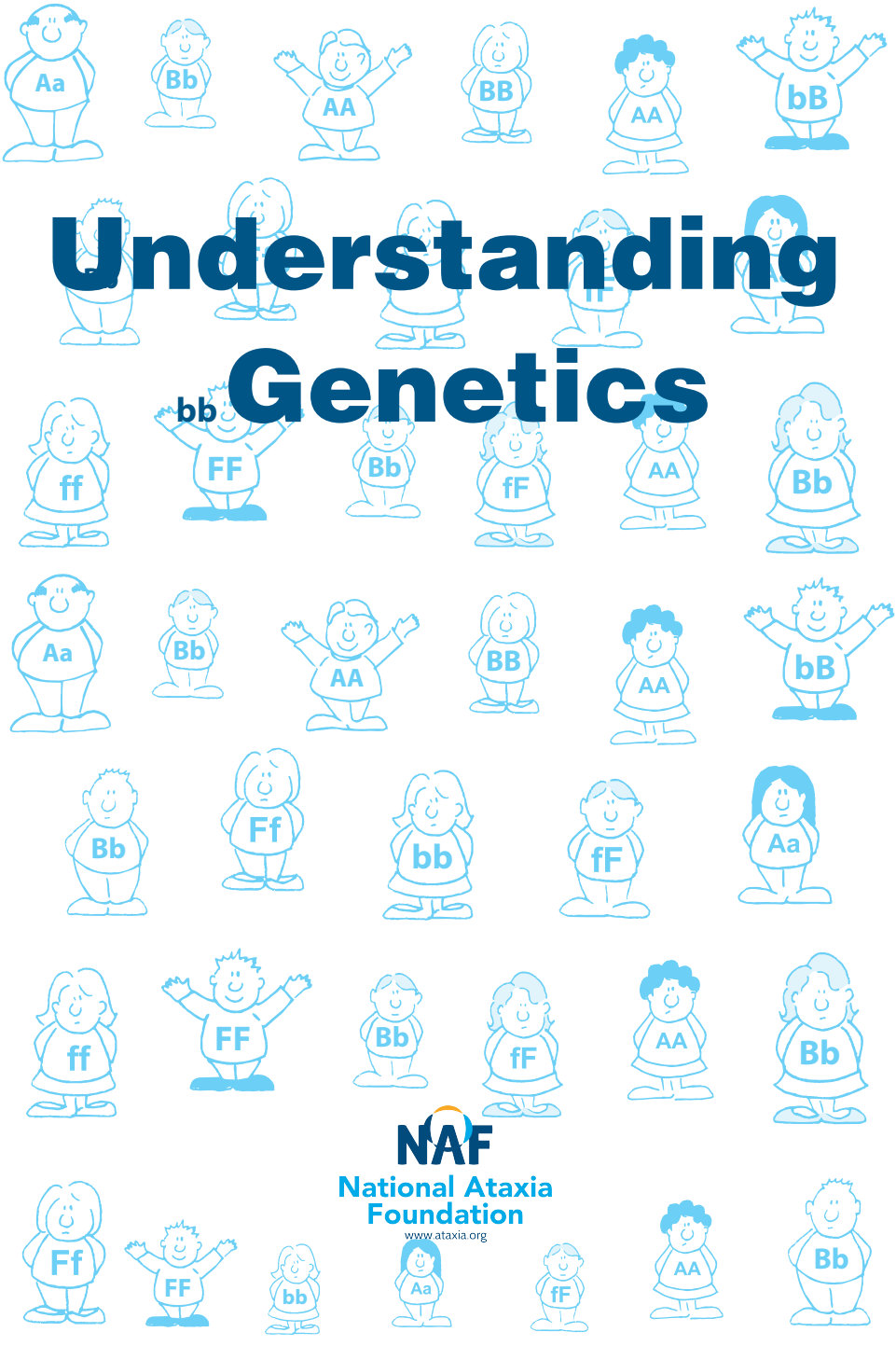

Understanding Genetics

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Understanding Genetics

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Understanding Genetics

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1.

