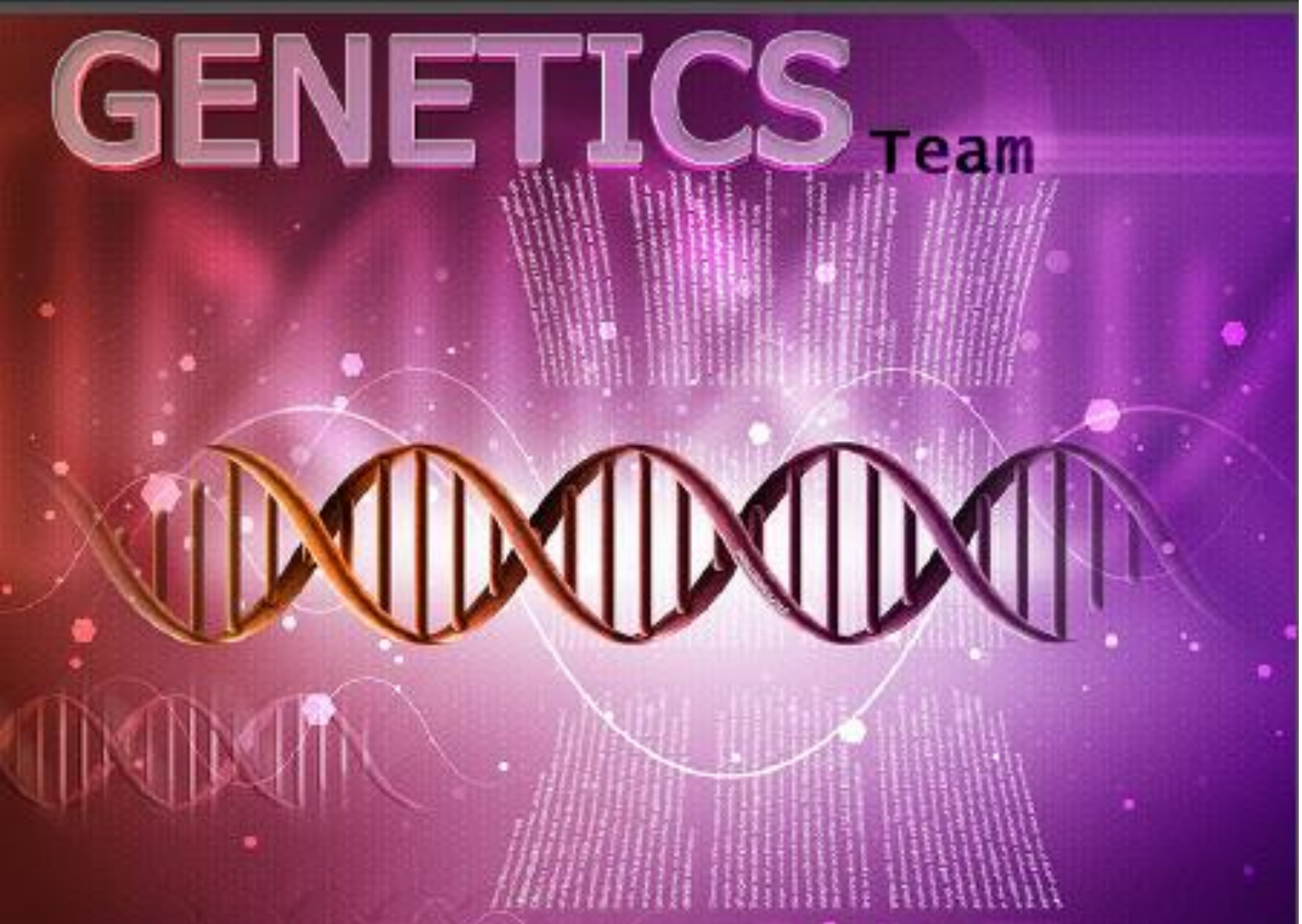
GENETICS Team



Klinefelter, Turner & Down syndrome

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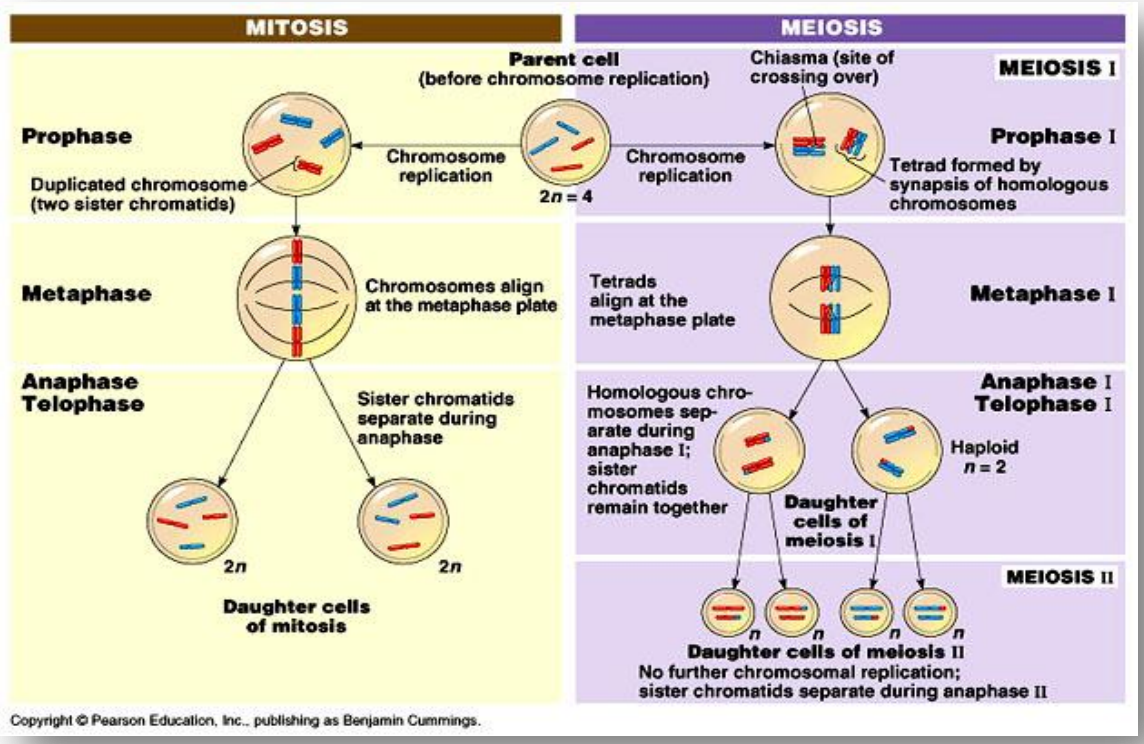
Mitosis

A process of asexual reproduction in which the cell divides in two producing a replica, with an equal number of chromosomes in each resulting **diploid cell**

Meiosis

The process of cell division in sexually reproducing organisms that reduces the number of chromosomes in reproductive cells **from diploid to haploid**, leading to the production of Gametes.



Non-disjunction in Meiosis:

Nondisjunction (Not coming apart) is the failure of chromosome pairs to separate properly during meiosis stage 1 or stage 2.

As a result, one daughter cell has two chromosomes or two chromatids, and the other has none.

The result of this error is a cell with an imbalance of chromosomes **(Aneuploidy)**

Autosomal

Trisomy 21 (Down syndrome)

Sex chromosome

- 47XXY (Klinefelter syndrome)
- 45X (Turner syndrome)

Meiotic non-disjunction:

- Can affect each pair of chromosomes
- Is not a rare event
- Non disjunction in first meiotic division produces 4 unbalanced gametes.
- Non disjunction in second division produces 2 normal gametes & 2 unbalanced gametes

