PRESENTING OUR

GKTEACH

STAGE 1 SERIES

MSA Education

~~FMS - CELL BIOLOGY AND SIGNALLING~~	~~MONDAY 13TH NOV 6PM~~
FMS - MOLECULAR AND CELL GENETICS	THURSDAY 16TH NOV 6PM
FMS - NUTRITION AND METABOLISM	TUESDAY 21ST NOV 6PM
ANATOMY OF RESPIRATORY AND CARDIOVASCULAR SYSTEMS	WEDNESDAY 29TH NOV 13:30PM
PHYSIOLOGY OF RESPIRATORY AND CARDIOVASCULAR SYSTEMS	WEDNESDAY 29TH NOV 4PM
FPP - PHARMACOLOGY	MONDAY 4TH DEC 6PM
RESPIRATORY PHYSIOLOGY	MONDAY 11TH DEC 6PM
RESPIRATORY ANATOMY	THURSDAY 14TH DEC 6PM

MAKE SURE TO COME ALONG!

MCG Essentials (it's not THAT hard)

GKTeach 2023/24
Arm Udomrat - Year 2

Learning Objectives

- Know what will come up in the exam
- Conditions (diseases) which will be examined
- SBAs

THIS IS NOT A LECTURE- ASK QUESTIONS THROUGHOUT

I will also be asking you questions so please volunteer yourselves!

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Exam Content

What will come up?

- Pretty much everything in lecture capture
- At least one question from every lecture
- More emphasis on conditions (e.g. CF, Huntington's)
- NOT a huge part of FMS but should be free marks

IMPORTANT POINT: learn this module properly because 50% of the content will be repeated in the GBE GEN module next semester!!

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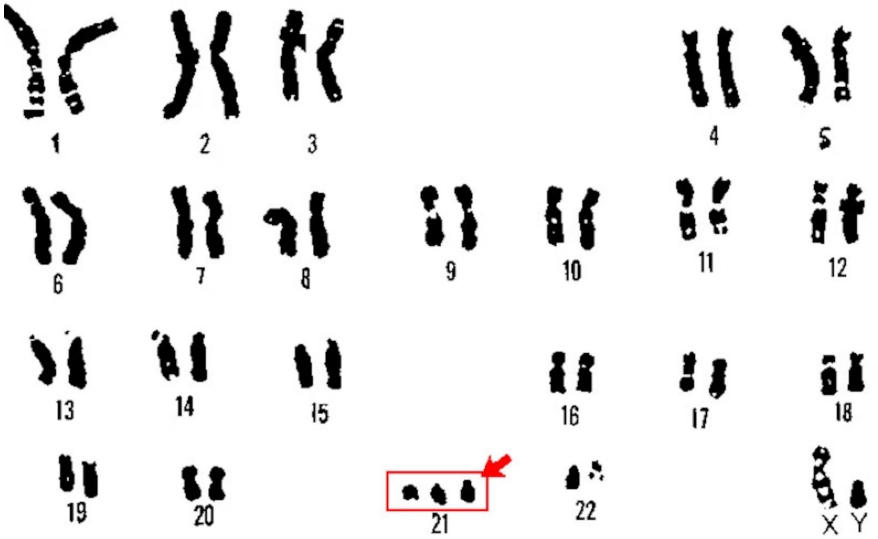
Questions?

Conditions

Trisomies



- Only three viable:
  - Down's Syndrome: T21
  - Edward's Syndrome: T18
  - Patau's Syndrome: T13
- Why just these three?
- Risk increases with maternal age
- Majority due to non-disjunction during oogenesis
- Diagnosis: amniocentesis (15-20 wks)
  - Foetal cells isolated
  - Quantification of chromosomes 13,18,21 using Q-PCR
  - Grown in culture medium
  - Karyotype (takes 2 weeks)

