Fakultas Farmasi
Universitas Pancasila
Program Strata 1 (S-1)

Penyakit Genetik dan Lingkungan

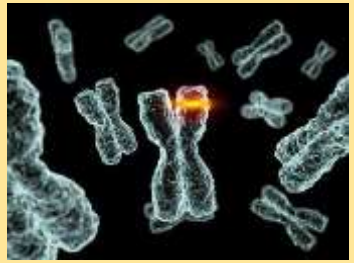
Tim Dosen Patofisiologi Manusia

Topik Bahasan

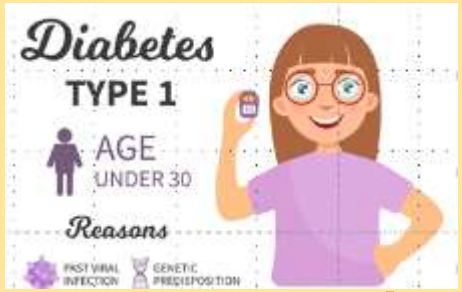
1. Penyebab penyakit
2. Alur masuk bakteri
3. Rangkuman skin disorder
4. Genetik
5. Mutasi genetik dan mutasi kromosom
6. Kelainan struktur dan/fungsi

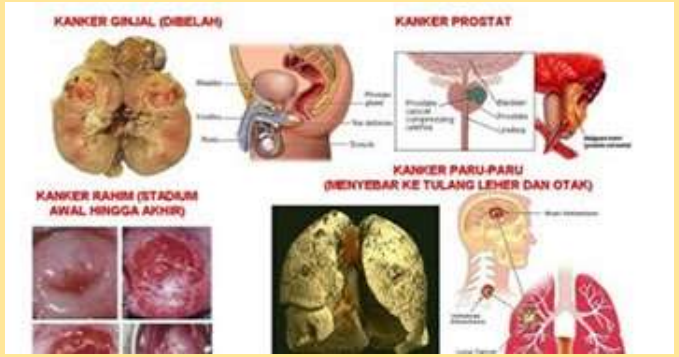
Penyebab/Etiologi Penyakit

1. Genetik

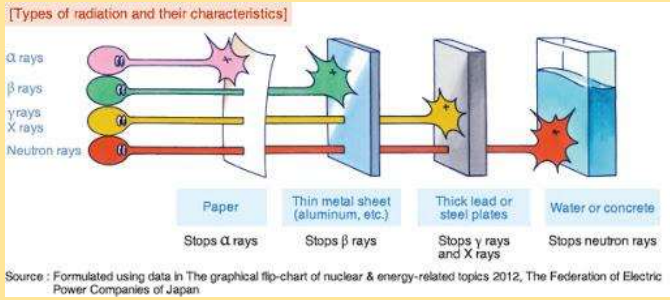


3. Kombinasi (1 &2)





2. Lingkungan



Penyakit akibat kerja

Definisi : semua kelainan / penyakit yang disebabkan oleh lingkungan kerja atau pekerjaan.

Menurut ILO & WHO :

Aspek / unsur kesehatan yang bertalian dengan lingkungan kerja dan pekerjaan yang secara langsung / tidak langsung dapat mempengaruhi kesehatan tenaga kerja.

Skin Disorders

Infections			
Virus	Fever blisters Genital herpes Shingles Chickenpox Warts	Bacterial	Follicullitis Boils Scalded skin syndrome Impetigo
Fungal	Ringworm Athlete's foot Blastomycosis Candidiasis	Parasitic	Swimmer's itch Scabies Pediculosis

Environmental Stress and Inflamation
Hyperkeratosis:Corns, calluses,psoriasis
Xerosis (some forms)
Decubitis ulcers
Dermatitis

Secondary Disorders	
Digestive systems	Jaundice
Endocrine	Addison's disease
	Acne
	Alopecia
	Hirsutism
Immune disorders	Vertigo
	Scleroderma
	Alopecia areata

Degenerative Disorders
Alopecia
Xerosis (age-related)

Nutritional Disorders
Hemanglomas
Carotene skin color

Tumors
Moles
Basal cell carsinoma
Squamous cell carcinoma
Melanoma

Trauma	
Wounds	Abrasions, incisions Lacerations, punctures, Avulsions, confusion
Burns	First degree Second degree Third degree

Congenital Disorders
Hemanglomas
Xenoderma pigmentorum

Table 8.1 Routes of Microbial Infection

Site	Major Local Defense(s)	Basis for Failure of Local Defense	Pathogens (Examples)
Skin	Epidermal barrier	Mechanical defects (punctures, burns, ulcers)	*Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*
		Needle sticks	Human immunodeficiency virus, hepatitis viruses
		Arthropod and animal bites	Yellow fever, plague, Lyme disease, malaria, rabies
		Direct penetration	*Schistosoma* spp.
Gastrointestinal tract	Epithelial barrier	Attachment and local proliferation of microbes	*Vibrio cholerae*, *Giardia duodenalis*
		Attachment and local invasion of microbes	*Shigella* spp., *Salmonella* spp., *Campylobacter* spp.
		Uptake through M cells	Poliovirus, *Shigella* spp., *Salmonella* spp.
	Acidic secretions	Acid-resistant cysts and eggs	Many protozoa and helminths
	Peristalsis	Obstruction, ileus, postsurgical adhesions	Mixed aerobic and anaerobic bacteria (*Escherichia coli*, *Bacteroides* spp.)
	Bile and pancreatic enzymes	Resistant microbial external coats	Hepatitis A, rotavirus, norovirus
	Normal protective microbiota	Broad-spectrum antibiotic use	*Clostridioides difficile*
Respiratory tract	Mucociliary clearance	Attachment and local proliferation of microbes	Influenza viruses
		Ciliary paralysis by toxins	*Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Bordetella pertussis*
	Resident alveolar macrophages	Resistance to killing by phagocytes	*Mycobacterium tuberculosis*
Urogenital tract	Urination	Obstruction, microbial attachment, and local proliferation	*Escherichia coli*
	Normal vaginal microbiota	Antibiotic use	*Candida albicans*
	Intact epidermal/epithelial barrier	Microbial attachment and local proliferation	*Neisseria gonorrhoeae*
		Direct infection/local invasion	Herpes viruses, syphilis
		Local trauma	Various sexually transmitted infections (e.g., human papillomavirus)

