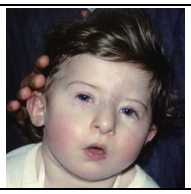
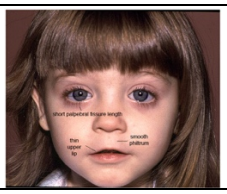
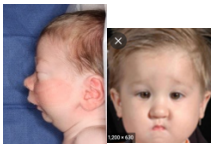
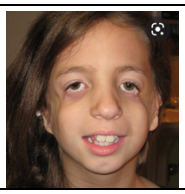
GENETIC/CHROMOSOMAL SYNDROMES

DiGeorge	Fetal alcohol spectrum disorder	Marfan syndrome	Pierre Robin sequence	Stickler syndrome	Treacher Collins syndrome
heterozygous chromosomal deletion at 22q11.2→ Defective development of the pharyngeal pouch system	prenatally exposed to alcohol (time, amount)	autosomal dominant CT disorder of fibrillin gene	hypoplasia of the mandible that occurs before 9th week of development	Inherited CT disorder	autosomal-dominant disorder of craniofacial development
CATCH-22 • Cardiac (TOF – cyanotic + FTT) • Abnormal facies (micrognathia, inward eyes) • Thymus absent (?MG) • Cleft palette • HypoPTH = hypoCa • Chr 22 Other: • **Recurrent chest infections** • Larynx-trachea-oesophageal anomalies	• Macrocephaly • Intrauterine growth restriction (IUGR) • Smooth philtrum • Joint abnormality	• **Marfanoid habitus** (tall, long limbs + high arched palette) • **Hypermobility** • **Arachnodactyly (test)** • Tricuspid valve prolapse	• Cleft palate • Micrognathia • Glossoptosis (tongue back in mouth)	• Flat face • Upturned nose • Prominent eyes • Hypotonia • Hypermobility	• Malar hypoplasia • Down slanting palpebral fissures • Lower lip defect • Ear + eye abnormality • Cleft palate
	• inattentive • Lung hypoplasia • Altered surfactant production • Poor academics, impulse control	• **Murmur** = MVP, AR • **Aortic dissection** • **Pneumothorax** • **Chest wall deformities** (kyphoscoliosis, pectus excavatum) • **Upward lens dislocation**		• Feeding/ breathing difficulties • Scoliosis	• **Underdevelopment of the facial bones** + airway can lead to airway obstruction • **Colobomas** (defect in iris)
		**Rx:** ➢ BB and ARB for HTN ➢ PT = strengthen joints ➢ Genetic counsel ➢ Yearly ECHO and ophthal reiew			

