Human karyotype preparation

1. Amniocentesis: sampling of fetal cells from amniotic fluid (cells)
2. Chorionic villi sampling: cells from chorion where placenta develops (tissue)
3. Cells are treated to arrest mitosis during metaphase when chromosomes are condensed
4. Chromosome spread is performed on fixed and stained cells
5. Computer is used to align paired chromosomes and determine karyotype
6. Find abnormalities.
Pedigree Charts

• A pedigree chart shows the pattern of inheritance for a particular disorder.
  – Males are designated by squares.
  – Females are designated by circles.
  – Shaded circles or squares are affected individuals.
  – Vertical line down represents a child, while an attached horizontal line across represents more children (siblings).

Royal Hemophilia Pedigree
Genetic counseling

Create pedigree of the family to determine genetic makeup of the family related to a particular trait.

Carriers possess the gene of interest, but are unaffected by it.

Recessive trait: masked by presence of a dominant gene.

Dominant trait: controls phenotype of individual.

Autosomal recessive disorders:
- Affected children can have unaffected parents.
- Heterozygotes (Aa) have a normal phenotype.
- Two affected parents will always have affected children.
- Affected individuals with homozygous dominant mates will have unaffected children.
- Close unaffected relatives who reproduce are more likely to have affected children if they have joint affected relatives.
- Both males and females are affected with equal frequency.

Key:
- aa = affected
- Aa = carrier (unaffected)
- AA = unaffected
- A? = unaffected (one allele unknown)

Autosomal dominant disorders:
- Affected children will have at least one affected parent.
- Heterozygotes (Aa) are affected.
- Two affected parents can produce an unaffected child.
- Two unaffected parents will not have affected children.
- Both males and females are affected with equal frequency.

Key:
- AA = affected
- Aa = affected
- aa = normal
Sex-linked disorder

X-linked disorder: defective gene carried on X chromosome
Expressed in male offspring because they only possess one X copy and the Y chromosome lacks an allele for the gene required to compensate.

Y-linked disorder: defective gene carried on Y-chromosome
Male-restricted defects, passed from a father to all sons.

Genetic testing by DNA markers

a. Normal fragmentation pattern
b. Genetic disorder fragmentation pattern
Genetic testing by DNA probe array

Screening for mutations in tagged DNA isolated from individual to test for multiple mutations known to associate with diseases.

Hereditary diseases that can be identified by genetic and/or biochemical screening

<table>
<thead>
<tr>
<th>Table 4.1</th>
<th>Tools and Treatments for Some Human Genetic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Description</td>
</tr>
<tr>
<td>Adundal Recurrence Disorders</td>
<td></td>
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<tr>
<td>Cystic Fibrosis</td>
<td>Mutations in the lung and digestive tract in thick and viscous, making breathing and digestion difficult</td>
</tr>
<tr>
<td>Tay-Sachs Disease</td>
<td>Neurological impairment and psychomotor difficulties develop early, followed by blindness and uncontrollable seizures, death at 3 years</td>
</tr>
<tr>
<td>Phenylketonuria</td>
<td>Inability to metabolize phenylalanine; if protein diet is not begun, mental impairment develops</td>
</tr>
<tr>
<td>X-linked Dominant Disorders</td>
<td></td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>Benign tumors occur under the skin or deeper</td>
</tr>
<tr>
<td>Huntington disease</td>
<td>Most disorders in balance and coordination develop in middle age and progress toward severe neurological disturbances leading to death</td>
</tr>
<tr>
<td>Complete Discontinue</td>
<td></td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td>Pain, swelling, anxiety, internal hemorrhage due to sickle-shaped red blood cells</td>
</tr>
<tr>
<td>X-linked Discontinue</td>
<td></td>
</tr>
<tr>
<td>Hemophilia A or B</td>
<td>Propensity for bleeding, often internal, due to the lack of a blood-clotting factor</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>Muscle weakness develops early and progressively until death occurs, usually before age 30</td>
</tr>
</tbody>
</table>
Harvesting eggs for genetic testing

Used by IVF clinics to screen for healthy eggs
Polar body of eggs examined for presence of defective gene - if present in polar body, then the gene in the egg is normal and egg is used. If the polar body chromosomes are normal, the egg carries the defective gene and is discarded.
Eggs that pass screening can be used for IVF to eliminate transmission of defective gene to offspring

Pre-pregnancy testing

Testing of embryo for presence of hereditary diseases
Allows parents who are carriers of severe genetic diseases to have healthy babies
By selecting characteristics of offspring, we are engaging in a form of evolutionary selection - which genes are passed on to offspring. Genetic screening allows for selection against deleterious alleles. Heterozygous carriers advised to opt for testing and screening to stop transmission to next generation (Tay-Sachs). Society is now asked to ponder the implications of knowing far more than ever before about the characteristics of a future child. Will the ability to screen for children who are expensive, emotionally demanding, or time consuming to raise alter future conceptions? Will this technology inevitably lead to eugenics: perpetuation of desirable human traits (intelligence, strong heart, healthy immune system)? In CA, Genetic Disease Branch estimates a savings of $108 million in 1993 through prenatal testing and abortion of fetuses with Downs Syndrome. What is the definition of health? Who should be allowed to survive?

Collision of scientific technology, desire for genetic fitness, societal and cultural imperatives.