REGISTRATION OF TUMOURS WITH MORPHOLOGICAL HETEROGENICITY: AGE-DISTRIBUTION OF THYROID CANCER IN DENMARK 1978-85.
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Registration of morphological heterogene tumours creates technical problems in the data collection as well as in the analysis. In the Danish Cancer Registry tumours have been coded according to the ICD-O since 1978. This classification includes a few combination codes, but most of the combined morphologies are coded with the higher number of the components. One of the combination codes is "Papillary and follicular adenocarcinoma" (M-8340/3). We have shown earlier that papillary carcinoma and follicular carcinoma of the thyroid have different agedistribution of the mixed type resembled the one or the other. In the Registry, 198 thyroid cancers were coded as follicular, 275 as papillary and 52 as mixed papillary and follicular. A test on agedistribution of the 3 subtypes showed a highly significant difference between follicular and mixed type ($p < 0.003$), whereas the resemblance between papillary and mixed type was so strong that a test for difference between the two distributions produced $p = 0.97$. It is concluded that in this example of morphological heterogenicity, the agedistribution and thus maybe some of the etiological factors could be assigned to one of the components.

HETEROGENEITY OF ESTROGEN RECEPTOR CONTENT IN PRIMARY BREAST CANCERS AND THEIR METASTASES.
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Immunohistochemical antibody techniques for detection of estrogen receptors (ER) were applied to formalin fixed, paraffin embedded sections from 62 primary breast cancers, metastases of the regional lymph nodes (29 cases), the bone marrow (43 cases), and the liver (20 cases). 40% of the primary tumors and 31% of the regional lymph node metastases were ER positive; less than 20% of liver and bone metastases were ER positive. The ER status of regional lymph node metastases was concordant with that of the primary tumor in 90% of the cases. The concordance rate was 75% for liver metastases and 58% for bone metastases. Patients with ER positive tumors had recurrence more often in bone; ER negative tumors recurred more often in the liver. The survival after recurrence (SAR) was related to the ER status of both the primary tumor and the lymph node metastases. The SAR was not associated with the ER status of bone marrow carcinosis or liver metastases. Regression analyses showed that ER status of the primary tumor was the most important independent prognostic factor when compared to other clinical, pathoanatomical and biochemical features. The study supports the hypothesis that tumor cell clones with different ER content are selected and adapted to grow in various anatomical sites.

SUBOPTIMAL CHEMOTHERAPY MAY BE BENEFICIAL IN THE TREATMENT OF HETEROGENEOUS TUMORS
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In the nude mouse model, it was shown that when a mixed tumor of human small cell carcinoma of the lung consists of a dominating subpopulation (592) sensitive to BCNU, and a dominated and silent (undetectable) subpopulation (NYH) which is resistant to BCNU, then treatment will kill the dominating cells only, resulting in a primary tumor response followed by early relapse of the resistant cells (Eur.J.Cancer Clin.Oncol.24:1550,1988). In this study, mixed tumors of the sensitive (592) and resistant (NYH) cells in nude mice were given suboptimal BCNU treatment, resulting in a minor reduction in tumor size without complete eradication of the sensitive and dominating subpopulation. At regrowth of the tumors, still only the sensitive 592 tumor could be detected by flow cytometric DNA analysis by which the two cell lines were distinguishable. Not until a subsequent optimal BCNU treatment had caused complete disappearance of the 592 cells, relapse of the resistant subpopulation (NYH) took place. Thus, it is concluded that suboptimal chemotherapy was beneficial in terms of temporary growth control of this tumor.

THE HETEROGENEITY OF SMALL CELL CARCINOMA OF THE LUNG (SCCL) IN SENSITIVITY TO CYTOSTATIC DRUGS REFLECTED IN A PANEL OF CELL LINES.
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SCCL has been shown to be heterogeneous, and treatment failure is caused by selection and overgrowth of resistant subpopulations. A large number of tumor cell lines have been established from patients with SCCL. If these cell lines reflect the heterogeneity in the parent tumor the patterns in sensitivity to different cytostatic drugs may reflect the range of sensitivities in the disease and enable selection of drugs and drug combinations for future treatment protocols. Using in vitro sensitivity assessments we have shown that SCCL cell lines established from treated and untreated patients vary in sensitivity to adriamycin, daunorubicin and mitoxantrone with a factor of five. The sensitivity to