

I have had two cases of cancer developing on lupus erythematosus scars, and have seen instances of a similar malignant development in the cicatrices of syphilitic ulcers. I have not seen a cancer develop on a primary chancre, though such have been described. The scars of burns, varicose ulcers, cellulitis, &c., may also become malignant. In every case which I have had examined the growth has been of the squamous type.

*Psoriasis, &c.*—Whitfield and Gray have described cases of rodent ulcer developing on psoriasis, but it must be remembered that in most cases of old psoriasis there has been prolonged treatment by arsenic, and this may be a factor in the malignant development.

*Multiple superficial carcinomata* are not infrequent. The majority of the cases are of the basal-celled variety, the lesions having the character of the superficial cicatrizing rodent ulcer. There is, however, a type which some authors have called "Pagetoid," from a superficial resemblance to Paget's disease of the nipple, but this is distinguished by a narrow, raised, smooth margin, as shown in the water-colour drawing exhibited. A type occurring on the face in young subjects, closely simulating lupus erythematosus, has been recently demonstrated by Dr. O'Donovan. In this the lesions are squamous carcinomata, with a very low malignancy. Here, again, a cancerous development on lupus erythematosus might be suggested, but careful examination has shown that the lesions are malignant *ab initio*.

*Bowen's dermatosis* demands attention. Bowen described a pre-cancerous dermatosis, occurring in late adult life, characterized by chronic papular lesions covered with a horny crust. These spread and form nodular swellings which may become grouped or confluent. Under the crust is a red, oozing, slightly papillomatous surface. Cancerous degeneration has been observed by Bowen and Darier.

Paget's disease may affect other parts than the nipple. I have seen it on the glans penis and about the umbilicus. I look upon it as malignant *ab initio*.

[The address was illustrated by numerous photographs and water-colour drawings, which included representations of cases of cancer following irritation by a wedding-ring, the repeated application of heat in the case of a baker, &c.]

Sir G. LENTHAL CHEATLE (President).

#### THE PRE-CARCINOMATOUS STATE IN THE BREAST.

There is a sequence of the events concerned in epithelial hyperplasia of the breast, and it corresponds exactly to the sequence of events observed in the skin of mice and men after the application of tar.

I believe that the forms of epithelial hyperplasia of the breast are either directly or indirectly concerned in the carcinoma problem, but I also believe there is only one of them that can be described as the actual pre-cancerous state. Changes that occur before the latter certainly lead up to it, and all of them, so far as concerns tissue, are distantly connected with the pre-cancerous and carcinomatous states.

The states preceding the pre-cancerous state are two types of desquamative hyperplasia, one of which is far more important than the other. The first and less important type is a generalized collection in terminal ducts and acini of small desiccated, irregularly-shaped, badly-staining cells. It may exist for years in the breast, it causes continuous pain, and cysts rarely, if at all, develop from this form. This type sometimes occurs in ordinary fibro-adenomata that do not arise from the intra-elastica.

The second, and by far the more important type of desquamative epithelial hyperplasia, also affects the terminal ducts and acini, but is never so generalized as the first type I have described. The epithelial cells lining the terminal ducts and acini become elongated and feathery in appearance—a process which, in the ducts, leads to a collection of colostrum-like cells that can be seen arising in all stages of formation

from the feathery cells of the ducts. When larger ducts are implicated, then the colostrum-like cells form in the duct epithelium which does not here become elongated or feathery in appearance. This second type of desquamative epithelial hyperplasia is the great factor in the formation of duct and acinous cysts.

A more important type of epithelial hyperplasia that is not desquamative occurs; to distinguish it from the desquamative type, I term it dysgenetic epithelial hyperplasia.

Dysgenetic epithelial hyperplasia also affects the terminal ducts and acini. In the ducts and acini the epithelial hyperplasia may be papillomatous, sessile (that is to say, without any fibrous tissue elements), or a mixture of the two. In the acini, the acinous papillomata possess very fine fibrillous stalks. The individual cells in dysgenetic epithelial hyperplasia may be present without marked signs of active division; their nuclei, size and shape are fairly regular. On the other hand, their shapes may be irregular, mitoses frequent, and marked nuclear hyperchromatosis may be present. Although all the last three cell changes may be seen in ducts and acini that are completely or partially filled by the actively dividing cells, yet all of them are contained within normal boundaries. I regard this stage as malignant and pre-carcinomatous; it cannot be said to be carcinoma, because there is no invasion of outside tissues. This pre-carcinomatous stage may, I believe, atrophy and disappear, but if it progresses it becomes part of the process of carcinoma, and can be observed in the centre of epithelial cells which have invaded the connective tissue. Hence, although it is impossible to describe a state of dysgenetic epithelial hyperplasia that must inevitably end in carcinoma, it is possible to describe one which, should it progress, must inevitably end in carcinoma. That is as near as one can get to undoubted carcinoma.

#### Mr. W. SAMPSON HANDLEY

said that in considering the pre-cancerous condition attention must not be focused exclusively upon the epithelial changes. The work of Bonney had shown that carcinoma was always preceded by long-standing, chronic, inflammatory changes in the immediately subjacent connective tissue, where collections of lymphocytes and plasma cells were invariably found. The lapse of time between the onset of these changes and the development of a cancer was a long one, and might roughly be stated as being from twenty to thirty years in those forms of cancer—such as lupus carcinoma, tar carcinoma, and carcinoma of the tongue following syphilis—where it was possible to estimate it with some approach to accuracy.

Breast cancer appeared to be no exception to the rule that carcinoma was preceded by a chronic inflammation of the connective tissue. In his (the speaker's) opinion these changes were conveniently and rightly described under the name of chronic mastitis. It was significant that both cancer and chronic mastitis showed a strong preference for the same region of the breast, namely, the upper and outer quadrant. Simple hypertrophic mastitis and early carcinoma with infiltration might often be seen in the same microscopic field. He (the speaker) acknowledged as fully as anyone the importance of the President's admirable work on the epithelial changes which preceded cancer of the breast, but those changes only constituted one chapter of the story. An equally important and earlier chapter related to the precursory changes in the connective tissue.

He (Mr. Handley) desired to draw particular attention to a factor which was very frequent, and perhaps constant, in the ætiology of carcinoma, namely, the pre-existence of chronic lymphatic obstruction in the region where the carcinoma began. This factor was certainly constant in lupus carcinoma, for lupus was essentially a destructive tuberculous lymphangitis. Syphilis, too, so often a precursor of mouth cancer, was essentially an infection of the lymphatic system and a cause of lymphatic