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department of genetics

((Down syndrome))

Name:-samer mutlag

Group:-8th

Course:-5th

DOWN SYNDROME

- Down's syndrome (DS) also known as trisomy 21:- is a genetic disorder caused by the presence of all or part of a third copy of chromosome 21.

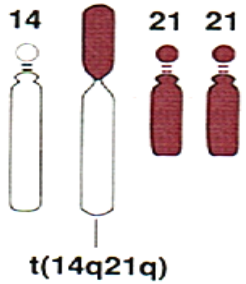
- It is typically associated with physical growth delays, characteristic facial features and mild to moderate intellectual disability

DOWN SYNDROME

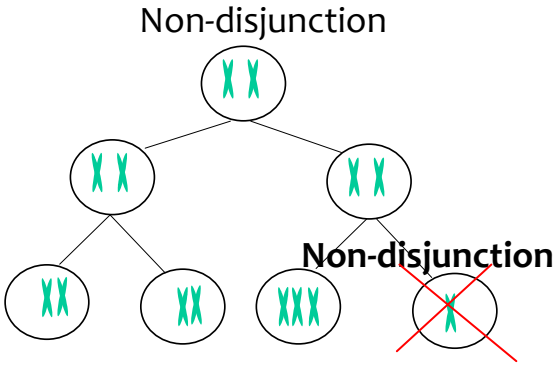
- in 700 live births
- >60% spontaneously aborted
- 20% stillborn
- Facial appearance permits diagnosis
- Marked muscle hypotonia as baby
- Single palmar crease may be present
- Learning difficulty (IQ usually <50)
- Congenital heart malformations (40%)
- Many other associated features

THREE DIFFERENT PATTERNS OF CHROMOSOMES CAN CAUSE DOWN SYNDROME

95% people have three separate copies of chromosome 21 - **trisomy 21**

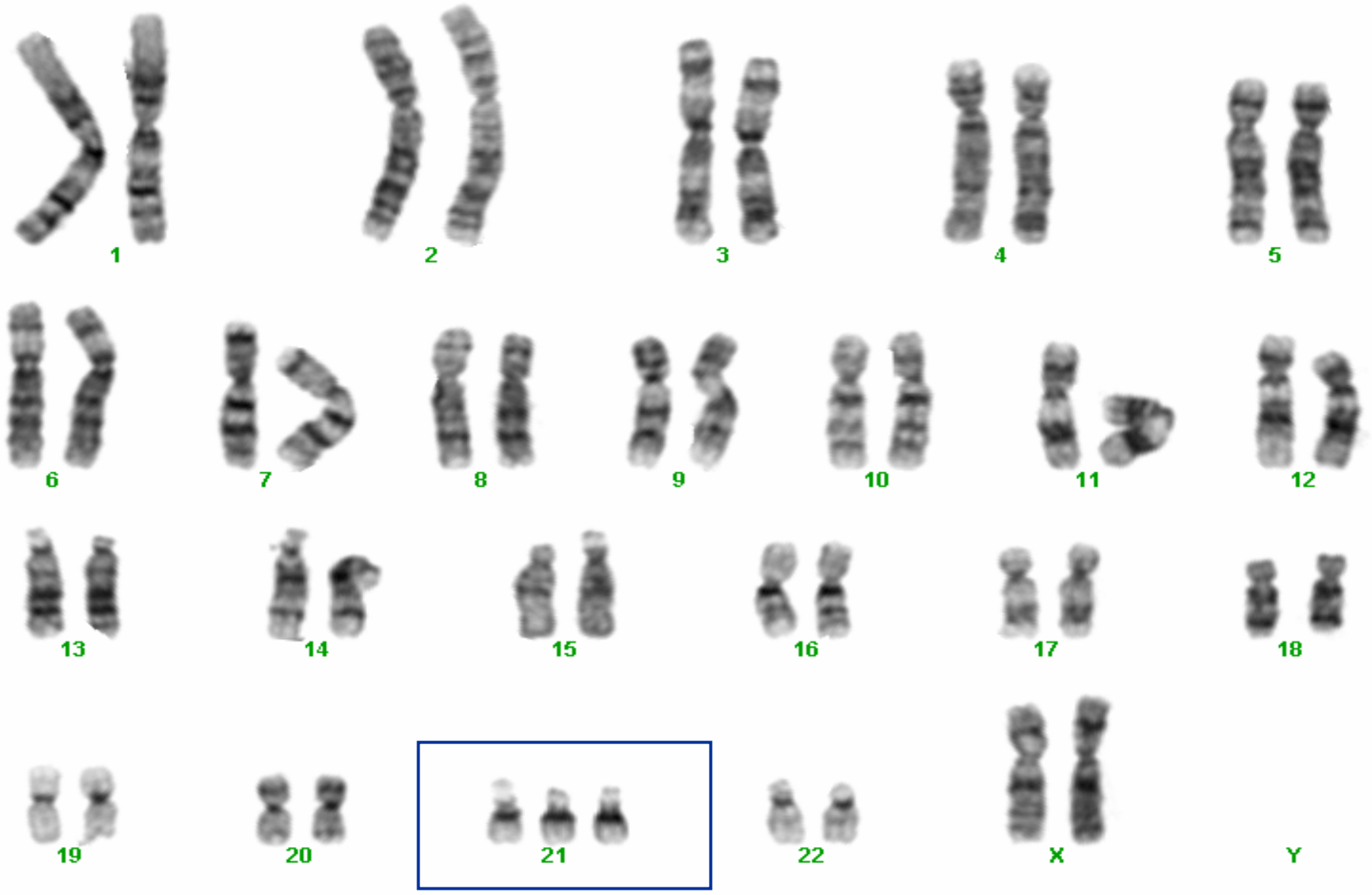


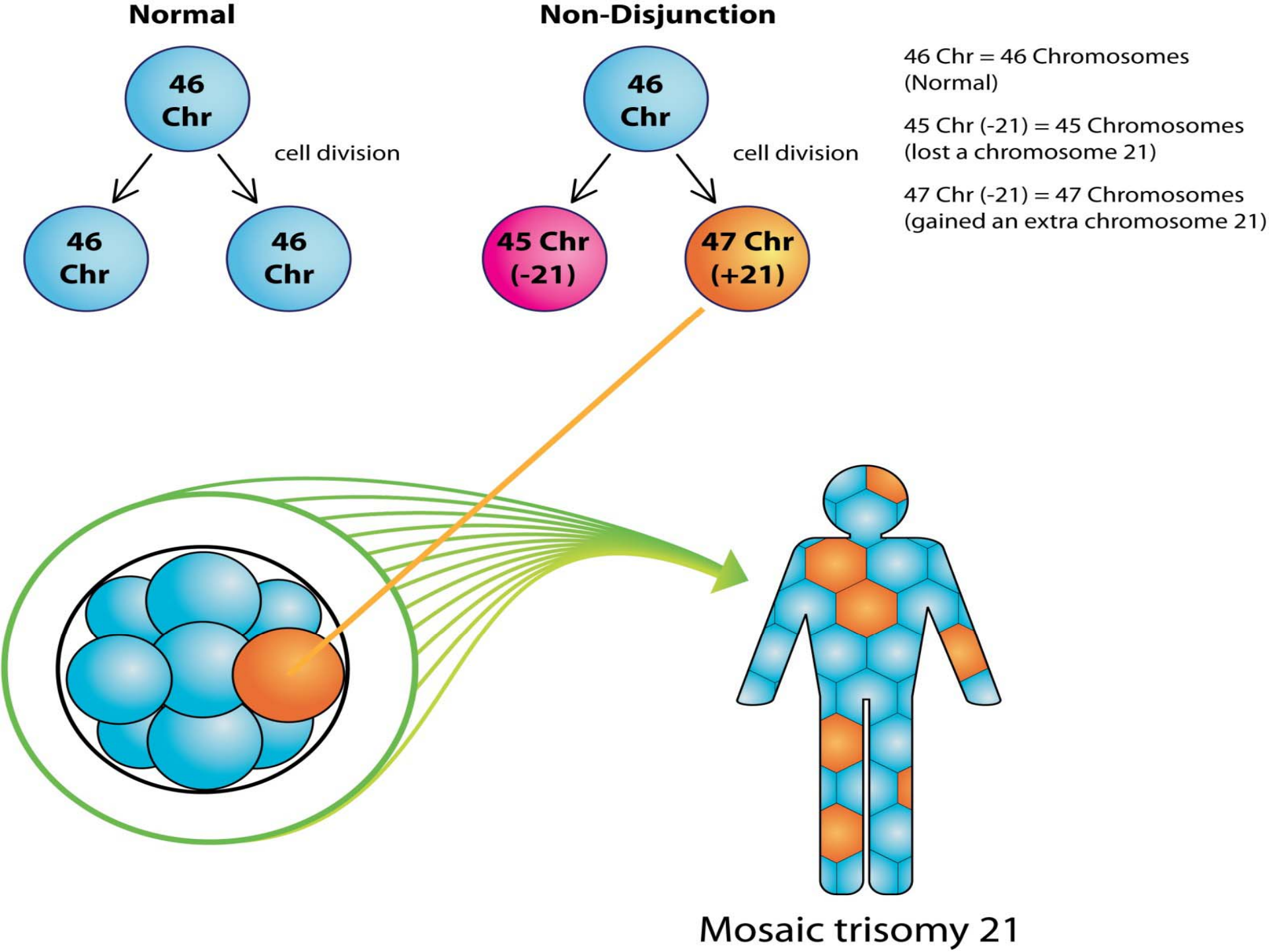
4% have the extra copy of chromosome 21 because of a **Robertsonian translocation**