What is genetics?

Genetics is the study of genes, which are found only in living cells. **Genes** are often called the "blueprints" of the cell because they contain the instructions for all its functions. This guide will discuss human genetics. To give a hint of how complex this field is, scientists estimate that the **genetic code** in one human cell would fill over a million pages if translated to letters of the English alphabet.

The field of genetics is relatively new. Much of our understanding of how genes work and how they are inherited has come in the past 60 years. New discoveries are being made all the time. Genetic studies have helped determine which diseases are inherited. In some cases, they have helped scientists locate the genes responsible for specific diseases, opening the doors to improved treatments, even cures.

Every individual has a unique gene code. The genetic information in your cells is inherited from your parents but is NOT exactly the same as that of your parents or siblings. You might have genes that code for red hair, while your sister has genes that code for blond hair. Your genes might instruct your body to only grown five feet tall, while your brother's genes instruct his to keep growing until he's well over six feet.

Scientists who study genes and how they work are called **geneticists**. These scientists are interested in:

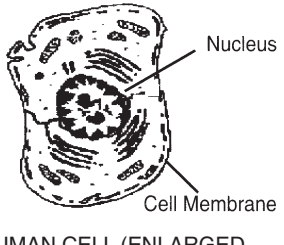
- The general nature of genes.
- The role of genes in development.
- How genes are passed from parents to offspring.
- How environmental factors impact genes.
- The diagnosis and treatment of genetic diseases.

2.

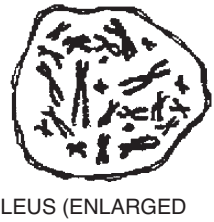
Cells, chromosomes and genes

The human body is made up of trillions of living cells of various types: heart cells, nerve cells, bone cells, skin cells, and egg cells, among others. Each of these cells are made up of thousands of parts that work together – like incredibly complex microscopic factories.

One essential component of every cell is the **nucleus**, which is the cell's control center. It contains 46 structures called **chromosomes**. The chromosomes are packages carrying all of our genetic material. Each chromosome is made up of thousands of genes. Overall, we carry approximately 25,000 genes. Nearly every cell in your body contains an identical set of chromosomes. The 46 chromosomes are arranged in 23 pairs. Therefore, we have two copies of each chromosome and two copies of each gene. One chromosome copy from each pair is received from your mother, one copy from your father. The first 22 pairs of chromosomes are the same in males and females. These 22 chromosome pairs are called **autosomes**. The 23rd pair of chromosomes is called the **sex chromosomes**. Males have an X and a Y chromosome and females have two X chromosomes.



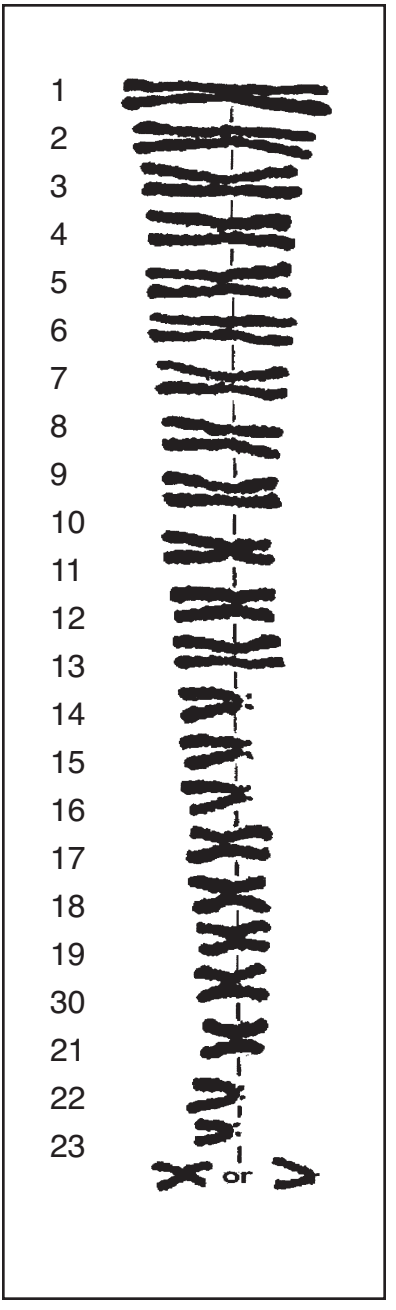
HUMAN CELL (ENLARGED THOUSANDS OF TIMES)



