TUBRCULOUS LYMPHADENITIS

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What is TBLN

- What is tuberculous lymphadenitis ?
- Tuberculous lymphadenitis is also know as **scrofula or king's evil**

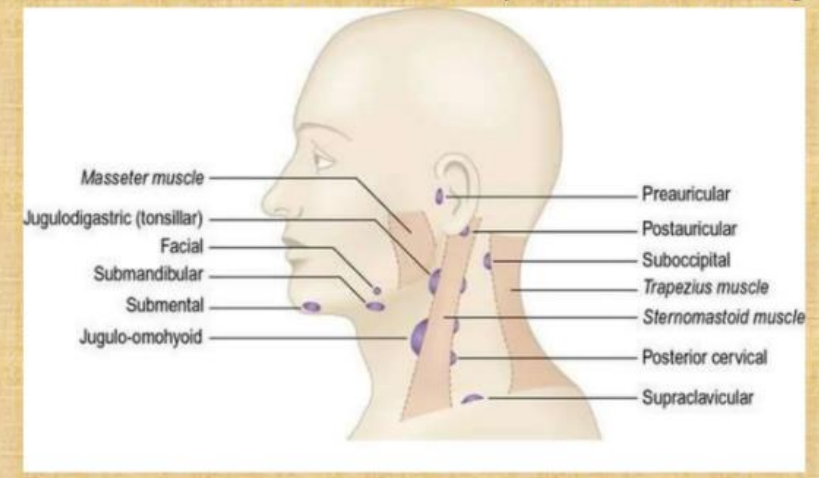
Etiology : Mycobacterium tuberculosis

It is the most **common site of extrapulmonary TB .**

Site of involvement

- Lymph nodes are the most common extrapulmonary site of disease
- Cervical and mediastinal glands are affected more frequently followed by axillary and inguinal
- Rich vascularity of head and neck and extensive network of lymphatics and drainage area of URT making these sites favourable
- Cervical nodes are rich in macrophages which are primary target cells for tb
- Delayed immune response is often robust immune response and is more common in cervical region than other nodes
- Other sites that can be involved are
- Abdominal LN
- Intercostal LN

- Commonest site to be affected is the lymph **nodes of the neck**
- Out of these jugulodigastric is usually infected
- Second most common is the posterior cervical group



MICROBIOLOGY

- M. tuberculosis is the usual cause of tuberculous lymphadenitis.
- Other infectious causes of chronic lymphadenitis include :
  - Nontuberculous mycobacteria (including M. scrofulaceum, M. avium, and M. haemophilum)
  - Pseudomonas pseudomallei
  - Toxoplasma species
  - Bartonella species
  - Fungi.

Mode of spread

- Disease may represent as primary infection, spread from contiguous sites or reactivation

  It may spread Through tonsils (Adenoids also)
- Occasionally through blood
- Rarely through Sibson's fascia from apex of lung

Pathogenesis

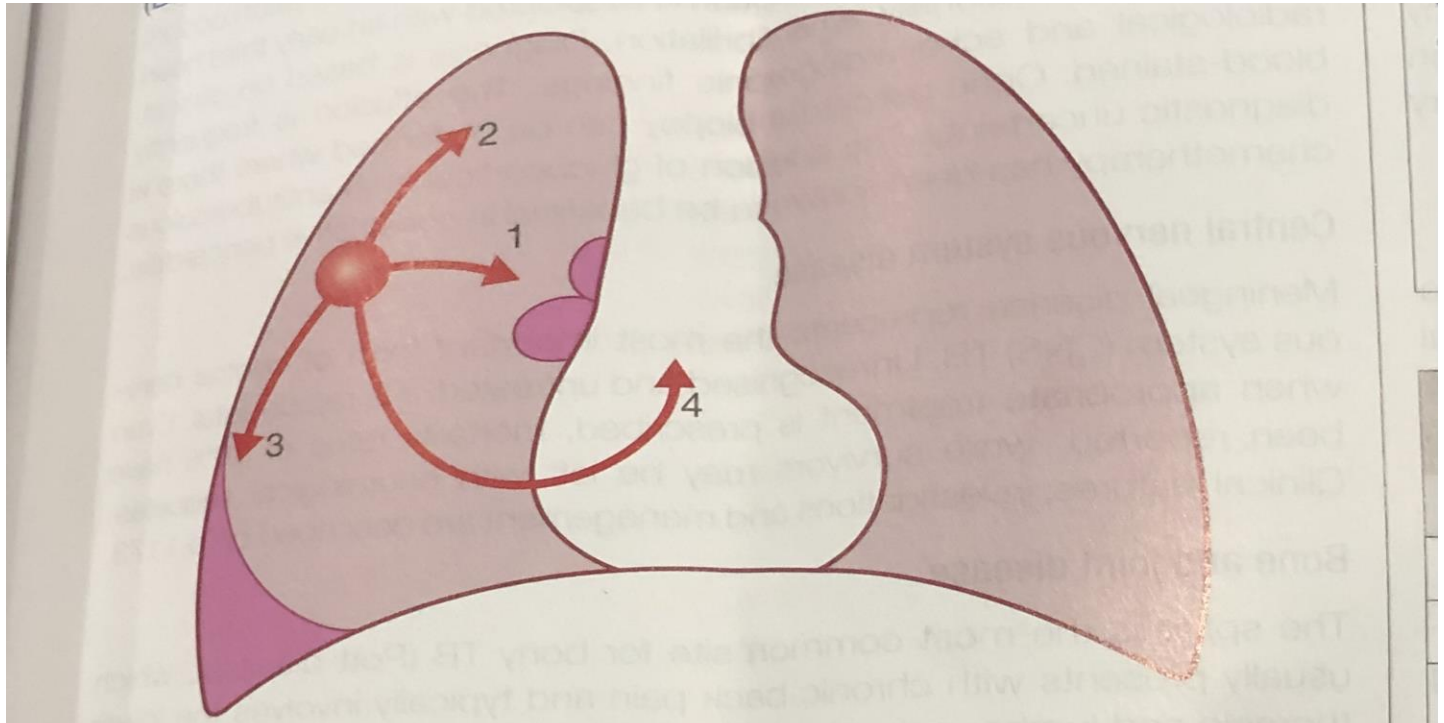


Fig. 17.36 Primary pulmonary tuberculosis. (1) Spread from the primary focus to hilar and mediastinal lymph glands to form the 'primary complex', which heals spontaneously in most cases. (2) Direct extension of the primary focus – progressive pulmonary tuberculosis. (3) Spread to the pleura – tuberculous pleurisy and pleural effusion. (4) Blood-borne spread: *few bacilli* – pulmonary, skeletal, renal, genitourinary infection, often months or years later; *massive spread* – miliary pulmonary tuberculosis and meningitis.

