin; and I believe that such cases sometimes occur on the breast, and after many months' duration are cured, or pass by, and are not followed by any other disease. But it has happened that 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 one year*. The eruption has resisted all the treatment, both local and general, that has been used, and has continued even after the affected part of the skin has been involved in the cancerous disease.

"The formation of 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 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 acute, some chronic, the majority following an average course, and all tending to the same end; recurring if removed, affecting lymph-glands and distant parts, showing nothing which might not be written in the ordinary history of cancer of the breast.

"The single noteworthy fact found in all these cases is that which I have stated in the first sentence, and I think it deserves careful study. For the

sequence of cancer after the chronic skin-disease is so frequent that it may be suspected of being a consequence, and must be always feared, and may be sometimes almost certainly foretold."

Paget believes that a nearly similar sequence of events may be observed in other parts. A persistent rawness of the glans penis, like a long-enduring balanitis, has been often followed after more than a year's duration by cancer of the substance of the glans. A chronic soreness or irritation (of whatever kind) on the surface of the lower lip often long precedes cancer in its substance, and superficial syphilitic diseases of the tongue are frequently followed, and not superseded, by cancers which do not always appear to commence in a diseased part of the tongue. For an explanation of these cases it is suggested that a superficial disease induces in the structures beneath it, in the course of many months, such degeneracy as makes them apt to become the seats of cancer; and that this is chiefly likely to be observed in the cases of those structures which appear to be, naturally, most liable to cancer, as the mammary gland, the tongue, and the lower lip. In other words, an adjacent disturbance of nutrition may hasten, and make prematurely sufficient, the degeneracy of parts which may come naturally in old age, and make them apt for cancer.

The object of this paper is set forth as concisely and as clearly as it is possible to do. It is most certainly to call attention to the fact that in a number of cases, some fifteen in all, in women of forty years of age and upwards—at the time they are most apt for cancer—after the skin of the nipple and areola had been diseased for some time—in none was it for longer than two years, and in only one did the affection pass into a deep ulceration after the manner of a rodent ulcer; scirrhus cancer followed in the mammary gland. And the fact is called attention to because the sequence of cancer after chronic skin-disease is so frequent that it may be suspected of being a consequence.

Since the appearance of this paper two papers have been published in *The American Journal of the Medical Sciences* having reference to it: one in the July number of 1883, entitled, "Two Cases of Paget's Disease of the Nipple;" the other in the January number of the present year, also relating two cases of disease, with the title, "Paget's Disease or Malignant Papillary Dermatitis (Thin)." Of these four cases, it is difficult to reconcile the description given with the symptoms so lucidly described by Paget. In one the disease of the nipple had existed for ten years, and no evidence of cancer was yet seen in the breast. In the other the disease of the nipple had begun six years before, and in this, it is said, the breast was in places distinctly lumpy, hard, and even knotted, feeling like an ordinary scirrhus in the early stage. This was a recent development, according to the patient. In the other paper, one case died of an affection in no way due to the disease in question some twelve years after it began, and there is nothing to show that the mammary gland had then become carcinoma-

tous. In the second case the disease of the nipples had existed more than three years, and yet nothing had shown itself in the mamma.

Now I cannot grant these cases to be those to which Paget calls attention, though one of the writers considers his as "well-marked typical cases of the disease he has described."

"The single noteworthy fact" in his cases, to use Paget's words, "is that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus cancer in the mammary gland." In none of these cases, though of so long standing, are we at all sure that this had occurred. In all of Paget's cases, it did before two years had elapsed, and it was because it did, and for no other reason, that he called attention to these cases. It is not as cases of obstinate sore nipples that he speaks of them, but as cases where cancer was a sequence to and may be a consequence of the sore nipple. The papers are valuable, nevertheless, as the authors, who are skilled clinical dermatologists, point out some distinguishing marks between the intractable disease they describe and ordinary eczema. The itching was insignificant until this disease had lasted several years, whereas in eczema it is one of the signs first noted. The outline of the lesion was sharply defined and circumscribed, and the border was slightly elevated. The colour was more brilliant and more marked. The infiltration was firm and hard, while in eczema it is soft.