NUCLEUS (ENLARGED FURTHER) CONTAINING THE 23 CHROMOSOME PAIRS

Cells, nuclei, and chromosomes can all be seen under a microscope. However, genes are too small to be seen even with the most powerful microscope. As tiny as they are, genes play a powerful role. Without them no cell could function. They tell the cell how to make the chemicals or proteins that are essential to life and health. They also tell the cell when and how much or each of these proteins to make.

All the information a cell needs is stored in its genes. However, the cell only uses bits of that information at a time.



Chromosomes are numbered according to their size. The 23rd chromosome pair looks different in males and females and are called sex chromosomes. All the other chromosomes are called autosomes.

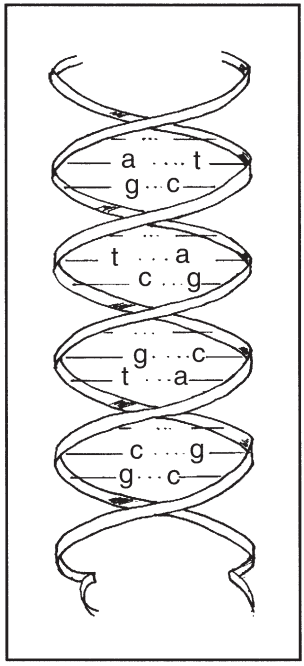
Some genes are only used in certain cells or at certain times. For instance, even though the gene responsible for eye color is located in your heart cells as well, it is not used in those cells. Genes might be only used or "turned on" when an organ is being formed, or only during puberty, or only when wound repair is needed. Other genes are always working because their job is to direct the cell's daily tasks.

3.

How is DNA related to genes?

We've learned that genes are the blueprints or instructions of the cell. But what is the genetic blueprint like?

With the aid of chemical techniques, scientists have broken apart chromosomes and identified a special substance that makes up genes – deoxyribonucleic acid or **DNA** for short. All chromosomes contain DNA.



No one has actually seen DNA, but by analyzing its chemical makeup scientists have constructed a model of it that looks kind of like a spiral staircase. The spiral "stairs" of the DNA are made up of four kinds of chemical bases. These chemicals are referred to by the first letters of their names, A, C, G and T (adenine, cytosine, guanine, and thymine). Just like letters can be put together to create words, sentences and whole books, the four DNA bases can be put together in various orders to create chemical "words." These chemical words are then linked to form genes. Thousands of genes are linked together in a chain to form chromosomes.

As the cell carries about its functions, it borrows only the genetic information it needs at the given time from the DNA. At the time the information is needed, the DNA spiral temporarily unwraps so its information can be copied. The information is then carried by chemical messengers from the nucleus to the part of the cell where proteins are assembled from **amino acids** present in the cell.

The DNA "letters" A, C, G and T combine in various ways to make three letter words. Each three-letter word codes for a particular amino acid and instructs the cell to insert that amino acid into the protein chain. For example GCA codes for the amino acid alanine and CAG codes for the amino acid glutamine. There are twenty different amino acids in all. Some proteins are simple chains of a few amino acids. Other proteins are complex structures made up of several amino acid chains.

4.

What role do genes play in who you are?

You have a unique set of genes inherited from your parents. Your genes have instructed your body how to grow, develop and function from the time you were conceived and will continue doing so until you die. Genes direct the development of your physical characteristics. For instance, your height, hair color, shape of ears and nose, and size of hands and feet were all largely determined by genes. More subtle traits, such as personality, mannerisms and talents can also be influenced by genes. People might tell you that you walk like your mother or laugh like your uncle. Or perhaps from the time you were very young you had a passion for taking things apart and putting them back together, while your sister was born with a great sense of rhythm. Some of your traits might be distinctly like those of a particular parent. Others might appear to be a blend of both your parents' traits.

