

Medical Characteristics of Down's Syndrome and Neural Tube Defects

Element B

Aims and Objectives

Aim

- To develop specific knowledge of the medical characteristics of Down's syndrome and neural tube defects

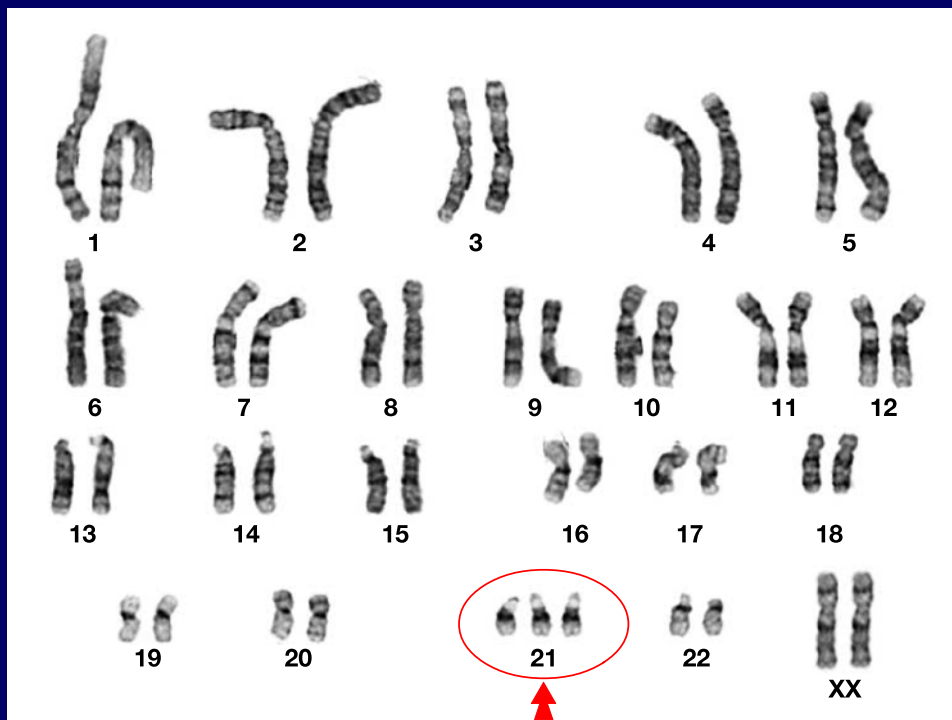
Objective

- To facilitate informed decision-making for women deciding whether to undertake screening for these conditions

Down's Syndrome

- Syndrome - a collection of signs or characteristics
- 1866 Dr John Langdon Down
'Observations on an ethnic classification of idiots'
- 1956 - 46 Chromosomes described
- 1959 Professor Jerome Lejeune
described extra copy of chromosome 21
- Incidence 1 in 700

