Approach to fever with lymphadenopthy

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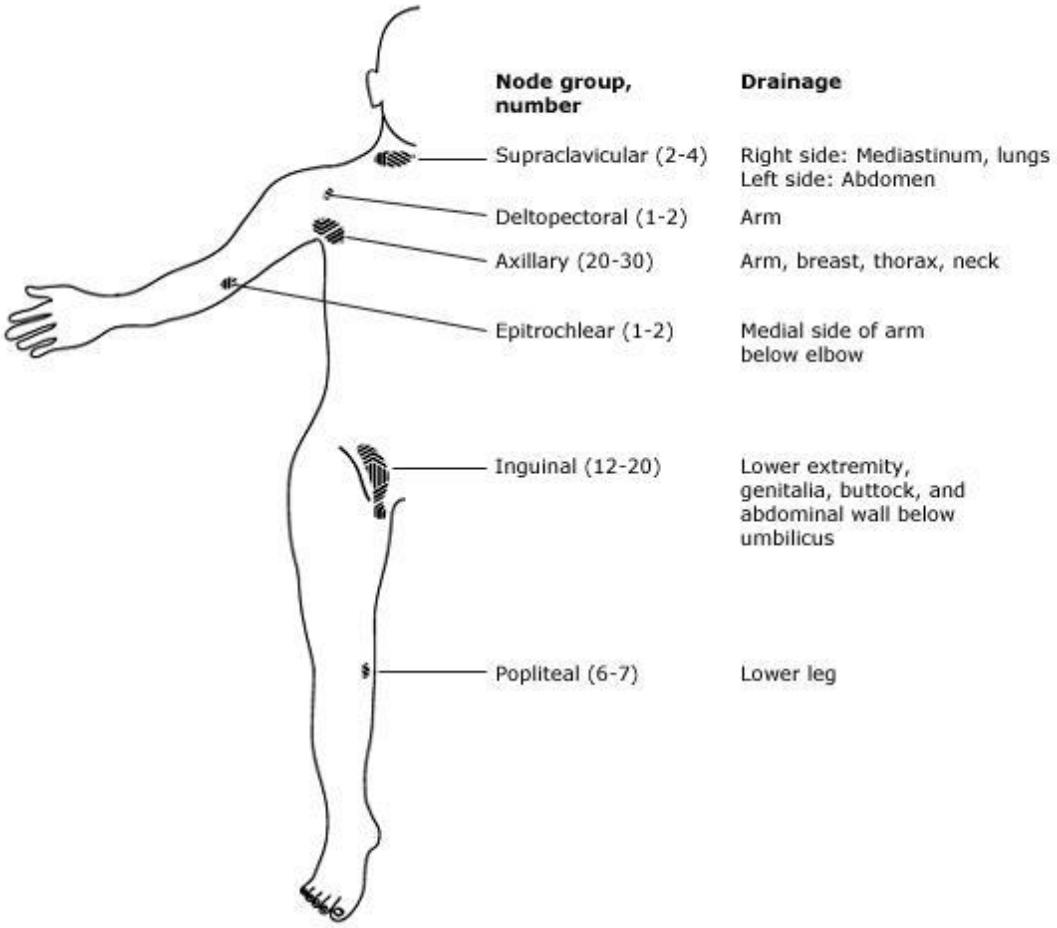
Learning Objectives

