بسم الله الرحمن الرحيم

Karyotyping, Chromosome Structure, and Nomenclature

Comprehensive study sheet based on the lecture slides

Built directly from the uploaded PDF lecture, with key slide figures included.

Slide coverage map

- 1-2: Why human chromosomes matter and the clinical burden of chromosomal abnormalities.
- 3-4: Research uses of cytogenetic evaluation and common tissue sources.
- 5-9: Karyogram, karyotype, ideogram, metaphase chromosomes, and clinical chromosome analysis.
- 10-13: Banding methods, with a focus on G-banding and R-banding.
- 14: Core culture, harvest, and slide-preparation workflow.
- 15-18: Chromosome shape, human chromosome ideogram, chromosome-region examples, and acrocentric structure.
- 19-20: High-resolution banding and how increasing resolution reveals sub-bands.
- 21-26: Chromosome components, centromere, telomere, subtelomere, and sequence homology between subtelomeres.

اللهم آتنا في الدنيا حسنة، وفي الآخرة حسنة، وقنا عذاب النار

اللهم ربِّ ارحمهما كما ربياني صغيرًا

1. Why human chromosomes matter (Slides 1-2)

• Chromosomes are central to both clinical medicine and research because chromosome abnormalities are common in humans.

• The lecture states that about 0.6-1% of all liveborns have a chromosomal abnormality.

• Chromosomal aberrations are especially relevant in sex reversal or pubertal anomalies, spontaneous miscarriages, repeated miscarriages, and leukemia/solid tumor samples.

• Slide 2 highlights the major disease burden: early embryonic loss, recognized embryonic and fetal death, infant and childhood deaths, birth defects, congenital heart defects, sex reversal/pubertal anomalies, multiple miscarriages, and neoplasms.

Why Study Human Chromosomes?

Morbidity/Mortality	Estimate of Cases with Cytogenetic Abnormality
Early embryonic death in unrecognized pregnancies	?? 33-67%
Recognized embryonic and fetal deaths (≥ 5 weeks)	About 30% total; rate varies from 50% at 8-11 weeks to 5% in stillbirths (≥ 28 weeks)
Infant and childhood deaths	5-7%
Birth defects	4-8%
Congenital heart defects	13%
Sex reversal/pubertal anomalies	20-27%
Multiple miscarriages in couples	2-5%
Neoplasms	20-80+%

Slides 1-2: clinical relevance of chromosomal abnormalities

2. Cytogenetic evaluation: why it is done and where it is done (Slides 3-4)

• Research uses of cytogenetic evaluation include localization of DNA on chromosomes, determination of the genomic complement, characterization of genetic changes, and recognition of chromosomal changes after treatment or in vitro culture.

• Common tissues for chromosome studies include peripheral blood lymphocytes, bone marrow, chorionic villi biopsy, amniotic fluid cells, and skin or organ biopsy.

Tissues for Chromosome Studies

•Peripheral blood (lymphocytes)
•Bone marrow
•Chorionic villi biopsy
•Amniotic fluid cells
•Skin or organ biopsy

Slides 3-4: research uses and tissue sources

3. Core chromosome terminology (Slides 5-9)

• A karyogram is a photograph or diagram showing chromosomes arranged in standard order, generally by length(1 is longest, 22 is shortest)

• In a karyogram, chromosomes are arranged as homologous pairs; each pair contains one maternally inherited and one paternally inherited chromosome,once a computer image of the chromosomes from a dividing cell is obtained.

• The normal human diploid chromosome number is 46.

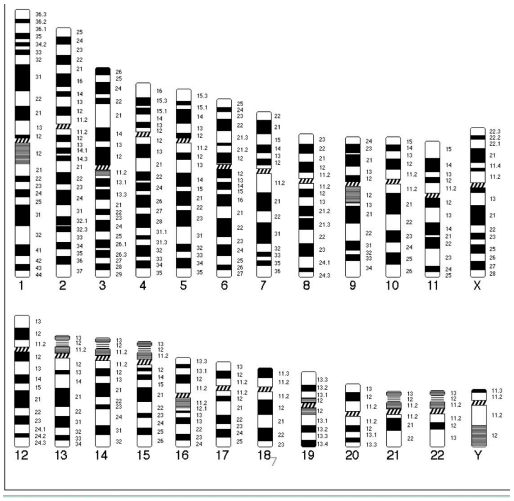
• A karyotype refers to the number and appearance of chromosomes in the nucleus.