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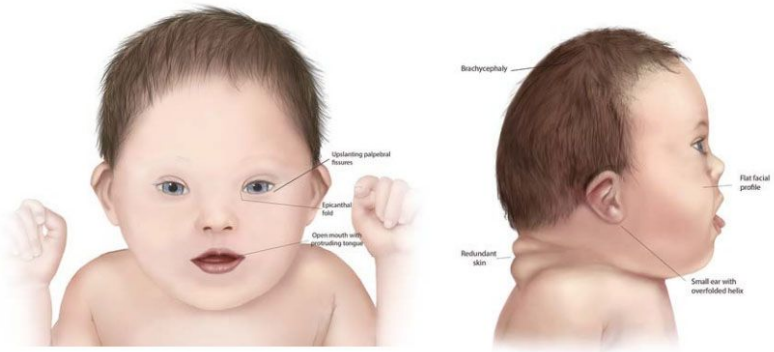
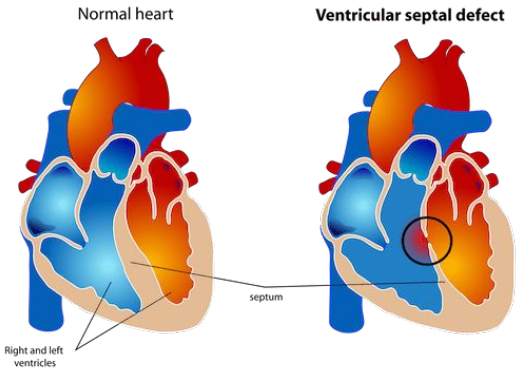
Down's Syndrome: 47,XX/ XY+21

- Signs +Symptoms:
  - Retarded growth and development
  - Mental retardation
  - Single (transverse) palmar crease
- Complications
  - Cardiac abnormalities (e.g. VSD)
  - Increased incidence of acute leukaemia
- Average life expectancy: 60 years





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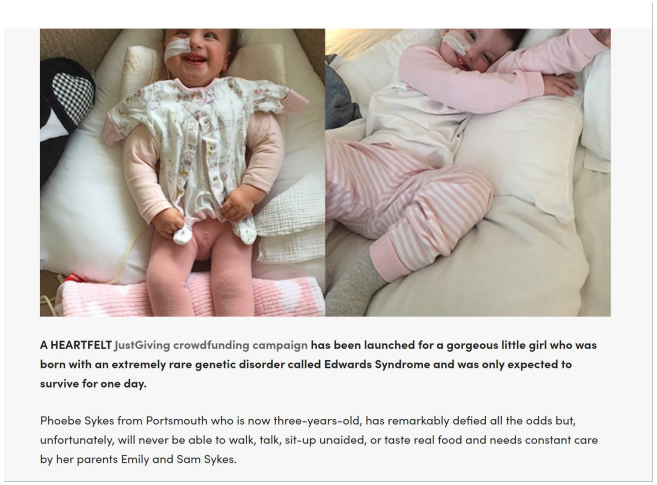
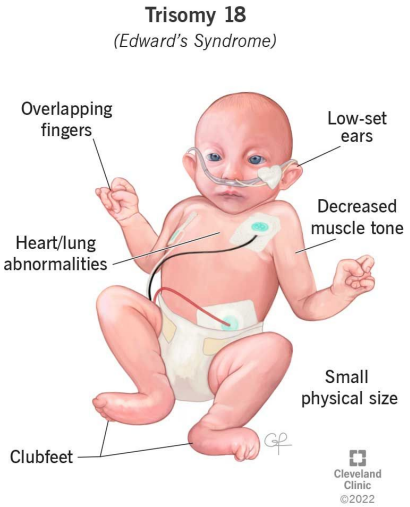
Edward's Syndrome: 47,XX/ XY+18

- Clinical Features
  - Prominent occiput
  - Low-set ears
  - Small jaw
  - Overlapping fingers
  - Rocker bottom feet
- Complications
  - Heart defects
  - Intestines protrude out
- Prognosis
  - 95% die in utero
  - 50% liveborn live 2 months
  - 5-10% live 1 year



A HEARTFELT JustGiving crowdfunding campaign has been launched for a gorgeous little girl who was born with an extremely rare genetic disorder called Edwards Syndrome and was only expected to survive for one day.

Phoebe Sykes from Portsmouth who is now three-years-old, has remarkably defied all the odds but, unfortunately, will never be able to walk, talk, sit-up unaided, or taste real food and needs constant care by her parents Emily and Sam Sykes.



