**TABLE 9-1** Classification of Eukaryotic DNA

<table>
<thead>
<tr>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein-coding genes</td>
</tr>
<tr>
<td>Solitary genes</td>
</tr>
<tr>
<td>Duplicated and diverged genes</td>
</tr>
<tr>
<td>(functional gene families and</td>
</tr>
<tr>
<td>nonfunctional pseudogenes)</td>
</tr>
<tr>
<td>Tandemly repeated genes encoding rRNA, 5S rRNA,</td>
</tr>
<tr>
<td>tRNA, and histones</td>
</tr>
<tr>
<td>Repetitive DNA</td>
</tr>
<tr>
<td>Simple-sequence DNA</td>
</tr>
<tr>
<td>Moderately repeated DNA (mobile DNA elements)</td>
</tr>
<tr>
<td>Transposons</td>
</tr>
<tr>
<td>Viral retrotransposons</td>
</tr>
<tr>
<td>Long interspersed elements (LINEs; nonviral</td>
</tr>
<tr>
<td>retrotransposons)</td>
</tr>
<tr>
<td>Short interspersed elements (SINEs; nonviral</td>
</tr>
<tr>
<td>retrotransposons)</td>
</tr>
<tr>
<td>Unclassified spacer DNA</td>
</tr>
</tbody>
</table>

**Box 6.4: The organization of the human genome**

1. 1% Exons
2. 24% Introns
3. 25% Genes
4. 75% Intergenic DNA

- Human genome 3000 Mb
- Genes and gene-related sequences 900 Mb
- 29% Coding DNA 90 Mb
- 24% Noncoding DNA 810 Mb
- 1% Pseudogenes
- 24% Gene fragments
- 24% Introns, leaders, trailers
- 24% Tandemly repeated DNA
- 24% Repetitive DNA 420 Mb
- 24% Unique and low copy number 1680 Mb
- 24% Interspersed genome-wide repeats
- 24% Satellite DNA
- 24% Microsatellite DNA
- 24% LTR elements
- 24% SINEs
- 24% Minisatellite DNA
- 24% LINEs
- 24% DNA transposons

Based on Strachan and Read (1996).
Table 7.11: Major classes of tandemly repeated human DNA

<table>
<thead>
<tr>
<th>Class</th>
<th>Size of repeat</th>
<th>Major chromosomal location(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Megasatellite’ DNA (blocks of hundreds of kb in some cases)</td>
<td>several kb</td>
<td>Various locations on selected chromosomes</td>
</tr>
<tr>
<td>RS447</td>
<td>4.7 kb</td>
<td>-50–70 copies on 4p15 plus several copies on distal 8p</td>
</tr>
<tr>
<td>untitled</td>
<td>2.5 kb</td>
<td>-400 copies on 4q31 and 19q13</td>
</tr>
<tr>
<td>Satelllite DNA (blocks often from 100 kb to several Mb in length)</td>
<td>5–171 bp</td>
<td>-50 copies on the X chromosome</td>
</tr>
<tr>
<td>α (alpheid DNA)</td>
<td>171 bp</td>
<td>Especially at centromeres</td>
</tr>
<tr>
<td>β (Sau3A family)</td>
<td>68 bp</td>
<td>Centromeric heterochromatin of all chromosomes</td>
</tr>
<tr>
<td>Satellite 1 (AT-rich)</td>
<td>25–48 bp</td>
<td>Centromeric heterochromatin of 1, 9, 13, 14, 15, 21, 22 and Y</td>
</tr>
<tr>
<td>Satellite 2 and 3</td>
<td>5 bp</td>
<td>Centromeric heterochromatin of most chromosomes and other heterochromatic regions</td>
</tr>
<tr>
<td>Minisatellite DNA (blocks often within the 0.1–20 kb range)</td>
<td>6–64 bp</td>
<td>Most, possibly all, chromosomes</td>
</tr>
<tr>
<td>telomeric family</td>
<td>6 bp</td>
<td>At or close to telomeres of all chromosomes</td>
</tr>
<tr>
<td>hypervariable family</td>
<td>9–64 bp</td>
<td>All telomeres</td>
</tr>
<tr>
<td>Microsatellite DNA (blocks often less than 150 bp)</td>
<td>1–4 bp</td>
<td>All chromosomes, often near telomeres</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dispersed throughout all chromosomes</td>
</tr>
</tbody>
</table>

**Figure 19.16** An overview of the various categories of repetitive DNA.
Figure 7.1 Occurrence of different kinds of unique and repeated DNA segments on chromosomal DNA.

