Chapter 2 Literature Review

Genetic and inherited diseases are major medical problems in the world. These diseases include mental disorders, birth defects and blood diseases that are passed down from one generation to another. Many common medical conditions such as diabetes mellitus, cancers and hypercholesterolaemia have familial predisposition. According to a study in the United Kingdom, 40.3% of patients who attended clinics for examination and consultation have one or more diseases with genetic component in their family history (Rose et al, 1999). Diseases with genetic components could have an effect on the patient’s health, and potentially that of their offspring.

Family history contains important information about each family member. It can be used in diagnosis and in genetic counselling. The social aspect of a family history has shifted to the evaluation of genetic or inherited conditions running in a family. Doctors inquire about family diseases as part of their medical evaluation process. This information is recorded in narrative form and may be difficult to analyse or interpret.

For example, Sarina’s grandmother died of breast cancer while two of her five aunts were diagnosed to have breast cancer. This statement does not indicate how her aunts are related to Sarina’s mother or father. Do the aunts have a biological relationship with Sarina’s grandmother who had cancer? The exact relationship of her aunt to Sarina, together with other details, will make a difference in the interpretation of the family history during genetic counselling. In view of this, the Center for Disease Control and Prevention (CDC) in the United States of America has advocated the Family History Public Health Initiative (2002). This was undertaken because a positive family history of a genetic disorder was found to be a risk factor for many common (multifactorial) diseases, and this knowledge is underutilised in preventive medicine. Many members of
the public are familiar with the charting of their own family tree as there is relatively widespread use of pedigrees in the public domain.

A pedigree or family tree chart is informative with regards to the relationship of a person with his family members and his/her ancestors, as well as the documentation of the phenotype and genotype, if available. It is a standard practice for genetic professionals to construct a genetic pedigree tree during encounters with patients seeking genetic services (Benkendorf et al, 2000). The pedigree tree may be used to analyse Mendelian inheritance of certain traits. This is particularly useful in paediatric practice, where a family may seek genetic counselling following the birth of a child with birth defects or severe learning disabilities. Other situations that may require a detailed pedigree include a positive family history of single gene disorders, members of a high-risk ethnic group, consanguineous marriages, prenatal diagnosis, inherited metabolic disorders and adult-onset genetic disorders such as Huntington’s disease and familial cancers (Bankhead et al, 2001).

There are many situations in general practice where the family history might be needed for genetic counselling.

i. Preconception

Prior to conception, there are a number of factors that might require patients to seek and benefit from genetic counselling. The reasons are shown below (Johnson and Christianson, 2006c):

- A positive family history of a genetic disorder (e.g., fragile X syndrome, muscular dystrophy, cystic fibrosis) and concerns about recurrence.
- Members of a high-risk ethnic group.
- Previous infertility or sterility problem.
- Exposure to potential teratogenic or mutagenic agents.
• Maternal health (e.g., diabetes, phenylketonuria or PKU, epilepsy).

• Consanguineous marriage.

• Anxieties over childbearing.

• Two or more prior miscarriages or pregnancy losses.

• A previous stillborn child.

• A previous child with a genetic or chromosomal disorder or birth defect (e.g., neural tube defect, Down’s syndrome, phenylketonuria or PKU).

ii. Prenatal

Women will benefit from prenatal diagnostic tests and genetic counselling. This will help them to determine whether the foetus has any abnormality in their chromosome or has certain single gene disorders. The reasons are shown below (Johnson and Christianson, 2006c):

• Women who are 35 years of age or older at delivery.

• A woman and/or her partner who are known to carry gene coding for a genetic disorder.

• A woman or her partner who is known to carry a chromosome rearrangement or abnormality.

• Couples with a family history of neural tube defect.

• Couples with a previous child born with multiple congenital anomalies or a chromosome abnormality.

• Women with an abnormal level of maternal serum alpha fetoprotein (AFP), human chorionic gonadotrophin (hCG), or estriol (uE3).

