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Genetics

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Introduction

One of the functions properly studied in Human Physiology is human reproduction and the passing on of genetic material to the next generation. Unfortunately in the text that I use genetics chiefly concerns itself with withered peas, (my apologies to Mendel) and apricot-eyed Drosophila. I would like to base this unit on human genetics, and the long hard research that has brought it to the "present state of the art." This study offers the opportunity to involve mathematics, chemistry, sociology, history, philosophy, ethics, a little molecular biology and, of course, anatomy and physiology. I hope this unit will interest my students and contribute to their understanding of their place in the stream of life as well as acquaint them with recent progress in genetics. They must also be informed so they may develop their own values about future investigations and movements in the fields of genetic engineering, genetic counseling, and the possible dangers to genetic material in their environments and lifestyles.

I have developed 10 lesson plans that scan the field from the text background to the current literature in this subject. The vocabulary is developed sequentially, as well as the complexity of the material. Objectives are stated for each segment, especially since the individual lessons are presented in a format based on a different discipline. Activities accentuating visual impact are used as much as possible and strategies for motivation will vary, almost daily.

This unit is designed for biology or human physiology students. It should last about three weeks. The use of supplementary materials from current scientific and popular magazines is encouraged.

Genetics in the Beginning . . .

I. Objectives:

1. To develop appreciation of scientists as human beings and the "timing" of developments in science.

2. To begin a vocabulary in genetics.
3. To urge students to examine their own potential as scientists.

II. Read the paragraph and use it to analyze these articles that follow in less than one page.

When an idea is “alive” in the minds of people called scientists many things can happen. Some scientists can make experiments and never realize the significance of their outcomes because the information for their interpretation is not available. Some scientists can look at results and misunderstand them. Some scientists understand the possibilities and really don’t know what to do with them. All of these have happened in the field we call genetics.

III. Genetics: In the beginning . . .

Human genetics, based on Mendelian Laws and ratios began with the “rediscovery” of Mendel’s studies in 1900, but it was preceded by observations of peculiarities in families as far back as the 1700’s. In order for a characteristic to be considered as carried from one generation to the following ones, the peculiarity had to be inborn, not acquired and it had to be free of rules of chance or coincidence. A mathematician (they’re the ones who give validity to genetics) named P.L.M. De Mauperius in 1752 found a family where extra fingers and toes occurred in four generations and since extra digits only occurred as one per 20,000 in that population (Berlin), he established a strong possibility that inheritance was responsible. Families who realized that color vision varied among them brought about pedigrees for color blindness. The natural division between those who were color blind and those who weren’t exhibited the law of segregation later explained by Mendel.

In 1883 Francis Galton, another British mathematician, completely unaware of Mendel’s work, but a compulsive measurer, started measuring what he termed “eugenics”. There was no recognition of separate packaging of positive or negative traits, but a general concept of “good blood” or “bad blood” passing the traits on. From 1870 to the 1930’s societies for “positive genetics” to encourage the “scientific” breeding of children for good traits arose.

One community in Oneida, N. Y. actually chose matings by the decision of a committee but the spiritual leader of the group seemed to be chosen more often for that heavy duty and the community disbanded in 1881.

On the other hand “negative genetics” also led to abuses Enthusiasts proposed that it might eliminate disease, producing supermen and a superior society. In America Social Darwinists were convinced that all mental retardation and unacceptable behavior (such as getting angry) were controlled genetically (post Mendel). They even urged the United States to avoid “pollution” of their genetics by restricting “undesirable” ethnic groups in immigration laws. They urged the passing of sterilization laws for the retarded or “socially-inadequate” persons. Pre-war and wartime Nazis in Germany carried this to the highest stage, the killing of the “socially unfit” and the control of mating and marriage. These practices were seen to be abominations and eugenics became an ugly word.

IV. Assignment: Outside research

A Contracts Read Mendel’s original publication and research one of the following for a short report

1. Karl Pearson
2. Francis Galton
3. Correns
4. DeVries
5. Tschermak
6. Morgan, Thomas A.

B Contracts Copy the three laws as presented in text and learn them. Research one of the above. Prepare a pedigree.

C Contracts Do one or the other of above.

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SO WHAT'S A CHROMOSOME?

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I. Objectives:

1. To update and consolidate student's concept of a chromosome.
2. To present visual material for physical and mentaL manipulation.
3. To encourage curiosity about the structure and function of the chromosome as the unit of inheritance.

