cases of carcinoma-in-situ treated by cone biopsy, 6 out of 49 subsequently developed carcinoma-in-situ or a positive smear. In those treated by amputation of the cervix 3 out of 54 developed carcinoma-in-situ and 1 invasive carcinoma. After hysterectomy 2 out of 270 developed carcinoma-in-situ, 1 invasive cancer of the vagina, and 1 invasive cancer of the vulva. After extended hysterectomy 3 out of 82 developed carcinoma-in-situ and 1 invasive cancer of the vagina.

In microcarcinoma 4 cases of extended hysterectomy had no later abnormalities, 16 cases of hysterectomy had one subsequent carcinoma-in-situ, and 2 cases of amputation of the cervix showed 1 case of carcinoma-in-situ later.

For 519 women with carcinoma-in-situ and microcarcinoma there were 2 deaths, 1 from later carcinoma of the cervix and 1 from treatment by hysterectomy followed by a pulmonary embolus. Hysterectomy carries the least risk of recurrence or recrudescence of some lesion in the vagina at 1·1%. For cone biopsy and amputation of the cervix the rate is 3%. Extended hysterectomy shows a rate of 5%, and the morbidity after operation was higher than in total hysterectomy.

Despite some imperfections, this survey suggests that gynaecologists who do cone biopsies or amputations of the cervix for good clinical reasons should excise a fairly large amount of the cervix and follow up their cases carefully. Those who perform hysterectomy seem to be on the safest ground, and they must ask themselves whether prolonged follow-up with its concomitant anxiety is justified for a 1·1% recurrence and recrudescence rate of carcinoma-in-situ. And there really appears to be no case at all for extended hysterectomy, even when there is proved microinvasion.

Two cases of carcinoma-in-situ of the vulva, and one of invasive cancer of the vulva in this cervical series, suggest once more the possibility of a "field change" in various epithelia in women of "cancer diathesis". The results of treatment suggest that the biology of unstable epithelia[2] may be more important in determining outcome than macrocsopic surgical intervention in a disease at the microscopical level.

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The Thyroid and Breast Cancer

Is there a relationship between thyroid dysfunction and carcinoma of the breast?[1-6] The problem has been recently reappraised by A. R. Moossa and his colleagues.[7]

They studied 71 patients with both breast cancer and thyroid disease, including patients with hyperthyroidism, non-toxic goitre, and primary hypothyroidism. All except one patient were clinically and biochemically euthyroid at the time of discovery of the breast cancer. Fifty-one of these patients have been followed up for 10 years, and their survival rate has been compared to that in a control group matched for age and staging of the breast cancer. The figures show that, though the incidence of thyroid disease in the patients with breast cancer was similar to that found in a normal population, those patients with breast cancer and a history of thyroid disease had lower average survival rates at both 5 and 10 years than the controls. This was true whether the patients had either treated hyperthyroidism or non-toxic goitres.

Thyroid disease could affect breast function in several ways. Patients with primary hypothyroidism may present with galactorrhoea and have high circulating levels of prolactin.[8] It is now known that thyrotrophin-releasing hormone releases prolactin in addition to thyroid-stimulating hormone.[9] H. Salih and his co-workers have recently shown a dependence on prolactin of 32% of breast cancers cultured in vitro.[10]

B. A. Eskin has investigated the role of iodine deficiency in the genesis of breast cancer.[11] Epidemiological surveys in the United States have shown a striking similarity between the areas where goitre is endemic and the areas with a high mortality from breast cancer.[4] Animal experiments have established a relationship between iodine deficiency and both breast dysplasia and neoplasia.[12 13] And further experiments suggested that thyroid-stimulating hormone is important in the induction of breast dysplasia in both iodine deficiency and primary hypothyroidism.[11] Little is at present known about the role of this hormone in the genesis or maintenance of human breast cancer. High levels of it could be suppressed by treatment with thyroxine. But this treatment did not improve the survival of patients with advanced breast cancer[14 15] or prevent metastatic spread.[16]

Changes in the metabolism of oestrogens and androgens or the plasma level of their binding protein, sex-hormone-binding globulin, induced by alterations in thyroid function could throw light on the effect of thyroid disease on breast cancer. Thyroid hormones are known to affect enzyme systems concerned with oestrogen and androgen metabolism.[17 18] For example, when levels of thyroid hormone are raised, the conversion of oestradiol to 2-methoxyoestrone is increased, as is the metabolism of testosterone to androsterone. In patients with thyrotoxicosis and after the administration of thyroid hormone there is a large rise in the concentration of sex-hormone-binding globulin.[19] Because of the different affinities of this binding protein for testosterone and oestradiol a rise in the level of this globulin results in a greater fall in the plasma level of unbound testosterone than of unbound oestradiol.[20] This may be the explanation for the development of gynaecomastia in some patients with thyrotoxicosis. At present the importance of these various factors in the development of breast cancer is unknown, but the solution of the problems they pose may have important implications for the treatment of the disease.

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