• Women exposed to an infectious disease, radiation, drugs or other environmental agents during pregnancy.
iii. Infancy and Childhood

An infant or a child might benefit from genetic counselling based on the following reasons (Johnson and Christianson, 2006c):

- A history of intrauterine growth retardation or failure to thrive.
- Abnormal growth patterns (short stature, obesity, excessive growth).
- Ambiguous or abnormal genitalia, earlier onset of puberty.
- Microcephaly, macrocephaly or craniosynostosis.
- Psychomotor delay or mental retardation.
- Hypotonia, hypertonia.
- A parent, sibling or relative who has problems similar to those observed in the patient.
- Abnormal or unusual facial features.
- Abnormal body and limb proportions, asymmetry.
- Major or minor congenital anomalies.
- Metabolic disorder.
- Muscular weakness.
- Bleeding tendency.
- Blindness or deafness.
- A significant regression in developmental progress.
- An unusual body odour.
- Excessive unexplained vomiting.
- Unusual behaviours, especially when associated with minor malformations (hand biting, hand flapping, autistic symptoms, abnormal sleep patterns, etc.).
iv. Adolescence and Adulthood

Adolescents and adults might be referred for genetic counselling based on the reasons below (Johnson and Christianson, 2006c):

- Abnormal sexual maturation.
- Amenorrhea (failure to menstruate), delayed puberty.
- Growth retardation.
- Excessive tall stature.
- A diagnosis of an adult onset genetic disease (e.g., Huntington’s disease, Marfan’s syndrome, myotonic dystrophy)
- A positive history of familial disorders (e.g., colon cancer, breast/ovarian cancer, familial hypercholesterolemia, psychiatric or behavioural disorders).
- Members of high-risk groups who want to pursue carrier testing for single gene disorders or chromosome abnormalities (e.g., Tay-Sachs’ disease, Duchenne’s muscular dystrophy, haemophilia, sickle cell anaemia, translocation carrier).
- Paternity testing.
- Questions about genetic diseases or birth defects in immediate or extended family members.

A pedigree chart can provide informative and important messages to enable us to understand the cause of these diseases. It is time-consuming for genetic counsellors to draw the pedigree chart manually. A good pedigree tree drawing system will save time compared to drawing it manually or writing it out. It also makes it easier when one needs to draw and update a pedigree tree for a large family hierarchy.
2.1 Pedigree Analysis

Pedigree analysis may alert genetic counsellors on the possibility of genetic factors running through a family, and thus, it might be necessary to establish the type of inheritance. It is also used to estimate the risk to other family members and to summarise an individual’s genetic data (Rose and Lucassen, 1999). The pedigree data play an important role in facilitating communication between clinical geneticists. The collection of extended pedigrees represents a powerful sampling design for quantitative genetic and linkage studies of both normal and disease-related quantitative traits (Williams-Blangero et al, 2006).

2.1.1 Family information required

A pedigree chart should contain some information related to the reason for recording the family history because this can reveal the important risk factors for several common diseases. The family history can also be a useful indicator of whether a patient may benefit from additional screening for certain conditions, such as breast or colorectal cancer (Bankhead et al, 2001). For family members who are looking for occurrence of a specific disease such as colon cancer, other medical information unrelated to this disease can be ignored. However, it is good to have more general information about family members on the pedigree.

In constructing a pedigree, information related to the reason for seeking genetic counselling is required. According to the National Society of Genetic Counselors (NSGC), family history, as well as medical and health information, should be collected (National Society of Genetic Counselors, 2006). The general information of family members may include their age or year of birth; year of death or age of death (for family members who are dead); cause of death and the year or age diagnosed (for
family members who are dead); relevant diseases with year and age at time of diagnosis and genetic testing results for those who are gene carriers/affected individuals. The Pedigree Standardization Task Force (PSTF) was established through the Professional Issues Committee of the NSGC to make recommendations for standardised human pedigree nomenclature (Bennett et al, 1995). There are some commonly recognised symbols used for constructing the pedigree chart.