II. At this time in the study of genetics an appropriate definition of a chromosome might be "a linear aggregation of genes to form a chain of DNA and proteins". The word chromosome comes from "chromo" meaning color and "some" meaning body. These colored bodies were named by Dr. W. Waldeyer in Germany in 1886 shortly after they were first seen by Schneider in 1883. Their ability to be stained by the dye, fuchsin, suggested by the name.

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Within the nucleus of the cells of each species there are a given number of chromosomes especially visible

during cell replication. In humans, the *euploid* number or normal number, of chromosomes present in all cells is 23, 1 pair of sex chromosomes (xx designating female) and xy designating male) and 22 pair termed *autosomal* that carry the genetic material for all other general body functions. The two chromosomes of a given pair are called *homologous* an abnormal number of chromosomes be *aneuploid* , the 23 pair or 46 chromosomes is the *diploid* number and in the gametes or sex cells there is one of each pair or 23 *haploid* number.

(figure available in print form)

Chromosomes are collected by bursting cells obtained from certain body tissues in hypotonic solutions after straining them with particular dyes for visibility they are assigned groupings and numbered. The groupings are determined by the size of the chromosome and the position of the *centromere* , the site of attachment of the microtubular spindle fibers present during the duplication of the chromosomes.

The setting up of chromosomes in this order is called karyotyping. Please use this chromosome group from a burst cell and make an arrangement of homologous chromosomes consisting of eight groups with 3, 2, 7, 3, 3, 2, 2 and the 1 sex chromosome pair in each. The sex chromosomes are circled. When you are finished let's compare your arrangement with the laboratory prepared karyotype. Remember that the chromosomes are arranged according to longest to shortest and subdividions by the centromere position.

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Is this individual a male or female?

(figure available in print form)

This human karyotype was prepared by a modified staining technique. What can you now observe in the chromosomes?

SOME HEAVY MOLECULES

I. Objectives:

1. To give information about the chemistry of DNA and RNA.
2. To introduce the concept of a coding mechanism for production of amino acids.
3. To allow students to manipulate their own code for amino acids.

II. In the course of studying biology you must learn some chemistry. The concept of a molecule of water as two atoms of hydrogen bonded to one atom of oxygen is not new to students. comfortable with 02, oxygen, and CO2, carbon dioxide in respiration and C6H12O as a hexose (6 carbon) sugar in digestion. Adenosine triphosphate, as the primary energy source in muscular tissue, seemed a large molecule but now you will make a big jump into macromolecules. Be assured that the laws that govern those simple molecules still apply in the giant molecules of heredity. It is now believed that there is no chemical reaction in life that a chemist with enough time, technology, and patience couldn't duplicate.

Molecular weights—comparative

H20 = 18 amu (atomic molecular units)

O2 = 32 amu C6H12O = 144 amu

CO 2= 38 amu Adenosine triphosphate = 372 amu

The macromolecules in genetics can have molecular weights in the hundreds of thousands of amu's. The macromolecules, called nucleic acids of the cell nucleus, were discovered by F. Meischer in 1897. Like many other scientific discoveries, their real significance was not appreciated for over 50 years, The two kinds of nucleic acids that are present are deoxyribonucleic acid, DNA, and ribonucleic acid, RNA. Evidence shows that DNA is possibly the genetic material of all living organisms.

DNA is composed of a nitrogen-containing base (either purine or a pyrimidine)

(figure available in print form)
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——and a *pentose* (5 carbon *sugar* called Deoxyribose) and a *phosphate* .

R N A is composed of the same elements except the sugar is ribose.

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Polynucleotides

The chains of units in DNA and RNA are called polynucleotides. ("poly" means many).

Structural Formula:

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Diagrammataic Representatic
(figure available in print form)
III. Task:

1. From information, name the nucleotides; tell what they bond for.
2. Construct two diagrammatic polynucleotides; example:-GaGTCT and CTCAGA.

Developed from diagrams in Beadle, *The Language of Life* , Garden City, 1966.

. . . . And Some Heavy Discoveries (part 2)

I. *Objectives*

1. To develop a little awe for patient, hard work paying off.

2. To develop understanding of the sharing of scientific knowledge and the necessity of its being analyzed with imagination.
3. To impress on students that today's understandings form the basis of tomorrow's discoveries.
4. To learn the facts that fit together to give us today's understanding of the DNA structure.