CONTINUOUS STRETCH OF GENES & INTERGENIC REGIONS!
Figure 2.28 In a simple tandem repeat polymorphism (STRP), the alleles in a population differ in the number of copies of a short sequence (typically 2–60 bp) that is repeated in tandem along the DNA molecule. This example shows alleles in which the repeat number varies from 1 to 10. Cleavage at restriction sites flanking the STRP yields a unique fragment length for each allele. The alleles can also be distinguished by the size of the fragment amplified by PCR using primers that flank the STRP.
VNTRs Are Sequence-Specific Tandem Repeats Present Throughout the Genome

Figure 22.8  Simplified diagram of the use of variable number tandem repeats in preparing DNA fingerprints.

VARY IN REPEAT LENGTH (2p or 2q!)  2L + UP!
VNTRs generally have many different alleles at a given locus.

**PCR Method**

Population of Alleles!

- **Repeat** = \((CA)n\)

(a) 1. Determine sequences flanking microsatellites

   - **Allele 1**
     - 5' \(\ldots CA\ldots\) 3'
     - 3' \(\ldots GT\ldots\) 5'

   - **Allele 2**
     - 5' \(\ldots CA\ldots\) 3'
     - 3' \(\ldots GT\ldots\) 5'

2. Amplify alleles by PCR

   - ** Allele 1**
     - 5' \(\ldots CA\ldots\) 3'
     - 3' \(\ldots GT\ldots\) 5'

   - **Allele 2**
     - 5' \(\ldots CA\ldots\) 3'
     - 3' \(\ldots GT\ldots\) 5'

3. Analyze PCR products

   ![PCR Products Diagram]

(b) Alleles present in population

   - **Allele 1**
     - \(\ldots CA\ldots\)
   - **Allele 2**
     - \(\ldots CA\ldots\)
   - **Allele 3**
     - \(\ldots CA\ldots\)

Diploid genotypes present in population

![Diploid Genotypes Diagram]

Figure 9.12 Detection of microsatellite polymorphisms by PCR and gel electrophoresis. (a.1) Microsatellite alleles differ from one another in length. (2) Sequence determination from both sides of a microsatellite enables the construction of primers that can be used to amplify the microsatellite by PCR. (3) Gel electrophoresis and ethidium bromide staining distinguish the alleles from each other.

(b) Microsatellites are often highly polymorphic with many different alleles present in a population. With just three alleles, there are six possible genotypes. With \(N\) (any number of) alleles, there will be \(2^N\) genotypes.

Useful for comparing individuals to populations (e.g., HCO70A).

Are there races?

Method used in HCO70A class!
Figure 1. *DIS80* Alleles in the Winter, 2004 HC70A UCLA Class Population.

Figure 2. *DIS80* Alleles in the Winter, 2004 HC70A Kyoto Class Population.
VNTR D1580 alleles vary in different human populations.

Figure 17.15 Range of allele frequencies found among human subpopulations for the VNTR D1580. [Data from B. Budowie et al. J. Forensic Science 1995. 40:38.]
Figure 17.14 Use of DNA typing in paternity testing. The sets of lanes numbered 1 and 2 contain DNA samples from two different paternity cases. In each case, the lanes contain DNA fragments from the following sources: M, the mother; C, the child; A, the accused father. The lanes labeled A + C contain a mixture of DNA fragments from the accused father and the child. The arrows in case 2 point to bands of the same size that are present in lanes M, C, and A + C. Note that the male accused in case 2 could not be the father because neither of his bands is shared with the child. [Courtesy of R. W. Allen.]
**Figure 2.22** Key concepts and terms used in modern genetics. Note that a single gene can have any number of alleles in the population as a whole, but no more than two alleles can be present in any one individual.
Multiple Single-Locus VNTRs Used in a Criminal Case