• Normal female complement: 46,XX. Normal male complement: 46,XY.

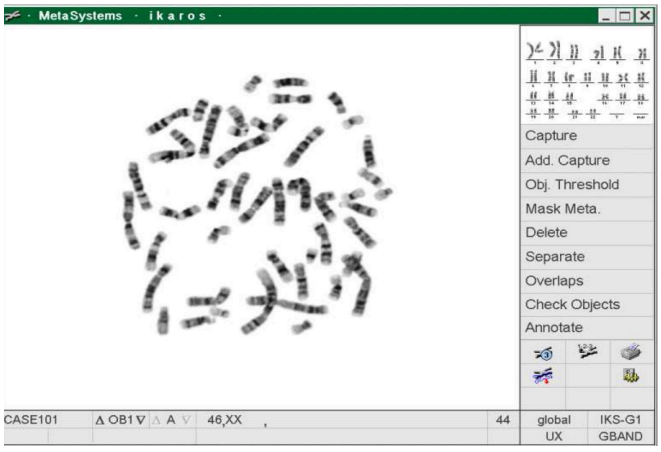
• For clinical chromosome analysis, cells must be able to proliferate in culture; the most accessible such cells are white blood cells, especially T lymphocytes.

• An ideogram is the diagrammatic representation of a karyotype.

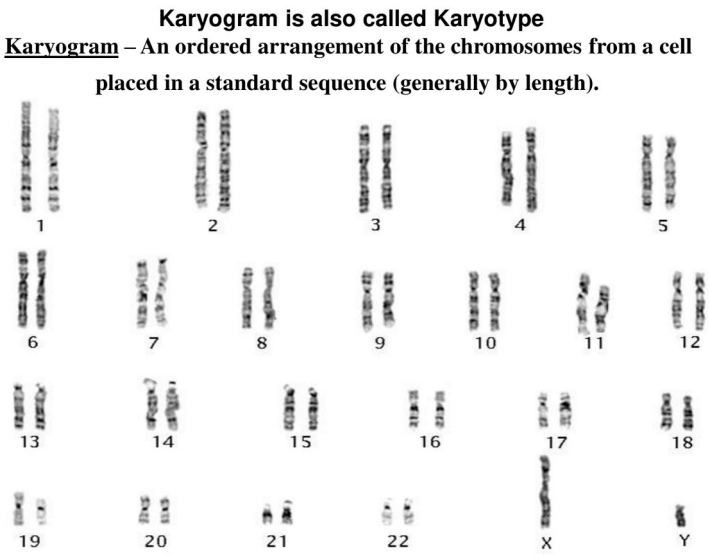
• Metaphase chromosomes are the condensed chromosomes visualized during metaphase for analysis.



Ideogram



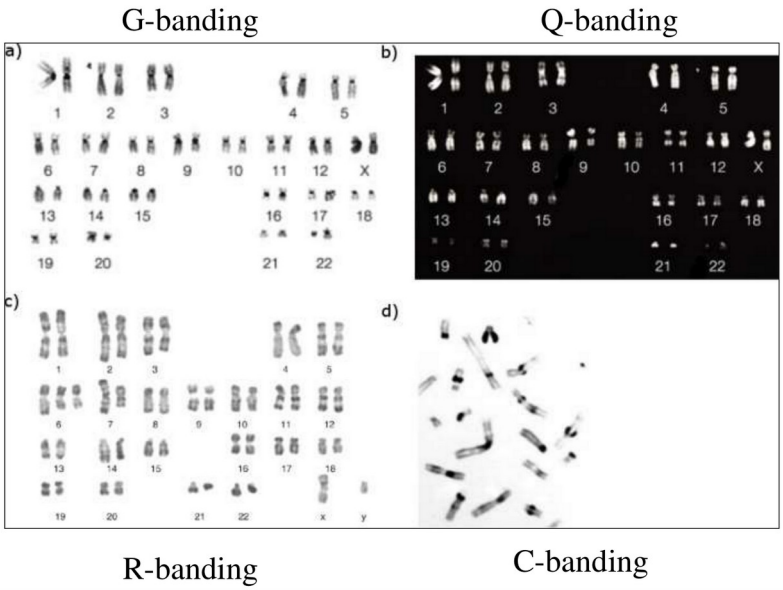
Metaphase chromosomes



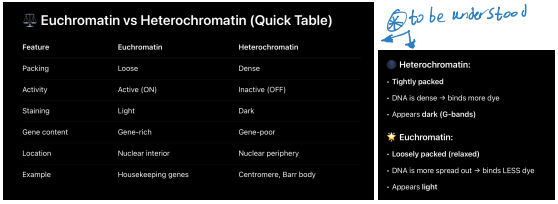
Slides 6-9: karyogram, ideogram, and metaphase chromosomes