Cotran, 349

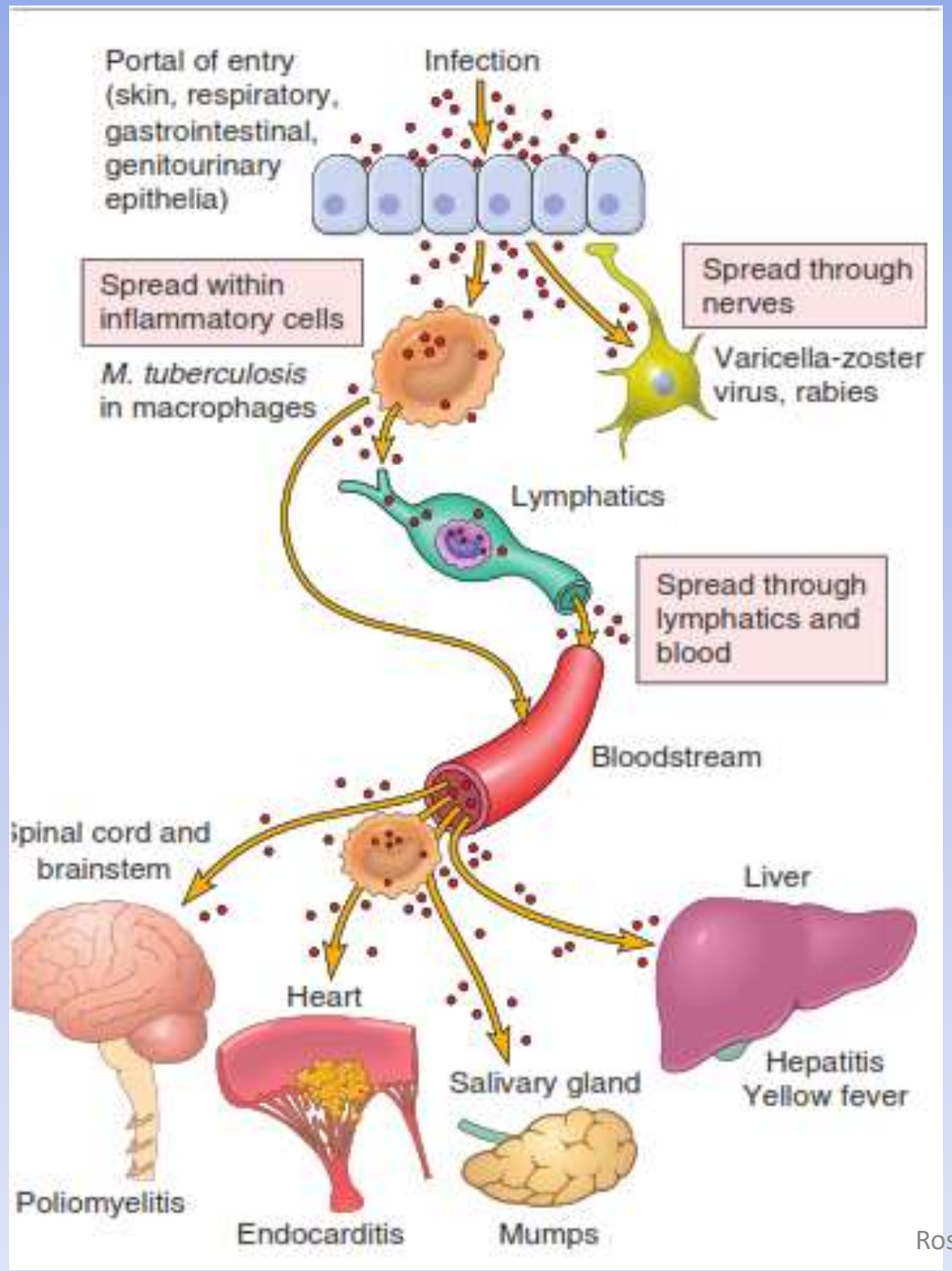
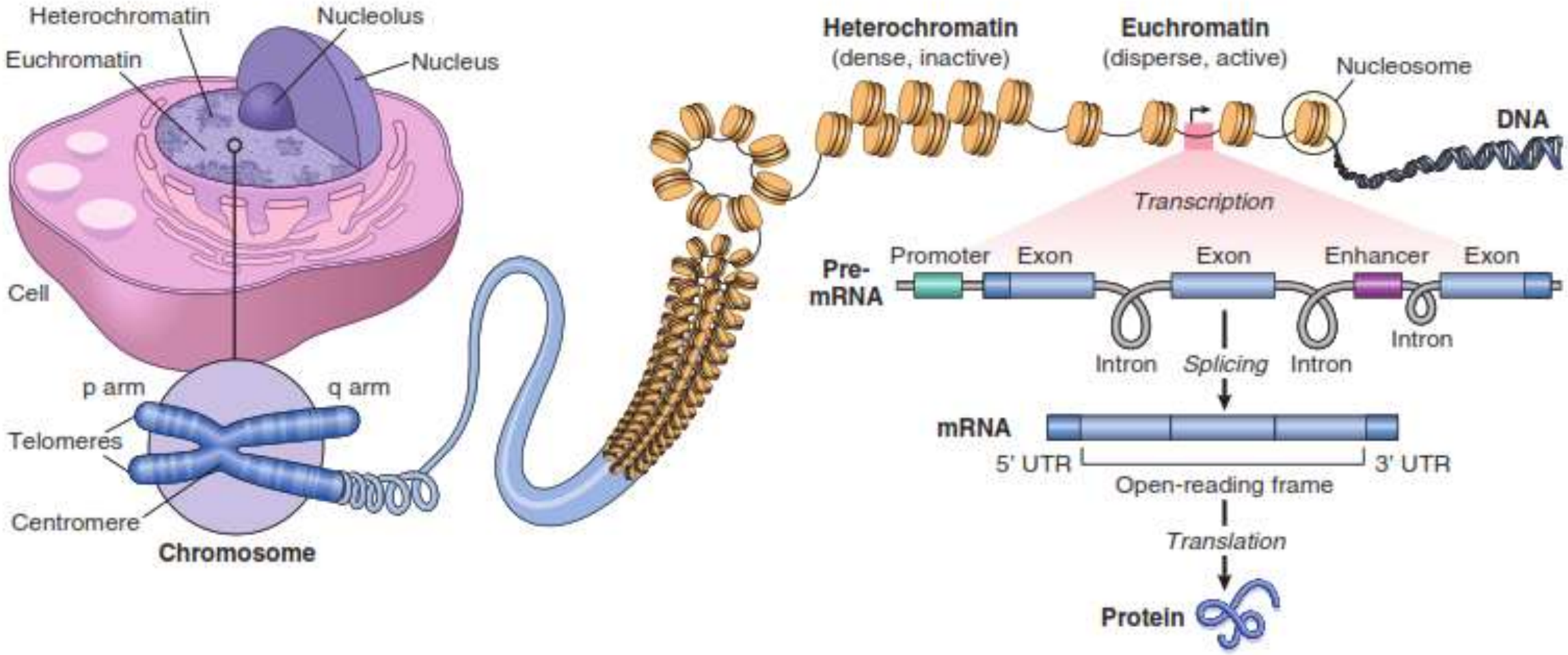


Figure 8.1 Routes of entry and dissemination of microbes. To enter the body, microbes penetrate the epithelial or mucosal barriers. Infection may remain localized at the site of entry or spread to other sites in the body. Most common microbes *(selected examples are shown)* spread through the lymphatics or bloodstream (either freely or within inflammatory cells). However, certain viruses and bacterial toxins may also travel through nerves. (Modified from Mims CA: *The Pathogenesis of Infectious Disease*, ed 4, San Diego, 1996, Academic Press.)

Table 8.3 Spectrum of Inflammatory Responses to Infection

Type of Response	Pathogenesis	Examples
Suppurative (Purulent) Infection	Increased vascular permeability Leukocyte infiltration (neutrophils) Chemoattractants from bacteria Formation of "pus"	Pneumonia (*Staphylococcus aureus*) Abscesses (*Staphylococcus* spp., anaerobic and other bacteria)
Mononuclear and granulomatous inflammation	Mononuclear cell infiltrates (monocytes, macrophages, plasma cells, lymphocytes) Cell-mediated immune response to pathogens ("persistent antigen") Formation of granulomata	Syphilis Tuberculosis
Cytopathic-cytoproliferative reactions	Viral transformation of cells Necrosis or proliferation (including multinucleation) Linked to neoplasia	Cervical cancer (human papillomavirus) Chicken pox, shingles Herpes
Tissue necrosis	Toxin- or lysis-mediated destruction Lack of inflammatory cells Rapidly progressive processes	Gangrene (*Clostridium perfringens*) Hepatitis (hepatitis B virus)
Chronic inflammation/ scarring	Repetitive injury leads to fibrosis Loss of normal parenchyma	Chronic hepatitis with cirrhosis (hepatitis B and C viruses)
No reaction	Severe immune compromise	*Mycobacterium avium* in untreated AIDS (T-cell deficiency) Mucormycosis in bone marrow transplant patients (neutropenia)

