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The Familial Cancer Program of the Vermont Cancer Center: Development of a Cancer Genetics Program in a Rural Area

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In response to many scientific discoveries linking cancer in certain families to inherited factors, the Vermont Cancer Center established the Familial Cancer Program (FCP) in December 1993. This multifaceted program combines the expertise of clinicians and researchers in many disciplines, including genetics, oncology, psychology, and molecular biology. The program's goals are identification of families in its region with excess cancer, provision of clinical services to such families, and use of research protocols when available and appropriate. This article describes the experience of setting up a familial cancer program in a rural area and discusses both successes and challenges in such an endeavor.

KEY WORDS: familial cancer; genetic counseling; cancer genetics; risk assessment; rural health care.

INTRODUCTION

The Vermont Cancer Center of the University of Vermont College of Medicine established its Familial Cancer Program (FCP) in December 1993. The FCP is a cancer risk assessment program that identifies families

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with increased risk for heritable cancer. The FCP offers clinical services, including genetic counseling, and the opportunity to participate in research protocols when available and appropriate.

The Lake Champlain Cancer Research Organization of Glens Falls, New York, a private foundation, provided start-up funding for the FCP as an exploratory project to include clinical and research activities. The program core consists of a genetic counselor, a clinical geneticist, a medical oncologist, a molecular geneticist, a clinical psychologist, a laboratory coordinator, and a program coordinator. In addition, other individuals at the University of Vermont with expertise in medical and surgical oncology, cytogenetics, health promotion and basic sciences participate in activities of the FCP. Besides collaborations within the University of Vermont, the FCP has established key working relationships with other academic cancer centers and community oncologists in the region. The FCP conducts its research activities under the approval of the University of Vermont College of Medicine's Institutional Review Board.

MULTIDISCIPLINARY APPROACH

Familial cancer is a complex issue and to address it effectively requires a variety of specialists from different disciplines (Josten *et al.*, 1986; Lynch *et al.*, 1989; Peters, 1994; Ponder, 1994). The complementary expertise of genetics professionals, oncologists, molecular biologists and psychologists has been key to the development of the FCP.

In evaluating families, each professional provides pertinent information and a unique perspective. The genetic counselor presents referrals to the core group, including questions and concerns raised by the consultand during the initial interview. In addition, the genetic counselor presents medical record information, relevant literature and other information specific to the family history (Peters and Stopfer, 1996). The genetic counselor and the clinical geneticist highlight issues relevant to families with inherited conditions, including ethical concerns (Garber and Patenaude, 1995; Reilly *et al.*, 1996). The medical oncologist discusses oncologic information relevant to the types of cancers in the family and provides information on appropriate screening and surveillance measures. The molecular biologist provides information on testing and laboratory issues. Together, the group discusses differential diagnoses, as well as the probability of the family having a specific mutation and the types of testing (research or clinical, chromosomal linkage, or direct mutation analysis) that may be appropriate (Narod, 1994; Shattuck-Eidens *et al.*, 1995). The psychologist raises issues relevant to both presymptomatic and cancer diagnosis and management

(Compas *et al.*, 1994; Stoll, 1996; Lerman *et al.*, 1993, 1994a,b). The psychologist is also available to those families that are at particular psychological risk. The laboratory coordinator assists with any genetic testing and DNA banking that may occur. The program coordinator oversees general operation of the program, including planning of meetings and assistance in developing educational brochures and marketing strategies.

A multidisciplinary approach also increases the ability of the FCP to perform worthwhile research (Ponder, 1987). The molecular diagnostic laboratory of the University's Department of Pathology has been an important resource to the FCP. The laboratory stores DNA samples for clinically-related banking purposes and for future research. The laboratory also has been instrumental in investigating interesting cases referred to the FCP (Wallace-Broder *et al.*, 1994; Weber *et al.*, 1996). The laboratory is certified under the Clinical Laboratory Improvement Act (1988) which enables it to confirm results from research laboratories for clinical use.