4. Banding systems used in cytogenetics (Slides 10-13)

- The lecture lists the main banding methods: G-banding, R-banding, C-banding, Q-banding, T-banding, and silver staining.
- G-banding and R-banding are emphasized as the most important routine complementary patterns for chromosome identification and abnormality detection.
- Banding patterns help distinguish chromosomes, identify structural changes, and compare homologous regions.



Slide 11: banding pattern comparison



Euchromatin vs Heterochromatin (Quick Table)

Feature	Euchromatin	Heterochromatin
Packing	Loose	Dense
Activity	Active (ON)	Inactive (OFF)
Staining	Light	Dark
Gene content	Gene-rich	Gene-poor
Location	Nuclear interior	Nuclear periphery
Example	Housekeeping genes	Centromere, Barr body

to be understood

Heterochromatin:
- Tightly packed
- DNA is dense → binds more dye
- Appears dark (G-bands)

Euchromatin:
- Loosely packed (relaxed)
- DNA is more spread out → binds LESS dye
- Appears light

5. G-banding versus R-banding (Slides 12-13)

• G-banding (GTG) produces dark bands in heterochromatic (AT-rich) relatively gene-poor regions, while light bands correspond to euchromatic (GC-rich) more transcriptionally active regions.

• Conventional G-banding typically yields about 300-400 bands among the 23 pairs of human chromosomes.

• A G-band represents several million to about 10 million base pairs, which is large enough to contain hundreds of genes.

• Before Giemsa staining, metaphase chromosomes are briefly treated with trypsin, which digests proteins and allows better dye access to DNAby relaxing the chromatin structure.

• R-banding is the reverse of G-banding: dark regions are GC-rich euchromatic regions, and bright regions are AT-rich heterochromatic regions.

• R-banding is especially useful for gene-rich regions near telomeres and is often used with G-banding to help detect deletions.

• R-banding uses heat treatment before Giemsa staining, which preferentially melts AT-rich DNA and leaves GC-rich regions to stain.

R-banding

- is the reverse of G-banding (the R stands for "reverse"). The dark regions are euchromatic (guanine-cytosine rich regions). The bright regions are heterochromatic (thymine-adenine rich regions)

- provide critical details about gene-rich regions that are located near the telomeres
- often used together with G-banding on human karyotype to determine whether there are deletions.

- the chromosomes are heated before Giemsa stain is applied. The heat treatment is thought to preferentially melt the DNA helix in the AT-rich regions that usually bind Giemsa stain most strongly, leaving only the comparatively GC-rich regions to take up the stain. R-banding

Slides 12-13: G-banding and R-banding principles

6. Culture establishment and harvest workflow (Slide 14)

• Primary steps: add mitogen when needed, perform hypotonic swelling, fix the cells, then analyze the chromosomes.

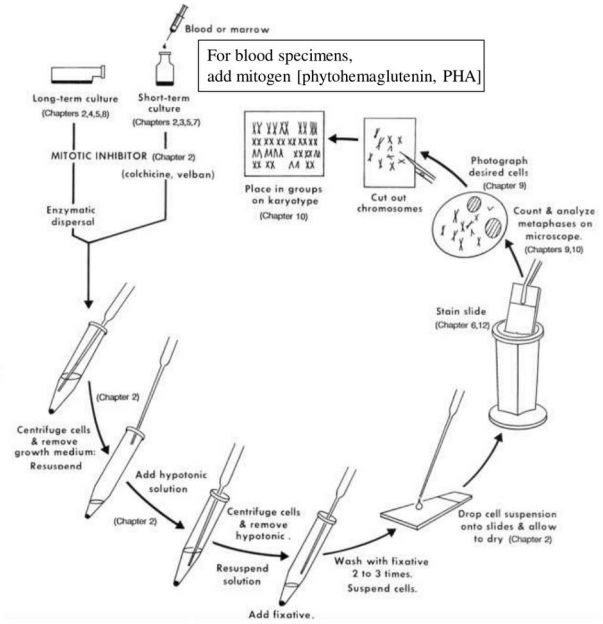
a substance that stimulates mitosis

• For blood specimens, the mitogen used is phytohemagglutinin (PHA).