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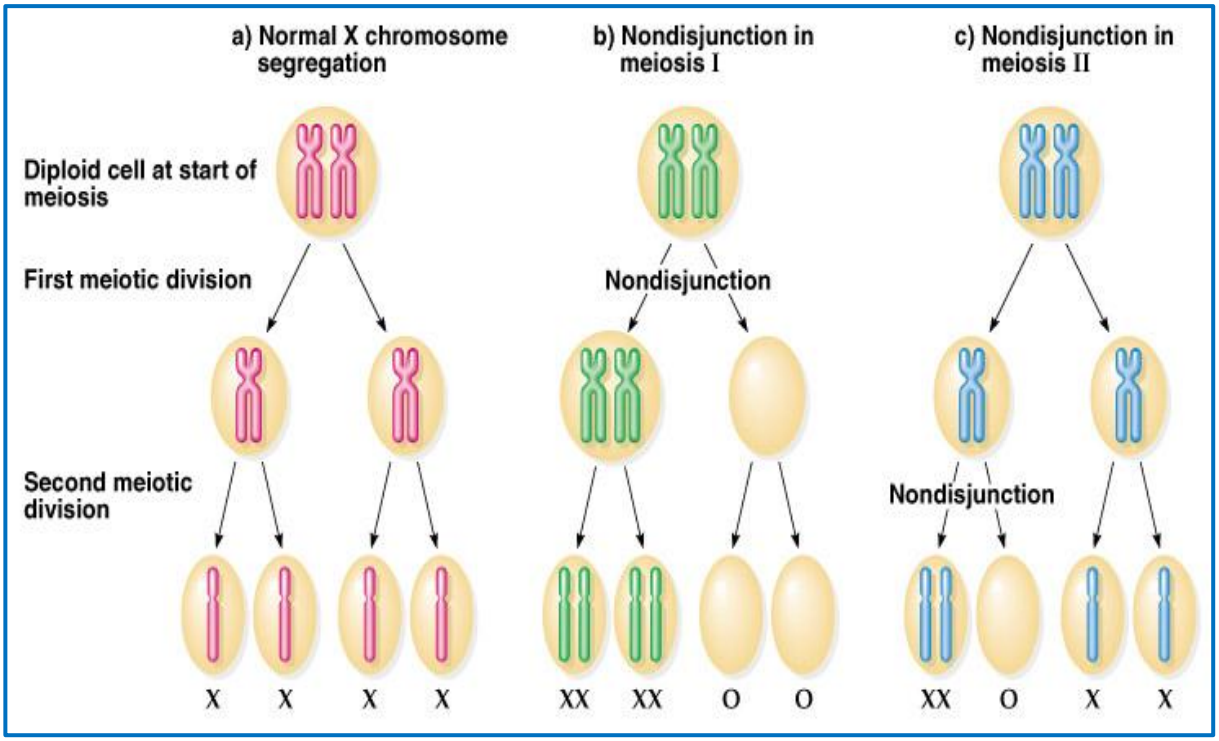
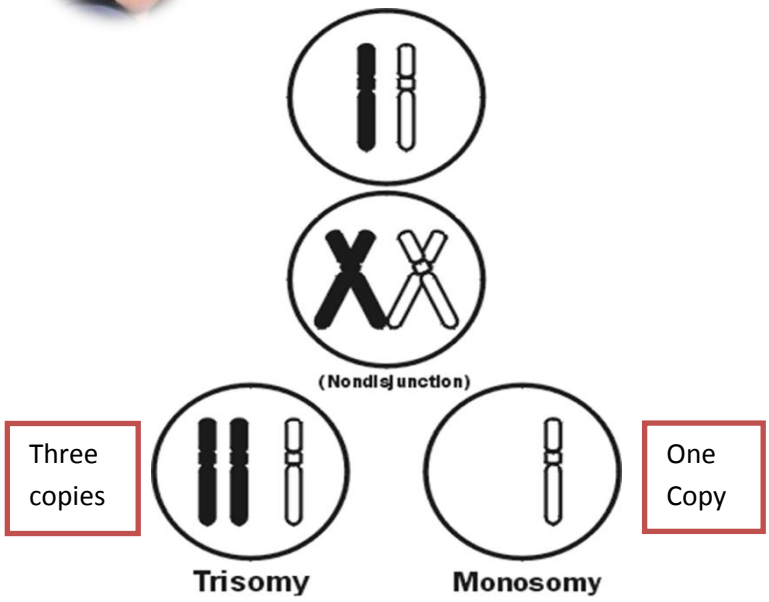
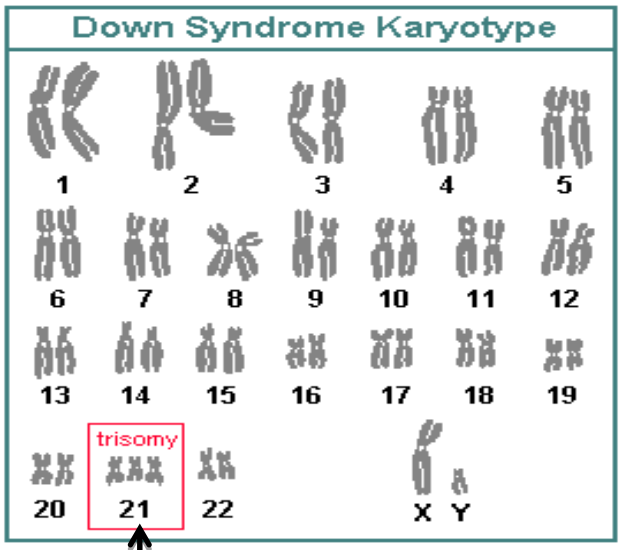
For your information

