Genetic Disorders

- Autosomal Genetic Disorders
- X-Linked Inheritance
- Tracking Traits With Pedigrees
- Changes in Chromosome Structure
- Aberrations in Chromosomal Sets: Polyploidy
- Incorrect Chromosome Numbers: Aneuploidy
- PGD: Screening for a Healthy Child

Autosomal Genetic Disorders

Most genetic traits and disorders are caused by a gene (or genes) on one of the 22 pairs of non-sex chromosomes
- Most genetic traits and disorders are _autosomal_
- Most genetic traits and disorders are not X-linked, but are found on the autosomes

Some genetic disorders are dominant
- One copy is sufficient to cause the disorder
- e.g., Marfan_s syndrome

A person with a dominant genetic disorder has a 50% chance of passing it on to any given offspring
- They usually have a heterozygous genotype

How can a person with a dominant genetic disorder live long enough to pass it on?
- Many of these disorders are not debilitating
  - e.g., Polydactyly
- The debilitating symptoms may not be exhibited until well into adulthood
  - Symptoms begin well into reproductive years
  - e.g., Neurological degradation from Huntington disease

Autosomal recessive disorders
- Homozygous dominant (AA) not affected
- Heterozygous (Aa) not affected
- Homozygous recessive (aa) affected
  - Only affects an individual who has 2 recessive copies of the gene

Two parents heterozygous for an autosomal recessive allele can have children with the disorder and without the disorder
- There is a 25% chance that any given child will have the disorder (aa)
- There is a 75% chance that any given child will not have the disorder (AA &Aa)

Individuals heterozygous (Aa) for an autosomal recessive allele are termed _carriers_ for the disorder

Galactosemia

Caused by autosomal recessive allele

Gene specifies a mutant enzyme in the pathway that breaks down lactose
Causes build-up of galactose-1-phosphate, which results in a spectrum of problems, possibly including death

Sickle Cell

In the Punnett square below
25% chance homozygous dominant
50% chance heterozygous (a _carrier_)
25% chance homozygous recessive

X-Linked Inheritance

Hemophilia is a genetic disorder in which blood fails to clot properly
- Multiple proteins interact to make blood clot
- About 80% of hemophiliacs lack a functional version of one of these proteins
  - Factor VIII
- Minor cuts can be life threatening to a hemophiliac

Hemophilia is an X-linked disorder
- So are red-green colorblindness and Duchenne muscular dystrophy
- Each of these disorders is caused by a defective gene on the X chromosome
  - This defective allele encodes either no protein or a protein with reduced function

X-linked disorders are more common in males than in females

We have two copies of most of our genes
- One copy on each chromosome in a homologous pair

Two recessive alleles are required to produce the recessive phenotype
- One functional allele is sufficient for the dominant phenotype in these cases

X-Linked genes are unique because they are on a sex chromosome

The X chromosome is fairly large
- Contains ~1,500 genes

The Y chromosome is very small
- Contains only 78 genes

Females possess two X chromosomes
- Two copies of all X-linked genes

Males possess a single X chromosome
- Only one copy of all X-linked genes
- Their Y chromosome does not contain copies of these genes

Females require two recessive alleles to have a recessive X-linked phenotype
- _Backup_ if one of their alleles is faulty

Males require only one recessive allele to have a recessive X-linked disorder
- No _backup_ if their allele is faulty

If a woman passes a recessive X-linked allele to her offspring
- Her son will be affected

He will not receive a copy of the gene from his father
His father will give him a Y chromosome
Her daughter will probably not be affected
She is likely to receive a functional copy of the gene from her father

Medical pedigrees can be helpful for genetic disorders
Provide a family history of the disease
Help to determine whether a condition is
Dominant or recessive
X-linked or autosomal
Help establish probabilities for future inheritance
Identification of carriers is an important part of this

Changes in Chromosome Structure

Chromosome structure can be changed
Random
Influenced by environmental influences
Main changes that occur
Duplication
Inversion
Deletion
Translocation

Polyploidy & Aneuploidy

Other genetic conditions can be caused by an aberrant (wrong) number of chromosomes
One or more additional full sets of chromosomes can be inherited
Polyploidy
A small number (generally 1) of extra or missing chromosomes can be inherited
Aneuploidy

Polyploidy is the condition in which one or more entire sets of chromosomes has been added to an organism_s genome
e.g., A sperm or egg contains two sets of chromosomes
Meiosis failed to separate these sets
e.g., An egg is fertilized by two sperm

Polyploidy is a disaster for humans and many other species
Polyploidy = death
Polyploidy is tolerated well by many species
Particularly plants
Cotton, soybeans, peanuts, bananas, and durum wheat are all polyploid

Aneuploidy is a condition in which an organism has either more or fewer chromosomes

than normally exist
Generally one chromosome too many or too few
Usually caused by nondisjunction during meiosis

Nondisjunction is the failure of homologous chromosomes or sister chromatids to separate during meiosis
Homologous chromosomes separate in meiosis I
Sister chromatids separate in meiosis II
If either event is imperfect, all or some of the gametes produced will have an aberrant number of chromosomes

Aneuploidy in humans in surprisingly common, yet goes largely unrecognized
Most aneuploid embryos will not survive
Generally miscarried during the pregnancy
This miscarriage is often so early in the pregnancy that the would-be-mother doesn_t even know that she was pregnant
She may only think that she is having a hard time getting pregnant

Some aneuploid embryos will survive
Only those with an extra copy of automosome 13, 18, or 21 have a greater chance of survival
These are relatively small chromosomes
Smaller genetic imbalance less likely to result in a miscarriage

Trisomy 21 results in a condition known as Down syndrome
Three copies of chromosome 21
Seen in 0.1% of all live births
Array of effects
Smallish, oval heads
IQs well below normal
Short stature
Reduced life span
Infertility in males

Aneuploidy can also affect sex chromosomes
Embryos often survive sex chromosome aneuploidies
Effects are usually debilitating
Examples include
XO - Turner Syndrome
XXY - Kleinfelter Syndrome
XXX, XYY also possible, but YO is not

PGD: Screening for a Healthy Child

Many debilitating human conditions have genetic causes
Many of these conditions can be detected very early
Embryonic cells can be gathered

Chromosomes and DNA can be analyzed
Such screening began in the 1960s

The screening of embryos produced through in vitro fertilization is termed
Preimplantation genetic diagnosis
PGD
Hormones stimulate egg formation
10 _ 12 mature eggs removed from ovaries
Fertilized in laboratory

Each fertilized egg divides to form an early embryo
Eight-cell embryo in three days
One cell is removed from this early embryo
Undifferentiated _embryonic stem cell_
Embryo is unaffected

DNA and chromosome testing is performed on removed cell from each embryo
e.g., Attach fluorescent molecules to each copy of chromosome 21 to allow them to be visualized easily with a microscope
Embryos deemed _acceptable_ are implanted