II. *Putting it together*

As early as 1907 Fleming noted that there was duplication of the nucleic acids in the nucleus of the cell. A scientist, E. Chargaff, established that there was a quantitative relationship between *Adenine* and *Thymine* and between *Guanine* and *Cytosine* . (In RNA, Uracil replaces Thymine) X-ray people (crystallographers) including *Maurice Wilkens* and his colleagues at King's College worked to determine the three dimensional aspects of the DNA structure for over 20 years. Research determined that the adenine *only* bonds with thymine (or uracil in RNA) and quinine *only* bonds with cytosine. Further, there are two weak hydrogen bonds between A and T (- . . . ..) and three weak hydrogen bonds between C and G (. . . . . ..) After many years of separate scientific studies, two scientists, Watson and Crick, consulted with Wilkens and together they published that DNA is a double helix structure, parallel and complementary in structure. It winds and unwinds and replicates itself. We receive this simple statement and accept it but it took the dedication, perseverance and imagination of many people to bring about "this discovery". And if that effort isn't impressive enough remember that these simple combinations of A = T and G = C probably took billions of years to find each other and arrange the code that brings about the replication of life.

Let's take a look at a diagrammatic representation of the double strand diagram, or chains going in opposite directions. The bonds between them are the "weak" hydrogen bonds that can only hold together because of the many linkages and that allows for easy breaking under the right conditions. These chains separate and each will become a mold or *templateon* which another strand can form. Watson and Crick and Wilkens were awarded the Nobel prize for their model piecing together this twisted ladder of phosphates, sugars, and nucleotides and information from many individual scientists' research.

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III. *Demonstration* : Overlays from Allyn and Bacon " *Molecular*

Biology on DNA Replication."

Use each chain in the diagram, fill in the possible initials of each nucleotide and predict the chain each is the template for. When you take the two new strands that are formed, what has happened?

IV. *Assignment* :

It is easier to see some of these features of the double helix in colorful drawings than in black and white so each student is to do one of the following:

1. Bring in an article from a magazine published within the last two years with a visual

conceptualization of the double helix and write a paragraph presenting his understanding of the drawing, or
2. Prepare his own model, drawn on three dimensional conceptualization. (lego can work) I'm bringing zippers myself.
3. Prepare a list of questions on the material thus far and predict where we're going.

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RNA—It Takes More Than One . . . . and The Code Pays Off . . .

I. *Objectives* :

1. To Learn the current information about the various kinds of RNA.
2. To follow the sequence of DNA—RNA—Protein.
3. To produce 20 amino acids from four nucleotides.

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II. *Information* :

Watson and Crick include in their published material this very simple model. It demonstrates the basic relationships between DNA, RNA and protein.

1. DNA is the *template* for its own duplication.
2. DNA is the template (code tape) for the synthesis of RNA, (this is called *transcription*).
3. RNA is the template in protein synthesis, (this is called *translation*).

Please note that after the replication of DNA the arrows only go in one direction.

II. A. *Task* :

Make an imaginary chain of DNA and predict the chain of RNA it would produce. (Remember that uracil (U) replaces thymine in RNA)

III. The RNA produced in the nucleus carries the genetic message of the DNA into the cytoplasm of the cell

where raw materials for the production of amino acids and, ultimately, proteins await organization. This RNA is caLled *messenger RNA* and is designated as mRNA. It is almost always a single strand, and has no regular hydrogen bonded structure. The DNA also seems to organize a chain of mRNA in the nucleus much longer than the chain of mRNA found in the cytoplasm. This has led scientists to believe that it is edited and some material is removed before mRNA leaves the nucleus. This longer form in the nucleus is called *heterogeneous nuclear RNA* and it contains gibberish sequences called *introns* . These introns form dangling material or loops and snip off, and the *axons* (the sensible segments) leave the cell via the endo-plasmic reticulum, and go forth to pass on the code. The introns intrigue scientists at this time since their function is not yet understood. Some hypotheses are:

1. They allow for less damage to the sensible segments. (If there's damage, it can happen in this extra material).
2. They serve as spacers and help regulate the system.
3. They control this RNA splicing mechanism.
4. They are freed and initiate the code for a companion section and the protein it will transcribe.