### 2.1.2 Symbols used in Pedigree

There are three main symbols that are used to keep track of human genetic traits and to infer genotype (Abedon, 1997):

a. Males are designated with square symbols.

b. Females are designated with round symbols.

c. Lines are drawn to indicate marriage, parent-offspring relationships, and relationships between siblings.

The recommendations for a genetic family history are shown in Figures 2.1 - 2.4. There are some commonly recognised symbols that are used for constructing the pedigree chart. Figure 2.1 shows the common symbols for an individual, the affected individual, multiple individuals with known number of family members and unknown number of family members, diseased individuals, stillbirth, pregnancy, proband and consultand.
Besides the common symbols shown in Figure 2.1, there are pedigree symbols to show the abbreviations for pregnancies not carried to term, as shown in Figure 2.2. There are four different types of symbols for Spontaneous abortion (SAB), Affected SAB, Termination of pregnancy (TOP) and Affected TOP.
Figure 2.2: Pedigree symbols and abbreviations for pregnancies not carried to term (Bennett et al, 1995)

The common relationship lines used to construct the pedigree are marriage, consanguineous marriage, extramarital union and divorce. The relationship line definitions are shown in Figure 2.3.

Figure 2.3: Relationship line definitions (University of Alberta, 2006)

Consanguineous marriage is the union of individuals having a common biological ancestor. It is important to know about a consanguineous marriage in a family history. A consanguineous mother has more stillbirths than a non-consanguineous mother and studies have shown that consanguinity is a factor of birth defect and must be taken into account for genetic counselling (Stoll et al, 1999). By identifying consanguinity in a family, there is suspicion of an autosomal recessive condition. It will also affect recurrence risks for multifactorial conditions (Bennett, 2002).
The definitions of the ‘relationship line,’ the ‘line of descent,’ the ‘sibship line’ and the ‘individual’s line’ are shown in Figure 2.4.

<table>
<thead>
<tr>
<th>Definitions</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>1. relationship line</td>
<td>If possible, male partner should be to left of female partner on relationship line.</td>
</tr>
<tr>
<td>2. line of descent</td>
<td>Siblings should be listed from left to right in birth order (oldest to youngest)</td>
</tr>
<tr>
<td>3. sibship line</td>
<td>For pregnancies not carried to term (SABs and TOPs), the individual’s line is shortened.</td>
</tr>
<tr>
<td>4. individual’s lines</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
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</thead>
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<tr>
<td>a. Relationships</td>
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<tr>
<td>b. Consanguinity</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Line of descent (vertical or diagonal)</th>
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</thead>
<tbody>
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</tr>
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<td>Twins</td>
</tr>
<tr>
<td>Mosaic, Diagonal</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Family history not available/known for individual</th>
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</thead>
<tbody>
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<td>No children by choice or reason unknown</td>
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<td>Indicate reason, if known.</td>
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</table>

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<th>4. Infertility</th>
</tr>
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<tbody>
<tr>
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<tr>
<th>b. Adoption</th>
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<tbody>
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</tr>
<tr>
<td>out</td>
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<tr>
<td>by relative</td>
</tr>
</tbody>
</table>

Figure 2.4: Pedigree line definitions (Bennett et al, 1995)

### 2.1.3 Generation on Pedigree Chart

A pedigree chart will not only show a record of an individual family but it can also be used to study the transmission of a hereditary condition from the last few generations. Figure 2.5 shows the common symbols for an individual, the affected individual,
multiple individuals with known number of family members and unknown number of family members, deceased individuals, stillbirth, pregnancy, proband and consultand from five generations (Roman numerals I to V).

Figure 2.5: Pedigree chart for five generations of a family

It is important to keep the generation lines clearly defined. Individual IV-4 (arrowed bottom right) is the consultand. She and her husband (IV-3) are first cousins (double lines). The consultand, her partner and two of their offsprings (V-2 and V-3) are carriers for an autosomal recessive condition. One of their offsprings (V-4) is affected with the disorder. Both the maternal and paternal grandfathers (II-1 and II-2) are deceased. Individuals of the same generation are placed on the same line, even though they have a big age difference. The generation lines should be numbered from top (oldest generation) to bottom (youngest generation) with Roman numerals I, II, III, and so on.
The individuals in each generation line should be numbered 1, 2, 3, and so on, moving from left to right (Johnson and Christianson, 2006a).

2.1.4 Interpretation of a pedigree

On the basis of the information represented in a pedigree, doctors may stratify risk to identify those who can be reassured and to refer those with an elevated risk to a genetic centre clinic for further testing (Knottnerus, 2003). A screening pedigree, when no particular diagnosis is expected, will be scrutinised for a common diagnosis or common theme running through. A pedigree with a positive finding may lead to further enquiries regarding risk factors that may point to a possible genetic cause or a particular mode of inheritance. Common Mendelian modes of inheritance such as autosomal dominant, autosomal recessive, X-linked dominant or recessive, chromosomal or mitochondrial inheritance may be inferred from a comprehensive pedigree. This may lead to estimation of the recurrence risk and recommendation of appropriate tests or preventive measures.

The following questions will help a novice to interpret a pedigree he is analysing (Rose and Lucassen, 1999):

- Is there a common diagnosis or common theme running through this pedigree?
  A common theme could be different cancers determined by the same gene; different diagnoses that could be euphemisms for the same diagnosis for example, depression, dementia, or chorea for Huntington’s disease.

- Does the family history fit a particular mode of inheritance?

- Are there other factors in the pedigree that alert you to a possible genetic cause?
  For example, common diseases such as cancers and heart disease occurring at an unusually early age in a number of relatives.
• Are there diseases present which are multifactorial but are known to have some genetic basis? For example, diabetes mellitus or rheumatoid arthritis.

The pedigree should also be looked at from the aspect of advising the patient what to do next (Rose and Lucassen, 1999):

• Is there enough information to estimate the person’s risk of being a gene carrier or developing the disease? This is unlikely to be the case after the initial history taking, unless there is no obvious genetic pattern. A discussion about general risk and preventive measures could ensue.

• What further information is required to make a firm diagnosis? How will this be obtained?

• Is there a gene test available for this disease?

• Is there a diagnostic test other than gene test to identify presymptomatic carriers, for example, colonoscopy to detect familial polyposis coli?

• Is presymptomatic screening available for the disease in question?

• Are other preventive measures or advice appropriate?

The following sections discuss the analysis of hereditary diseases based on family history by constructing the pedigree.

i. **Autosomal Dominant Inheritance**

Autosomal dominant inheritance refers to disorders that are expressed in the heterozygote, i.e., the affected person has a mutated allele and one allele that is functioning normally (U.S. National Cancer Institute, 2006).
The following are the characteristics of an autosomal dominant pedigree, and they are also illustrated in Figure 2.6 (Johnson and Christianson, 2006b):

- Affected individuals are usually present in each generation, creating a vertical pattern of inheritance.

- Approximately 50% of the children born to an affected individual will be affected, provided the partner is unaffected.

- Both males and females can be affected, therefore, male to male transmission is possible.

![Figure 2.6: A typical autosomal dominant pedigree](image)

**ii. Autosomal Recessive Inheritance**

Autosomal recessive inheritance refers to an inheritance pattern in which an affected person must be homozygous, i.e., carry 2 copies of a mutant gene, one from each parent (U.S. National Cancer Institute, 2006).

The following are the characteristics of an autosomal recessive pedigree, and they are illustrated in Figure 2.7 (Johnson and Christianson, 2006b):
• The parents of an affected child are usually clinically normal and, as a rule, they are not aware that they carry a recessive gene until after the birth of an affected child.

