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

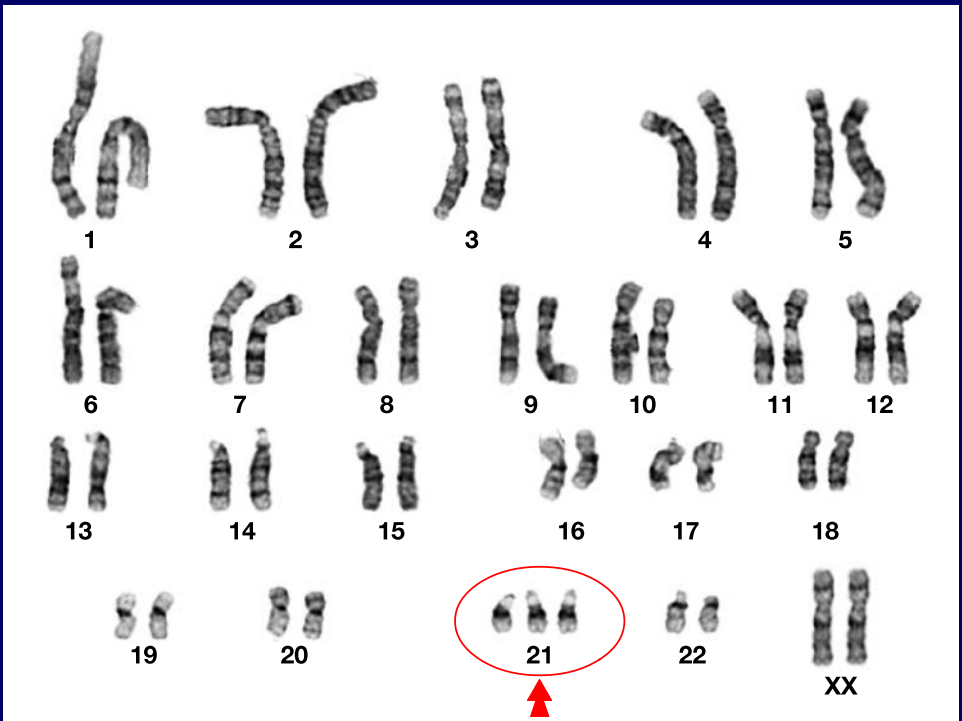
Objective

- 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

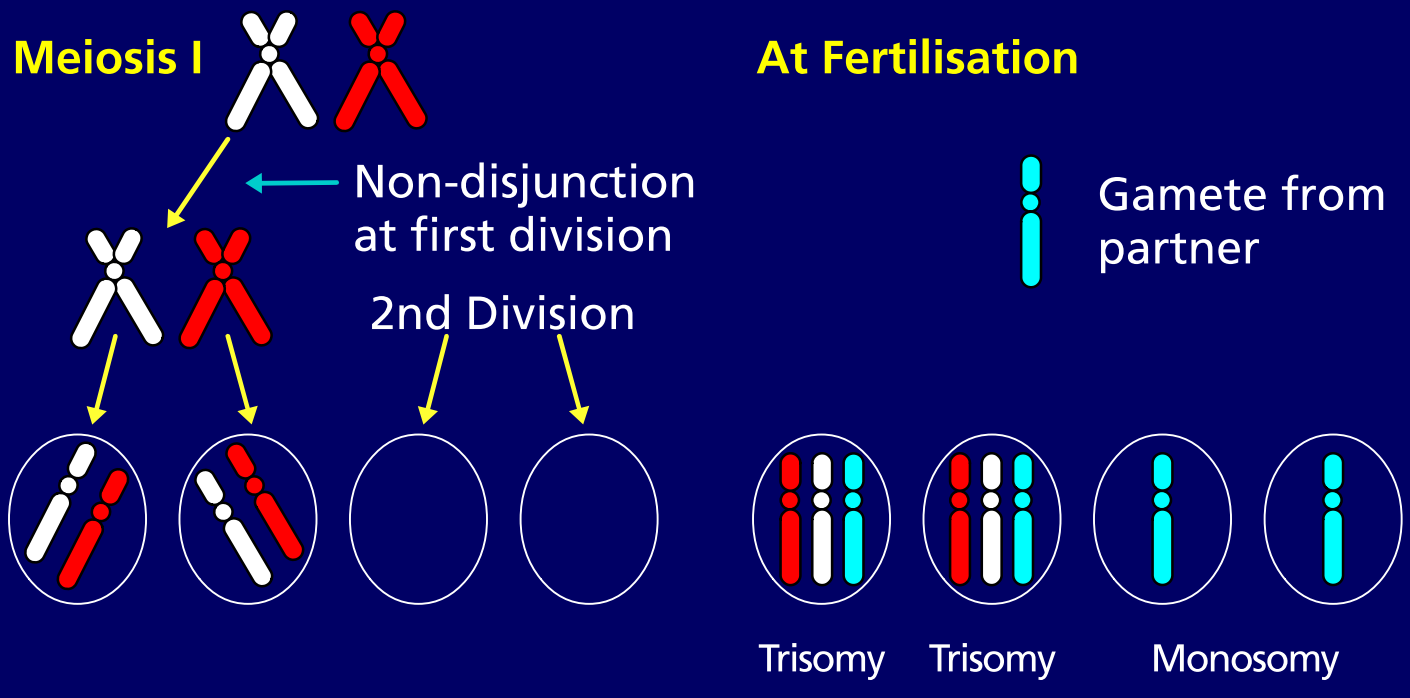


47, XX+21

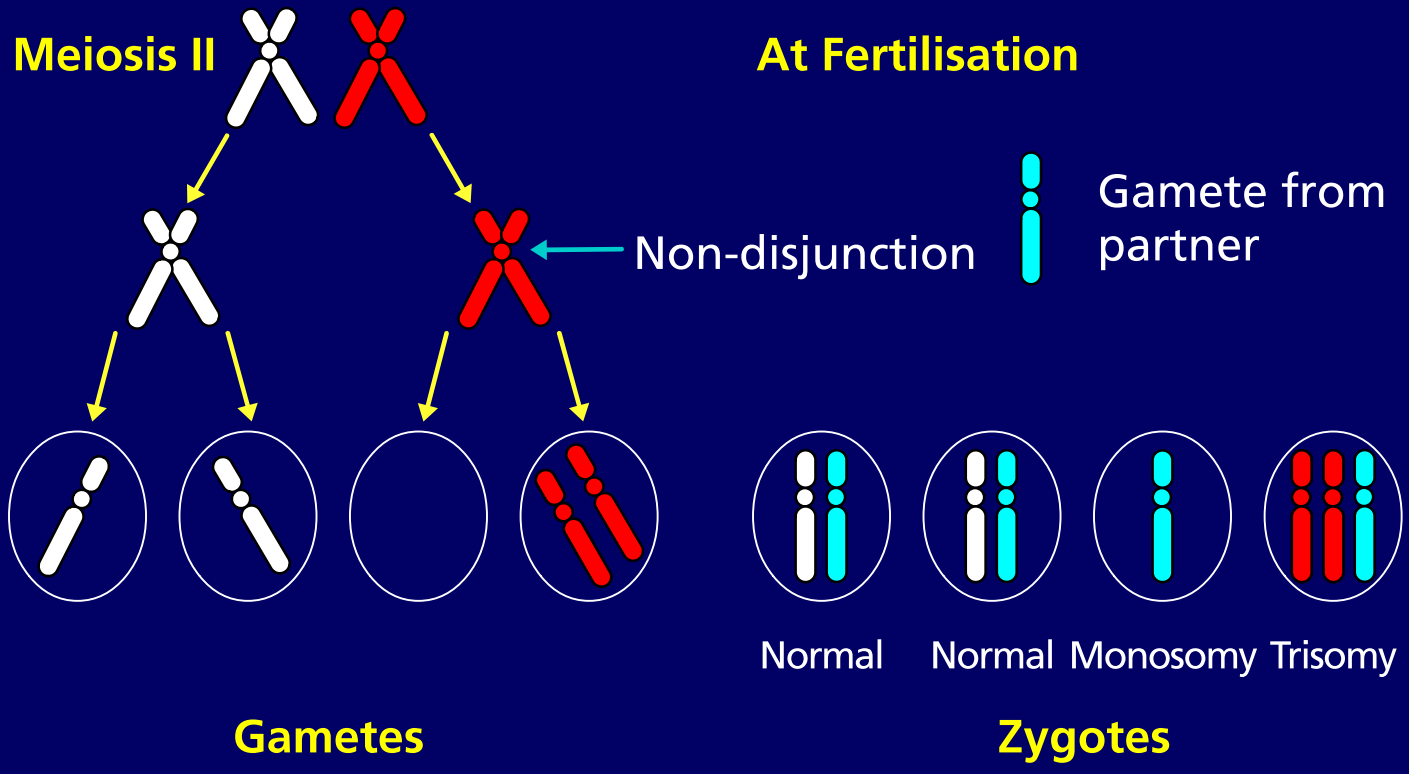
Aetiology

- 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

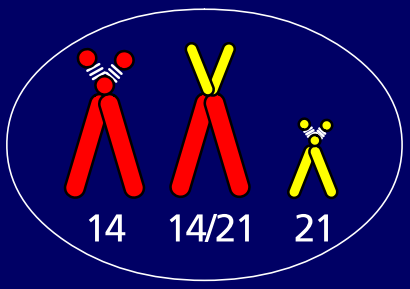


Robertsonian Translocation

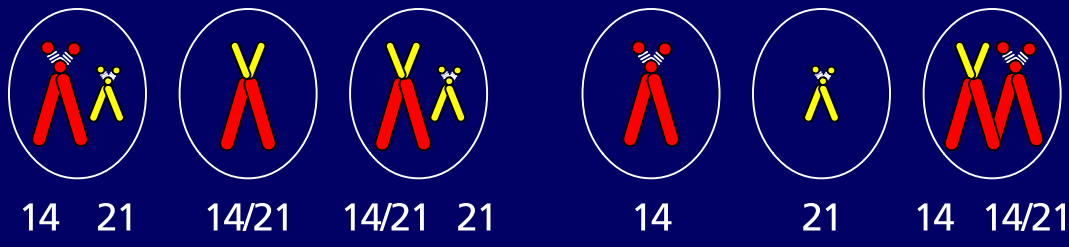
Normal Chromosomes