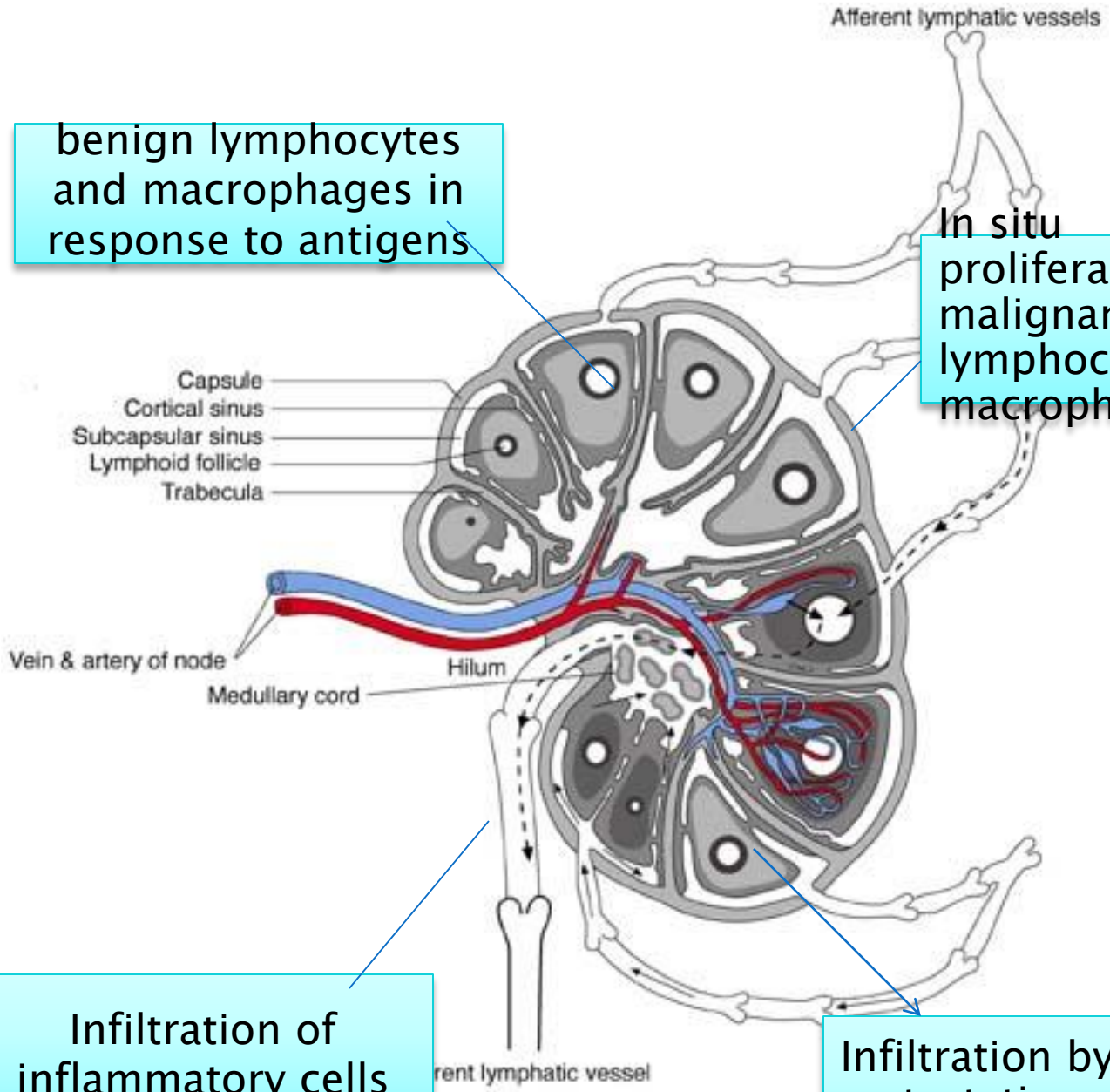
- Knowledge of nodal distribution and anatomic drainage
- Provide an approach to the patient with peripheral lymphadenopathy with case scenarios
- Be able to differentiate between benign and serious illness
- Present a substantial differential diagnosis
- Indications for nodal biopsy

Drainage of LN



benign lymphocytes and macrophages in response to antigens

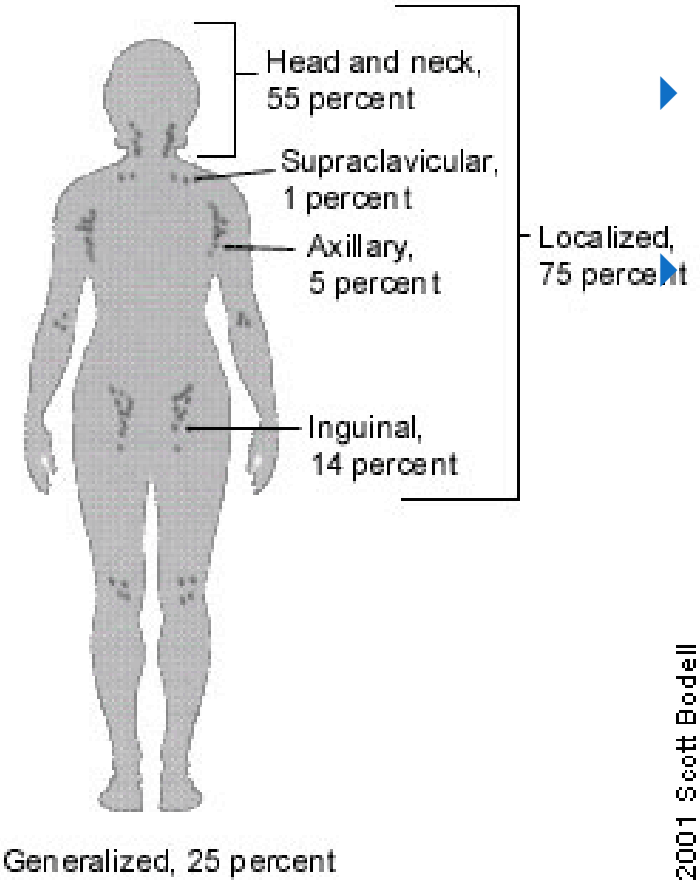
In situ proliferation of malignant lymphocytes or macrophages