PATHOGENESIS

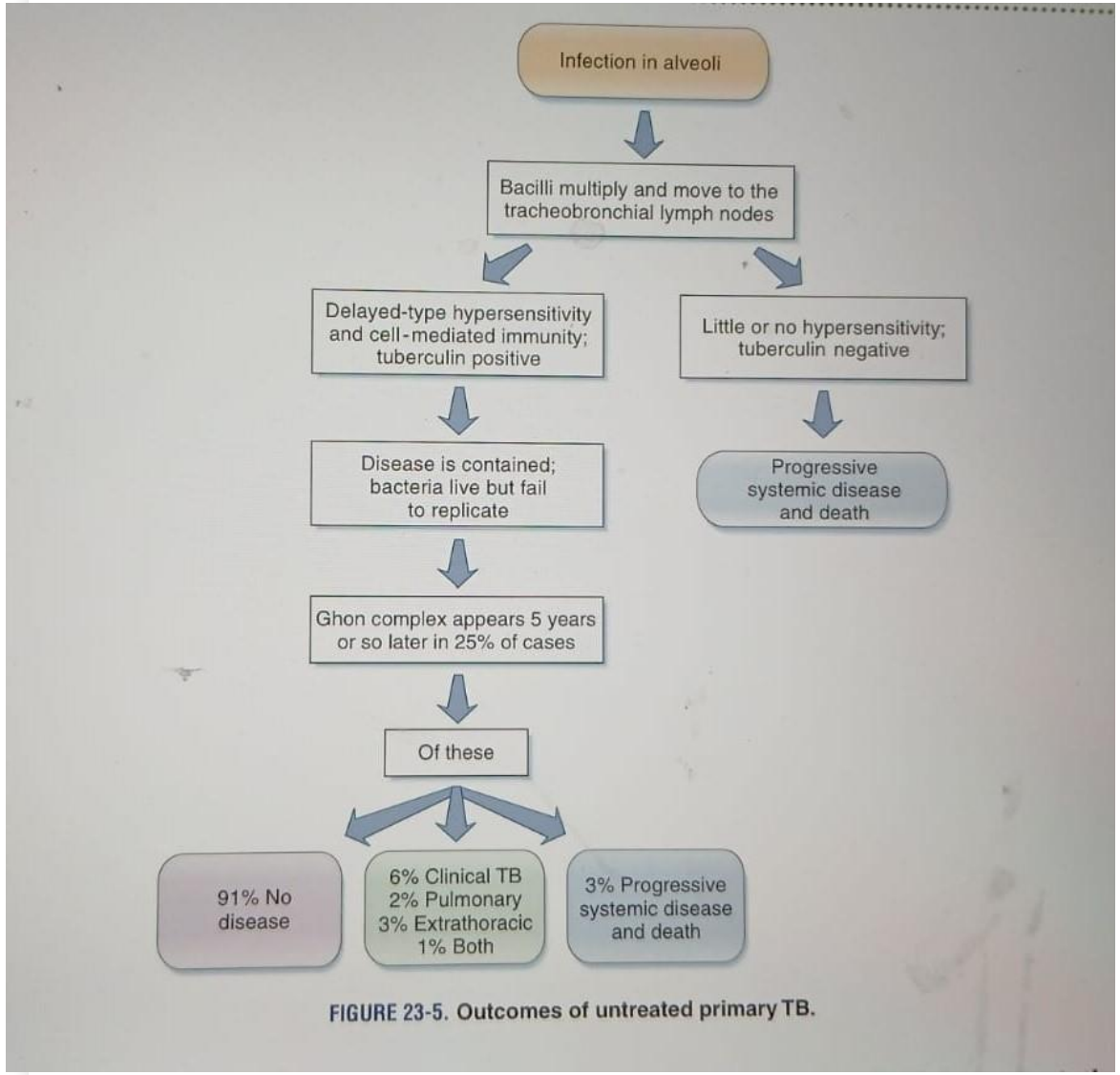
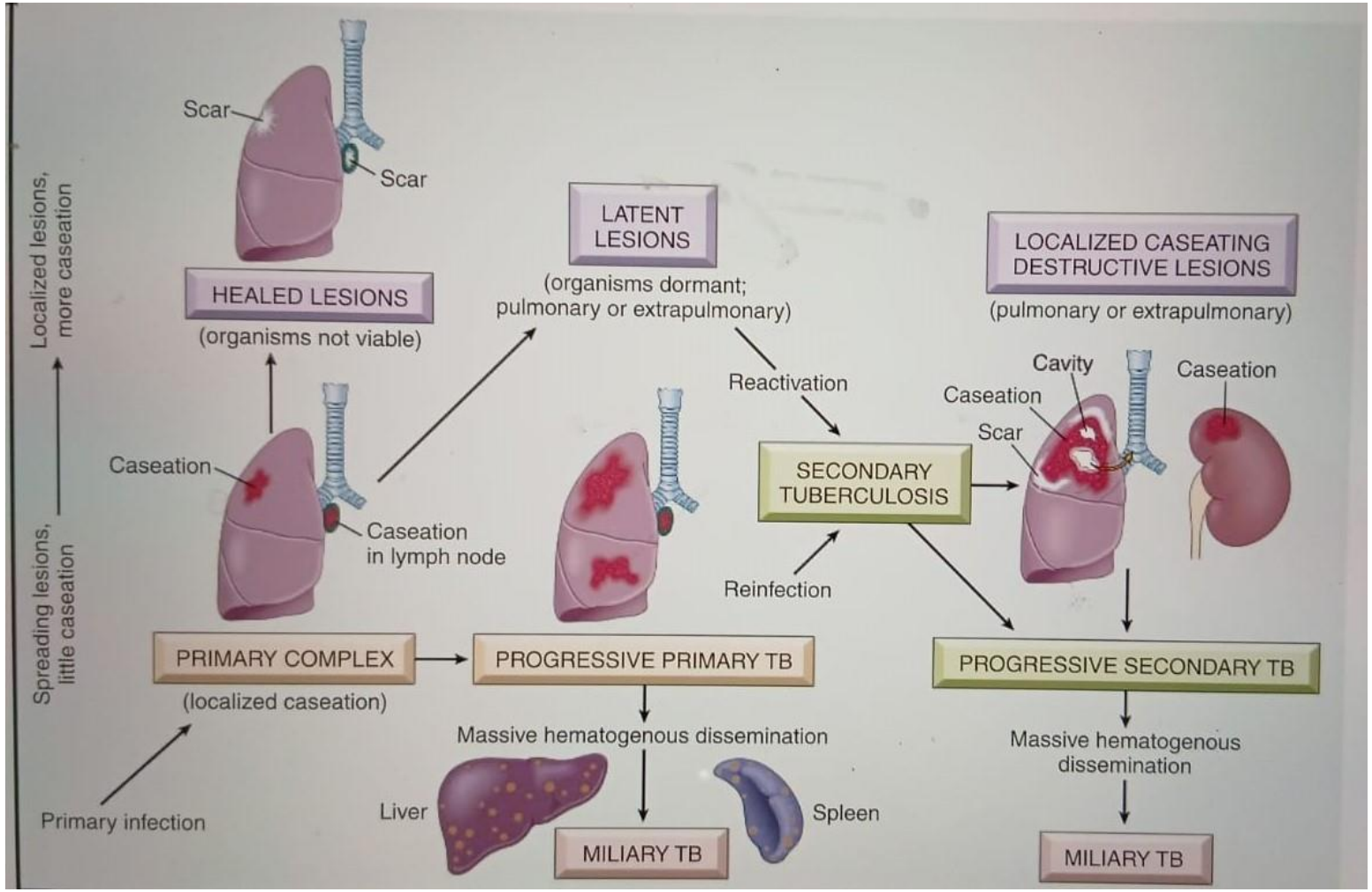