When the mRNA has exited into the cytoplasm it serves as a template for a new form of RNA called transfer RNA or tRNA. It is activated by ATP. This form of RNA seems to have two affinities, one to bond to some particular amino acid and one for its codon. Therefore, it can bring an amino acid to site A on the ribosome and from there the amino acid attaches to a protein building from a chain of amino acids at site P *on* the *ribosome* . Voila! Proteins for cell growth and for export.

There seems to be only two sites per ribosome.

IV. *Task:*

However, when cell metabolism is taught, students learn that there are 20 amino acids in human cells. How then, can only four kinds of nucleotides in DNA or RNA accomplish separate coding for the synthesis of all twenty? We will use a colored grid; each color will represent one of the nucleotides of RNA. We'll label them U, C, A and G. These could only code for four at the most. Now we'll overlay a similar set of color strips and find sixteen possible combinations UU, UC, UA, UG, CU, CA, etc. One more set of strips combining each of these doubles with the original four brings about 64 combinations, more than enough *codons* to cue the synthesis of all 20 amino acids. In fact, these *triplet* codons do just that and, in many cases, more than one triplet causes the synthesis of the same amino acid.

(figure available in print form)
Do the write out sheet for codons. Place the overlay, (clear plastic) over the write out and it is clear which triplets code for which. In some cases only doubles are necessary to bring an amino acid together and some triplets serve as *terminations* of the chains of amino acids. Formylmethianine is the activator. Chains grow from the 3' end (third carbonatom) to the 5' or vice versa.

V. *Assignment:*

1. Take chain of these codons and “synthesize” a chain of amino acids. CUC, GUG, GCU, GAC, CAU, UAA.
2. Make up a chain of codons and predict the amino acids.
3. In your text, find the polypeptide *chains* for normal hemoglobin and list their codons.

Genes, Alleles and Possibilities

I. *Objectives* :

1. To relate the molecular biology to genetics from Mendel and text.

II *Information* :

At this time we consider a *gene* to be a stretch along a chromosome that codes for a functional product. (Either RNA or its translation product, a polypeptide). We know that each parent in humans (and sexual reproduction, of course), donates one of each pair of chromosomes to the genetic makeup of the zygote. We know that the chromosomes that make up the zygote’s complement of genes differ from that of its parents because:

a. two parents contribute.
b. crossing over has occurred in the diplotene stage of prophase I in meiosis.

One parent has a pair of alleles AA. This parent can donate either of these to the Zygote. This parent is said to have a genotype of AA and a phenotype (what shows up) of black hair. The other parent (Mom) has a genotype of aa and a phenotype of some other color hair. Both of these parents are homozygous genotypes. *Homozygous* means having identical members of an allelic gene pair coding for the same protein, therefore, for the same trait, or contributing to the same trait.
(figure available in print form)
In every case the dominant gene will be expressed and all four will exhibit the black-hair phenotype. They are all *Heterozygous* . Heterozygous means having an allelic pair that is not identical and which can possibly code for different proteins and therefore traits.

III. *Tasks* :

A

1. Make crosses (like Punnett square above) between two of those heterozygous genotypes. Indicate the resulting genotypes and phenotypes. Does it agree with Mendel's Law?

2. Make a cross between a heterozygous genotype and a homozygous recessive genotype. Indicate the outcome in genotypes and phenotypes.

B If each gene pair contributes one allele and there are 23 chromosomes the possible variation at one site could be $2.^{23}$. Use a calculator and figure the possibilities. Now, when combined with the contribution of the other parent, what are the possibilities? What would this mean in terms of all the sequences in DNA that constitute genes?

IV. *More information* :

When the coding is from any of the chromosomes other than the sex chromosome, it is called autosomal, and codes in terms of other body functions. Some normal monogenic autosomatic characteristics you may do classes on are:—curly hair, straight hair, long eyelashes, short eyelashes, unattached earlobes, attached earlobes. Some of the abnormal autosomal dominant diseases are Polycystic kidneys, some kinds of dwarfism, (lack of growth hormone) and Neurofibromatosis (elephant man disease). These abnormal congenital defects are caused by mutation of a single autosomal gene.

Since Mendel's time, we have learned that linkage exists between certain inherited traits because of the proximity of genes on the chromosome and the odds of those genes crossing over together. We also can understand in terms of the coding for proteins accomplished by genes that certain traits are a result of several genes functions.

Example:—Skin color is an excellent characteristic to show how genes still segregate separately and yet determine a strain in combination.

