

“Here are few corrections we have found in our book. Hope you find them useful.” – Amit Ashish

97. A patient with limited systemic sclerosis for the past 10 years complains of shortness of breath for the past one year. His pulmonary function tests are as follows – (AIIMS Nov 09)

PFT	OBSERVED	PREDICTED
FVC	2.63	2.82
FEV1	88%	80%
DLCO	5.2	16.3

Which among the following is the probable diagnosis

- Interstitial lung disease
- Pulmonary artery hypertension
- Pneumothorax
- Diaphragmatic weakness

97. Ans. is ‘b’ i.e., Pulmonary artery hypertension [Ref: Harrison 17th/e p. 1587-1588; 16th/e p. 1499, 1500]

- We overlooked an important fact
- The forced vital capacity (FVC) is not decreased in this case.**

The forced vital capacity in the question is

$$\frac{2.63}{2.82} \times 100 = 93.26\%$$

- FVC is 93% which is quite normal.**
- (Any pulmonary function test which is 80-100% of the predicted value is considered normal)
- The FEV1 is also mentioned as normal.
- So, the only pulmonary function abnormality is decrease in DLCO.**
- This strongly suggests pulmonary artery hypertension.**
- Systemic sclerosis is associated with both pulmonary artery hypertension and interstitial lung disease.
- They are quite difficult to distinguish clinically because pulmonary function test are almost similar.
- Both presents with restrictive pattern of disease and decrease in DLCO.
- Features of pulmonary function test which favours pulmonary artery hypertension are : -**
- Decrease in DLCO in the absence of any other abnormality on pulmonary function test i.e., isolated decrease in DLCO.
- **Decrease in DLCO is out of proportion to the decrease in FVC.**

If FVC/DLCO ratio

- > 1.5 → Pulmonary artery hypertension
- < 1.5 → Interstitial lung disease.

The definitive diagnosis of : -

- Pulmonary artery hypertension → Pulmonary artery catheterization.
- Interstitial lung disease → Helical CT scan
- In the question the patient shows decrease in DLCO in the absence of any other abnormality.
 - This strongly suggests pulmonary artery hypertension.**

126. Most common cause of sepsis in India within 2 months - (AIIMS Nov 09)

- H influenza
- E. coli
- Coagulase positive staph aureus
- Group B streptococcus

126. Ans. is ‘c’ i.e., Coagulase positive staph aureus [Ref: www.Indianjournals.com, Dr. Ashok K Deorari, M Jeeva Sanker, Ramesh Agarwal, Vinod K. Paul, Division of neonatology, Department of pediatrics AIIMS, Journal of Neonatology year 2009, Vol.23, issue]

It was a typing error

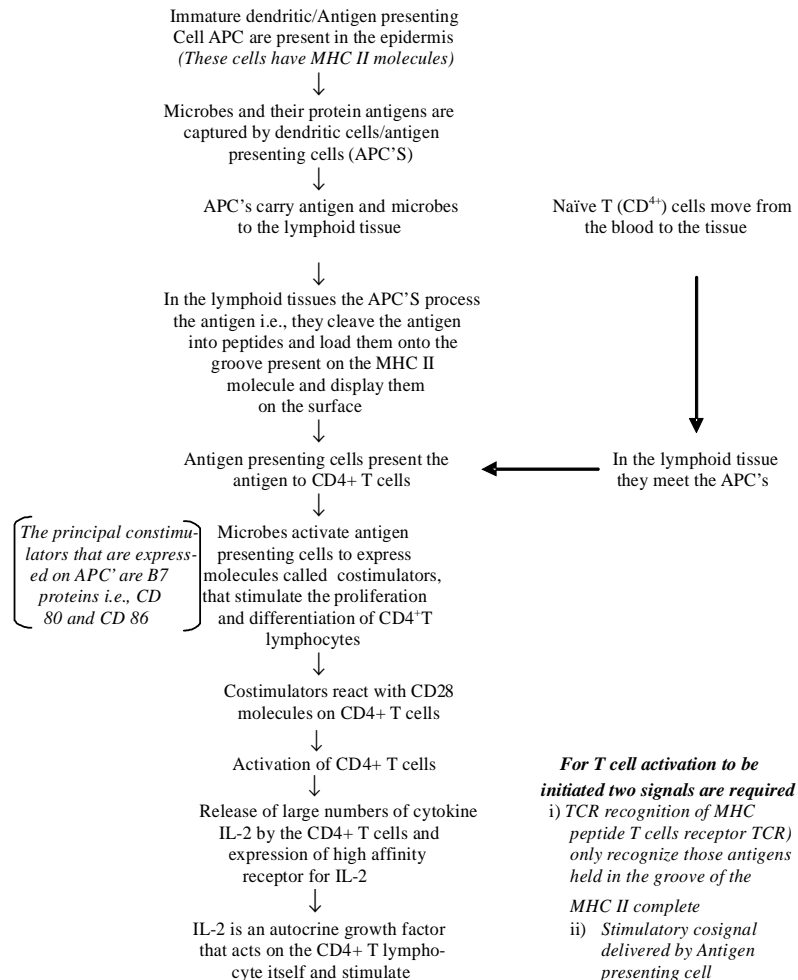
- *In developing countries sepsis is the commonest cause of mortality responsible for 30-50% of 5 million total neonatal deaths each year.*
- *National neonatal perinatal database from India has reported an incidence varying from .1 to 4.5% from 18 hospitals across India.*

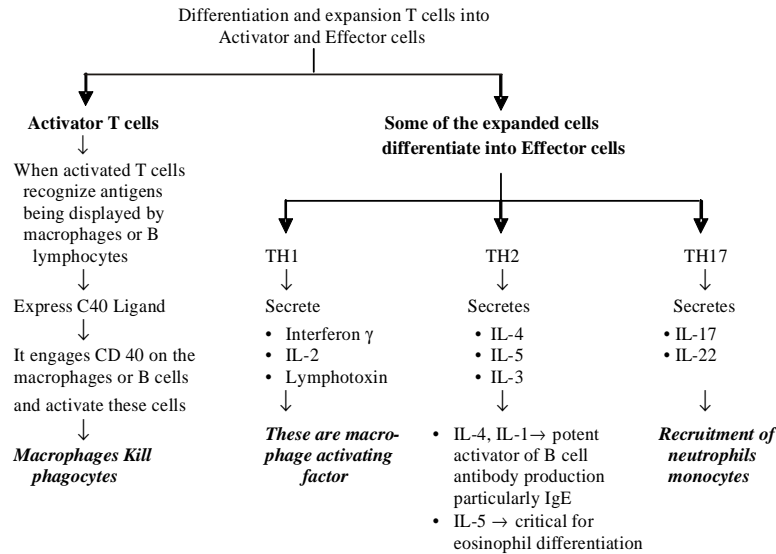
“Klebsiella pneumonia, S. aureus and E.coli are the most common organism isolated in both early and late sepsis in intramural and extramural births”

