The demand for services for predicting, diagnosing, and managing genetic diseases or diseases with a genetic component is likely to increase faster than the availability of services from medical geneticists and genetic counselors. Health care systems may also impose limitations on referrals to these specialists. If genetic problems are not to be missed and excessive referrals are to be avoided, non-geneticist practitioners will have to recognize when genetic problems should be considered, and initiate diagnosis and even management. Primary-care-centred systems offer the greatest potential for maximizing overall cost-effectiveness, by reducing the demand for specialty services not essential for improving health. But primary-care-centred systems may pose a risk of underdetection and undermanagement of genetic problems if practitioners are not actively supported by information and other educational networks. Several models for dealing with these challenges are presented, including algorithms that aid in recognizing genetic problems.

Keywords: genetics, primary care

Until about 1970, referrals to geneticists were primarily for the diagnosis of children with unusual clinical features and for counseling parents on risks of recurrence or occurrence. Referrals for genetic counseling increased with the advent of mid-trimester amniocentesis and carrier and prenatal serum screening. To meet this demand, nurses and master's level graduates were trained to provide genetic counseling, usually under the supervision of medical geneticists.

During the past decade the number of relatively rare disorders for which a precise genetic diagnosis can be made has increased remarkably. Nevertheless, there has been no parallel increase in genetic specialists. Consequently, other practitioners will have to deal with many genetic problems.1 The importance of primary care has been stressed2 and the potential role of general practitioners in genetic testing demonstrated.3 In the first part of the paper, we examine how the provision of genetic services is likely to emerge in different European countries, based on current patterns of services.

Different cultures of health care systems may well lead to different modes of dealing with the emerging challenges.4 In the second part of the paper, we present schemes to help primary care and other practitioners decide when genetic contributions to a patient's problem merit consideration.

POTENTIAL MODELS FOR GENETIC SERVICES

Direct access to geneticists
In this model, which operates in several European countries, including Germany, patients who suspect genetic problems may self-refer to a genetic specialist. Expansion in service provision could be achieved by increasing training posts in the speciality. Task delegation from doctors to trained nurses is believed to enhance efficiency in clinical areas5,6 including genetics.7

Direct access systems generally offer the highest quality of care for specific diagnosed clinical conditions (although not generally for concomitant other health conditions8) because specialists in those conditions may reasonably be supposed to be the most knowledgeable and up-to-date in their field.9 They also are likely to be more knowledgeable about the implications of the genetic problem for the family. The high volume and flow of patients within a specialist practice facilitates the maintenance of technical skills and ensures ready access to specialist equipment and technologies. The outcomes of care are generally good for those problems that are in the purview of the specialist.10

There are, however, disadvantages. Inequities in care will arise because less-educated and less-knowledgeable members of the public will be less good at making appropriate self-referrals. Specialists may also see a high proportion of patients who have no real need for specialist care but who believe themselves to be at risk. Specialists are also less efficient and more likely to make false positive diagnoses when patients are self-referred.11 There is a tendency towards overprovision of care by specialists who carry out more tests and interventions than are commensurate with patients' needs.12,13 For these reasons, direct access systems are more expensive and potentially less cost-effective than other models of care.

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Gate-keeping by specialists
In the specialist gate-keeper model, access to specialist genetic care is by referral from another specialist. In many systems (e.g. Holland) where patients might theoretically have direct access to geneticists, in practice they are often referred by other specialists such as ‘specialoids’ who care for population groups defined by age, e.g. by pediatricians, or other specialists. The system is dependent on the ability of the specialoid physician to make a preliminary assessment and refer appropriately to a genetic specialist. This could be achieved by training those physicians whose practices may be at higher risk of encountering certain types of genetic diseases in their specialty (e.g. endocrine specialists already deal with some inherited metabolic disorders and oncologists are already involved in caring for cancers with a genetic component); developing genetic referral guidelines; and/or introducing liaison and outreach services whereby genetic specialists advise and support other specialists in settings where genetic problems are likely to be particularly prevalent. This model may be appropriate for certain types of genetic problems, for example, in neonatal intensive care units with a higher likelihood of genetic metabolic and chromosomal problems and whose patients already are likely to be in a specialty-oriented environment.
This model requires fewer geneticists but a wider knowledge of genetics among the physicians initially seeing the patient. Gate-keeping reduces inequities in access to specialist care due to variations in patients’ knowledge of genetics. For these reasons, the specialist gate-keeper model may be more cost-effective than the direct access model. A disadvantage is potentially lower quality of care if more patients who could benefit from referral are, instead, treated by poorly trained non-geneticist specialists. A corollary is that specialists often do not see the commoner polygenic conditions whose genetic implications are only beginning to become understood.