1% have **mosaicism** with normal and trisomy 21 cell lines (and usually have much milder features because of the presence of the normal cells); - occurs postzygotically

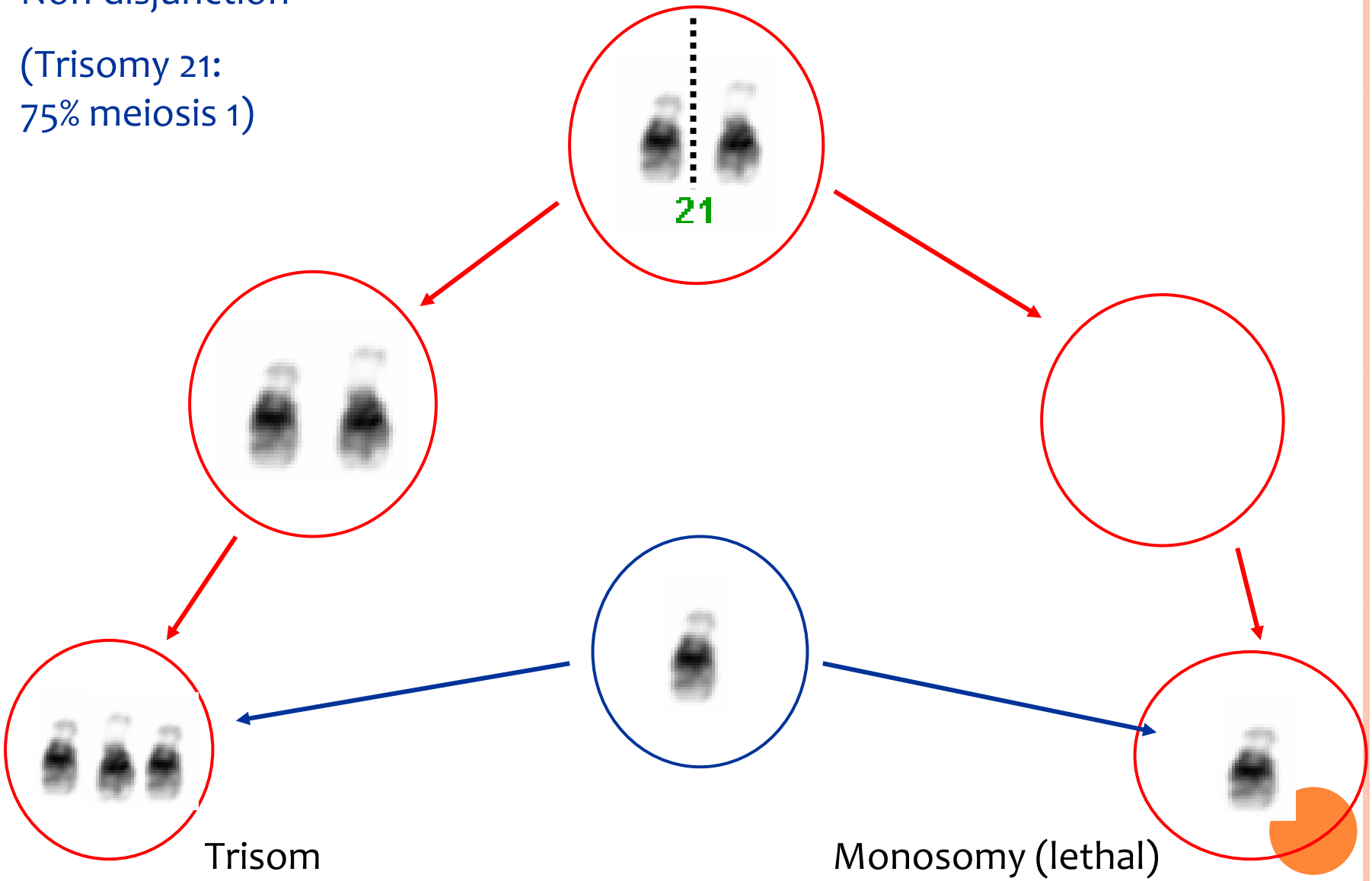
TRISOMY 21: 47,XX,+21



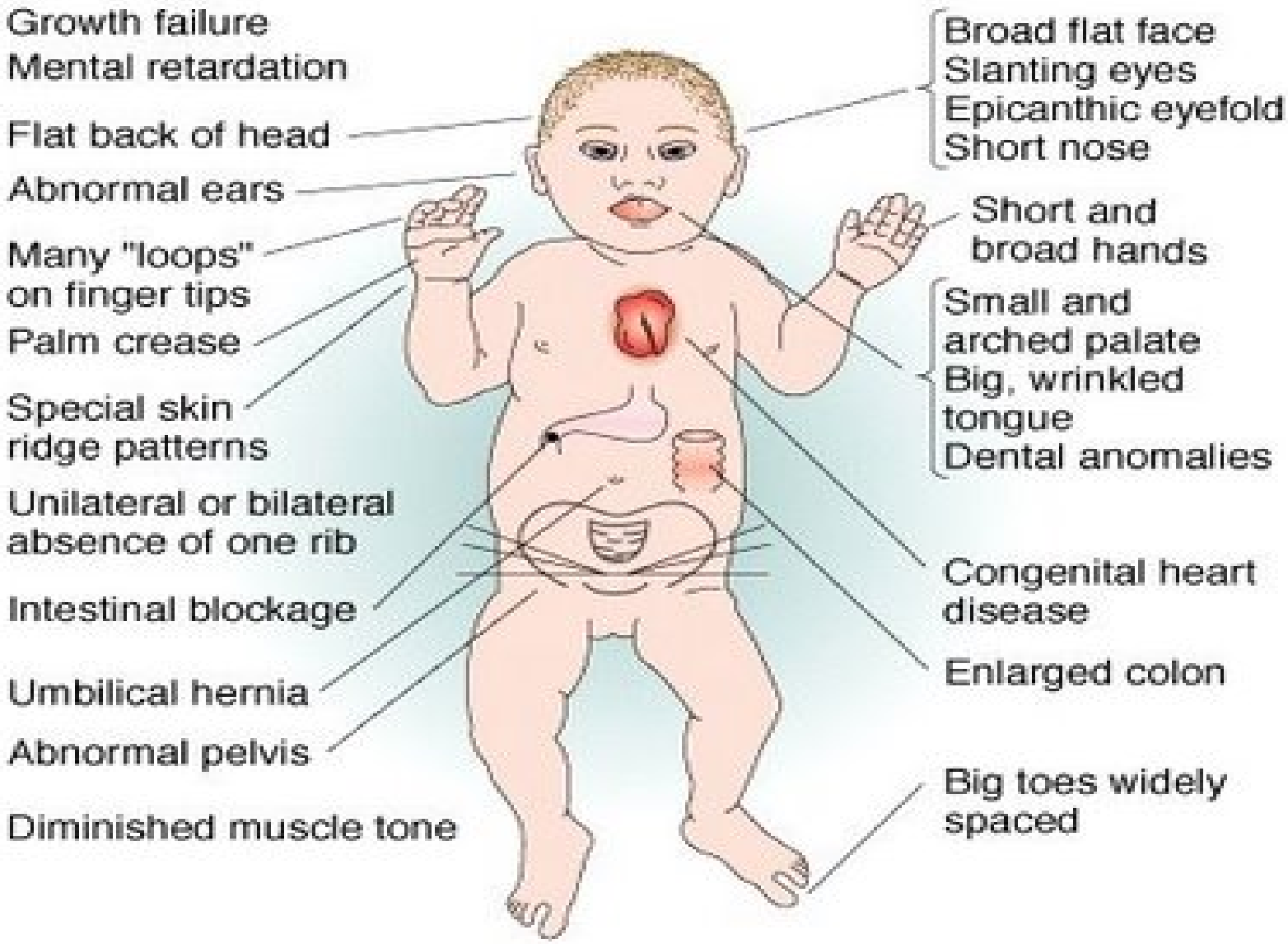

Normal
46 Chr
cell division
46 Chr
46 Chr
Non-Disjunction
46 Chr
cell division
45 Chr (-21)
47 Chr (+21)
46 Chr = 46 Chromosomes (Normal)
45 Chr (-21) = 45 Chromosomes (lost a chromosome 21)
47 Chr (-21) = 47 Chromosomes (gained an extra chromosome 21)
Mosaic trisomy 21

Meiotic
Non-disjunction

(Trisomy 21:
75% meiosis 1)



SIGNS AND SYMPTOMS



Characteristics	Percentage	Characteristics	Percentage
Mental impairment	99%[15]	Abnormal teeth	60%[16]
Stunted growth	90%[17]	Slanted eyes	60%[14]
Umbilical hernia	90%[18]	Shortened hands	60%[16]
Increased skin back of neck	80%[11]	Short neck	60%[16]
Low muscle tone	80%[19]	Obstructive sleep apnea	60%[11]
Narrow roof of mouth	76%[16]	Bent fifth finger tip	57%[14]
Flat head	75%[14]	Brushfield spots in the iris	56%[14]
Flexible ligaments	75%[14]	Single transverse palmar crease	53%[14]
Large tongue	75%[19]	Protruding tongue	47%[16]
Abnormal outer ears	70%[11]	Congenital heart disease	40%[16]
Flattened nose	68%[14]	Strabismus	~35%[2]
Separation of 1st and 2nd toes	68%[16]	Undescended testicles	20%[20]

PHYSICAL

- *People with Down syndrome may have some or all of the following physical characteristics((small chin, slanted eyes, poor muscle tone, a flat nasal bridge, a single crease of the palm, and a protruding tongue due to a small mouth and large tongue))*

- *These airway changes lead to obstructive sleep apnea in around half of those with Down syndrome*

- *Other common features include: a flat and wide face, a short neck, excessive joint flexibility, extra space between big toe and second toe, abnormal patterns on the fingertips and short fingers.*

- *Hip dislocations may occur without trauma in up to a third of people with Down syndrome.*