Klebsiella pneumonia > S. aureus > E.coli

83. CD4 - is not important for which of the following - (AIIMS May 10)
- a) Antibody production
 - b) Cytotoxicity of T cells
 - c) Memory B cells
 - d) Opsonisation

83. Ans. is 'None' ?? [Ref: Robbin's 8th/e p. 194, 195]





Memory cells

- **CD4 helper T cells are part of adaptive immune system.**
 - Memory cells persist after initial (primary) exposure to an antigen allowing an accelerated response if there is further (second) infection.
 - **During primary immune responses naïve T cells proliferate, acquire effector functions and die. However, some persist and form memory cells.**
 - These allow an accelerated response, if the same antigen stimulus is encountered.
- **Naïve, memory T cells display characteristic surface marker that can be used to distinguish b/w them.**
 - **Naïve T cells** → Express high molecular weight from of CD 45 (CD45RA)
 - **Memory T cells** → Express low molecular weight from of CD 45 (CD45RO)

An important function of CD4 T helper cells is to help the cytotoxic T cells.

Response of cytotoxic T cells (CTL) can be divided in two stages: -

- i) During acute phase the naïve CD8 or cytotoxic T cells (CTL) expand, differentiate into effector cells and fight the antigen (virus). This is called primary response. It can result in resolution of the infection.
 - ii) At this stage the CTL's enter the memory phase i.e., the effector cells differentiate into memory CTL, that can persist at elevated levels in the long term. Upon further antigenic stimulation, the memory cells can become activated, proliferate and differentiate into effector cells again that fights the virus. **This is called the secondary response.**
 - If an infection is not cleared but persists in the host this cycle of memory cell stimulation, proliferation and differentiation is repeated continuously.
- **Experimental datas have shown that primary response develops normally in the absence of help. It is therefore called "helper independent".**
 - **On the other hand efficient restimulation of memory cytotoxic T cells requires CD4 help.**
 - The exact mechanism by which CD4 cells deliver help to cytotoxic T cells are still unclear.
 - **Two main hypothesis can be found in literature.**
 - i) Traditionally the main role of CD4 T cells was thought to be the secretion of cytokines upon contact with antigen. These cytokines especially IL-2 are thought to stimulate cytotoxic T cell production promoting their expansion and maintenance. This mechanism would be referred as the "**classical pathway**".
 - ii) **However recently it has become clear that a more complicated pathway might be involved in the generation of help for cytotoxic T cells responses.**
 - Experiments suggests that CD4 T cells can specifically interact with antigen presenting cells (APC's) there by activating them. Activated APC's in turn can specifically interact with cytotoxic T cells delivering help in the form of "**costimulatory signals**".

T helper cells in humoral immune response (antibody response)

- Humoral response begins with an encounter between pathogen or toxin and B cells.
- Antigens stimulating the process are derived from bloodstream, such as those associated with bacterial cells viruses and certain organic substances.

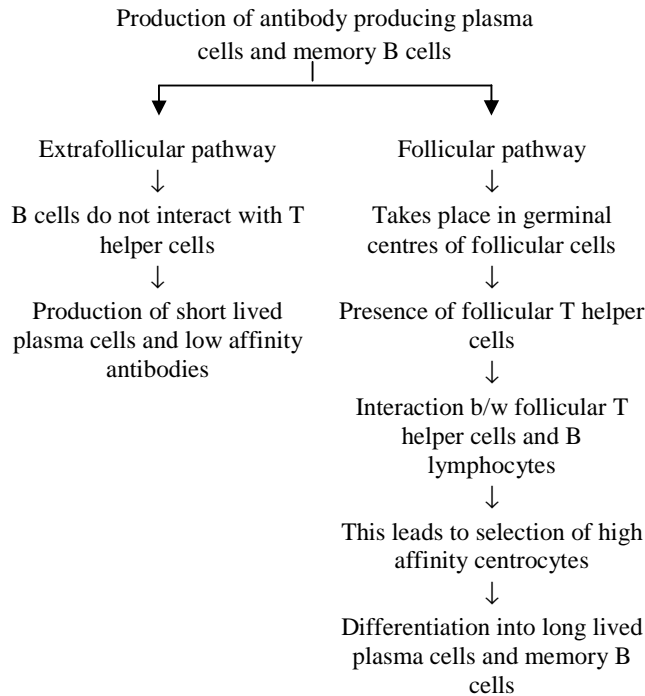
- **Antigen binds with surface receptor on the B cells.**
 - The combination of antigen and receptor (protein) is taken into the cytoplasm of the B cell.
 - Then the B cell displays the antigen/receptor (peptide) on its surface within a MHC II molecules.
- **Antigen/receptor complex is recognized by activated TH2 cells and it binds to B cell.**
 - TH₂ cells release certain cytokines IL-4, IL-5. These spurs the B cells to enlarge and divide into a clone of plasma cells and memory cells. **The plasma cells produce antibodies.**
- Antigen evoking this sort of response are called T dependent antigens because they require the services of TH₂ cells. However a few antigen are T independent these substances (such as bacterial capsule and flagella) do not require the intervention of TH₂.

CD4 helper cells help in production of memory B cells

- A critical CD4 T helper cell function is B cell help.
- **Recent studies have demonstrated that an additional effector subset, follicular T helper cell is largely responsible for B cell help during an immune response.**
- **T helper follicular cells are located within germinal centres and are responsible for**
 - High affinity
 - Class switching
 - Long lived plasma and memory cells

Interaction b/w T helper cells and B cells are required for B cell memory and antibody response.

- This process particularly involves T helper cells the follicular B helper T cells.
- The generation of memory B cells require T cells because T independent response do not usually show memory B cells.
- The T helper cell which interacts with B cells B cells is called follicular T helper cells.
- **Follicular T helper cells develop independent from Th1, Th2 and Th17 cells and are critical for humoral immunity including the generation of long lived and high affinity plasma cells and memory cells crucial for long term protection against infection.**
 - T follicular helper cells express CXCR5
 - They are localized in germinal centre.
 - Their development is driven by BCL6.
 - They help B cell by producing IL-21 which provides stimulus for development of B cells into memory cells.



CD4T helper cells are also required in opsonisation:-

- *Opsonisation is the coating of the bacteria so that they are easily phagocytosed by the white blood cells. WBC's can phagocytose the bacterias even without opsonisation, but opsonised bacteriase are more easily phagocytosed.*
- **The main chemicals causing opsonisation are:-**
 - Complement C3b
 - IgG (Fc) fragment, some serum proteins

According to Robbin's 8th/e p.196

The production of most opsonizing and complement-fixing IgG anti bodies is stimulated by T_H1 helper cells, which respond to many bacteria and viruses is driven by T_H1 cells.