Lost fragments of chromosomes

Balanced 14/21 carrier



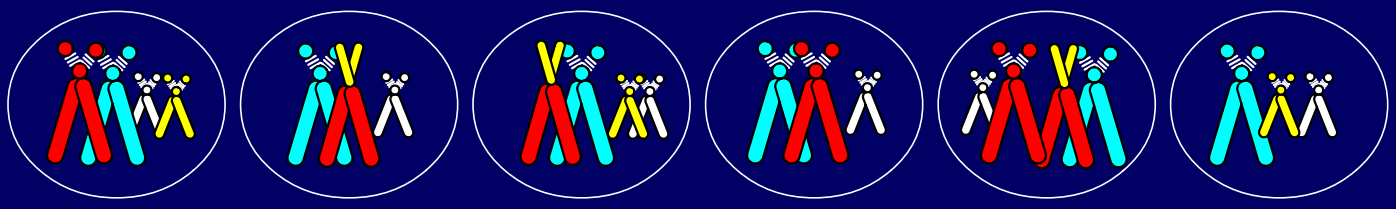
Gametes



Robertsonian Translocation

At Fertilisation

Partner gamete



Normal | Balanced 14/21 Translocation | Trisomy 21 | Mono 14 | Tri 14 | Mono 21

Viable zygotes | **Non-viable zygotes**

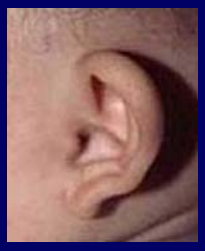
Recurrence Risk

- 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

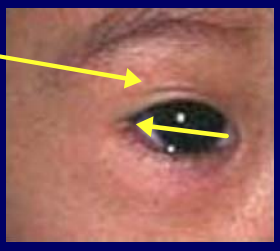
