Curriculum Units by Fellows of the Yale-New Haven Teachers Institute
1982 Volume VII: Human Fetal Development

Hereditary Defects—Down Syndrome and Sickle Cell Anemia

Curriculum Unit 82.07.06
by Anthony P. Solli

Teaching Level:

For elementary school teachers, grades 5 and 6, and middle school teachers, grades 7 and 8. Individual students or small groups may follow the curriculum independently. The unit may also be used as a summary or motivational part of an eight grade science or mathematics course.

The length of time needed to teach this unit could be one or two weeks, depending on the amount of time you would spend on each disease.

Prerequisite:

Students should have at least a working knowledge of the human cell. For a beginning class studying the human cell, the reader is referred to another unit in this volume. In particular, the unit by Nancy Wyskiel.

Background Information:

The characteristics of living organisms are determined by the hereditary factors inherited from the parents. The person who formulated many of the basic principles of heredity was the Austrian monk, Gregor Mendel (1822-1884), although the importance of his work was not realized until 1900. Working in his monastery gardens over a period of eight years and using 20 varieties of garden peas, Mendel came to some significant conclusions:

1. There are hereditary traits controlled by units (the term ‘gene’ was introduced long after Mendel’s work) that go unchanged from generation to generation.
2. Each hereditary trait is produced by two factors (genes), one from each parent. At fertilization, the two hereditary factors are brought together.
3. Hereditary factors are of two types: dominant and recessive. (The traits Mendel selected to

study did not show incomplete dominance.) For his historic work, Mendel is called the “Father of Genetics.” Three other people working independently of one another rediscovered the Mendelian principles: Correns in Germany, DeVries in the Netherlands, and von Tschermak also of Austria.

As evidence accumulated about inheritance, scientists became increasingly curious about the chemical identity of the genetic material that controlled inheritance. Early experiments focused on the nucleus as the source of the hereditary traits. A German psychologist, Frederich Miescher, discovered DNA (he referred to it as nuclein) in cells as early as 1869, but Miescher did not associate it with inheritance. Miescher was not familiar with Mendel’s work.

A number of biologists in the 1880’s proposed that the transmission of hereditary traits was associated with nuclein, but it was not generally accepted for more than 50 years.

Francis H. Crick, working with James D. Watson, built a model of the DNA molecule that looked like a twisted ladder. The Watson-Crick model helped to explain the way in which DNA replicates. Watson and Crick established that the cross pieces of the “ladder” were made up of a specific order of bases, A, T, C, and G, that acted as a code during replication. The double-helix model set forth by Watson and Crick in 1953 has withstood rigorous experimentation by scientists throughout the world, and it satisfactorily explains the chemical basis of heredity. It (the double-helix DNA model) provides an adequate explanation of the duplication, mutation, and transmission of genetic material.

The determination of the sex of human offspring had been the subject of some rather vague notions up until the twentieth century. The chromosome theory (now proven) clearly explains sex determination. The critical factor is whether the sperm (male gamete) carries an X or a Y chromosome. If the sperm carries an X chromosome to the egg at fertilization, the offspring will be female (Figure 1). If, however, the sperm carries a Y chromosome, the offspring will be male (Figure 2). The female contributes only X chromosomes.

Traits other than those having to do with determination of sex are located on the X and Y chromosomes. These are known as sex-linked traits.

Finally, many characteristics are manifestations of multiple genes with incomplete dominance. There are also differences in the expected genetic expressions because of mutation in the chromosomes and genes themselves.

Figure 1. Normal female karyotype.
(figure available in print form)
Figure 2. Normal male karyotype.
(figure available in print form)

Enrichment Activities 1:

1. Emphasize Mendel's fortunate selection of garden peas for his experiments. The varieties he chose had many clear-cut traits: red vs. white flowers, green vs. yellow seed pods, and so on. Then, have your students write a brief essay on why they think Mendel chose plants rather than animals for his experiments.
2. Obtain pea seeds bred for dominant and recessive factors from a biological supply house. Have your students simulate Mendel's experiments in class.
3. Have some students read and report on the award-winning book *The Double Helix* by Watson and Crick, and have other students prepare a report on the famous DNA model set forth by Francis Crick and James Watson.
4. Have interested students construct models of the double-helix, using Tinker Toy pieces or colored construction paper.

Down Syndrome:

In recent years, scientists have found the genetic basis for Down syndrome. This unfortunate condition results from an extra twenty-first chromosome in all of the body cells, resulting from nondisjunction during meiosis, in egg or sperm formation. Down syndrome is often referred to as trisomy-21 because of the presence of three twenty-first chromosomes (Figure 3). All other chromosomes are present in normal numbers.

