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The family medical history

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The family history is the gateway to identify individuals at risk for genetic disorders

> "Even when an individual's genome can be displayed on a personal microchip, interpreting that information will depend in large part, on the biological and environmental contexts in which the genome is expressed, and the family milieu is as good a guide as any." Reed Pyeritz, MD [1]

With the increasing number of amazing genetic tools that are available to fill a physician's diagnostic armamentarium, it is tempting to presume that the need for family history information will become obsolete. In fact, the medical family history remains the single most cost-effective approach to identifying individuals at risk for common disorders with a genetic etiology [2]. The family history can help determine a diagnosis and identify genetic and medical screening needs. For example, screening for colon cancer would be offered to a person at age 25 years instead of age 50 years if the parent had colon cancer at age 35 years [3].

A graphical family history

Although sometimes specific questions suffice when screening for familial diseases, recording family history information graphically in the form of a pedigree (also called a genogram) is a quick visual tool for incorporating and interpreting key medical information. A medical pedigree truly represents the popular saying that a picture is worth a thousand words. Box 1 summarizes major health and demographic information to include when obtaining a family medical history.

Time constraints on the busy medical practitioner continue to increase. How can developing a pedigree be incorporated into the confines of an already time-limited patient appointment? Many medical encounters require

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Box 1. Key information to include on a family pedigree

Age
Age at death (and year if known)
Cause of death
Siblings (denote if half or full siblings)
Children (note if with separate partners)
Parents and grandparents
Ideally aunts and uncles and their offspring
Age at diagnosis (use key in pedigree to note affected status)
Ethnic background of all four grandparents (if known)
Consanguinity (note how related)
Date pedigree recorded
Note name of person who took the pedigree
Include a key/legend to explain any symbols

at least some family history information to aid in diagnosis or risk assessment [4,5]. It is unrealistic to assume that every patient visit requires an extensive pedigree. A *targeted* family history and pedigree diagram, however, can be recorded easily in less than 5–10 minutes. It actually may be quicker to draw a pedigree than to dictate the family history. With a pedigree, pages of medical information can be compressed into an association of simple symbols—circles, squares, lines, and triangles. A pedigree begun at one visit can be updated easily at future appointments. Furthermore, computerized, self-administered family medical history questionnaires are becoming available that can construct a pedigree in digital form, as discussed later [3,4,6].

Primary care physicians routinely triage and prioritize multiple medical issues with each patient during a clinic visit. A pedigree targeting selective family history issues can be used as an instrument to help practitioners prioritize patient concerns [4]. The pedigree can be used to educate the patient about health priorities. Take Jim, age 50 years, who is concerned that he will die of colon cancer because his seemingly healthy father, age 71 years, recently died of colon cancer 6 months after his diagnosis. A quick family pedigree shows that there is no additional history of colon or other cancer in Jim's siblings, grandparents, great-grandparents, aunts, or uncles. In fact, the most significant health factor is premature death in several close relatives in their fifties from heart disease. Jim can be reassured that a screening colonoscopy will identify and remove precancerous colon lesions and that he is at the age that all men and women should begin screening for colon cancer. You can also refocus Jim's concerns about disease prevention to address his significant family history of heart disease (see article by Scheuner elsewhere in this issue). He really should stop smoking and begin a weight loss and exercise program, given that he smokes and is 30 pounds

overweight. These measures have potential to reduce his risk for developing several types of cancer, coronary disease, and diabetes [6].

When clinicians record family history information in text form it is common to record only the "positive" family history information. Actually it is equally important to record the "unremarkable" or "negative" family history. Textual recording of family history information may miss key information. Consider the following example: "Ms. Smith, age 29 years, has an aunt, grandmother, and first cousin who died of breast cancer." What ages did these women develop breast cancer? Is the cousin the daughter of the aunt with breast cancer? Is the cousin a paternal or maternal relative? Is this cousin related through a male relative or through a female relative who lived to be elderly without developing cancer? Is the grandmother a paternal or maternal relative? The exact relationship of these relatives to Ms. Smith and the age at diagnosis can make a critical difference in Ms. Smith's cancer risk assessment and the approach to genetic testing. A pedigree would provide the clinician with this information at a glance (Fig. 1).

