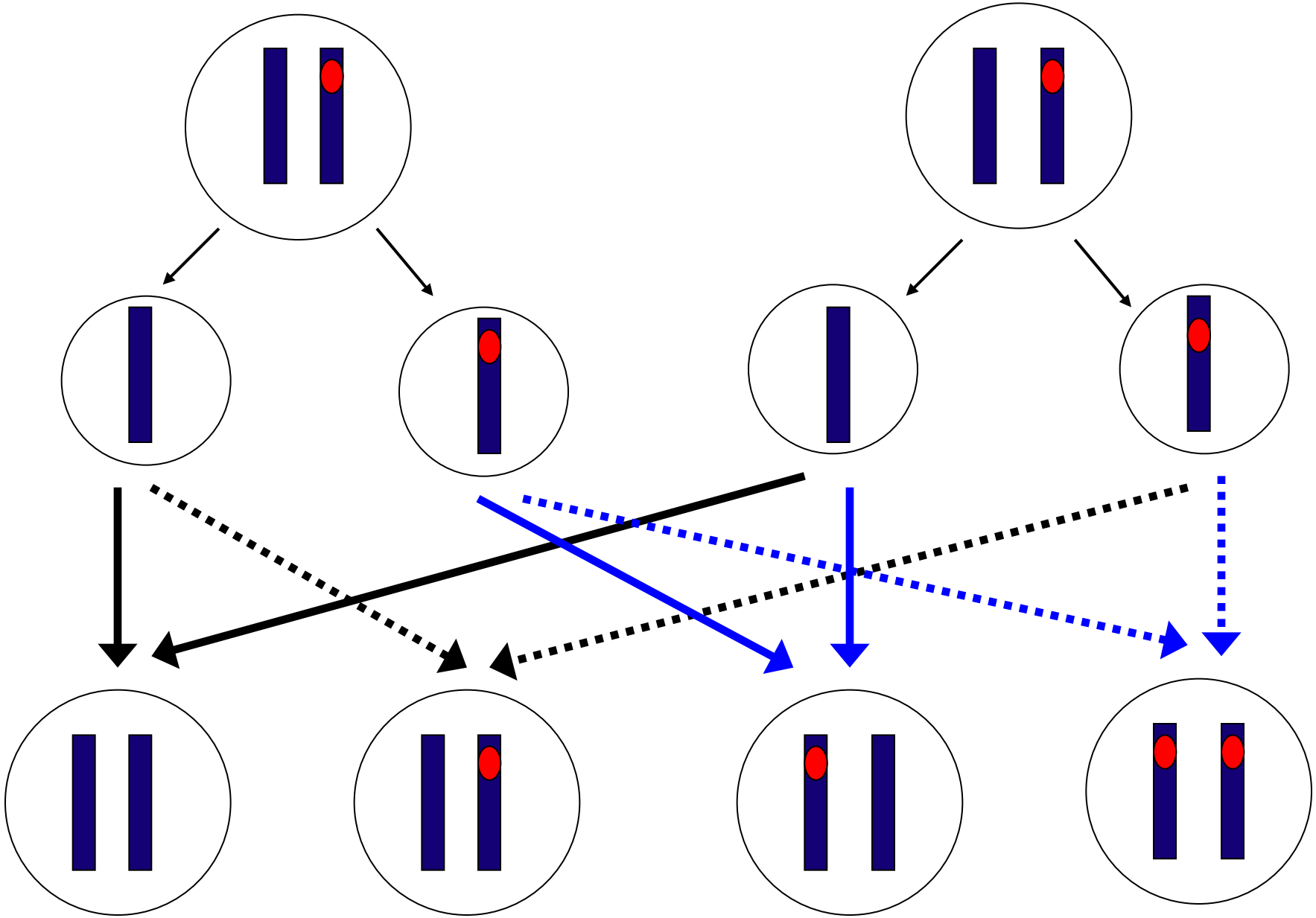
Common Genetics Conditions seen in General Practice

- Haemochromatosis
- Alpha 1 anti-trypsin deficiency
- Familial hypercholesterolaemia
- Suspected Marfan syndrome

Haemochromatosis

- Autosomal Recessive with incomplete penetrance
- Causes progressive iron overload resulting in cirrhosis, diabetes, skin pigmentation and testicular failure
- Incidence about 1/2000, carrier rate about 1/10
- Iron studies show increased serum ferritin and raised transferrin saturation levels
- 2 common mutations C282Y and H63D
- 90% of symptomatic patients are C282Y homozygous, remainder are compound heterozygotes
- Treated by venesection
- Genetic testing can be requested by primary care