Some characteristics have a stronger genetic component and are more likely to appear in offspring. Normal variations in genes, known as polymorphisms, also impact development. Polymorphisms in our genetic code make each individual unique. Chapter 7 discusses the difference between normal gene variations and those that can cause serious problems.

However, scientists now understand that most traits are the result of several genes and external factors working together and NOT the result of a single gene. For instance, height depends on a dozen or more genes acting together.

Remember that genes provide instructions for what can be done, not necessarily what actually happens. External factors such as poor nutrition, injuries or environmental pollutants can hinder healthy development. On the other hand, good eating habits and proper exercise can influence development in a positive way.

5.

What happens to genes during growth and development?

During growth and development, existing cells divide over and over again to make new cells. However, before one cell divides into two, all the genetic information in the original cell is duplicated so it can be passed on to the new cell. This type of cell division, in which cells produce exact copies of themselves, is called **mitosis**.

When a female egg cell is fertilized by a male sperm cell, a new cell is formed. That cell immediately starts dividing and for a time many divisions happen quite rapidly. Each division produces smaller and smaller copies of the original egg cell. After a while, the cells take a break from dividing, and the new cells take in food to grow larger. Eventually, these new cells begin dividing again.

But growth is not just a matter of gaining size. As an individual organism grows from a fertilized egg to an adult, lots of changes take place. What starts as a single cell eventually grows into billions of cells of many different types – skin, muscle, bone, nerve and heart cells (to name a few), which all look and function uniquely.

How can many cells look and act so differently when they all contain the same genetic information?

Even though all cells contain the same information, not all of the information is used at once. Cells use the information stored in genes selectively – similar to the way we use information in computers. How cells know when to stop duplicating and start selecting and using specific information is a mystery.

Under powerful microscopes, chromosomes packed with thousands of genes usually look like long tangled threads. During this stage, they are called **chromatin**. When a cell is ready to divide, these chromatin threads coil and tighten into compact dark rods. It is during this stage they are referred to as chromosomes.

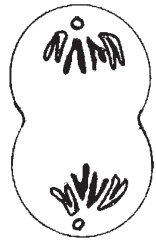
A closer look at mitosis

1. The cell swells as the DNA is duplicated and it prepares to divide.

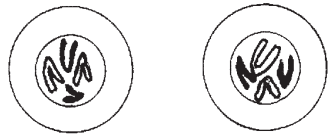
2. The membrane around the nucleus disappears. The material that was inside the nucleus draws itself in threads. These threads get shorter and thicker and separate.

3. Each chromosome now looks like two threads stuck together at one spot. The doubled threads move close to the center of the cell.

4. The double stranded chromosome is pulled in two directions at once. Each chromosome splits apart. The two threads of each chromosome move to opposite ends of the cell (along with half the other contents of the cell).



