

# Chapter 1

## *The Language of the Pedigree*

*Pedigrees are a challenge. With their intricate patterns of geometric symbols, pedigrees are like biological crossword puzzles which dare the clever and creative geneticists to solve them for clues about inheritance, family dynamics, or the localization of a gene.*

—Robert G. Resta (1995)

### 1.1 WHY TAKE TIME TO RECORD A GENETIC FAMILY HISTORY

The field of human genetics has revolutionized the practice of medicine. The cyberspace bible of human genetics—Victor McKusick's *Online Mendelian Inheritance in Man* (better known as OMIM)—lists more than 10,000 hereditary traits and conditions. Identification of genetic mutations through the International Human Genome Project makes genetic testing for most of these conditions a reality. Genetic susceptibility mutations are being identified as part of the causal nexus for complex medical conditions such as cancer, diabetes, heart disease, Alzheimer disease, and mental illness. Human genetics is no longer just a topic for obscure medical journals. Headlines heralding genetic advances are splashed across the fronts of newspapers and popular magazines. The gripping stories of people making heart-wrenching decisions about genetic testing and diagnosis increase the Nielsen ratings of Oprah Winfrey-style talk shows and hospital-based television medical dramas. Patients come to *you* wanting to know if they need to worry about a genetic disease during their pregnancies, in their children, or in relation to their own healthcare.

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How can you as a clinician identify individuals at risk for genetic disorders? Often, the first step is to take a genetic family history, recorded in the shorthand form of a pedigree. A pedigree, commonly referred to as a family tree, is a graphic representation of a medical-family history using symbols. A concise pedigree provides both critical medical data and biological relationship information at a glance. In many circumstances, the pedigree is just as important for providing medical services to the patient as any laboratory test. In fact, the pedigree has been described as the “first genetic test.” This is both a historical reference to the fact that pedigrees have been used in medicine for over 100 years and also that a pedigree is the first step for genetic evaluation. The pedigree is truly the symbolic language of clinical genetic services and of human genetic research.

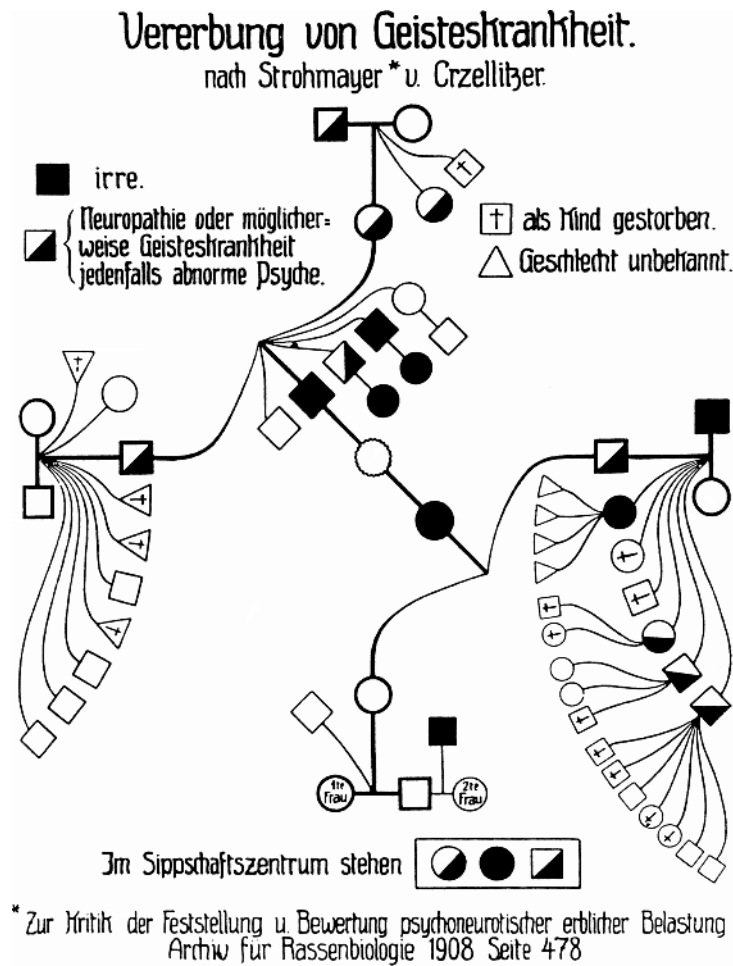
Genetic diseases affect all organ systems. Therefore health professionals from all specialties need to learn to think genetic. You need not be a “clever and creative geneticist” (Resta, 1995) to take a genetic family history. The purpose of this book is to provide you with practical screening tools to make an assessment as to whether your client might benefit from more extensive genetic evaluation and/or testing. My goal is provide you with not just the family history questions to ask but the logic behind this questioning. Health professionals working with clients in family practice, internal medicine, pediatrics, neurology, oncology, and obstetrics will find these screening tools particularly useful.

