# Familial ovarian cancer. How rare is it?

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SUMMARY. This paper reports an apparently hereditary ovarian carcinoma in the authors' family. A grandmother, her daughter and five granddaughters have been affected. Three of the granddaughters were sisters. The mode of transmission appears to be autosomal dominant, with males capable of being carriers. Present methods of record-keeping make it difficult to link affected females in a family. Further studies are required to find the true incidence of familial ovarian cancer.

## Introduction

THE incidence of cancer of the ovary is steadily rising, with the highest incidence in the 55-65 age group. It is the fourth most common cause of death from cancer in British women and the commonest fatal gynaecological cancer *(British Medical Journal,* 1979). There are 15 reported familial aggregations of ovarian cancer (Liber, 1950; Lewis and Davidson, 1969; Li *et al.,* 1970; Fraumeni, 1975; Skinner *et al.,* 1977; Philipp, 1979). These are thought to be rare, although well recognized *(British Medical Journal,* 1979).

## Family history

For many years there seems to have been a dread of cancer in our family and a despairing acceptance that it is inevitable. The subject was taboo and hardly ever discussed.

In 1968 one aunt of S.A.A. and H.M. (Figure, III/3), aged 45 years, became ill with a 'gynaecological' cancer and died two years later. Subsequently, a second aunt (III/6) visited her general practitioner on several occasions, expressing anxiety about contracting a similar cancer, and was reassured repeatedly that she had no need to worry. In 1975 she was diagnosed as having cancer of the ovary and died a year later at the age of 45 years. In 1977, a third aunt (III/5), aged 47 years, presented with an advanced ovarian carcinoma and died in 1978.

At the time of the third aunt's illness we became convinced of the possibility of a family predisposition to cancer. This was confirmed for us by the report of Skinner and colleagues (1977) describing a family in which four out of seven female siblings died of ovarian cancer.

We proceeded to investigate the cause of death of as many members of the family as could be found. By means of death certificates we discovered that a cousin (III/12) had died of ovarian cancer in 1970, aged 49 years, and that a grandmother (I/1) had died in 1930, aged 60 years, of the same condition. At the same time we found that our first aunt to have died (III/3) had also suffered from cancer of the ovary. In the second generation II/1 had died of a renal tumour, II/2 had carcinoma of the large bowel, II/3 was reported as having cancer of the stomach and II/6 had died of breast cancer. Two years after our initial enquiries, histological review has shown that II/3 died of a primary cancer of the ovary, and not of the stomach as was originally reported. The remaining siblings, II/4 and II/5, died of non-malignant disease.

Our family was very helpful at this stage: members willingly provided the necessary information, and we were aware of a great sense of relief that at last something was being done. We then discussed our findings with a consultant gynaecologist, who was willing to look after the family and who encouraged us to continue our research.

Unfortunately, during this time, another cousin (III/10) had become ill with the same disease and is at present receiving treatment.

## Genetics

It appears that in this family ovarian cancer was transmitted through both males and females. Transmission through males has previously been noted only once (Li *et al.,* 1970). Genetic opinion is that the mode of transmission is autosomal dominant. The age of the affected members of the third generation was younger

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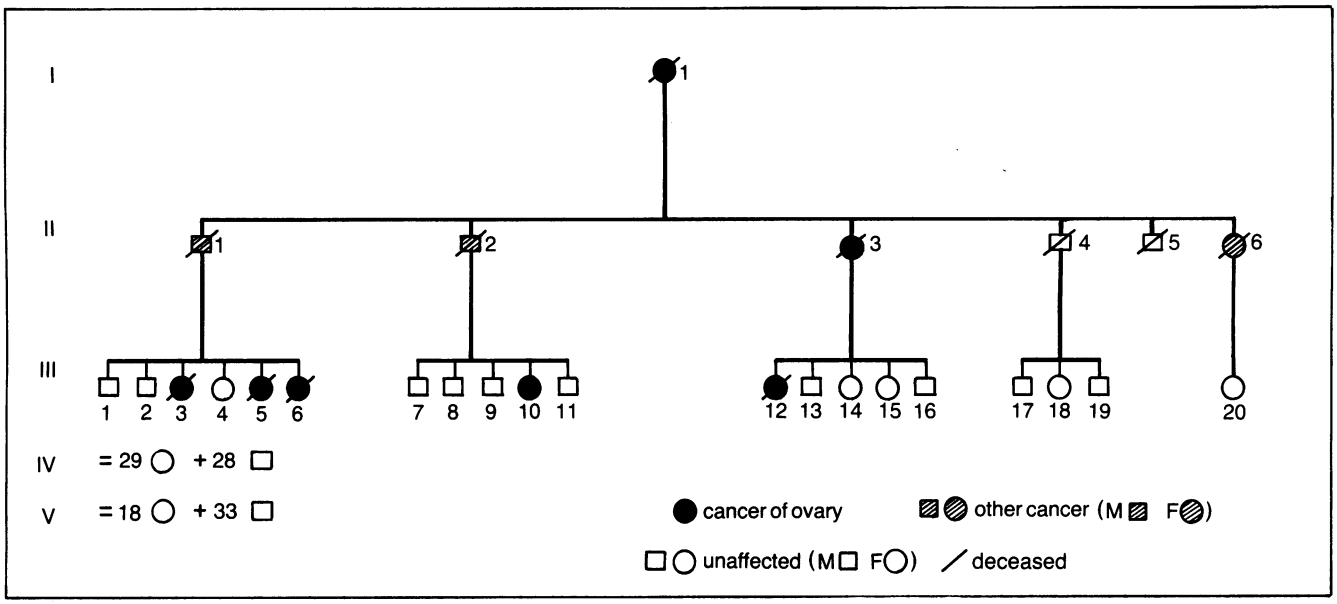