A pedigree is just as useful in determining if a condition does not require genetic evaluation as it is in establishing a diagnosis, especially when the patient has a family history of a common disorder such as cancer. In the case of Ms. Smith, one is more likely to be concerned that she is at risk for an inherited predisposition to breast cancer if her relatives had premenopausal breast cancer than if they developed breast cancer in their sixties or seventies [3,7]. As her primary care clinician, examination of the family medical history might enable you to reassure her that her risk is not much above average, ie, with a family history of cancer in only two elderly relatives. An example of how information as simple as the age at diagnosis can change risk assessment is shown in Fig. 1. This figure highlights the dramatic difference in empiric risks for Ms. Smith to develop breast cancer based on the age that her mother and maternal aunt developed breast cancer [7].

Pedigrees: an opportunity for developing patient rapport and determining the patient's needs for information

The process of taking a medical family history provides an excellent opportunity to develop a relationship with one's patient (Box 2). Patients are more likely to heed medical recommendations if they feel their physicians are caring individuals who are interested in their lives. A pedigree (sometimes called a genogram [8]) is a visual tool for assessing the extent of the medical, emotional, and social impact of a disorder on the patient and the entire family. For example, it may show that the patient is the only person who has survived the disease in the family. The patient may experience a strong sense of "survivor guilt." One may note from the pedigree that the patient is approaching the age when other people have died from the disease in the family, and thus the patient may be experiencing

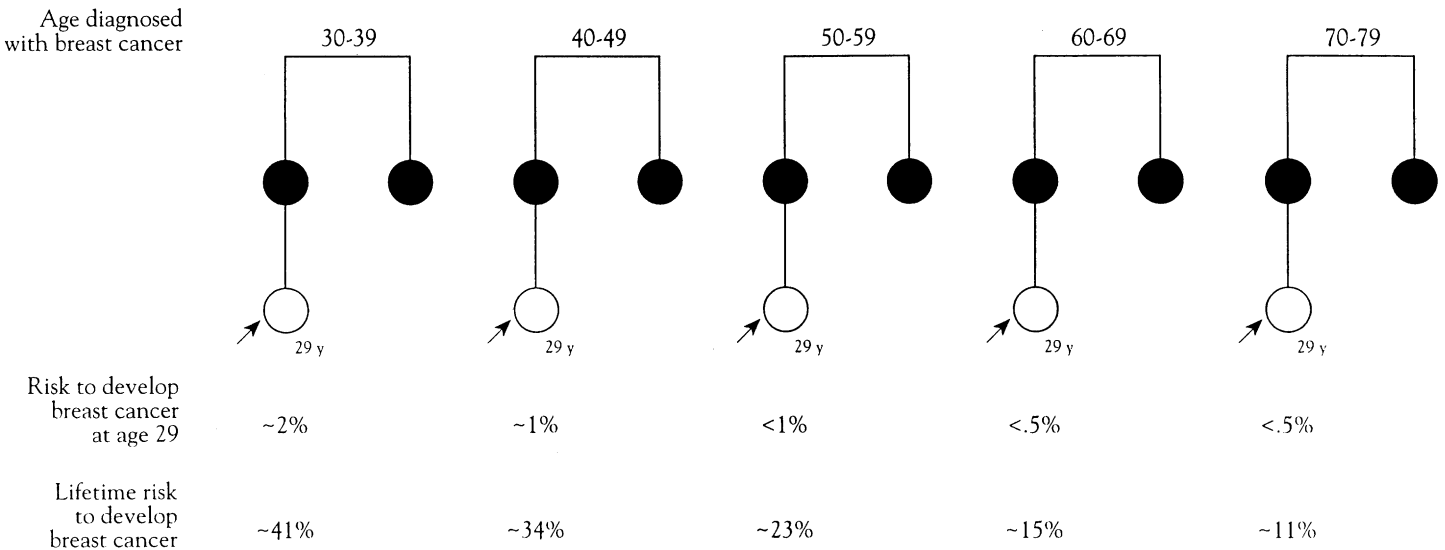

Fig. 1. Comparison of the empiric risk to develop breast cancer with the age of onset of breast cancer in a mother and maternal aunt. *Data from* Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. Cancer 1994;73:643–51.