NEUROLOGICAL

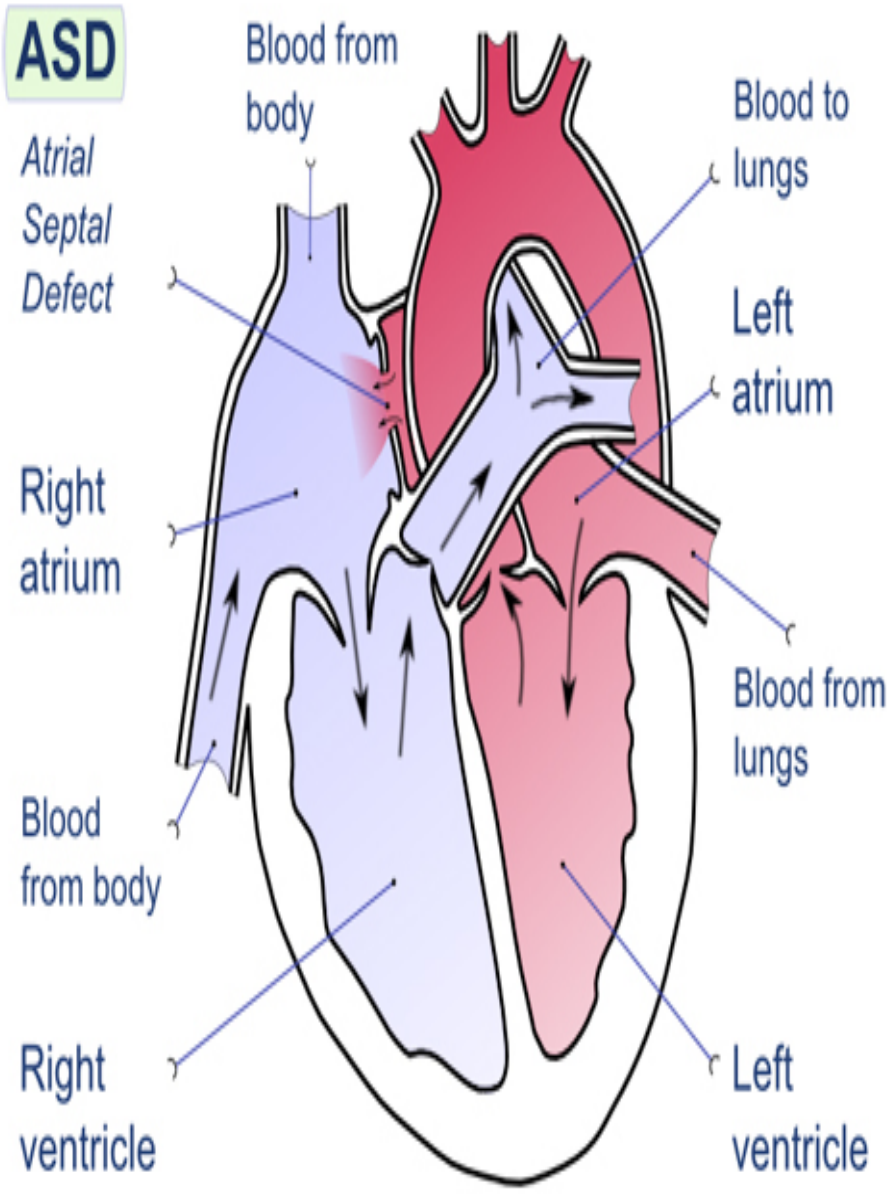
A. Most individuals with Down syndrome have mild (IQ: 50–70) or moderate (IQ: 35–50) intellectual disability with some cases having severe (IQ: 20–35):-
B. Some patinets with DS after 30 years of age may lose their ability to speak
C. Behavior problems are not generally as great an issue as in other syndromes associated with intellectual disability
D. In children with DS mental illness occurs in nearly 30% with autism occurring in 5–10%
E. Children and adults with Down syndrome are at increased risk of epileptic seizures which occur in 5–10% of children and up to 50% of adults. This includes an increased risk of a specific type of seizure called((infantile spasms))
F. Many (15%) who live 40 years or longer develop dementia of the((Alzheimer's type))

SENSES

- Hearing and vision disorders occur in more than half of people with DS..
- Vision problems occur in 38 to 80% .Between 20 and 50% have **strabismus**, in which the two eyes do not move together
- Cataracts (cloudiness of the len of the eye) occur in 15%...
- Keratoconus (a thin, cone-shaped corneas),and glaucoma (increased eye pressure)...
- Brushfield spots (small white or grayish/brown spots on the outer part of the iris) are present in 38 to 85%
- Hearing problems are found in 50–90% of children
- This is often the result of otitis media with effusion which occurs in 50–70%

HEART

- The rate of congenital heart disease in newborns with DS is around 40%.
- those with heart disease about 80% have an (*atrioventricular septal defect* or *ventricular septal defect).* Mitral valve problems
- Other problems that may occur include: tetralogy of Fallot and patent ductus arteriosus
- People with Down syndrome have a lower risk of ((hardening of the arteries)).



GASTROINTESTINAL

- Constipation occurs in nearly half of people with DS, and may result in changes in behavior
- One potential cause is Hirschsprung's disease, which is due to a lack of nerve cells controlling the colon, which occurs in 2 to 15%
- Other frequent congenital problems include: duodenal atresia, pyloric stenosis, Meckel diverticulum and imperforate anus . Celiac disease affects about 7–20% and gastroesophageal reflux disease is also more common

FERTILITY

- Males with DS usually don't have father children
- while females have lower rates of fertility relative those who are unaffected. Fertility is estimated to be present in 30–50% of women

- Menopause typically occurs at an earlier age

- The poor fertility in men is thought to be due to problems with sperm development. however, it may also be related to not being sexually active

#As of 2006 there have been three recorded instances of males with Down syndrome fathering children and 26 cases of women having children!!!