• It is highly unusual to find other affected individuals in preceding or succeeding generations. The disorder is generally found only in siblings, thus, resulting in a horizontal pattern of inheritance.

• Either sex can be affected, on average, in equal numbers.

• When both parents are carriers, there is a 25% chance with each pregnancy of having an affected child.

• Consanguinity is noted more often among the parents of individuals with rare recessive disorders. A consanguineous relationship noted in the parents of a patient with an unidentified genetic disorder suggests the possibility of an autosomal recessive single gene disorder.

![Figure 2.7: A typical autosomal recessive pedigree](image)

iii. X-Linked Inheritance

X-linked inheritance refers to inheritance of genes located in the X chromosome (U.S. National Cancer Institute, 2006).
The following are the characteristics of an X-linked inheritance, and they are illustrated in Figure 2.8 (Johnson and Christianson, 2006b):

- The hallmark of X-linked inheritance is that there is no male to male transmission, since males pass on Y chromosomes to their sons.
- Unaffected males cannot transmit the disorder because they do not carry the abnormal X-linked gene.
- Affected males have clinically normal offspring. Their sons receive a Y chromosome and are free of the trait. Their daughters receive an X chromosome and are normal, but obligate carriers.
- Female carriers have a 50% chance, with each pregnancy, of passing on the abnormal gene. Sons who inherit the gene will be affected and daughters will be carriers like their mothers.
- Female carriers may be mildly symptomatic due to unequal inactivation of the X chromosomes.
- Although unlikely, a female can express an X-linked disorder if her father is affected and her mother is a carrier. Even rarer is an affected female with Turner’s syndrome (female who have only one X chromosome).
- Females are considered obligate carriers if they have more than one affected son, or have an affected son and another affected male relative.
iv. Polygenic Multifactorial Inheritance

Multifactorial inheritance is used to describe the conditions caused by genetic and environmental factors (U.S. National Cancer Institute, 2006). An individual who has a first or a second degree relative with such a disorder should be referred for counselling, given that their risk of having an affected child is higher than the general population risk (Johnson and Christianson, 2006b). Figure 2.9 shows a pedigree suggestive of a polygenic or multifactorial pattern of inheritance.
2.2 Existing Pedigree Tree Software Packages

Existing pedigree software packages available in the market are briefly described and compared in the subsections below. These software packages normally come in the form of compact discs and some are accessible on the Internet. Screenshots of some of the packages are provided.

2.2.1 Family Tree Maker 2005

This package, developed by MyFamily.com. Inc., is a system for creating a family tree. This system allows the user to enter the family members’ names, and their detailed information (FamilyTree Maker 2005, 2006). This software is simple to use and the input method is user-friendly. FamilyTree Maker has a number of functions such as pedigree view, individual data maintenance, family members photo insert, scrapbook, and Internet online link. Stand-alone help file and online help are also provided. The software does not utilise standard human pedigree symbols for the family relationships.
and does not use medical symbols to denote genetic information. Figure 2.10 and Figure 2.11 show the standard pedigree tree and Pedigree View in Family Tree Maker 2005, respectively.

Figure 2.10: Standard Pedigree Tree in Family Tree Maker 2005

Figure 2.11: Pedigree View in Family Tree Maker 2005
2.2.2 Cyrillic 2.02

This package was developed by C.J. Chapman and published by Cherwell Scientific Publishing Ltd (Chapman, 1996). This system was developed specifically for the drawing of the pedigree chart. Cyrillic has a number of functions such as adding individual data, information about spouse, siblings, parents, relatives as well as haplotypes with the arrangement performed sequentially. The pedigree can also be printed. It has many useful functions, including the ability to document multiple pregnancies and twin status, and there is a help file that contains explanations of each function in the system. However, this software package lacks security feature as it can be accessed on a local workstation without user authentication. Any person may gain access to the pedigree chart information after logging into the local workstation. Each pedigree chart is stored in a single file and there is the risk of missing important data if there is damage to the local workstation or if the file is accidentally deleted. Figure 2.12 shows Pedigree Chart drawing in Cyrillic 2.02.