V. Task 1. Set up a square on a full sheet of paper

ABAB = black

abab = white

4 (ABAB) = black (dominants)
3 = dark
2 = medium
1 = light
0 = white

(figure available in print form)

Task 2. Do a chart of blood type possibilities for offspring of parents AAX AA, AOXAA, AAXBB, etc.

* Before doing this task, read material on codominance.

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Mitosis and Meiosis Revisited

I. *Objectives*

1. To learn the cell cycle as it relates to mitosis and meiosis.
2. To update information about gametogenesis.
3. To predict the usefulness of this information in genetics.

II. A. *Information* : The Cell Cycle

Mitosis , or cell duplication, is only a short segment of the cell cycle. During the interphase or time between, duplications, the cell synthesizes materials, undergoes growth and carries on its catabolic functions. The entire cycle, in a mouse cell for instance, would take 18 to 24 hours. All but one hour, which corresponds to the actual mitotic cycle, would correspond to interphase. The DNA is duplicated before the onset of mitOsis so the daughter cell will have the same genetic information as the mother cell.

(figure available in print form)

B. *Appearance of the chromatin material during mitosis* .
1. Interphase-material evenly dispersed.
2. Prophase—coiling to give thread like appearance. The thread is stranded, therefore the duplication of the DNA has already taken place (2 strands are called chromatids).
3. Metaphase—nuclear membrane breaks down, spindle of microtubules forms, chromatids are held together at centromeres.
4. Anaphase—centromere divides, homologues (chromatids) separate, centromere first, to opposite poles of spindle.
5. Telophase—new membrane forms around each set of daughter chromosomes.

C. *Stages of meiosis-First division* :

Meiosis is the division of gametes or germ cells. A second division takes place to reduce the number of chromosomes to the haploid number where only one of each kind of chromosome ends up in the “daughter” cells. The *prophase* I of meiosis is further broken down into leptotence, zygotene, pachytene, diplotene and diakinesis.

1. Leptotene—threadlike structure—2 of each (homologues)
2. Zygotene—homologues begin to pair (zipperlike, point for point.)
3. *Pachytene* —complete pairing, thicker, tightly coiled, called bivalent.
4. *Diplotene* —bivalent opens lengthwise, becomes four chromatids; *centromeres are not split* and *chiasmata* or points of contact exist along the chain, (possible sites of *crossing* over).
5. *Diakinesis* —shortening at height, appears tightly coiled.

Metaphase I— same as mitosis, 2 centromeres for each tetrad, independently arranged (not as pairs of homologues). Crossings over have taken place.
Anaphase I —undivided centromeres and sister chromatids move to opposite sides.
Meiosis II. second division
Metaphase II as in mitosis.
Anaphase II —centromere finally divides—and 4 cells have been produced each with one half the original number of chromosomes.

D. *Gametogenesis revisited* :
1. The sex cells in the human female are originated during fetal life. At the time of birth, the normal female has all the primary cocytes present. Of these only 3 to 4 hundred will be released throughout her life between menarche and menopause. They are at a resting stage in meiosis and must undergo the second meiotic division as long as 40 years after their first division.
2. Most of the cytoplasm in gametes is in the ovum about 20 or 50 times as much as in the sperm.
3. Male gametes or germ cells, (sperm) production, begins at puberty and is more subject to insult from external stimuli.

Assignment:

Relate the information above to the sheet illustrations of phases of meiosis in an organism from Levine,

Genetics , Holt, Rinehart and Winston, 1968, pages 36-37.

Sex Chromosomes . . . and others . . .

I. *Objectives* :

1. To see what can go wrong with chromosomes in general.
2. To learn about sex chromosome abnormalities in particular.
3. To become aware of sex linked and sex limited characteristics.
4. To recognize abnormal karyotypes.

II. *Information* :

The X and Y chromosomes are of different size, and each has areas without a comparable section on the other. If a trait is coded for by a gene or genes in this area of the X chromosome it is said to be sex-linked. Color-blindness and hemophilia are transmitted genetically as sex-linked traits. If a trait is carried on the Y chromosome without a homologue on the X it is said to be sex limited.

III. *Task* :

Predict the offspring in cases of sex.linked disorders. These are all recessive alleles. Differentiate between male and females and their own genotypes.

