The *European Journal of Cancer* is happy to invite cancer registries to submit short synopses of their recent data for publication. The articles should be in a format similar to that of the article contained in this issue (Levi *et al.*, p. 207). In particular, a short description of the registry and registration practice should be followed by pointers to recent reports from the registry and a brief description of the most important findings either regarding cancer levels, cancer trends or cancer survival. Registries should endeavour to provide a figure similar to Fig. 1 of Levi *et al.* containing annual rates age-standardised to the World Standard Population [4] together with the numbers of cases that these are based on.

Descriptive epidemiology has provided important information in the past which has led to the formulation of the environmental theory of carcinogenesis and it is currently thought that upwards of 80 and perhaps 90% of human cancers may be due to environmental factors, defining "environment" in its broadest sense to include a wide variety of aspects of lifestyle [5, 6]. The development of cancer registration in the recent past has an important role to play in refinement of the influence of environmental ("lifestyle") factors on cancer risk. Thus, it is important that cancer registries, one of the major contributors to descriptive epidemiology, have the opportunity to present their data to a wider audience than can generally be reached by their own reports. Thus, this journal is happy to provide a forum for descriptive epidemiology whether as described above or in general terms by publishing longer articles on the subject.

P. Boyle
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Establishment of a European Registry for Familial Ovarian Cancer

BACKGROUND

EPIDEMIOLOGICAL STUDIES have provided little data useful for the identification of women at risk of developing ovarian cancer. Furthermore, there are no cheap, reliable screens, and this malignancy is almost invariably diagnosed at an advanced stage. During the past decade, genetic evidence of the aetiology of ovarian cancer has rapidly accrued. The apparent increase in the incidence of genetically determined ovarian cancer may be due to improved data collection. We need to be able to identify risk factors and markers for early detection and control.

Three carcinoma-prone conditions have been recognised in which malignant epithelial ovarian neoplasm show significant familial concentration: (1) site-specific ovarian carcinoma, where familial risk is restricted to ovarian cancer; (2) breast/ovarian cancer syndrome, where carcinoma of the breast is associated with ovarian carcinoma; and (3) cancer family syndrome (Lynch syndrome II), consisting of hereditary non-polyposis colorectal cancer with proximal colonic cancer predominance, associated with endometrial and/or ovarian carcinoma [1]. Families with two or more first-degree relatives affected by ovarian cancer have been conventionally considered suitable for epidemiological and genetic analyses.

Studies on such families at high risk for ovarian carcinoma showed that the hereditary pattern is consistent with the segregation of an autosomal dominant mutation with variable penetrance [1–5]. However, the data have not conclusively clarified the mode of genetic transmission. Both genetic and environmental factors, alone or in combination, could account for familial aggregation of ovarian cancer cases. However, in a subset of ovarian cancer families, genetic background plays a major role, as shown by the linear decrease in tumour incidence with lower degree of kinship. Lynch estimated that this hereditary subgroup represents 5–10% of all ovarian cancers [2]. Although the real frequency of genetically controlled ovarian cancer may be overestimated, it is clear that familial ovarian cancer should no longer be looked on as rare.

Formal genetic analysis of such kindreds has not been done systematically. Nevertheless, the available data do not show any consistent chromosomal abnormality except for *in vitro* hyperploidy associated with cancer proneness in families with hereditary single tumours, including that of the ovary [6]. Furthermore, low IgA levels and serum alpha-L-fucosidase levels have been detected in some ovarian cancer aggregates [1].

For molecular genetic studies, different research groups are trying to identify regions of the genome that are frequently rearranged in ovarian tumour samples. Once these have been characterised, the next step would be to search for predisposing mutations at these loci in high-risk families. Concurrently, a search for predisposing genetic lesions could be done by linkage

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analysis in ovarian cancer families. For this purpose, it must be stressed that the number and size of such families should be adequate, and a common effort in their identification is desirable. Since recent molecular genetic studies have shown that non-hereditary and hereditary forms of the same tumour may share the same genetic pathway of development—such as in retinoblastoma and colon cancer—these results would be relevant to ovarian cancer in general.

Genetic counselling in individuals from such kindreds is obviously of great importance for surveillance, management and an adequate approach to psychological problems. Nevertheless, the assessment of the expected risk for ovarian cancer in "high-risk" family members remains difficult, even though their probability of developing ovarian carcinoma has been calculated as 11–18 times higher than that in the average population [7, 8]. Sisters and daughters of probands in families with a history of ovarian cancer have approximately a 50% chance of developing the disease. This compares with a 1.4% chance in women without this family history.

A US Familial Ovarian Cancer Registry (recently re-named the Gilda Radner Familial Ovarian Cancer Registry to honour the comedienne who died from ovarian cancer) was established in 1981 at the Roswell Park Memorial Hospital, Buffalo, for the accession of families that contain two or more first-degree relatives with ovarian cancer. By May 1990, 435 families had been registered, accounting for more than 1000 patients with ovarian cancer. The preliminary analysis of data from the US registry showed that characteristics such as number of pregnancies, parity, religion, histotype and FIGO stage are consistent with those of ovarian cancer patients in general. However, there appears to be a trend towards more poorly differentiated adenocarcinomas among familial cases than among cases of ovarian cancer in general [9, 10]. Interestingly, in mother/daughter relationships (136 cases among the first 298 families accessioned) the disease developed by the daughters occurred at a significantly younger age than in their mothers (mean 60.3 vs. 47.7 years, respectively; $P < 0.001$) and in the ovarian cancer patients accessioned into the SEER data from 1973 to 1986 (mean age 59.9; $P < 0.001$) [10]. The earlier onset of the disease in successive generations adds new evidence that familial ovarian cancer can be the result of gene-initiated events. Furthermore, other investigators found that a history of breast cancer was significantly more frequent among probands and their first-degree relatives; the probands showed a nearly sixfold excess over patients with sporadic cancer [11]. This finding adds new strength to previous evidence from case-control studies that ovarian and breast cancer share aetiological and/or pathogenetic mechanisms, some of which could be related to genetic predisposition [12, 13].