Several other units within the university, including the Department of Psychology, the Office of Health Promotion Research, and the Vermont Mammography Registry, have been helpful in addressing important research questions regarding familial cancer. Areas of research interest include: genes that predispose to cancer; psychological aspects of increased familial cancer risk; methods of provision of genetic counseling for cancer; individuals' and providers' perceptions and acceptance of genetic testing in cancer; and development of regional protocols for health care management for those with a family history of cancer.

PROGRAM OPERATION

Initial Contact, Data Gathering, and Evaluation

Individuals referred to the FCP speak, usually over the telephone, with a genetic counselor, who obtains a family history, including types of cancer and ages at diagnosis. The counselor identifies those medical records that are necessary to assess the family history adequately and mails medical record release forms and an informational brochure about the FCP to the consultand. To allocate records to the correct family and to maintain confidentiality, each family receives a unique identifying number. Upon receipt, all medical records are kept in a confidential file and are coded using the family number. Upon receipt of adequate medical record information, the core group of the FCP reviews the family history in a triage meeting. The group discusses the availability and appropriateness of DNA-based testing,

research protocols, and surveillance recommendations specific to the family history.

Scoring of the family follows group discussion and is based on a 5-point scale. A score of "1" indicates that the family history strongly suggests a known inherited cancer syndrome and an individual with a high likelihood of carrying a known gene mutation is available for testing (see Fig. 1 for specific criteria). A score of "2" means that the family history strongly suggests an inherited cancer syndrome, but no living affected relative is available for research or testing. A score of "3" signifies that the family does

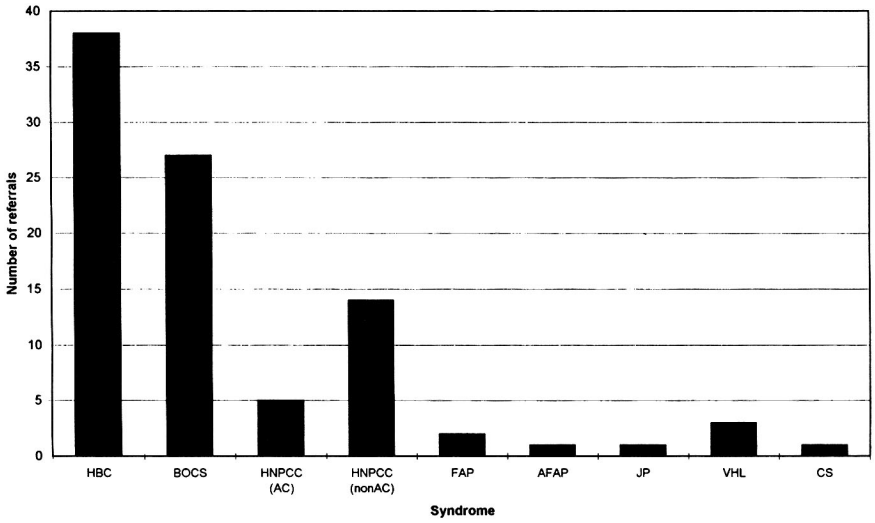

Fig. 1. Number of referrals with family histories strongly suggestive of an inherited cancer syndrome (score of 1 or 2) (family history includes a minimum of two first degree relatives with breast cancer < 50; or one individual with bilateral breast cancer, the first diagnosis of breast cancer < 50; or family history of breast cancer and the presence of male breast cancer). HBC = Hereditary Breast Cancer (family history includes a minimum of one individual with breast cancer < 50 and a first degree relative with ovarian cancer at any age; or two first degree relatives with ovarian cancer at any age; or one individual with breast cancer < 50 and ovarian cancer at any age). BOCS = Breast/Ovarian Cancer Syndrome (Amsterdam criteria are defined as a family history consisting of three individuals with colon cancer in two successive generations, one individual being a first degree relative of the other two and at least one individual diagnosed < 50. Familial Adenomatous Polyposis has been excluded). HNPCC (AC) = Hereditary Non-Polyposis Colon Cancer (Amsterdam criteria) (family history of colon cancer, but lacks one criteria of Amsterdam definition of HNPCC; presence of colon cancer in addition to other HNPCC-associated tumors). HNPCC (nonAC) = Hereditary Non-Polyposis Colon Cancer (Non-Amsterdam criteria) FAP = Familial Adenomatous Polyposis AFAP = Attenuated Familial Adenomatous Polyposis JP = Juvenile Polyposis VHL = von Hippel-Lindau CS = Cowden Syndrome.