Infiltration of inflammatory cells

Infiltration by metastatic malignant cells

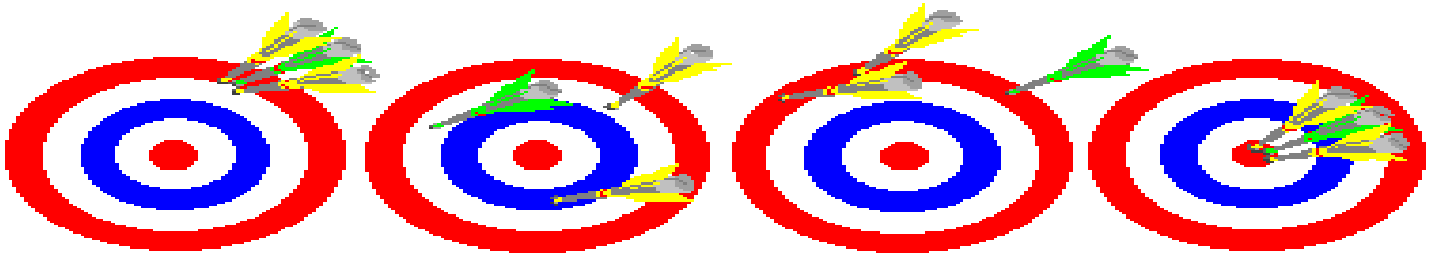
Presentation of lymphadenopathy



- 3/4 presents with localized
- 1/4 present with generalized

Peripheral lymphadenopathy

- Primary or secondary manifestation of 100 illnesses
- Most cases benign, self limited illness
- The CHALLENGE is to decide if it is representative of a serious illness…



Case 1

- 25 yr male school teacher presents to you with right sided cervical lymphadenopathy -1 week
- Nil other localisation
- His past medical history is significant for hypertension and dyslipidemia .

.

- On physical exam 2cm anterior cervical lymph node which is firm, non-tender and mobile.
- ENT exam is unremarkable.
- No skin lesions are evident.
- No other palpable lymphnodes

How should you proceed with this patient?

Have your patient follow up for annual physical next year.

Proceed to fine needle aspiration.

Check a CXR and CBC.

Have patient follow up in 3-4 weeks.

Epidemiology

- 925 biopsy.
- Age <30 79% benign 15% lymphomatous 6% carcinomas
- Age >50 40% benign 16% lymphomatous 44% carcinomas
- Age 30-50 indeterminate values

Lee Y, Terry T, Lukes RJ. Lymph node biopsy for diagnosis: a statistical study. J Surg Oncol. 1980;14:53-60.

How should you proceed with this patient?

A. Location and duration typical for viral etiology. Have your patient follow up for annual physical next year.
B. Proceed to fine needle aspiration.
C. Check a CXR and CBC.
D. Have patient follow up in 3-4 weeks.

- It has been reported in general practice, less than one percent of patients with LAP have malignancy
- Prevalence of malignancy is 0.4% in patients under 40 years and 4% in those over 40 years of age in the primary care setting.
- Prevalence rises to 17% in referral centre and soars to 40-60% in highly suspicious patients.

CASE 2

- 23 year girl , Puduchery
- h/o fever low grade last 15 days,
- h/o neck swelling for 1wk
- No h/o weight loss , loss of appetite
- No h/o cough
- No h/o travel
- PMH / Family / Personal history- non contributory

EXAM–

- B/L Cervical LN, erythematous rash,
- No hepatosplenomegaly

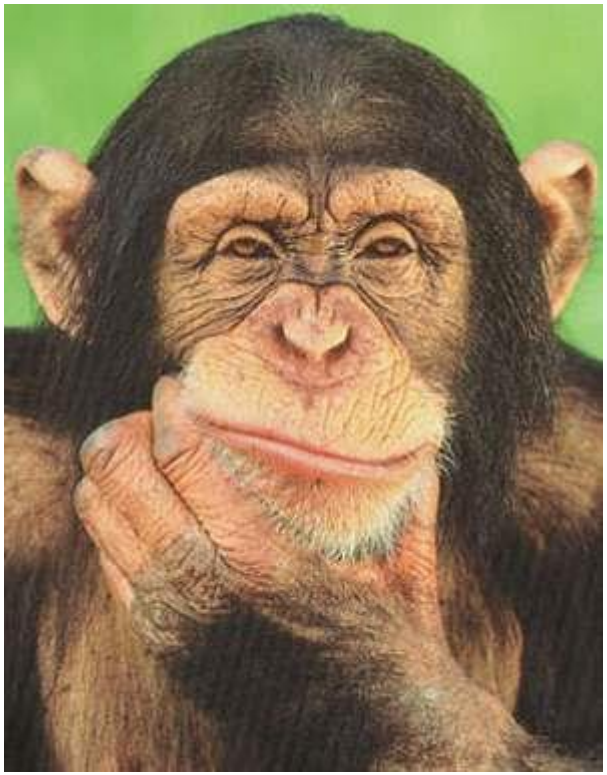
Labs–

- Hb - 8.2, Platelet - 1.1 lakh
- WBC - 4500 (N-35 %,L-60 %,M-5 %)
- LFT - S.bil -1.2, ALT- 124, ALP-156, GGTP-56
- Chest X-ray – normal
- Usg Abd - normal

What next

A. Get the FNAC / biopsy done
B. Ask for PET CT scan
C. Review your history / exam
D. Refer to ID specialist /oncologist
E. Start on antibiotics