![Pedigree Chart drawing in Cyrillic 2.02](image_url)
2.2.3 GenoPro version 1.91b

This package was developed by Monica McGoldrick and Randy Gerson (GenoPro Inc., 2002), specifically for the recording of medical history and to show genetic traits. It includes various mental health symbols to allow psychological medicine professionals and therapists to identify and understand social patterns in the family history. It has functions for adding information of new individuals, their parents and offsprings. A photograph of the person and a family table layout can also be added. It allows the user to preview the family tree before it is printed. The family ‘wizard’ is included in the family members’ data. A help file with a simple tutorial is provided to guide the user as well as to explain the functionality and tools provided. However, this software package does not produce the standard pedigree chart and some of the genetic symbols used are not the standard pedigree genetic symbols. This software package lacks security features and the chart is stored in a single file like Cyrillic 2.02. Figure 2.13 shows a pedigree chart in GenoPro version 1.91b.

![Pedigree chart in GenoPro version 1.91b](image)

Figure 2.13: Pedigree chart in GenoPro version 1.91b
2.2.4 GenealogyJ 2.3.2

The system was developed under the terms of the GNU General Public Licence and published by the Free Software Foundation (GenealogyJ, 2005). GenealogyJ is a viewer and editor for genealogic data and it allows nested information to be edited in its hierarchical form. GenealogyJ has a number of functions such as adding data for child, parents, spouse and siblings. It also provides a tree view, timeline view, print preview and a help file. GenealogyJ does not produce a standard pedigree chart and some of the genetic symbols do not follow the standard pedigree symbols. It also lacks system security features as it can be accessed without authentication. Figure 2.14 shows a pedigree view in GenealogyJ.

![Pedigree View in GenealogyJ](image)

Figure 2.14: Pedigree View in GenealogyJ
2.2.5 PED 5 Pedigree Drawing Software

PED 5 was first introduced at the European Society of Human Genetics (ESHG) Conference in 1997. PED 5 can retrieve family information from a data file using a comma-separated value (CSV) format, where each line describes an individual by the pedigree ID, the individual's ID, the IDs of his/her father and mother, the gender, the phenotype or affection status, and any other data related to the individual (PED 5, 2005). In PED 5, only the menu bar and the buttons on the toolbar are used to create a pedigree chart. PED 5 complies with the "Recommendations for standardized human pedigree nomenclature." It has the usual functions such as adding son, daughter, ancestors, and annotating, editing pedigree comments, and importing and exporting family information into a CSV file. However, an auto-drawing input window in PED 5 does not indicate generation by using the Roman numerals, and each individual is not assigned a specific number. Although the drawing input module in PED 5 uses most of the pedigree symbols, it is difficult to construct a pedigree tree showing the relationship between individuals because the drawing module does not provide auto-relationship checking during construction of the pedigree tree. Thus, it will take a longer time to construct a pedigree tree. Although PED 5 can produce a standard pedigree chart, it lacks system security features as it can be accessed without authentication. Figure 2.15 shows a pedigree chart in PED 5.
2.2.6 Pedigree Assistant

Pedigree Assistant was developed by C.J. Chapman, author of Cyrillic (Pedigree Assistant Pedigree Drawing Software, 2006), for drawing the pedigree chart. It uses the human pedigree symbols similar to Cyrillic. Pedigree Assistant uses Microsoft Access as its database. Pedigree Assistant has a number of functions such as adding individual data, adding parents and siblings’ names, pedigree chart printing, picture export, import family from Cyrillic, interface with patient database and questionnaire. It has symbols for multiple pregnancy and twins status. It has a security feature that secures the pedigree data from unauthorised access. However, Pedigree Assistant does not indicate the generation number using Roman numerals. In addition, while each individual is assigned a specific number, it does not follow the recommended numbering system of moving from left to right. Figure 2.16 shows a pedigree chart created using Pedigree Assistant.
2.2.7 Progeny