In England several papers have appeared having reference to Paget's communication. One is by Henry Trentham Butlin, "On the Minute Anatomy of Two Breasts, the Areola of which had been the seat of long-standing Eczema," in vol. lix. of the *Medico-Chirurgical Transactions*. In neither of these cases, as in those just mentioned, was cancer present, although the eczema had been of long duration; but the changes found on microscopical examination, after removal of the breasts, are given, and they are very striking. The alterations in the ducts, and more especially in their epithelial elements, remind one forcibly of the early stages of proliferating intra-cystic growths.

Another paper in the ensuing volume of the *Transactions* is one entitled, "On the Minute Anatomy of Two Cases of Carcinoma of the Breast, preceded by Eczema of the Nipple and Areola." In one case the carcinoma had been noticed only for seven weeks, and had been preceded by an eczematous condition of the nipple and areola only about a fortnight. In the second case—which was one of Paget's himself—the patient had suffered from the eczema about three years, and the breast became affected three or four months before its removal. In these cases the same changes were found at the microscopical examination as those before described by Mr. Butlin, and they had extended further. The acini and ducts were more enlarged, so that they had frequently become confluent from the breaking down of the partition walls, and their contents had made their way into the surrounding tissues.

From these and the two former cases the following conclusions may, Mr. Butlin thinks, fairly be drawn :—

1. That a certain relation existed between the eczema of the nipple and areola and the carcinoma of the breast.
2. That one of the first effects of the eczema was to produce proliferation of the mucous layer of the epidermis of the parts affected.
3. That in time the epithelium lining the galactophorous ducts became affected in like manner.
4. That the disease travelling along the large ducts reached the smaller ducts and acini, which became dilated and filled with proliferating epithelium, which was, at length, so to speak, discharged into the surrounding tissues.
5. That the carcinoma thus formed was, therefore, essentially a disease of epithelium.

In vol. lxiii. of the *Transactions* of the same society is a paper by Henry Morris, entitled, "On Two Cases of Carcinoma of the Breast, preceded by so-called Eczema of the Nipple and Areola." These cases differ from any others hitherto reported, by giving the complete clinical history and the conditions found after death. In one the so-called eczema of the nipple and areola, beginning at thirty-five years of age, was followed after six years by ulceration of the nipple and carcinoma of the mamma; and after its removal the cancerous disease recurred in the periosteum, liver, and cicatrix, and caused death in about two years from the time of the operation. In the second case, after some five years, a similar disease, beginning when the patient was twenty-nine, was followed by cancer of the mamma and lymphatic glands; she died of broncho-pneumonia within three months after an operation for their removal, and cancerous infiltration was found in the lungs, bronchial glands, liver, and supra-renal capsules.

The differences between these cases of Mr. Morris and those of Sir James Paget are, that the eruption extended beyond the areola and the ulceration of the skin was somewhat deeper, that the eruption preceded the cancer some four or five years at least, and the patients attacked were younger. This paper of Mr. Morris ends as follows :—

"During the years from 1872 to 1878 inclusive, I have seen in the cancer outpatient department of the Middlesex Hospital 585 cases of cancer or imputed cancer, in 305 of which the seat of disease was the mamma. The above cases are the only instances in which eczema of the nipple and areola has been associated with cancer of the breast. Nor have I learnt from the subjects of the mammary cancer that they had previously suffered from either eczema or psoriasis of the nipple. In eighty instances there was eczema of the nipple, but no cancer."

These two cases of Mr. Morris, together with two others of a similar kind, are the subject of a paper by Dr. George Thin, published in the *British Medical Journal*, May, 1881. It is entitled "Malignant Papillary Dermatitis of the Nipple and the Breast-tumour with which it is found associated. Illustrated by specimens exhibited in the pathological museum of the British Medical Association at Cambridge." This paper is

illustrated by twenty-one wood-cuts. It shows that the peculiar condition of the nipple and areola in these four cases was not one of eczema. In eczema, even in the most severe cases, the connective tissue remains undestroyed, while in these cases the connective tissue had disappeared. The rete mucosum and the papillary layer of the skin had undergone almost complete destruction; beneath the papillary layer the tissues of the skin were undisturbed. As Dr. Duhring and Dr. Sherwell, in the papers above referred to, Dr. Thin says the disease can be distinguished clinically from eczema. In the one the margin is well defined, which is not the case in eczema, and when the tissue is grasped between the fingers there is evidence of infiltration into the papillary layer. Microscopical examination showed, moreover, that the breast tumours were not cases of ordinary scirrhus or parenchymatous cancer. In these the terminal vesicles of the acini, after they begin to enlarge, rapidly lose their symmetry, and offshoots pierce the connective tissue in all directions. In the tumours examined, the tendency was to regular symmetrical growth on the circumference, more like what used to be called adenoma. They are duct cancers.