Clinical Features

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

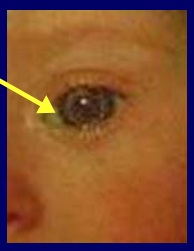
- Low set simple ears



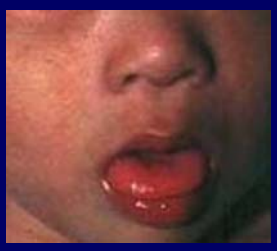
- Epicanthic folds
- Upslanting palpebral fissures



- Brushfield spots



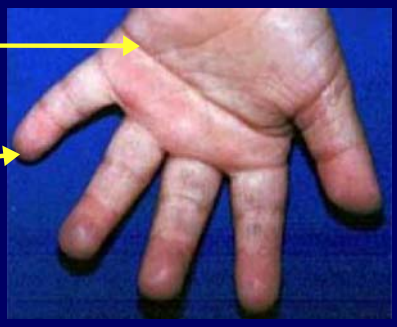
- Small carp-shaped mouth, protruding tongue



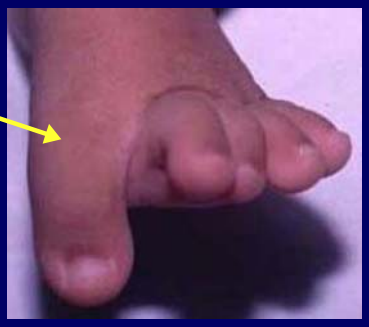
(With kind permission of the Down's Syndrome Association)