FIGURE 23-5. Outcomes of untreated primary TB.

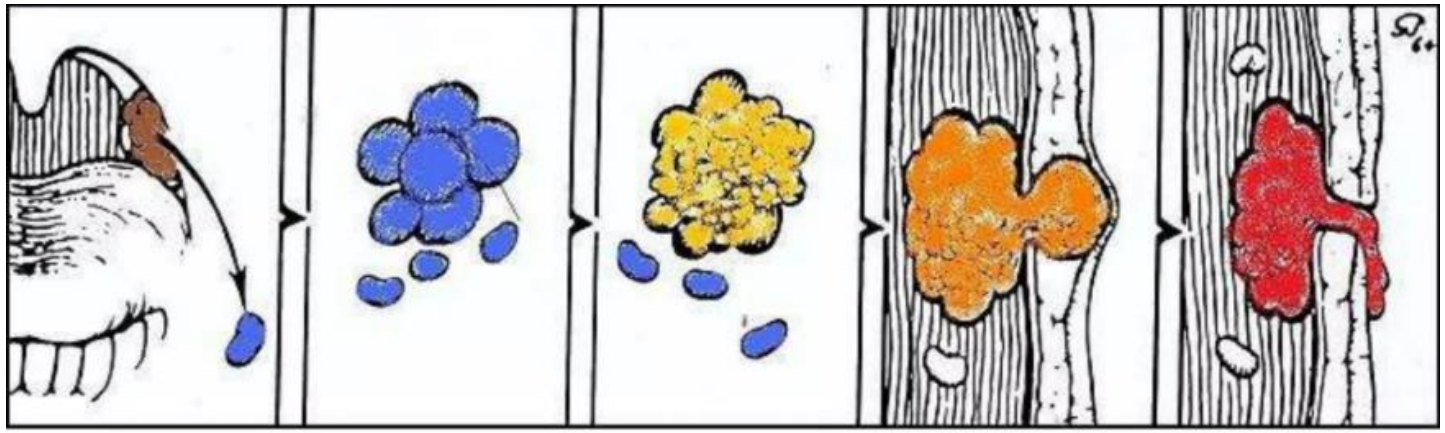
Pathogenesis



Other forms of Extrapulmonary TB

	Symptoms	Signs
Pulmonary TB	Cough productive of purulent sputum Haemoptysis Shortness of breath	Often nil to auscultate, but can have coarse crepitations (usually lung apices affected Pleural effusion
Extrapulmonary TB		
CNS: meningitis	Neck stiffness Headache Photophobia	Neck stiffness, Kernig's sign
Eyes: choroiditis	Blurred vision Ocular pain unusual Red eyes	Reduced visual acuity Ciliary injection
Skin: lupus vulgaris	Brown lesions, may have ulcers	Brown plaques which may ulcerate; can occur at mucocutaneous junctions
Lymph nodes, including scrofula	Swollen glands in neck or groin which may discharge pus via a sinus to skin	Cervical or inguinal lymphadenopathy with sinuses discharging purulent material (cold abscesses)
CVS: constrictive pericarditis	Chest pain Shortness of breath	Pericardial rub if no effusion Quiet heart sounds with an effusion Signs of heart failure
GI: ileocaecal GI: peritoneal Adrenals: Addison's disease	Abdominal pain Distended abdomen Weakness, collapse Nausea, vomiting, diarrhoea Abdominal pain Myalgia Confusion	Mass in right iliac fossa Ascites Postural hypotension Pigmentation, e.g. buccal, scars, palmar creases Dehydration
GU: renal	Dysuria Haematuria	Sterile pyuria
Skeletal: arthritis and osteomyelitis	Joint/bone pain Inability to weight-bear	Localized swelling (not hot, i.e. cold abscess) Localized pain