Down syndrome is marked by moderate mental retardation and abnormal physical characteristics, including an enlarged tongue, slanted eyes, and muscle weakness. Palm and footprints are also abnormal.

About one in 800 babies are born with Down syndrome. The number is lower, about one in 1300 in mothers under 20 years of age, but increases to one in 32 in mothers over 45 years of age (Figure 4). Some scientists feel the result is from the decreased likelihood of the two chromosomes (pair 21) to separate during oogenesis in the older woman. Factors involved in faulty spermatogenesis are not yet discovered. It is known that one-quarter or more of Down syndrome persons have an extra chromosome 21 that originated with their fathers.

Figure 3. Female chromosome 21 trisomy (Down syndrome).
(figure available in print form)
Figure 4. Maternal age and the production of Down syndrome offspring.
(figure available in print form)

Student Activities:

Have students solve problems like the following examples:

1. If you have 10,000 women, age 30, who have babies and one in 900 of these births will result in a Down syndrome baby, how many will have this disease?
2. 5,000 babies are born; 2,000 to women age 20, 3,000 to women age 40. How many of each group will give birth to a Down syndrome baby? (Hint, see graph; Figure 4).

Sickle Cell Anemia:

This serious blood disease is one of several hereditary anemias. Recent figures indicate the frequency of sickle cell anemia among North American Negroes varies considerably. One survey indicates that 8 1/2 percent of the Negro population carry the trait, but do not have the disease, and 0.3 to 1.3 percent have the disease. Sickle cell anemia disease is even more widespread among natives of central and western Africa, where it is present in as much as 4 percent of the Negro population (Figure 5).

Sickle cell anemia was first observed in 1910, when the blood of patients was found to contain abnormal sickle-shaped red corpuscles. However, it was not until 1949 that the corpuscles were found to contain an abnormal hemoglobin. The chemical structure of this abnormal hemoglobin was determined in 1957. In the protein chain containing more than 500 amino acids, one amino acid, valine, was substituted for glutamic acid in normal hemoglobin. This slight variation alters the chemical properties of the hemoglobin and causes the red corpuscles to change from the normal disk shape and become sickle-shaped when the blood circulates through tissues where the oxygen supply is low. The abnormal corpuscles disintegrate in the blood stream. Thus, loss of red corpuscles causes anemia.

Sickle cell anemia usually appears during the latter months of the first year of life. The gene associated with sickle cell anemia is recessive. Therefore, the disease appears only in homozygous individuals. Heterozygous individuals, with a normal allele, may transmit the disease to offspring but do not develop it.

Figure 5. A distribution of sickle cell anemia.
(figure available in print form)

Student Activities:

Have students solve problems like the following examples:

1. Given 100,000 North American Negroes, of which, 8.5 percent carry the sickle cell anemia trait.

How many of the 100,000 carry this trait?
2. Given 100,000 natives of central Africa, 4 percent of this population have sickle cell anemia. How many of this population have sickle cell anemia?

Enrichment Activities 2:

1. Give your students some human genetics problems to solve. For example: Blond hair in humans is recessive to darker hair; right handedness is dominant to left handedness; and so on.
2. Have your students make a list of breeding examples in which people have taken advantage of incomplete dominance of traits to produce variations. Examples may include variations in roses, cattle, and so on.
3. Have students research and prepare reports on diseases and research related to genes such as cystic fibrosis, diabetes, and Tay-Sachs disease.

GLOSSARY OF GENETIC TERMS

allele—one of a pair of genes responsible for contrasting traits.
amino acids—substances from which organisms build protein.
anaphase—a stage of mitosis during which chromosomes migrate to opposite poles.
chromosome—a rod-shaped gene-bearing body in cell nucleus, composed of DNA joined to protein molecules.
daughter cells—newly formed cells resulting from the division of a previously existing cell, called a mother cell. The two daughter cells receive identical nuclear materials.
diploid—term used to indicate a cell that contains a full set of homologous pairs of chromosomes.
division plate—a wall of cellulose that forms across the dividing cell, forming a common boundary between daughter cells.
DNA (deoxyribonucleic acid)—a supermolecule consisting of alternating units of nucleotides, composed of deoxyribose sugar, phosphates, and nitrogen bases.
dominance—principle first observed by Mendel, that one gene may prevent the expression of an allele.
double cross—genetic process in which four pure-line parents are mixed in two crosses.
environment—all the external forces that influence the expression of an organism’s heredity.