IV. Sex chromosomes show more abnormalities than most of the autosomal chromosomes. Changes can occur in the phenotype of the individual that affect him or her both sexually and physically, often limiting his or her ability to become a parent and even to earn a living. In an article on sex chromosome disorders in the New England Journal of Medicine (March 25, 1978) Dr. Park S. Gerald measures the incidence of such disorders as 1/380 males and 1/1100 females.

Doctors have two ways to ascertain if there are sex chromosome abnormalities.

1. Examination for Barr bodies and F bodies. Barr bodies can be seen as dark spots near the nuclear membrane. There is always one less Barr body than the number of X chromosomes. The F body appears as a bright spot with a florescent staining method. The number of F bodies is equal to the number of Y chromosomes.

Chromosome examination is done by karyotyping methods

A. The main dysfunction in sex chromosomes (and frequently in autosomal chromosomes as well) is the failure of the pairs to separate during meiotic reduction division. This is called non-disfunction. It occurs more in oogenesis than in spermatogenesis. Can you relate this to when the gametes are produced in females and when they complete meiosis.

What genotypes could this produce?

Task A Normal Non-disjunction in Female In Male

XX and XY XX or O and XY XX and XY or O

When 3 chromOsomes occur in the zygote, the condition is called a *trisomy* (like XXX). When the non-disjuntion causes only one chromosome of a pair in the zygOte it is called a *monosomy* . Monosomies, other than the XO in the sex chromosomes, seem to be unfit to survive. Trisomies do survive but often exhibit phenotypic and genetic problems.

In the above offspring:.

1. The YO does not survive. An X chromosome is a prerequisite for life.
2. The XO female, Turner's syndrome.
    a. How many Barr bodies, how many chromosomes?

These are females,with rudimentary or nO ovaries, underdeveloped breasts, short stature, and with a peculiar webbing of the neck and often sub-normal in intelligence. They cannot reproduce and occur about 1/25,000 births.

3. The XXX—Super female:
    a. How many Barr bodies? F bodies, chromosomes? These females can reproduce normal males and females. The possible genotypes for eggs would be XX and X. Only about 1/6 Of their offspring have chromosome abnormalities so XX code doesn't seem to function well. Some of these females do nOt menstruate.
4. The XXY male, Klinefelter's syndrome, 6/1,000 males.
    a. Barr bodies? F bodies? chromosomes? These males do not look abnormal until puberty when underdeveloped gonads, long limbs, and often, development of breasts become evident. Most are sterile and many are mentally defective.

Task B.:

Predict the testosterone level, sperm production, bodily hair, musculature and voice of XXY.

5. The XYY genotype also exists and it is believed in a ratiO of 1/300 males. These males are usually taller than average, have barely normal IQ's and often suffer persistence.
6. Tetro X (XXXX) females occur. How many Barr bodies? Chromosomes? They exhibit same characteristics as XXX.
7. Klinefelter with XXXY, XXXXY genotypes also occur. Barr bodies? F bodies? Chromosomes?

Assignment:

A
1. Research one of the above or
2. Research testicular feminization or
3. Research new findings in hemophilia research.

B Everyone examine these karyotypes, paste in notebook and describe problems Of each.

Autosomal Recessive Disorders

I. *Objective:*

1. To learn the characteristics of autosomal recessive genetic disorders.
2. To become aware of techniques available for diagnosis.
3. To allow students to discuss their feelings on these matters.

II. *Information* :

Autosomal recessive diseases result from genes that cause carriers without symptoms in the heterozygous genotypes and the disease occurs when the offspring of these receive the two mutant non-functional genes. Some exhibit inborn errors of metabolism. These are caused by deficiencies of enzymes that are catalysts for some metabolic reactions. Carriers don't exhibit the disorder because their normal gene produces enough of the enzyme to sustain the individual.

Some autosomal recessive disorders are:
Sickle cell anemia
Spino-cerebellar ataxias.
Inborn errors of metabolism include those of: Carbohydrate-galactosemia
Amino acid—phenylketonuria
Lipids—Tay-Sachs disease
Mucopoly-saccharide—Cystic fibrosis
Others:
Albinism
Congenital Adrenal hyperplasia

Multi factorial:

Anencephaly	Spinal Bifida
Cleft Lip and Palate	Club Foot
Congenital heart diseases Congenital Hip Dislocation	
Diabetes Mellitus	Epilepsy

III. *Assignment* :

1. Research one Of the above for a report.

Learn (a) Who it affects?——— At what ages?
(b) How can it be diagnosed?