Figure 17.13 An example of DNA typing in a criminal case. Each panel is the result of DNA typing for a different VNTR. The lanes marked S1, S2, and S3 contain DNA from blood samples of three male suspects; those in columns U1 through U7 contain DNA from semen samples collected from seven female victims of rape. The lanes marked M contain molecular-weight markers. In each case, the DNA from suspect S2 matches the samples obtained from the victims. [Courtesy of Steven J. Redding, Office of the Hennepin County District Attorney, Minneapolis, and Lowell C. Van Berkom and Carla J. Finis, Minnesota Bureau of Criminal Apprehension.]
Figure 9.4 Minisatellites are highly polymorphic because of their potential for misalignment and unequal crossing-over.

Minisatellites are composed of relatively long tandem repeating units of identical sequence. (a) Misalignment and (b) unequal crossing-over produce (c) recombinant products that contain different numbers of repeating units than either parental locus; each new recombinant product is a new allele.
The human genome is packaged into chromosomes.

Figure 8-60  (a) Generalized diagram of eukaryotic nucleus showing identifiable structural elements. (b) Electron micrograph of nuclear pore–lamin complexes isolated from rat nuclei. Nuclear pores (arrows) are embedded in fibrous lamin proteins (la). (c) A transmission electron micrograph of a whole mount of a HeLa cell, showing a skeletal network within the nucleus. The cell was prepared by removing lipids and soluble factors with a mild detergent. The remaining skeletal structure was then treated to remove most of the DNA. The sample was fixed with glutaraldehyde, but no heavy-metal shadowing was done. [See S. Penman et al., 1982, Cold Spring Harbor Symp. Quant. Biol. 46:1013.] Photograph (b) courtesy of N. Duryer. Reproduced from the Journal of Cell Biology, 1976, by copyright permission of Rockefeller University Press. Photograph (c) courtesy of S. Penman.

Nucleus = 6 μm diameter
DNA = 6×10⁶ μm in length

Figure 28.10
Levels of chromatin structure. The beaded string structure is a 10-nm fiber, which folds into a "solenoidal" 30-nm fiber with about six nucleosomes per turn. This can further fold to form thick 200-nm fibers that can be observed in electron micrographs of chromosomes or nuclei.

DNA tightly coiled
Hundred of genes per chromosome

DNA tightly coiled
Historides
by name/ tailing chromosomes
**Figure 19.12** General model of the association of histones and DNA in the nucleosome, illustrating the way in which the chromatin fiber may be coiled into a more condensed structure, ultimately producing a mitotic chromosome.
Chromosomes can be characterized using a microscope and constructing a karyotype.

Preparation of a Karyotype

Chromosome typing for the identification of gross chromosomal abnormalities is being carried out at an increasing number of genetic counseling centers throughout the United States. The result of the procedure is a graphic display of the chromosome complement, known as a karyotype. The chromosomes shown in a karyotype are mitotic metaphase chromosomes, each consisting of two sister chromatids held together at their centromeres. To prepare a karyotype, cells in the process of dividing are interrupted at metaphase by the addition of colchicine, a drug that prevents the subsequent steps of mitosis from taking place by interfering with the spindle microtubules. After treating and staining, the chromosomes are photographed, enlarged, cut out, and arranged according to size. Chromosomes of the same size are paired according to centromere position, which results in different “arm” lengths. From the karyotype, certain abnormalities, such as an extra chromosome or piece of a chromosome, can be detected.

Karyotypes are needed to detect chromosomal abnormalities.