When an epithelial growth in the mamma takes its origin in the duct epithelium, if the development of columns and tubes is localized and encapsulated by a growth of connective tissue, the ordinary adenoma is produced; if, on the other hand, there is progressive destruction of connective tissue and continued growth, we have a duct cancer as the result. The stamp of origin in the duct epithelium is, however, always retained; and in some parts of the tissue round-cell masses, with columnar epithelium, will be found, making the radical distinction between this kind of tumour and scirrhus or parenchymatous cancer or cancer developed from the secreting epithelia of the acini.

The present state of our knowledge, the result of the investigations prompted by the paper of Sir James Paget, may, I take it, be stated as this: A disease is met with in the nipple and areola, resembling eczema, but capable of being clinically distinguished, and under the microscope showing distinguishing appearances, that extends into the lactiferous tubes and causes duct cancer. Moreover, in some cases the cancerous disease becomes general throughout the body.

We do not yet know, however, whether this disease is the one to which Paget called attention. His cases may, indeed, have been cases not to be distinguished from true eczema, followed by breast trouble, without direct and continuous extension through the lactiferous tubes. He says expressly, that *always a clear interval of apparently healthy tissue* existed. We do know that, in some cases, carcinoma is derived from the endothelium of the lymphatics. We have all seen, for example, after a scaly affection of the lower lip, undoubted malignant disease of the lymphatic submaxillary glands, which we were sure was not only a sequence, but a consequence.

I would call attention to the fact that before the paper of Sir James Paget, attention has been directed to this connection between affections of the nipple and malignant disease of the breast by another most eminent surgeon, and that such connection has been published. Some twenty years before the publication of Paget's paper, a clinical lecture, in which this is referred to, was delivered by Nélaton; this was published in my *Clinical Lectures on Surgery*, by M. Nélaton, published in 1855. It is as follows:—

“November, 1852. A woman, forty-five years of age, with a tumour of the mammary gland, of which she gave the following history. Six or eight months before her entrance she commenced to suffer at the extremity of the nipple; there was smarting, the epidermis disappeared, small blisters formed; in short, there was eczema of the nipple. This ulceration, at first superficial, extended and covered the whole nipple, and, after some time, the breast became hard.

“When she came into the wards there was induration of the mammary gland, the nipple was not retracted, and the gland itself was perfectly movable, both as respects the skin and the subjacent parts; and yet the tumour seemed to be very near the skin, a condition favourable to the formation of adhesions. When the pectoral muscle was made to contract, the tumour could still be moved perfectly well. The tumour, however, was very hard and lumpy; the hardness was cartilaginous, and it extended throughout the whole mass. The ganglions in the axilla were hard and enlarged, they were not painful to the touch.

“The first idea in regard to this tumour was that it was cancerous, and yet the usual circumstances did not exist. The retraction of the nipple was wanting, and also there were not adhesions with the skin, in spite of the existence of circumstances favourable to their formation. Since he had been in practice M. Nélaton said he had never seen a case of cancer without one or other of these things. He asked himself *if the affection had not arisen from the ulceration on the nipple* as an affection of the testicle follows an affection of the urethra, so this glandular affection might follow that of the nipple. As to the glands in the armpit, they are often seen everywhere where there is an inflammatory action. The question was still too new to be answered, and M. Nélaton thought it to be his duty to cut out the tumour; if not a cancer, so much the better.

“Upon examination after its removal, M. Nélaton said the tumour was evidently a cancer, in spite of the absence of signs of which he spoke. The mass was very hard, and in the galactiferous ducts was a gray matter; the tumour, he said, was evidently scirrhus, and the ducts were also affected; the glands also presented evident marks of degeneration. To explain the absence of adhesions to the skin something was found, the cancerous degeneration was deeply seated, reposing on the pectoral muscles, and *there was a portion remaining healthy*, towards the surface. No microscopical examination, so far as I know of, was made of this tumour. This patient got well without any bad symptom, and she went out with the wound entirely closed, but M. Nélaton said a relapse was probable.”