Autosomal Recessive Inheritance



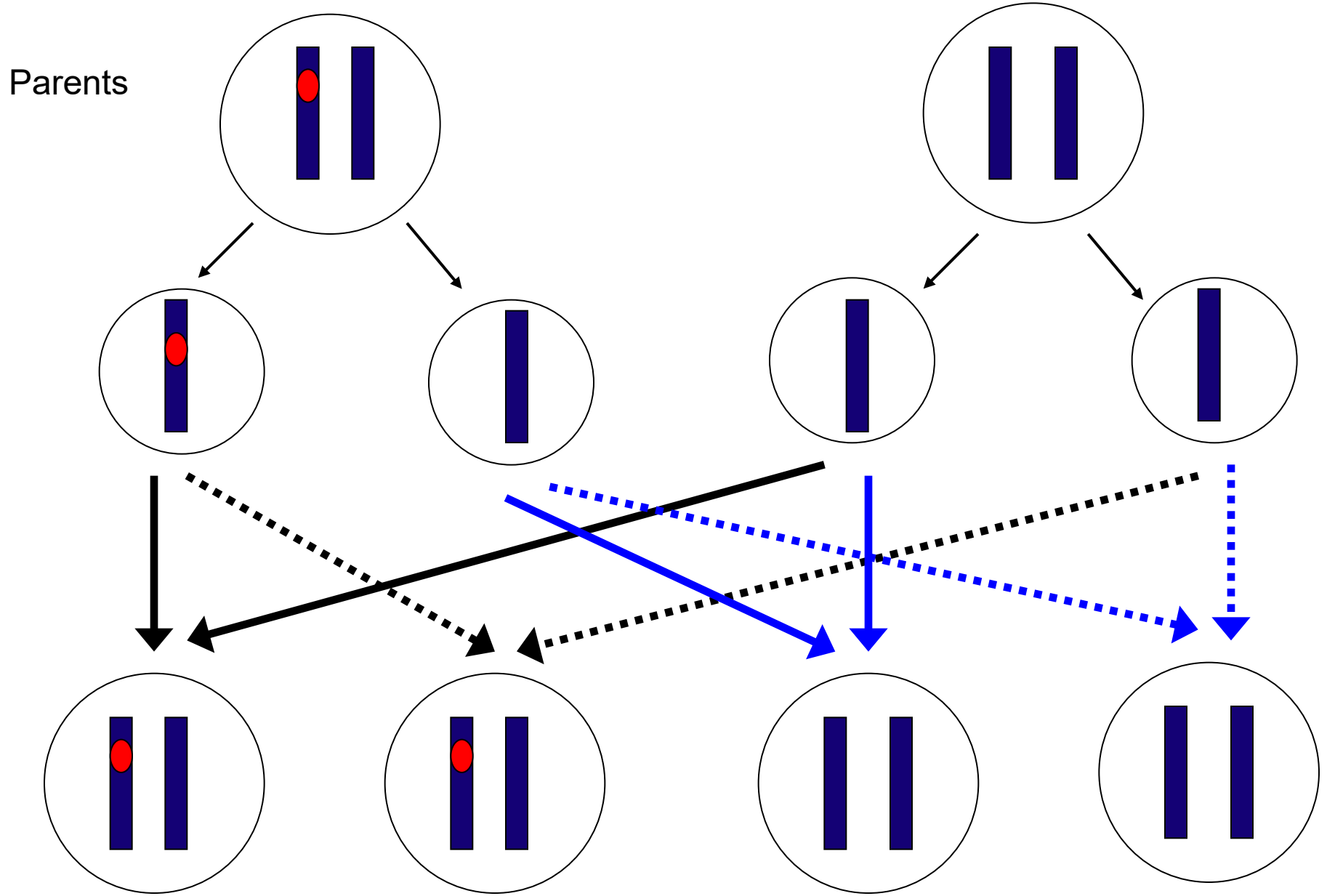
Alpha 1 antitrypsin Deficiency

- Autosomal Recessive with variable expression
- Incidence 1/1600 – 1/1800, carrier rate 1/10
- Predisposes to emphysema and cirrhosis
- Normal variant – M variant
- S variant 40% reduction in alpha 1 antitrypsin levels in SS individuals
- Z variant 85% reduction in homozygotes
- Rarely ZZ homozygotes will develop severe neonatal liver disease
- Genetic testing can be requested by primary care