SCREENING

- Guidelines recommend that screening for Down syndrome be offered to all pregnant women, regardless of age
- A number of tests can be used, with varying levels of accuracy. They are usually used in combination to increase the detection rate, while maintaining a low false positive rate
- None can be definitive, thus if screening is positive either amniocentesis or chorionic villous sampling is required to confirm the diagnosis
- Screening in both the first and second trimesters is better than just screening in the first trimester . The different screening techniques in use are able to pick up 90 to 95% of cases with a false positive rate of between 2 and 5%

FIRST AND SECOND TRIMESTER SCREENING

Screen	Week of pregnancy when performed	Detection rate	False positive	Description
Combined test	10–13.5 wks	82–87%	5%	Uses ultrasound to measure nuchal translucency in addition to blood tests for free or total beta-hCG and PAPP-A.
Quad screen	15–20 wks	81%	5%	Measures the maternal serum alpha-fetoprotein, unconjugated estriol, hCG, and inhibin-A.
Integrated test	15–20 wks	94–96%%	5%	Is a combination of the quad screen, PAPP-A, and NT
Cell-free fetal DNA	From 10 wks[60]	96-100%[61]	0.3%[62]	A blood sample is taken from the mother by venipuncture and is sent for DNA analysis.

ULTRASOUND

- Ultrasound imaging can be used to screen for Down syndrome. Findings that indicate increased risk when seen at 14 to 24 weeks of gestation include
- a small or no nasal bone, large ventricles, nuchal fold thickness, and an abnormal right subclavian artery, among others
- Increased fetal nuchal translucency (NT) help identify higher chances for chromosomal conditions including Down syndrome in a fetus, indicates an increased risk of Down syndrome picking up 75–80% of cases and being falsely positive in 6%

BLOOD TESTS

- Several blood markers can be measured to predict the risk of DS during the first or second trimester:-

A. In the second trimester often two or three tests are used in combination with two or three of: ((α-fetoprotein, unconjugated estriol,total hCG,and free βhCG)) detecting about 60–70% of cases..

B. Testing of the mother's blood for fetal DNA is being studied and appears promising in the first trimester

C. Accuracy has been reported at 98.6% in the first trimester of pregnancy..

D. Confirmatory testing by invasive techniques (amniocentesis, CVS) is still required to confirm the screening result.

MANAGEMENT

1) Efforts such as early childhood intervention, screening for common problems, medical treatment where indicated..

2) a good family environment, and work related training can improve the development of children with DS.

3) Education and proper care can improve quality of life.

4) Typical childhood vaccinations are recommended.

HEALTH SCREENING

- A number of health organizations have issued recommendations for screening those with DS for particular diseases. It is recommended that this be done systematically.
- At birth all children should get an ECG and ultrasound of the heart
- Surgical repair of heart problems may be required as early as three months of age
- Heart valve problems may occur in young adults, and further ultrasound evaluation may be needed in adolescents and in early adulthood
- Due to the elevated risk of testicular cancer, some recommend checking the person's testicles yearly.

RECOMMENDED SCREENING

Testing	Children[71]	Adults[3]
Hearing	6 months, 12 months, then yearly	3–5 years
T4 and TSH	6 months, then yearly	
Eyes	6 months, then yearly	3–5 years
Teeth	2 years, then every 6 months.	
Coeliac disease	Between 2 and 3 years of age, or earlier if symptoms occur.	
Sleep study	3 to 4 years, or earlier if symptoms of obstructive sleep apnea occur.	
Neck X-rays	Between 3 and 5 years of age	

EPIDEMIOLOGY

- Globally, as of 2010, Down syndrome occurs in about 1 per 1000 births and results in about 17,000 deaths..
- It occurs more commonly in countries where abortion is not allowed and in countries where pregnancy more commonly occurs at a later age..
- About 1.4 per 1000 live birth in the United States[90] and 1.1 per 1000 live births in Norway are affected
- The number of pregnancies with DS is more than two times greater with many spontaneous abortion. It is the cause of 8% of all congenital disorders.
- Maternal age affects the chances having a pregnancy with DS

TREATING DOWN'S SYNDROME

- There is no "cure" for Down's syndrome, but there is much that can be done to help someone with the condition lead a healthy, active and more independent life,this includes:-

1) good parenting skills and an ordinary family life
2) education and support groups to provide information and help to parents, friends and families
3) early intervention programmes to provide support for children and parents
4) access to good healthcare, including a range of different specialists

THANKS FOR ATTENTION