Progeny is a pedigree drawing system developed by Progeny Software, LLC (Progeny Software, 2006), specifically, for the recording of genetic data. It assigns the human pedigree symbols into the pedigree chart one by one. Progeny uses Sybase SQL Anywhere database. Progeny can run on Microsoft NT or Novell Netware Server on a local area network. The software package comes in an Enterprise edition and a Desktop edition. The Enterprise edition allows multiple users concurrent access to the same pedigree data. It also provides user security management and row assignment module to enhance the system security. The desktop edition is a stand-alone single user pedigree drawing system. Progeny has a number of functions such as adding individual, parents and siblings data, pedigree chart printing, export of pedigree chart as an image with properties of each individual and an individual palette. However, the pedigree chart does not indicate the generation number and each individual is not assigned specific numbers moving from left to right. Although it provides many icons and tabs in the user interface, the user still needs to undergo training in order to construct and maintain
the pedigree. Many steps are involved when updating each individual genetic symbol and the data. Figure 2.17 shows a pedigree chart created using Progeny.

![Pedigree chart created using Progeny](image)

2.3 **Comparative Analysis of Existing Pedigree Drawing Software Packages**

The existing pedigree drawing software packages were compared, based on system features, pedigree analysis functions and the use of pedigree symbols.

2.3.1 **System Features View**

All the pedigree software packages discussed above can run on Microsoft Windows operating system. Except for Progeny, the others are stand-alone applications, which can support multi-users. Most of the packages store the pedigree data in a binary file. However, Pedigree Assistant and Progeny, use Microsoft Access database and the Relational Database Management System (RDBMS), respectively. With regards to system security, Pedigree Assistant and Progeny enforce user authentication. All the systems described above have import/export, print, and help functions. Only Family
Tree Maker 2005, GenoPro version 1.91b, GenealogyJ 2.3.2 and Pedigree Assistant provide reports such as family group report, family members listing and generation chart report from the pedigree data. Only Progeny provides application users’ management and user role function. The development technology information is not available for other software packages, except GenealogyJ. Java Applet and HTML programming language are used to develop GenealogyJ 2.3.2. With regard to the price, Family Tree Maker 2005 costs USD14.99, PED5 costs USD299, GenoPro version 1.91b costs USD24 and GenealogyJ 2.32 is a freeware. Information on the price is not available for Cyrillic 2.02, Pedigree Assistant and Progeny. Table 2.1 shows a comparison of the system features of the pedigree software packages.

### 2.3.2 Pedigree Analysis

Cyrillic 2.02, GenoPro, Pedigree Assistant and Progeny provide detailed pedigree information and structure sufficient for analysis. Although PED 5 contains the pedigree structure, it does not incorporate features to indicate twin pregnancy, multiple pregnancy and multiple marriages. It also does not have provisions to join family branches. Family Tree Maker 2005 can indicate marital status but not multiple marriages. GenealogyJ does not contain any of the pedigree analysis items because it does not use any standard pedigree symbol. Pedigrees constructed using Cyrillic 2.02, GenoPro, PED 5, Pedigree Assistant and Progeny may be used for analysis and interpretation of four of the most common patterns of inheritance such as autosomal recessive and dominant inheritance, X-linked inheritance and polygenic or multifactorial inheritance. However, the pedigrees created using Family Tree Maker 2005 and GenealogyJ do not facilitate analysis and interpretation of the modes of inheritance, and hence, are not suitable for pedigree analysis. Table 2.2 shows a comparison of pedigree analysis of the pedigree software packages.
Table 2.1: Comparison of pedigree software packages based on system features