Clinical Features

- Single palmar crease (Simian crease)
- Clinodactyly

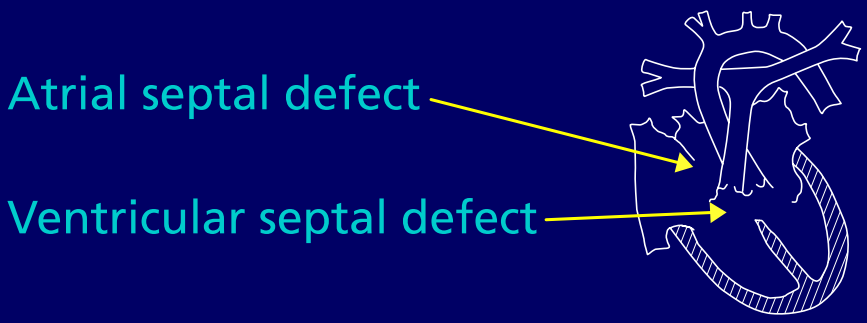


- Sandle gap toes
- Hypotonia and poor feeding
- Developmental delay



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 Opthalmic

- 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 opthalmological 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)*

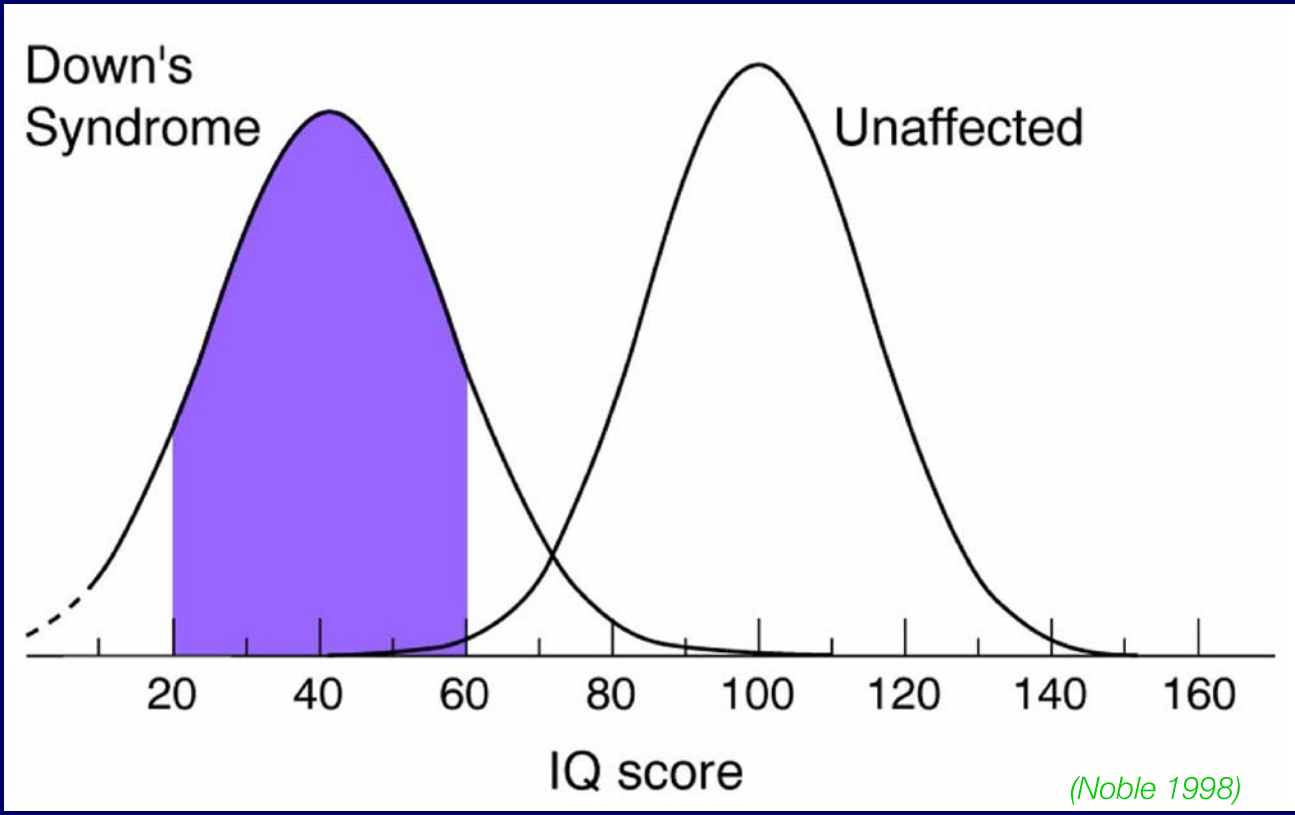
Gastrointestinal Tract

- 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



Median IQ: 40 (range 25 - 60)

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)*