• The workflow shown in the slide includes culture, mitotic inhibition, enzymatic dispersion, hypotonic treatment, fixation, slide preparation, staining, and microscopic analysis.

Primary Steps for Culture Establishment and Harvest of Specimens

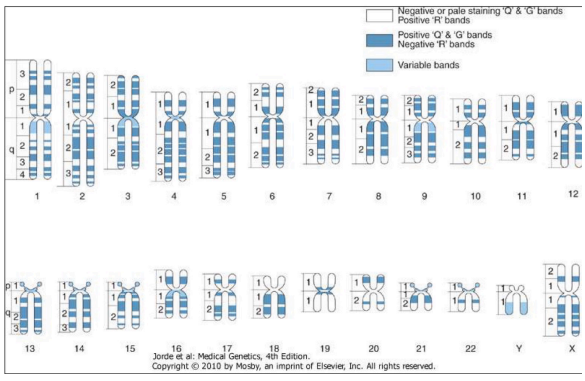
- **Add Mitogen (when needed)**
- **Hypotonic Swelling**
- **Fixation**
- **Analysis**



Slide 14: core chromosome culture and harvest workflow

7. Chromosome shape and chromosome maps (Slides 15-18)

- Metacentric chromosomes have the centromere in the middle.
- Submetacentric chromosomes have the centromere displaced from the center.
- Acrocentric chromosomes have the centromere near the end.
- The human chromosome ideogram is a diagrammatic representation of a karyotype, showing banding patterns and chromosome landmarks.
- Slide 17 gives examples of region counts: chromosome 3 has p: 2 regions and q: 2 regions; chromosome 7 has p: 2 regions and q: 3 regions; chromosome 14 has p: 1 region and q: 2 regions.
- Slide 18 illustrates an acrocentric chromosome (21) with a stalk and satellite and shows the organization of telomere, satellite DNA, rRNA genes, and band-rich p/q landmarks.

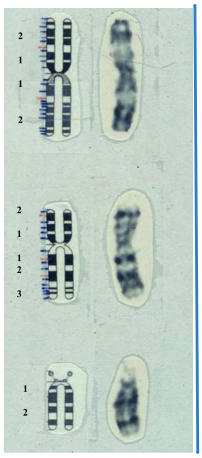


slide17

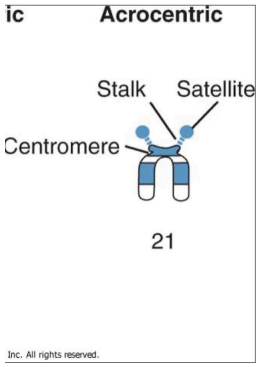
Chromosome 3
p: 2 regions
q: 2 regions

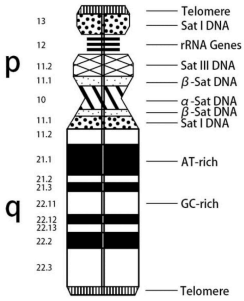
Chromosome 7
p: 2 regions
q: 3 regions

Chromosome 14
p: 1 region
q: 2 regions



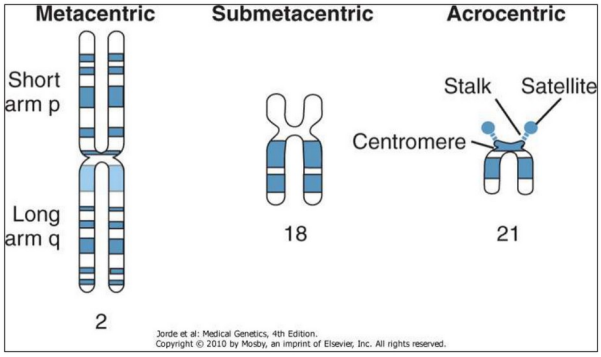
Slide 18

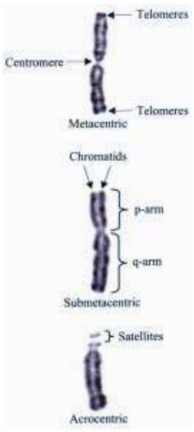




Chromosome Shape

Metacentric- centromere is located in the middle of chromosome
Submetacentric- centromere is displaced from the center
Acrocentric – centromere is placed near the end





Slides 15-18: chromosome shape and regional organization

8. High-resolution banding and band subdivision (Slides 19-20)

• High-resolution banding stains chromosomes during prophase or prometaphase, before maximal condensation.

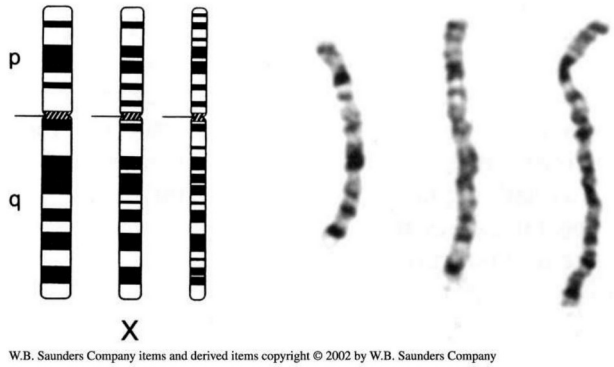
• Because these chromosomes are more extended than metaphase chromosomes, the number of visible bands increases from about 300 to 450 and can reach as many as 800 per haploid set.

• This higher resolution helps detect less obvious abnormalities that may not be seen with conventional banding.

• The banding-resolution figure on slide 20 shows how chromosome 4 bands can be resolved into bands, sub-bands, and sub-sub-bands as resolution increases.

High Resolution Banding

High-resolution banding involves the staining of chromosomes during prophase or prometaphase, before they reach maximal condensation.
Because prophase and prometaphase chromosomes are more extended than metaphase chromosomes, the number of bands observable for all chromosomes increases from about 300 to 450 to as many as 800 per haploid set. This allows the detection of less obvious abnormalities usually not seen with conventional banding.



Slide20:

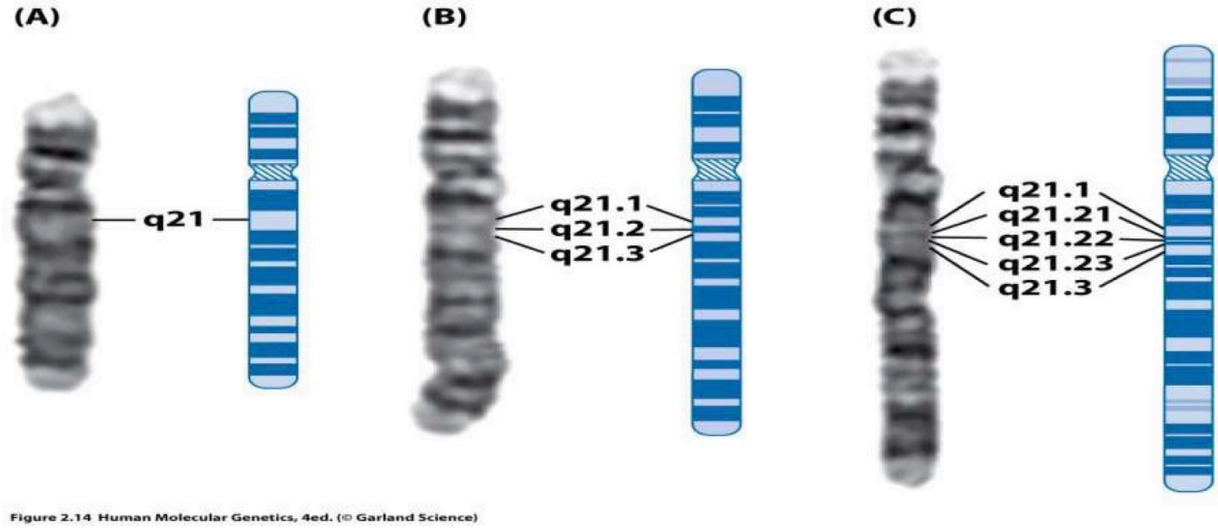


Figure 2.14 Different chromosome banding resolutions can resolve bands, sub-bands, and sub-sub-bands.