Patau's Syndrome: 47,XX/ XY+13

- Clinical Features
  - Learning difficulties
  - Microphthalmia/anopthalmia
  - Cleft lip and palate
  - Polydactyly
  - Holoprosencephaly
  - Rocker bottom feet
- Complications
  - Heart defects
  - Incomplete brain development
- Prognosis
  - Mean survival: 130 days
  - Only 10% survive to 1 year

Figure 29.3 An adolescent femal with Patau syndrome.

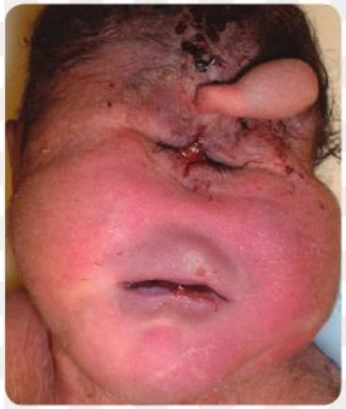


Figure 29.4 An infant with a more severe case of Patau syndrome demonstrating cyclopia and a proboscis.

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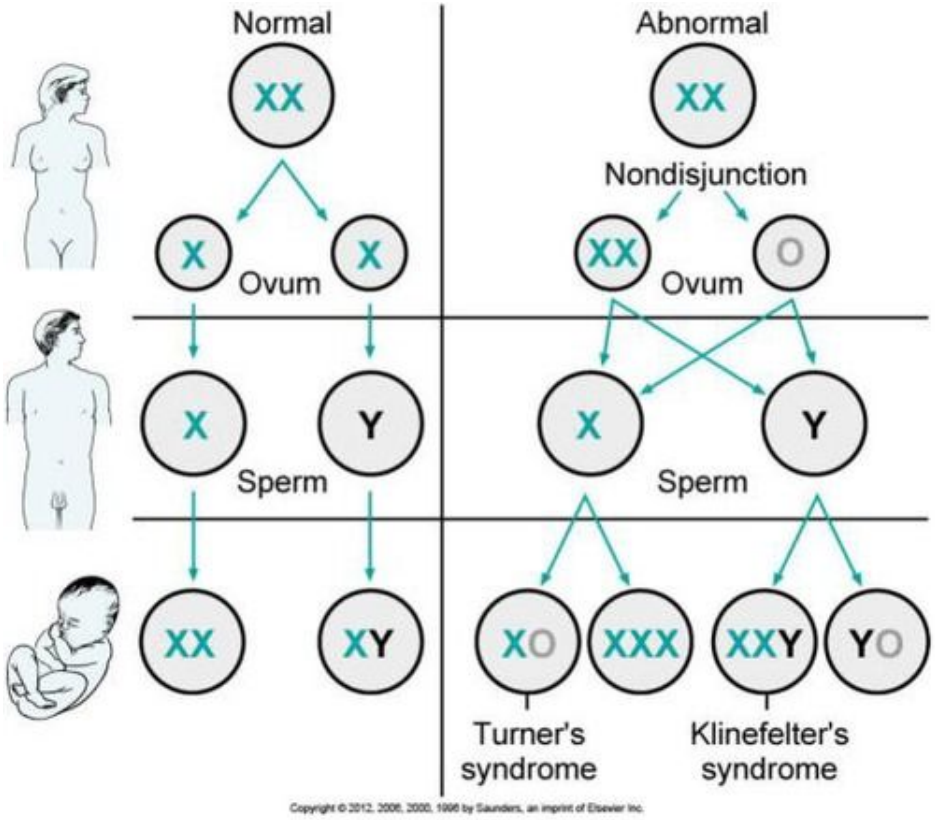
Sex Chromosome Aneuploidies