Fever with regional lymphadenopathy



1) Suppurative lymphadenitis-

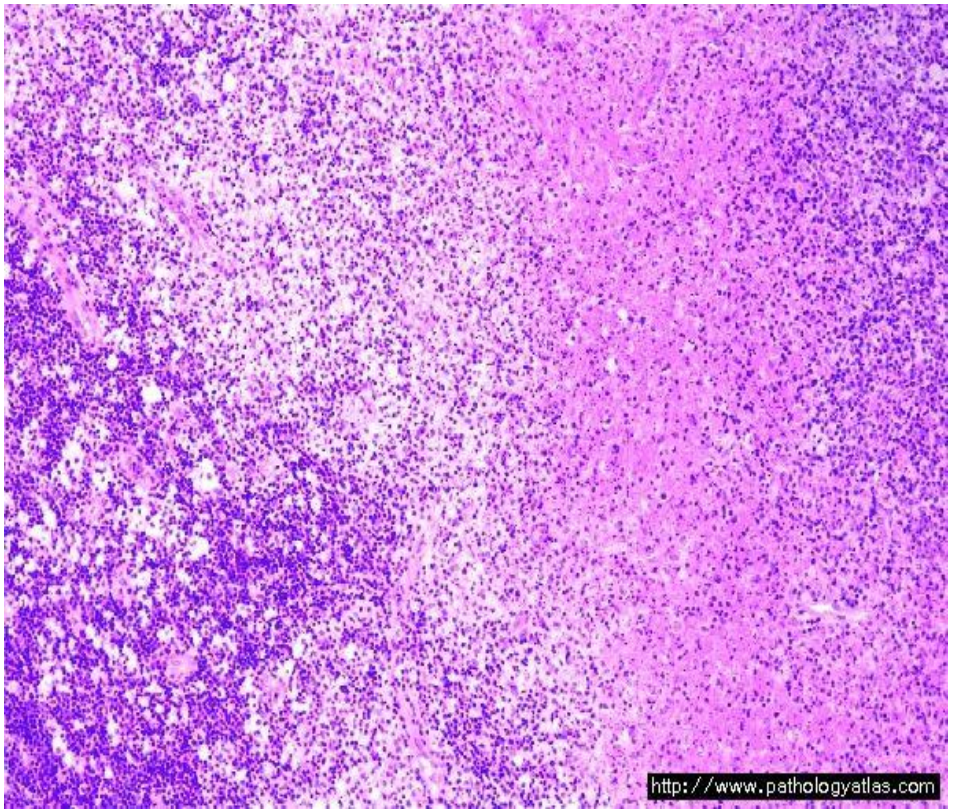
Staphylococcus aureus
Streptococcus
Anerobes (oral)

2) Non suppurative lymphadenitis-

Tuberculosis
Toxoplasmosis
Cat-scratch
Kawasaki's disease
Kikuchi's disease
Malignant, metastatic ,etc

This case

- FNAC – histiocytic necrotising picture



Necrosis → TB ?

- Granulomas & caseation necrosis–
  MTB,NTM
- Necrotizing granulomas–
  cat scratch disease, yersinia, tularemia
- Necrotizing non granulomatous –
  kikuchi's disease,
  SLE,
  kawasaki's disease

Kikuchi disease

- uncommon, idiopathic, self-limited cause of lymphadenitis.
- Cervical lymphadenopathy , with or without systemic signs and symptoms.
- Clinically and histologically , the disease can be mistaken for lymphoma or SLE

- No specific cure. NSAIDS,Steroids

Case 3

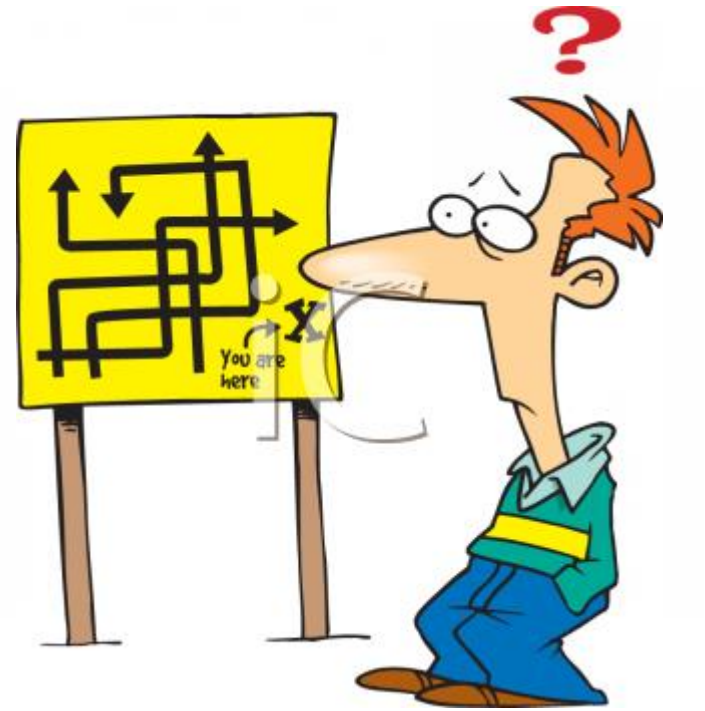
- 18male, h/o fever 7 days, no weight loss, no systemic localisation, no joint pain .
- He has cat ,recently delivered two kittens
- k/c seizure disorder on phenytoin since last 5 yrs

- On exam has generalised LN, hepatosplenomegaly
- Labs mild thrombocytopenia ,lymphocytosis with atypical lymphocyte predominance & mild hepatitis