A focus of this book is genetic screening questions for clinical specialists by disease system (see Chapter 4). The emphasis in Chapter 5 and Appendix 3 is family history tools for identifying individuals with an inherited susceptibility to cancer. Researchers in human genetics will find useful information on how to obtain family history information, as well as ethical issues to consider in family studies and the publication of pedigrees (see Chapter 10). For the benefit of professionals involved in adoption, in Chapter 7 I discuss the unique issues surrounding a genetic family history and adoption. In Chapter 8 I delve into some of the challenging aspects of family history in the context of assisted reproductive technologies and the use of donor gametes. Appendix 4 is a medical-family history questionnaire that could be used for a child being placed for adoption, or for health information for an egg or sperm donor, or surrogate mother.

### 1.2 WHAT DO CRANES HAVE TO DO WITH ANYTHING?

The word *pedigree* comes from the French *pie de grue*, or “crane’s foot.” The term first appeared in the English language in the 15th century. It described the curved lines resembling a bird’s claws that were used to connect an individual with his or her offspring (Resta, 1993). Such vestiges of a bird’s talons are obvious in the example of the *sippschaftstafel* drawn by Ernst Rüdin shown in Figure 1.1. The *sippschaftstafel* was a form of depicting family ancestry used by German eugenicists in the early 20th century (Mazumdar, 1992; Resta, 1993).

A pedigree is of limited value if the symbols and abbreviations cannot be easily interpreted. Historically, many different pedigree styles have been used in the



**Figure 1.1** A sippschaftstafel drawn by German eugenicist Ernst Rüdin in 1910. Note the proband (circle with irregular edge) is placed in the center of the pedigree and the maternal and paternal lineages radiate from curved lines drawn to the proband). Here the proband is shown being crushed by the weight of her dysgenic ancestry. (Reprinted with permission from Mazumdar, 1992; and Resta, 1993.)

published literature and in patient medical records (Bennett et al., 1993; Resta, 1993; Steinhaus et al., 1995). In fact, genetics professionals probably use as many pedigree dialects as there are forms of the human language. As Francis Galton (an early geneticist and cousin to Charles Darwin) observed, “There are many methods of drawing pedigrees and describing kinship, but for my own purposes I still prefer those that I designed myself” (Galton, 1889). By using uniform symbols, it is possible to reduce the chances for incorrect interpretation of patient, family, medical, and genetic information.

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Through a peer-reviewed process, the Pedigree Standardization Task Force (PSTF) of the National Society of Genetic Counselors (NSGC) developed standardized nomenclature for symbolizing pedigrees (Bennett et al., 1995). These have become an international standard, and the symbol set has required little revision since the original publication (Bennett et al., 2008). All pedigree symbols in this book conform to these standards.

### **1.3 THE PEDIGREE IS A COST-EFFECTIVE TOOL FOR GENETIC DIAGNOSIS AND RISK ASSESSMENT FOR MANY DISEASES**

“But who has time to take a family pedigree?” is a common lament from the busy practitioner. Most clinicians record some information about a patient’s family illnesses in textual form. This can be just as time-consuming as recording a pedigree, and the text may be both lengthier and less informative than a pedigree. For example, consider this excerpt from a medical record:

Linda’s grandmother and two aunts died of breast cancer.

Did the cancer occur in Linda’s maternal or paternal grandmother? Are the aunts the sisters of Linda’s mother or her father? Did they have breast cancer before or after onset of menopause? The exact relationship of these affected relatives to Linda, their ages at diagnosis, and if the breast cancer was unilateral or bilateral can make a critical difference in your clinical assessment of Linda’s lifetime risk of developing breast cancer. Instead, using the associative icons of a pedigree, the relevant family and medical information can be recorded quickly and precisely, in an easily interpretable format. A family pedigree has many functions; it is a tool for:

- Making a medical diagnosis.
- Deciding on testing strategies.
- Establishing the pattern of inheritance.
- Identifying at-risk relatives.
- Calculating disease risks.
- Determining reproductive options.
- Distinguishing genetic from other risk factors.
- Making decisions on medical management and surveillance.
- Developing patient rapport.
- Educating the patient.
- Exploring the patient’s understanding.

Each of these benefits of collecting a pedigree will be explored further in this chapter.

## 1.4 JUST DO IT®

The popular advertisement “Just Do It” from the sports company Nike (Center for Applied Research, 2008) is applicable to the attitude that should be assumed by most health professionals regarding documenting a patient’s medical-family history. Taking a directed genetic history is a primary step in the evaluation of many medical disorders. Barton Childs (1982) predicts that “to fail to take a good family history is bad medicine and someday will be criminal negligence.” Notation of a genetic family history is likely to become an essential component of a patient’s electronic medical record (Bennett et al., 2008). The family history that is placed in a newborn’s electronic medical record may travel through the health system during that person’s life, with the pedigree undergoing various iterations as the individual faces age-related health risks and changing familial risks as diseases develop in relatives.

The ability to elicit a comprehensive medical family history including a family pedigree, is stated as a fundamental skill for all health professionals, according to the National Coalition for Health Provider Education in Genetics (NCHPEG, 2007). Peter Schwartz of Yale University School of Medicine states that for early screening and detection of gynecological malignancies, “Family history is crucial, and it’s not a superficial history. You have to go into depth” (Stone, 1998). Both the American College of Obstetrics and Gynecology (ACOG) and the American Society of Clinical Oncologists (ASCO) have had long-standing statements recording the importance of family history in obstetrics evaluations and cancer risk assessment, respectively (ACOG, 1987; ASCO, 1997).

