1. GENETICS

INHERITANCE

I. Mutant gene (Mendelian disorder)
II. Polygenic inheritance: Hypertension/Diabetes
III. Chromosomal aberration: Mongolism, Turners, Klenfelter's syndrome

MENDELIAN TYPES

I Autosomal dominant [AD]
2. Autosomal recessive [AR]
3. Sex linked inheritance{SLD]
4. Multifactorial inheritance

	AD	**AR**	**SLD**
One affected parent	50%	None	Mother to son
Two affected carrier	100%	25% affect; 50% carry	50% son affect; 50% Daughter career
Age of onset	Onset delayed	Onset is early	Delayed
Penetrance	Variable penetrance	More uniform	Uniform
Consanguineous Marriage	Not affected	Affected	Royal family
Mutation	Common	Rare	Uncommon

AD	AR	SLD
Achondroplasia	Enzyme defect	**Dominant**
Neurofibromatosis	Sickle cell anaemia	Hypophosphatemic rickets (Vitamin D refractory rickets)
Osteogenesis imperfecta	Osteogenesis imperfect	
Marfan's syndrome	Hypophosphatasia	
Ehlers Danlos syndrome	Vit D dependent rickets	
Multiple epiphyseal dysplasia	Homocystinuria	**Recessive**
Spinal epiphyseal dysplasia		Haemophilia
Multiple diaphyseal dysplasia		Duchene muscle dystrophy
Polydactyly		Hunter's syndrome

POLYGENIC OR MULTIFACTORIAL INHERITANCE

When one parent affected, 5% chance to I degree relative (son)

5% changes of recurrence with each pregnancy

10% if two siblings affected

Monozygotic twins: range is 20-40%

Examples: Diabetes, hypertension, gout, Schizophrenics
Talipes, CDH: Scoliosis: incidence sibling 5-30%
Rheumatoid arthritis

FEW EXAMPLES GENETIC DISORDER AND ABNORMAL PROTEIN

Disease	Chromosomal defect	Defective protein
Achondroplasia	4	FGFR3
Marfan's	15	Elastin
Osteogenesis imperfecta	17	Collagen I
Charcot Marie Tooth disease	17	Connexon
Neurofibromatosis	17	Neurofibrin
Fredrick's	9	Frataxin
Fibrous dysplasia		Gs protein

TRISOMIES

DOWN'S SYNDROME [TRISOMY 21]

Cardiac Malformation
Risk of Leukaemia
Risk of Infection
Early onset of Dementia

EDWARD SYNDROME [TRISOMY 18]

Micrognathia
Mental retardation
DDH
Rocker bottom feet
Congenital heart

PATAU SYNDROME [TRISOMY 13]

Cleft lip and palate
Cardiac
Mental retardation
Polydactyl

KLENFELTER'S [XXY]

Tall
Infertility; testicular atrophy
Low IQ
Acne
Scoliosis

TURNERS [XO]

Short stature
Amenorrhea
Infertility
Webbed neck
No mental retardation
Cubitus valgus, Widely spaced nipple
Coarctation of aorta
Horse shoe kidney
Malignant Hypothermia

DOWN'S SYNDROME

Trisomy 21; Translocation 21-14 (4%);Mosaic type (1%)
Do not use the term "Mongol"

Effect of maternal age: older the mother, high the risk of child with Down's syndrome

(1 in 25 in >45 years)

Diagnosis

Prenatal	Amniocentesis
Clinical	Mongoloid facies: Flat occiput
	depressed nasal bridge
	inner epicanthic fold and eyes are up slanted
	Brushfield spots
	Short neck
	Trident hand
	Lax joints
	Congenital heart problem
	Dementia

Non-orthopedic manifestation

Congenital heart disease	50%
Duodenal atresia	
Hirschprung disease	
Anorectal atresia	<10%
Leukemia	1-2%
Hypothyroidism	40%
Diabetes	2%
Premature ageing/ Alzheimer's	Majority
Higher risk of infection	
Higher risk of anesthesia	
Sensitive to atropine	

Cervical instability may be present [C1-C2]

In 20% incidence, A-A distance is more than 5 mm
High risk for neurology
High incidence of Pseudarthrosis following spinal fusion
Careful neurological assessment: in patient participating in sports [X rays at 10 yrs]

Hip instability

10% and usually seen at 10 yrs and not at birth
Multidirectional
Young patient hip spika

Older: Capsular plication, osteotomy or femur and acetabuloplasty
Results are poor compared to CDH
For painful hip in adults: THR

Ligamentum laxity and excessive femoral anteversion

Patello-femoral subluxation or dislocation

Metatarsus adductus and Metatarsal. Primus Varus

Tarsal coalition may be more frequent.

Hand: Simian Hand

Little finger deviates radially (Delta phalanx)

Scoliosis: Thoracolumbar (50%)