Regular Down's Syndrome

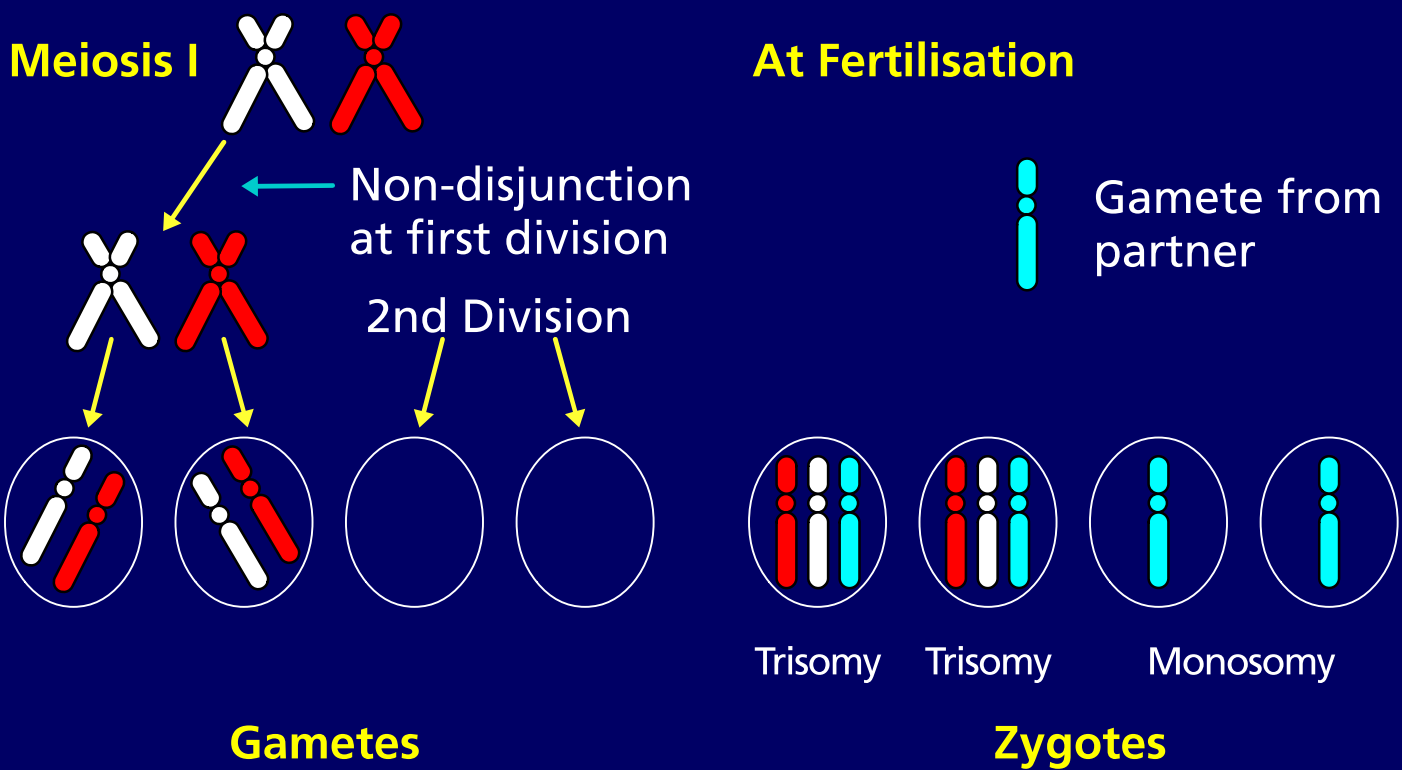


47, XX+21

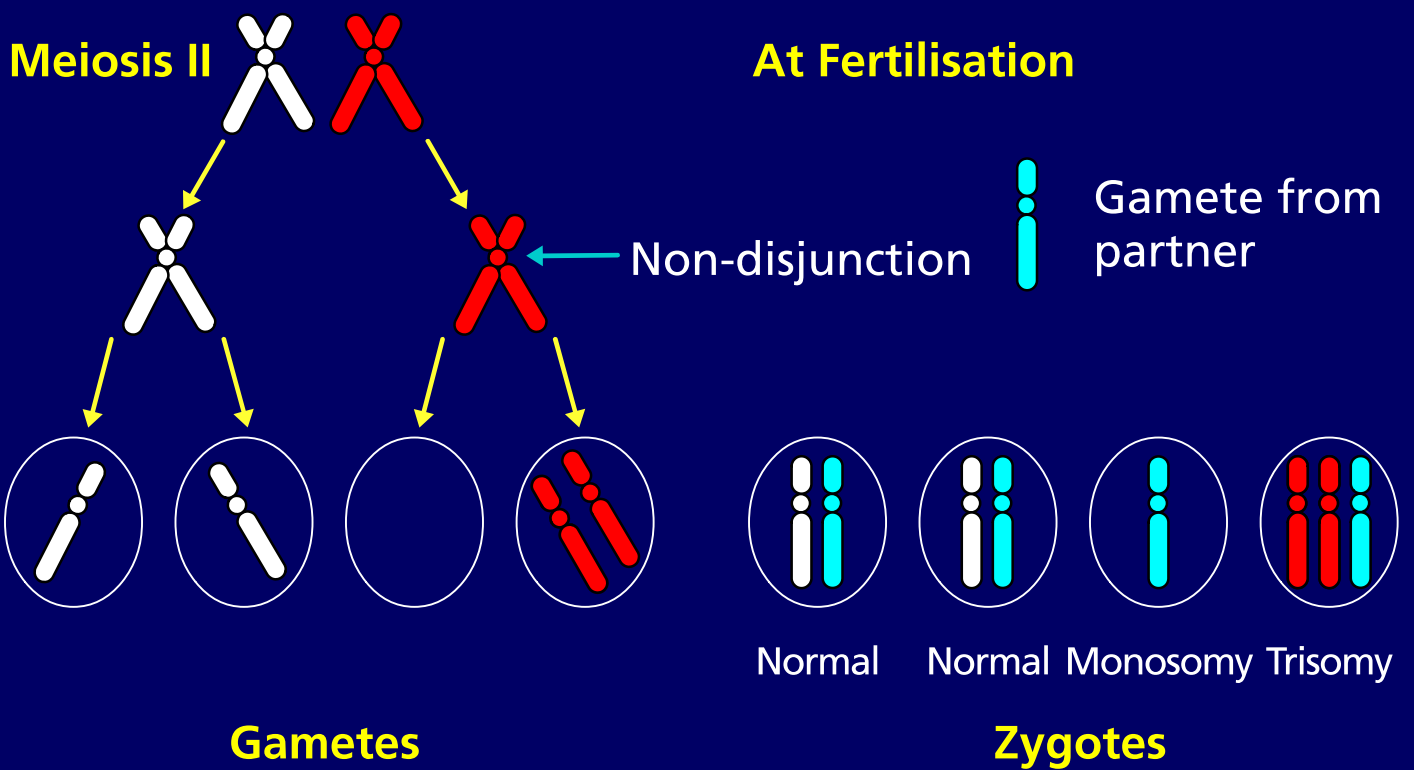
Aetiology

- 95% are regular Trisomy 21 due to non-dysjunction
 - 85% maternally derived,
 - 15% paternally derived
- 4% due to translocation usually Robertsonian
- 1% mosaicism