Using a pedigree to symbolize a patient’s medical and genetic history is no more time-consuming than dictating a detailed summary for the medical chart. A pedigree is a way to compress pages and pages of medical information on to an 8½ by 11-inch piece of paper, or the screen of an electronic medical record. I always keep the patient’s pedigree in the front of his or her medical file. This saves me time at subsequent visits because most of the critical information I need is readily accessible and succinctly summarized in one page. The pedigree gives me an immediate image of the family’s health and sociological structure without the need to wade through stacks of medical records. Once a pedigree is obtained, the patient’s family history can be easily updated on return visits.

## 1.5 THE PEDIGREE AS A DIAGNOSTIC TOOL

Reviewing a family pedigree can aid the clinician in diagnosis. For example, in making a diagnosis of a familial cancer syndrome, it is imperative to know the cluster of types of cancers; the ages of the individuals diagnosed with cancer; and how closely the individuals with cancer are related to each other (i.e., first- or second-degree relatives) (see Chapter 5). The family history will even influence the kind of genetic diagnostic tests that are ordered.

Take, for example, the family history of Susan, a 30-year-old computer software engineer and the mother of three. She is interested in information about how she can

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be screened for renal cell cancer because her father, Sam, was recently diagnosed with clear-cell renal carcinoma. Additional family history information is needed to help determine if his cancer was sporadic (the most likely scenario), resulting in a relatively low risk for Susan to develop renal cell cancer, or if Sam has an inherited cancer syndrome for which genetic testing might be available. Some inherited cancer syndromes to consider might include von Hippel-Lindau syndrome, Birt-Hogg Dubé, tuberous sclerosis complex, Lynch syndrome, and Cowden syndrome (see Chapter 5). Many of these inherited cancer syndromes are associated with other tumors besides renal cell carcinoma, thus an accurate diagnosis is important for both Susan and Sam. Taking a multigeneration pedigree (Figure 1.2) can help identify cost-effective approaches to genetic testing for Sam and Susan.

### **1.6 USING THE PEDIGREE TO DECIDE ON TESTING STRATEGIES AND FOR EVALUATING AT-RISK RELATIVES**

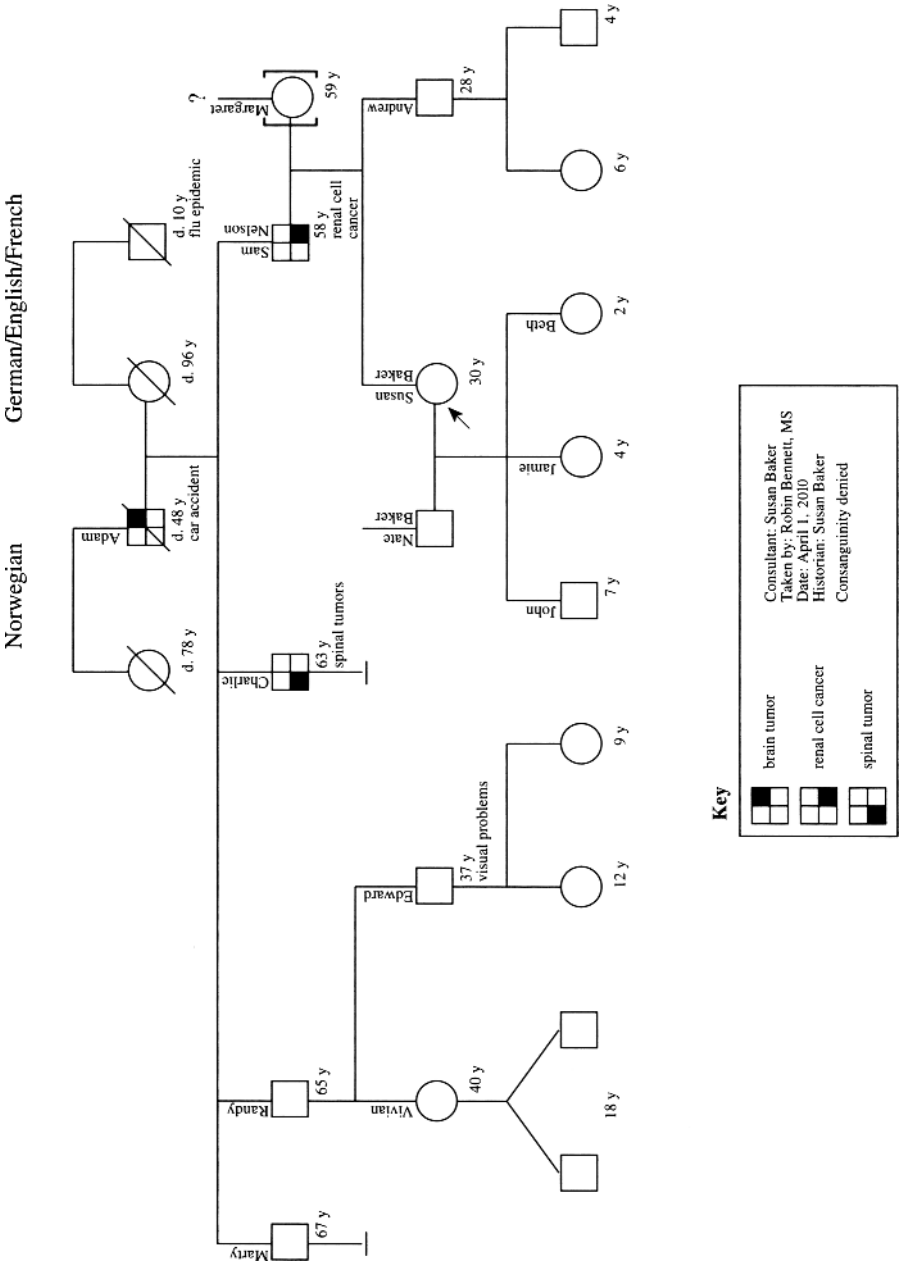
Susan's pedigree suggests von Hippel-Lindau (VHL) syndrome, given the history of spinal tumors in her paternal uncle Charlie and the history of a brain tumor in her paternal uncle Adam. Ideally the DNA testing should begin with Sam. If a mutation is identified in Sam, then accurate mutation analysis is available for Susan, her siblings, and other relatives. The pedigree helps you determine the appropriateness of genetic testing, the first person to test, and who else in the family should be tested.