D/D-

A. Tuberculosis
B. Lymphoma
C. SLE
D. Drugs
E. Mononucleosis syndrome

Algorithm to evaluate Lymphadenopathy



Attention to history and physical exam

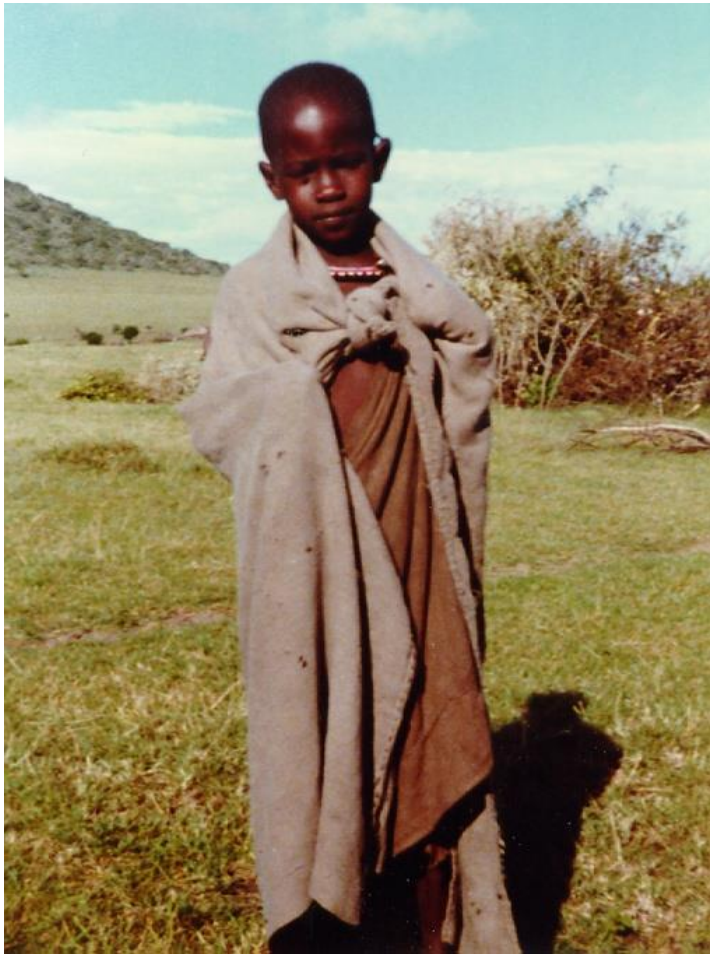
Confirmatory testing

Environmental Exposures

- Cat Exposure - Cat-scratch disease, Toxo
- Under-cooked meat - Toxo
- Tick-Bite - Lyme's Disease Tularemia
- Recent Blood transfusion - CMV
- High-Risk Sexual Behavior - HIV, syphilis, HSV,
- Hep B, CMV
- IVDU - HIV, , Hep B, Hep C