THE EUROPEAN REGISTRY

Overall, data on familial ovarian cancer are still insufficient—most being retrospectively collected—and a larger prospective recruitment of ovarian cancer families is needed for analysis of epidemiology and pedigree. Moreover, cases from Europe have been only occasionally reported, and, if sufficient suitable families could be collected, a bank of biological samples from family members would be extremely important for marker and molecular genetic studies.

In this respect, a European Registry on Familial Ovarian Cancer was established in 1989 under the auspices of the EORTC Gynecological Cancer Cooperative Group and in collaboration with the US Registry directed by Dr M.S. Piver, with the following purposes: (1) identification and registration of families prone to ovarian cancer (families with at least two first-degree relatives affected by ovarian cancer); (2) recording of detailed epidemiological characteristics of familial ovarian cancer; (3) establishment of a bank of blood and tumour samples from family members on the registry; (4) study of genetic transmission pattern and identification and registration of high-risk subjects; (5) counselling and surveillance of high-risk subjects; and (6) exchange of data with the US Registry.

Data are elicited on social background, personal and obstetric/gynaecological history, personal history of cancer, familial history of cancer and pedigree, and are strictly confidential. Serum and blood samples from probands and their first-degree relatives are requested for biochemical marker and molecular genetic studies. Genetic counselling is provided with a follow-up programme for high-risk subjects.

To date, about 50 European institutions, including most European cancer institutes, have been accepted to participate in the registry from the following countries: Italy, France, Germany, Belgium, Holland, Austria, Denmark, Sweden, Iceland, the USSR, Hungary, Turkey and Greece. 59 families have been registered so far. In the meantime, there is close collaboration between the registry and a joint Cancer Research Campaign/Imperial Cancer Research Fund group in the UK coordinated by Dr B. Ponder, which is doing a similar study on a national basis.

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Papers

Oestrogen and Progesterone Receptor Status in Bone Biopsy Specimens from Patients with Breast Cancer

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Of 16 breast cancer patients with histologically proven, tumour-infiltrating biopsy specimens most had low ER and PR values; the ER and PR contents varied between 0 and 135 and 0 and 44 fmol/mg protein, respectively. With the conventional clinical threshold of 10 fmol/mg protein, 8 specimens (50%) were ER−PR−, 4 (25%) ER−PR+, 3 (19%) ER+PR+ and 1 (6%) ER+PR−. ER levels were significantly lower in the tumoral bone lesion compared with the primary tumour. For 15 patients with negative biopsies and without endocrine treatment, ER and PR concentrations were quantifiable (2 fmol/mg protein or more) in 9 (60%) and 11 cases (73%), respectively. 8 of 9 patients over 55 (89%) were ER+ (2 fmol/mg protein or more). Conversely, for patients under 55, 1 of 6 (17%) was ER+ ($P < 0.001$). Results for PR were similar. These data strongly suggest that steroid receptors are present in healthy bone tissue.
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INTRODUCTION

THE RESPONSE rate to endocrine therapy in breast cancer is higher for oestradiol (ER) and progesterone receptor (PR) positive tumours than for receptor negative tumours [1, 2]. Analysis of the response rates in 51 clinical trials in which tamoxifen was the major endocrine treatment revealed that bone metastases are among the least responsive sites [3]. This can be partly explained by the difficulty of evaluating the response of bone lesions. Moreover, the steroid receptor content tends to differ in the primary tumour and in synchronous [4, 5] and asynchronous distant sites [6–11]. Most information about ER and PR concentrations in metastatic sites concerns soft tissue or nodal metastases [4–7, 9]. Overall, the percentage of receptor positive estimations is lower in metastatic tissue than in primary tumours. Although bone metastases are one of the most frequent secondary sites of breast cancer, we are aware of only two reports on steroid receptor measurements in bone metastases of breast carcinoma [12, 13]. Furthermore, because of the limited quantity of biological material generally available from bone biopsies, only ERs were measured in these studies. We have used the micromethod we developed for measurement of both ER and PR in small tumour fragments [14] to obtain additional data on these hormone receptors in bone biopsy samples from 38 female patients.

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MATERIAL AND METHODS

The characteristics of the 38 female patients summarised in Tables 1 and 2 were obtained from the clinical records (age, TNM classification [15], ER and PR levels in primary tumours and bone biopsies, initial and palliative treatments, time between ER and PR measurement in primary tumour and bone sites, response to treatment). Bone metastasis was suspected on the basis of clinical, radiological and/or scintigraphic findings. Patients were separated into two groups: those with histologically proven tumour-infiltrating bone biopsy specimens (positive biopsies) and those with tumour-free bone biopsy specimens as proven by histological examination (negative biopsies). The