5. The chromosomes uncoil and are surrounded by a membrane. The two new nuclei now look just like the original nucleus.



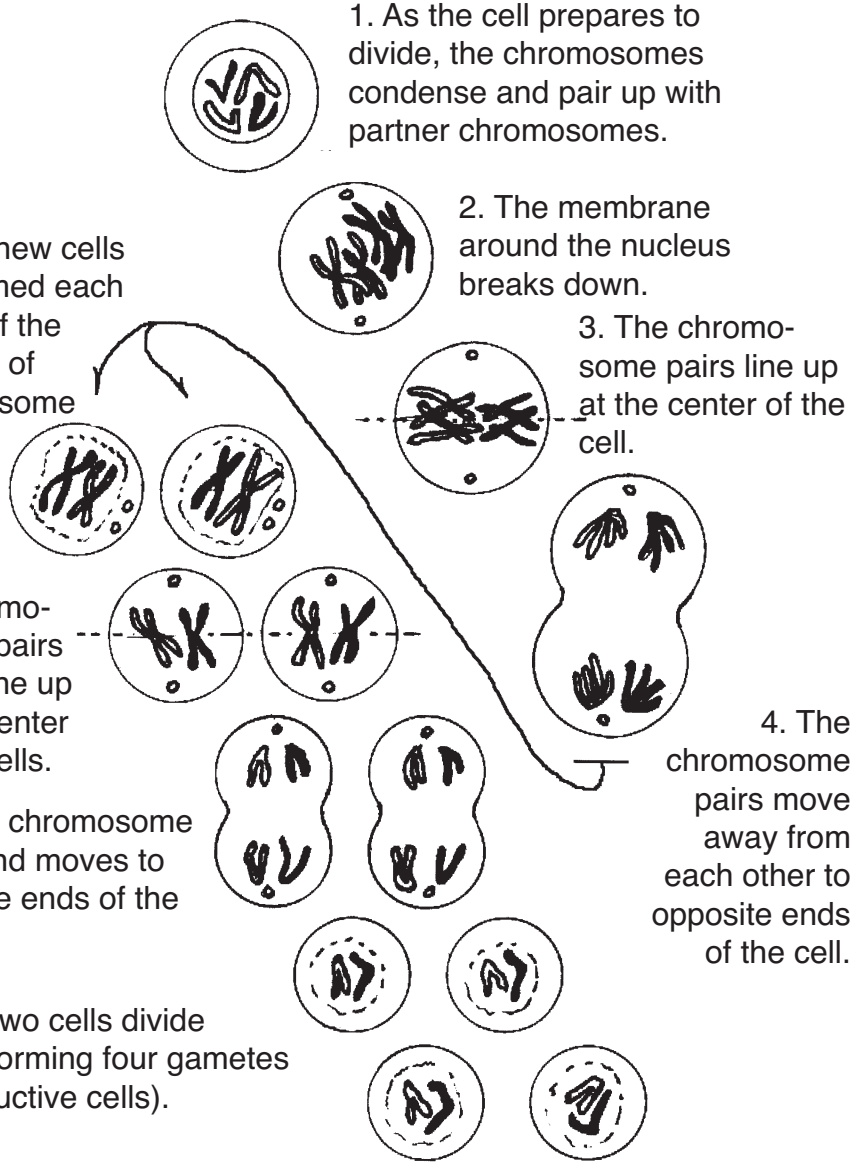
Each new cell has a copy of everything that was in the nucleus.

6.

How are genes inherited?

In the last section, we looked at mitosis, the type of cell division in which each new cell gets a copy of the original cell's genetic information. However, a different type of cell division is involved in making egg and sperm cells. This special kind of division, called **meiosis**, results in cells that contain only 23 chromosomes or half of the genetic material from the original cell. Egg and sperm cells are also known as **germ cells**, or **gametes**. In sexual reproduction, the gametes of the two parents are brought together to produce a fertilized egg. In the nucleus of this fertilized egg cell, 23 chromosomes (from each parent) combine to make a full new set with 46 chromosomes. In this way, genetic information from the parents is passed to offspring. The new fertilized cell then begins dividing and growing, through the process of mitosis. (see Chapter 5).

A closer look at meiosis



1. As the cell prepares to divide, the chromosomes condense and pair up with partner chromosomes.

2. The membrane around the nucleus breaks down.

3. The chromosome pairs line up at the center of the cell.

4. The chromosome pairs move away from each other to opposite ends of the cell.

5. Two new cells are formed each with half the number of chromosome pairs.

6. Chromosomes pairs again line up at the center of the cells.

7. Each chromosome splits and moves to opposite ends of the cell.

8. The two cells divide again, forming four gametes (reproductive cells).

7.

What causes genetic disease?