Non-Disjunction in Meiosis



Non-Disjunction in Meiosis



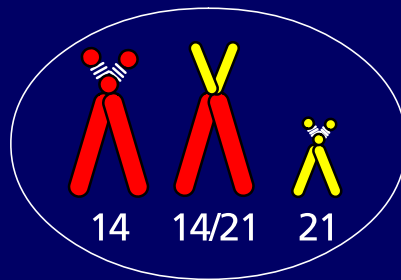
Robertsonian Translocation

Normal Chromosomes

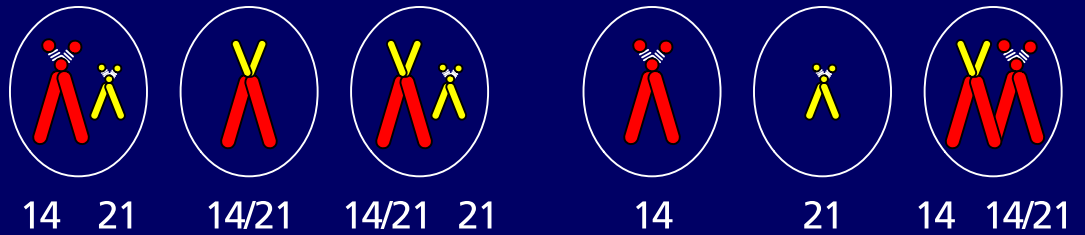


Lost fragments of chromosomes

Balanced 14/21 carrier



Gametes

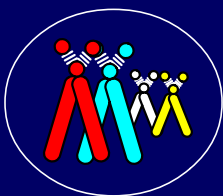


Robertsonian Translocation

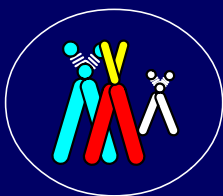
At Fertilisation



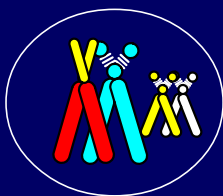
Partner gamete



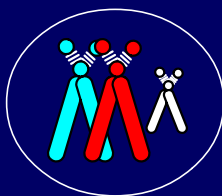
Normal



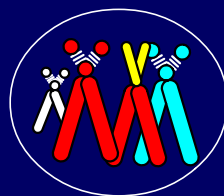
Balanced 14/21
Translocation



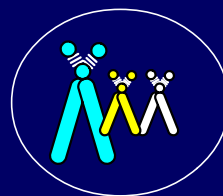
Trisomy 21



Mono 14



Tri 14



Mono 21

Viable zygotes

Non-viable zygotes

Recurrence Risk

- Following a regular trisomy 21, the recurrence risk is 0.75% at 12 weeks (*Nicolaides et al 1999*)
- 0.42% mid trimester and 0.34% at term (*Noble 1998*) plus the background age risk
- Following a trisomy due to a translocation the recurrence risk is dependent on type of translocation and which partner carries the translocation
- Affected persons rarely reproduce.
No evidence of paternal offspring.
Of maternal offspring < half are affected

Clinical Features

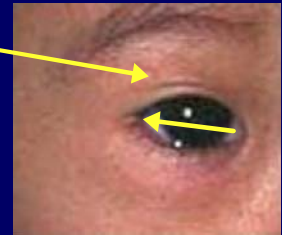
- Brachycephaly excess neck folds, small nose, flattened broad bridge of nose, flat facial profile



- Low set simple ears



- Epicanthic folds
- Upslanting palpebral fissures



- Brushfield spots



- Small carp-shaped mouth, protruding tongue



Clinical Features

- Single palmar crease (Simian crease)



- Clinodactyly

- Sandle gap toes

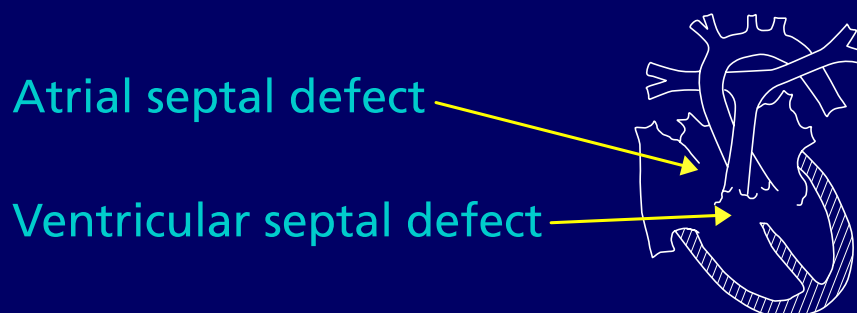


- Hypotonia and poor feeding

- Developmental delay

Cardiac Anomalies

- 40-50% have Congenital Heart Defect
 - 30-40% have complete AVSD (*Tubman et al 1991*) (*Frid et al 1999*)
 - Common others include VSD and PDA (*Noble 1998*)



- All babies should have a clinical screen and an echocardiogram (*DSMIG*)

Hearing and Ophthalmic

- Over 50% have significant impairment, sensorineural and/or conductive loss
- Need lifelong audiological surveillance
- High incidence, 5 X more likely to wear glasses
- Cataracts and/or glucoma may occur in infancy (*Traboulsi et al 1988*)
- Neonatal testing for cataracts and continued ophthalmological screening is required

Thyroid Disorder

- At all ages more frequent than in general population, usually hypothyroidism. Around 10% of school age have uncompensated hypothyroidism. Prevalence increases with age
- Biochemical screening essential throughout life
- Hyperthyroidism is rare

Musculoskeletal

- Joint laxity - knee problems, patello-femoral instability, genu valgus, pes planus (*Merrick et al 2000 Jun*)
- High BMI - feet problems, vertical talus, spinal problems, genu valgum (*Merrick et al 2000 Jun*)
- Cervical spine instability - atlantoaxial joint. There is a small risk for acute or chronic neurological problems (*DSMIG*)