evolution—the slow process of change by which organisms have acquired their distinguishing characteristics.
gene—that portion of a DNA molecule that is genetically active and capable of replication and mutation.
gene frequency—the extent to which a gene occurs in a population.
gene linkage—the assemblage of genes in a linear arrangement on a chromosome.
gene pool—all the genes present in a given population.
genetic code—the sequential arrangement of the bases in the DNA molecule, which controls traits of an organism.
genetics—the science of heredity.
genotype—the hereditary makeup of an organism.
habitat—place where an organism lives.
haploid—a term used to indicate a cell that contains only one chromosome of each homologous pair.
heredity—the transmission of traits from parents to offspring.
homozygous—refers to an organism in which the paired genes for a particular trait are identical.
incomplete dominance—a blend of two traits, resulting from a cross of these characteristics.
individual characteristics—traits that are inherited but that make an organism different.
interphase—the period of growth of a cell that occurs between mitotic divisions.
law of independent assortment—a law based on Mendel's hypothesis that the separation of gene pairs on a given pair of chromosomes, and the distribution of the genes to gametes during meiosis, are entirely independent of the distribution of other gene pairs on other pairs of chromosomes.
law of segregation—Mendel's first law, based on his third hypothesis, stating that a pair of genes is segregated during the formation of gametes.
lethal gene—one that bears a characteristic that is usually fatal to the organism.
meiosis—the type of cell division in which there is a reduction of chromosomes to the haploid number.
metaphase—the stage of mitosis in which the chromosomes line up at the equator.
mitosis—the division of chromosomes preceding the division of cytoplasm.
monohybrid—an offspring from a cross between parents differing in one trait.
monosomy—the presence of a single homologous chromosome in all body cells.
mother cell—a cell that has undergone growth and is ready to divide.
multiple alleles—one of two or more pairs of genes that act together to produce a specific trait.
mutation—a change in genetic make-up resulting in a new characteristic that can be inherited.
nucleus—the part of the cell that contains chromosomes.
phenotype—the outward appearance of an organism as the result of gene action.
prophase—the stage of mitosis in which chromosomes shorten and appear distinctly double and the nuclear membrane disappears.
recessive—refers to a gene or character that is masked when a dominant allele is present.
RNA (ribonucleic acid)—a nucleic acid in which the sugar is ribose. A product of DNA, it serves in controlling certain cell activities, including protein synthesis.
sex chromosomes—the two kinds of chromosomes X and Y that determine the sex of an offspring.
sex-influenced character—a characteristic that is dominant in one sex, recessive in the other.
sex-linked character—a recessive characteristic carried on the X type of sex chromosome.
telophase—the last stage of mitosis, during which two daughter cells are formed.

trisomy—the presence of three homologous chromosomes in all body cells.
X chromosome—a sex chromosome present singly in human males and as a pair in females.
Y chromosome—a sex chromosome found only in males.

REFERENCES

Kaercher, Dan, “Genetic diseases and birth defects: What every family needs to know”, Better Homes and Gardens, March, 1980, pp. 66-72.

Mahoney, Dr. M. Jeremiah, Associate Professor, Human Genetics, Pediatrics and Obstetrics and Gynecology, Yale University.

Suzuki, David T., Griffiths, Anthony J. F., and Lewontin, Richard C., *An Introduction to Genetic AnalYsis* , W. H. Freeman and Company, San Francisco, 1981.

United States Department of Health and Human Services, “Amniocentesis for Prenatal Chromosomal Diagnosis”, Public Health Service, Center for Disease Control, Atlanta, Georgia, 1980.

ACKNOWLEDGEMENTS

The author wishes to express his appreciation to Dr. Jeremiah Mahoney and Dr. Cara Smith for their unrelenting time and invaluable assistance in making this report possible.

STUDENTS’ ANNOTATED BIBLIOGRAPHY

Fast, Julius, *Blueprint* for Life, St. Martin’s Press, Inc., New York, 1964. (The story of modern genetics.)

Goldstein, Phillip, *Genetics is Easy* , Lantern Press, Inc., New York, 1961. (Introduction to the study of genetics for the average biology students.)

Ludovici, L. J., *Links of Life* : *The Story of Heredity* , G. P. Putnam’s Sons, Inc., New York, 1962. (Helpful to the slower reader in understanding how heredity works.)

Papazian, Haig P., *Modern Genetics* , W. W. Norton and Co., Inc., New York, 1967. (Updated and authoritative, a book that will give the better-than-average students a rare insight into genetics.)