STAGES OF LNTB
Jones and Campbell classified peripheral tuberculous lymph nodes into following five stages:

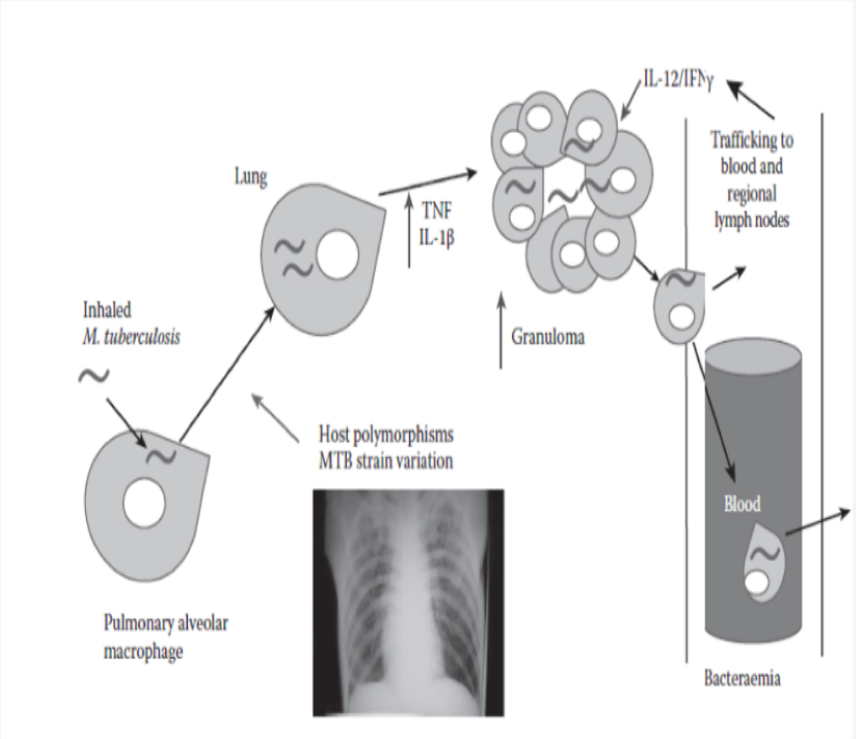


Stage I	Stage II	Stage III	Stage IV	Stage V
Enlarged firm mobile discrete nodes (Lymphoid hyperplasia with formation of tubercles & granuloma)	Large rubbery nodes fixed to surrounding tissue due to periadenitis (Caseation starts)	Central softening due to abscess formation (progressive Caseation necrosis)	Collar stud abscess formation. skin over is inflamed (Rupture of caseous material)	Sinus tract formation

Pathogenesis of LNTB

In the initial stage of superficial lymph node involvement, **progressive multiplication of M. tuberculosis occurs.** The onset of delayed hypersensitivity is accompanied by marked hyperaemia, swelling, necrosis and caseation of the centre of the nodes.

- This can be followed by **inflammation, progressive swelling and matting** with other nodes within a group.
- Adhesion to the adjacent skin may result in **induration and purplish discolouration**.
- The centre of the enlarging gland becomes soft and caseous material may **rupture into surrounding tissue** or through the skin with sinus formation.
- Tuberculous mediastinal lymphadenitis may enlarge and cause **compression of major blood vessels, phrenic or recurrent laryngeal nerves or cause erosion of bronchus**.



SYMPTOMS

Patients do not generally report significant pain at presentation.

Node tenderness during examination is noted in only 10%–35% of cases.

A draining sinus may be present in 4%–11% of cases.

Unilateral involvement of 1–3 nodes has been noted in 85% of cases.

Cervical chain involvement is most common (45%–70%) with 12%–26% in the supraclavicular region; 20% of cases are bilateral.

Clinical Features

- Usually presents as a slowly progressive , painless swelling of a single group of lymph nodes .The lymph nodes are usually initially mobile but become matted together with time
- When cessation and liquefaction occurs the swelling becomes fluctuant and may discharge through skin with formation of a collar stud abscess and sinus formation
- Approximately half of cases fail to show any constitutional features such as night sweats and fever
- The duration of symptoms at time of presentation is typically 1-2 months , varying from 3 weeks to 8 months