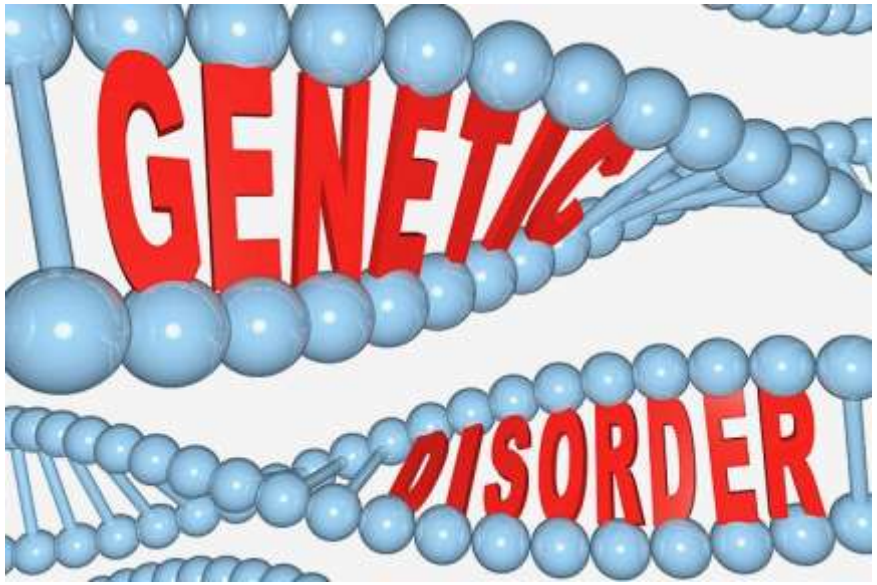
Genetik

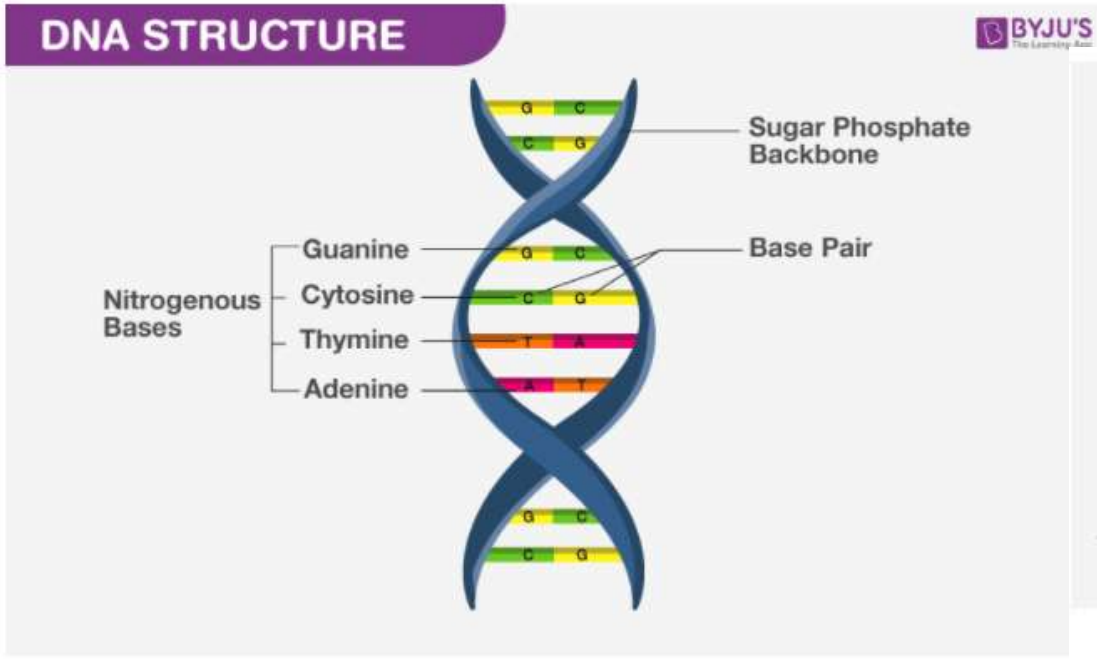


Cotran, p.15

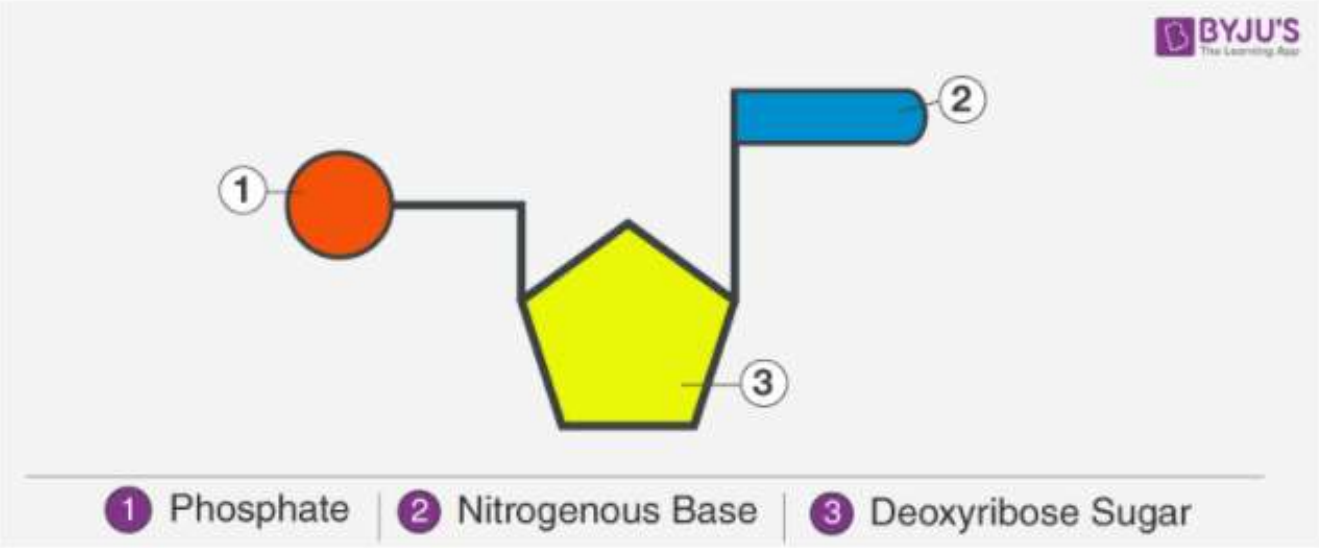
Genetik: ilmu tentang gen
DNA (=deoxyribonucleic acid)
adalah material genetik yang mengontrol sifat-sifat makhluk hidup,
Ekspresi:

- A. polipeptida/protein
- B. RNA, memiliki reaksi katalitik

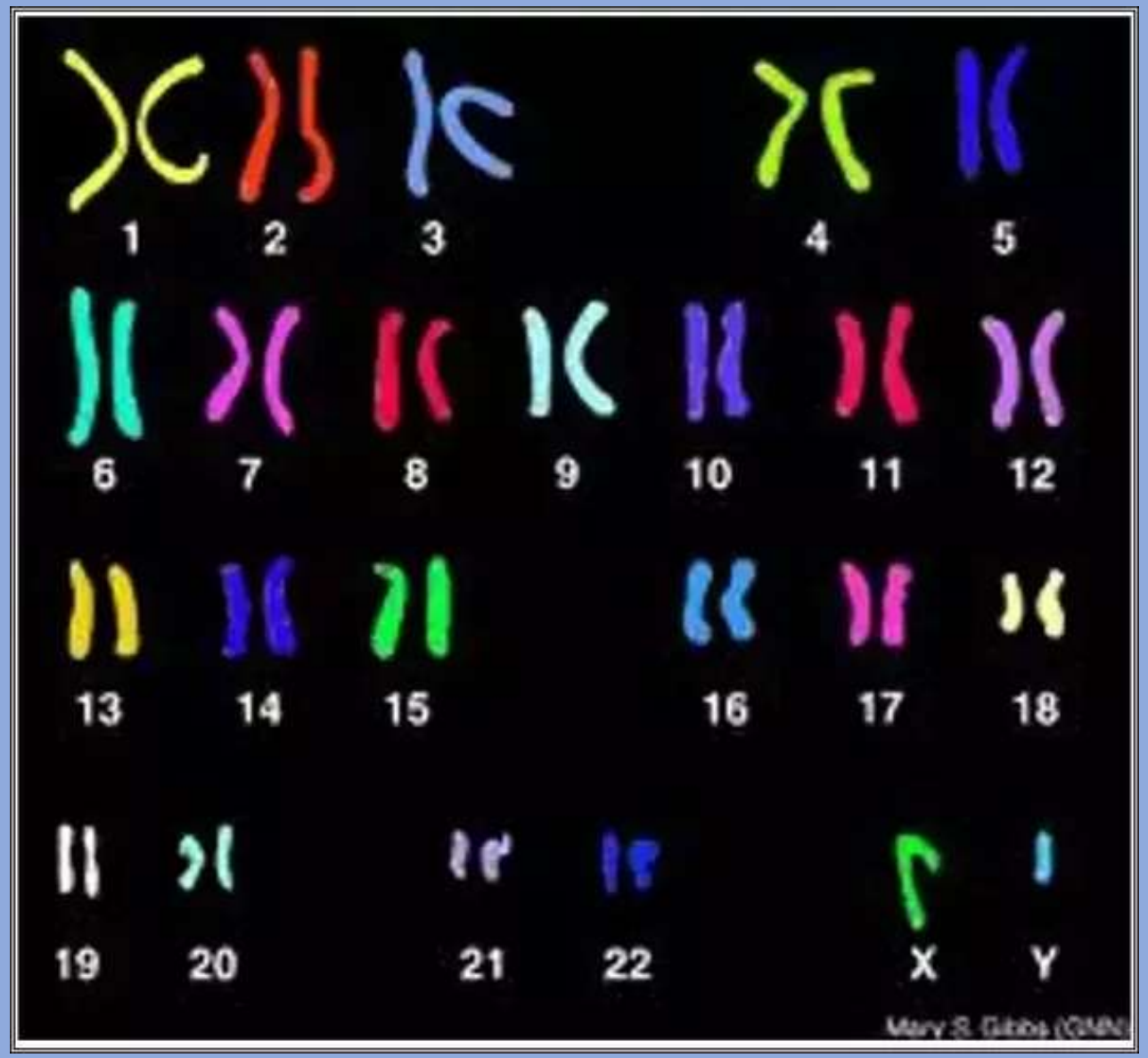


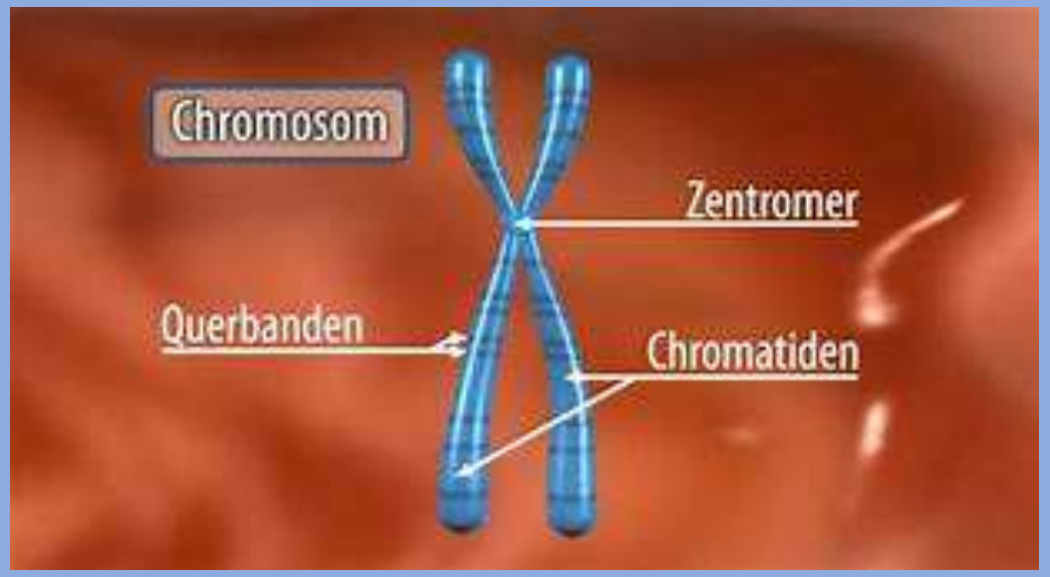


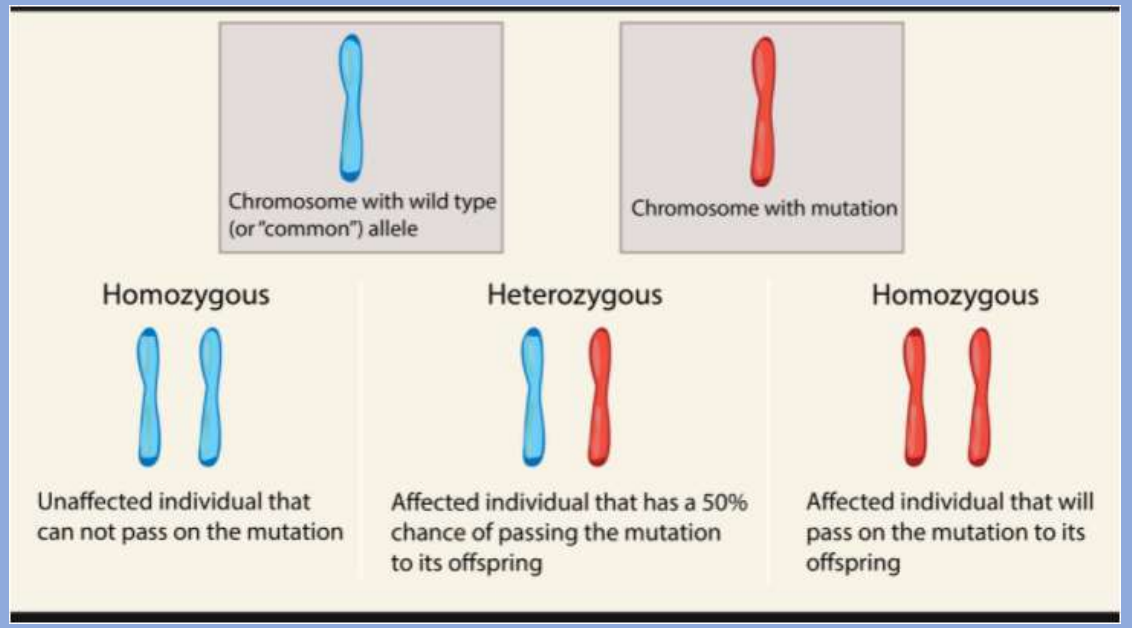
DNA Diagram representing the DNA Structure