not fit a known inherited cancer syndrome, but appears to have more cancer than expected by chance alone, cancers at younger than expected ages, or cases of rare cancers. Families that have an unremarkable history of cancer receive a score of "4." Family histories that require further clarification, such as medical record confirmation of cancer diagnoses, receive a score of "5."

Follow-up

Once the family has been scored, the genetic counselor re-contacts the consultands from families in groups 1, 2, and 3 and offers an appointment for genetic counseling. The FCP instructs consultants from families with a score of 5 how to gather further information, and on its receipt re-evaluates and re-scores the family. A consultand from a family with a score of 4 receives a standardized letter that summarizes the family history and reviews why the history does not suggest heritable cancer. This letter also includes the American Cancer Society screening recommendations for the general population. The FCP encourages all consultands to remain in contact with the FCP as research progresses or family history changes.

For consultands from groups 1, 2, and 3, the 60 to 90-minute genetic counseling session includes review of family history and discussion of the conclusions of the triage meeting. The genetic counselor obtains a personal medical and psychological history, as well as information about potential risk factors, such as diet and smoking. The counselor asks the consultand to talk about experiences with cancer in himself/herself and/or relatives. The counselor inquires about the individual's perception of his/her own risk for inherited cancer in the future and then provides a more formal risk assessment derived from published models (Gail *et al.*, 1989; Claus *et al.*, 1993; Houlston *et al.*, 1992; Hoskins *et al.*, 1995; Fuchs *et al.*, 1994). Often a range of risk is given because the family history does not fit neatly into any specific category. The counselor reviews the inheritance pattern and natural history of any suspected inherited cancer syndrome. He/she also emphasizes the incomplete nature of knowledge about penetrance and expression of cancer susceptibility genes, particularly with respect to age of onset, tumor spectrum, pathology, and prognosis. After inquiring about the individual's current screening practices, the counselor discusses surveillance options and any recommendations from the FCP's review of the family history and medical records. When appropriate, the genetic counselor offers a referral to the medical oncologist of the FCP to discuss surveillance or other oncologic issues in more detail. The counselor encourages individuals to discuss screening options with their primary doctors to derive an

optimal individualized screening plan. Individuals have different informational needs and varying emotional responses to information (Kelly, 1992; Biesecker *et al.,* 1993, Lerman and Croyle, 1996), and therefore, each counseling session is individualized toward specific needs and emotional responses.

After this genetic counseling session, the consultand receives a detailed follow-up letter reiterating information communicated during the genetic counseling session. This letter serves as a safety check that all salient points have been communicated to the individual. This letter also provides education in cancer genetics, for which limited materials exist. In addition, individuals may misunderstand or forget verbal communication and the letter serves as a resource for future reference (Evans *et al.*, 1994). The consultand decides to whom he/she wants copies of the letter sent (physicians, relatives, etc.). If the letter is sent to physicians and relatives, it provides education to those individuals. The consultand also receives educational materials such as booklets pertaining to specific cancer syndromes, and materials from the American Cancer Society regarding specific cancers.

If the consultand's physician receives a copy of the clinic letter, enclosed with it is literature to support recommendations for screening and management. The FCP also emphasizes to the physician that the field is in a state of flux and that it is not always clear which are the best screening or management methods for a specific individual.

Genetic Testing

When the FCP started, genetic testing for breast, ovarian, and colon cancer existed only on a research basis; however commercial testing is now available. The availability of research based genetic testing is discussed with the consultand if the family history meets the researcher's eligibility criteria.