### **1.7 USING THE PEDIGREE TO ESTABLISH THE PATTERN OF INHERITANCE AND CALCULATE RISKS**

John was born with a profound hearing impairment. He and his fiancée are planning a family, and they want to know if they have a high probability of having children who will also have severe congenital hearing impairment. This question is impossible to answer without obtaining a family history. Congenital deafness can have an autosomal recessive, autosomal dominant, X-linked, or mitochondrial inheritance pattern or it could have a maternal teratogenic etiology (see Section 4.3). How to use a pedigree to identify patterns of inheritance is detailed in Chapter 2. Once an inheritance pattern is identified or suspected, John and his fiancée can be given appropriate genetic counseling and possibly genetic testing.

### **1.8 A PEDIGREE CAN HELP DISTINGUISH GENETIC FROM OTHER RISK FACTORS**

A pedigree can be just as useful in determining that a condition is not genetic as in establishing that a condition is inherited in a family. This is particularly true for common complex health conditions such as mental illness, heart disease, and cancer. For example, Jean is a 42-year-old premenopausal woman with unilateral



**Figure 1.2** A hypothetical pedigree representative of a family with von Hippel-Lindau syndrome.

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breast cancer. Her mother is healthy at age 65 years, but Jean's maternal grandmother, Pamela, died of breast cancer at age 53. This limited family history may raise your initial suspicion for a familial breast cancer. Yet, when you take an extended family history, you find that Jean's mother has three healthy sisters between the ages of 68 and 72 years. You also find that Pamela had two sisters who died of heart disease in their mid-70s, but they had never developed cancer. For Jean, this "negative" family history is just as important as the "positive" family history of cancer for her cancer risk assessment and determining a strategy for cancer screening and risk reduction.

### **1.9 A PEDIGREE CAN DOCUMENT SHARED ENVIRONMENT AND SHARED GENETIC RISK FACTORS**

Families share their genes and often their environment. Relatives who are raised together often share the same environmental risks (such as secondhand smoke, pesticide exposure, and dietary preferences), lifestyle factors (such as patterns of exercise and alcohol use), styles of coping (such as how stress is dealt with), and even attitudes about health and wellness (for example, whether they use herbal supplements or seek medical care). A pedigree is a simple and accessible place to record these nongenetic factors that can influence wellness and disease processes.

### **1.10 A PEDIGREE CAN HELP IDENTIFY MEDICAL SCREENING NEEDS FOR HEALTHY INDIVIDUALS**

A brief family history can identify genetic and medical screening needs for an otherwise healthy person. For example, a healthy couple of Ashkenazi Jewish ancestry can be offered carrier testing for several genetic autosomal recessive disorders that occur with higher frequency in persons of this ancestry than in some other populations (Gross et al., 2008). Serum cholesterol screening can be considered for someone with a strong family history of coronary artery disease. A person with a first-degree relative with colon cancer before age 50 should be offered colonoscopy screening at a younger age than usual. A young woman with a strong family history of breast cancer might be offered breast cancer screening at an earlier age than is typically recommended, particularly if her relatives are premenopausal at the time of breast cancer diagnosis.

### **1.11 TAKING A FAMILY HISTORY IS A WAY TO ESTABLISH CLIENT RAPPORT AND FACILITATE PATIENT DECISION MAKING**

Your patients are more likely to comply with your recommendations if they trust you and have a relationship with you. The process of taking a medical-family history provides a prime opportunity to establish rapport with a client. A clear picture of family dynamics, family crisis and loss, ethnic and cultural background, and the patient's life experiences usually unfold while taking a patient's medical-family



history. These family relationships and life experiences will influence a patient's decisions about medical care and genetic testing.

Querying a patient about his or her family history puts the client in the role of the expert (McCarthy et al., 2003). This can empower a patient who may feel powerless in the healthcare setting or mistrustful of health professionals (Erlanger, 1990). A client may feel more like an active participant in decisions about his or her healthcare. Through the process of taking a family history, a client is likely to feel listened to, and the process may even decrease patient anxiety (Erlanger, 1990; Rogers and Durkin, 1984; Rose et al., 1999).