Add colchicine

Add water

White cells

Causes cells to swell

White cells settle out

Fix with alcohol and stain

Spread one drop

Centrifuge

Stop all cells at metaphase

Red cells settle out and are removed

Cells at metaphase have burst

Photograph and enlarge

Cut out individual chromosomes

C. Metaphase chromosomes

Paste in order of diminishing size with centromere on pencil line

2 Chromatids cyto 2n RRNA replication = 2 0.4 units

Before or after DNA replication?
CHROMOSOMES HAVE STRUCTURES THAT ARE VISIBLE IN LIGHT AND ELECTRON MICROSCOPES

**Figure 1.3 Human chromosomes.**

- Light micrograph of human chromosomes (enlarged 600 times)
- Electron micrograph of fixed chromosome (enlarged 30,000 times)
- Transmission electron microscope
- Schematic diagram

- Chromatids
- Satellite DNA
- Telomeres
- A chromosome during division
- One chromosome/one DNA molecule

**Legend:**
- Light microscope
- Electron microscope
Figure 10.3 The human karyotype: Banding distinguishes the chromosomes. (a) Photograph of a complete set of human chromosomes at metaphase. Staining with Giemsa dye accentuates the bands and interbands. (b) Idiograms for the complete set of human chromosomes. An ideogram is an idealized diagram of the banding pattern associated with a stained chromosome.

(c) Chromosome 7 at three different levels of banding resolution. As staining techniques improve, it becomes possible to resolve what previously appeared as a single band into a series of bands and interbands, producing more and more bands along each chromosome. Thus, at one resolution, 7q31 appears as one band. At a slightly higher resolution, 7q31 becomes two bands (7q31.1 and 7q31.3) flanking an interband (7q31.2); and at an even higher resolution, 7q31.3 itself appears as two bands (7q31.31 and 7q31.33) and an interband (7q31.32).

What causes banding patterns of chromosomes to be unique?
Sign 2 bands?
### Table 9.1 Conventional karyotype symbols used in human genetics

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A–G</td>
<td>Chromosome groups</td>
</tr>
<tr>
<td>1–22</td>
<td>Autosome designations</td>
</tr>
<tr>
<td>X, Y</td>
<td>Sex-chromosome designations</td>
</tr>
<tr>
<td>p</td>
<td>Short arm of chromosome</td>
</tr>
<tr>
<td>q</td>
<td>Long arm of chromosome</td>
</tr>
<tr>
<td>ter</td>
<td>Terminal portion: pter refers to terminal portion of short arm, qter to terminal portion of long arm</td>
</tr>
<tr>
<td>+</td>
<td>Preceding a chromosome designation, indicates that the chromosome or arm is extra; following a designation, indicates that the chromosome or arm is larger than normal</td>
</tr>
<tr>
<td>−</td>
<td>Preceding a chromosome designation, indicates that the chromosome or arm is missing; following a designation, indicates that the chromosome or arm is smaller than normal</td>
</tr>
<tr>
<td>mos</td>
<td>Mosaic</td>
</tr>
<tr>
<td>/</td>
<td>Separates karyotypes of clones in mosaic—e.g., 47, XXX/45, X</td>
</tr>
<tr>
<td>dup</td>
<td>Duplication</td>
</tr>
<tr>
<td>dir dup</td>
<td>Direct duplication</td>
</tr>
<tr>
<td>inv dup</td>
<td>Inverted duplication</td>
</tr>
<tr>
<td>del</td>
<td>Deletion</td>
</tr>
<tr>
<td>inv</td>
<td>Inversion</td>
</tr>
<tr>
<td>t</td>
<td>Translocation</td>
</tr>
<tr>
<td>rcp</td>
<td>Reciprocal translocation</td>
</tr>
<tr>
<td>rob</td>
<td>Robertsonian translocation</td>
</tr>
<tr>
<td>r</td>
<td>Ring chromosome</td>
</tr>
<tr>
<td>i</td>
<td>Isochromosome (two identical arms attached to a single centromere, like an attached-X chromosome in <em>Drosophila</em>)</td>
</tr>
</tbody>
</table>
BANDING PATTERNS CAN BE USED TO DISTINGUISH CHROMOSOMES AND LOCATE GENES.

