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VI.3 DNA Content in Tamoxifen-induced Endometrial Carcinoma

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DNA measurements and histopathological evaluation were performed in 17 patients treated with adjuvant tamoxifen in early breast cancer and who developed endometrial carcinoma during or after tamoxifen therapy. The tumours were exclusively characterised by low grade malignancy and euploid DNA pattern except for two cases. The hazards of giving long-term tamoxifen thus seem to be low.
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TAMOXIFEN IS the most commonly used drug in breast cancer treatment with a well documented effect in clinical studies on recurrence-free interval. Several reports [1–3] have appeared in the last few years on tamoxifen as a risk factor for polyps, hyperplasia and endometrial cancer. Tamoxifen is considered to have an oestrogenic property and is thus implicated in the development of endometrial carcinoma. Recently, DNA-adducts were found in human endometrium using high performance liquid chromatography [4].

The prediction of prognosis in the individual patient is essential in medical practice. Significant methods are available to distinguish highly malignant types of endometrial carcinomas from less biologically aggressive ones. Measurement of nuclear DNA content adds information which is additional and superior to clinical and morphological parameters [5–7].

17 patients with early breast cancer, who were included in the Stockholm adjuvant tamoxifen trial initiated in 1976, and who developed endometrial cancer during or after tamoxifen treatment were studied. The patients had a FIGO stage I in 14 cases, 2 stage II and 1 stage IV. The ages ranged from 54–73 years.

DNA measurements were performed on 4 μ sections of the paraffin blocks from curettings of the 17 tamoxifen-treated patients. The sections were stained with Feulgen and analysed in a TV-based image system (Ahren's, Bargteheide, Germany). The optical density of 100 nuclei was obtained at 546 nm for each specimen.

Histograms were considered near-diploid in 10 cases, tetraploid in 5 cases and aneuploid in 2. The histopathological examination revealed 8 grade 1 and 8 grade 2 tumours. One case could not be evaluated because of scarce material. The subtypes were adenocarcinomas, 13 cases, adenoacanthomas, 3 cases, mixed mesodermal carcinoma, 1 case.

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Cancers with euploid DNA pattern are considered as being of low potential malignancy grade with favourable prognosis [5–7]. Sixty per cent of endometrial carcinomas are adenocarcinomas and usually have good prognosis. About 25% have squamous differentiation and 15% are adenacanthomas, which are considered low malignant [8]. This study based on retrospective material with a careful follow-up showed 15 cases with hormone-dependent carcinoma all of grades 1 and 2. One case could not be graded. Only one highly malignant tumour was identified. 2 cases showed aneuploid DNA pattern, the mixed mesodermal tumour and one adenocarcinoma, of which the patient also died.

The undoubted oncogenic effect of tamoxifen on the endometrial mucosa obviously leads to tumours with low malignancy according to histopathology and DNA content.

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