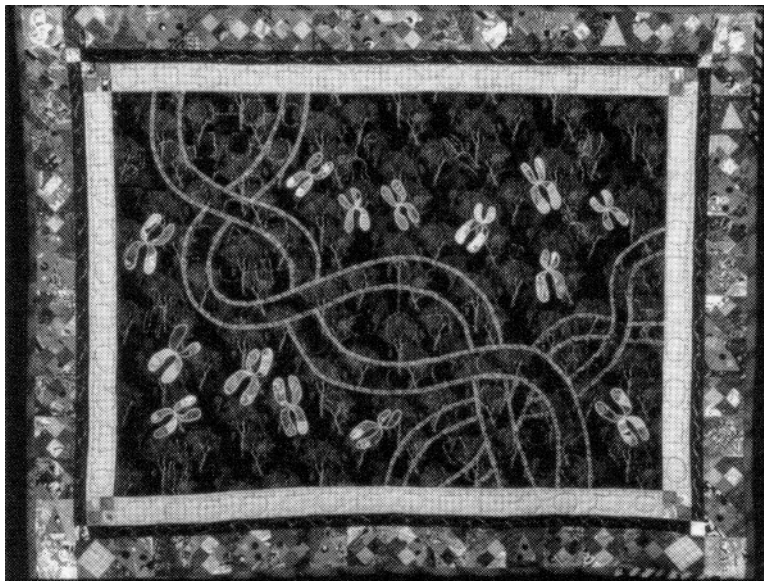
Compare Amanda, a healthy 37-year-old pregnant woman who has experienced 10 years of infertility, with Beth who is also 37 years old and pregnant but has two healthy children. Both women have the same age-related risk to have a child with a chromosome anomaly, yet each woman may make different choices about genetic testing during her pregnancy. Or consider two 45-year-old women who each have a mother diagnosed with breast cancer at age 38 years; one has a mother who survived her breast cancer, the other has a mother who died 2 years after diagnosis. Their genetic cancer risk assessments (drawn from factual empiric risk models) are similar, but the emotional feelings each woman has about the magnitude of her cancer risk, the effectiveness of breast cancer screening, and usefulness of genetic testing are likely to differ based on each woman's experience with her mother's illness.

The symbols of a pedigree represent more than the "geometric pieces of a biological crossword puzzle," as described by Resta (1993) in the introductory quote to this chapter. I view a pedigree like a quilt, stitching together the intimate and colorful scraps of medical and family information from a person's life (Figure 1.3). Familiar pedigree patterns are the clinician's matrix for providing pedigree risk assessment as well as clinical and diagnostic recommendations. Yet just as the quilter takes artistic liberty with tried-and-true patterns to make each quilt a unique work of art, each pedigree has a unique human story behind it. It is from the interwoven fabric of a patient's family, cultural, and life experiences that the patient pieces together his or her decision-making framework.

## 1.12 A PEDIGREE CAN BE USED FOR PATIENT MEDICAL EDUCATION

"A picture is worth a thousand words," or so the popular saying goes. Reviewing the pedigree with a patient is a vital tool in patient education (Table 1.1). Let us return to Susan's family in Figure 1.2. Susan's pedigree can be used to explain autosomal dominant inheritance: There are people affected in more than one generation, both men and women are affected, and there is male-to-male transmission of the disease. To establish the diagnosis of VHL, you may want to obtain medical records on the people you suspect are affected in the family (such as Susan's father, her uncle Charlie, and her paternal grandfather). By reviewing the pedigree with Susan, it is easy for Susan to see which family members she needs to obtain medical records from and why. The pedigree clearly defines who is at risk to develop VHL syndrome

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**Figure 1.3** *The Family Tree. Designed and stitched in 1997 by Josephine B. Rice of Gambier, Ohio, in celebration of her grandson Brian Alan Forthofer. Brian lived one day before dying from complications of trisomy 13 on March 6, 1997. (Photographed by Ted Rice, reprinted with permission.)*

in Susan's family. You can discuss with Susan a plan for contacting extended family members. Strategies for helping a patient obtain medical records are presented in Chapter 6.

Reviewing a pedigree is a simple tool for showing the variability of disease expression in a family. In Susan's family it is obvious that some people with VHL have lived to an old age with few problems, whereas others are more severely affected. Susan's family history also nicely illustrates the various tumors that can occur together

**TABLE 1.1 The Pedigree As a Valuable Tool in Patient Education**

The clinician can use a pedigree to:

- Review with the patient the need for obtaining medical documentation on affected family members.
- Help the patient recognize the inheritance pattern of the disorder.
- Provide a visual reminder of who in the family is at risk for the condition and discuss plans for sharing information with relatives.
- Demonstrate variability of disease expression (such as ages of onset).
- Assist the patient in exploring his or her understanding of the condition.
- Discuss shared familial environmental risk factors (such as tobacco).
- Clarify patient misconceptions.

or in isolation in association with VHL. Seeing this visual representation of her family may help motivate Susan to follow your medical screening recommendations because, at a glance, she is reminded of the effect that VHL has had on her extended family.

The visual representation of a pedigree is a stark reminder that a genetic disease is a shared condition; a whole family is influenced. A clinician can use this as a compelling reminder to the patient that it is never any one person's fault that a genetic disease is present in a family.

### 1.13 USING A PEDIGREE TO EXPLORE A PATIENT'S UNDERSTANDING AND TO CLARIFY MISCONCEPTIONS

Reviewing the pedigree with Susan is an excellent way to explore her feelings about being at risk for VHL as well as her understanding of the disease:

- Should Susan's children have genetic testing and medical screening for VHL?
- How will Susan feel if she finds she is affected with VHL and that her children are at risk for this condition?
- Should Susan's children have genetic testing and medical screening for VHL?
- If Susan has VHL, what type of support does she have from her extended family to deal with her chronic illness?
- How will Susan feel if she is unaffected with VHL, but her sister is affected or vice versa?

Almost invariably a person seeking information about a genetic disease or genetic testing has already reached some of his or her own conclusions about the inheritance of their "family's curse." In fact, considerable family lore may center on complicated theories about the inheritance of the disease in question. For example, Susan might think that she is not a risk for VHL in her family because mostly men are affected. You can point out to Susan that her father did not have any sisters. Or Susan may falsely believe that the eldest sibling is spared from disease. A pedigree can be a wonderful way to clarify patient misconceptions. Table 1.2 lists many of the common misconceptions patients have about the inheritance of a condition in their family.

### 1.14 OTHER FAMILY DIAGRAMS: GENOGRAMS AND ECOMAPS

Genograms are common tools of therapists and some family practice professionals. They include demographic information (age, dates of birth and death), functional information (data on medical, emotional, and behavioral functioning of different family members) and critical family events (McGoldrick et al., 1999). Nonbiological relationships (such as a housemate or office co-worker) can be included on a genogram.

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**TABLE 1.2 Common Patient Misconceptions and Beliefs about Inheritance**

- Ø If no one else in the family is affected, the condition is not inherited.
- Ø If several people in the family have the same condition, it must be inherited.
- Ø All birth defects are inherited.
- Ø The parents (particularly the mother) must have done something before conception or during the pregnancy to cause the condition in their fetus or child.
- Ø An external event caused the problem (such as radiation from flying in airplanes, living near a power line or a nuclear reactor, a lunar eclipse).
- Ø An evil spirit or an angered ancestor caused the disease.
- Ø With a 25% recurrence risk, after one affected child, the next three will be unaffected.
- Ø With a 50% recurrence risk, every other child is affected.
- Ø The disease skips a generation.
- Ø Birth order influences disease status (for example, only the eldest or youngest child can be affected).
- Ø If the affected individuals in the family are all women, the condition must be sex-linked.
- Ø A person will inherit the genetic condition because he or she looks or acts like the affected relative(s). Or the opposite—a person will not inherit a condition because he or she bears no resemblance to the affected relative(s).
- Ø For a condition with sex-influenced expression (such as breast cancer), individuals of the opposite sex cannot transmit the condition (for example, a male cannot pass on a gene alteration for breast cancer).

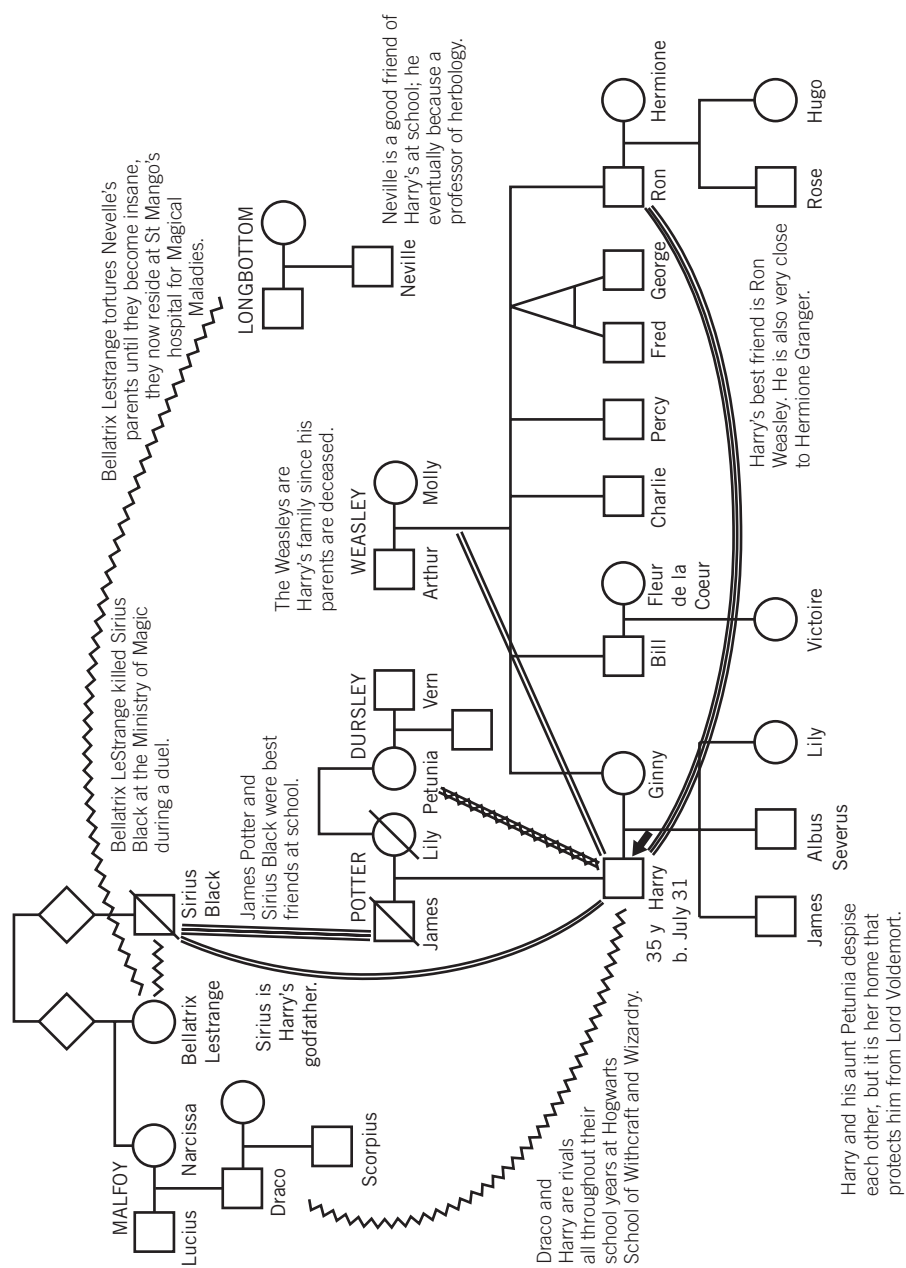
Source: Modified from Connor and Ferguson-Smith, 1997.