Components of DNA Structure

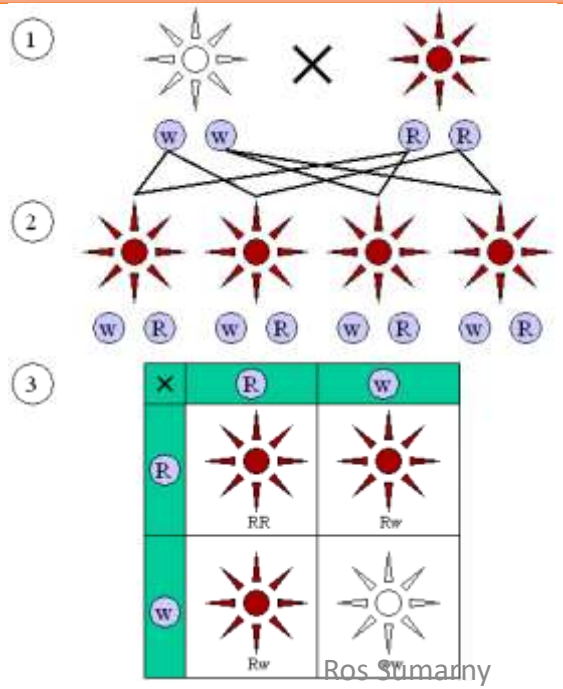

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y

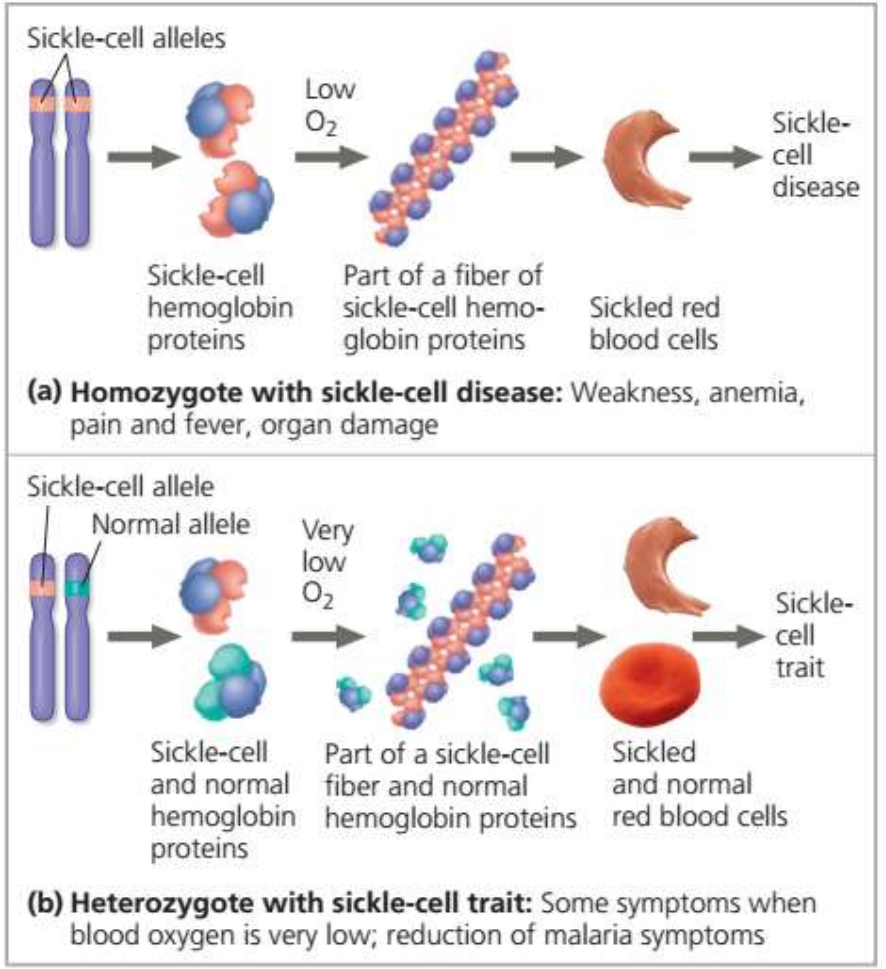

Chromosom
Zentromer
Querbanden
Chromatiden


Chromosome with wild type (or "common") allele
Chromosome with mutation
Homozygous
Unaffected individual that can not pass on the mutation
Heterozygous
Affected individual that has a 50% chance of passing the mutation to its offspring
Homozygous
Affected individual that will pass on the mutation to its offspring

Ciri Penyakit Genetik

1. Diwariskan dari gen keluarga (hereditas);
2. Tanda dan gejala muncul pada usia anak-anak;
3. Insiden/kejadian → jarang/langka

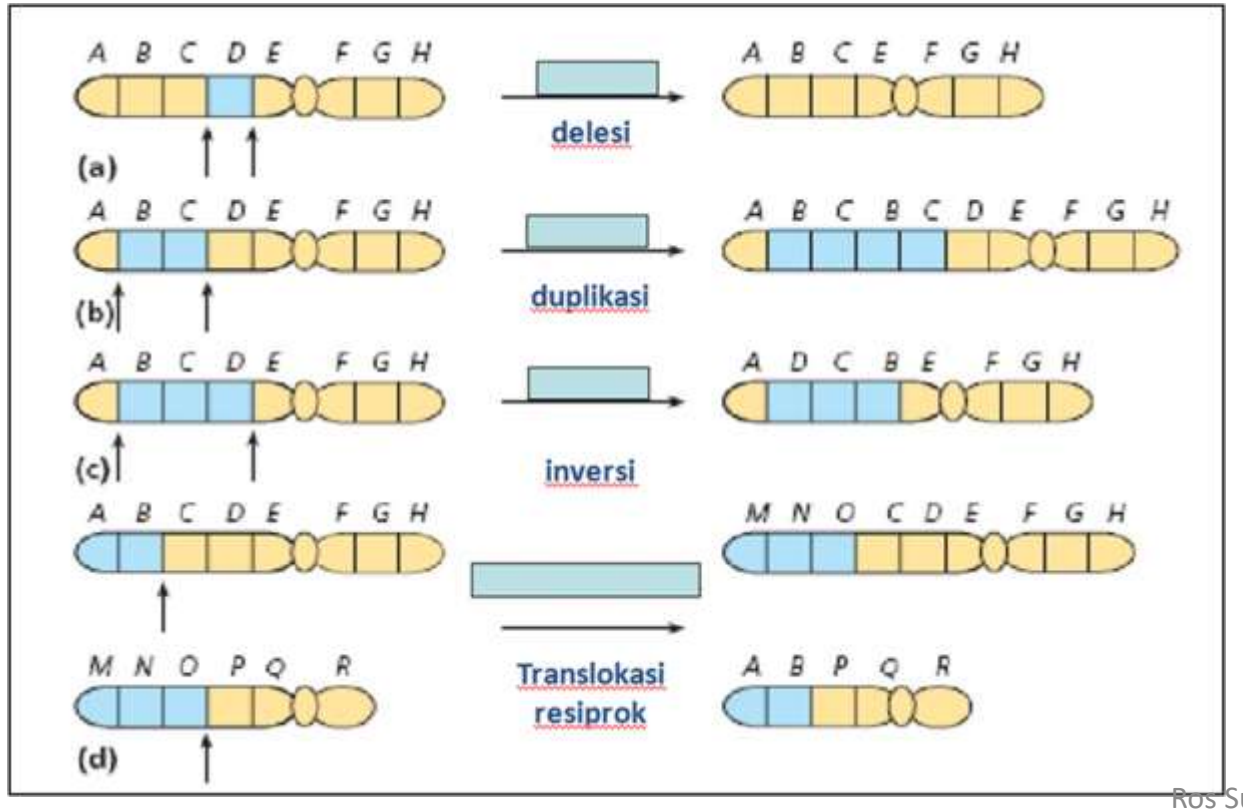


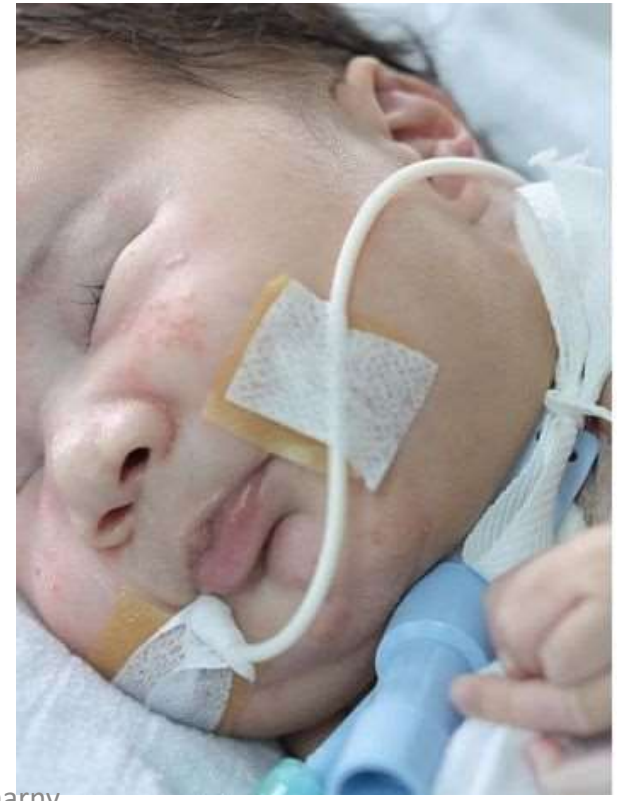


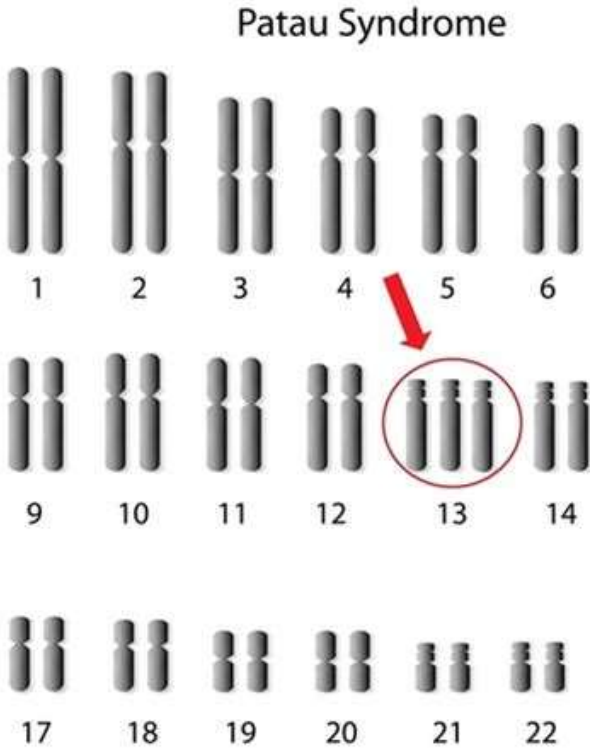
Defek/cacat materia genetik→ mutasi

1. Mutasi titik/gen: perubahan pada basa N dari DNA atau RNA

2. Mutasi kromosom: perubahan jumlah dan susunan dalam kromosom (trisomi)







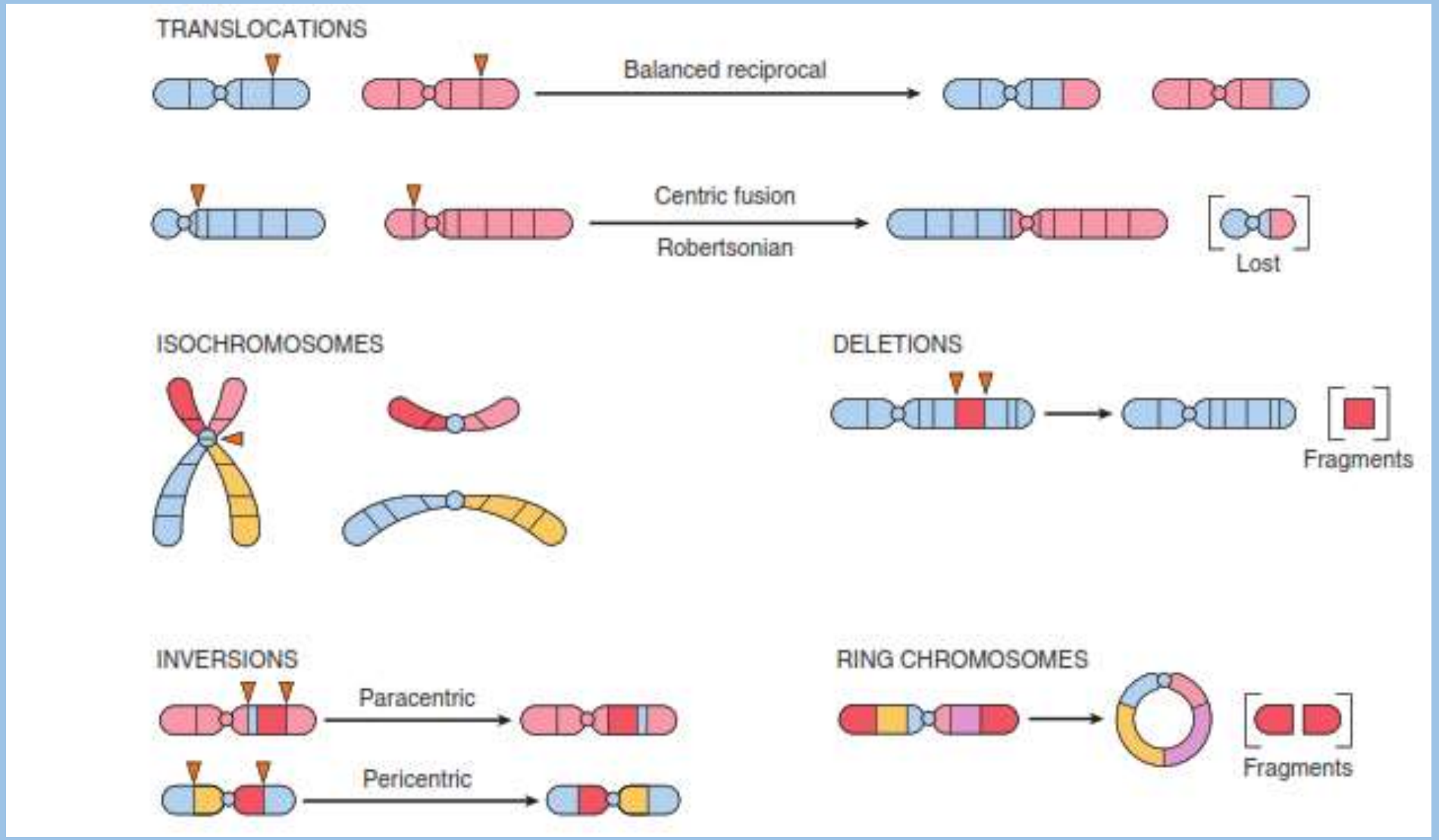


Figure 5.18 Types of chromosomal rearrangements.

Cotran, 175

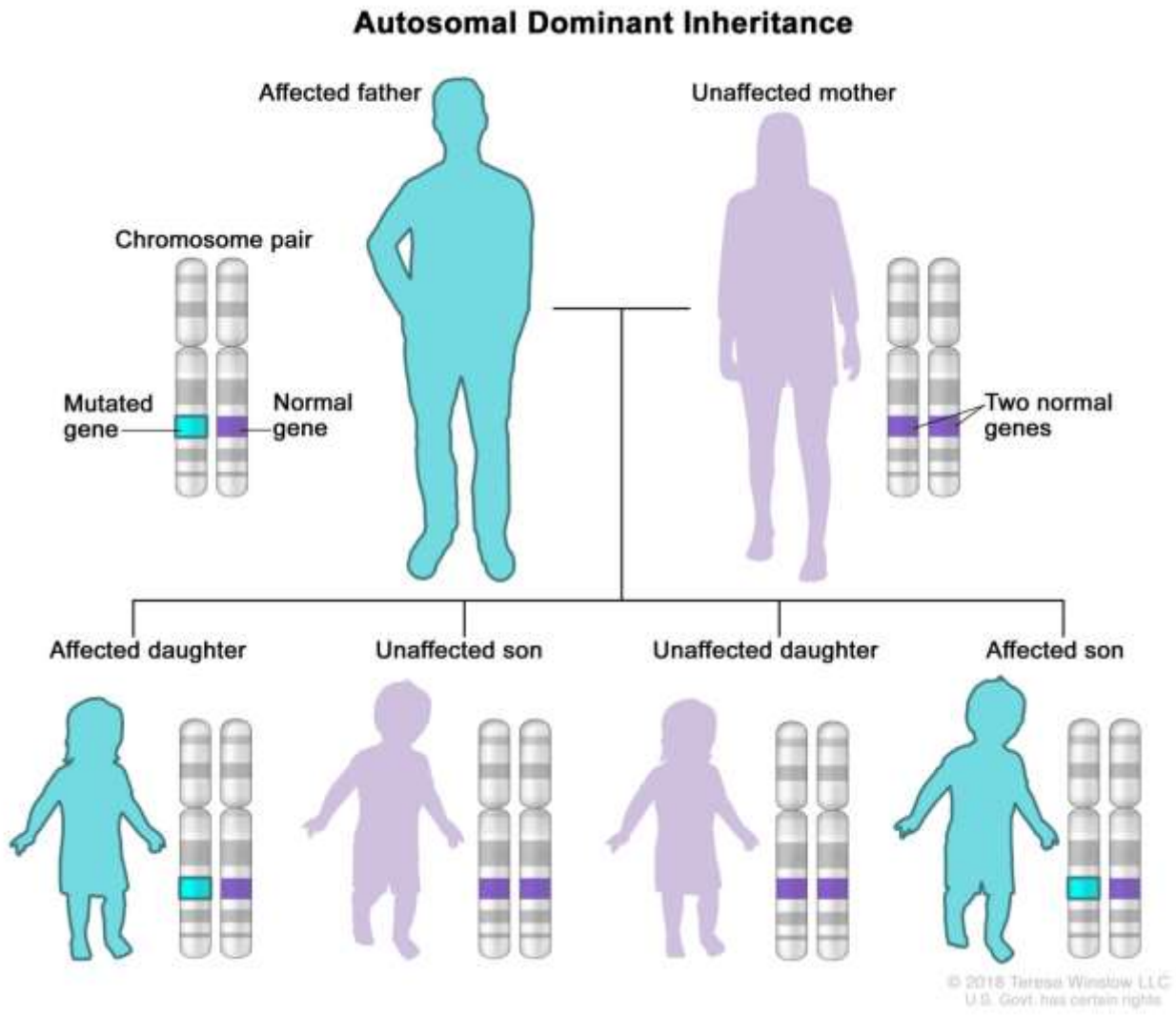


Table 5.1 Autosomal Dominant Disorders

System	Disorder
Nervous	Huntington disease Neurofibromatosis Myotonic dystrophy Tuberous sclerosis
Urinary	Polycystic kidney disease
Gastrointestinal	Familial polyposis coli
Hematopoietic	Hereditary spherocytosis von Willebrand disease
Skeletal	Marfan syndrome[a] Ehlers-Danlos syndrome (some variants)[a] Osteogenesis imperfecta Achondroplasia
Metabolic	Familial hypercholesterolemia[a] Acute intermittent porphyria

[a]Discussed in this chapter. Other disorders listed are discussed in appropriate chapters in the book.

Cotran, 154-155


Huntington's disease is a progressive disorder, meaning the symptoms gradually worsen over the course of the disease until the patient's death.

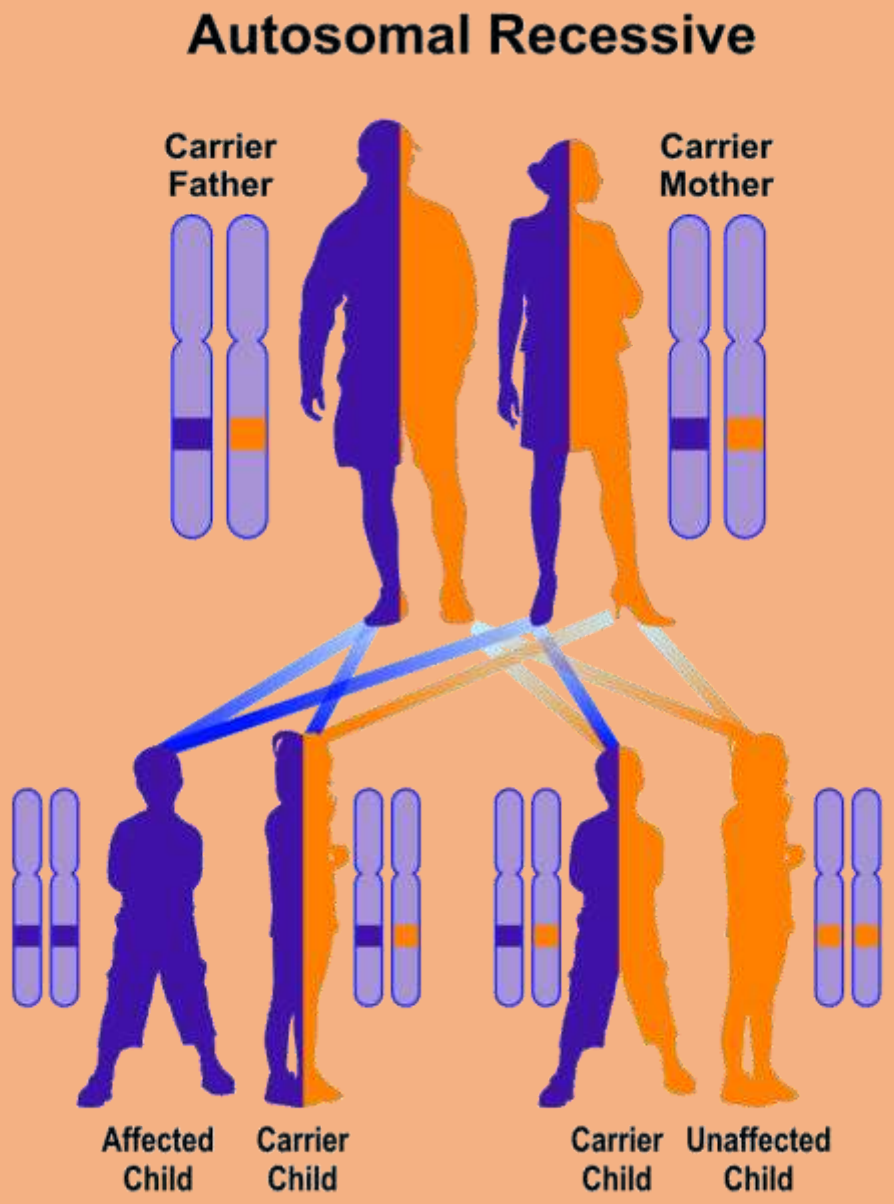


Table 5.2 Autosomal Recessive Disorders

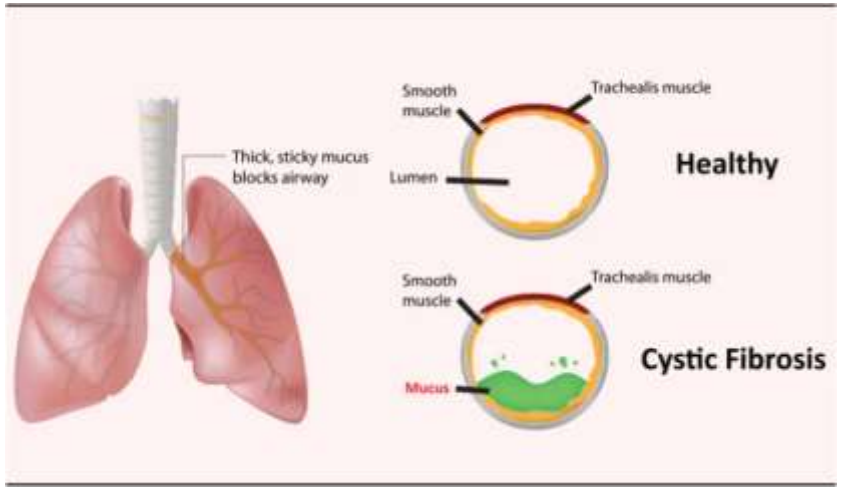
System	Disorder
Metabolic	Cystic fibrosis Phenylketonuria Galactosemia Homocystinuria Lysosomal storage diseases[a] α_1-Antitrypsin deficiency Wilson disease Hemochromatosis Glycogen storage diseases[a]
Hematopoietic	Sickle cell anemia Thalassemias
Endocrine	Congenital adrenal hyperplasia
Skeletal	Ehlers-Danlos syndrome (some variants)[a] Alkaptonuria
Nervous	Neurogenic muscular atrophies Friedreich ataxia Spinal muscular atrophy

Cotran, 154-155

Cystic Fibrosis (Fibrosis kistik) Kowalak, h. 115

Deskripsi:

- Disfungsi kelenjar endokrin
- Angka harapan hidup ; rerata 32 tahun



Penyebab (etiologi)

- Pengkodean abnormal 350 alel CFTR , kromosom 7q; kode untuk protein membran sel (CFTR; *cystic fibrosis transmembran regulator*)
- Pewarisan autosom resesif

Tanda dan gejala

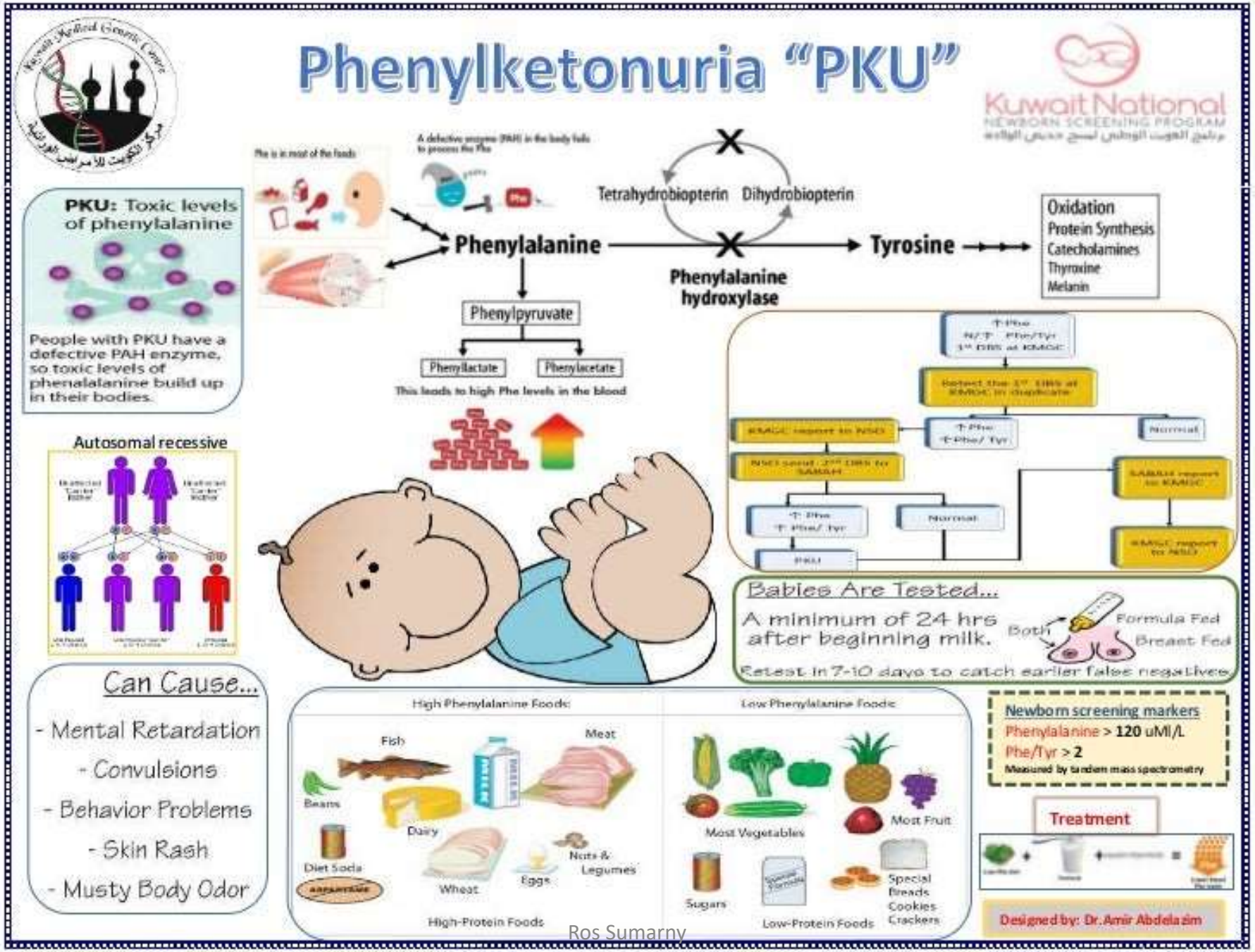
- Sekresi yang kental dan dehidrasi akibat ketidakseimbangan ion;
- Infeksi jalan napas kronis oleh *S. aeroginosa* dan *P. cepacea;*

Patofisiologi/patogenesis

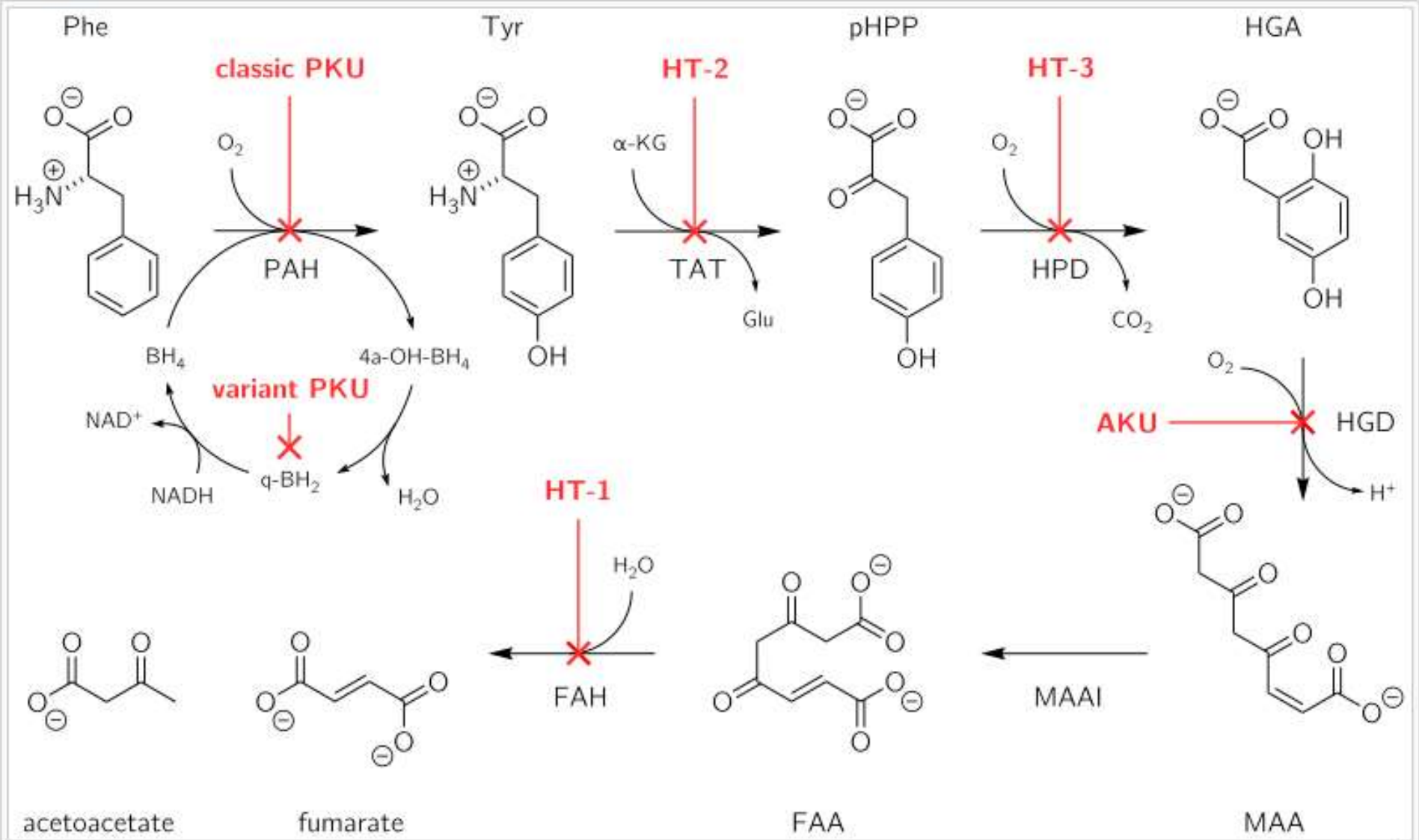
- Mutasi pengkodean genetik asam amino , sehingga CFTR tidak berfungsi
- gangguan absorpsi garam oleh sel epitel
- Kekurangan fenilalanin akan menyebabkan dehidrasi dan peningkatan viskositas sekret mukus

Komplikasi

- Obstruksi saluran kelenjar akibat peningkatan viskositas sekret bronkus, pankreas dan kelenjar lendir ;
- Atelaksis atau emfisema;
- Malnutrisi dan malbasorpsi vitamin larut lemak


Phenylketonuria "PKU"
Kuwait National
NEWBORN SCREENING PROGRAM
PKU: Toxic levels of phenylalanine
People with PKU have a defective PAH enzyme, so toxic levels of phenalalanine build up in their bodies.
Phe is in most of the foods
A defective enzyme (PAH) in the body fails to process the Phe
Phe
Tetrahydrobiopterin
Dihydrobiopterin
Phenylalanine
Phenylalanine hydroxylase
Tyrosine
Oxidation
Protein Synthesis
Catecholamines
Thyroxine
Melanin
Phenylpyruvate
Phenyllactate
Phenylacetate
This leads to high Phe levels in the blood
Autosomal recessive
Can Cause...
- Mental Retardation
- Convulsions
- Behavior Problems
- Skin Rash
- Musty Body Odor
Babies Are Tested...
A minimum of 24 hrs after beginning milk.
Both
Formula Fed
Breast Fed
Retest in 7-10 days to catch earlier false negatives
High Phenylalanine Foods:
Fish
Meat
Beans
Dairy
Diet Soda
Wheat
Eggs
Nuts & Legumes
High-Protein Foods
Low Phenylalanine Foods:
Most Vegetables
Most Fruit
Sugars
Special Breads Cookies Crackers
Low-Protein Foods
Newborn screening markers
Phenylalanine > 120 uMl/L
Phe/Tyr > 2
Measured by tandem mass spectrometry
Treatment
Designed by: Dr. Amir Abdelazim

Metabolic pathways [edit]

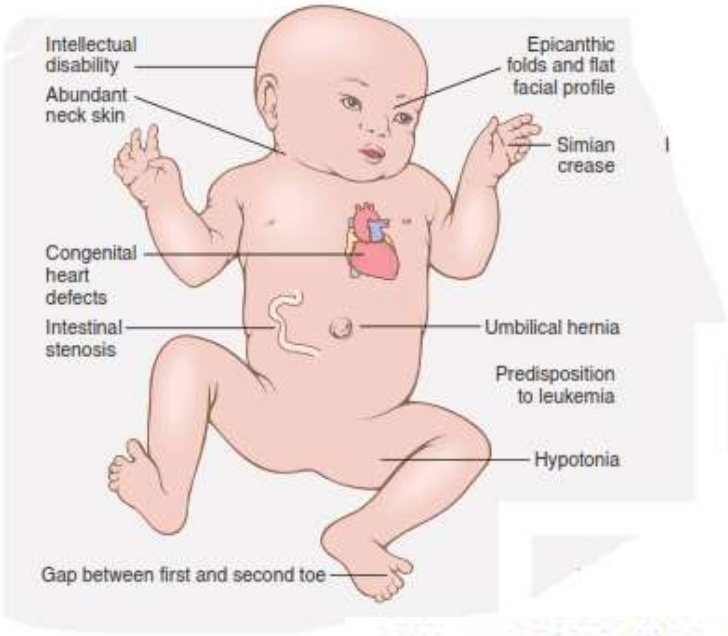


Pathophysiology of phenylketonuria, which is due to the absence of functional phenylalanine hydroxylase (classical subtype) or functional enzymes for the recycling of tetrahydrobiopterin (new variant subtype) utilized in the first step of the metabolic pathway.

Disorder of autosomal chromosome

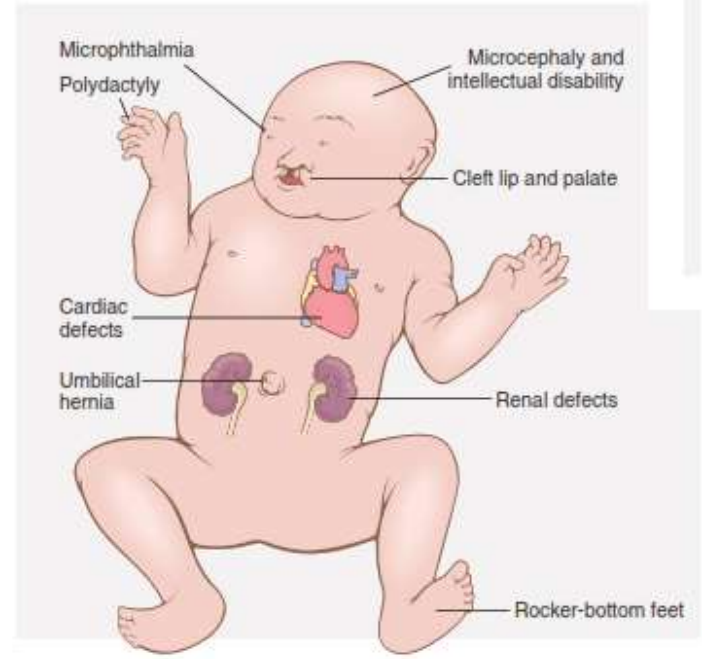
TRISOMY 21: DOWN SYNDROME

Incidence: 1 in 700 births
Karyotypes:
Trisomy 21 type: 47,XX, +21
Translocation type: 46,XX,der(14;21)(q10;q10),+21
Mosaic type: 46,XX/47,XX, +21



TRISOMY 13: PATAU SYNDROME

Incidence: 1 in 15,000 births
Karyotypes:
Trisomy 13 type: 47,XX, +13
Translocation type: 46,XX,+13,der(13;14)(q10;q10)
Mosaic type: 46,XX/47,XX, +13



TRISOMY 18: EDWARDS SYNDROME

Incidence: 1 in 8000 births
Karyotypes:
Trisomy 18 type: 47,XX, +18
Mosaic type: 46,XX/47,XX, +18

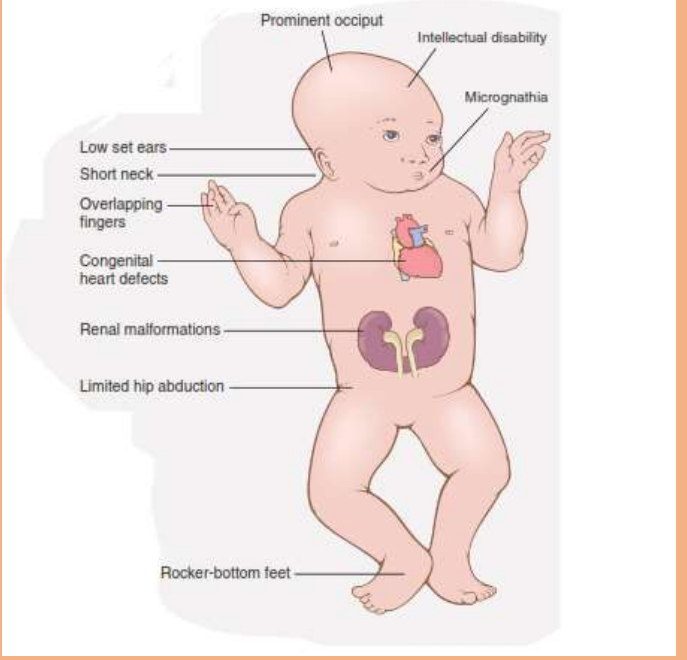
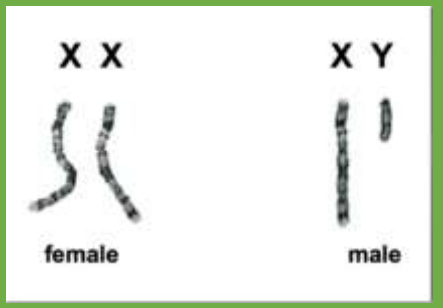
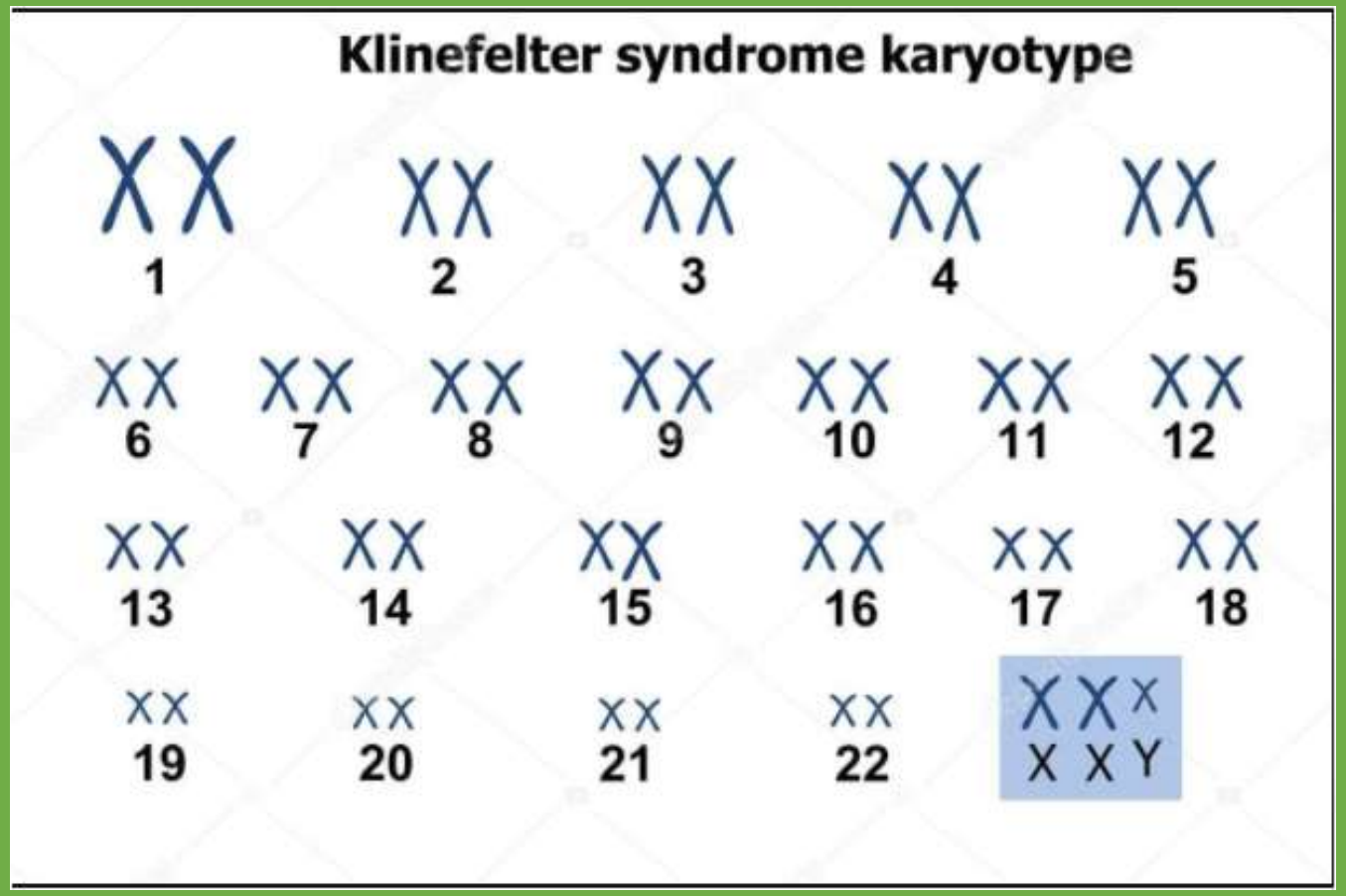


Figure 5.20 Clinical features and karyotypes of selected autosomal trisomies.

Cotran, 177

Disorders of sex chromosome





Disorders Associated With Defects in Structural Proteins

Several diseases caused by mutations in genes that encode structural proteins are listed in Table 5.4. Many are discussed elsewhere in the text. Only Marfan syndrome and Ehlers-Danlos syndromes (EDSs) are discussed here because they affect connective tissue and hence involve multiple organ systems.

Coltran, 156

Table 5.4 Biochemical and Molecular Basis of Some Mendelian Disorders

Protein Type/Function	Example	Molecular Lesion	Disease
Enzyme	Phenylalanine hydroxylase	Splice-site mutation: reduced amount	Phenylketonuria
	Hexosaminidase A	Splice-site mutation or frameshift mutation with stop codon: reduced amount	Tay-Sachs disease
	Adenosine deaminase	Point mutations: abnormal protein with reduced activity	Severe combined immunodeficiency
Enzyme inhibitor	α_1-Antitrypsin	Missense mutations: impaired secretion from liver to serum	Emphysema and liver disease
Receptor	Low-density lipoprotein receptor	Deletions, point mutations: reduction of synthesis, transport to cell surface, or binding to low-density lipoprotein	Familial hypercholesterolemia
	Vitamin D receptor	Point mutations: failure of normal signaling	Vitamin D–resistant rickets
Transport			
Oxygen	Hemoglobin	Deletions: reduced amount	α-Thalassemia
		Defective mRNA processing: reduced amount	β-Thalassemia
		Point mutations: abnormal structure	Sickle cell anemia
Ion channels	Cystic fibrosis transmembrane conductance regulator	Deletions and other mutations: nonfunctional or misfolded proteins	Cystic fibrosis
Structural			
Extracellular	Collagen	Deletions or point mutations cause reduced amount of normal collagen or normal amounts of defective collagen	Osteogenesis imperfecta Ehlers-Danlos syndromes
	Fibrillin	Missense mutations	Marfan syndrome
Cell membrane	Dystrophin	Deletion with reduced synthesis	Duchenne/Becker muscular dystrophy
	Spectrin, ankyrin, or protein 4.1	Heterogeneous	Hereditary spherocytosis
Hemostasis	Factor VIII	Deletions, insertions, nonsense mutations, and others: reduced synthesis or abnormal factor VIII	Hemophilia A
Growth regulation	Rb protein	Deletions	Hereditary retinoblastoma
	Neurofibromin	Heterogeneous	Neurofibromatosis type 1

Struktur tugas presentasi pada P-7
Setiap kelas dibagi 8 kelompok @ 4-6 mhs
Presentasi sebelum dan setelah UTS @ 4 judul
Judul tugas diumumkan via LMS

1. Deskripsi
2. Penyebab
3. Patofisiologi/patogenesis
4. Tanda dan gejala
5. Komplikasi
6. Penanganan (untuk gangguan umum)
7. Pustaka

Berkolaborasi dalam mengerjakan tugas Pasti ada kenangan indah