In an earlier section, we described how genetic information is copied from DNA in the cell nucleus, then transferred to the part of the cell where proteins are assembled. The process of copying and reading DNA takes place more times than anyone can count. With so much copying and assembling going on, mistakes occasionally occur. However, these occasional mistakes in copying the DNA or assembling a protein do not usually damage the cell or cause a disease because fresh copies of the DNA "master copy" of the gene are being made all the time.

Widespread damage to the DNA of body cells, or changes in certain specific genes, can be caused by ultra-violet radiation or chemical toxins and carcinogens. These changes, or **mutations**, in the DNA of body cells do not cause genetic disease, but can speed up the aging process or, in some cases, cause cancer.

Some DNA changes present in the "master copy" do not affect how the protein works and are considered normal. These changes are called polymorphisms instead of mutations because they do not cause genetic diseases. An example of a polymorphism is the ABO blood types – Type A, Type B and Type O blood are coded by three different variations in the DNA sequence of the blood type gene. They combine to form Types A, B, AB, and O, all of which are normal.

However, mutations in the DNA present at the time of conception CAN lead to genetic diseases. These diseases are passed from parent to child when a gene mutation is present in a sperm or egg cell. At the time of fertilization, the inherited mutation will be copied and recopied into every cell of the embryo. These germline mutations can lead to genetic disease.

Scientists estimate that in every individual, five or six out of the 25,000-30,000 genes have mutations in them. Some genetic diseases are associated with only minor problems; others are so serious that they lead to death. Genetic conditions, like ataxia, can be inherited in different patterns. The most common inheritance patterns are **autosomal dominant, autosomal recessive**, and **X-linked**. Autosomal and X-linked tell information about where the gene is located. Autosomal conditions have genes located on one of the 22 chromosomes that are found in both males and females. Therefore, both males and females can be affected with these disorders. X-linked conditions have genes located on the X chromosome. In contrast to autosomal conditions, the X-linked diseases primarily affect males and are inherited from unaffected females. One form of ataxia that is inherited as an X-linked condition is Fragile X-associated Tremor/Ataxia Syndrome.

The terms dominant and recessive refer to the number of copies of the abnormal gene that are required in order for the disease to occur. Each of the thousands of gene pairs in your body works as a team. In the case of a dominant condition, only one abnormal copy of the gene is needed in order for an individual to be symptomatic. Dominant conditions are usually inherited from an affected parent, who carries one normal and one abnormal

copy of the gene. Since each parent passes on one copy of every gene there is a 50% chance of passing along the normal gene and a 50% chance of passing along the abnormal gene. That is why some siblings are affected and others are not. The spinocerebellar ataxias are examples of autosomal dominant inheritance.

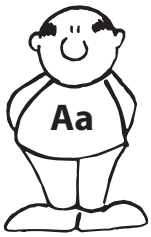
In the case of a recessive condition, two copies of the abnormal gene are needed in order to show symptoms of the disease. Therefore, each parent passes on one abnormal copy of the gene. In most cases, the parents are unaffected and carry one normal and one abnormal copy of the gene. Each parent can pass along either the normal or abnormal copy. When both parents pass along the abnormal copy, the child is affected with the recessive condition. If they both pass along the normal copy the child is unaffected and is not a carrier. When one parent passes along a normal copy and one passes along an abnormal copy the child will be an unaffected carrier like the parents. An example of autosomal recessive inheritance is Friedreich's ataxia.

How an Autosomal Dominant Disorder is Passed on in a Family

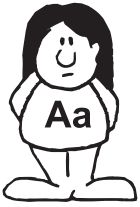
Father with one **A** and one **a** (has ataxia)

Mother with two **a**'s (does not have ataxia)

A = disease gene
a = normal gene



When a parent with autosomal dominant ataxia and a parent without ataxia produce offspring, each of the offspring will either inherit ataxia or not inherit ataxia depending on which genes are passed on.



Offspring who inherit one ataxia-causing gene will have ataxia.

Offspring who inherit two normal genes will not have ataxia.