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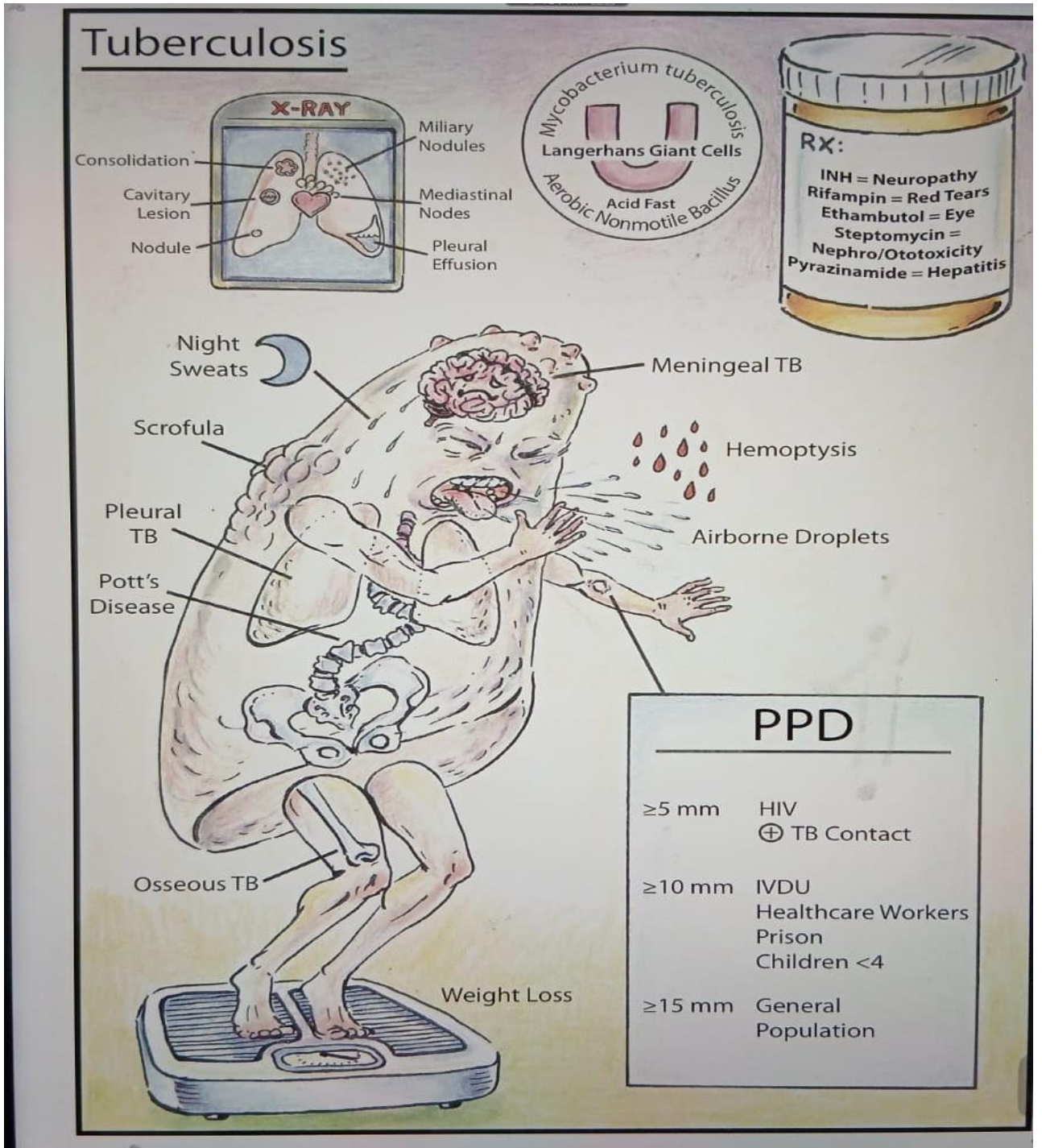

Tuberculosis
X-RAY
Consolidation
Cavitary Lesion
Nodule
Miliary Nodules
Mediastinal Nodes
Pleural Effusion
Mycobacterium tuberculosis
Langerhans Giant Cells
Acid Fast
Aerobic Nonmotile Bacillus
RX:
INH = Neuropathy
Rifampin = Red Tears
Ethambutol = Eye
Steptomycin = Nephro/Ototoxicity
Pyrazinamide = Hepatitis
Night Sweats
Scrofula
Pleural TB
Pott's Disease
Osseous TB
Weight Loss
Meningeal TB
Hemoptysis
Airborne Droplets
PPD
≥5 mm HIV ⊕ TB Contact
≥10 mm IVDU Healthcare Workers Prison Children <4
≥15 mm General Population

Progressive generalised lymphadenopathy

It can present as progressive generalised lymphadenopathy

Symmetrical adenopathy with nodes typically <3cm

HIV patients with tuberculous lymphadenitis have higher rate of disseminated disease than HIV negative patients

TBLN and HIV

- HIV infection has been presumed to be responsible for the rise in number of tuberculous lymphadenitis cases.
- Clinical manifestations depends on CD 4+ count.
  - >250 – granuloma &/or caseation necrosis-AFB ±
  - < 200–poor granuloma formation – AFB +
  - <100 –acute pyogenic abscess – AFB +++

Trends of EPTB under RNTCP: A study from south Delhi, V.K. Arora & Rajnish Gupta. Ind J Tube vol 53 No. 2 April 2006: 76-83

How to clinically differentiate different types of nodes ? For diagnosis and better management

Clinical differences between benign and malignant nodes

Feature	Malignant	Benign
Size	>2 cm	<2 cm (<1 cm)
Consistency	Hard, firm or rubbery	Soft
Duration	>2 weeks	<2 weeks
Mobility	Fixed	Mobile
Surroundings	Attached (invasion)	Not attached
Location	Supraclavicular, epitrochlear, or generalized	Inguinal, submandibular
Tenderness	Usually non-tender	Usually tender

Clinical features to differentiate benign from malignant lymphadenopathy

Matted and non matted nodes

Key Differences:

Feature	Matted Lymph Nodes	Non-Matted Lymph Nodes
Appearance	Feel fused or connected, moving as a unit	Feel separate and move individually
Possible Causes	Malignancy, infection, sarcoidosis, lymphoma	Benign conditions, infections, lymphoma
Significance	May indicate a more serious condition	More likely associated with benign causes

Consistency :based on consistency a rough guide to differentiate between benign and malignant nodes

- SOFT :inflammation/infection
- FIRM/RUBBERY: lymphomatous process
- HARD/FIXED: carcinomatous/metastasis
- FLUCTUANT: suppurative
- MATTING: infective/malignant
- PAIN: due to stretching of capsule/inflammation but can also be due to rapid growth ,hemorrhage or necrosis within enlarging node hence it is not now considered useful in differentiating benign from malignant

Lymphadenitis and lymphoma

- How to differentiate clinically ?

Lymphadenitis	Lymphoma
Surrounding inflammation	Sharply delineated
Heterogeneous structure of LN	Homogeneous disruption of LN
Central Liquefaction	Hypoechogenic on Ultrasound
Unilateral, often one level only	Several levels involvement
Tender/mobile LN	Non-tender/ non-mobile LN
Young age, adolescent	Adults, elderly persons
Favorable prognosis	Less favorable prognosis

MANAGEMNT

DIAGNOSIS /TREATMENT OPTIONS AVAILABLE

DIAGNOSTICS

- A definitive diagnosis of tuberculous lymphadenitis can be made by culture or polymerase chain reaction demonstration of M tuberculosis in an affected lymph node, thereby permitting distinction from other mycobacteria that may cause lymphadenitis.