Gate-keeping by primary care physicians
In an increasing number of countries, primary care physicians (PCPs) are the main source of first contact care for new problems, ongoing care for long-term problems, and preventive care/health promotion. In some countries (e.g. the UK, Spain, Denmark, Netherlands), patients may not see a specialist without first being referred by their general practitioner. The challenge to the primary care practitioner is to be alert to symptoms and signs, including family histories, that suggest a potential for a genetic condition. Computerized decision support systems may further facilitate the management of genetic problems by non-geneticists.
Primary-care-centred health care systems have four key characteristics which generally enhance the quality and cost-effectiveness of care as compared with health care systems centred on specialists. We now consider how these characteristics of primary care can be brought to bear to maximize recognition of potential genetic problems as well as to coordinate management when they occur.

CHARACTERISTICS OF PRIMARY CARE IN THE CONTEXT OF GENETICS

First-contact care
Except when public health activities assume a role in organizing community-wide screening programmes, primary care is the main point of entry for all potential and actual genetic services, whether for routine testing or because of a family history in individuals or family members. Primary care settings are the most equitable, as almost everyone will have better access to them compared with access to other specialists. For many conditions, the primary care practitioner may be the ONLY point of contact with medical care. Primary care physicians must be knowledgeable about the likely modes of presentation of various types of genetic conditions and aware of those or combinations of those that signal a need to refer to a genetic specialist. It has to be the responsibility of specialists to develop mechanisms for the continual education of family physicians and other generalists. This is likely to be a major task. Clinical practice can be improved by involving practitioners in the planning and execution of clinical research, in reviewing evidence, and in developing guidelines. Computerized protocols developed jointly by genetic specialists and primary care practitioners could potentially provide a method not only of advice on indications for referral but also on tests that should be done prior to the referral and tests that are not indicated.

Longitudinal (ongoing) care
The long-term person-focused nature of primary care is more conducive to the existence of a base of knowledge about patients in the context of their families and communities. Therefore, a primary care practitioner freely chosen by patients is more likely to be able to ascertain family histories, even by means less formal than standardized history-taking, than is a specialist or other professional who knows the patient less well. Moreover, primary care practitioners, as compared with specialists, more often recognize psychological factors that may facilitate or inhibit the elicitation of information or the discussion of options for intervention. As a result, potential ethical issues are likely to be more readily recognized and dealt with because of greater knowledge of individual and family considerations. The second strength of the longitudinal relationship which primary care physicians offer their patients is that the issues and problems related to genetic disorders may stay relevant over many years.

Comprehensiveness
Comprehensiveness means that primary care physicians undertake responsibility for all health problems in populations except those that arise too uncommonly for them to maintain competence in dealing with them. Genetic problems sometimes present with very common symptoms, and the practitioner must be able to distinguish, for the purpose of diagnosis, those that are likely to be the result of a genetic disorder from those that
are a manifestation of some acute illness. From the viewpoint of treatment, common genetic problems are in the purview of primary care, and primary care practitioners must be educated in the skills required to deal with them and provided with new information about them as it becomes available. Geneticists, working with family physicians, can help establish criteria for deciding what is a primary care problem and what should be referred to other specialists for ongoing management.

**Co-ordination**

The fourth key function of primary care is co-ordination of care provided within the primary care setting with care provided elsewhere. Since many genetic problems, particularly the uncommon ones, will require ongoing care from a range of professionals, mechanisms for effectively and efficiently transferring information from primary to specialty care need to be established. The specialist needs information not only about the problem itself but also about the family and cultural context in which the problem occurs. The primary care physician, in turn, requires information not only about the problem but also about possible alternative interventions and the merits and disadvantages of each, in order to help patients choose the option best for them and for their families. Even when the specialist takes over complete management of the genetic problem (as in the case of existing rare or very complex disorders), there is a continuing need for communication with the primary care physician who may be caring for the other aspects of the patient’s health and the health problems of family members.