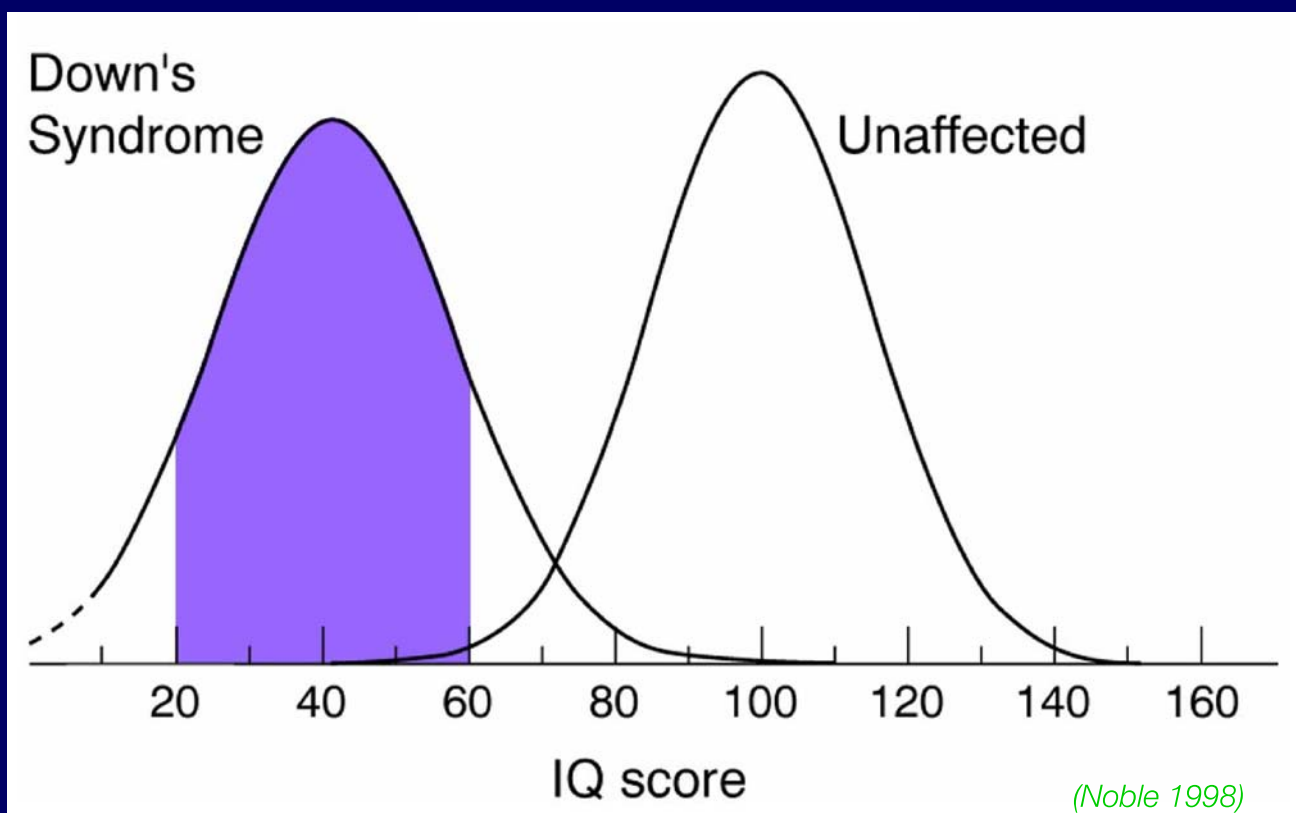
Gastrointestinal Tract

- 10 - 12% have abnormalities of the gastrointestinal tract. Most prevalent are TOF (Tracheo-oesophageal fistula), duodenal obstruction with or without pyloric stenosis, imperforate anus and Hirschsprungs disease (*Levy 1991*)
- Constipation is very common at all ages
- Coeliac Disease (*Roizen et al 2003*)

Other Associated Problems

- Epilepsy 10% in late fifties, 1-2% in children
- Leukaemia 1% in first 2-3 years
- Alzheimer's disease is common affecting 45% from age 45 (*Cunningham 1984*)
- Dentition hypoplasia - less caries, more gum disease
- Skin is dry, some hyperkeratotic areas, less elastic, prone to chapping. Fine and sparse hair some balding

Distribution of IQ



Down's Syndrome

- Most common cause of learning difficulties - some will cope with extra help in mainstream schools, others will need to attend special schools.
- Some adults will live semi-independent lives, others will always be dependent
- Life expectancy is 50-55 years
44% of live births survive to age 60 (*Noble 1998*)