Ultrasound

- Ultrasound is an excellent first-line investigation as it assess cervical lymphadenopathy and also enables guided fine needle aspiration cytology.
- The combination of grey-scale imaging and FNAC as a sensitivity of 92% and specificity 97% in distinguishing benign from malignant nodal disease.
- Differentiating features from neck metastasis include:
  - Nodal matting
  - Surrounding soft tissue oedema (less marked than one would expect given the size of the collections)
  - Homogeneity
  - Intranodal cystic necrosis and
  - Posterior enhancement.

continued

Ultrasound

- Doppler examination is particularly useful in helping distinguish tuberculous infection from necrotic metastatic disease.
- Reactive nodes (including those in tuberculous lymphadenitis) demonstrate prominent vascularity, but mostly confined to the hilum, whereas malignant nodes demonstrate more peripheral/capsular vascularity.

CT SCAN

CT SCAN

- CT appearances of tuberculous lymphadenitis is variable depending on the degree of caseation.
- Nodes may initially appear merely enlarged, often with attenuation similar to muscle.
- Eventually, central caseation develops and the nodes become centrally low density and eventually frankly cystic.
- They are , usually, matted together with only minor surrounding inflammatory changes.

continued

- On a CT scan, differentiating between tuberculous lymphadenopathy and lymphoma involves analysing the anatomical distribution and enhancement patterns of lymph nodes, with tuberculous lymphadenopathy often showing peripheral or multilocular enhancement, while lymphoma typically displays homogeneous enhancement
- Key CT Features to Differentiate Tuberculosis and Lymphoma in Lymph Nodes:
- **Anatomic Distribution:**
  - **Tuberculosis:** May show involvement of specific lymph node regions like the mesentery, anterior pararenal space, upper para-aortic regions, and lesser omentum.
  - **Lymphoma:** May show involvement of different lymph node regions, such as the lower para-aortic nodes and inguinal lymph nodes.
- **Enhancement Patterns (after contrast administration):**
  - **Tuberculosis:** Often exhibits peripheral or multilocular enhancement, frequently with a cystic or necrotic center.
  - **Lymphoma:** Typically shows homogeneous enhancement.
- **Other Features:**
  - **Tuberculosis:** May demonstrate calcifications in some cases.
  - **Lymphoma:** May demonstrate a "sandwich sign" (enlarged lymph nodes at the margin of the small bowel).

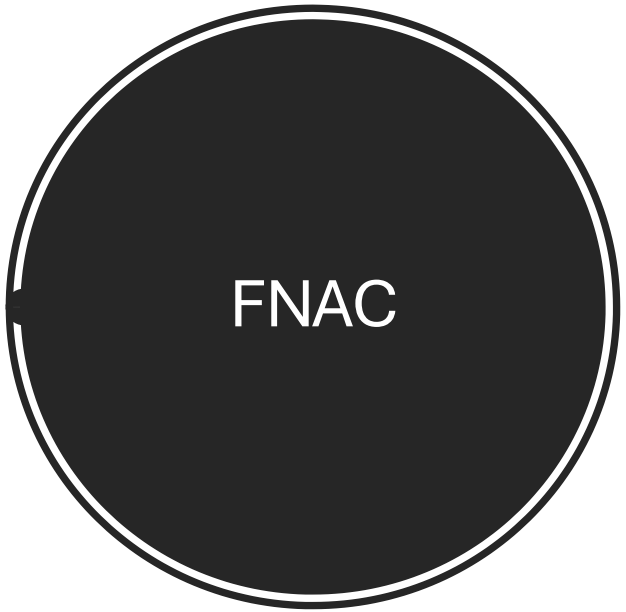
CONTINUED

WithContrast-enhanced CT, tuberculous lymphadenitis is associated with higher incidence of peripheral enhancement with multilocular appearance and heterogeneous attenuation, compared with lymphoma.

MRI

MRI

- MRI appearances are similar to those of CT, ranging form homogeneously enlarged nodes, to cystic transformation with peripheral enhancement.



FNAC

- FNA is first-line diagnostic technique, especially in tuberculosis-endemic countries, where the test is both sensitive and specific.
- FNA is safer, less invasive, and more practical than biopsy, especially in resource-limited settings.
- Yield : 48 - 83%

Culture

- Culture remains the gold standard for diagnosis, but may take 2–4 weeks to yield results.
- A positive acid-fast bacilli (AFB) stain result indicates a mycobacterial etiology and has excellent specificity for M. tuberculosis in adults.
- Following Histologic features support a diagnosis of probable tuberculosis in AFB-negative, culture-negative cases,
  - nonspecific lymphoid infiltrates,
  - noncaseating granulomas,
  - Langerhan giant cells in areas of extensive caseous necrosis.

Limitations of Culture:

- Culture remains the gold standard for diagnosis but may take 2-4 weeks to yield results ,leading to delay in initiating treatment
- The paucibacillary nature of lymph node specimen means the number of bacteria present can be too low to detect by culture leading to false negative results

BIOPSY

- Excisional biopsy is the most invasive approach to diagnosis; however, it has the highest sensitivity and may produce a more rapid and favorable symptomatic response and has been recommended in cases involving multiple nodes.
- Complications of biopsy include postsurgical pain, wound infection, sinus formation and scar.