Polyploidy When a cell contains more than two sets of chromosomes, polyploidy occurs. So it alters the chromosome number in a cell. Polyploidy can be seen frequently in flowering plants including important crop plants but rarely in animals, except vertebrates and invertebrates. Several types of polyploidy occur through several processes. Autopolyploidy is one type that is formed by multiplication of the genome of same species. Autopolyploidy is produced in sexual reproduction during meiosis by the non disjunction of homologous chromosomes in metaphase I or abnormal cell division in mitosis. Allopolyploidy occurs due to the combination of genomes of different species such as in hybrid species. Polyploidy also can be induced using various chemicals such as colchicine by inhibiting cell division.



Down's syndrome "trisomy 21 Karyotype: 47, XY, +21"





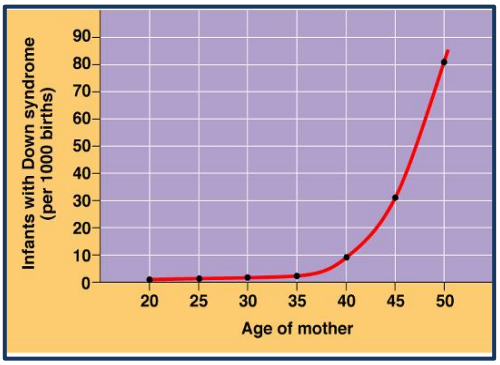
Three copies of chromosome 21

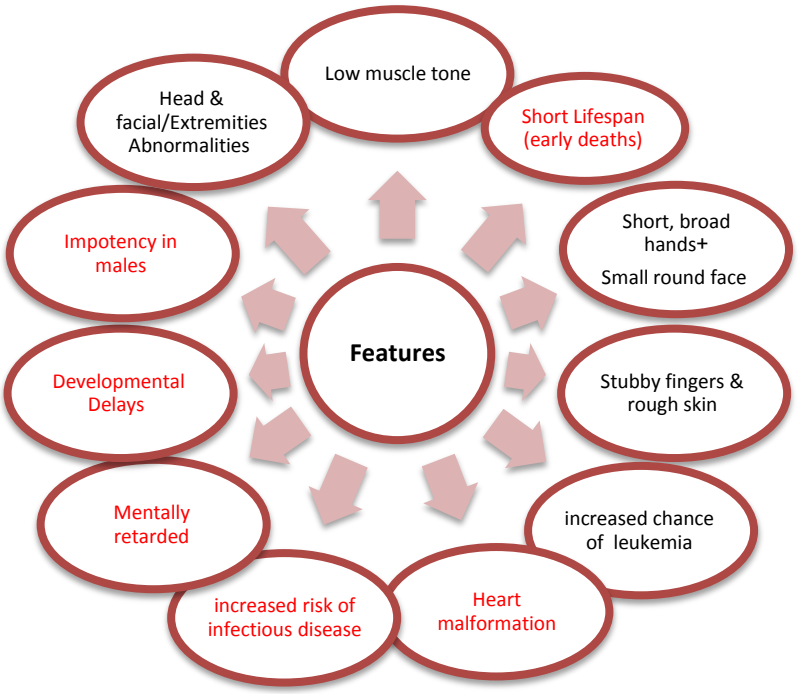
The incidence of trisomy 21 rises sharply with increasing maternal age.

Most cases arise from non disjunction in the first meiotic division

The father contributing the extra chromosome in 15% of cases (i.e. Down syndrome can also be the result of nondisjunction of the **father's** chromosome 21)

A small proportion of cases are mosaic and these probably arise from a non disjunction event in an early zygotic division

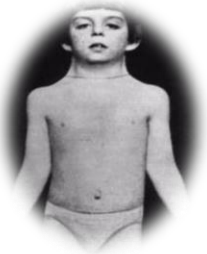




Mosaic Down syndrome

In this rare form of Down syndrome, children have some cells with an extra copy of chromosome 21. This mosaic of normal and abnormal cells is caused by abnormal cell division after fertilization.

IQ level = 40-50 (They survive in school but have low IQ levels)



Turner's Syndrome" Monosomy X: 45, XO"

- Monosomy of sex chromosome(only one X chromosome present)
- Occurrence – 1 in 2500 live Phenotypic female births (Incidence is considered high)
- Approximately 60,000 girls and women are affected in the United States with around 800 new cases diagnosed every year.
- The only viable monosomy in humans (The only human example of monosomy that survive)
- **Characteristics:** Webbed neck, Individuals are genetically female, not mature sexually, Broad chest, Low hairline, Streak ovaries, Normal intelligence, Normal life span

Features of Turner's syndrome:

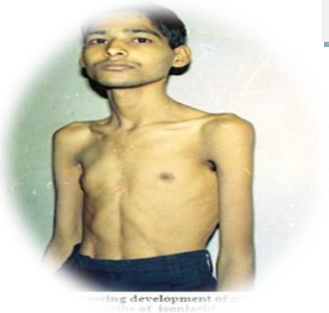
Cardiovascular	Skeletal	Reproductive	
Increased risk of Cardiovascular constriction	Short fourth metacarpal/matatarsal bone may be short (+/- short 3rd and 5th).	Lack of ovarian development	Short stature
Bicuspid aortic valve	Osteoporosis (due to lack of estrogen)	Women with Turner syndrome are almost universally **infertile**.	Neck abnormalities
Coarctation of the aorta	Scoliosis		Diabetes
Thoracic aortic aneurysm (aortic root dilatation)			Kidney and thyroid problems

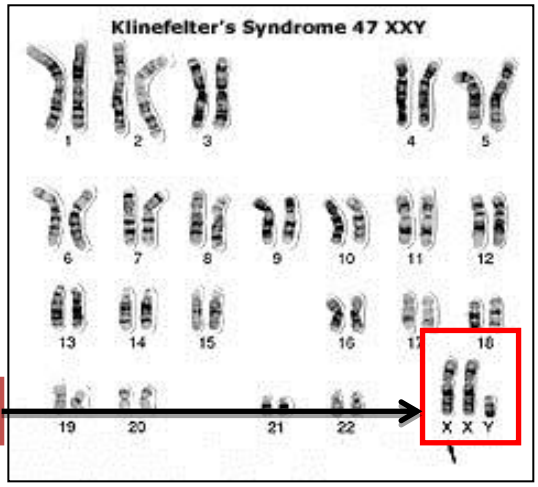
- It is also important to note that unlike Trisomy 13, Trisomy 18, and Down syndrome, developmental delays are not associated with Turner Syndrome
- There is no association between developmental delays and any sex chromosomal abnormality. This indicates that genes affecting mental development and ability lie only on autosomal chromosomes. Early death is also not associated with any of the sex linked chromosomal abnormalities

Treatment:

growth hormones, and estrogen replacement therapy. Additionally, reproductive technology can help women with Turner syndrome become pregnant.

Klinefelter's Syndrome "Trisomy 47,XXY males"





#23 Trisomy Nondisjunction

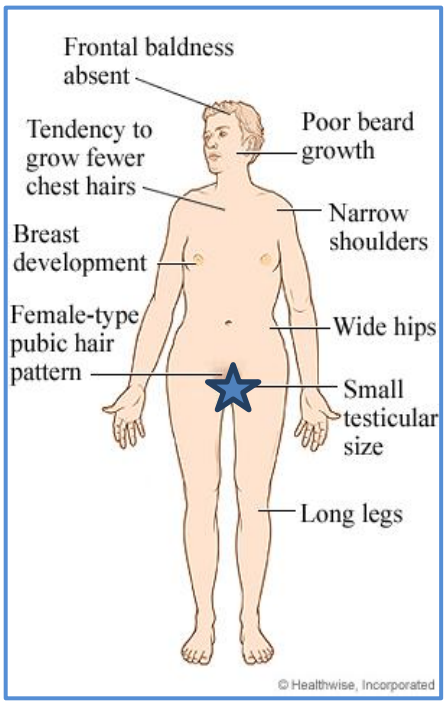
Incidence: 1:1000 male births (very high)

47 chromosomes XXY only

Male sex organs: unusually small testes which fail to produce normal levels of testosterone→ breast enlargement (gynaecomastia)and other feminine body characteristics

No spermatogenesis → sterile

Very rarely more extreme forms of Klinefelter syndrome occur where the patient has 48, XXXY or even 49, XXXXY karyotype. These individuals are generally severely retarded.



Features of Klinefelter's Syndrome:

Scarce beard	No facial and body hair
Longer fingers and arms	Sterile(infertility)
Tall	sexually underdeveloped
Delicate skin	Slight reduction in IQ levels
Low mental ability	Developmental Delays
Normal lifespan	Brown spots (nevi)
↑risk of autoimmune disorders	↑ risk of breast cancer
Osteoporosis	leg ulcers
dental problems	depression

In some cases testicular function is preserved, delay in speech and motor skills as well as deficits in attention.

Treatment

Testosterone therapy and assisted learning

Down syndrome typically is recognized at birth, Turner syndrome often is not recognized until adolescence, and many men with Kleinefelter syndrome are never diagnosed

Sex chromosome unbalance

(much less harmful)

47, XYY	**XXX females**
May be without any symptoms. Males are tall but normally proportioned. 10 - 15 points reduction in IQ compared to others	It seems to do little harm, individuals are fertile and do not transmit the extra chromosome. They do have a reduction in IQ comparable to that of Kleinfelter's males

When to do a Chromosome test?

Prenatal

Maternal age>37yrs; USS changes; Family history

Triple test = increased risk

Postnatal

Learning & developmental disability; growth retardation

Infertility

Recurrent miscarriage, primary infertility

How Do we know there is chromosome abnormality?

Rapid Aneuploidy Screening by FISH (Fluorescence InSitu Hybridization)	New techniques	
	qf (quantitative) PCR	Fetal DNA
(FISH) is a test that "maps" the genetic material in a person's cells. This test can be used to visualize specific genes or portions of genes	Able to measure number of copies of a chromosome – used for trisomy & monosomy screening	At 6-8 weeks to determine sex – look for presence of Y chromosome material
Available on amniocentesis sample		
Uncultured amniocytes		
FISH probes for X,Y, 21		
Result in 24-48 hours		
Proceed onto full karyotype (11-14 days)		

Summary

Down syndrome	Turner's Syndrome	Klinefelter's Syndrome
1) trisomy 21 2) Karyotype: 47, XY, +21 3) Most cases arise from non disjunction in the first meiotic division 4) Features : ➢ Mentally retarded ➢ Short lifespan ➢ Impotency in males	1) Monosomy of sex chromosome (only one X chromosome present) 2) genetically female 3) The only viable monosomy in humans 4) Features: ➢ Webbed neck ➢ Normal intelligence ➢ Normal life span ➢ Increased risk of osteoporosis, cardiovascular constriction ➢ Women are almost universally infertile 5) treatment: growth hormones, and estrogen replacement therapy. Additionally, reproductive technology can help women with Turner syndrome become pregnant	1) 23 Trisomy Nondisjunction 2) 47,XXY 3) No spermatogenesis → sterile 4) Features: ➢ Gynaecomastia ➢ Normal lifespan ➢ Tall 5) testosterone therapy and assisted learning

Questions

1) **Which one of the following is not a feature of Turner Syndrome?**
   A- Sterile
   B- Short stature
   C- Broad chest
   D- ab*normal life span*

2) **which one of the following syndromes is Monosomy?**
   A- Down syndrome
   B- Turner's Syndrome
   C- Klinefelter's Syndrome

1	2
D	B