WHAT CAN GO WRONG and Teratogens

I. *Objectives:.*

1. To review methods of genetic screening
2. To give realistic information about birth defects and flaws in genetic replication.

3. To allow students to form their own outlook in terms of this unit.

II. *Information:*

A. Of the 3,000,000 children to be born this year in the United

States it is estimated that 215,000 will have some genetically or teratogenically caused disorders.

Those that are genetically caused would be:

1. Point mutations, producing either autosomal or sexual dominant disorders. These can be the result of defects in the sequence of bases in the codons (interchange of base pairs, insertion of a base pair or deletion of a base pair which does not have the opportunity to correct itself). It can even be the result of the loss of a gene.
2. “Negative” recessive disorders. These are most difficult to deal with because of carrier guilt and need for recognition of the “masked” effect.
3. Abnormalities in the number of chromosomes or makeup and arrangement of chromosomes, such as translocations, deletions and nondisjunctions.
4. Combinations of these factors and environmental teratogens.

B Teratogens:—A teratogen is a drug, chemical, virus, physical agent or deficiency state that, by acting during the embryonic or fetal period, alters morphology or function in post-natal period. The amount of damage during the 0-14 days of gestation is very low because either the ovum dies or regenerates completely. Until the 60th day (organogenetic period) the embryo is extremely sensitive and structural damage is most likely to occur from exposure to teratogenic agents. In the later part of pregnancy, the fetal period, venerability to transplacental insults is greater. A 50% increase in the number of birth defects, when an agent is present, would be considered an indication that the agent is teratogenic.

Materials with proven effects are certain drugs, alcohol, tobacco, some chemicals and large dosages of radiation. We must realize that 2,000 or so chemicals and drugs are added to our environment each year and this alone precludes adequate monitoring. Testing really can only be carried out on laboratory animals and the animal may not show the same results as in humans. For instance, thalidomide that caused reduction of arms and legs in the children of women, who were given that drug, wouldn't affect rabbits or rats but would show up in monkeys and humans . . . . . Testing done in rats leads to questions about aspirin, cortisone and vitamin deficiencies. Also, variation in dosages and individual susceptibility are factors. Medications that have done damage are usually prescribed for problems unrelated to pregnancy and the risk is often before pregnancy is diagnosed. Natural occurrences from the genetic factors also cause 2-3% of the infants to have birth defects.

III. *Assignment* :

Some proven teratogens are:

alcohol		DES	
cancer chemotherapy drugs	hyperthermia (14-28 days)		
thalidomide		tetracycline	
			rubella

Research one of these and their discovery and effects.

IV. *More Information* :

Diagnosis of birth defect possibility is through:

1. Medical monitoring in normal prenatal visits.
2. Alpha fetoprotein measurements (for anencephaly and spinal bifid a.
3. Amniocentesis
4. Fetoscopy
5. Screening of karyotypes
6. Awareness of the parents

V. *Assignment* :

As a sensitive informed person, write up a code for medical people who are involved in genetic screening and counseling.

Genetic Engineering Curse or Blessing . . .

I. *Objective* :.

1. To acquaint students with simple version of recombinant techniques.
2. To present the ethical question without bias, (if possible), .
3. To predict some positive and negative effects that may be realized from genetic engineering.

II. *Information* :

No matter how we feel about it, genetic engineering is progressing by leaps and bounds. Viruses, which are no more than a few genes joined together and surrounded by a protein coat,have been known to be able to replicate in the cytoplasm of cells. Now, these and fast producing and reproducing bacteria are being used to produce protein chains. A repression protein is used to splice or turn off the action at one site on the circular E coli (a bacteria which exists in the human digestive tract) and turn on another part (by a transcribing enzyme) where genes have been inserted, and production of the protein chains that those genes code for begins. DNA can be spliced from one kind of cell to another. These methods can also be used to turn on and off so that the mechanisms of genes may be studied.

Commercial companies are vieing for patent rights and they and commercial biologists are using these recombinant techniques to produce interferon (hopefully effective in virally caused disorders such as flu, hepatitis and even cancer. Human insulin, (a two amino acid chain) has been produced from coding with man-made genes that have been inserted into the plasmids of E.coli. They are activated by (turned only) a mechanism called a lacoperon and the bacteria turned out insulin chains. Other hopes are for pituitary growth hormone for dwarfism and Factor VIII. blood protein for hemophiliacs. It is dreamed that someday the faulty genetic material in humans may be altered by introduced corrective genes.