Family tree.

than the average incidence of ovarian cancer. The histology (where known) is shown in the Table.

Histology.

| Pedigree | Age at diagnosis | Survival time | Histology |
|---|---|---|---|
| I/1 | Not known | Died aged 60 years | Not known |
| II/3 | 66 years | 6 months | Papillary adenocarcinoma |
| III/3 | 45 years | 2 years | No biopsy taken at laparotomy |
| III/5 | 47 years | 1 year | Poorly differentiated adenocarcinoma |
| III/6 | 44 years | 1 year | Cytology confirmed ovarian carcinoma |
| III/12 | 49 years | 6 months | Poorly differentiated adenocarcinoma |
| III/10 | 44 years | 15 months' treatment | Poorly differentiated adenocarcinoma |

## Discussion

Ovarian carcinoma is insidious in its onset, producing non-specific symptoms which make for late diagnosis. A pelvic mass, ascites or evidence of metastases are commonly the presenting signs. Treatment offers little hope for the patient (Tobias, 1980; Barker and Pring, 1981). The median survival rate is approximately eight months from diagnosis *(British Medical Journal,* 1979). Although there is progress in treatment regimes, the screening methods available are still invasive and unreliable—ovarian biopsy or brushings; castration is the only prophylaxis. Subsequent hormone replacement therapy brings its own risks.

Since we presented the family with this information, the surviving women in the third generation have become markedly reluctant to seek medical advice, despite their awareness of the family history and their expressed fear of developing cancer. This is a well-recognized reaction (Li *et al.,* 1970).

It has been suggested for many years that families such as ours could be used to develop methods of screening which would lead to a better understanding of the aetiology of ovarian cancer (Liber, 1950; Li *et al.,* 1970; Skinner *et al.,* 1977). However, our recent experience showed that there is difficulty in linking affected females. Although III/3, III/5, III/6, III/10 and III/12 all presented to the same hospital group within eight years, there appears to be no method by which the medical staff could have been alerted to the family connections. Further, III/3 and III/12 were patients of the same practice and died in the same year. Although the women all came from the same area, it was impossible to link them because they changed their names on marriage; most moved to a different practice area. The main difficulty encountered in relating sisters with a similar disease is the fact that the maiden name is not always recorded in general practitioner records (E.C.6 & 7) and hospital inpatient record sheets. This simple piece of information is essential if family studies are to be carried out. It was only because of the medical knowledge of two members of the family that the extent of the problem was recognized. The circumstances were further obscured by ignorance of the anatomy of the female reproductive system in a traditional farming community. For example, III/3 was thought by her family to have had cervical cancer; this confusion caused a delay of several years in noting the high incidence of ovarian cancer in the family.

Is it possible that there are other families, like ours, as yet not recognized? It has been suggested by Simpson and Photopulus (1976) that "genetic factors are probably more important in the aetiology of gonadal neoplasia than generally appreciated". If so, is it also possible that presently unsuspected familial trends may be found for other malignancies? It is now 30 years since Liber (1950) suggested that "each case of ovarian cancer be the occasion of a complete family study and life-time follow-up of all relatives". There is no indication that this has been carried out. We have witnessed the suffering caused by the untimely deaths of women with maturing families, and hope that further deaths from ovarian cancer have been prevented in our family.

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## Wholesome

The National Food Survey shows that, in recent years, the purchase of brown and wholemeal bread has risen in relation to white bread. In 1978 brown and wholemeal accounted for 12 per cent of bread purchased, in 1979, 15 per cent and in 1980, 18 per cent.

Source: DHSS, 6 May 1981.