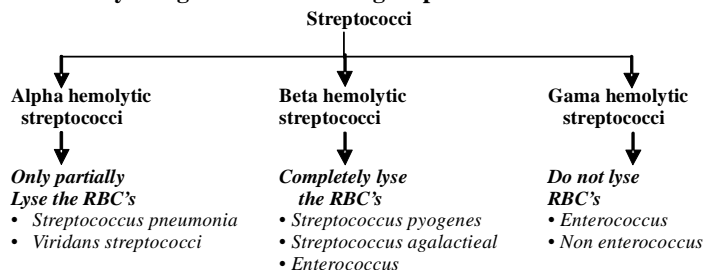
We can also find this on following sites : - <http://ndt.oxfordjournals.org/content/23/3/816.full>,
www.medscape/viewarticle/431127

74. A 65 year old man presenting with complaints of chest pain fever, cough with sputum. O/E of sputum pus cells with gram positive cocci present. Blood agar showed positive result. How will you differentiate this from other gram positive cocci?
- Bacitracin sensitivity (AIIMS Nov 09)
 - Optochin sensitivity
 - Bile solubility
 - Positive coagulase

74. Ans. is 'c' i.e., Bile solubility > 'b' i.e., Optochin sensitivity [Ref: Ananthnarayan 8th/e p. 219, 205, 206]

This question is about the differential diagnosis of streptococcus.

Streptococcus can be broadly categorized into three groups.



Alpha hemolytic group of streptococci

- *Alpha hemolytic streptococci may be pathogens such as streptococcus pneumonia or a part of the normal flora of the upper respiratory tract i.e., Viridans streptococci.*
- **Collectively commensal streptococci are often called viridians streptococci which refers to their α hemolytic property.**
 - *Viridans is the Latin for "green" and most of the viridians streptococci are alpha hemolytic, Not quite logically this term also includes few streptococci (e.g., the salivarius and mutans groups of streptococci that induce neither α nor β hemolysis).*

Moreover

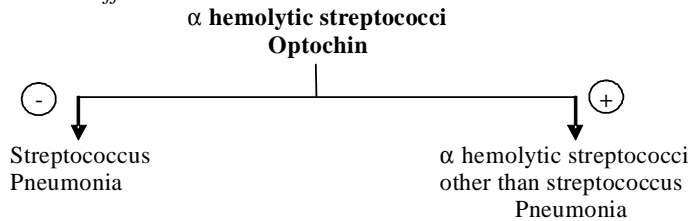
- *In common usage this term excludes streptococcus pneumonia although this species is also α hemolytic.*
- **Streptococcus pneumonia is the major cause of community acquired bacterial pneumonia and the most frequent cause of otitis media and bacteremia in infants and children.**
 - *Thus it is important to distinguish streptococcus pneumonia from other alpha hemolytic streptococci which are commensals.*

Two tests are commonly employed for distinguishing streptococcus pneumonia from the viridians streptococcus i.e.,

- Optochin sensitivity test
- Bile solubility test

Optochin sensitivity test

- **Optochin (or ethylhydrocupreine) is a chemical used for distinguishing streptococcus pneumonia from other α hemolytic streptococci.**
 - *Streptococcus pneumoniae* is sensitive to optochin i.e., it is lysed by optochin.
 - Other α hemolytic streptococci are resistant to (not killed by) optochin.
- Bacteria that are optochin sensitive will be inhibited to grow around optochin disc while the bacteria that are optochin resistant will be unaffected.



Bile Solubility test

- **Bile solubility test is used to distinguish streptococcus pneumoniae from other α hemolytic streptococci.**
 - Bile will selectively lyse colonies of streptococcus pneumoniae while other streptococci are immune to bile's activity.
 - When a bile salt such as deoxycholate is added directly to streptococcus pneumoniae growing on an agar plate or in a broth culture the bacteria will lyse and the area becomes clear. Other alpha hemolytic streptococci are resistant to (not lysed by bile) and will stay viable or turbid.

β hemolytic group of streptococci

- **β hemolytic group of streptococci includes most of the pathogenic streptococci: -**
 - *Streptococcus pyogenes*
 - *Enterococcus*
 - Non enterococcal group D species.
- The enterococcal strain of streptococci are more resistant to antimicrobial agents than are the nonenterococcal strain therefore it is important that the enterococcal strains be rapidly and accurately identified.
- **Two tests are used for this purpose**
 - PYR test
 - Bacitracin sensitivity test

PYR test (L-pyrolididnyl beta naphthylamide test)

- **It is used for presumptive identification of enterococci.**
 - The rapid and accurate identification of enterococci can provide clinician's decision making of antimicrobial therapy because enterococci are usually multiresistant to commonly used antimicrobial agents.
- The conventional method of identifying the enterococci using **bile esculin and 6.5% NaCl tolerance** is accurate but requires upto a 48 hr incubation period.
- **A 4 hr method was devised using PYR to differentiate the non beta hemolytic streptococci into three categories.**
 - All of enterococci and streptococcus pyogenes are positive in PYR test while all of Beta hemolytic streptococci other than *S. pyogenes* and non-beta hemolytic streptococci were negative in the PYR test.

Bacitracin sensitivity test

- **It is used to differentiate beta hemolytic streptococci.**
 - Group A beta hemolytic streptococci are sensitive to Bacitracin and the group B beta hemolytic streptococci are not sensitive to it.

Bile solubility Vs Optochin sensitivity in pneumococci

- So two options seems correct in this question. i.e., bile solubility and optochin sensitivity.
- **I would prefer bile solubility**
 - Though optochin sensitivity is an easier test and is routinely done in all laboratories.
 - It is the first test to be performed for the detection of pneumococcus. But now days, optochin resistance has emerged in pneumococci. These cases, when further tested with bile solubility test were found to be pneumococcus. Thus any organism demonstrating optochin resistance has to be further confirmed by bile solubility.

90. Both hyperplasia and hypertrophy is found in – (AIIMS May 09)
a) Pregnancy uterus

- b) Cardiac muscle in cardiomegaly
- c) Skeletal muscle in atelelectasis
- d) Breast development in lactation (earlier option was puberty)

90. Ans. is 'a' i.e., Pregnant uterus ?? [Ref: Robbin's 8th/e p. 6, 7, 8; 7th/e p. 6, 7]

There are some confusion because of the changes in 8th/e Robbin's

Robbin's 7th/e clearly states that (p7)

- The massive physiologic growth of uterus during pregnancy is a good example of hormone induced increase in the size of an organ that results from both hypertrophy and hyperplasia

But Robbin 8th/e says (P 6-7)

- The massive physiological growth of the uterus during pregnancy is a good example of hormone induced increase in the size of an organ that results mainly from hypertrophy of muscle fibres. The cellular enlargement is stimulated by estrogenic hormones acting on smooth muscle estrogen receptors.

About Breast enlargement during pregnancy and puberty

Robbin's 8th/e p. 8 says

- Hormonal hyperplasia is well illustrated by the proliferation of glandular epithelium of female breast at puberty and during pregnancy usually accompanied by enlargement (hypertrophy of glandular epithelial cells).