Box 2. The pedigree: a cost-effective tool for genetic diagnosis and risk-assessment and for establishing patient rapport

A pedigree is useful for
- Developing a differential diagnosis
- Identifying genetic and environmental risk factors for disease
- Establishing a pattern of inheritance for genetic counseling and risk assessment
- Identifying medical risks for other relatives
- Deciding an approach to genetic testing (eg, whom to test)
- Planning medical management, prevention, and surveillance
- Assessing reproductive options
- Developing patient rapport and trust
- Recording a snapshot of family's health-related experiences
- Seeing family dynamics: sources of conflict or support
- Patient education; clarifying misconceptions

increased anxiety over this. On the other hand, having lived past the usual age for disease onset in his family, another patient may feel ''immune'' and may imagine that no further preventive measures are necessary. From a pedigree it is easy to see if a patient has an extended family that may provide emotional support in a time of illness or crisis. Important qualities of family relationships can be diagramed on a genogram. For example, bold lines can be used to show exceptionally close relationships, interrupted lines can indicate cutoffs with lack of communication, and jagged lines can show strong conflicts between individuals [8].

The visual nature of a pedigree also makes it a valuable tool for patient education (see Box 2). The chances of a son or daughter inheriting a genetic alteration can be explained using this visual tool. A pedigree can demonstrate variation in the expression of the condition, such as the varying ages of disease onset or degrees of disease severity. The intergenerational pattern of health risks in the family may become obvious to the patient when shown the pedigree. Some patients may be motivated to break the chain of behaviors or inherited genetic alterations that transmit ill health. For example, family violence and substance abuse, though multifactorial in cause, can appear in one generation after another. Viewing the pedigree can prompt productive discussion of the ways in which family might contribute to changing these patterns [8].

Recognizing patterns of inheritance

A pedigree helps to identify patterns of inheritance. Knowing the pattern of inheritance can help to establish a diagnosis [2]. Parents who are first

cousins or more closely related have a higher likelihood of having a child with an autosomal recessive condition than non-related couples [9]. A patient with neurologic findings of cerebellar ataxia may have many conditions to consider in the differential diagnosis, ranging from single gene and mitochondrial etiologies to environmental toxins [10]. If the ataxia presents in more than one generation and there is male-to-male transmission, an autosomal dominant pattern can be assumed. With such a family history, testing for the more common autosomal dominant causes of ataxia would be the most cost-effective approach as compared with testing for the rarer X-linked, autosomal recessive, or mitochondrial forms of ataxia.

Table 1 reviews some clues to classic patterns of inheritance. Refer to the article on Basic Genetics in this issue for sample pedigrees that illustrate these patterns. There are several factors that complicate identifying patterns of inheritance [2]. One of the biggest problems is small family size, which can be a particular dilemma in recognizing autosomal dominant or X-linked conditions. Limiting the family history intake to only first-degree relatives (parents, siblings, and children) underestimates familial risk, especially if the condition has an adult onset [2,11]. The rate of misattributed paternity in a population ranges from 1% to as high as 30%; thus, this can be a common problem in genetic risk assessment [12]. Delayed onset of symptoms or mild expression of the disease can complicate identifying patterns of inheritance and can lead to a missed diagnosis. Sex-limited disease expression can mask an inheritance pattern. For example, a woman who has no history of breast or ovarian cancer in her mother's family may be considered at low risk for breast or ovarian cancer, when actually her healthy father has sisters with breast or ovarian cancer, thus influencing his daughter's lifetime risk for developing breast or ovarian cancer.

Getting started: drawing a pedigree

Although as Francis Galton noted, "There are many methods of recording kinship, but for my own purposes, I prefer those I designed myself," a system of symbolization that is not interpretable by others has little usefulness [2]. Recognizing that there was wide variation in the pedigree symbols used in practice, in 1995 the Pedigree Standardization Task Force of the National Society of Genetic Counselors used a consensus process to develop standardized pedigree nomenclature [13,14]. This system of pedigree nomenclature is recognized as an international standard and is included in the American Medical Association's Manual of Style (10th edition) [15]. The standardized pedigree symbols used most commonly are shown in Figs. 2 and 3. Fig. 4 is a hypothetic pedigree using all of the standard pedigree symbols.

The following method is used often by genetic professionals to construct a complete pedigree. These pointers may be helpful to anyone in making an accurate representation of the family medical history. The pedigree drawing

begins with the consultand (the person seeking medical attention) or the proband (the affected individual who brings the family to medical attention), and radiates up the page to include relatives by ascent—that is parents, full siblings and half siblings, grandparents, aunts, uncles, half aunts, and half uncles. Next draw the descendants (children and grandchildren). It is important to clarify with the patient the exact relationships and that you are concerned about biologic relationships. Someone may not distinguish between an adopted sibling, half sibling, or full sibling. Descriptions of relationships of cousins also may be confused.

It is easiest to begin drawing the pedigree with your informant near the middle of the page. By convention, couples are drawn on the pedigree with the male partner placed to the left of the female partner. Siblings are recorded in birth order when possible from left to right, usually beginning with the oldest. Draw an arrow toward the square or circle representing your client (the consultand). Adding names or initials can help keep track of who is who on the pedigree. For healthy relatives who are related distantly to the consultand, it is acceptable to record the number of healthy individuals inside a square or triangle. For example, a square with a "5" inside represents five males, or a diamond with a "4" inside symbolizes four individuals of either gender.

Critical information to record

Typically a three-generation pedigree from the consultand (the person requesting the medical or genetic information) is recorded. Information is usually collected on first-degree relatives (children, siblings, and parents), second-degree relatives (half-siblings, aunts, uncles, nieces, nephews, grandparents, and grandchildren), and sometimes third-degree relatives (eg, first cousins). When a condition is suspected of being inherited, it is important to extend the history back as many generations as possible to include any additional affected relatives.

The health information to record on a pedigree is shown in Table 1. The square or circle representing an affected relative can be shaded. More than one condition can be shown on the pedigree by partitioning the circle or square into two to four sectors and shading the appropriate sector or by using different patterns. A pedigree key is necessary for accurate interpretation of the shading or any unusual abbreviations and less commonly used symbols (eg, adoption, donor gamete).

Recording the ethnic background of a client is important in genetic diagnosis. Certain genetic disorders are more common in specific populations, because individuals are likely to have a common gene mutation inherited from a distant ancestor. For example, the preconception or prenatal genetic screening that is offered to a couple who is of Ashkenazi Jewish ancestry differs from what would be offered to a couple of Southeast

Table 1
Examples of clues for recognizing basic patterns of inheritance and variables that can mask recognition of these patterns

Inheritance pattern	Mode of transmission	Pedigree clues	Confounding factors	Disease examples
Autosomal dominant	50% risk to each son or daughter	Male-to-male transmission Condition in multiple successive generations Males and females affected Often variability in disease severity Homozygotes may be affected more severely Homozygous state may be lethal (eg, achnodroplasia)	Reduced penetrance Mild expression of disease can miss diagnosis in relatives New mutations may be mistaken for sporadic if small family size	Familial hypercholesterolemia Postaxial polydactyly Neufibromatosis 1 Myotonic muscular dystrophy Marfan syndrome Huntington disease Breast-ovarian cancer syndrome Familial adenomatous polyposis (FAP)
Autosomal recessive	Parents "healthy" 25% risk to each son or daughter	Usually one generation Males and females affected Often seen in newborn, infancy, childhood Often inborn errors of metabolism May be more common in certain ethnic groups Sometimes see parental consanguinity	May be mistaken as sporadic if small family size	Cystic fibrosis Hemochromatosis Sickle cell anemia Phenylketonuria Tay-Sachs disease Beta-thalassemia Alpha-thalassemia Nonsyndromic neurosensory deafness Medium-chain-acyl-dehydrogenase (MCAD) deficiency
X-linked dominant	Heterozygous women affected with 50:50 risk to have affected daughter and 50:50 chance for affected male (though lethal)	No male-to-male transmission Often lethal in males so see paucity of males in pedigree May see multiple miscarriages (ie, lethal in male fetus) Females usually express condition but have milder symptoms than males	Small family size	Incontinentia pigmenti Orofacial digitial syndrome 1 Rett syndrome

X-linked	Women have 50% chance to have an affected son and 50% chance to have heterozygous daughter Heterozygous daughter may be affected Affected men cannot have son with condition	No male-to-male transmission Males affected Females may be affected but may be often milder and/or with later onset than males	May be missed if paucity of females in family Lyonization	Duchenne muscular dystrophy Red-green color blindness Hemophilia A (factor VIII deficiency) Fragile X syndrome
Chromosomal	Increased risk for trisomy seen with advanced maternal age Risk for affected fetus depends on specific chromosomal rearrangement (range 1%–15% though may be higher for some)	Suspect if individual has 2+ major birth defects or 3+ minor birth defects Fetus with structural anomalies Unexplained MR (static) especially with dysmorphic features Unexplained psychomotor retardation Ambiguous genitalia Lymphedema or cystic hygroma in newborn Couples with 3+ pregnancy losses Individual with multiple congenital anomalies and family history of MR Unexplained infertility		Trisomy 21 (Down syndrome) Trisomy 18 Turner syndrome (45,X) Robertsonian translocations

(*continued on next page*)

Table 1 (*continued*)

Inheritance pattern	Mode of transmission	Pedigree clues	Confounding factors	Disease examples
Mitochondrial	0%–100%	Father does not transmit condition to children; only mother does Highly variable clinical expression Often central nervous disorders Males and females affected, often in multiple generations May be degenerative		Mitochondrial encephalopathy with ragged-red fibers (MERRF) Mitochondrial encephalomyopathy, lactic acidosis, strokes (MELAS) Neuropathy with ataxia and retinitis pigmentosa (NARP)
Multifactorial	Based on empiric risk tables	Males and females affected No clear pattern Skips generations Few affected family members	May actually be single gene	Neural tube defects Scoliosis Cleft lip Schizophrenia Bipolar disorder

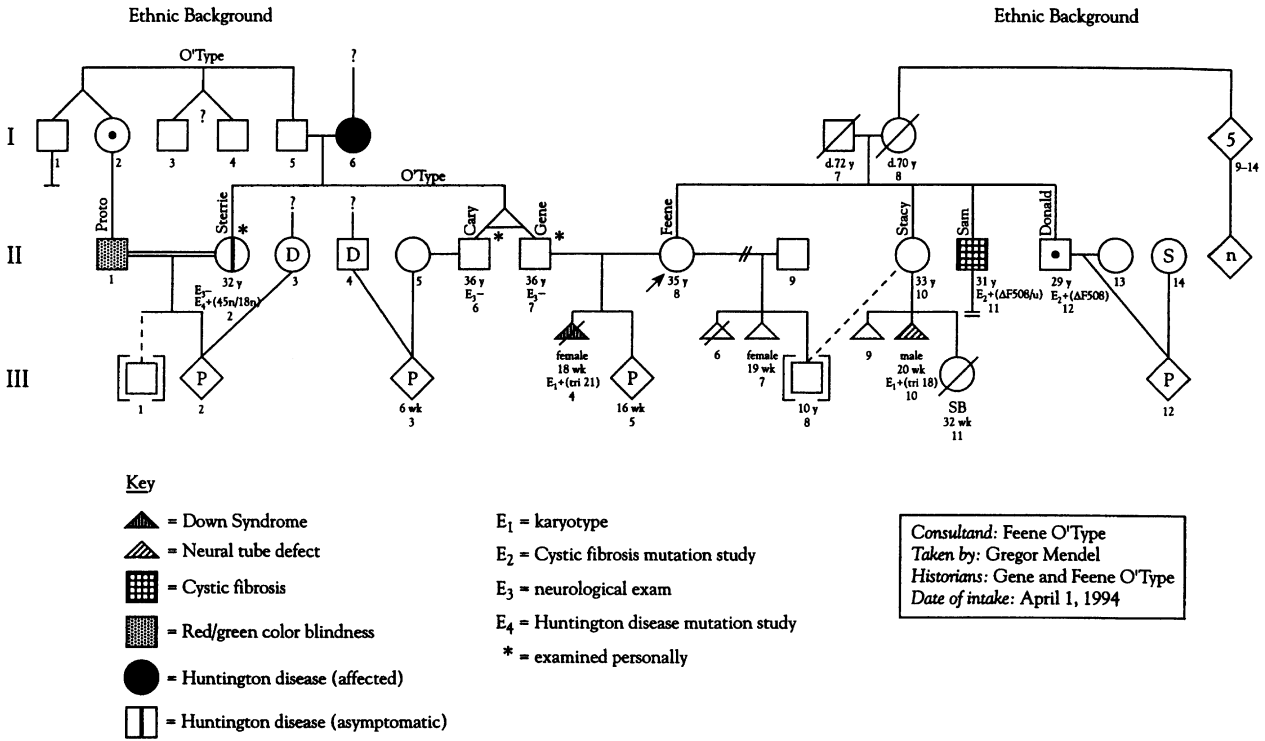

Fig. 2. Hypothetic clinical pedigree using standard pedigree nomenclature. *From* Bennett RL, Steinhaus KA, Uhrich SB, et al. Recommendations for standardized pedigree nomenclature. Am J Hum Genet 1995;56:745–52.

Pedigree Symbols

	Male	Female	Sex Unkown
Individual (assign gender by phenotype)	b. 1925	30	4 mo
Clinically affected individual (define shading in key/legend) Affected individual (> one condition)			
Multiple individuals, number known	5	5	5
Multiple individuals, number unknown	n	n	n
Deceased individual	d. 35 y	d. 4 mo	
Stillbirth (SB)	SB 28 wk	SB 30 wk	SB 34 wk
Pregnancy (P)	P LMP: 7/1/94	P 20 wk	P 16 wk
Spontaneous abortion (SAB), ectopic (ECT)	male	female	ECT
Affected SAB	male	female	16 wk
Termination of pregnancy (TOP)	male	female	12 wk
Affected TOP	male	female	12 wk
Consultand	b. 4/24/59	35y	
Proband	P	P	

Fig. 3. Commonly used pedigree symbols. *From* Bennett RL. The practical guide to the genetic family history. New York: Wiley-Liss; 1999. p. 141. Used with permission.

Asian ancestry (see article by Bubb and Matthews elsewhere in this issue). A woman with ovarian cancer who is of Ashkenazi ancestry has a higher probability of having a mutation in BRCA1 or BRCA2 (~26%) than a woman with ovarian cancer who is of northern European ancestry (~7%) [16]; therefore, the approach to genetic testing may differ [3].

Remember to include the name and professional background (eg, MD, PA, ARNP) of the person who recorded the pedigree and the date the

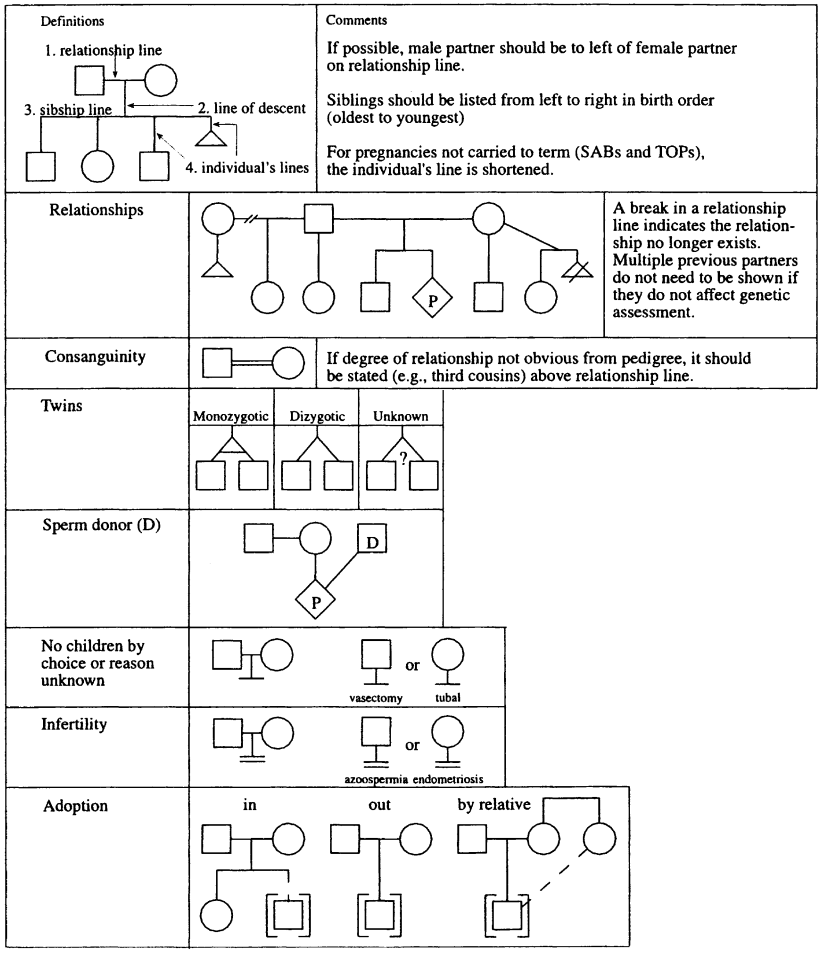

Fig. 4. Pedigree line definitions. *From* Bennett RL. The practical guide to the genetic family history. New York: Wiley-Liss; 1999. p. 141. Used with permission.

information was obtained. This way when other health professionals review the pedigree they know how long ago the information was recorded and if the pedigree should be updated. It is also helpful to record the name of the historian (such as the patient, parent, grandparent, or foster parent) in case additional information is needed.

The family history interview

Open-ended questions are the best way to obtain a range of health information. A line of questioning that begins, "Are your parents healthy?"

is likely to get a reply of "Yes," even if this is not correct. Instead the query, "Describe any medical problems that affect your mother and father" is more likely to disclose important health information. Some clinicians approach family history-taking by asking about a series of medical conditions [2], instead of or in addition to the query mentioned. For example, "Do any of your blood relatives have problems with their eyesight, hearing, bones, skin conditions, and so on?" It is worth inquiring about potential environmental or occupational exposures in extended family members, particularly smoking or alcohol abuse, or occupational exposure to toxins such as lead, asbestos, or other carcinogens. Consider closing the interview by asking, "Are there any conditions that you think 'run in' your family? Is there anything that I have not asked about that you feel it is important for me to know?" [2].

Remember that family medical history often contains emotionally charged information. The person giving the history may have been bereaved by miscarriages or by family members' premature deaths and may have witnessed suffering or helped to care for a chronically ill family member. Some diseases in some families are not discussed openly. Patients may be struggling with feelings of personal susceptibility, shame, or guilt about inherited conditions. Or they may be concerned about revealing secrets about family relationships, for example, a relative's true parentage, adoption, or incest. Skills of empathic interviewing thus are needed for family medical history-taking, as for any sensitive aspect of patient care. Furthermore, lay people may feel hurt or confused by terms commonly used in medical parlance; choice of descriptive words can help communication and develop rapport. For example, a family history can be called "free of X disease" or "noncontributory" rather than "negative" [2]. One can inquire about "miscarriages" or "pregnancy losses" rather than "spontaneous abortions." "Genetic alteration or change" is sometimes preferable to "mutation."

Approaches to obtaining and recording family history

Patients can be encouraged to bring their own family history to a medical appointment. Most people have a fascination with their ancestors. The popularity of the genealogy movement of tracing the social history of one's ancestors can be modified to include information about causes of demise and the age at death. There are many reasonably priced genealogy software programs that could enable clients to record family health information. Family gatherings can be occasions for communicating about family medical history.

Although most people have fairly accurate information about the health history of their parents, children, and often their siblings, the accuracy of their knowledge tends to decline for more distant relatives [2]. Appropriate interpretation of medical history information depends on the accuracy of

the information provided. Encouraging clients to confirm the diagnoses of relatives with medical records or death certificates is important in cases in which genetic risk assessment or diagnosis depends on accurate knowledge of relatives' diagnoses.

Creating a universal family history tool

In theory, a tool that would collect family history and then interpret it would seem to be the answer to the problem of primary care physician finding time to systematically record medical pedigrees [4,17]. There are many challenges to developing such an instrument. The type of family history information needed for a pediatric clinic visit, an adult clinic visit, a sports medicine visit, or a prenatal visit may be different. What health information is important to record? How accurate is the information collected? Who collects and records the family history information (ie, the clinician or the patient)? Does the tool consider cultural sensitivity and provide equal client access to the tool (eg, internet access, language barriers). How is the information collected? Is the tool web-based, a mail-in form, through a computer kiosk in a waiting area, or through a computerized phone interview? What is the purpose of collecting the health information? Is it to make a diagnosis in a patient, to identify a patient for further evaluation, or possibly to identify a set of family members who could benefit? The answers to these questions are complex and require a coordinated approach [11]. Currently the Office of Genomics and Disease Prevention in the Centers for Disease Control and Prevention is taking a public health approach to family history by funding projects that develop medical family history tools and test their clinical validity and usefulness [6]. Such studies generate evidence about whether simple, computer-administered family history tools are useful to stratify populations into those at low, medium, and high risk for disease. More important, can preventive measures targeted to families at increased risk be more effective than prevention recommended for everyone? And do people actually modify health behavior in response to medical advice based on the interpretation of such instruments?