Figure 30-1
The haploid human genome. This is a schematic drawing of 1 of each of the 23 human chromosomes, showing the pattern of staining seen with the Giemsa banding method. Chromosomes are first treated with trypsin and then stained with Giemsa. The patterns of light and dark bands are characteristic for each chromosome, and translocations, deletions, and other structural abnormalities can be identified. Typically 400 bands can be seen per haploid genome, and each band represents on average \(7.5 \times 10^6\) bp, or twice as many base pairs as in the entire \(E. coli\) genome! Chromosome 1 constitutes 8.4 percent, and the \(Y\) chromosome about 2.0 percent, of the human genome. Taking the \(E. coli\) genome as a unit of genome size, a cytogenetic band is 2 genome units, and the \(Y\) chromosome is 15 genome units.

The band size is \(7.5 \times 10^6\) at \(25 \times 10^6\) bp larger than the size of \(E. coli\) genome!
Figure 9.1 Human chromosome painting, in which each pair of chromosomes is labeled by hybridization with a different fluorescent probe. (A) Metaphase spread showing the chromosomes in a random arrangement as they were squashed onto the slide. (B) A karyotype, in which the chromosomes have been grouped in pairs and arranged in conventional order. Chromosomes 1–20 are arranged in order of decreasing size, but for historical reasons, chromosome 21 precedes chromosome 22, even though chromosome 21 is smaller. [Courtesy of Johannes Wienberg and Thomas Ried.]

Table 7.2: DNA content of human chromosomes a

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Amount of DNA (Mb)</th>
<th>Chromosome</th>
<th>Amount of DNA (Mb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>263</td>
<td>13</td>
<td>114</td>
</tr>
<tr>
<td>2</td>
<td>255</td>
<td>14</td>
<td>109</td>
</tr>
<tr>
<td>3</td>
<td>214</td>
<td>15</td>
<td>106</td>
</tr>
<tr>
<td>4</td>
<td>203</td>
<td>16</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>194</td>
<td>17</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>183</td>
<td>18</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>171</td>
<td>19</td>
<td>67</td>
</tr>
<tr>
<td>8</td>
<td>155</td>
<td>20</td>
<td>72</td>
</tr>
<tr>
<td>9</td>
<td>145</td>
<td>21</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>144</td>
<td>22</td>
<td>56</td>
</tr>
<tr>
<td>11</td>
<td>144</td>
<td>X</td>
<td>164</td>
</tr>
<tr>
<td>12</td>
<td>143</td>
<td>Y</td>
<td>59</td>
</tr>
</tbody>
</table>

a The DNA content is given for chromosomes prior to entering the S (DNA replication) phase of cell division (see Figure 2.2). Data abstracted from electronic reference 1.
In situ hybridization with fluorescent probes can identify genes and chromosomes.

(a) Steps in performing in situ hybridization:
1. Squash cells on slide.
2. Treat with 0.07 N NaOH for 2 min.
3. Incubate with radioactive DNA, then wash to remove unhybridized single strands of DNA.
4. Coat slide with emulsion, expose, and develop autoradiograph.

(b) Autoradiograph showing chromosomal locations of mouse satellite DNA sequences.

(c) Visualization of human telomeres by using fluorescent dyes and in situ hybridization.

Visible color in microscope specific wavelength.
Mapping Genes to Chromosomes and Specific Regions

In situ Hybridization

Chromosome 11

Unwind

Anneal with fluorescent probe for β-globin gene

DNA tagged at β-globin gene

**β-globin gene**

ACTCTGGAGAG

Fluorescent tag

Figure 7.5 Locating the position of the β-globin gene on human chromosome 11.
This task is now complete with the completion of the human genome sequence.
Genes can be mapped to specific bands of each chromosome.

How locate these genes if no probe or sequence?

