Achievable

USMLE STEP 1 DUMP SHEET

Genetics

Inheritance patterns

Pattern	Clues and risk	Examples
Autosomal dominant	Every generation; both sexes. One affected parent: 50% per child	Marfan, Huntington, achondroplasia, familial hypercholesterolemia, NF1
Autosomal recessive	Skips generations; consanguinity. Two carriers: 25% affected, 50% carrier	Most enzyme deficiencies (PKU, galactosemia, Gaucher), CF, sickle cell, Friedreich ataxia
X-linked recessive	Mostly males; no male-to-male transmission. Carrier mother: half of sons affected; affected father: all daughters carriers	Hemophilia, DMD, G6PD, Fabry, Hunter, Lesch-Nyhan, Bruton, Wiskott-Aldrich, color blindness
X-linked dominant	Affected father: all daughters, no sons. Affected mother: half of all children	Hypophosphatemic rickets, Rett, Alport, fragile X
Mitochondrial	Mother to all children, never from father; heteroplasmy, threshold effect	MELAS, Leber hereditary optic neuropathy, mitochondrial myopathies
Codominant	Both alleles expressed	ABO blood groups, HLA, α1-antitrypsin

Terms

- **Incomplete penetrance:** carries the genotype, no disease (BRCA)
- **Variable expressivity:** same genotype, different severity (Marfan)
- **Allelic heterogeneity:** different mutations in one gene
- **Locus heterogeneity:** one phenotype from different genes (nephrogenic DI: AQP2 or AVPR2)
- **Dominant negative:** mutant product blocks the normal one
- **Haploinsufficiency:** one working copy is not enough; acts dominant
- **Uniparental disomy (UPD):** both copies from one parent

Repeats and imprinting

- **Anticipation:** repeats expand, so onset is earlier and more severe each generation
- **CAG:** Huntington, spinocerebellar ataxias. **CGG:** fragile X
- **GAA:** Friedreich ataxia. **CTG:** myotonic dystrophy
- **Imprinting:** only one parent's copy is active; the silent copy is methylated
- **Prader-Willi:** paternal 15q loss or maternal UPD; hypotonia, hyperphagia, obesity, small hands
- **Angelman:** maternal 15q loss or paternal UPD; happy demeanor, ataxia, seizures, hand flapping
- **Beckwith-Wiedemann:** 11p15; macroglossia, omphalocele, hypoglycemia, Wilms tumor

Chromosomal disorders

Disorder	Features
Trisomy 21	Meiotic nondisjunction (maternal age), Robertsonian t(14;21), mosaic. Epicanthal folds, single palmar crease, heart defects, ALL, early Alzheimer
Trisomy 18	Edwards: clenched fists, prominent occiput, small jaw, low ears, VSD
Trisomy 13	Patau: cleft lip and palate, polydactyly, holoprosencephaly
47,XXY	Klinefelter: tall, hypogonadism, gynecomastia, infertility; breast cancer risk
45,X	Turner: short, webbed neck, streak ovaries, lymphedema, coarctation
47,XYY	Tall males, learning disability
5p−	Cri du chat: cat-like cry, microcephaly
7q del	Williams: elfin face, supravalvular aortic stenosis, hypercalcemia

- **Karyotype** (metaphase, Giemsa): number and large rearrangements. **FISH:** microdeletions (Prader-Willi, Angelman, DiGeorge)
- **Robertsonian:** acrocentric long arms fuse (13, 14, 15, 21, 22)
- **Balanced reciprocal:** carrier normal; miscarriage risk. **t(9;22)** Philadelphia: CML
- **Isochromosome:** two copies of one arm, the other arm lost

Population genetics

- **Hardy-Weinberg:** $p + q = 1$; $p^2 + 2pq + q^2 = 1$
  In an AR disease, q^2 = incidence and $2pq$ = carriers
- **CF:** $q = 1/50$: incidence $1/2500$; carriers $2pq \approx 2q = 1/25$
- **X-linked:** males affected $= q$, females $= q^2$. If $q = 0.08$, $p = 0.92$
- **LOD score:** over 3 supports linkage (1000:1 odds); under −2 excludes it
- **Shared DNA:** identical twin 100%; parent, sibling 50%; grandparent, aunt, half-sibling 25%; first cousin 12.5%
- **HLA in siblings:** 25% identical, 50% haploidentical, 25% none. **Heritability (h^2):** 0 to 1