How an Autosomal Recessive Disorder is Passed on in a Family

Father with one **F** and one **f**
(does not have ataxia)

Mother with one **f** and one **F**
(does not have ataxia)

F = normal gene
f = disease gene

The above parents each have one recessive ataxia-causing gene. Each of their offspring could inherit one of four possible gene combinations:

F from father, **f** from mother
(child does not have ataxia but can pass disease gene on to future children)

f from father, **F** from mother
(child does not have ataxia but can pass disease gene on to future children)

F from father, F from mother
(child does not have ataxia and has no disease gene to pass on to future children)

f from father, **f** from mother
(double-dose of ataxia-causing gene means child will have ataxia and will pass disease gene on to all future children)

8.

Types of mutations

Remember from Chapter 3 that there are four chemicals used to make genetic words. They are represented by the letters A, C, G, and T. These are combined in various sequences to form three letter "words."

There are several types of mutations:

1) **Point mutation (or substitution)** – A mistake in the DNA word resulting in the substitution of a wrong chemical letter.

For instance a normal DNA sequence might be:

ACT – TTA – GGA

but in copying the message, a T might be substituted for the first C, resulting in a sequence that reads:

ATT – TTA – GGA.

The result will be a change in one amino acid in the protein.

2) **Insertion** – A mistake in a DNA word resulting from the insertion of an extra letter.

For instance, a normal DNA sequence might start as:

ACT – ATT – ACT – ATT

An extra letter might be added and disrupt the entire sequence resulting in a different amino acid chain:

ACT – TAT – TAC – TATT

3) **Deletion** – A letter is accidentally left out as the DNA message is read:

Rather than ACT – ATT – ACT – ATT

The first T is not read and the message becomes:

ACA – TTA – CTA – TT

The result is a different amino acid.

4) **Repeat expansion** – A DNA word is repeated over and over. For instance a normal sequence might read:

ACC – CAG – CAG – TTA

In repeat expansion, the message gets stuck on CAG so that it reads:

ACC – CAG – CAG – CAG – CAG for many more sequences than it should and results in a protein that is longer than normal.

The following charts list some of the hereditary ataxias caused by the types of mutations discussed in this chapter:

Autosomal Recessive Ataxias

DISEASE TYPE	LOCATION OF GENE	TYPE OF MUTATION
Friedreich's ataxia	Chromosome 9	GAA expansion
Ataxia telangiectasia	Chromosome 11	Deletion & insertion
Ataxia with vitamin E deficiency	Chromosome 8	Deletions & other point mutations

Autosomal Dominant Ataxias

DISEASE TYPE	LOCATION OF GENE	TYPE OF MUTATION
Spinocerebellar ataxia 1	Chromosome 6	GAG expansion
Spinocerebellar ataxia 2	Chromosome 12	GAG expansion
Spinocerebellar ataxia 3 (Machado-Joseph disease)	Chromosome 14	GAG expansion
Sensory ataxia neuropathy 2	Chromosome 16	Unknown
Spinocerebellar ataxia 5	Chromosome 11	Inframe deletions: missense point mutation
Spinocerebellar ataxia 6	Chromosome 19	GAG expansion
Spinocerebellar ataxia 7	Chromosome 3	GAG expansion
Spinocerebellar ataxia 31	Chromosome 16	Pentanucleotide repeat insertion
Dominant Episodic ataxia 1	Chromosome 12	Point mutations
Dominant Episodic ataxia 2	Chromosome 19	Point mutations

9.

Exploring the genes in your family tree

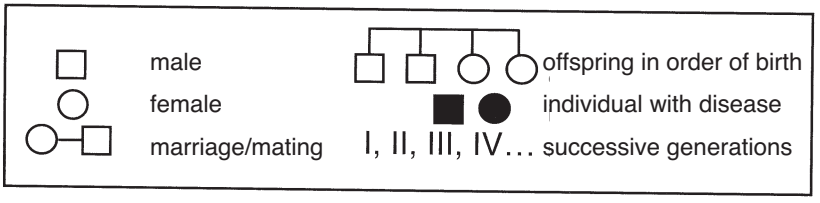
In order to learn about the genes in an individual or family, one can study their effects – the observable features – rather than the genes themselves. An observable characteristic is called a **phenotype**. Specific genes that code for blue eyes are your genotype for eye color.