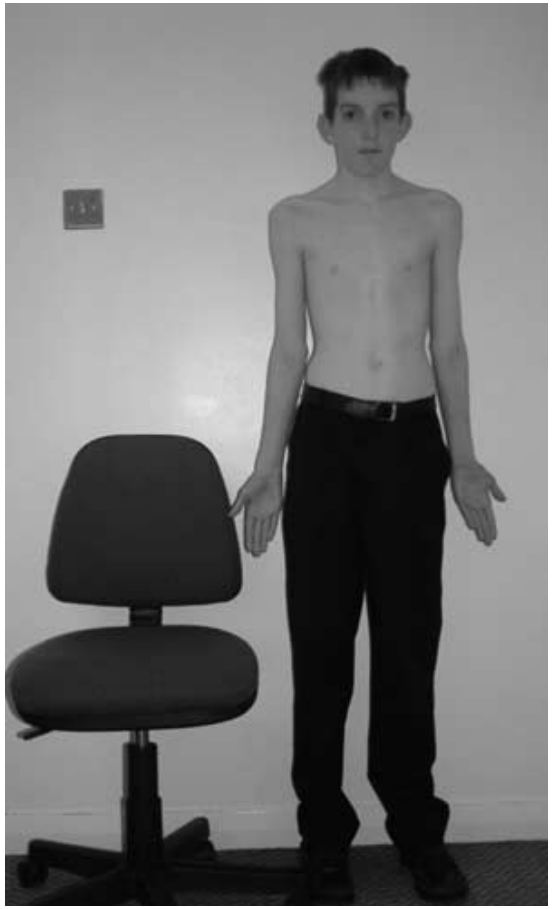
Familial Hypercholesterolaemia

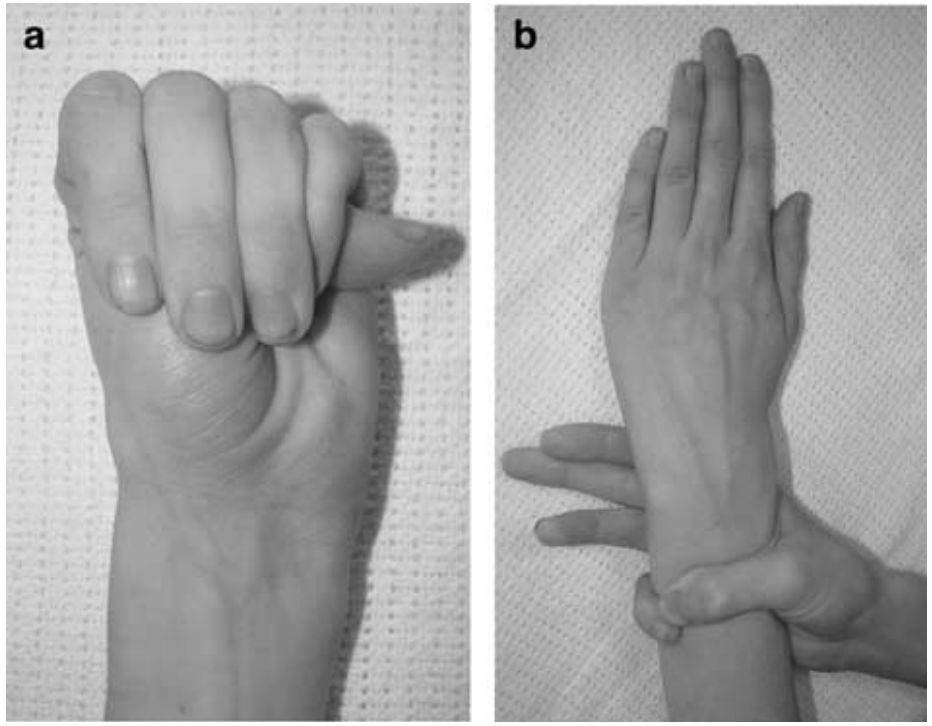
- 1 in 250 people
- Autosomal dominant
- 13X risk of coronary artery disease
- LDLR, APLB, PCSK9
- Think about if
  - Total cholesterol > 7.5 mmol/L and / or
  - Personal or first degree relative with premature coronary artery disease under 60
- Referral to lipid clinic or inherited cardiac conditions clinic

Autosomal Dominant Inheritance



Marfan Syndrome





From Dean JCS (2007) *Eur J Hum Genet* **15:** 724-33

Marfan Syndrome

Table 1 Ghent diagnostic nosology

System	*Major criterion*	*Involvement*
Skeletal	At least 4 of the following features: • Pectus carinatum • Pectus excavatum requiring surgery • ULSR <0.86 or span:height >1.05 • Wrist and thumb signs • Scoliosis >20° or spondylolisthesis • Reduced elbow extension (<170°) • Pes plenus • Protrusio acetabulae	2 of the major features, or 1 major feature and 2 of the following: • Pectus excavatum • Joint hypermobility • High palate with dental • Crowding • Characteristic face
Ocular	Lens dislocation (ectopia lentis)	Flat cornea Increased axial length of globe (causing myopia) Hypoplastic iris or ciliary muscle (causing decreased miosis)
Cardiovascular	Dilatation of the aortic root Dissection of the ascending aorta	Mitral valve prolapse Dilatation of the pulmonary artery, below age 40 Calcified mitral annulus, below age 40 Other dilatation or dissection of the aorta
Pulmonary	None	Spontaneous pneumothorax Apical blebs
Skin/Integument	None	Striae atrophicae Recurrent or incisional hernia
Dura	Lumbosacral dural ectasia	None
Genetic findings	Parent, child or sibling meets these criteria independently Fibrillin 1 mutation known to cause Marfan syndrome Inheritance of DNA marker haplotype linked to Marfan syndrome in the family	None

Abbreviations: ULSR, Upper:lower segment ratio.
Having one of the features listed constitutes a major criterion or system involvement for all systems except the skeletal system, where more than one feature is needed.

From Dean JCS (2007) *Eur J Hum Genet* **15:** 724-33