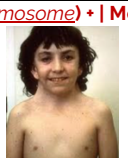
	Cause	Physical dysmorphia	Assoc	Mx
Down's	**Trisomy 21**	• Low set ears, • epicanthic folds, • upslanting palpebral fissures, • single palmar crease • clinodactyly (bending of 5th finger) • inguinal hernia (crypto-orchidism)	• **ENT –conductive hearing loss (recurrent otitis media, glue ear)** • **Vision loss** *(myopia, cataracts, strabismus)* • **CVS**: **AVSD (ASD, VSD),** PDA, TOF, aberrant SCA • **Resp:** small nose → OSA, Recurrent chest infections • **GIT:** ***Duodenal atresia, Hirschsprungs disease*** • **Endo: hypothyroidism (10-20%)** • **Cancers** = *leukeamia*	**Ante-natal screening** • **NIPT** • **NT scan** • **Biochemical (B-HCG, PAPP-A)** • **CVS or amniocentesis**
Patau	**Trisomy 13**	• small eyes, cleft palette and lip • polydactyly	• **structural brain defect → learning delay** • **cardiac and renal malformations**	
Edward	**Trisomy 18**	• Prominent occiput and micrognathia • Rocker bottom feet • Flexed overlapping fingers	• **LBW** • **cardiac and renal malformations**	
Turner	**45XO**	• Short stature • webbed neck + widely spaced nipples • wide carrying angle (**cubitus valgus**) • koilonychia	• **Recurrent AOM and UTI** • **Aortic Coarctation** • **Hypothyroidism** • HTN, DM, OP, obesity • **Ovary dysgenesis = amenorrhoea, early miscarriage**	• **GH therapy (for short stature)** • **E2 + PG (for 2nd sex characteristics and regulate [periods)** • **Fertility support**
Klinefelter	**46XXY**	• **Tall thin men** ○ XS central adiposity • Wide hips + less facial/body hair • **small testes + gynecomastia**	• Seminiferous tubules dysgenesis → Infertile • Reduced libido • Learning difficulties (e.g. dyslexia and shy • **COMP (rare) ➔ BC, OP, DM, anxiety and depression**	• **TT injections** • **Breast reduction surgery** • **MDT – speech path, OT, PT, educational support**
Noonan	**AD mutation**	• Short stature • Broad forehead • webbed neck + widely spaced nipples • **hypertelorism (wide space between eyes)** • Downsloping eyes + ptosis • Lymphodema	• POOR FEEDING – FTT , puberty delay • CHD (ASD, pulm. Stenosis, HOCM) • Renal malformation • Hearing loss • Behavioural problems • Crypto-orchidism – infertility • **COMP (rare) ➔ Leukaemia and neuroblastoma**	*MDT and supportive Rx:* • ECHO referral for CHD • Audiology assessment • FBC + APTT • Yearly check up • Plot growth curves – need GH supplementation
Velocardiofacial syndrome	**AD mutation**	• Cleft palette • High-arched palette • Broad nose ridge	• Cardiac malformation (Carotid artery anomaly) • ADHD • Assoc. PTH and thymus hypoplasia (DiGeorge Syndrome)	• FISH to diagnose • CMP – (check for hypoCa) • FBC + complement
Williams syndrome	**Chr 7 deletion**	• Broad forehead, short nose, • **Starburst eyes (star-like pattern on iris)** • WIDE MOUTH + big smile	• **VERY SOCIABLE PERSONALITY** • Hypercalcemia → Nephrocalcinosis • Supravalvular AS • ADHD • HTN	**No cure → MDT approach** • **BP monitor** • **ECHO** • **Low Ca diet**
Cri du chat	**Chr 5 deletion (part only)**	• Developmental, delay	• Learning and speech delay	• **MDt**
Fragile X syndrome	**Tri-repeat FMR1**	• Big head + big testes (macro-orchid) • **Long face + large everted ears** (mickey mouse) • **Large testes after puberty**	• CVS – MVP • MSK – *scoliosis, joint laxity (hypotonia)* • **Intellectual disability**– ADHD, hyperactive (IQ 20-80) • **Seizures**	• **Genetic test – measure # of CGG repeats > 50)** • **MDT approach →** *e.g. Speech path* • **OCD = SSRI** • **ADHD - Stimulants**
Charcot-Marie-Tooth	**Chr 17 duplicate**	• Pes cavus (high foot arch)	• Sensory and motor neuropathy	•
Angelman syndrome (*UBE3A gene*) ***MALE***	**Chr 15 – both copies from father**	• Blond hair, blue eyes and fair skin • Microencephaly, sunken nasal ridge • **Widely spaced teeth** • Prominent lower lip and small chin • **Fascination with water**	• **"happy puppet demeanour** • **Wide-based ataxic gait + flexed elbows and wrist** • **Severe intellectual disability (non-verbal) –** ADHD, epilepsy	**No cure- MDT approach** • Parental education • PT, OT, psychology, social worker • Anti-epileptics if needed
Prader-Willi syndrome [FEMALE]	**Chr 15 – both copies from mother**	• Narrow forehead + almond shaped eyes • Triangular mouth • Short stature and small hands/feet • Underdeveloped genitals= infertility	• Initially feeding difficulties **→FTT + Neonatal hypotonia** • After **– constant hyperphagia → XS wt gain** • MH issues + moderative learning disability	**No cure – supportive care (control wt)** • Give GH – for muscle development • Dietician (control diet) • Social workers • PT, OT, psychologists
Beckwith-Wiedemann syndrome	**Overgrowth disorder**	**Macroglossia** **Hypoglycemia**	• **Omphalocele** • **Hyperinsulinemia (B-cell hyperplasia)** • **Wilms' tumour & Kidney anomalies**	•
Alagille syndrome	**JAG1 mutant gene**	• Prominent forehead, bulbous nose tip • Pointed chin, deep set eyes	• Biliary atresia **–** Jaundice (conj. Bilirubin) • Also: PS, ToFallot	
Thalassemia	**Variant globin gene**	• Chipmunk face – XS bone turnover and proliferation of bone marrow	• **Massive splenomegaly**	

*****Other chr. Issue = Translocation** *e.g. AML T9;22 (ph chromosome)* **+ | Mosaicism =** *Chromosomal abnormality occurs after conception* *****


Down's


Patau


Edward


Turner


Klinefelter


Fragile X


William's


Alagille