Other test include

AFB SMEAR MICROSCOPY

- **Can be used to detect MTB in various extrapulmonary samples like pleural fluid, cerebrospinal fluid (CSF), urine, pus, and lymph node aspirates.**
- **Specificity :** 80.95% to 100%
- **Limitations:**
- Low sensitivity 34.6% to 74.1%, especially in samples with low bacterial load.
- Cannot detect rifampicin resistance

GENE XPERT

- Offers higher sensitivity compared to AFB smear microscopy, 71.6% to 90.1% and specificity (around 78.8% to 100%) compared to AFB smear microscopy. leading to earlier and more accurate diagnosis
- Can detect rifampicin resistance, which is crucial for guiding treatment decisions
- May have lower sensitivity in some extrapulmonary specimens, like ascitic fluid.
- Cost can be higher than AFB smear microscopy.
- Requires specialized equipment and trained personnel

Combined Approach

- Combined Approach:
- In practice, a combined approach using both AFB smear microscopy and GeneXpert is often recommended for diagnosing EPTB.
- AFB smear microscopy can be used as a preliminary test, and GeneXpert can be used to confirm the diagnosis and detect rifampicin resistance.
- The choice of which test to use first or which test to use in combination depends on the specific clinical context, available resources, and the type of sample being tested.

Tuberculin skin test

- The tuberculin skin test (TST), or Mantoux test, can be a useful tool in diagnosing tuberculous lymphadenitis, but it's not definitive and should be interpreted in conjunction with clinical findings and other diagnostic tests.
- A small amount of PPD is injected under the skin, and a reaction (induration) is measured 48-72 hours late
- **Limitations:**
- **False-positives:** Can occur due to previous BCG vaccination or sensitization to non-tuberculous mycobacteria.
- **False-negatives:** Can occur in immunocompromised individuals, elderly patients, or those with advanced TB

Tuberculin skin test interpretation

≥ 5 mm

- HIV positive
- Recent contact with an active TB patient
- Nodular or fibrotic changes on chest X-ray
- Organ transplant

≥ 10 mm

- Recent arrivals (< 5 yrs) from high-prevalence countries
- IV drug users
- Resident/employee of high-risk congregate settings
- Mycobacteriology lab personnel
- Comorbid conditions
- Children < 4 yrs old
- Infants, children, & adolescents exposed to high risk categories

≥ 15 mm

- Persons with no known risk factors for TB

Interferon gamma release assays (IGRAs)

GRAs are blood tests that measure the immune response to TB antigens (like ESAT-6 and CFP-10) by detecting the release of interferon-gamma (IFN-γ) by T-cells.

IGRAs can be helpful in diagnosing extrapulmonary TB (TB that affects organs other than the lungs) because they can detect TB infection even when the disease is not readily apparent through sputum samples

- **Body Fluid IGRAs:** IGRAs can be performed on body fluids (like cerebrospinal fluid, pleural fluid, etc.) to diagnose extrapulmonary TB.
- **Blood IGRAs:** Blood IGRAs can be used to assess overall TB infection status, which can be helpful in diagnosing extrapulmonary TB

Limitations:

- IGRAs cannot distinguish between active and latent TB infection.
- IGRAs may not be as accurate in diagnosing certain types of extrapulmonary TB, such as osteoarticular TB

- Isoniazid, Rifampin, Pyrazinamide and Ethambutol for 2 months, followed by Isoniazid and Rifampin for another 4 months.
- The 6-month recommendation is supported by studies that showed no difference between 6 and 9 months of treatment in cure rates (89%–94%) or relapse rates (3%).

TREATMENT

STEROIDS /ARE THEY USEFUL?

Steroid Therapy

- The benefit of *routine* corticosteroid therapy for peripheral tuberculous lymphadenitis is unknown.
- A double blind, placebo controlled trial involving 117 children with endobronchial tuberculosis revealed a significantly greater improvement in those who received a 37-day tapering course of steroids.

CONTINUED

- Adjunctive use of corticosteroids in TB may have
  - anti inflammatory effect
  - Inhibitory actions on the release and activity of lymphokines and cytokines leading to rapid regression of LN size & obviate potential complications.
  - Directly suppress the pathologic effects of cytokine TNF & from activated CD4+
- Even in Rifampicin containing regimen significant clinical advantage is observed.
- Prevent Paradoxical reactions.