Hypertrophy

- Hypertrophy refers to an **increase in the size of cells** resulting in an increase in size of the organ.

Hyperplasia

- It is an **increase in the number of cells** in an organ or tissue usually resulting in increased volume of the organ or tissue.
- Hyperplasia takes place if the cellular population is capable of synthesizing DNA, thus **permitting mitotic division**, in contrast, hypertrophy involves cell enlargement without cell division.

Although hyperplasia and hypertrophy are two distinct processes, sometimes they may occur together.

- For example hormone induced growth in the uterus during pregnancy involves both **increased number of smooth muscles and epithelial cells and the enlargement of these cells** (i.e. both hypertrophy and hyperplasia).
- The cellular hypertrophy is stimulated by estrogenic hormones acting on smooth muscle estrogen receptors, eventually resulting in increased synthesis of smooth muscle proteins and an increase in cell size.

Muscular hypertrophy

- One of the most common and visible forms of organ hypertrophy occurs in **skeletal muscles** in response to strength training.
- The muscle cells in both the heart and the skeletal muscles are **capable of tremendous hypertrophy** perhaps because they **cannot adequately adapt to increased demands** by mitotic division and production of more cells to share the work.
- The most common stimulus for muscle hypertrophy is **increased workload**. For example the bulging muscles of bodybuilders engaged in "pumping iron" result from an **increase in size of the individual muscle fibres** in response to increased demand.
- The workload is thus **shared** by a greater mass of cellular components and each muscle fibre is spared excess work and so escapes injury.
- The enlarged muscle cell achieves a new equilibrium, permitting it to function at a higher level of activity.
- **In the heart**, the stimulus for hypertrophy is usually a **chronic hemodynamic overload** resulting from either **hypertension** or faulty valves.
- Synthesis of more proteins and filaments occur, achieving a **balance b/w** the demand and the cell's functional capacity. The greater number of myofilaments per cell permits an increased workload with a level of metabolic activity per unit volume of cell not different from that borne by the normal cell.
- **Breast enlargement during lactation occurs due to hypertrophy of the cells caused by the action of prolactin and estrogen on breast. Breast hyperplasia occurs during puberty and pregnancy.**

102. All the following is found in Primary Sjogren syndrome except – (AIIMS May 09)

- a) Lymphoma

- b) Connective tissue disorder
- c) Xerostomia
- d) Xerophthalmia

102. Ans. is 'b' i.e., Connective tissue disorder; 'd' i.e., Xerophthalmia [Ref: Harrison 17th/e p. 2107, 2108]

- Dryness of the eye occurs in Sjogren's syndrome but it cannot be termed xerophthalmia
- It can be termed xerosis .
- Xerophthalmia is a term exclusively used for eye manifestations in Vitamin A deficiency.

So, two options are wrong

Most probably, they would have asked about Sjogren's syndrome, not primary Sjogren's syndrome.

- **Sjogren's syndrome** is a chronic disease characterized by -
 - Dry eyes (*keratoconjunctivitis sicca*)
 - Dry mouth (*xerostomia*)
- It results from **immunologically mediated destruction of the lacrimal and salivary glands.**
- The characteristic **decrease in tears and saliva** is the result of **lymphocytic infiltration and fibrosis** of the lacrimal and salivary glands. The infiltrates are predominantly activated **CD4⁺ helper T cells.**
- There has been some association of **Hepatic C infection** with sjogren's syndrome.
- Sjogren's syndrome is associated with antibodies directed against two ribonucleoprotein antigens **SS-A (Ro)** and **SS-B (La).** These antibodies are seen in upto **90%** of the patients.

Sjogren's syndrome can occur in two forms:-

- **Primary form** (*isolated disorder*) also known as **Sicca syndrome.**
- **Secondary form** (*associated with other connective tissue disease*).

Connective tissue disorders associated with Sjogren's syndrome

- Rheumatoid arthritis
- SLE
- Polymyositis
- Scleroderma
- Vasculitis
- Mixed connective tissue disease
- Thyroiditis

Clinical features

- Sjogren's syndrome occurs most commonly in **older women** typically between ages 50-60.
- Symptoms result from **inflammatory destruction** of the exocrine glands.

Keratoconjunctivitis produces

- Blurring of vision
- Burning & itching
- Thick secretions accumulate in conjunctival sac.

Xerostomia

- Difficulty in swallowing solid food
- Cracks and fissures in the mouth
- Dryness of buccal mucosa

Parotid gland enlargement

- Seen in **50%** of patients

• **Sjogren syndrome is also associated with extraglandular involvement** (*in upto 1/3rd of patients*).

Extraglandular manifestation of sjogren's syndrome :-

- Arthralgias / arthritis
- Raynaud's phenomenon
- Lymphadenopathy
- Lung involvement
- Vasculitis
- Kidney involvement
- Liver involvement

- Lymphoma
- Splenomegaly
- Peripheral neuropathy
- Myositis

Two options are wrong in this question. Most probably they have not asked about primary Sjogren's syndrome. The question would have been about Sjogren's syndrome only.

Earlier we had given the question as -

163. All are true about aneuploidy except – (AIIMS May 09)
- a) 30% of trisomy 21 fetus die in utero
 - b) 80% of trisomy 18 fetus die in utero
 - c) Occurrence of aneuploidy has no relation with the progression of mother's age
 - d) Not recalled

Now we are getting feedback that the correct options are as below -

163. All are true about aneuploidy except – (AIIMS May 09)
- a) 30-40% of trisomy 21 fetus die between 12 weeks and 40 weeks
 - b) 50-60% of trisomy 18 fetus die between 12 weeks and 40 weeks
 - c) Occurrence of triploidy has no relation with the progression of mother's age
 - d) In previous pregnancy with trisomy 21 due to non disjunction, the risk in future pregnancy is .75% higher

163. Ans. is 'b' i.e., 50-60% of trisomy 18 fetus die between 12 weeks and 40 weeks

[Ref: Fernando Arias high risk pregnancy 3rd/e p. 33, 34, 35]

"80% of trisomy 18 fetus die between 12 weeks and 40 weeks"

- **The risk of having a baby with chromosomal abnormalities depend upon the maternal age and the gestational age at the time of evaluation.**
 - In general there is increased risk of chromosomal abnormalities with advanced maternal age.
- **There is decreased risk of chromosomal abnormalities associated with gestational age.**
 - *The decreased risk associated with gestational age occurs because fetuses with abnormalities tend to die "in utero".*

An important point

- **Triploidy is a chromosomal abnormality whose incidence does not depend upon either maternal age or paternal age.**

Triploidy

- **Triploidy is the most frequent chromosomal aberration in first trimester spontaneous abortions.**

"In contrast to aneuploidies due to non disjunction, increased maternal age is not a risk factor".