Occupational Exposures

Travel History

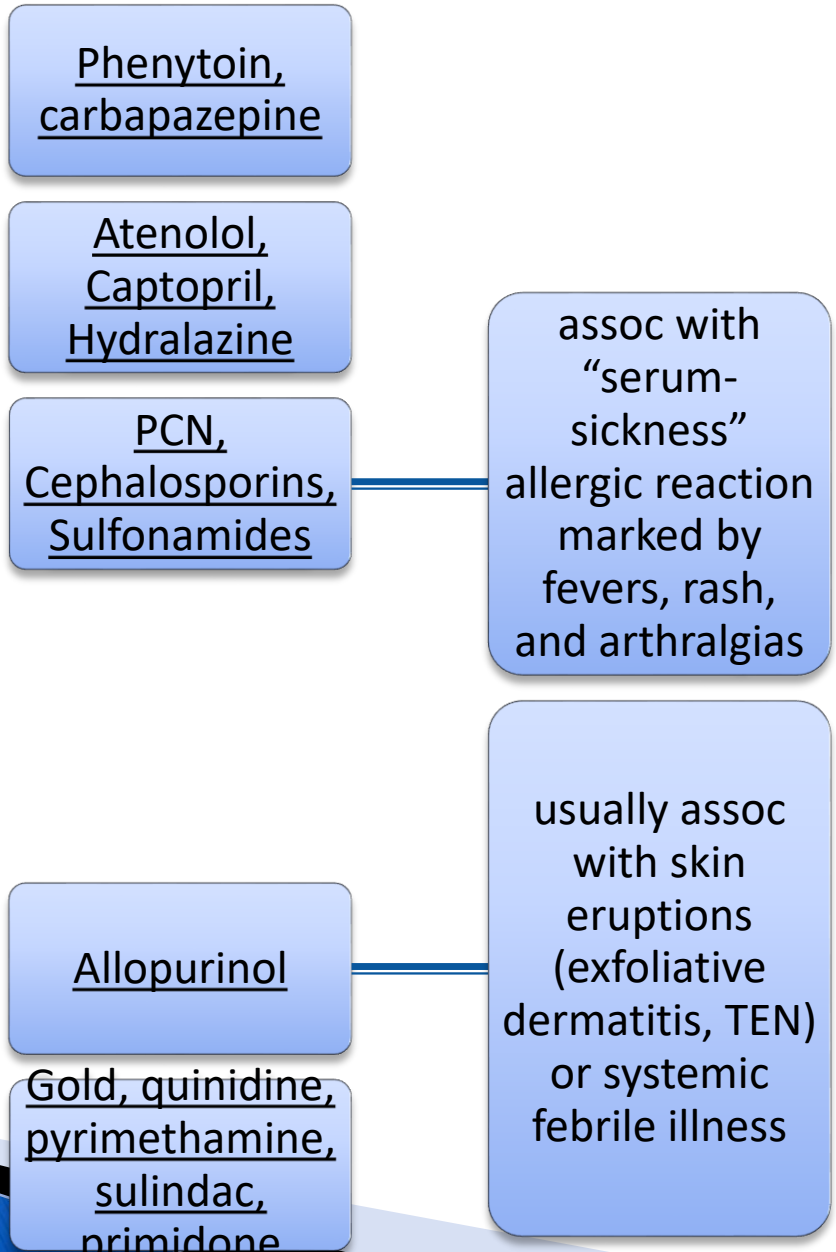


Where you stand depends on where you sit”

Epidemiological clues

Occupational	
Hunters, trappers	Tularemia
Fishermen, fishmongers, slaughterhouse workers	Erysipeloid
Travel-related	
Arizona, southern California, New Mexico, western Texas	Coccidioidomycosis
Southwestern United States	Bubonic plague
Southeastern or central United States	Histoplasmosis
Southeast Asia, India, northern Australia	Scrub typhus
Central or west Africa	African trypanosomiasis (sleeping sickness)
Central or South America	American trypanosomiasis (Chagas' disease)
East Africa, Mediterranean, China, Latin America	Kala-azar (leishmaniasis)

Medications which can cause LN



This patient

- Fever, Gen LN , hepatosplenomegaly
- Lymphocytosis , atypical lymphocyte , Generalized lymphadenopathy

Mononucleosis syndrome

Mononucleosis Syndrome

- Symptoms-

  sorethroat , fever , fatigue , malaise , pharyngeal Inflammation ,

- Signs-

  lymphadenopathy , splenomegaly , hepatitis ,

- D/D–

  EBV, CMV, Toxoplasmosis, Acute seroconverion syndrome (HIV)

- Suspect if

  lymphocytosis with atypical lymphocyte

(>50% lymphocyte,>10% atypical lymphocyte)

- Serologies-

  CMV ,EBV VCA IgM, Toxo IgM

CASE 4

- 10 year old; Male
- Swelling in the neck 5 months
- Fever for one month
- Weight: 15 Kg; Height: 113 cms
- Physical Exam – Multiple lymph nodes in the neck; vertical and horizontal; non tender; mobile;
- other: unremarkable

Investigations

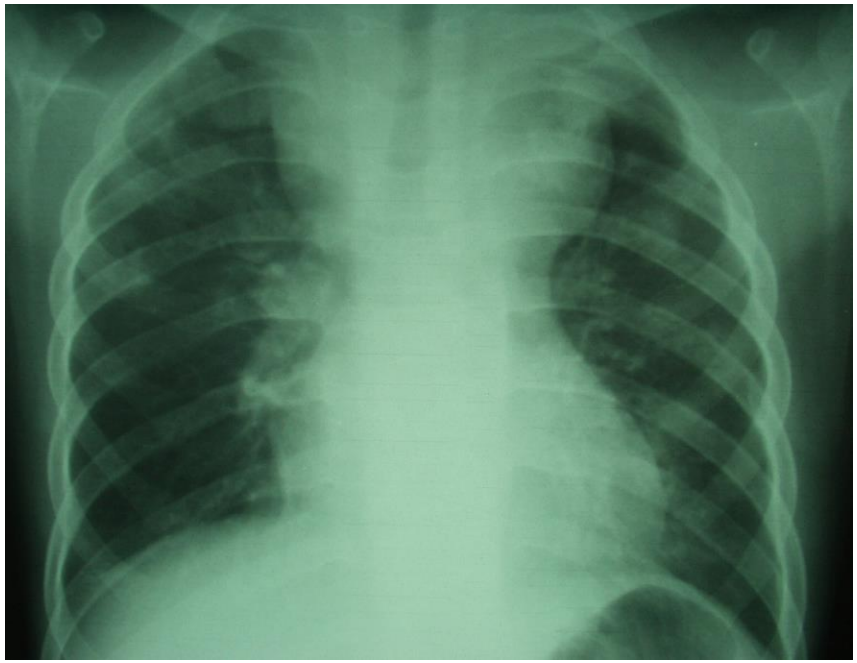
- Had a routine CXR
- Blood: WBC: 7,000/cmm; N: 72%; L: 28%; Hb: 8.4gm%.