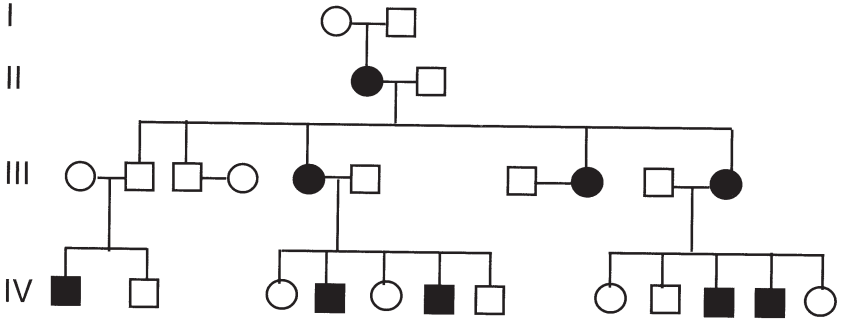
In studying the genetic makeup of a particular family, looking at phenotypes among generations of family members reveals information about the genotypes or the genetic makeup of a family.

Since humans have lots of traits, studying genotypes can be complicated. Most of what is known about human inheritance comes from interviewing families. By gathering information from several families about the same trait, scientists have learned more about how specific traits are passed along from generation to generation. Family trees or pedigrees help visualize how traits are carried along. When it comes to genetic diseases, physicians often rely on patients to help construct family trees, which help them make diagnoses and develop disease management plans.

In designing family trees, circles are often used to represent females and squares to represent males. Married men and women are connected by horizontal lines. Starting with the oldest generation at the top, each succeeding generation is drawn below with the most recent generation at the bottom of the graph. Once all the figures available are added to the graph, traits of interest are recorded on the same pedigree; too much information on the same chart might get confusing. Therefore, it is often better to record them on separate charts. Traits can be represented by words, dots, shading or letters, and explained with a key.

Sample pedigree of family with a hereditary disease:





Glossary:

amino acids – Often called the building blocks of life, amino acids are linked together to build proteins. There are 20 amino acids in all. They are assembled in different ways to produce proteins that do different jobs.

autosomal disease – A disease caused by a mutation in a gene of an autosome.

autosomes – All 22 human chromosomes that are not sex determining chromosomes.

chromatin – Chromosomes in their less compact state. During this stage, they appear under a microscope as long tangled threads.

chromosome – A thread-like structure in the cell which contains genetic material. Humans have 46 chromosomes in all (23 pairs).

DNA – Deoxyribonucleic acid, the double-stranded chemicals that make up genes.

dominant gene – A gene whose effect will appear whether its partner gene is of the same type or different.

genes – The cell's blueprints or instructions for growth and development.

genetic code – The collection of genes within a cell.

genetic disease – A disease caused by a gene mutation.

geneticists – Scientists who study genes or medical doctors specializing in genetic disorders.

genotype – The genetic makeup of an individual.

germ cells or gametes – Reproductive cells. Male gametes are called sperm. Female gametes are called eggs. Gametes have only 23 chromosomes.

meiosis – The type of cell division that results in new cells with half the number of chromosomes and genes as the original cell.

mitosis – The type of cell division that results in exact duplicates of the original cells.

mutation – A mistake in the DNA.

nucleus – The cell control center. It houses the chromosomes containing the genes.

pedigrees – Charts showing how members of various generations are related. Also known as family trees.

phenotype – The observable traits or characteristics of an individual.

polymorphism – A normal variation in a gene.

proteins – Chemicals essential to life and health. The genes code for all the types of proteins required for life.

recessive gene – A gene whose effect will only appear when its partner gene is the same type.

sex chromosomes – The 23rd chromosome pair. Human males have one X and one Y sex chromosome. Females have two X sex chromosomes.

x-linked disease – A disease caused by a mutation in a gene of a sex chromosome.

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