For individuals and families that choose to participate in genetic testing on a research basis or to bank samples, the FCP utilizes an IRB approved, two-phase informed consent process. In the first phase, subjects agree to provide blood and/or tissue samples for research and indicate whether they want to be informed of any research finding that might have clinical implications for themselves or their families. Any subject re-contacted for this reason undergoes a second consent process that includes counseling regarding the risks, benefits, and limitations of learning the results of specific available tests. If the subject chooses to learn this information, re-testing of a second blood sample in a licensed clinical laboratory (CLIA compliant) occurs before provision of results. The consent process allows research samples to be shared with other institutions.

A Certificate of Confidentiality from the Department of Health and Human Services protects information gathered in research projects from subpoena. However, once information from a research project is used for clinical purposes and enters the medical record, the certificate no longer is protective (Earley and Strong, 1995).

The availability of commercial, fee-for-service genetic testing for breast, ovarian, and colon cancer susceptibility has created controversy within the medical and scientific communities with regards to use of these tests (Collins *et al.,* 1994, 1996; Bowcock *et al.,* 1994; Offit *et al.,* 1996; Mark *et al.*, 1996). Currently, insufficient information exists regarding the full consequences of testing (Collins, 1996; Holtzman, 1996; Schneider *et al.,* 1995; Kahn, 1996). However, genetic testing may offer reassurance or improve medical care for some individuals and families. The FCP believes that genetic testing, whether research or commercial, should only be offered in conjunction with pre-test education and genetic counseling to ensure informed consent and to minimize potential harm to those individuals and families who request genetic testing. If an individual or family history suggests inherited factors, the risks, benefits, and limitations of genetic testing are discussed. This discussion includes the potential for adverse psychological consequences, the potential for disrupted family relationships (Northhouse, 1994), current options for surveillance and their limitations, and the possibility for insurance and employment discrimination. The genetic counselor distinguishes between genetic testing after disease diagnosis and predisposition testing.

If a family is eligible for both commercial and research testing, the pros and cons of testing by each mechanism are discussed. The program encourages individuals to take time to think about their motivations and the possible ramifications of genetic testing. The genetic counselor offers a follow-up visit to individuals interested in pursuing testing or to discuss further the implications of testing. When indicated, psychological counseling is made available.

Cost and Billing Procedures

Participation in any aspect of the program, except for DNA-based testing from the commercial sector, has been without charge until January 1997. Since that time, genetic counseling services have been billed using the 99245 CPT code ($243.00). An ICD9 V code is used and the diagnosis listed is either that of a personal history of a specific cancer or a family history of a specific cancer. The FCP will evaluate whether this deters some individuals and families from scheduling genetic counseling appointments

and whether insurance will cover such services for those that do proceed with genetic counseling.

PROGRAM EXPERIENCE

Two primary marketing mechanisms have promoted referrals to the FCP. Grand Rounds presentations and other educational forums to health professionals in the region have been the greatest source of referrals. Local and national media coverage regarding genetics has also influenced referrals to the program.

From December 1993 through December 1996, the FCP received 285 referrals. Approximately 40% were self-referrals, 25% came from oncologists, and 15% were identified during routine genetic counseling for advanced maternal age. The remaining 20% came from genetics professionals, general surgeons, primary care physicians, medical subspecialists, and Title X (family planning) clinics. Referral patterns have changed over time. In the program's first year, media attention focused on the discovery of MSH2 and MLH1 (Fishel *et al.*, 1993; Leach *et al.*, 1993; Bronner *et al.*, 1994), genes involved in the development of Hereditary Non-Polyposis Colon Cancer (HNPCC) which resulted in a self referral rate of over 50%. In the second and third years of the program, self- referrals declined to 15% and referrals from oncologists grew to nearly 50%.

Thirty-five percent of families referred to the FCP have a history that suggests hereditary cancer (score of 1 or 2). These families represent a variety of hereditary cancer syndromes (Fig. 1). While they do not fit a defined hereditary cancer syndrome, another 25% of family histories are concerning because they include more affected individuals than expected by chance alone and/or the ages at diagnosis are younger than expected in the general population, and/or there are cases of rare cancers in the family (score of 3). Approximately, 10% of referrals have unremarkable histories with regard to hereditary cancer (score of 4) and 30% of referrals remain indeterminate due to incomplete medical record documentation (score of 5).