Summary

All primary care practitioners should have basic competence in obtaining and interpreting a family medical history and pedigree or genogram. There are standardized pedigree symbols that are used to record a family history. A family pedigree remains a cost-effective and basic approach to identifying individuals at risk for genetic disorders, particularly for disorders that are common (such as heart disease, stroke, familial dementia, gait and movement disorders, and cancer). A pedigree can help to establish the pattern of inheritance and guide the practitioner in making choices about

molecular genetic testing. Medical geneticists and genetic counselors are experts in recording and interpreting family history information and can serve as a resource to family practitioners in making decisions about appropriate referrals for genetic counseling and testing. A pedigree not only serves as a basis for diagnosis and making recommendations for medical management and surveillance, but also is a primary method for patient education and developing patient rapport.

Resources for family history information

Centers for Disease Control Office of Genomics and Disease Prevention (Family History Public Health Initiative) www.cdc.gov/genomics/fHix.htm

The American Medical Association (genetics web pages, with sample family history forms) www.ama-assn.org

The National Coalition for Health Care Professional Education in Genetics www.nchpeg.org

The National Society of Genetic Counselors (web pages with guide for family history-taking) www.nsgc.org

March of Dimes, Genetics and Your Practice www.marchofdimes.org

References

[1] Pyeritz RE. Family history and genetic risk factors. Forward to the future. JAMA 1997; 278:235–60.
[2] Bennett RL. Practical guide to the genetic family history. New York: John Wiley and Sons; 1999.
[3] Hampel H, Sweet K, Westman JA, et al. Referral for cancer genetics consultation: a review and compilation of risk assessment criteria. J Med Genet 2004;41:81–91.
[4] Acheson L. Fostering applications of genetics in primary care: what will it take? Genet Med 2003;5:63–5.
[5] Medalie JH, Zyzanski SJ, Langa D, Stange KC. The family in family medicine: is it a reality? J Fam Pract 1998;46:390–6.
[6] Yoon PW, Scheuner MT, Khoury MJ. Research priorities for evaluating family history in the prevention of common chronic diseases. Am J Prev Med 2003;24:128–35.
[7] Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. Cancer 1994;73:643–51.
[8] McGoldrick M, Gerson R, Shellenberger S. Genograms: assessment and intervention. 2nd edition. New York: WW Norton & Company; 1999.
[9] Bennett RL, Motulsky AG, Bittles A, et al. Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the National Society of Genetic Counselors. J Genet Counsel 2002;11:97–119.
[10] Pulst SM, Perlman S. Hereditary ataxias. In: Pulst SM, editor. Neurogenetics. New York: Oxford University Press; 2000.
[11] Scheuner MT. Family history: where to go from here? Genet Med 2003;5:66–8.
[12] Lucassen A, Parker M. Revealing false paternity: some ethical considerations. Lancet 2001;357:1033–5.
[13] Bennett RL, Steinhaus KA, Uhrich SB, et al. The need for developing standardized family pedigree nomenclature. J Genet Counsel 1993;2:261–73.

[14] Bennett RL, Steinhaus KA, Uhrich SB, et al. Recommendations for standardized pedigree nomenclature. Am J Hum Genet 1995;56:745–52.
[15] Iverson C. American Medical Association manual of style: a guide for authors and editors. In press.
[16] Frank TS, Deffenbaugh AM, Reid JE, et al. Clinical characteristics of individual with germline mutations in BRCA1 and BRCA2: analysis of 10,000 individuals. J Clin Oncol 2002;20:1480–90.
[17] Frezzo TM, Rubinstein WS, Durham D, et al. The genetic family history as a risk assessment tool in internal medicine. Genet Med 2003;5:84–91.