- A normal human conceptus possessed 46 chromosomes 23 derived from the mother and 23 from the father.
- Triploidy is a chromosomal abnormality where three complete sets of the haploid genome instead of the normal two sets that are present within the conceptus.
- A triploid conceptus will possess 69 chromosomes.

There are three different mechanisms that may produce triploidy

- (i) Nondisjunction in meiosis I or meiosis II of spermatogenesis
- (ii) Nondisjunction in meiosis I or meiosis II of oogenesis
- (iii) Double fertilization of a normal egg

- **Maternal age has not been found to be associated with any of the three mechanisms by which triploidy occur.**

- *Neither maternal age nor paternal age has been associated with increased risk of triploidy (infact some reports say that incidence decreases with increased maternal age).*

Trisomy 21 or Down's syndrome

- **Risk of Down's syndrome in previously affected pregnancy with Down's syndrome**
When a pregnant woman has a history of a previous child with Down's syndrome, it is important to know the type of chromosomal defect found in the affected child because the risk of recurrence in a future pregnancy will be different depending on the type of defect.
 - a) **Recurrence risk for Nondisjunctional 21**
 - The recurrent risk for nondisjunctional T21 is .75% higher than the maternal and gestational age risk.
For example
 - The background risk for a women 25 years old at 16 weeks of gestation is 1 in 933(0.10%). If she has a history of T21 in previous pregnancy, her risk will be $0.10 + 0.75\% = 0.85\% = 1$ in 117
 - b) **Recurrence risk when Down syndrome is caused by an unbalanced translocation**
 - The recurrence risk when Down syndrome is caused by an unbalanced translocation varies depending on the chromosomal composition of the parent.
If both parents have a normal Karyotype
 - The translocation in the affected child occurred denovo and the risk of affected child is < 1%
 - Mother's karyotype normal but the father has balanced 13/21, 14/21, 15/21 or 21/22 translocation**
 - The risk of affected child will be 2-3%.
 - Father's karyotype normal and the mother is the carrier of balanced 13/21, 14/21, 15/21, or 21/22 translocation**
 - The probability of having another affected child is 11.9%.
 - c) **Recurrence risk when Down syndrome is caused by balanced translocation (21/21)**
 - If either parent has a balanced 21/21 translocation the risk of having an affected child in a future pregnancy will be 100%
 - d) **Risk of recurrence when a previous child has been born with Down's syndrome due to mosaicism.**
 - It is unknown but is probably small 2-3%.

Death rates for aneuploidy b/w 12 weeks and term (40 weeks)

• Down's syndrome	→	30%
• Trisomy 18	→	80%
• Trisomy 13	→	80%
• Triploidy	→	100%

195. Formication and delusion of persecution, both are together seen in - (AIIMS May 09)
- a) LSD psychosis
 - b) Amphetamine psychosis
 - c) Cocaine psychosis
 - d) Cannabis psychosis

195. Ans. is 'c' i.e., Cocaine psychosis

[Ref: Nimboodiri 3rd/e p. 334; Essentials of clinical psychiatry 4th/e p. 580]

- This question is tricky one as tactile hallucination (formication) and delusion of persecution are seen both in cocaine as well as amphetamine abuse.
- Read the question carefully, examiner has asked about the presence of formication and delusion of persecution together.
- In amphetamine abuse these two do not occur together
 - **Formication (tactile hallucination) is seen in** → **Chronic abuse.**
 - **Paranoid ideation (delusion of persecution) occurs in** → **Acute intoxication.**
- On the other hand both delusion of persecution and formication are seen together in chronic cocaine abuse.

"Cocaine abuse can present with auditory hallucinations, tactile hallucination including formication and paranoid delusion (delusion of persecution)".

— BK Puri 3rd/e 356

113. All of the following statements regarding progressive multifocal leucoencephalopathy are true except -
 a) Patient commonly presents with visual disturbances and speech defects (AIIMS Nov 08)
 b) It is most commonly seen in immunocompromised persons
 c) Exclusively diagnosed by brain biopsy
 (earlier the option 'c' was -**Diagnosis is frequently suggested by MRI**)
 d) Patient usually dies within 6 months

113. Ans. is 'c' i.e., Exclusively diagnosed by brain biopsy [Ref: Harrison 17th/e p. 2634, 2635]

Progressive multifocal leucoencephalopathy :-

- Progressive multifocal leucoencephalopathy is a progressive disorder cause by **J.C. virus**^o.
- The main cells affected in the disease are **oligodendrocytes**^o.
- Since oligodendrocytes are concerned with myelination, progressive multifocal leucoencephalopathy is characterized by multifocal areas of **demyelination**^o of varying size distributed throughout the brain but **sparing** the spinal cord and optic nerves.

Pathology

- Besides demyelination there are characteristic cytological alterations in both astrocytes and oligodendrocytes :-
Astrocytes^o
 - Enlarged and contain, hyperchromatic, deformed and bizarre nuclei and frequent mitotic figures.**Oligodendrocytes**^o
 - These have enlarged densely staining nuclei that contains virus inclusions formed by crystalline arrays.

Symptoms of progressive multifocal leucoencephalopathy :-

- Focal neurological signs → Speech defect (aphasia), dysarthria hemiparesis, Ataxia
- Visual defects (45%) → Homonymous hemianopia
- Mental impairment (38%) → Dementia, confusion, personality changes
- Weakness → Hemi or monoparesis and ataxia
- Seizures (20%)
- **Progressive multifocal leucoencephalopathy is predominantly seen in patients with immunosuppressive disorders :-**
 - **Most commonly associated conditions are :-**
 - AIDS (80%)^o
 - Hematological malignancies (13%)
 - Transplant recipients (5%)
 - Chronic inflammatory disease (2%)

Prognosis of progressive multifocal leucoencephalopathy

- In most cases death occurs in **3-6 months** from onset of neurological symptoms and even more rapidly in patients with AIDS unless aggressive intertrivial treatment is undertaken.

Diagnosis

- **MRI** is used for the diagnosis of PML.
- **MRI is better than CT scan in the diagnosis of PML and is frequently used for the diagnosis of PML.**
- On MRI the lesion appears as multifocal asymmetric coalescing white matter located periventricularly.

Brain biopsy in diagnosis of progressive multifocal leuco encephalopathy

- It has a sensitivity of 74-92% and specificity of 92-100%.
- **PML lesions are classically nonenhancing**^o.
- **Brain biopsy demonstrates multiple demyelinative foci in cerebral, cerebellar and brainstem white matter.**
- Perivascular inflammatory infiltrates are seen
- Nuclear inclusions may be seen
- **Microscopic hallmark of the disease is intranuclear basophilic or eosinophilic inclusions within the swollen nuclei of oligodendrocytes often at the periphery of lesions.**
- Large multinucleated astrocytes are also seen.