The degree of risk in the family history is significantly related to the source of referral. The majority of self-referrals receive scores that either require more information to evaluate the family history adequately, or have histories that do not suggest heritable cancer. In contrast, the majority of referrals from oncologists appear to have an increased risk of heritable cancer (Fig. 2).

The FCP has provided genetic counseling to over half of the referrals scoring 1, 2, or 3. The other half are not interested in genetic counseling services or pertinent medical records have not been received. Figure 3

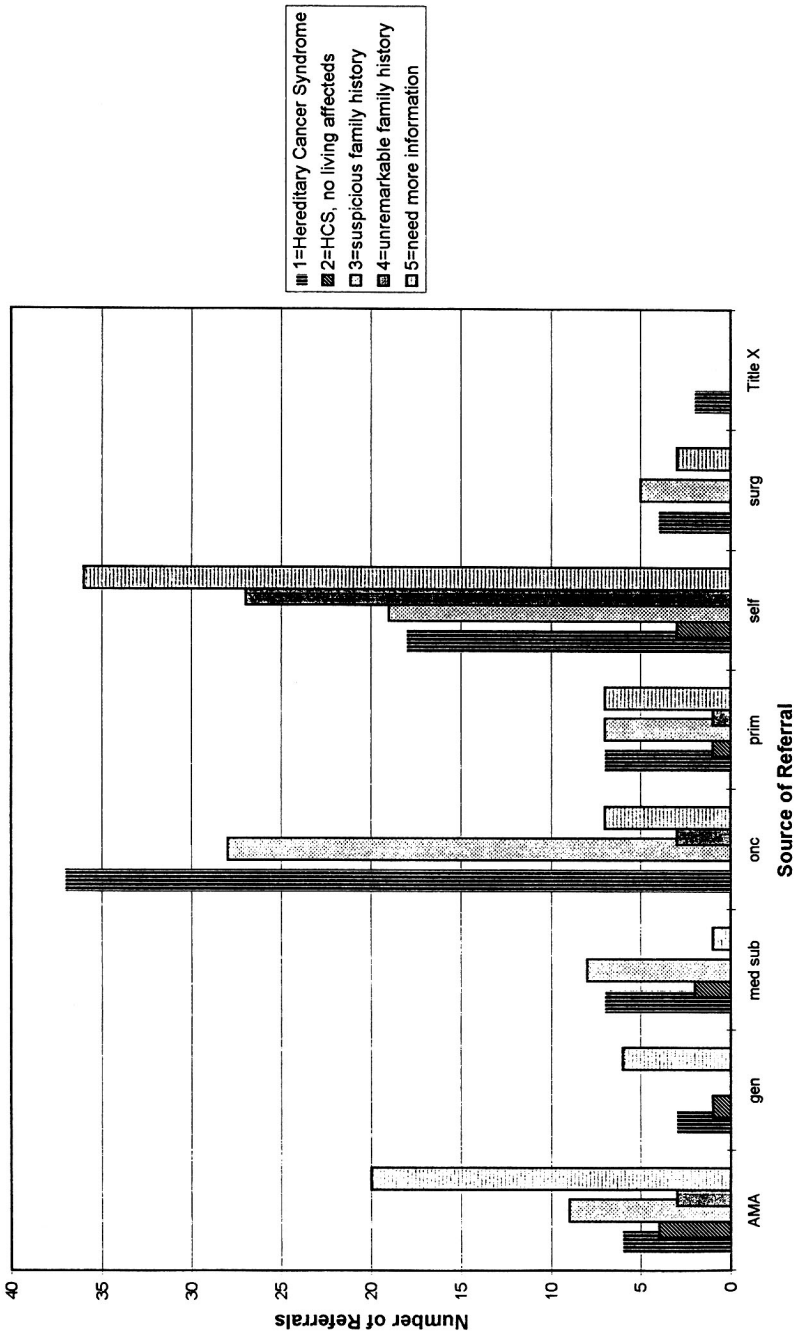

Fig. 2. Comparison of mode of referral with level of risk as determined by the FCP scoring method. AMA = family histories identified through genetic counseling for Advanced Maternal Age, gen = referrals from genetic professionals, med sub = referrals from medical subspecialists (Ob/Gyn, derm, etc.), onc = oncology referrals, prim = referrals from primary care physicians, self = self-referrals, surg = referrals from general surgeons, Title X = referrals from family planning clinics.