Mediastinal mass:

a. Malignancy

b. Tubercular

c. Sarcoidosis

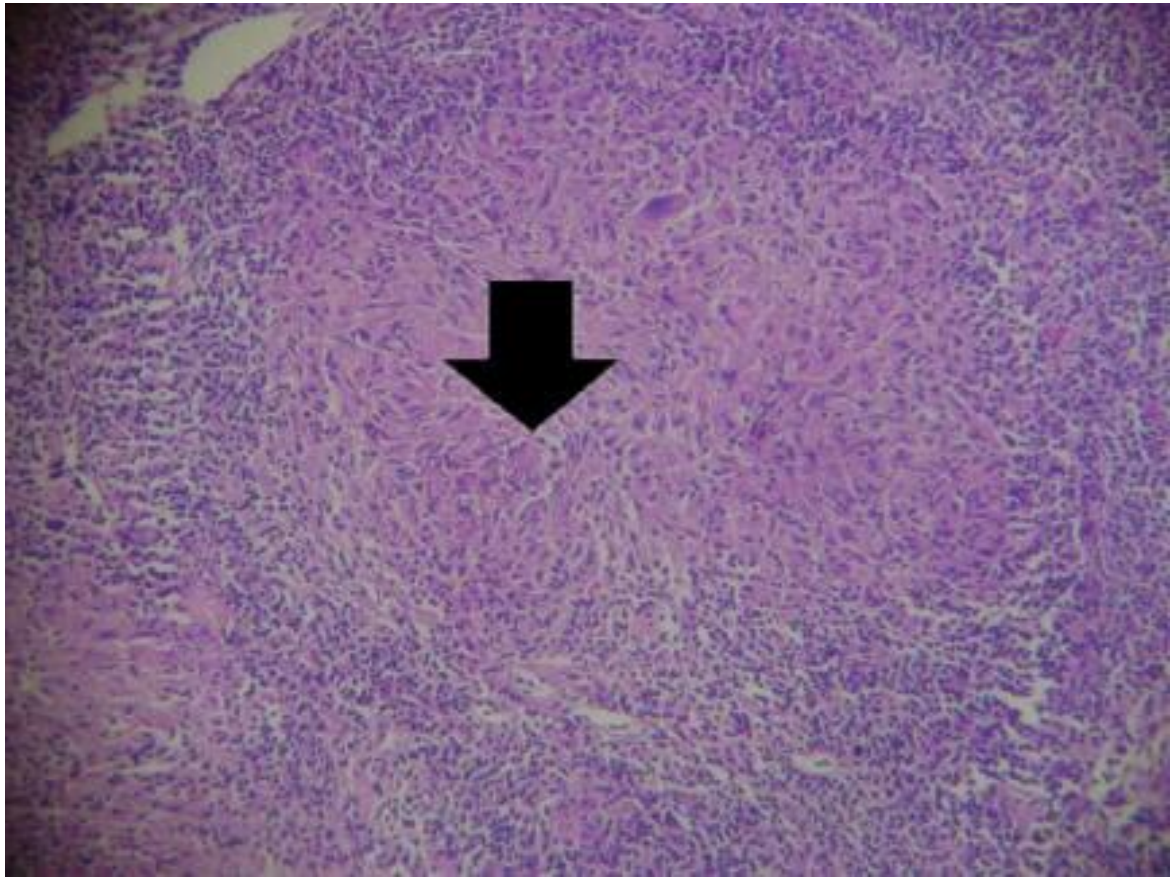


This case

- Nospecific- no pressure effect of mass sorrounding structures
- Chronic onset with fever and loss of weight
- mass detected on CXR
- Physical findings : cervical lymphadenopathy; fever; loss of weight.
  - **50% mediastinal masses are malignant in children**

What next???

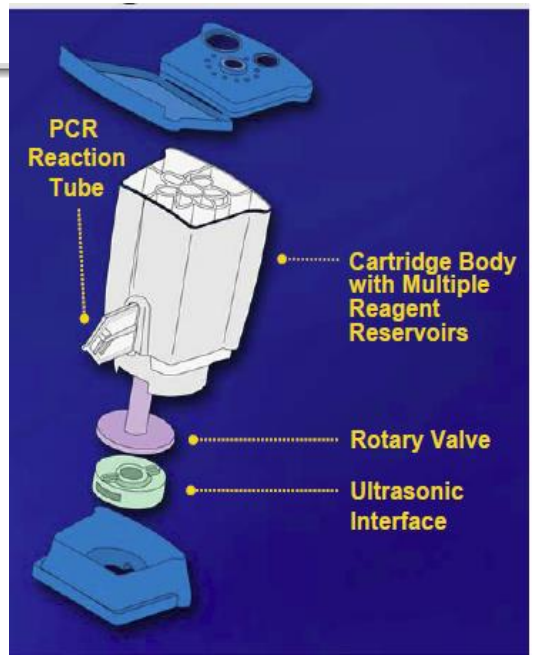
- BIOPSY



- What tests would you send the sample for?
  - HPE
  - AFB smear and culture
  - Xpert MTB RIF

GeneXpert® – a Molecular Lab in a Cartridge
Fully-Integrated Sample Preparation, Amplification and Detection

- **Has dramatically improved the rapid diagnosis of lymph node TB**
- **The sensitivity and specificity of the Xpert assay is 91.5% and 70.4% respectively.**



(International Journal of Mycobacteriology Volume 4, Supplement 1, March 2015, Pages 112)