The symbols of a genogram are construed similar to a pedigree (with males as squares and females as circles), with usually three generations pictured. Pertinent relationships are further described by *communication lines* that connect the symbols (McGoldrick et al., 1999):

- == Close, open communication with few secrets.
- ≡ Very close or fused; open communication without secrets.
- ^^^ Poor communication, conflictual, many disagreements and secrets.
- ..... Distant communication (may be from geographic or lifestyle differences).
- ⊣ Estranged or cut off (no communication; may be from conflict or separation such as divorce).
- #### A relationship can be both close and conflictual (a double line with a zigzag through it).

A sample genogram is shown in Figure 1.4 deduced from the fictional families of Harry Potter and Ron Weasley from the acclaimed book series by J. K. Rowling.

Pedigrees also often include information about levels of communication but not in the explicit format of a genogram. For example it may be noted on a pedigree that a person is adopted and has no contact with his or her birth family or that a person is estranged from certain relatives. In general, genograms seem most useful for a



**Figure 1.4** Genogram of the fictional families of Harry Potter and Ron Weasley from the J. K. Rowling Harry Potter series. (Illustration courtesy of Leslie Clarleglio.)

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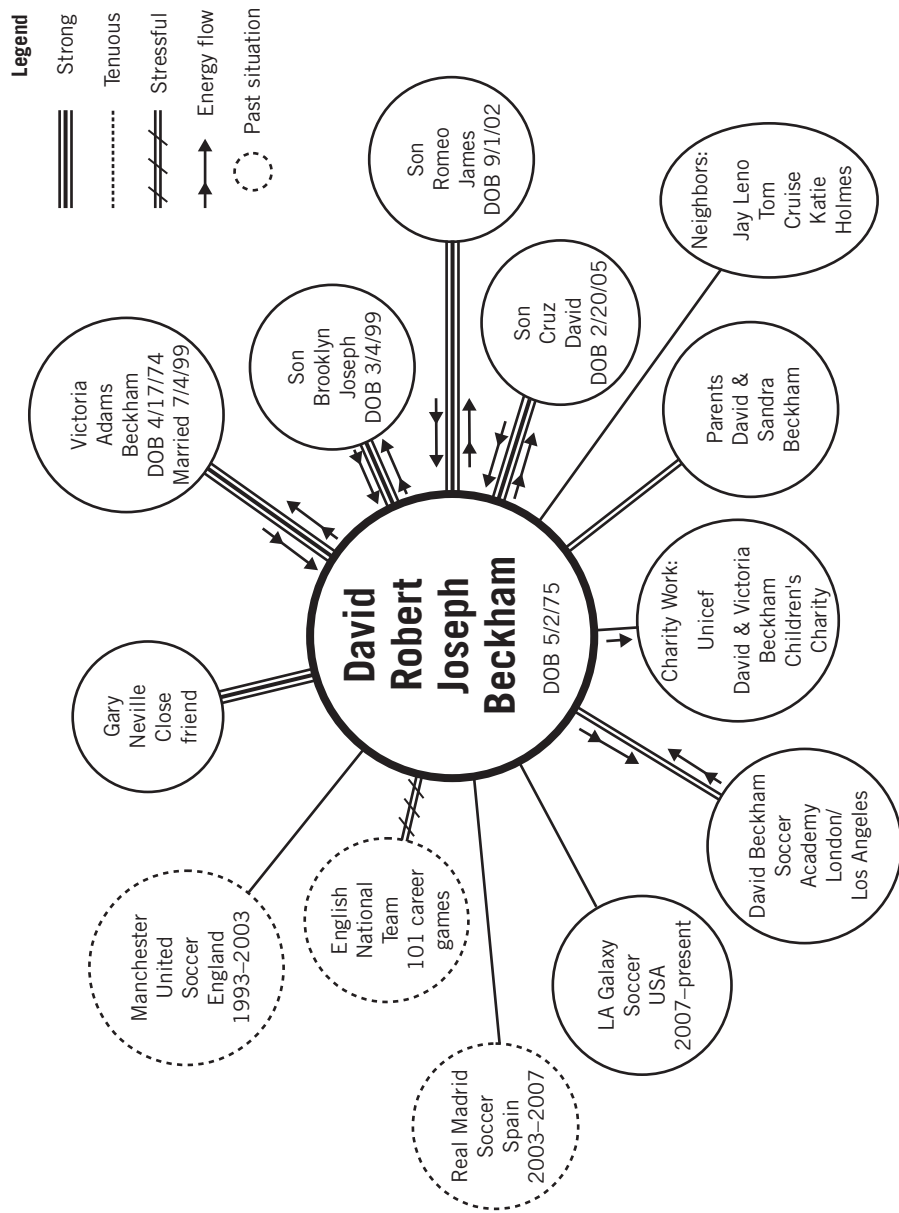
therapist's chart or process notes when working with a client in long-term therapy; this documentation is traditionally not part of a patient's common medical record that is shared with other health professionals. As construed currently, a genogram is not as multifunctional as a pedigree, particularly for disease risk assessment and informing strategies for genetic testing. The crisscross effects of the multiple communication lines of a genogram may actually clutter the family graphic to the extent that it becomes difficult for the clinician to attend to the most relevant health information for that office visit.

Ecomaps are also a tool used primarily in personal and family therapy. The format resembles a wheel, with the client in the center, and the social relationships (some of which are also biologic) and agencies (such as church, employer, etc.) are in a circle surrounding the client. The clients "circle of life" may include his or her employer, teacher, sports coach, church and/or religious leader, friend, neighbor, and relatives (partner or spouse, children, parents, etc.). The "spokes" of the wheel are similar to the communication lines of genograms, showing them as close, conflictual, distant, etc. (Rempel et al., 2007). The Ecomap is then used to assess the client's or family's support network. Consideration of how this approach may piggy-back with a traditional genetic pedigree is a future area of research (Kenen and Peters, 2001). A sample ecomap is shown in Figure 1.5 using information on the professional soccer player David Beckham ([http://en.wikipedia.org/wiki/David\\_Beckham](http://en.wikipedia.org/wiki/David_Beckham); [http://en.wikipedia.org/wiki/Victoria\\_Beckham](http://en.wikipedia.org/wiki/Victoria_Beckham); <http://www.davidbeckham.com/>; <http://la.galaxy.mlsnet.com>).

The professional genetics organizations should coordinate efforts with the professional societies of family therapists and those of family practice practitioners (such as nurses, physicians assistants and physicians) to consider the potential benefits of melding pedigrees and genograms (and possibly ecomaps) into a standardized format. There is a tricky balance between recording enough information to make the family diagram useful and including so much information that the graphic can no longer be quickly and concisely interpreted. The pedigree's utility lies in its ability to simply and graphically depict complex information so that disease patterns and risks, and biological relationships are immediately and obviously visible. The pedigree can already be used as a psychosocial assessment tool as discussed in Section 9.2.

### 1.15 THE CONTINUING EVOLUTION OF THE PEDIGREE IN THE AGE OF GENOMIC MEDICINE

Genomics describes the study of the interactions among genes and the environment (Guttmacher and Collins, 2002). The ability to practice genomic medicine by potentially viewing the molecular status of each patient's individual genome has an effect on all medical disciplines. Yet it is absurd to think that a complete genomic reference map will then lead to the understanding of all that is human or that we are all the direct and inevitable consequence of our genome. The genetic family history will continue to play an essential role in the medicine of the 21st century. As Reed Pyeritz



**Figure 1.5** Ecomap of professional soccer player David Beckham, based on information from the public domain as of February 2009. (Illustration courtesy of Leslie Clarleglio.)

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(1997), former president of the American College of Medical Genetics succinctly summarized:

The importance of the family history will only be enhanced in the future. 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 context in which the genome is expressed, and the family milieu is as good a guide as any. Physicians can help define those contexts through careful family and social histories. How those histories can be obtained and interpreted, when the average time for patient interaction with a physician continues to diminish, are crucial areas for research.

Variation is the hallmark of humans—even within well-established diseases with known patterns of inheritance, there is remarkable disease variability. Pedigree assessment will continue to play a critical role in our understanding of gene expression. A patient who has a genetic disorder or one who carries a genetic susceptibility mutation cannot be viewed in isolation from the background of his or her family history. How is it that five relatives with the same gene mutation can all have different ages of disease onset and varying clinical manifestations of the same genetic disorder? The patient and his or her genotype must be examined in the context of his or her genetic and environmental exposures. The clues from buried ancestors can reach out to the present to provide solutions for the future.

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