The major problems are that natural genes have regulatory mechanisms we don’t understand completely, and mapping of genes on chromosomes has really just begun. Therefore, how to install helpful genes into the appropriate cells of the human body is the big question. The closest so far is that Ruddle installed interferon in mouse cells in the embryo and the gene was later passed on to the mouse’s offspring.

III. *Assignment* :

1. Organize a debate among the class members. One half is to argue for genetic engineering; one half is to argue against. Information is to be collected from outside readings. Three days will be given to prepare.
Everyone in class must write a summary of the pertinent points in the debate.
2. “Research” the research going on in any of the disorders mentioned or choose one of your own.

BIBLIOGRAPHY GENETICS

Teacher Bibliography

Beadle, George and Muriel, *The Language* of Life, Garden City, New York 1966.

Cavalli-Sforza, L. L. and Bodner, W. F., *The Genetics of Human Populations* , San Francisco: W. H. Freeman and Co., 1971.

Karp, Laurence F., *Genetic Engineering, Threat of Promise* , Chicago: Nelson-Hall, 1979.

Levine, Robert Paul, *Genetics* , 2nd edition, New York: Holt Rinehart and Winston, Inc., 1968. A nice combination of theory and corroborating experiments of period clearly expressed in wording graphics.

Luria, S. E., *Life, The Unfinished Experiment* , New York: Charles Scribner and Sons, 1973. Easily read, material gradually introduced, humanistic approach, by 1969 Nobel Prize Winner.

Moore, John A., *Heredity and Development* , New York: Oxford University Press, 1957, 1963. Background for historical aspects of genetics, written during Watson-Crick helix period.

Olby, Robert C., *Origins of Mendelism* , New York: Schocken Books, 1967. The book presents a human view of the background of the Mendelian experiments, the man, and an appendix with original sources.

Penrose, L. S., *Outline of Human Genetics* , New York: John Wiley and Sons, 1959. Beautifully written, cogent, pleasant to read, strong section on color blindness.

Scientific American, *The Molecular Basis of Life Biotics* , San Francisco: W. H. Freeman and Co., 1968. Selected articles from Scientific American including “Gene Action in Protein Synthesis” and “Modifications of Gene Action”.

Volpe, E. Peter, *Human Heredity and Birth Defects* , Indianapolis: Pegasus, division of Bobb-Merrill Company, Inc., 1971. This book details chromosomal and gene defects. It contains pictures and it is not for the squeamish.

Watson, James D., *Molecular Biology of the Gene* , 3rd edition, Menlo Park, California: W. A. Benjamin, Inc., 1977. This is Watson’s book. It contains very good summaries at the end of each chapter on all phases of gene molecular biology.

BIBLIOGRAPHY GENETICS

Articles

Bank, Arthur, Mears, J. Gregory and Ramirez, Francisco, “Disorders of Human Hemoglobin,” *Science* , 1, February 1980.

Chedd, Graham, “Genetic Gibberish in the Code of Life”, *Science* , November 1981, pp. 50-55.

Jones, K. L. “Teratogens, What We Know and Don’t Know About Them,” in *Genetic Issues in Pediatric and Obstetric Practice* , Ed. M. M. Kaback: Yearbook Medical Publishers, 1981.

Miller, Orlando J. and Berg, William Roy, “Autosomal Chromosome Disorders and Variations,” *New England Journal of Medicine* , 11” March 1976

Newsweek , March 17, 1980, “The Miracles of Spliced Genes” pp. 62-72.

Gerald, Park S., “Current Concepts in Genetics: Sex Chromosomes and Disorders”, *New England Journal of Medicine* , 25, March 1976

Patrusky, Ben, “How Do Cells Know What To Become?”, *Science* , May 1981 Rensberger, Boyce, “Tinkering With Life”, *Science* , November 1981, pp. 44-50

Student Bibliography

Beadle, George and Muriel, “ *The Language of Life* ”, Garden City, New York: 1966

Interesting lively account of fundamentals of genetics for the lay person.

Morrison, Thomas F., et al,” *Human Physiology* ” Holt, Rinehart and Winston, Inc., New York: 1976. Accepted secondary source for physiology, chapters on cells and Mendelian genetics. Short chapter on human genetics.

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