- These lesions have increased signals on T2 and FLAIR images and decrease signal on T₁-weighted images.
- Other important diagnostic tool in PML is the **PCR amplification of JCV DNA**.
- **The PCR amplification of JCV DNA in association with typical MRI lesion in the appropriate clinical setting is diagnostic of PML.**

119. Microangiopathic hemolytic anaemia is seen in all of the following diseases except - (AIIMS Nov 08)
- Antiphospholipid antibody syndrome
 - Thrombotic thrombocytopenic purpura
 - Microscopic polyangiitis
 - Metallic cardiac valves

119. Ans. is 'd' i.e., **Metallic cardiac valves** [Ref: Harrison 17th/e p. 658; Wintrobe Hemato 11th/e p. 1232, 1234; Tejinder Singh p. 65]

- **Metallic cardiac valves do not cause microangiopathic hemolytic anemia.**
- Don't mix microangiopathic hemolytic anemia with fragmentation syndrome.
- They are two separate entities, according to most standard text in hematology.

Fragmentation syndrome

- Red cells when subjected to mechanical trauma may undergo fragmentation in circulation. These fragment cells have shapes like triangular cells, helmet cells and are known as schistocytes and are easily made out in a well made peripheral blood film.

Schistocytes are the hallmark of diagnosis of this group of hemolytic anemia.

Fragmentation of the red cell can occur either in large vessels or small vessels of capillaries and arterioles.

Microangiopathic hemolytic Anemia

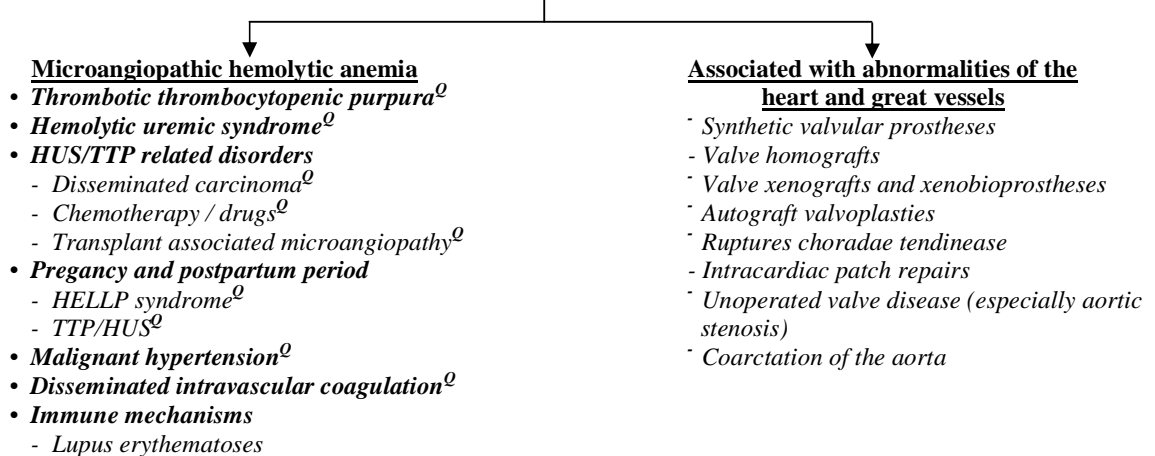
- When fragmentation occurs in small vessels of capillaries and arterioles due to the presence of thrombotic lesions, it is called microangiopathic hemolytic anemia.
- Microangiopathic hemolytic anemia is characterized by hemolytic anemia due to red cell fragmentation. There is associated small vessel disease of capillaries and arterioles with thrombotic lesions. As the red cells pass through these microthrombi, red cells get attached to them and part of RBC's get fragmented by high shear forces.

But the problem is that Harrison does not make any distinction between these two:-

- It is clearly mentioned in Harrison table 101-6 page 658 that microangiopathic hemolytic anaemia occurs in prosthetic heart walls.
- C.M.D.T also shares same views.

We may have to go against Harrison in this case (may be they might have loosely used the term microangiopathic hemolytic anemia).

Causes of Red cell Fragmentation



- Acute glomerulonephritis^Q
- Scleroderma^Q
- Microscopic polyangitis^Q
- Wegner granulomatosis
- **Hemangiomas**
 - Giant hemangioma^Q (Kasabach - Meritt syndrome)
 - Hemangioendothelioma^Q of the liver.
 - Plexiform lesions^Q in pulmonary hypertension

Both microscopic polyangitis and antiphospholipids antibody syndrome can cause microangiopathic hemolytic anemia.

128. A 29 yr old unmarried female presents with dyspnea her chest X-ray is normal, FVC is 92%, FEV₁/FVC is 89% and DLCO is 59% of normal. On exercise her oxygen saturation drops from 92% to 86%. What is the likely diagnosis - (AIIMS Nov 08)
- a) Alveolar hypoventilation
 - b) Primary pulmonary hypertension
 - c) Interstitial lung disease
 - d) Anxiety

128. Ans. is 'c' i.e., Primary pulmonary hypertension [Ref: Harrison 17th/e p. 1643]

Once again we remind you
What is FEV₁% ???

- FEV₁ is also expressed as a ratio or percentage of the FVC and can be written as %FEV₁ rather than FEV₁/FVC.

Once again make it clear

"FEV₁ expressed as percentage (FEV₁%) is actually FEV₁/FVC."

- **If the individual being tested displays a low FEV₁ and the FEV₁% is also low, then the clinician should suspect the presence of obstructive pathologies.**
- **In patients with restrictive lung diseases**
 - FVC → low
 - FEV₁ → is also low, (but there is less reduction in comparison to FVC).
- **Since both of these values may be equally affected in restrictive lung disease the %FEV₁ is normal or sometimes it is increased because the decrease in FEV₁ is less compared to decrease in FVC.**
- Hence when % FEV₁ is between 85% - 100% of the normal and if both FEV₁ and FVC are low then you should suspect the patient of having restrictive lung disease.

Major clues given in the question are :-

- **Decreased DLCO** → (Normal predicted range is 75-120%)
- **Normal FEV₁/FVC** → (Normal predicted range is 88% - 90%)
- **Normal FVC** → (FVC > 80% is considered normal)
- Beside these patient is having decrease in oxygen saturation on exercise.
- **These abnormalities suggest primary pulmonary hypertension.**
- Interstitial lung disease can be ruled out because of **normal FVC** (FVC is reduced in restrictive lung disease).
- Obstructive lung disease can be ruled out because of **normal FEV₁/FVC and normal FVC.**

Primary pulmonary hypertension

Age group

- Most common in young women (20-40 years of age).

Symptom

- Most commonly present with exertional dyspnoea.