PARADOXICAL REACTIONS /TB-IRIS

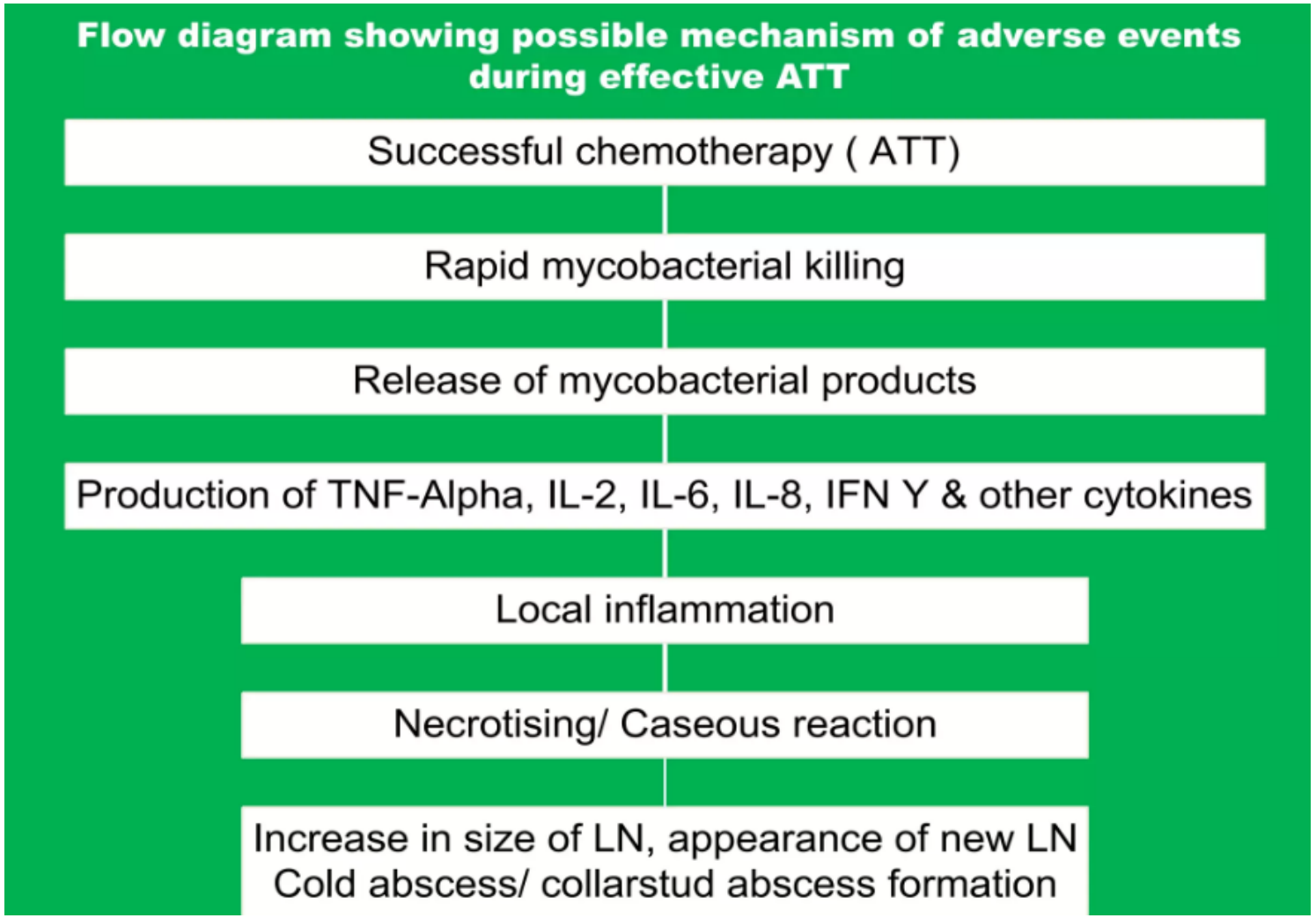
Paradoxical Upgrading Reactions

- Worsening of symptoms during treatment (ie, paradoxical upgrading reaction [PUR]).
- One definition is the development of enlarging nodes, new nodes, or a new draining sinus in patients who have received at least 10 days of treatment.

PUR

- PUR has been reported in 20%–23% of HIV-negative patients.
- It occurred at a median of 1.5 months
- Manifestations of PUR have included
  - enlarging lymph nodes in 32%–68% of cases
  - New nodes in 27%–36%
  - pain in 60%
  - draining sinuses in 12%–60%
- In addition, increased adenopathy has also been reported in 9%–11% of patients a mean of 27 months after successful treatment

MECHANISM OF ADVERSE EVENTS AFTER ATT



PUR /HOW IT CAN BE TREATED ?

- Biopsy or culture of nodes involved in PUR typically shows granuloma formation and negative culture results with or without positive AFB stains.
- Steroids have been considered as a means to reduce the robust immune response in PUR, but their use is controversial.
- Intra LN injection of depot Methylprednisolone averts most of these, if given at earliest warning signal.

INDICATIONS FOR SURGERY

- Guidelines recommend surgical excision in unusual circumstances :
  - For patients who have discomfort from tense fluctuant lymph nodes.
  - For paradoxical upgrade reactions.
  - As an adjunct to antibiotic therapy for diseas cause by drug resistant Organisms.
  - Cervical lymphadenitis due to nontuberculou mycobacteria.

NTM LYMPHADENITIS

NTM Lymphadenitis

- M. avium complex. – commonest
- M. scrofulaceum (predominant before 1970), M. malmonse & M. kansasii
- Unilateral & nontender
- Submandibular, submaxillary
- Cervical or preauricular LN in young children of 1-5 years of age
- Truly localized disease
- 92% U.S. children (1-5yrs age) have NTM disease.
- In Australia & Canada NTM LN are 10 times more common.
- Mycobacterial adenitis, caused by nontuberculous mycobacteria, such as M. avium complex, is typically seen in non-BCG immunized children in developed countries.

CONTINUED

Diagnosis

1. Simple diagnostic biopsy / incision and drainage - may lead to fistula formation.
2. FNAC is controversial.
3. Skin tests with NTM antigens.
4. NTM antigen specific Gamma interferon.

Treatment

Treatment of NTM adenitis is surgical and achieves cure rate > 70%.

Bacille Calmette-Guérin lymphadenitis

- Most common complication of BCG vaccination.
- Two forms of BCG lymphadenitis can be recognised in its natural course :
  1. Simple or non-suppurative lymphadenitis, usually regresses spontaneously.
  2. Suppurative BCG lymphadenitis distinguished by the development of fluctuations in the swelling, with erythema and oedema of overlying skin.

BCG LYMPHADENITIS

BCG LYMPHADENITIS

DIAGNOSIS

Diagnosis of BCG lymphadenitis

- Isolated axillary (or supraclavicular/cervical) lymph node enlargement.
- History of BCG vaccination on the same side.
- Absence of tenderness and raised temperature over the swelling.
- Absence of fever and other constitutional symptoms.
- Chest radiography, Mantoux reaction, and haematological analysis are not helpful. Fine needle aspiration cytology corroborates the clinical diagnosis in doubtful cases.

MANAGEMENT

Management of BCG lymphadenitis

- No role for antibiotics or Antituberculous drugs.
- Needle aspiration –
  - Recommended for suppurative BCG lymphadenitis.
  - Prevents discharge and associated complications.
  - Shortens the duration of healing.
  - Safe.
- Surgical excision

  Useful in cases with failed needle aspiration, multiloculated or matted lymph nodes, and draining sinuses.
- Non-suppurative BCG lymphadenitis is a benign condition and regresses spontaneously without any treatment.

Conclusion

- Good FNAC / needle biopsy / ZN staining / MT test & ESR make diagnosis in almost all cases.
- Optimal management of comorbid conditions.
- LNTB enlarge during ATT or appear afresh will eventually respond to treatment.
- Development of fluctuation requires immediate attention - Early surgical intervention.
- Residual LN at end of ATT should be closely monitored.

SUMMARY

Thankyou