Karyotype Analysis

• Number of chromosomes
• Sex chromosome content
• Presence or absence of individual chromosomes
• Nature or extent of chromosomal aberrations
Chromosome Painting Using Fluorescent Dyes

- DNA sequences attached to fluorescent dyes
- The sequences attach to the chromosome and "paint" specific regions
- Using several different DNA sequences and fluorescent dyes produces a unique pattern for each of the 24 types of human chromosomes
Chromosome Painting

Normal Cell

Cancer Cell with Translocations

Fig. 6.9
Cells Used for Chromosomal Analysis

- Any cell with a nucleus
- Lymphocytes
- Skin cells
- Tumor cells
- Amniotic cells
- Chorionic villi
- Rare fetal cells from maternal blood
Amniocentesis

- Collects fetal cells for chromosomal and biochemical studies
- Generally performed in the 16th week
Conditions that May Suggest the Use of Amniocentesis

- Advanced maternal age (>35)
- Previous child with chromosomal aberration
- Parent with chromosomal rearrangement
- X-linked biochemical disorder carrier
Chorionic Villus Sampling

- Can be done at 8-10 weeks
- Somewhat risky for mother and fetus
Variations in Chromosome Number

- **Polyploidy** – a chromosome number that is a multiple of the normal haploid set
- **Aneuploidy** – a chromosomal number that varies by something less than a set
  - **Monosomy** – having only one member of a homologous pair
  - **Trisomy** – having three copies of a single chromosome
Aneuploidy Is a Major Cause of Reproductive Failure

It is estimated that

- Humans have a rate of aneuploidy 10x higher than other mammals, including primates
- 1 in 2 conceptions are aneuploid
- 35–70% of early embryonic deaths and spontaneous abortions are caused by aneuploidy
- 1 in 170 live births are at least partially aneuploid
- 5–7% of early childhood deaths are related to aneuploidy
Polyploidy

Caused by

- Errors in meiosis
- Events at fertilization
- Errors in mitosis
Triploidy

- Three sets of chromosomes (69)
- Most common form of polyploidy
- 15–18% of all spontaneous abortions
- Approximately 75% have two sets of paternal chromosomes
- Probably due to polyspermy
- 1% conceptions are triploid but 99% die before birth (lethal condition)
Tetraploidy

- Four sets of chromosomes (92)
- 5% of all spontaneous abortions
- Extremely uncommon in live births
- May result from failure of cytokinesis in the 1st mitotic division
- Mosaics occur
- Life threatening
Most Common Cause of Aneuploidy Is Nondisjunction in Meiosis

- **Nondisjunction** is the failure of homologs or sister chromatids chromosomes to separate in meiosis or mitosis
- Produces abnormal gametes
- Phenotypic effects of aneuploidy vary widely
Nondisjunction

Chromosome alignments at metaphase I

Nondisjunction at anaphase I

Alignments at metaphase II

Anaphase II

Chromosome number in gametes:

$n + 1$

$n + 1$

$n - 1$

$n - 1$

Fig. 6.14
Autosomal Monosomy

- Lethal condition
- Aneuploidy during gamete formation produces equal numbers of monosomic and trisomic gametes and embryos
- Rarely seen in spontaneous abortions and live births
- Majority are lost early in development
Autosomal Trisomy

- Most are lethal

- 50% of cases of chromosomal abnormalities that cause fetal death are autosomal trisomies

- Varies by chromosome
Autosomal Trisomy

Survey of 4,088 spontaneous abortions

Fig. 6.16

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Examples

• Trisomy 13: Patau syndrome (47,+13)
• Trisomy 18: Edwards syndrome (47,+18)
• Trisomy 21: Down syndrome (47,+21)
Trisomy 18: Edwards Syndrome (47,+18)

- 1/11,000 births
- Average survival time 2–4 months
- Affected infants small at birth grow slowly and are mentally retarded
- Malformation of heart, hands, and feet
- For unknown reasons 80% of all trisomy 18 are female
- Advanced maternal age is a risk factor
Trisomy 13: Patau Syndrome (47,+13)

- 1/15,000 births
- Lethal; mean survival time 1 month
- Facial malformations, eye defects, extra fingers or toes, and large protruding heels
- Severe malformations of brain, nervous system, and heart
- Parental age only known risk factor
Trisomy 21: Down Syndrome (47,+21)

- First chromosomal abnormality discovered in humans (1959)
- 1/900 live births
- Leading cause of mental retardation and heart defects in US
- Wide flat skulls, skin folds in the corner of the eyes, spots on the irises, and thick, furrowed tongues
- 40% congenital heart defects
Risk for Autosomal Trisomy

- Advanced maternal age

- Risk increases rapidly after 35 years of age
Maternal Age and Trisomic Conceptions

Maternal age and trisomic conceptions

Paternal age?

Fig. 6.20

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Sex Chromosome Aneuploidy

• 45, X  Turner’s syndrome

• 47, XXY  Klinefelter syndrome

• 47, XYY  XYY syndrome
Turner’s Syndrome: 45, X

- 1/10,000 births
- **Females**: short, wide chest; rudimentary ovaries; and abnormal sexual development
- Puffiness of hands and feet
- Abnormalities of the aorta
- No mental dysfunction
- Single X chromosome; two X chromosomes are required for normal female sexual development
- Complete absence of an X chromosome is lethal—(So, no Y monosomies)
XYY Syndrome: 47, XYY

- 1/1000 births
- Above average in height
- No established link with possible antisocial behavior
Klinefelter Syndrome: 47, XXY

- 1/1000
- Features do not develop until after puberty
- Affected individuals are male with low fertility and may have mental dysfunction
- Significant number are mosaics
- 60% due to maternal nondisjunction
- Other forms XYYY, XXXY and XXXXY