Rowland, John, *The Insulin Man* , Roy Publishers, Inc., New York, 1965. (The story of Sir Frederick Banting and his search for a weapon against diabetes.)

Singer, Sam, *Human Genetics* , W. H. Freeman and Co., San Francisco, 1978. (An illustrated introduction to the principles of heredity.)

Webb, Robert N., *Gregor Mendel and Heredity* , Franklin Watts, Inc., New York, 1963. (Tells of the patient research of the Austrian monk whose pea-plant experiments established the basic laws of heredity.)

Webster, Gary, *The Man Who Found Out Why* , Hawthorn Books, Inc., New York, 1963. (Describes Gregor Mendel’s pioneering work.)

TEACHERS' ANNOTATED BIBLIOGRAPHY

Engel, Leonard, *The New Genetics* , Doubleday and Co., Inc., Garden City, New York, 1966. (Deals with some of the latest findings in the field of genetics.)

Gabriel, Mordecai L., (ed,), *Great Experiments in Biology* , Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1955. (A presentation of scientific writings in the original including those of the great geneticist, Hermann J. Muller.)

McKusick, Victor A., *Human Genetics* , Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1964. (One of a few authoritative books available to the layman, written in a readable style and incorporating the latest findings.)

Milunsky, Audrey, *Know Your Genes* , Avon Books, New York, 1979. (A clear, accurate, and readable book on medical genetics; hereditary disorders, genetic counseling, prenatal diagnosis, sex selection, twins, and more. Ethical, moral, and legal issues are given thoughtful consideration.)

Peters, James A., *Classic Papers in Genetics* , Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1959. (Several original papers from the outstanding men of genetics including Mendel up to those of the present day.)

Scheinfeld, Amram, *Your Heredity and Environment* , J. B. Lippincott Co., Philadelphia, 1964. (Explains how heredity works to produce a unique individual and the effect of the environment on the person.)

Sullivan, Navin, *The Message of the Genes* , Basic Books, Inc., Publishers, New York, 1967. (A lucid account of the mechanisms of heredity showing that today's molecular biologists have arrived at a clear understanding of life itself.

Swanson, Carl P., *The Cell* , Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1964. (A discussion of the structure of cells, and the tools involved in the investigations of cells.)

MAGAZINE ARTICLES

Cohen, Stanley N., "The Manipulation of Genes", *Scientific American* , July, 1975. (A summary of recombinant DNA techniques by one of the main innovators.)

Crow, James F., "Genes that Violate Mendel's Rules",

Scientific American , February, 1979. (An interesting article on a topic called segregation distortion and its effects in populations.)

McKusick, Victor A., "The Royal Hemophilia", *Scientific American* , August, 1965. (An account of the gene for hemophilia and how it is found in the royal families of Europe.)

AUDIO VISUAL MATERIALS

35-mm Transparencies

Elementary Genetics Set , Carolina Biological Supply Company, Burlington, North Carolina. (Uses inheritance of kernel color and texture in maize to explain dominance, recessiveness, and the simple Mendelian ratios resulting from monohybrid and dihybrid crosses, 55 slides with narrative cassette.)

Filmstrip

Elementary Genetics Set , Carolina Biological Supply Company, Burlington, North Carolina. (Uses inheritance of kernel color and texture in maize to explain dominance, recessiveness, and the simple Mendelian ratios resulting from monohybrid and dihybrid crosses, 55 slides with narrative cassette.)

Video and 16-mm Programs

Genetics , Carolina Biological Supply Company, Burlington, North Carolina. (Heredity is used to show how anatomical and physiological traits are produced. One example used is how we become right- or left-handed, a trait inherited as a simple autosomal dominant gene. Polydactylism (many fingers or toes) and blood groups (ABO) in humans are used to further illustrate inheritance.)

COMPUTER SOFTWARE

Genetics , Apple II (32k) Diskette. (Covers results of various crosses of peas, fruit flies, and sex-linked diseases. Question/information format.)

Linkover , Apple II (48k) Diskette. (Allows students to plan and execute a program of experiments to draw a genetic map of a single chromosome. Interaction format.)

OTHER SOURCES FOR INFORMATION AND MATERIALS

National Genetics Foundation, Incorporated

9 West 57th Street

New York, New York 10019

Telephone 212-759-4432

The March of Dimes Birth Defects Foundation National Headquarters

Box 2000

White Plains, New York 10602

or local March of Dimes chapter

National Clearinghouse for Human Genetic Diseases for the Department of Health, Education, and Welfare, Bureau of Community Health Services, Genetic Services Program