Joint Clinical Meeting
A Case of fever

January 2008

Dr. Cheng Hei Wan Lian

NDH

Demographic data

- 38/F
- Indonesian Maid
- Working in Hong Kong for 5 years
- c/o fever x 2/7

At triage

- Ambulatory
- Alert & conscious
- Temp 39.2°C
- BP 124/80, P 106
- RR 16 SpO2 98% (room air)

How to approach this patient?

- History
- Physical Examination
- Investigation
- Treatment

History?

- Chief complaint
  - Fever
- Any other history ?
  - Fever
  - Headache
  - Vomit & Vomitus details
  - Associated symptoms
  - Travel history
  - Past medical history

Fever

- Definition
  - Oral temp :> 37.5°C
  - Anal/ tympanic temp: > 38°C
- Grading
  - Low grade 37.3 – 38°C
  - Moderate grade: 38-39°C
  - High grade: 39.1-41°C
  - Hyperthermia fever > 41°C

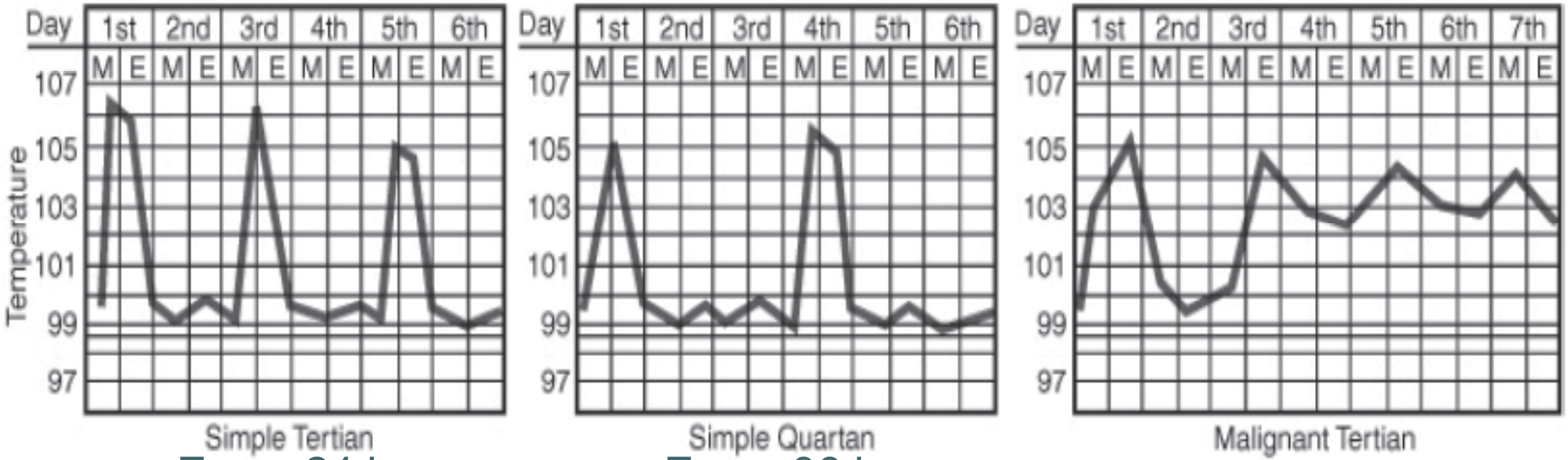
Continuous	Temp varies < 1'C over several days	Pneumoia, UTI, typhus
Biphasic	Recurs only once	Dengue, leptospirosis
Relapsing	Recurrent over days or weeks	Malaria, lymphoma
Remittent	Temp do not return to normal each day	TB, endocarditis, typhoid
Intermittent	Elevated temp for some hours of the day	Abscess, malaria
Pulse-temp dissociation	Pulse slower than normal temperature rise	Typhoid rickettsia

Fever pattern

P. vivax
P. ovale

P. malariae

P. falciparum



Every 24 hrs

Every 36 hrs

Variable

History

- Diffuse headache, myalgia & malaise
- Vomiting > 10 times, undigested food and fluid
- No abdominal pain/ diarrhea
- No LOC/seizure/ HI
- No URI symptoms
- No urinary symptoms or PV discharge
- No rash
- No bite/ sting
- TOCC –ve
- Unremarkable past health

Physical Examination

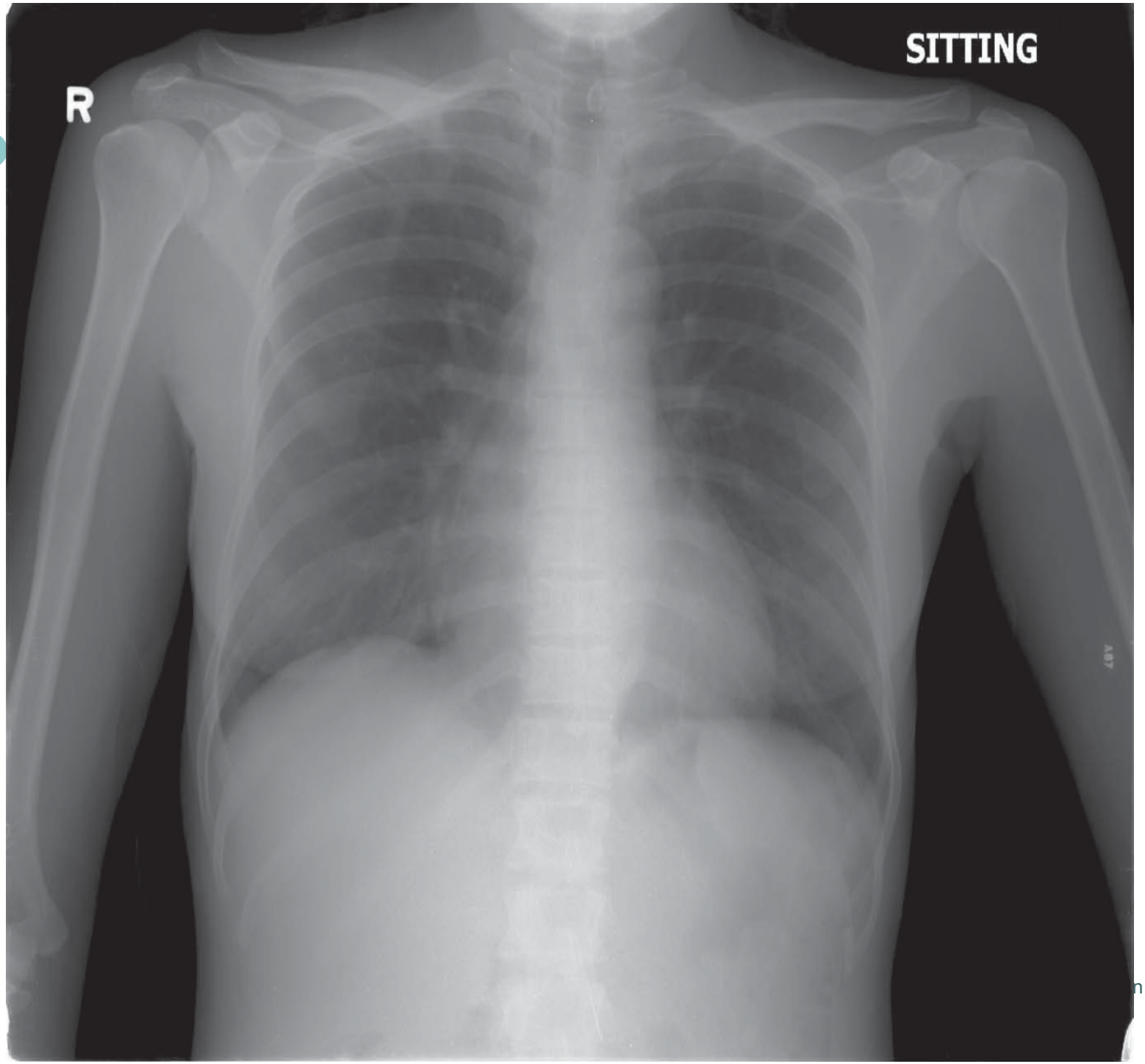
- Temp (tym) 39.2°C
- Non toxic looking
- BP 124/80, P 106, Hydration fair
- No LN, no skin rash/lesion
- HS dual, no murmur
- RR 16 Chest clear
- Abdomen soft, non-tender, no mass

Physical Examination

- Alert neck soft, no stiffness
- Cranial nerves grossly normal
- Motor & sensory normal
- Fundi no papilloedema

Investigation in A&E?

- WBC 5.6
- Neu 81.3%, Lym 13.6%
- Hb 13.2, Plt 296
- RLFT, albumin normal
- Amylase 265
- CXR clear lung field, no hilar mass
- Urine multistix WBC 2+



n 2008

Differential diagnosis

- Gastroenteritis
- Flu
- Genitourinary causes e.g. UTI/ PID
- Meningitis/ encephalitis
- Systemic infection

Differential diagnosis

- ? UTI
- Pyuria

UTI	**Urethritis**
TB	**Renal or bladder calculi**
Glomerulonephritis	**Chemical cystitis**
Contamination (false +ve)	**Pelvic appendicitis**

Management

- Antipyretic
- ?Discharge home
- ?Admit observation room
- ?Admit to medical unit

Progress

- Admitted to observation room
- Treatment:
  - panadal, gravol, oral Augmentin
- Fluctuating temp, up to 39.6°C
- Still persistent headache with malaise
- Vomited once

- How will you manage this patient?

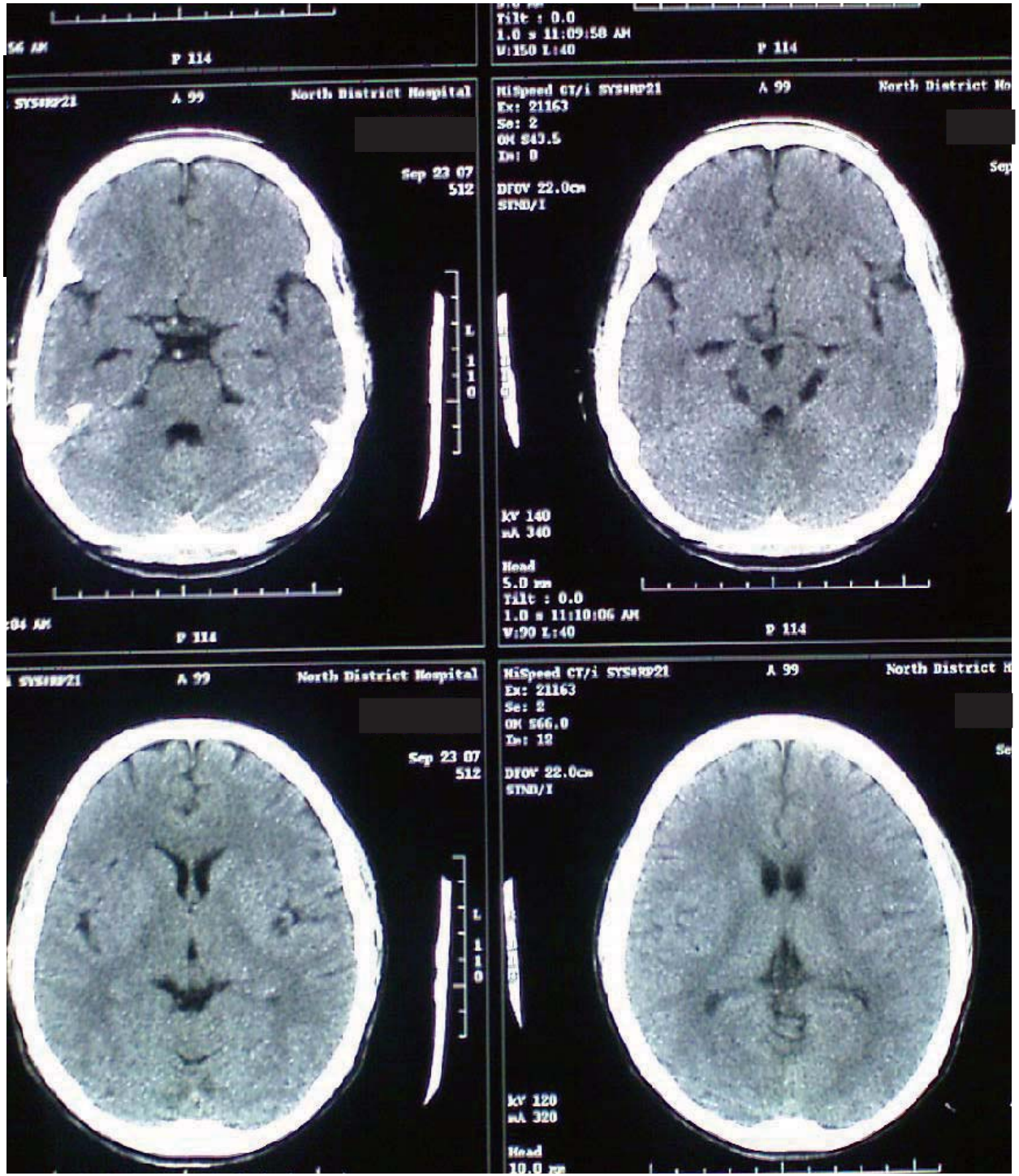
Progress D2/D3

- Admitted to Medical ward
- Initial ddx : fever/ ? URTI
- IV Augmentin started

- Still persistent Fever+
- Nausea & vomiting
- What further Investigation ?
  (D5 fever)

Further Investigation

- ESR 42, CRP<1
- NPA –ve, sputum AFB smear –ve
- MSU
  - moderate no. of WBC (10,000-100,000),
  - insignificant growth
- EMU AFB -ve
- Blood C/ST –ve
- Malaria, widal test –ve
- CT brain performed


P 114
A 99
North District Hospital
Sep 23 07
512
Tilt : 0.0
1.0 s 11:09:58 AM
W:150 L:40
HiSpeed CT/i SYS#RP21
Ex: 21163
Se: 2
DFOV 22.0cm
STND/I
kV 140
mA 340
Head
5.0 mm
Tilt : 0.0
1.0 s 11:10:06 AM
W:90 L:40
kV 120
mA 320
Head

2 Jan 2008

Progress D4

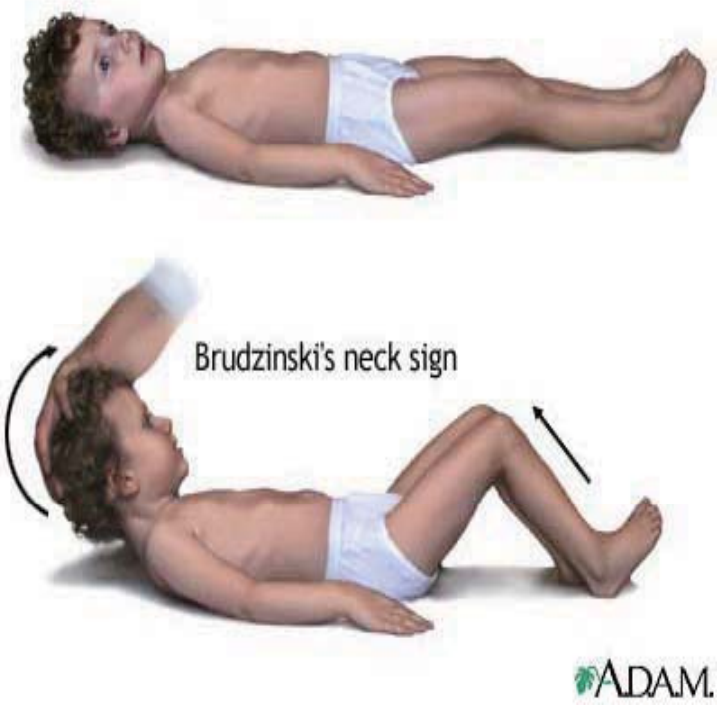
- Fever persisted, up to 40°C
- Headache, nausea & vomiting
- Vomiting 1-2 times per day, fluid

- What other ddx?
- What other investigation?

Meningitis

- Neck stiffness
- Kernig's sign
  - *Severe stiffness of the hamstrings causes an inability to straighten the leg when the hip is flexed to 90 degrees*
- Brudzinski's sign
  - *Severe neck stiffness causes a patient's hips and knees to flex when the neck is flexed.*


Kernig's sign
A.D.A.M.


Brudzinski's neck sign
A.D.A.M.

What other investigation?

- Lumbar puncture on D4
  - Opening pressure (10cm)
  - CSF color (clear CSF)
  - Cell count, gram stain
  - Protein. Glucose
  - C/St, ZN stain, AFB culture,
  - Cryptococcus
  - Herpes simplex/ varicella zoster
- Blood glucose

Meningitis

- Any empirical treatment?
- *COC guideline on Antibiotic use in A&E (July 2007)*
- Cefotaxime (Claforan) 2g OR Ceftriaxone (Rocephin) 2g

- *HAHO CPG o Antibiotics use*
- Penicillin G 4MU q4h IV and
- Cefotaxime 1.5-2g q4h IV OR
- Ceftriaxone 2g q12h IV

Empirical Treatment

- Started on IV Rocephin
- To cover for suspected meningitis and persistent fever

Date Collected: 25/09/07 15:08
Date Arrived: 25/09/07 16:35
Specimen:- CSF
Site:- LP

Appearance : Clear

Gram stain : No organisms seen

Cell count : WBC : 162 x 10 E6/L
RBC : 12 x 10 E6/L

Differential count : Polymorphs : 25 %
Lymphocytes : 75 %

India Ink : Cryptococcus not seen

Routine culture :-

Please see comment below

No growth after 7 days incubation.

Authorized By: 02/10/07 12:07

*** This Laboratory is NATA & RCPA accredited ***

********** End of report **********

Collect Date	25/09/07	25/09/07		
Collect Time	15:07	15:08		
Arrive Date	25/09/07	25/09/07		
Arrive Time	15:44	16:05		
Request No	L1202621	L1202786		
Urgency	URGENT	URGENT	Reference Range	Units
CSF Protein	--	1.36 H	0.15 - 0.45	g/L
CSF Glucose	0.9 L	--	2.8 - 4.4	mmol/L

Footnotes:
CGLU - CSF glucose must be interpreted with that of plasma. In 70% of bacterial meningitis cases, CSF/plasma glucose ratio is <0.31 while in 99% of cases, CSF glucose is <1.9 mmol/L and CSF/plasma glucose ratio is <0.23 (vs viral meningitis).

Authorized by : Eleanor Chantel

********** End of report **********

Final report for permanent retention in patient's record.

Report Destination : NDH/--/4C - 4C, NDH NDH - MR20201/ND

- Glucose (spot) 6.1

So what is your opinion

- ? Bacterial
- ? Viral
- ? TB
- ? Fungal

CSF results

Typical CSF findings in meningitis

	Normal	Viral	Bacterial	TB / Cryptococcal
Appearance	clear	clear	turbid	turbid/viscous
Mononuclear cells (/mm^3)	<5	10-100	<50	100-300
PMN (/mm^3)	nil	nil	200-3000	0-200
Protein (g/l)	0.2-0.4	0.4-0.8	0.5-2.0	0.5-3.0
CSF/blood glucose	>1/2	>1/2	<1/2	<1/2

Progress(D6)

- CSF reviewed →ZN –ve
- Started Pen G/ Claforan & IV acyclovir

- SR : compatible with TBM
- Acyclovir off
- Started anti-TB treatment
- Notification to DH
- Transferred to IT ward

Standard treatment for TB

- Which drugs would you start?
- Duration of anti-TB medication

Extrapulmonary TB	Treatment
TBM	3HRZE+/-S → 9HR+/-E
Miliary	3HRZ + (E or S)→ 9HR+/-E
Bone & joints	2HRZ + (E or S)→10HR
Lymphendenitis (cervical)	2HRZ + (E or S) →4HR
Pericarditis, peritonitis, GU tract	Same as uncomplicated PTB Total 9 months

Progress

- Fever downward trend
- Complicated with deranged LFT due to anti-TB medication
- Titration of medication
- CSF broth culture showed AF bacilli (D19)

TB drug related Hepatoxicity

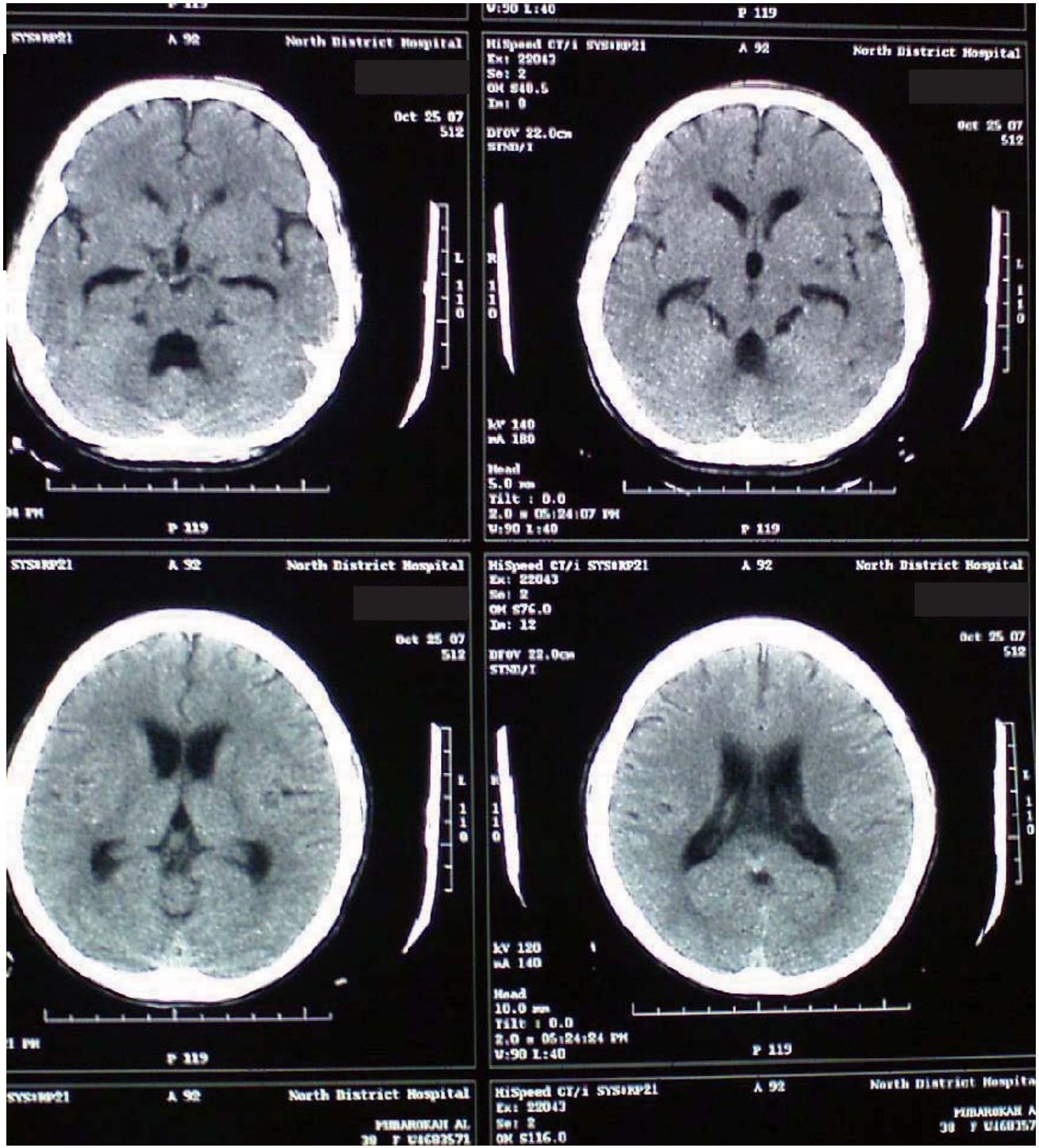
- *Isoniazid, rifampicin, pyrazinamide,*
- *Prar-aminosalicylic acid, prothionamide & ethionamide*

Progress

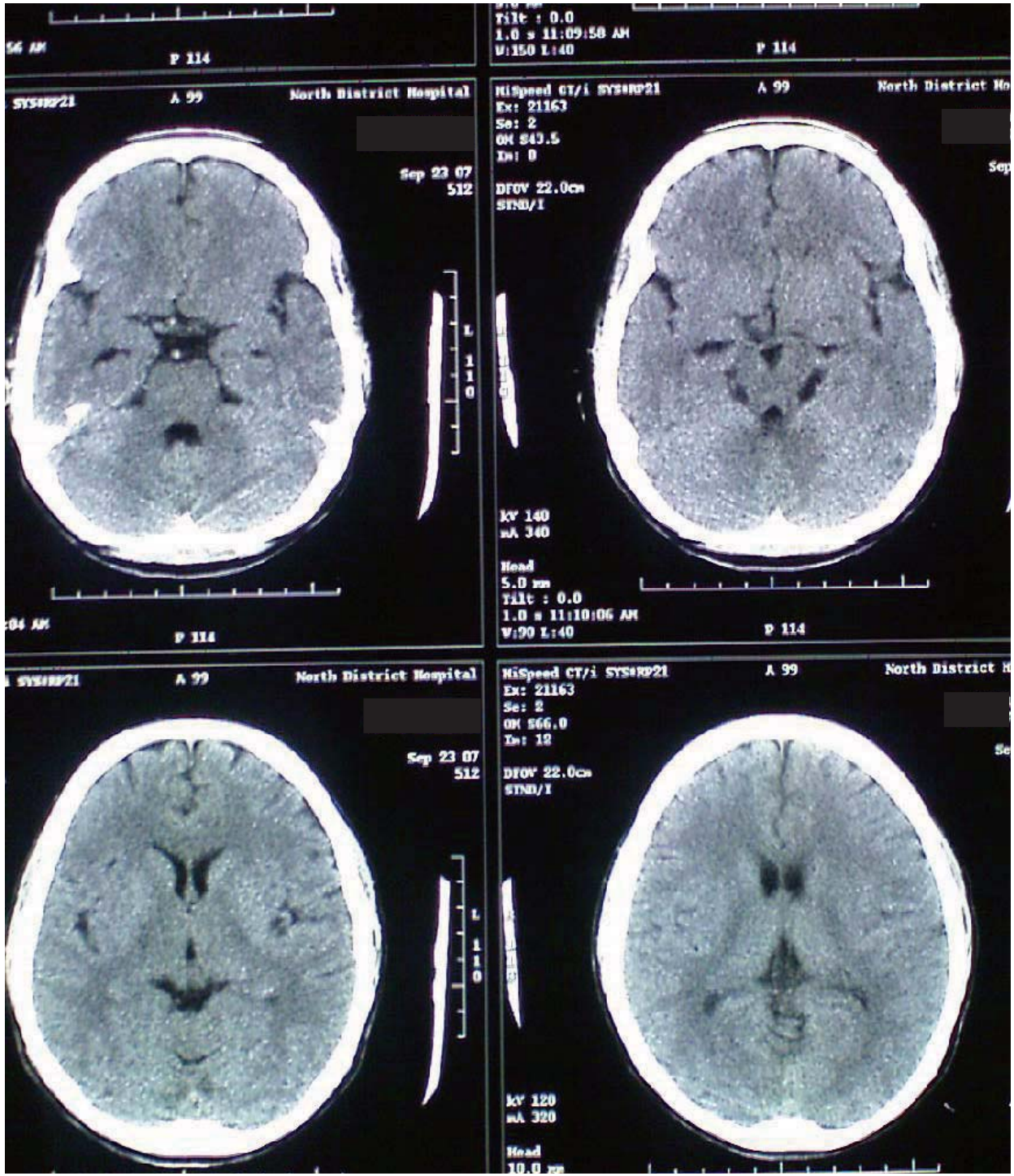
- Found increased vomiting after anti-TB med
- GCS 15/15
- Managed conservatively
- Treated as S/E of anti-TB med
- Vomiting gradually subsided

Progress

- Developed vomiting again D 25 of antiTB med
- 2-3 times per day
- CT brain repeated 3 days later


A 92
North District Hospital
Oct 25 07
512
P 119
HiSpeed CT/i SYS#RP21
Ex: 22043
Se: 2
Dfov 22.0cm
Head
5.0 mm
Tilt : 0.0
V:90 L:40
kV 140
mA 180
kV 120
mA 140
10.0 mm
PM

2 Jan 2008


P 114
North District Hospital
A 99
Sep 23 07
512
HiSpeed CT/i SYS#RP21
Ex: 21163
Se: 2
DFOV 22.0cm
STND/I
kV 140
mA 340
Head
5.0 mm
Tilt : 0.0
1.0 s 11:10:06 AM
W:90 L:40
kV 120
mA 320

2 Jan 2008

Hydrocephalus

- Headache, neck pain
- Nausea, vomiting
- Blur vision, diplopia (6^{th} nerve palsy)
- Gait disturbance
- Drowsiness
- Cognitive disturbance
- Papilloedema

Hydrocephalus

- Pathophysiology
  - Communicating
  - Non-communicating
- Causes for hydrocephalus?

Hydrocephalus in TBM

- Bacteraemia seeding in meninges
- Ruptured into subarachonoid space
- Reactive thick exudates formed
- Adhesion in basal cistern → hydrocephalus
- Or obstruction of arachnoid granulation

Progress

- Transferred to Neurosurgical unit
- Dexamethazone IV started
- Repeat CT brain → no interval change
- Transferred back to NDH 1 week later
- Sputum C/St & EMU – mycobacterium tuberculosis

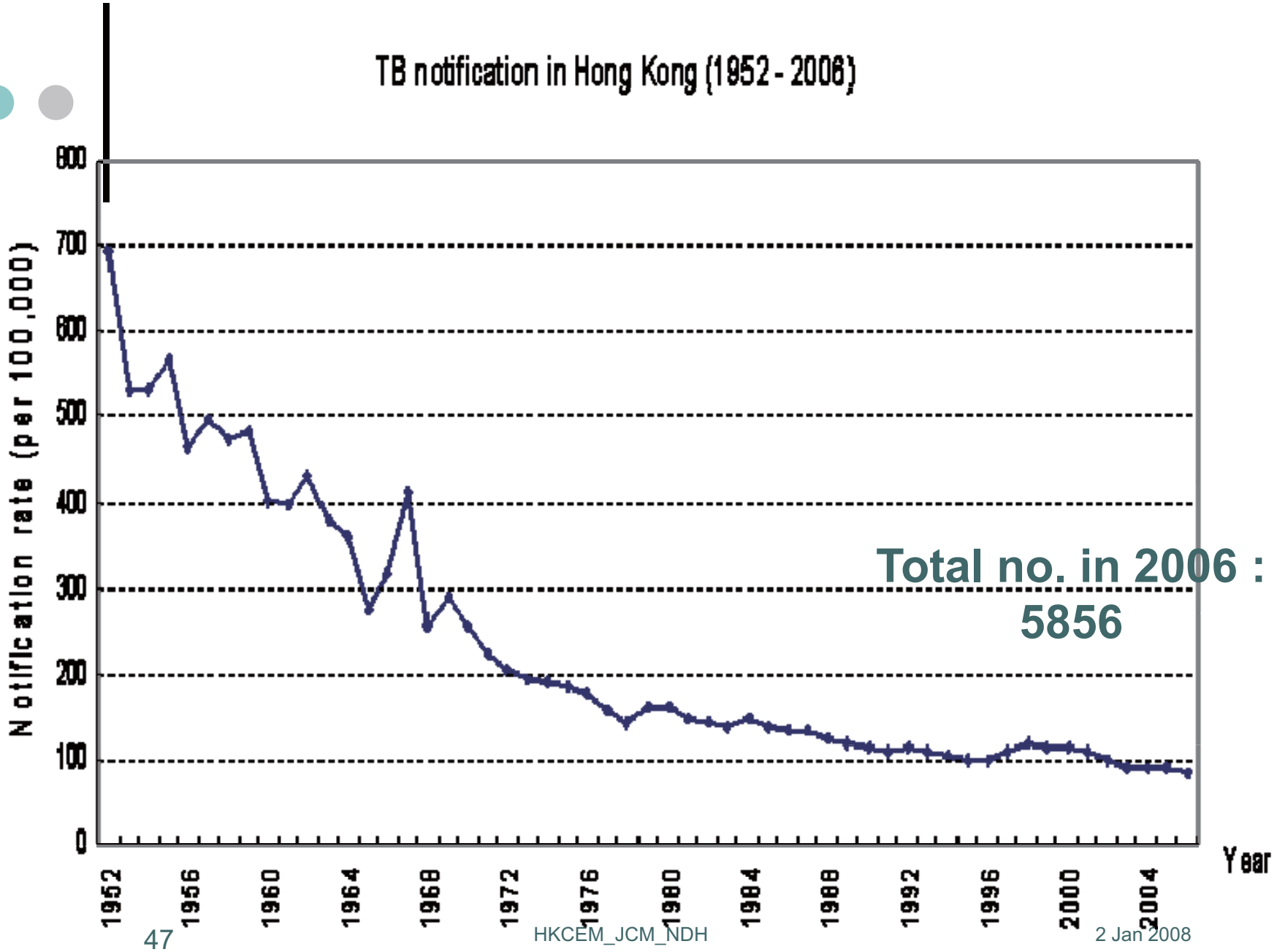
Latest Progress

- Transfer to WTS hospital for TB bed
- Continued on anti-TB medication titration
- LFT improved
- Patient discharged and returned back to Indonesia

Tuberculosis

TB in Hong Kong

- Important infectious disease in HK
- Notification rate ~6000 to 7000 per year
- 10 times higher than western developed countries
- Listed by WHO as intermediate burden of TB
- Lifetime risk 1 in every 13 persons


TB notification in Hong Kong (1952 - 2006)
Notification rate (per 100,000)
800
700
600
500
400
300
200
100
0
1952
1956
1960
1964
1968
1972
1976
1980
1984
1988
1992
1996
2000
2004
Year
Total no. in 2006 : 5856

Transmission

- Air-borne transmission
- Through cough, sneeze, speaks
- Chance of infection
  - Immunity, virulence, duration of exposure
- Only 1 in 10 patients → full blown TB
  - 50% of them develop disease within first 2 years
- Death rate ~ 4-5 %

Clinical features

- In Hong Kong
- 90% involve lungs
- 1/3 of them smear positive
  - 2/3 smear negative
- ~ 25% extrapulmonary TB
  - Commonest site: LN & pleural
  - Other common sites: meninges. brain

Clinical features

- Constitutional symptoms
  - non-specific
- Fever, weight loss, night sweat, malaise
- