DNA are made of Genes which are coiled together by histone proteins; which forms the chromatids in rest phase, which makes chromosome in dividing phase.

Gene → Segment of DNA, which coded for proteins called Codones.

DNA → Deoxyriboenucleic acid which is a double helix model which has a nitrogenous base (Nucleotides)

Purine as guide → Purines → Adenine and Guanine (Same in RNA)

Pyrimidine → Cytosine and Thymine (Uracil in RNA)

which look oppositely.

Chromosome → When DNA are packed together they form chromatids and chromosome

Autosome: Except germ cell (Sperm and eggs → Haploid) and RBC, all cell contain, Diploid 2n (23 pairs of chromosome), one from maternal and one from paternal.

Autosomes → 22 pairs. except 1 sex chromosome

Sex chromosome → X and Y in male, XX in female.

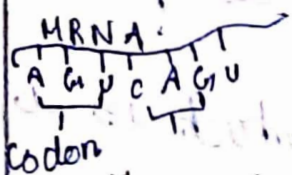
Transcription:

Gene (segment of DNA) coder for protein chain of amino acids (o-oo-o-o-o)

↓

Sends MRNA to ribosomes (helps of RNA polymerase)

↳ (single stranded and Thymine replaced by Uracil)



Translation of the message into proteins (code)

↓

Protein synthesis (20 amino acids)

Genetics

- DNA (Gene) makes the chromosomes.
- Autosomal → 22 pairs
- Sex chromosome → 1 pair XX / XY
  - XX → Female
  - XY → Male

Pattern of Inheritance

1) Autosomal
   - Recessive
     - Consanguinity in marriage.
     - Recurrence in sibling is possible in 25%.
   - Dominant
     - 50% of the children in affects.
     - More than one generation.

System	Autosomal dominant	Autosomal Recessive
1) Nervous	Huntington disease Neurofibromatosis	Neurogenic Muscular atrophy
2) Skeletal	Marfan's syndrome Achondroplasia	
3) Metabolic	Familial Hypercholesterolemia	Cystic fibrosis Phenyl ketonuria, Haemochromatosis, Glycogen storage disease.
4) Haematopoietic	Hereditary Spherocytosis.	Sickle cell anemia Thalassemia.
5) Renal	Polycystic kidney disease	
6) GIT.	Familial polyposis coli	

Sexual Inheritance

$X\alpha$ $X\ Y$

$X'X\ X'Y$ ~~XX~~ ~~XY~~

↳ α can compensate.

X-linked — Dominant
↳ Females more affected
from father equal to mom ← daughter if affected.

~~Autosomal~~ Recessive
↳ Always women carriers. never from father.
Sons are affected, daughters are carriers.

Diseases of X linked recessive:

1) Nervous → Fragile ~~X syndrome~~
2) Muscular → Duchenne (Becker) muscular dystrophy.
3) Metabolic → Diabetic insipidus.
4) Blood → Hemophillia A & B. G6PD deficiency.
5) Immune → Agammaglobulinemia. Colour Blindness, Night Blindness

X linked dominant → Rare.
↳ Hypophosphatemic type Vitamin D resistant rickets, fragile X syndrome

Autosomal Disorders

Down's Syndrome (Trisomy 21)

- Chromosome number 21 is present in triplicate, making the total number of 47.

Maternal age → Strong influence.
- <25 years → 1 in 1500 live births
- >40 years - 1 in 100 births
- >45 years - 1 in 40 births.

Risk Factors → Exposure to pesticides, electromagnetic fields, anaesthetic, coffee, alcohol.

Causes → 1) Non-Disjunctional - 95%, (Chromosome does not separate)
2) Translocation - 4%.
3) Mosaic - 1%.

Clinical Features
1) Marked Hypotonia 2) Poor Moro's Reflex
3) Flat facies 4) Upward slant of eyes.
4) Dysplastic ear 5) Dysplastic middle phalynx of little finger 6) Dysplastic pelvis
7) Fold of skin near neck.

Physical → 1) ↑ Simian Crease (Transverse Crease)
2) Gap between first two toes.
3) Flat facial profile.
4) Epicanthal fold.

Organ → 1) Brain → Retardation, Alzheimer.
2) Blood → Acute leukemia
3) Heart → Congenital Heart disease (CSD, ToF Fallot) Atrial Septal Defect
4) GIT → Duodenal atresia
5) Reproductive → ↓ Fertility

Screening during pregnancy

Decrease	Increase
1) Alfa peta protein AFP	1) HCG
2) Unconjugated estriol	2) Inhibin A

- Imaging - Ultrasound seeing how much light passes through neck - Nuchal translucency.
- Karyotyping

Treatment → ↑ Quality of life.

Edward syndrome (Trisomy 18)

- Chromore number 18 is present in triplicate making the total number of 47.
- Maternal age increases the risk.

Causes → 1) Non-Disjunction 2) Translocation, 3) Mosaic.

C/F: Organs → 1) Heart → Congenital Heart defect (VSD)

2) GIT → Atrophagia atresia → Small & Amniotic fluid → Polyhydramnios.
→ Omphalocele.

3) Kidney → Horseshoe kidney
↑ Wilms tumor & Hepatoblastoma.

- Child usually dies Before Birth, if survives dies after birth.

Physical → Microcephaly, Low set ears, Cleft lip/palate, Rocker bottom feet, Digit overlapping.

Screening → USG → Nuchal translucency.

Prenatal sonogram → Polyhydramnios.

Serum → 1st trimester → ↓ HCG & Inhibin A
and trimester → ↓ AFP & uE Conjugation

- Karyotyping → before Birth → Amniocentesis.
after → Blood test.

Trisomy 13 (Patau Syndrome)

- Very rare only 1 in 10,000 births.
- Chromosome number 13 is present as a triplate → making the total number 47.

Cause → 1) Non-disjunction 2) Translocation, 3) Mosaic

↑ Maternal age.

C/F:

Organ → 1) Microcephaly.
2) Holoprosencephaly (No division of 2 Hemisphere.
3) Spina bifida.
4) Heart → Septal defect.
5) GIT → Omphalocele 6) Kindney → PKD -

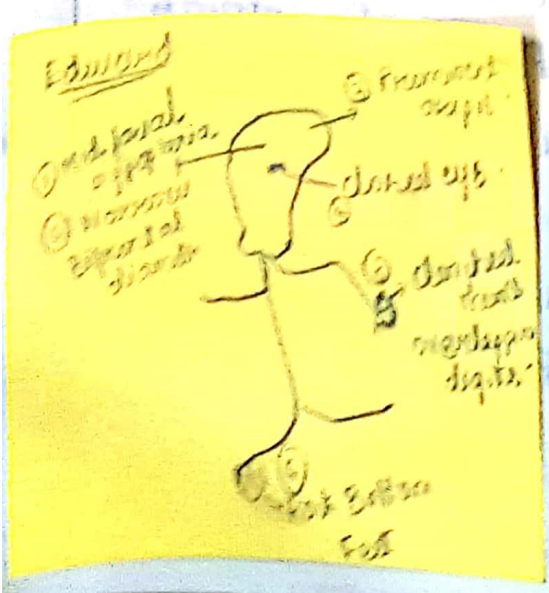
Physical → Cleft Lip & Palate.
Cyclopia → (Fusion of Eyes no division)
Proboscis → (Nose absent).
Multiple fingers (polydactyly)
Rocker bottom feet.

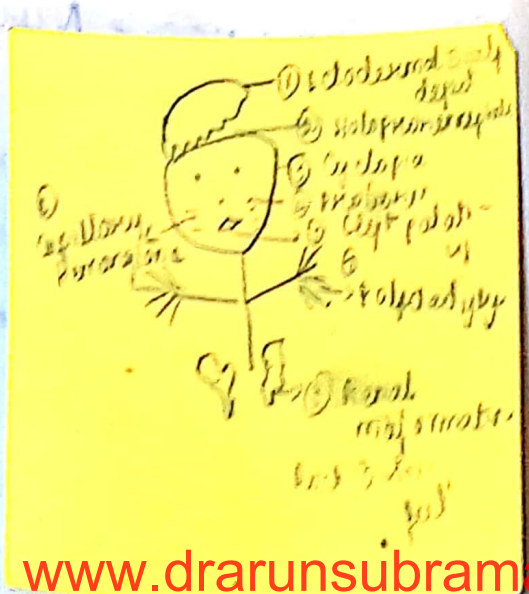
Investigation

USG → Nuchal translucency.

Serum → 1st Trimester → HCG & PAPP-A ↓.
2nd Trimester → AFP, UE3 & HCG, Normal.

Karyotyping.





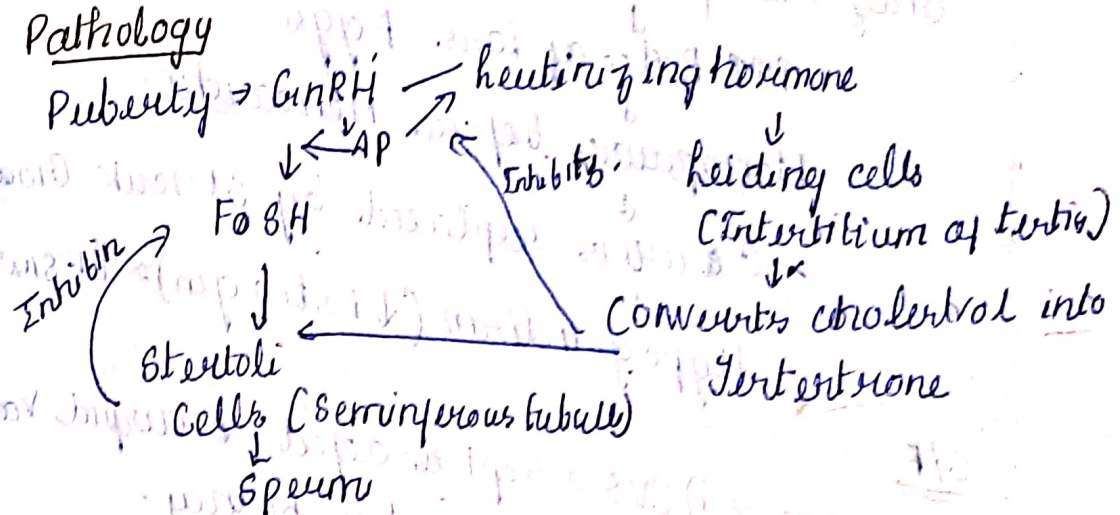
Sex Chromosomal Disorder:

Extra X chromosome - Klinefelter syndrome
Deletion X chromosome → Turners syndrome.

Klinefelter Syndrome

- Male ~~fear~~ is affected usually. and addition of one X extra chromosome cause XXY.
- Male = Sex. Not gender or identity.

Pathology



→ In Klinefelter syndrome no production of the ↓ Testosterone ∴ ↓ Inhibin ∴ ↑ Production of Estrogen
↓ Small testes
Sterility.
↓
↑ Breast tissue

C/F- Most after puberty, hive as men or female gender identity.
1) Hypogonadism - Small Testis + Penis → Sterility.
2) A The span is big than height and lower segment bigger than upper segment.
3) Gynecomastia, 4) Loss Muscle mass, ~~facial~~ ~~hair~~ ~~pubic~~ hair.
5) Lower Estrog levels.
6) Increased risk of Breast Cancer & Osteoporosis.

Investigation → ↑ Estrogen ∴ FSH ∴ LH, ↓ Testosterone.
Karyotyping - Amniocentesis → XXY.
→ Blood

Treatment → Long acting testosterone.

Turner's Syndrome (Monosomy)

- Missing of but or Partial X chromosome (Monosomy). (X O)

Cause: 1) Non-Disjunctional.
2) Mosaic Pattern (XX/XO).
3) Deletion of Parts

Pathology:
only 1 Complete X chromosome.
↓
↑↑↑ Rate of loss Eggs.
↓
Menopause before Menarche.
↓
Ovaries replaced by Streak Gonads.
↓
Hypogondism (↓ Estrogen) ∝ ↑FSH ↑LH.

C/F:
Organs → 1) CVS → Septal defect, Coarctation, Bicuspid valve.
2) Kidney → Horseshoe kidney.
3) ↑ Risk of Type II Diabetes + Hypothyroidism
4) Lymph obstruction → Cystic hygroma, odema.
5) Female →
Physical → Underdeveloped breast, Hypoplastic uterus. + presence of Fatty streak in ovaries, Less hair. Amenorrhea.

Physical → 1) Low Seat Ears Cystic.
2) Neck Webbing.
3) Broad chest & Wide Nipples.
4) Arm turns outward (Cubitus valgus)
5) Short stature.

Investigation:
Karyotyping → Aminocentesis
Ultrasound

Genetic disorders

1) Single Gene Mutation
   - ↳ Substitutions → Sickle Cell (Glutamate to Valine)
   - → Insertions -
   - → Deletions.

2) Polygenic →

3) Chromosomal disorders:
   - 1) Structural:
     - ① → Deletion
     - ② → Duplication
     - ③ → Insertion
     - ④ → Inversion
     - ⑤ → Translocation → Eg: (Philadelphia chromosome) 9 : 22
     - ⑥ → Non disjunction → Ring chromosome.
   - 2) Numerical chromosomal abbnebration:
     - 1) Aneuploidy → Chromosome number not a multiple of 23 (Haploid Normal) By addition or deletion.
       - a) Trisomy → (2n+1). (47 XX + 21)
         - → Autosome → Trisomy 21 → Down syndrome
           - Trisomy 13 → Patau Syndrome (47 XY + 13)
           - Trisomy 18 → Edward syndrome (47 XY + 18)
         - → Sexual → Klinefelters syndrome: (XXY)
       - b) Monosomy → (2n-1).
         - Turners syndrome (45 XO)
     - 2) Poly ploidy: chromosome number that is multiple of 23, but greater than 2n (2 haploid)
       - 69 → Triploid. 92 → Tetraploid → Spontaneous abortion.

3) Mixoploidy
   a) Moraicism
   b) Chimerism.

Prader Willi Syndrome.

→ Defect in chromosome 15 (Imprinting disorder).
Absence of expression of paternally active gene on long arm chromosome 15 (Tf maternal active ~~chromosome~~ gene → Angel man's Syndrome).

Infancy
→ Poor Hypotonia
↓ Asphyxia ↓ Suckling reflex
↓ Failure to thrive
↓ GnRH → Hypogonadism
Hypothalamus
↓ GH → Short stature.

Late Infancy
· Overeating
always felt
· Hungry.

Childhood
↓ Obesity,
Type II diabetes
Obstructive
Sleep apnea.

Mnemonic
'SOM' eat too much. Though He Has Small hands & feet
Fish shaped mouth & almond shaped eyes.
S - Short stature
O → Obesity, Obstructive sleep apnea
M → Mental retardation
T - ~~H~~ Tone decreased (Asphyxia, Suckling reflex)
HH → Hypogonadotropic Hypogonadism
Small hands & Feet
Fish shaped mouth
Almond shaped eyes

Management → Restrict amount of food.
↑ GH supplements.

Angelman's Syndrome:

→ Imprinting disorder.

→ Absence of expression of maternally active genes or long arm of 15 expression

"SAMI the happy puppet"

S - Seizures

A - Ataxia

M → Mental retardation

I → Inappropriate laughter.

Happy

Puppet → Cogwheel rigidity.

Developmental milestone delayed.

Williams Syndrome

Autosomal dominant disorder of chromosome 7 where small portion is deleted.

W - Weight low at birth slow to

I - Iris Stellate Iris

L - Long philtrum

L - Large mouth.

I → Increased Ca^{++} (↑ vitamin D) Tonic.

A → Aortic stenosis (Supravalvular stenosis) Pulmonary stenosis,

M - Mental retardation

S - Swelling over eyes (Periorbital)

H - Hoarse voice

E - Elfin Facies.

L - Loquacity personality.

Di george Syndrome (CATCH 22)

→ Deletion of chromosome 22q11.2 deletion. which coder for pharyngeal pouch ~~cause~~ for parathyroid & thymus.

C → Cardiac abnormality (Tetralogy of fallot)

A → Abnormal Facies.

T → Thymic aplasia, T cells dysf.

C - Cleft Palate & Lip.

H - Hypocalcemia/Hypoparathyroidism.

Werners Syndrome (WRN gen, Recessive)

- Adult Progeria
- Premature ageing syndrome
- Senile cataracts, premature balding and grays, Scleroderma like illness.
- Muscle wasting, Osteoporosis.

→ ↑ Malignant risk and diabetes.