G-banding patterns for human chromosome 4 (with accompanying ideogram at the right) are shown at increasing levels of resolution. The levels correspond approximately to (A) 400, (B) 550, and (C) 850 bands per haploid set, allowing the visual subdivision of bands into sub-bands and sub-subbands as the resolution increases. [Adapted from Cross & Wolstenholme (2001). Human Cytogenetics: Constitutional Analysis, 3rd ed. (DE Rooney, ed.). With permission of Oxford University Press.]

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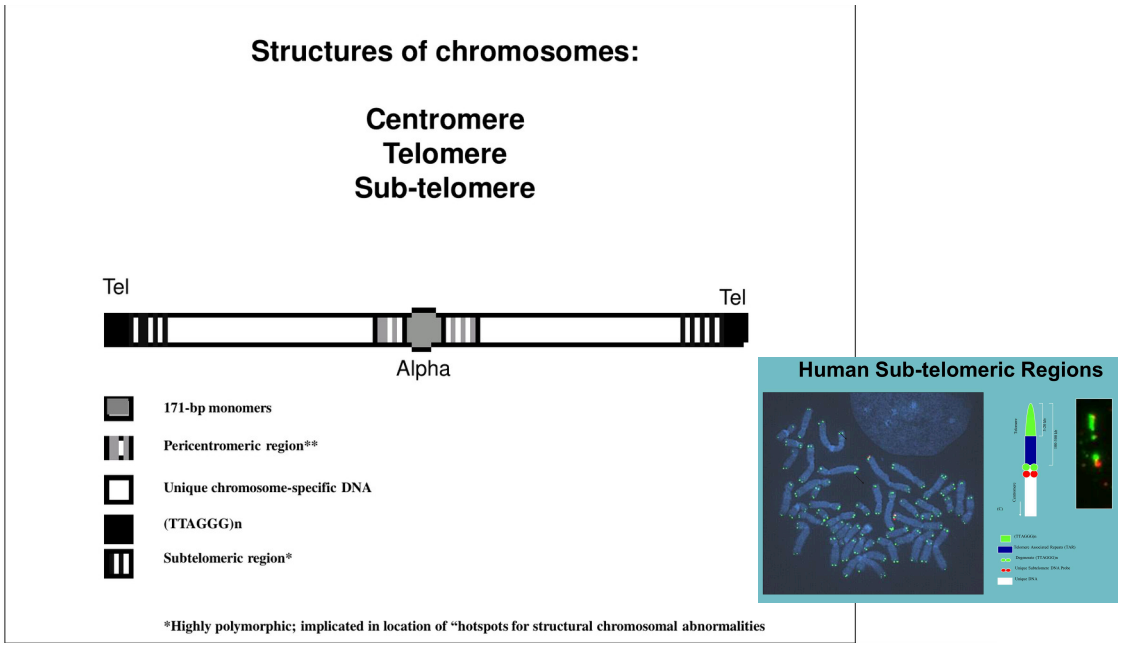
19/07/2026

Slides 19-20: high-resolution banding

9. Chromosome components: centromere, telomere, and subtelomere (Slides 21-26)

- The main components highlighted in the lecture are the centromere and the telomeric/subtelomeric regions.
- The centromere is the genetic locus required for chromosome segregation; it contains DNA and proteins that form the kinetochore. a complex of proteins associated with the centromere of a chromosome during cell division, to which the microtubules of the spindle attach
- Telomeres are specialized structures at the ends of eukaryotic chromosomes; they maintain chromosomal integrity by preventing end-to-end fusion. Their sequence is (TTAGGG)n.
- Subtelomeric regions are highly polymorphic and are implicated as hotspots for structural chromosomal abnormalities.
- Human subtelomeric regions contain telomere-associated repeats, unique subtelomere DNA probes, unique DNA, and degenerate TTAGGG repeats.
- The final slide notes that there is some sequence homology between subtelomeres.



Slides 22-26: chromosome-end architecture and subtelomeric structure

High-yield revision points

- Karyogram = ordered chromosome picture; karyotype = number and appearance of chromosomes.
- 46,XX is the normal female complement; 46,XY is the normal male complement.
- G-bands are dark in AT-rich, gene-poor regions; R-bands are the reverse and are useful near telomeres.
- High-resolution banding reveals more bands because chromosomes are less condensed in prophase/prometaphase.
- Centromere = segregation site; telomere = chromosome-end protector; subtelomere = variability-rich region near the end.
- Acrocentric chromosomes have the centromere near the end, often with stalk/satellite structures.