Genetic counseling: what is important to know in your clinic

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Patient expectations

It is important to establish early on in the consultation what the patient expects to derive from the consultation [1]. In cancer genetic clinics the primary patient, or proband, is often a well person who has not developed cancer, but who is concerned about their risk of developing the disease. There are a number of different situations which lead to an individual being concerned about their own individual risk. They may have a significant family history of cancer, as outlined in the section below. They may have a family history of cancer which would be assessed as not significant because there are a number of individuals in the family who have different types of cancer, which are not thought to be linked to each other, as described in more detail at the end of this article. There may be a small number of relatives with relevant cancers, but occurring at an older age or not frequently enough to be considered significant [2].

A good example of this is found in familial ovarian cancer; if there is only one close female relative with ovarian cancer in a family, then that is usually considered not significant. However, the scientific assessment of the strength of the family history may be very different from the relative’s impression of that family history. A well woman whose mother died in her fifties from ovarian cancer may well be concerned about her own risk, and may well feel that she has not been looked after properly if she feels her concerns have been dismissed. It is important to allow enough time in the out-patient clinic to take an adequate family history, and then to give a reasoned explanation for why the particular clinical circumstances do not suggest a genetic cause [3–5]. It is important to be reasonably confident of that judgment, as lack of clarity from the health professional usually results in a lack of clear understanding by the patient, and therefore continuing uncertainty, and a poor outcome to the consultation. Patients left in this position will worry that there is something sinister about that particular family, and may well feel that there is something sinister about that particular individual cancer risk. One rather unexpected finding was that many people become concerned about cancer because of circumstances involving friends, neighbors, other acquaintances and sometimes those with high publicity profiles rather than family members. A woman who has three friends who all developed breast cancer in their forties, may well be very concerned. Similarly, a lady who knows five women who have developed breast cancer, all living in a small village, may well worry that there is something sinister about that particular village which may increase her breast cancer risk. We have seen a married couple in which both the husband and the wife developed breast cancer at different times, and the husband was convinced that he had infected his wife with the cancer.

Once the patient’s expectations have been understood, it is important to offer explanations in a reasonable, sympathetic fashion, which takes account of the patient’s preconceptions and fears. Outright dismissal may be intellectually correct, but may often be seen by the patient as arrogant and inappropriate. It is not unreasonable for a woman to fear breast cancer because several of her friends have had it, even if none of them are directly related to her.

All cancer is genetic

There is a widespread apparent misconception that all cancer is genetic. Only a relatively small percentage of all cases of breast or bowel cancer are secondary to inherited genetic variation. However, all cancer cells have accumulated a number of alterations as they progress from being completely normal to
being a malignant cell, including major changes in their genetic material, as illustrated in Figure 1. All cancer cells carry somatic genetic alterations, but only a minority are secondary to inherited, and therefore germ-line genetic variants. This important point is often misunderstood by health professionals as well as the public.

Recent technological advances make it possible to assess the activity of thousands of genetic sequences simultaneously. These genetic signatures may allow the detailed characterization of the many steps involved in the multi-step pathway of carcinogenesis. As cancer cells develop more powerful metastatic potential, they continue along a pathway similar to that depicted in Figure 1. These genetic signatures may give useful prognostic information, as recently reported in breast cancer by the Amsterdam group [11–13].

In those who carry an inherited genetic mutation, all cells carry one mutated copy. When these cells become malignant one of the changes which occurs in the multi-step process is the loss of the normal copy of the gene. So tumor cells carry no normal copies of the susceptibility gene. This is illustrated in Figures 2 and 3.

There is thus a theoretical opportunity to exploit this fact by targeting treatment of tumors in those who carry a susceptibility gene. This opportunity is being tested in carriers of the breast cancer susceptibility genes BRCA1 and BRCA2. Laboratory experiments suggested that tumor cells in carriers were more sensitive to platinum compounds [14–17], and an international randomized clinical trial examining toxicity and efficacy of platinum and taxane in known gene carriers with relapsed metastatic breast cancer is now running. It is coordinated by the Cancer Research UK Cancer Trials Centre in University College London, and hopes to recruit widely from as many countries as possible across Europe and further afield [18].

**assessing family history**

Figure 4 illustrates the clinical situation in those cancers which have an inherited component. There has been a lot of publicity for the high penetrance susceptibility genes, particularly in breast cancer, but the majority of breast cancers are not secondary to inherited genetic variation. There is a clinical need to establish understandable criteria for each of the risk groups. Unfortunately the traditional labels used to denote these groups can be very misleading [19, 20]. The high-risk group will be offered genetic testing as described in subsequent articles. The moderate-risk group may be offered extra screening: either from a younger age or more frequently than normally offered to the general public. However, the largest group, representing those with a family history of cancer not considered strong enough to warrant further intervention, are not well catered for in most healthcare systems, and yet the overall burden of anxiety may well be highest in total in this group, because of the large numbers of people involved [21–23]. In an effort to provide care for this group, the UK charity Cancerbackup has developed a user friendly program which is available to the general public on the website www.cancerbackup.org.uk, called OPERA (Online Personal Education and Risk Assessment) [24]. This program is based on guidance issued by the National Institute of Health and Clinical Excellence (NICE) to the UK National Health Service [19]. This guidance is relatively specific but is similar to other guidelines which have previously been used [20, 25]. The program gathers information on the individual’s personal and family history of breast and ovarian cancer, and then derives a personal information sheet based on an analysis of the information given. This information sheet outlines the available options for the individual using the program without making any reference to the traditional label for the group, thus avoiding possible misleading reassurance caused by the ‘low-risk’ label. Considerable attention has been paid within the program to the possible triggers which would drive an individual to search for and spend time on such a program, particularly for those individuals who actually do not have a significant family history; the largest circle in Figure 4. The theoretical basis underlying the information sheet comes from the ‘Theory of Argumentation’ initially expounded by
A clinical situation which may cause particular concern to both health professionals and patients is illustrated in Figure 5. This family contains a number of cancer patients, although there is no known genetic link between the various different cancers. Patients naturally worry that there may be genetic variants which predispose to cancer in general, and that a family history as illustrated is evidence of more general cancer predisposition. There are a small number of genetic variants which predispose to several different cancer types, but these cancer patterns have been generally well described, and consist of very specific cancer types [28]. It is important to point out to patients from families like the family in Figure 5, that with our current knowledge we do not recognize the conglomeration of these different cancer types as representing a significant pattern. However, as knowledge advances it is quite possible that the position may change. For example if a gene predisposing to lung, prostate and ovarian cancer was identified, then the current knowledge we do not recognize the conglomeration of very specific cancer types [28]. It is important to point out to patients and family members that a family history of breast cancer is a significant risk factor in identifying patients who are at increased risk for breast cancer in general practice. This family contains a number of cancer patients, although there is no known genetic link between the various different cancers. Patients naturally worry that there may be genetic variants which predispose to cancer in general, and that a family history as illustrated is evidence of more general cancer predisposition. There are a small number of genetic variants which predispose to several different cancer types, but these cancer patterns have been generally well described, and consist of very specific cancer types [28]. It is important to point out to patients from families like the family in Figure 5, that with our current knowledge we do not recognize the conglomeration of these different cancer types as representing a significant pattern. However, as knowledge advances it is quite possible that the position may change. For example if a gene predisposing to lung, prostate and ovarian cancer was identified, then the family history in Figure 5 would be considered significant. As a point of good medical practice in general it is sensible to ensure that important points covered verbally in the outpatient consultation are reinforced in a personal letter sent after that consultation.

**disclosures**

No significant relationships.

**references**

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