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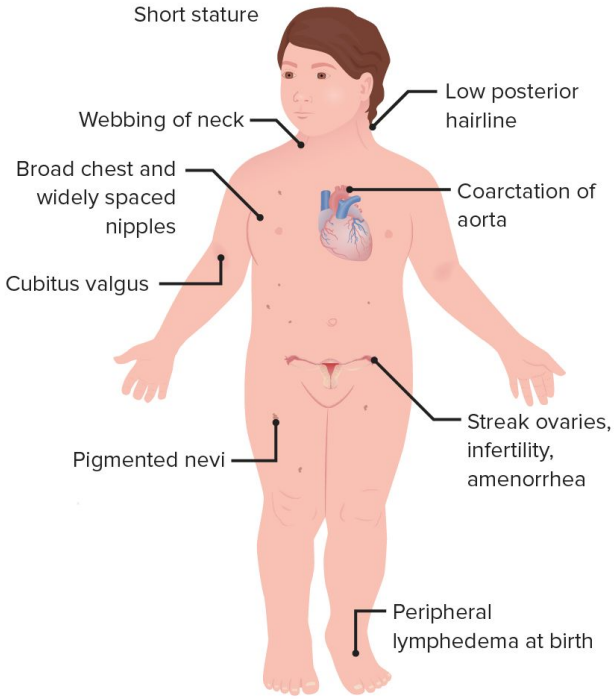
Turner's Syndrome: 45,X

- Clinical Features
  - No growth spurt → shorty
  - Infertility: ova degenerate in gestation
  - Less development of SSCs
  - Amenorrhea
  - Webbed neck
  - Widely spaced nipples
  - Congenital heart defects→ risk of CVD
  - Normal intellect
- Diagnosed by Karyotype
- No cure: HRT only
- Prognosis: slightly reduced life expectancy



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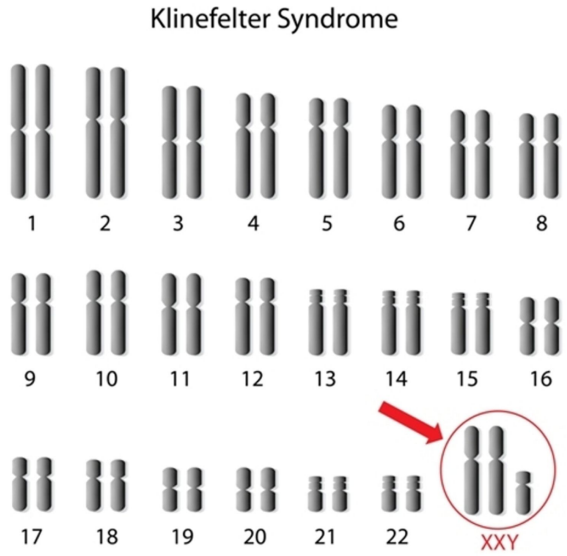
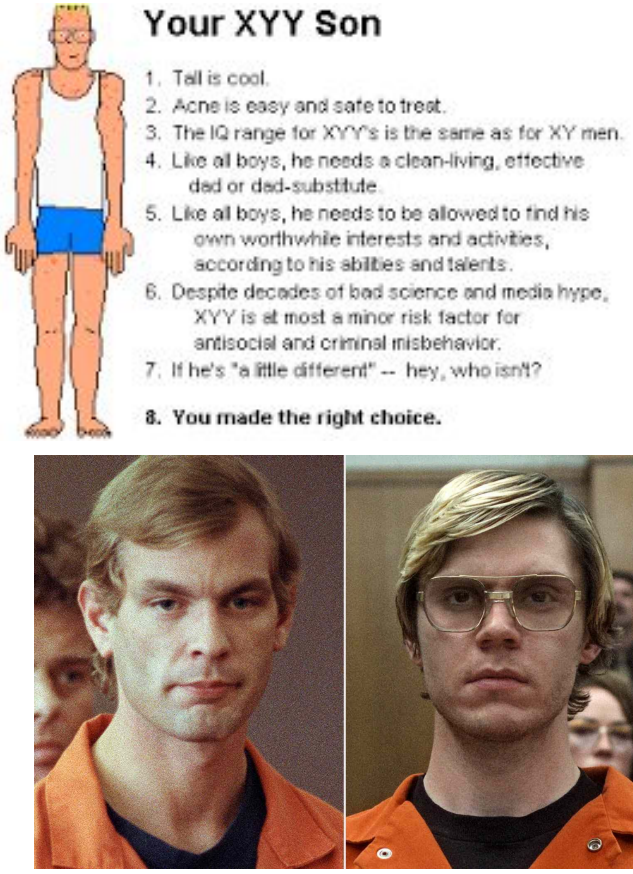
Klinefelter Syndrome: 47, XXY