**ALGORITHMS FOR RECOGNIZING AND MANAGING GENETIC DISORDERS**

Genetic diseases involve virtually every organ, tissue, or functional system and can begin at any time in life. Although primary care practitioners cannot be aware of all diseases in which genes play a prominent role, they should be alert to a genetic factor when the patient has a family history of the disease under consideration. They also should be aware of those common diseases for which allele penetrance is high. (An ‘allele’ is the actual DNA sequence of a gene on a chromosome. A person inherits one allele from each parent. The extent to which other factors must be present determines the ‘penetrance’ of the allele. For many Mendelian diseases, most of which are rare, no other factors are needed and penetrance of the disease-causing genotype approaches 100%.) Primary care practitioners should also be aware of those common disorders for which the discovery of an inherited factor would present opportunities for prevention or require special management. They should also know that patients belonging to a population subgroup that has been geographically or culturally isolated historically may be at increased risk for certain inherited disorders. They should also recognize that certain frequent symptoms and signs may result from the presence of rare inherited disorders. We emphasize these factors in the following algorithms, which are intended to help primary care practitioners recognize situations in which a genetic problem may exist while keeping both missed cases and over-referrals to a minimum.

**Patients with symptoms present**

*Figure 1* shows how a clinician might manage patients who present with symptoms or signs that may result from an underlying inherited disorder. The greater the prevalence of the symptoms or signs the more likely PCPs will deal with them directly rather than refer. In most cases, the findings will respond to routine management. When they do not, or when they recur, genetic conditions should be considered. Persistence of vomiting, lethargy,
and poor feeding in young infants, or their recurrence with the reintroduction of milk, may indicate the presence of any one of a large number of inherited metabolic disorders. Recurrent infection, unresponsive failure to thrive, persistent anemia, short stature, developmental delay, and hearing or visual impairment are some other signals of genetic disorders. As most genetic-metabolic conditions are recessive (requiring inheritance of an abnormal allele from each parent), previous generations are unlikely to be affected. However, parents should be queried about unexplained deaths or problems in siblings of the patient. A history of consanguinity also increases the probability of a recessive disorder. Family history could be helpful when X-linked (e.g., Duchenne muscular dystrophy) or dominant conditions (e.g. Huntington’s disease) enter into the differential diagnosis. Patients or parents may be more likely to admit that relatives have an unusual disease to a primary care practitioner with whom they have a long-standing relationship than to a specialist. Some rare findings, such as the facies and palm creases of Down syndrome, or cleft lip and palate, or uncontrollable bleeding following circumcision, or swollen hands and feet in a child of African origin, may suggest a diagnosis but not necessarily enable the primary care practitioner to provide management without the help of a specialist. Such unusual findings should prompt referral unless perusal of texts or searches of the literature reveal the likely diagnosis and initial treatment. Online Mendelian Inheritance in Man (OMIM) may be particularly helpful (available at http://www3.ncbi.nlm.nih.gov/Omim/). Problems that occur commonly in older people may indicate a genetic problem when they occur in young adults. Deep vein thrombosis in women on oral contraceptives may indicate a genetic problem when they occur in young adults. Genetic considerations play little role in the immediate management of acute and life-threatening problems. For example, stabilization is the main priority for a young adult with acute chest pain or for a full-term infant with signs of dehydration or metabolic acidosis. The likelihood of an underlying genetic problem should be considered later, particularly if the presence of a genetic condition will alter subsequent management or increase the risk to relatives. Occasionally, however, establishing a genetic diagnosis will affect acute management, as in salt-losing adrenal hyperplasia.

Primary care practitioners should refer to specialists if they lack experience, time or expertise to perform genetic diagnostic procedures, such as chorionic villus sampling or amniocentesis, or because the test is only available when requested by a specialist. When specialists return patients with genetic diseases, primary care practitioners should be alert for relapses or complications of the treatment. Patients and families may seek advice from primary care practitioners about the recommendations for specialists. Primary care practitioners may also be in a good position to counsel about reproductive risks and to serve as ombudsmen for the family in discussions with specialists, e.g. in considering the benefits and risks of investigational procedures or when different options are available. When no definitive treatment is available, such as with severe developmental retardation, the primary care practitioner has the major responsibility for palliative care (although consultations may be needed) and to comfort and counsel the family. Other special services may be needed and the primary care practitioner should coordinate them. When no interventions are available, there may still be reasons to pursue a genetic diagnosis when it is likely that a family’s anxiety would be relieved by just getting a diagnosis. Recognition of a Mendelian disorder also gives parents a precise and accurate risk of recurrence and enables them to choose prenatal diagnosis in subsequent pregnancies.