Pulmonary function test

Usually presents with restrictive pattern of disease

- FVC → Normal to decrease
- FEV₁/FVC → Normal to decrease

- DLCO → Decrease out of proportion to FVC
- *Patient with primary pulmonary hypertension can presents with restrictive pattern of disease but the decrease DLCO is out of proportion to the decrease in FVC.*

Exercise tolerance

- Markedly reduced

Chest X-ray

- **Clear lung field, enlargement of pulmonary artery.**

75. About HUS all are true except – (AIIMS May 08)
- Not commonly caused by verocytogenic E coli in Asia (*earlier the option did not mention Asia*)
 - Causes mild to severe Coombs positive hemolytic anemia
 - Recurrences rare
 - Transient thrombocytopenia

75. **Ans. is 'b' i.e., Causes mild to severe Coombs positive hemolytic anemia** [Ref. Nelson 17th/e p 2181, 2182]

- **Hemolytic-uremic syndrome** (H.U.S.) is the most common cause of acute renal failure in young children.
- **It is classically characterized by the triad of**
 - Microangiopathic hemolytic anemia
 - Thrombocytopenia
 - Uremia

Etiology

- Hemolytic uremic syndrome is preceded by **bacterial infections**
- **The bacterias commonly associated are :**
E.coli (*Verocytogenic E.coli is the most common cause of hemolytic uremic syndrome*)

Nelson states

“An acute enteritis with diarrhoea caused by shiga-like toxin producing escherichia coli (verocytogenic E. coli) 0157:H7 precedes 80% or more of HUS cases in developed countries”

An important point

Some say that option ‘a’ was
- *“Not commonly caused by verocytogenic E.coli in Asia”*

If this was the option then it is a true statement.
- *The infection associated with H.U.S. varies with region*

In developed countries (North America and Europe)
- *Verocytogenic E coli or Shiga like toxin producing Eschererichia coli is the most common cause (80% of all the cases).*

In Asia (India)
- *Shigella dysenteriae is the chief pathogen.*

- The anemia associated with hemolytic uremic syndrome is **coomb’s negative hemolytic anemia**
- **Coomb’s positive** hemolytic anemia occurs when the anemia is caused due to **autoantibodies** produced in the body.
- In **H.U.S.** the hemolytic anemia is caused by **mechanical damage to R.B.C.** when they **pass through microthrombi** (*which are formed in capillaries due to platelet aggregation*).
- The red cells while passing through these capillaries get attached to the thrombus and gets fragmented causing hemolysis.
- Autoantibodies have nothing to do with hemolytic uremic syndrome. So the anemia **will not be coomb’s positive**.

Thrombocytopenia in H.U.S.

- A low platelet count can usually but not always be detected early in the illness, **but it may then become normal or even high.**
- If a platelet count obtained within **7 days** after onset of the acute gastrointestinal illness is not **<150,000/mm³**, other diagnosis should be considered.

Recurrence in H.U.S.

- Recurrence is **rare** in H.U.S. There may be disease recurrence only in familial or non diarrhoea associated cases.

160. Regarding Alpha Fetoprotein true statement is - (AIIMS May 08)

- Major source of fetal life is yolk sac
- Commonly elevated in Wilm's tumor
- Max level at 20th week
- Half-life 5-7 days

160. Ans. is 'd' i.e. **Half-life 5-7 days** [Ref. Dutta 6th/e p 107, Williams's obstetric 22nd/e p 319-322; Immunoassay handbook p. 601; Cancer in children p. 413; Cancer of testis M picar p. 69]

Major source of alpha fetoprotein in fetal life is liver (not yolk sac)

- Yolk sac synthesizes alphafetoprotein mainly during the first trimester of fetal life (especially during the first one month). After this the major source of alphafetoprotein is liver and it remains so throughout the pregnancy.
- Alpha fetoprotein is first synthesized by yolk sac and liver and subsequently predominantly in liver.
- So, the major source of alphafetoprotein in fetal life is liver.

Half life of alpha fetoprotein

- There are doubts regarding this one
 - we have looked into numerous books for this one.
 - Even the standard text books vary on this one.
 - According to the books the half life of alpha fetoprotein is either 3-5 days, 4-6 days or 5-7 days.
 - Most of the books say it is 5-7 days, some say it is 3-5 days, while the rest of them consider it 4-6 days.
 - we will consider 5-7 days as correct option (you will have to confirm it from your own source).
- AFP concentration in fetal serum is **maximal at approximately 3 mg/ml by 12-14 weeks** gestation and declines throughout the rest of pregnancy.
 - AFP levels in the fetal serum continues to decline following birth and by one year of age the serum AFP is approximately **1 ng/ml** a level, that persists throughout adult life.

How is alpha fetoprotein transferred to amniotic fluid.

- Because the fetus passes AFP into its urine, it can also be detected in amniotic fluid.
- The concentration of alpha fetoprotein in amniotic fluid is approximately **100 folds less** than in fetal serum, peaks at **13-14 weeks** and then decreases in the second trimester by approximately 10% per week.

How does alphafetoprotein reach maternal serum.

- AFP can **diffuse** across **the amniotic membranes** and can also be transferred via the *placenta* to maternal serum.
- The level of AFP in *maternal serum* is **1000 fold** less than in amniotic fluid.

Association between alpha fetoprotein and neural tube defects

- AFP level is **increased during neural tube defects**.
- The elevations occur following **leakage of fetal serum into amniotic fluid from exposed neural membranes and blood vessels in an open NTD**.
- This elevated alpha fetoprotein is subsequently transmitted to amniotic fluid.

185. All of the following are used to maintain proper oxygen flow to the patient *except* - (AIIMS May 08)

- Placement of nitrogen flowmeter downstream of the oxygen flowmeter
- A proportionater between N₂ and O₂ control valve
- Different pin index for nitrogen and oxygen
- Calibrated oxygen concentration analyses

185. Ans. is 'a' i.e., **Placement of nitrogen flowmeter downstream of the oxygen flowmeter**

[Ref. Morgan's Anaesthesia 4th/e p. 47]

"Oxygen is last gas to be added for safety in event of leak from top of rotamotor, so most downstream."

The systems used to prevent hypoxia:-

- | | | |
|---|---|--|
| • Low oxygen pressure alarm | → | <i>It detects oxygen supply failure at the common gas inlet that activates a gas whistle or electric alarm</i> |
| • Minimum oxygen/nitrous oxide ratio controller device (hypoxic guard) | → | <i>Prevent delivery of less than 21% oxygen</i> |
| • Oxygen must enter the common manifold down-stream to other | → | <i>Prevent hypoxia in event of proximal gas leak.</i> |

- gases*
- **Oxygen concentration monitor and alarm** → Prevents administration of hypoxic gas mixtures in event of a low pressure system leak; precisely regulate oxygen concentration

We are still confused about option ‘c’

- **Pin index safety system** for cylinders prevents **incorrect cylinder attachments**.
- It is a safeguard introduced **to eliminate cylinder interchanging and the possibility of accidentally placing the incorrect gas on a yoke designed to accomodate another gas. It has nothing to do with hypoxia.**

125. A 21 year old male presents with anemia and mild hepatosplenomegaly. His hemoglobin is 5 gm/dL history of single blood transfusion is present till date. Most probable diagnosis is - (AIIMS May 07)
- Thalassemia major
 - Thalassemia minor
 - Thalassemia intermedia
 - Autoimmune hemolytic anemia

125. **Ans. is ‘d’ i.e. Autoimmune hemolytic anemia > Thalassemia intermedia** [Ref. Harrison 16th/e p 634, Nelson 17th/e p 1630-1633]

It is a close diagnosis between autoimmune hemolytic anemia and thalassemia intermedia. *We are more in favour of autoimmune hemolytic anemia.*

Factors which favour Autoimmune hemolytic anemia

- **Age and sex of the patient**
 - AIHA is more common in adult females
- **Severity of anemia**
 - In many cases of AIHA, anemia is severe with Hb < 6 mg/dl.

Factors which goes against Autoimmune hemolytic anemia

- **Adequate response with blood transfusion only**
 - Patients with AIHA are managed by glucocorticoid therapy not by blood transfusion.
 - Severe anemia in AIHA requires immediate blood transfusion but the patient will not remain asymptomatic in the absence of glucocorticoid therapy, other immunosuppressant or splenectomy is definitely needed to keep the patient asymptomatic.
- **So adequate response to blood transfusion without any other therapy strongly favours thalassemia intermedia.**

Features which goes against thalassemia intermedia

- **Severe anemia (Hb < 5)**
 - Patients with thalassemia intermedia presents with moderate degree of anemia (10g/dl)
 - Even in severe cases of thalassemia the Hb level rarely go below 7g/dl.

More on t/t of Autoimmune hemolytic anemia

Autoimmune hemolytic anemia	
• Mild	→ • Watch
• Moderate	→ • Begin with glucocorticoids • If no response, splenectomy / immunosuppressants
• Severe	→ • Either glucocorticoid or splenectomy

138. Common to both acute and chronic malnutrition is – (AIIMS May 07)
- Weight for age
 - Weight for height
 - Height for age
 - BMI

138. **Ans. is 'a i.e. Weight for age** [Ref: Indian academy of pediatrics 3rd/e p 127; O.P. Ghai pedia 7th/e p. 62 (confirmed by WHO book on malnutrition)]

- **Height is affected only in chronic malnutrition.**
“A child can loose weight but not height”.
- **Loss in weight can be seen in both acute and chronic malnutrition.**

Indicators of malnutrition		
Indicator	Interpretation	
• Stunting	Low height for age	Indicator for chronic malnutrition, the result of prolonged food deprivation and/or disease or illness
• Wasting	Low weight for height	Suggests acute malnutrition, the result of more recent food deficit or illness
• Under weight	Low weight for age	Combined indicator to reflect both acute and chronic malnutrition

More explanation is needed for weight for height.

- *Weight for height is the ratio of the patients actual weight to ideal weight for the patients height.*
- *When acute medical condition results in short term nutritional deprivement the body weight is depleted out of proportional to the length for height and the weight for height value is low.*
- *Conversely chronic malnutrition affects both weight gain and linear growth resulting in a small child with a body weight that is more proportional to length, So weight for height cannot diagnose chronic malnutrition.*

Weight for age

- *If there is acute malnutrition there will be weight loss.*
- *Weight loss will occur in chronic malnutrition to.*
- *So weight for age decreases in both acute and chronic malnutrition.*
- *But it can not distinguish between acute and chronic malnutrition.*

B.M.I

- *we don't have much information regarding BMI.*
- *we are not sure if BMI is used in children below 12 years.*
- *Please check this out from your own sources.*
- **The common anthropometric measurements used are:**
 - **Weight,**
 - **Length/height**
 - **Arm circumference**
 - **Skinfold thickness**
 - **Chest circumference.**
- *These are one time measurement and can assess only acute malnutrition. They cannot be used for chronic malnutrition.*

Dear students,

This post is to clarify one of the controversial questions in May 10, i.e.

Leprosy involves all except:

- a) Uterus
- b) Ovary
- c) Nerve
- d) Eye

We had given option a i.e. Uterus as the answer.

Many students have raised controversy that Ovary is the answer. **But let us clarify once again that Uterus is the right answer.**

We had given the reference of the book: "Blaustein's Pathology of the Female Genital Tract" which stated that "*Although Leprosy rarely involves the female genital tract, the ovary is the most commonly involved gynaecological site*"

Now here is one more very reliable reference in support of our answer. This is an article from very reputed and highly authoritative journal "International Journal of Dermatology" – "**Visceral leprosy** Andria M. Klioze MD, Francisco A. Ramos-Caro MD" [Volume 39, Issue 9, pages 641–658, September 2000](#)

This article has classified visceral organs into 3 categories:

Organs with significant degree of infiltration or dysfunction

Skin	Eyes
Peripheral nerves	Nasopharynx
Kidney	Larynx
Liver	Testicles

Organs with mild to moderate degree of infiltration or dysfunction

Tongue	Autonomic nervous system
Spleen	Bone marrow
Adrenals	Bone
Lymph nodes	Joints
Peripheral vasculature	

Organs with none or minimal degree of infiltration or dysfunction

Brain	Striated muscle
Cerebellum	Ureter
Leptomeninges	Bladder
Spinal cord	Urethra
Pancreas	Prostate
Lungs	Seminal vesicles
Heart	External genitalia
Great vessels	Breasts
Gallbladder	Vagina

Organs with significant degree of infiltration or dysfunction

Pancreas	Uterus
Esophagus	Ovaries
Stomach	Thyroid gland
Small intestine	Parathyroid gland
Large intestine	Pituitary gland
Striated muscle	Pineal gland

So according to this article both uterus and ovaries are none or minimally involved. Now this article further describes leprosy involvement of each and every organ system in detail.

Under its description of **Female reproductive system** the article describes involvement of only ovary and *does not even mention uterus*. The exact lines are quoted below:

“There is little or no involvement of the female genital tract. ³ *The reported incidence of involvement of the ovary ranges from none or very little,^{63,75,141} to almost half (47%) of cases.* ¹¹⁸ Menarche, menstruation, fertility, and menopause do not seem to be affected. ¹⁴⁴ Pregnancy and lactation may predispose the patient (even the apparently cured) to worsening, relapse, or reactivation of leprosy, but with proper management a successful outcome can be obtained. ^{145,146,147} Transplacental transmission is rare and most neonates are healthy; ¹⁴⁵ however, low birth weight and prematurity, especially in mothers with high AFB count, may be a problem in some patients. ¹⁴⁵⁻¹⁴⁸ Low birth weight in infants born to mothers with lepromatous leprosy has been attributed to low placental weight, placental insufficiency, and low estrogen levels. ^{75,149}”

So now we have 2 Reference clearly stating that female genital tract is very rarely involved, and if there is any involvement, ovary is the most common genital organ to be involved.

**All the best for your upcoming exams
 Amit Ashish**