- Clinical Features
  - Small testes
  - Less development of SSCs
  - Very tall
  - May appear normal
- Diagnosed when presenting with infertility

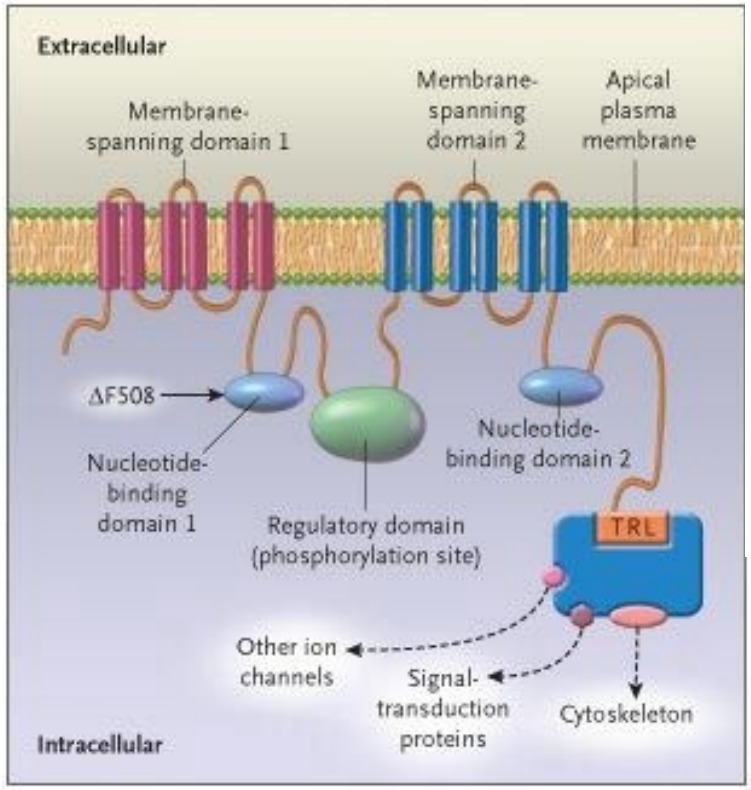


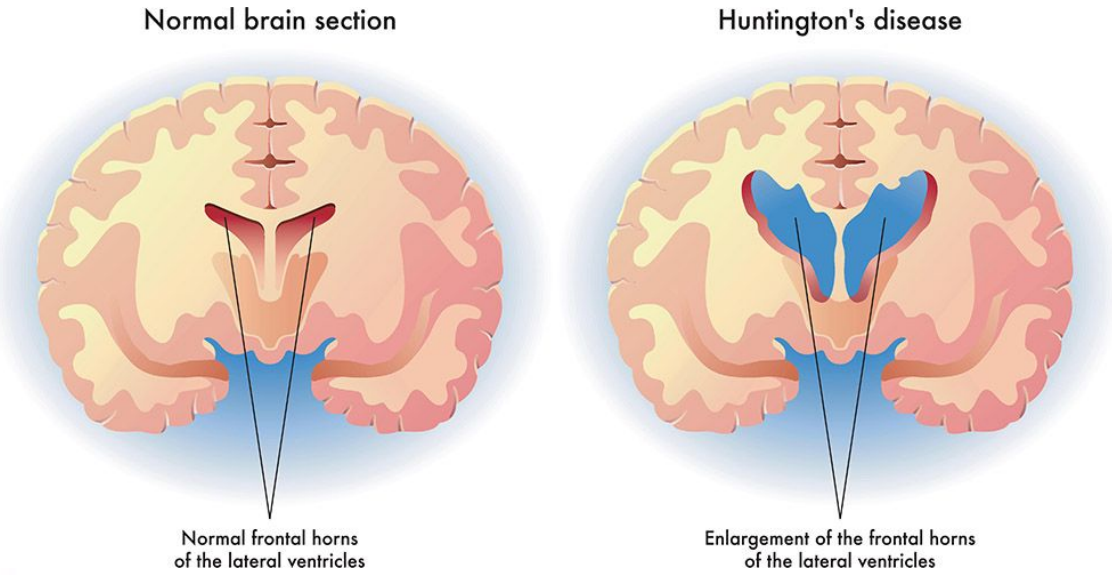
Super Male Syndrome: 47, XYY

- No abnormalities
- May be very tall
- NOT associated with violence (or serial killing!)



Single Nucleotide Polymorphisms (SNPs)





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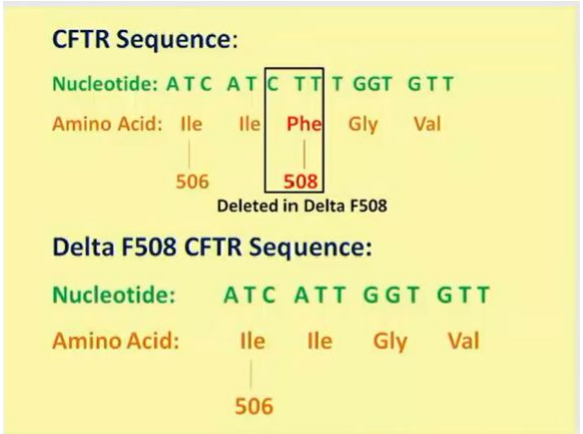
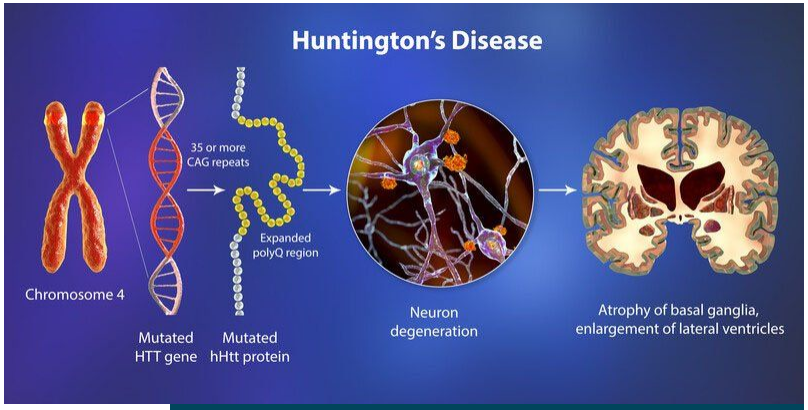
Cystic Fibrosis: autosomal recessive

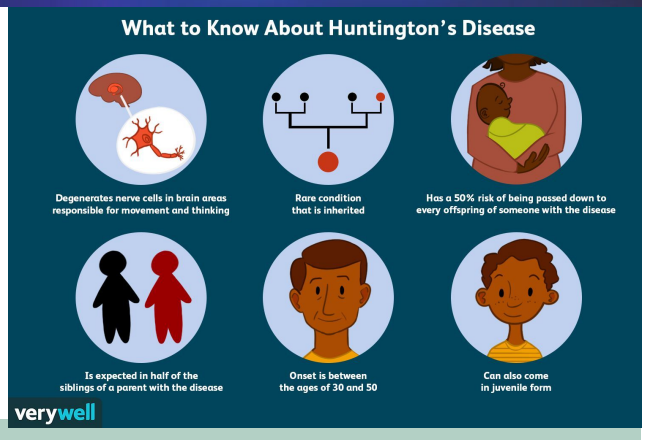
- Gene: cystic fibrosis transmembrane conductance regulator (CFTR)
- ΔF508: deletion of 3 nucleotides
  - No phenylalanine at 508th position
- Pathophysiology:
  - Cl- ion channel protein misfolded and trapped in ER
  - Not active when at membrane
- Clinical Features
  - Abnormal levels of thickened mucus in lungs, GI tract
  - Breathing problems, respiratory infections
  - Badly damaged mucosal epithelium
  - Bowel obstruction for first few days of life
- Long term consequences
  - Osteoporosis
  - Malnutrition
  - Diabetes
  - Liver problems
  - Reproductive problems
  - Arthritis



Huntington's Disease: autosomal dominant

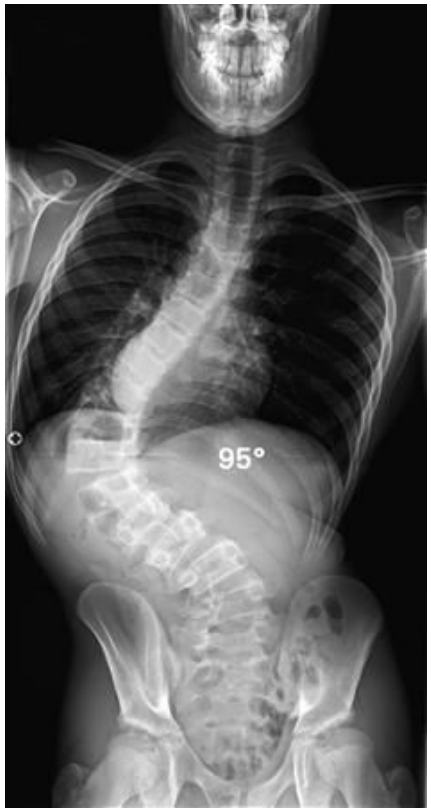
- Mutation: expansion of short tandem repeat CAG on HTT gene
  - 6-35 repeats = unaffected
  - 36-39 = incomplete penetrance
  - >40 = adult onset HD within normal lifespan
  - >60 = juvenile onset HD
- Clinical features: progressive degenerative (accumulation)
  - Personality changes
  - Motor and cognitive impairment
  - Chorea
  - Dystonia
  - Tremor
  - Depression
  - Irritability
- No effective therapy





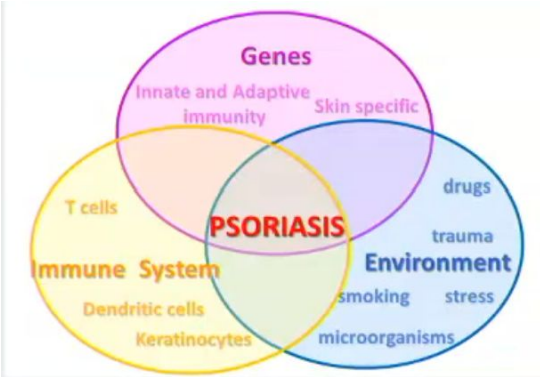
Friedreich's Ataxia: MT genetic disorder

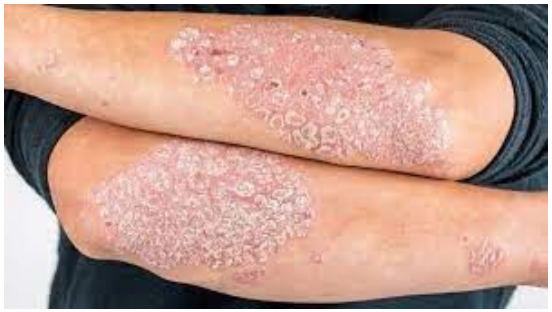
- Mutation: trinucleotide GAA repeat in intron 1 of FXN (tandem repeat polymorphism)
  - FXN binds iron so required for mitochondrial function
  - Expression of frataxin diminished
  - Encoded in nuclear genome
- Key Symptoms
  - Gait abnormalities
  - Frequent falls
  - Cerebellar signs
  - Mixed upper and lower motor neuron signs
  - High-arched palate
  - Pes cavus
  - Kyphoscoliosis



Psoriasis: multifactorial disease

- Red, inflamed scaly plaques due to excessive keratinocyte proliferation and immune cell activation
- Comorbidities
  - Psoriatic arthritis
  - Obesity
  - CVD
  - IBD
  - Depression
- Interaction of genetic susceptibility, environmental triggers, abnormal immune activation
- Therapies: range of topical to immunomodulatory drugs





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Questions?

SBA 1

A 55 y.o man is diagnosed with Huntington's. Which of the following is characteristic of the disease?

1. Over 35 repeats of CAG codon
2. Rapid cognitive decline
3. Less than 28 repeats of CAG codon
4. Double vision
5. Slow accumulation of HD aggregates

SBA 1

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3. Less than 28 repeats of CAG codon
4. Double vision
5. **Slow accumulation of HD aggregates**

SBA 2

Which of the following is not a complication of Down Syndrome?

1. Retarded growth and development
2. Single crease on palm of hand
3. Increased incidence of acute lymphoma
4. Mental retardation
5. VSD

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SBA 2

Which of the following is not a complication of Down Syndrome?

1. Retarded growth and development
2. Single crease on palm of hand
3. **Increased incidence of acute lymphoma**
4. Mental retardation
5. VSD

SBA 3

Which of the following is not true about cystic fibrosis?

1. It is recessive
2. Causes accumulation of mucus
3. Limits ability to breathe
4. Caused by an addition in F508
5. Causes bowel obstruction

SBA 3

Which of the following is not true about cystic fibrosis?

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3. Limits ability to breathe
4. **Caused by an addition in F508**
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SBA 4

What is the mutation involved in Friedreich's ataxia?

1. GCC repeats in intron 1 of FXN
2. GAA repeats in intron 1 of FXN
3. GCC repeats in exon 1 of FXN
4. GAA repeats in exon 1 of FXN
5. GAA deletion in intron 1 of FXN

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SBA 4

What is the mutation involved in Friedreich's ataxia?

1. GCC repeats in intron 1 of FXN
2. **GAA repeats in intron 1 of FXN**
3. GCC repeats in exon 1 of FXN
4. GAA repeats in exon 1 of FXN
5. GAA deletion in intron 1 of FXN

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SBA 5

A 15 year old girl presents to the GP for short stature. She is currently on the 2nd centile for height. She has not had her first period. She has a low posterior hairline and a shield-shaped chest. She is on the 50th centile for weight.

What is the most likely diagnosis?

1. Friedreich's Ataxia
2. Huntington's Disease
3. Cystic Fibrosis
4. Turner's Syndrome
5. Klinefelter's Syndrome

SBA 5

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What is the most likely diagnosis?

1. Friedreich's Ataxia
2. Huntington's Disease
3. Cystic Fibrosis
4. **Turner's Syndrome**
5. Klinefelter's Syndrome

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SBA 6

Which of the following is not a multifactorial disease?

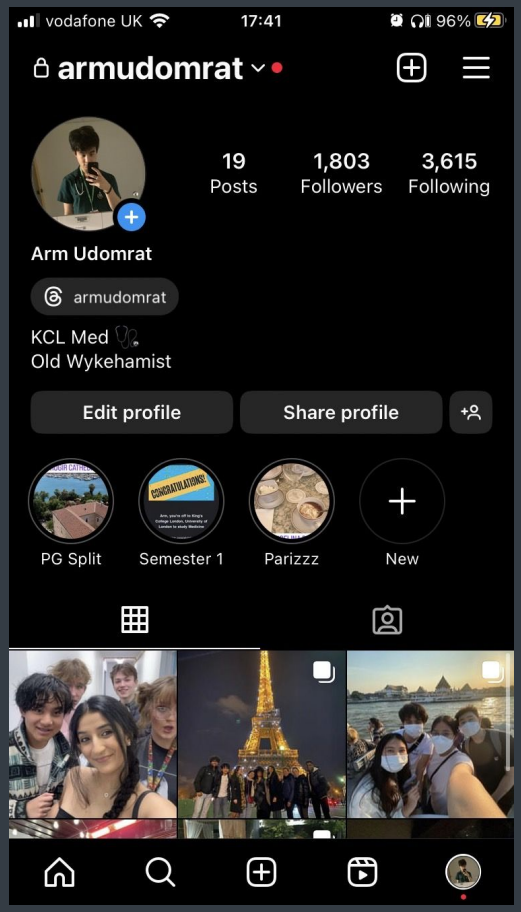
1. IBD
2. Diabetes
3. Psoriasis
4. Obesity
5. Huntington's disease

SBA 6

Which of the following is not a multifactorial disease?

1. IBD
2. Diabetes
3. Psoriasis
4. Obesity
5. **Huntington's disease**

Questions?



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Thank you for attending the session -

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