Patients without symptoms

The presence of a family history of certain disorders will indicate some but not all high risk situations (figure 2). The primary care practitioner can either take a complete pedigree of morbidity and mortality in first and second degree relatives (self-administered family history forms are available) or limit the inquiry to situations that raise a flag for genetic etiology (such as unexplained deaths of young children) or to those disorders for which a positive family history would alter the management of the asymptomatic patient. For example, prophylactic mastectomy and oophorectomy may increase survival in asymptomatic women with BRCA1/2 mutations. In healthy people with a family history leading to discovery of mismatch repair mutations predisposing them to hereditary nonpolyposis colon cancer (HNPCC), total colectomy will eliminate the risk of colon cancer. COX2 inhibitors also may prevent colon cancer in some people at risk for HNPCC.

A family history of a common disease will more often be explained by shared environment, life style, or patterns of nurturing than by the presence of highly penetrant alleles.
If the family history is negative, the patient’s geographic or cultural background might prompt the primary care practitioner to counsel about carrier testing for disorders that have a higher frequency in the patient’s ethnic group, such as sickle cell anaemia in African-Americans, thalassemia in people from Mediterranean countries or South Asia, or Tay Sachs in Ashkenazi Jews. A practice serving such subpopulations should have heightened sensitivity to the possibility that patients will be carriers. For some autosomal recessive conditions (for which a negative family history is expected), screening may be available. In many countries, newborn screening is not the responsibility of primary care, although the primary care practitioner may be notified if the test is positive and be responsible for contacting the family, arranging followup, and almost certainly playing a role in long-term management (e.g. prescribing prophylactic antibiotics and pneumococcal vaccines in infants found to have sickle cell anaemia or advising parents to avoid prolonged fasts in infants and children with medium chain acyl-Co-A dehydrogenase (MCAD) deficiency).

The primary care practitioner or obstetrician will usually be the one to raise the issue of prenatal screening for fetal Down syndrome or neural tube defects as well as for carrier screening. For women who indicate prior to pregnancy that they are opposed to abortion, either by volunteering the information or by judicious questioning by a primary care practitioner who suspects this might be the case, carrier screening available for Mendelian disorders should be offered before pregnancy so options other than prenatal diagnosis and abortion can be considered (e.g. artificial insemination or adoption).

Primary care practitioners who lack confidence in managing genetic problems may refer to specialists; if the risk is to future offspring, reproductive counseling is important. PCPs should, however, eventually acquire sufficient expertise to manage many situations (and provide counseling) without referral, regardless of whether the risk is to the patient or to future offspring.

CONCLUSION: ESSENTIALS FOR EFFECTIVE GENETIC CARE

Each of the four key elements of primary care has high relevance for the planning and delivering of genetics services, regardless of which model is chosen. Each should be assured in the design and execution of an organized system for the effective and efficient ascertainment and management of diseases with a major genetic component. Primary care services offer the greatest potential for maximizing overall cost-effectiveness, but may not be achievable or acceptable in some countries. They also may pose the greatest risk of underdetection and under-management of genetic problems if they are not actively supported by information and other educational networks. The requirements for good quality genetic care, in any case, must include:

- First contact physicians sufficiently knowledgeable about genetics to provide appropriate genetic care themselves and/or make an appropriate referral to a specialist in genetics. All physicians need to be aware of any unusual origins of the patients and the possibility of genetic disorders, to be able to take a family history to identify affected relatives, and to know when to refer to specialists;
- Development and implementation of guidelines for referral to genetic specialists. The use of computerized and other decision support systems is likely to be crucial in achieving access to the exponentially rising amount of needed information;
- Achieving equity of access to appropriate specialist genetic care for patients with genetic problems, irrespective of age, ethnicity, or socio-economic...
circumstances. Nurses and other health professionals with special genetic training may prove cost effective alternatives to physician care at all levels in a health service.

Most health care systems are unprepared for the anticipated rise in demand for genetic care. There is an urgent need for countries to decide how genetic care is to be provided, to institute appropriate training programmes, and to provide ongoing support to enable primary care physicians to carry out their functions adequately.

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REFERENCES