<table>
<thead>
<tr>
<th>Pedigree Software Packages</th>
<th>Family Tree Maker 2005</th>
<th>Cyrillic 2.02</th>
<th>GenoPro version 1.91b</th>
<th>GenealogyJ 2.3.2</th>
<th>PED 5</th>
<th>Pedigree Assistant</th>
<th>Progeny</th>
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<td>Standalone</td>
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<td>Standalone</td>
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<td>Yes</td>
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<tr>
<td>Patient Record</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Price</td>
<td>USD14.99</td>
<td>Not Available</td>
<td>Shareware, USD 24</td>
<td>Freeware</td>
<td>USD 299</td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
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</table>
Table 2.2: Comparison of pedigree software packages based on pedigree analysis functions

<table>
<thead>
<tr>
<th>Pedigree Software Packages</th>
<th>Family Tree Maker</th>
<th>Cyrillic 2.02</th>
<th>GenoPro ver 1.91b</th>
<th>GenealogyJ 2.3.2</th>
<th>PED 5</th>
<th>Pedigree Assistant</th>
<th>Progeny</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Pedigree Symbols</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Marital Status</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pregnancy with Twins</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Multiple Pregnancy</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Adoption</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Multiple Marriages</td>
<td>Yes *</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>(Polygamous)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to Join Family Branches</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pedigree Analysis to</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Determine Mode of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inheritance</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

* Unable to show multiple marriages in the pedigree tree.

2.3.3 Pedigree Symbols Used

There are some differences in the use of pedigree symbols in the different software packages. The symbols used in Cyrillic 2.02, PED 5, Pedigree Assistant and Progeny comply with the recommended Standardized Human Pedigree Nomenclature. PED 5 uses most of the symbols except for identical twins, consanguineous marriage, extramarital marriage and divorce. GenoPro version 1.91b does not have the symbols for abortion, affected status with different phenotypes and obligate carrier status. Family Tree Maker 2005 and GenealogyJ 2.3.2 do not use the recommended pedigree symbols. Pedigrees constructed using the systems reviewed above, except for Cyrillic, do not show the generation and individual number for each generation line. Pedigrees created using Cyrillic show the generation number in Roman numerals and the
generation line of each individual is shown below the individual symbols. Table 2.3 shows a comparison of the use of pedigree symbols among the various software packages.

Table 2.3: Comparison of the pedigree symbols used in various software packages

<table>
<thead>
<tr>
<th>Pedigree Software Packages</th>
<th>Family Tree Maker</th>
<th>Cyrillic 2.02</th>
<th>GenoPro ver 1.91b</th>
<th>GenealogyJ 2.3.2</th>
<th>PED 5</th>
<th>Pedigree Assistant</th>
<th>Progeny</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male / Female</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Unknown Gender</td>
<td>No</td>
<td>Yes</td>
<td>Yes *</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Affected Status</td>
<td>No</td>
<td>Yes</td>
<td>Yes *</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Affected with Different Sectors (q1, q2, q3, q4)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Obligate Carrier</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Possibly Affected</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Unaffected</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Spontaneous Abortion (SAB) and Its Status</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes *</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Termination of Pregnancy (TOP) and Its Status</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes *</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Individual Death</td>
<td>No</td>
<td>Yes</td>
<td>Yes *</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Multiple Individuals with Number Known</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Adoption</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Proband</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Identical Twins</td>
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<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Marriage</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Consanguineous Marriage</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Extramarital Marriage</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<td>Divorced</td>
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<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Generation Number in Roman Numerals I, II, III, etc.</td>
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<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Individual Number 1, 2, 3, etc.</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

* Different symbols used from the common pedigree symbols recommended.
2.4 Summary

This chapter reviews a few situations in general practice where the family history information is used during genetic counselling. It also discusses the standard symbols used in a pedigree, indication of generation in a pedigree chart and interpretation of some common disorders using pedigree. The last section of this chapter describes and compares existing pedigree software packages available in the market, including the development technology used for the software packages and their prices.