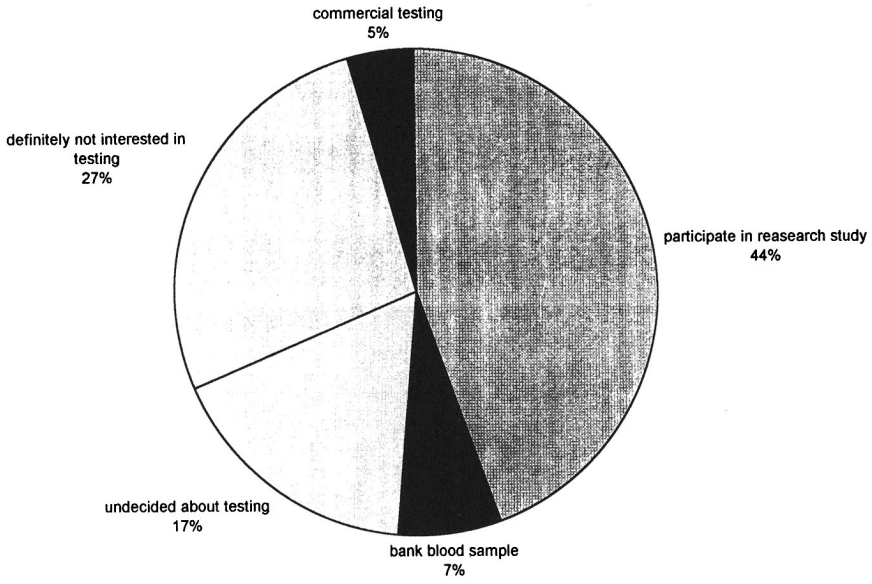

Fig. 3. Decisions regarding genetic testing.

shows the variety of decisions those individuals and families, with histories strongly suggestive of an inherited cancer syndrome, make regarding genetic testing after receiving genetic counseling.

DISCUSSION

The development of the FCP has been an exciting and challenging experience. Using the accepted definition of rurality as the percentage of the population living outside a metropolitan statistical area (MSA), Vermont is the most rural state in the country, with 73% of its population living outside its single MSA (Bureau of the Census, 1992). Developing a familial cancer program in a rural area presents both opportunities and barriers. Two characteristics of a rural population, lower socioeconomic status and poor access to health care, have been linked to increased psychological distress and less adequate health behaviors (Lerman *et al.*, 1993, 1994a,b; Northouse, 1994; Rutter and Quine, 1994). Limited access to health care resources decreases opportunities for early detection and prevention of cancer and for participation in research studies. Working with colleagues and outreach clinics throughout the region, allows the FCP to reach a larger sector of the population and to lessen barriers to appropriate

services. By adding professional expertise and patient numbers, these collaborations also increase the ability of the FCP to answer important research questions regarding familial cancer.

However, especially in a rural area, regular communication with colleagues can be difficult due to distance. Constraints on time and resources make face to face meetings on a regular basis nearly impossible. To address this problem, the FCP has incorporated videoconferencing as a way to communicate on a regular basis without having to travel large distances. Videoconferencing allows many colleagues at different sites to meet on a regular basis to discuss referred families, as well as a host of other issues related to familial cancer. Many hospitals are now incorporating telemedicine technology which enables these resources to be used for videoconferencing (Wootton, 1996).

The development of a scoring system allows stratification and triage of family histories based on level of risk. However, it became apparent that assigning a specific level of risk to families is difficult and labor intensive. Many families have excess cancer, but do not fit a known inherited cancer syndrome. A major challenge has been the issue of how to improve health care for the many individuals with a positive family history of cancer for whom precise DNA-based testing is not yet available. Indeed, at the present, such families appear to far outnumber those relatively few families for whom DNA-based testing can be definitive or those families who choose to have DNA-based testing. The FCP believes that establishment of guidelines for the management of such patients and evaluation of these guidelines in clinical research studies will be an important contribution of cancer genetic programs.

The importance of medical record documentation is well established (Love *et al.*, 1985; Lynch, 1991; Aitken *et al.*, 1995). However, medical record retrieval is often the program's greatest obstacle, and without documentation of the reported cancer history, the FCP often cannot provide an accurate assessment for the family. In addition, counseling families with inadequate information may lead to inappropriate, costly screening tests and an unnecessary elevation in anxiety. On the other hand, a lack of information may lead to inadequate screening and surveillance procedures.

Retrieval of medical records can be difficult for some families because it must involve cooperation of other family members who may be resistant. Involvement of other family members in the testing process has been frustrating for many consultands, as well. In many situations, genetic testing must first be performed on a family member who has had cancer who lives in another part of the country. In these cases, a referral is made to a genetic counselor in that relative's region, ideally with experience in cancer genetics. However, the relative may differ in his/her opinions regarding the im-

plications of genetic testing, presenting a barrier to the individual seeking information regarding their genetic status.

With the availability of commercial testing for BRCA1 and HNPCC, the FCP anticipated a high level of interest in testing for these genes. Several publications have suggested a high level of interest in genetic susceptibility testing among first degree relatives of persons with breast, ovarian, or colon cancer (Croyle and Lerman, 1993; Lerman *et al.,* 1994a,b; Lerman *et al.,* 1996; Smith and Croyle, 1995). However, our data reflect a lower level of interest in commercial genetic testing than we expected based on these preliminary studies. Anecdotal comments from families suggest that privacy issues, including the potential for insurance discrimination, the cost of commercial testing, and the scientific uncertainties in the interpretation of results and the uncertainty of clinical recommendations based on the results of testing, are the main concerns regarding testing. The current state of genetic testing creates a dilemma for many high risk families. After receiving genetic counseling, people realize that commercial testing is costly and that the investigational status of testing leaves many unanswered questions. The possibilities for families to participate in research is decreasing, as many research labs are currently overwhelmed with specimens and express interest only in very unusual family histories. If a family is eligible for research-based genetic testing, they realize it may take years to receive any information. Despite this, the FCP's experience suggests that families eligible for research and commercial testing usually choose research-based testing over commercial testing (Fig. 3). Therefore, the focus of the FCP's activities have been genetic counseling and education regarding surveillance recommendations, rather than referral for commercial genetic testing.

In the multidisciplinary work of the FCP, we have observed that health professionals from different backgrounds tend to bring diverse perspectives to the consideration of both patients and of clinical and research issues. Perhaps because of dissimilar education, training, and work experience, and personality styles, oncologists, for instance, often approach issues differently than do genetic counselors. In the FCP, the genetic counselor is the primary person the individual or family has contact with after referral to the program. The genetic counselor can be in the position of "protecting the patient's interests" and may come in conflict with the other members of the multidisciplinary team. In many situations, we found that no one approach is "correct," but that the best practice comes from a distillation of differing views. Indeed, an unanticipated benefit of the FCP's multidisciplinary approach has been the opportunity to learn from colleagues not only new knowledge, but new ways to think about patients and other issues.

CONCLUSIONS

A multidisciplinary approach to familial cancer enriches the expertise of the program and brings a variety of perspectives to the many difficult issues that arise. From a genetic counselor's perspective, being involved in developing such a program can be an exciting and challenging experience, offering the opportunity to learn about a new and emerging area of genetics and medicine and to interact with a different group of professionals. Basic scientists, clinical geneticists, and genetic counselors, medical and surgical oncologists, public health professionals, and psychologists challenge each other to consider new perspectives in order to work together toward the benefit of the families referred to familial cancer programs. Collaborations with regional clinicians and scientists broaden the scope of services provided to individuals and families and create research opportunities which will ultimately lead to enhanced care for individuals and families affected by cancer.

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