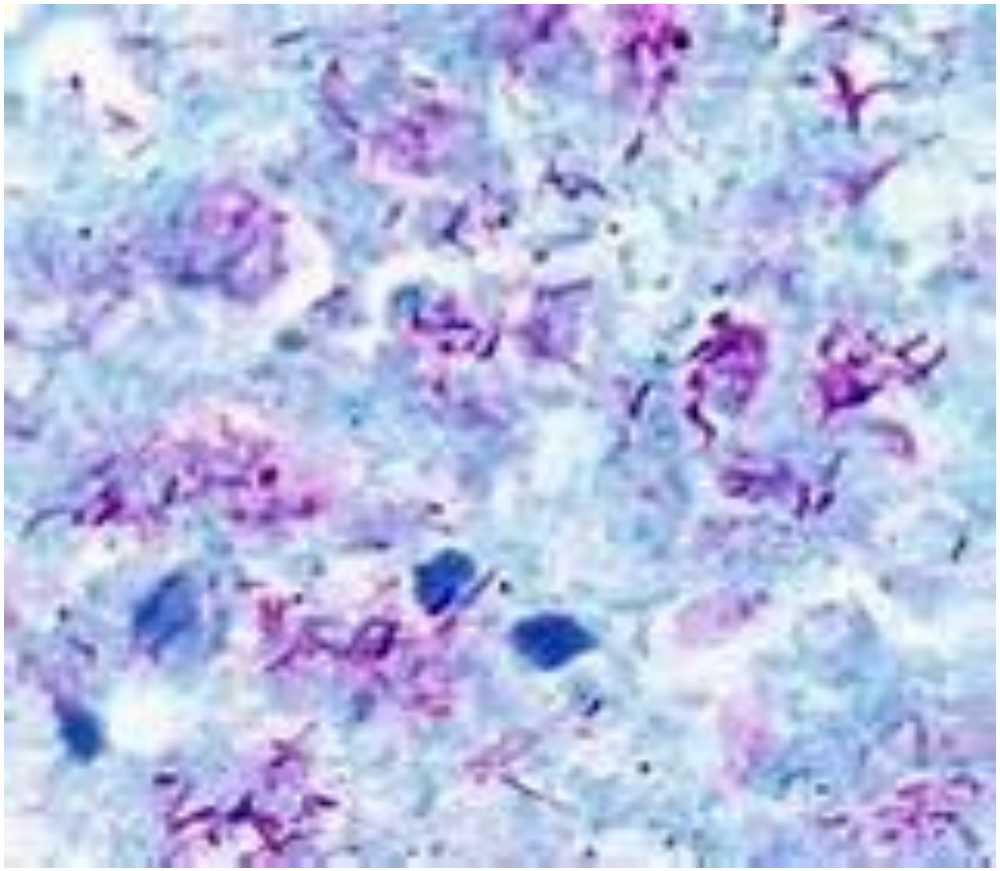
JOURNAL OF CLINICAL MICROBIOLOGY, July 2011, p. 000
0095-1137/11/$12.00 doi:10.1128/JCM.02319-10

Xpert MTB/RIF: a New Pillar in Diagnosis of Extrapulmonary Tuberculosis?[▽]

Viral Vadwai,[1] Catharina Boehme,[2] Pamela Nabeta,[2] Anjali Shetty,[1] David Alland,[3] and Camilla Rodrigues[1]*

Specimen	Xpert Sensitivity			Xpert Specificity
	All C +	S – C+	S + C +	
Biopsies	54/ 70 (77)	21 /34 (62)	33/36 (92)	157/208 (75)
Pus / Abscess	54 / 56 (96)	8 /9 (89)	46/47 (98)	39/84 (46)
Body Fluids	16/ 21 (76)	8 /13 (62)	8/8 (100)	63/71 (89)
CSF	1/ 3 (33)	1/3 (33)	0/0 (0)	18/19 (95)

AFB smear and cultures positive



This case

- Importance of tissue diagnosis
- Cultures are crucial

What's appropriate??

Fine Needle Aspirate

- Convenient, less invasive, quicker turn-around time
- Discordance of 17% between FNA and BX

Examples of appropriate patient to refer on to biopsy

- Solitary hard cervical nodule in older patient
- Supraclavicular lymphadenopthy
- Generalized firm/rubbery lymphadenopathy with systemic symptoms

Rules for Excisional Biopsy

- Use the largest/most abnormal node palpable.
- Avoid previously irradiated areas if possible
- Supraclavicular> cervical> axillary>> inguinal
- Always ask for cultures

Yes and No No's in lymphadeopathy

Considerations for histological diagnosis:

- Lymphoma suspects -excisional lymph node biopsies are preferred,
- If suspicion for an underlying malignancy is high, an unrevealing lymph node biopsy should be considered non-diagnostic rather than negative for malignancy, and further work-up should be pursued.

Report…..

- Atypical lymphoid hyperplasia should be considered non-diagnostic rather than negative for a malignancy,

- Patients should be carefully followed and an additional lymph node biopsy strongly considered

No-No's of LN

- DO NOT use glucocorticoids unless LN is life-threatening or systemic illness dictates
  - eg. SLE flare, airway obstruction, cord compromise, SVC syndrome
    a. Steroids can obscure some diagnoses (lymphomatous disorders)
  - b. Steroids and delay healing or activate indolent infections
  - Inguinal node biopsy should be avoided, since the diagnostic yield at this site is often low

Conclusions

- Generalized LN should always prompt further clinical evaluation
- Repeated examination helps
- **Most important is detail & elaborate history**
- Planning BIOPSY/ FNAC in time is important
- Cultures are crucial


Thank You!