**X Chromosome**

Ichthyosis, X-linked
Placental steroid sulfotase deficiency
Kallmann syndrome
Chondrodysplasia punctata,
X-linked recessive

Hypophosphatemia
Aicardi syndrome
Hypomagnesemia, X-linked
Ocular albinism
Retinoblastoma

Adrenal hypoplasia
glycerol kinase deficiency
Ornithine transcarbamylase deficiency
Incontinentia pigmenti
Wiskott-Aldrich syndrome
Menkes syndrome

Androgen insensitivity
Charcot-Marie-Tooth neuropathy
Charcot-Marie-Tooth neuropathy
Cleft palate, X-linked
Spastic paraplegia, X-linked, uncomplicated
Deafness with stapes fixation

Sideroblastic anemia
Aarskog-Scott syndrome
PGK deficiency, hemolytic anemia
Anhidrotic ectodermal dysplasia

Agammaglobulinemia
Kennedy disease

Pelizaeus-Merzbacher disease
Alport syndrome
Fabry disease

Immunodeficiency, X-linked, with hyper IgM
Lymphoproliferative syndrome
Albinism-deafness syndrome

PRPS-related gout
Low syndrome
Long-Pierre syndrome
HPRT-related gout
Hunt syndrome
Hemophilia B

Hemophilia A
G6PD deficiency: favism
Drug sensitive anemia
Chronic hemolytic anemia
Manic-depressive illness, X-linked
Colorblindness, (several forms)
Dyskeratosis congenita

TKCR syndrome
Adrenal muscular dystrophy
Adrenomyeloneuropathy
Emery-Dreifuss muscular dystrophy
Diabetes insipidus, renal
Myotubular myopathy, X-linked

Fragile-X syndrome

AOL = Lorenzo's disease

Self-mutation

**Figure 12-22**
The human X-chromosome gene map. Over 50 diseases have now been traced to specific segments of the X-chromosome. Many of these disorders are also influenced by genes on other chromosomes. *KEY: PGK, phosphoglycerate kinase; PRPS, phosphoribosyl pyrophosphate synthetase; HPRT, hypoxanthine phosphoribosyl transferase; TKCR, torticollis, klooids, cryptorchidism, and renal dysplasia.
Disease genes can be localized to specific chromosomes.

Figure 1-6 The 23 chromosomes of a human being, showing the positions of genes whose abnormal forms cause some of the better-known hereditary diseases. (Time)
Figure 2.19: Origins of triploidy and tetraploidy.

About two-thirds of human triploids arise by fertilization of a single egg by two sperm (A). Other causes are a diploid egg (B) or sperm (C). Most human triploids abort spontaneously; very rarely they survive to term, but not beyond. Tetraploidy (D) results from failure of the first mitotic division after fertilization, and is incompatible with development.

What causes lethality with xtra genes/chromosomes?

What are the consequences of xtra chromosomes & chromosome sets?
HOW CAN CHANGES OCCUR IN THE HUMAN GENOME?

**TABLE 12.1 Chromosomal Rearrangements and Changes in Chromosome Number (or Ploidy).**

<table>
<thead>
<tr>
<th>How Detect?</th>
<th>Chromosomal Rearrangements</th>
<th>Changes in Chromosome Number or Ploidy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deletion: Removal of a segment of DNA</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Duplication: Increase in the number of copies of a chromosomal region</td>
<td>1 2 3 4</td>
<td>5 6 7 8</td>
</tr>
<tr>
<td>Inversion: Half-circle rotation of a chromosomal region</td>
<td>1 2 3 4</td>
<td>5 6 7 8</td>
</tr>
<tr>
<td>Translocations:</td>
<td>Nonreciprocal: Unequal exchanges between nonhomologous chromosomes</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>Reciprocal: Parts of two nonhomologous chromosomes trade places</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>Transposition:</td>
<td>Movement of short DNA segments from one position in the genome to another</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

**Euploidy:** Cells that contain only complete sets of chromosomes

- Diploidy (2x): Two copies of each homolog
- Monoploidy (x): One copy of each homolog
- Polyploidy: More than the normal diploid number of chromosome sets
  - Triploidy (3x): Three copies of each homolog
  - Tetraploidy (4x): Four copies of each homolog

**Aneuploidy:** Loss or gain of one or more chromosomes producing a chromosome number that is not an exact multiple of the haploid number

- Monosomy (2n - 1)
- Trisomy (2n + 1)
- Tetrasomy (2n + 2)

Note that it is more accurate to denote monoploids, triploids, and tetraploids as multiples of x, which represents the number of different chromosomes in a complete set, rather than as multiples of n, the number of chromosomes in the genome. In this table, as throughout the chapter, nonhomologous chromosomes are drawn in different colors. Different shades of the same color highlight different regions of the same chromosome.
Amniocentesis and Chorionic Biopsy: Procedures to Detect Aneuploidy in Human Fetuses

The Andersons, a couple living in Minneapolis, were expecting their first baby. Neither Donald nor Laura Anderson knew of any genetic abnormalities in their families, but because of Laura’s age—38—they decided to have the fetus checked for aneuploidy.

Laura’s physician performed a procedure called amniocentesis. A small amount of fluid was removed from the cavity surrounding the developing fetus by inserting a needle into Laura’s abdomen (Figure 1). This cavity, called the amniotic sac, is enclosed by a membrane. To prevent discomfort during the procedure, Laura was given a local anesthetic. The needle was guided into position by following an ultrasound scan, and some of the amniotic fluid was drawn out. Because this fluid contains nucleated cells sloughed off from the fetus, it is possible to determine the fetus’s karyotype (Figure 2). Usually the fetal cells are purified from the amniotic fluid by centrifugation, and then the cells are cultured for several days to a few weeks. Cytological analysis of these cells will reveal if the fetus is aneuploid. Additional tests may be performed on the fluid recovered from the amniotic sac to detect other sorts of abnormalities, including neural tube defects and some kinds of mutations. The results of all these tests may take up to three weeks. In Laura’s case, no abnormalities of any sort were detected, and 20 weeks after the amniocentesis, she gave birth to a healthy baby girl.

Chorionic biopsy provides another way of detecting chromosomal abnormalities in the fetus. The chorion is a fetal membrane that interdigitates with the uterine wall, eventually forming the placenta. The minute chorionic projections into the uterine tissue are called villi (singular, villus). At 10–11 weeks of gestation, before the placenta has developed, a sample of chorionic villi can be obtained by passing a hollow plastic tube into the uterus through the cervix. This tube can be guided by an ultrasound scan, and when it is in place, a tiny bit of material can be drawn up into the tube by aspiration. The recovered material usually consists of a mixture of maternal and fetal tissue. After these tissues are separated by dissection, the fetal cells can be analyzed for chromosome abnormalities.

Chorionic biopsy can be performed earlier than amniocentesis (10–11 weeks gestation versus 14–16 weeks), but it is not as reliable. In addition, it seems to be associated with a slightly greater chance of miscarriage than amniocentesis, perhaps 2 to 3 percent. For these reasons, it tends to be used only in pregnancies where there is a strong reason to expect a genetic abnormality. In routine pregnancies, such as Laura Anderson’s, amniocentesis is the preferred procedure.

Figure 1 A physician taking a sample of fluid from the amniotic sac of a pregnant woman for prenatal diagnosis of a chromosomal or biochemical abnormality.

Figure 2 Amniocentesis and procedures for prenatal diagnosis of chromosomal and biochemical abnormalities.
FIGURE 27-1
Amniocentesis and chorionic villus sampling. (a) A sample of amniotic fluid (mostly fetal urine and other secretions) is taken by inserting a needle into the amniotic cavity during or around the sixteenth week of gestation. The fetal cells are separated from the fluid by centrifugation. The cells can be used immediately, or more usually they are cultured so that a number of biochemical, enzymatic, and chromosomal analyses can be made. The cultured cells can also be a source of DNA. (b) Chorionic villus sampling is performed between the eighth and twelfth weeks of gestation. A catheter is introduced through the vagina or transabdominally, and a small sample of chorionic villi is drawn into the syringe. DNA can be isolated directly from the tissue, or cell cultures can be established. Note that the various elements of this figure are not drawn to scale.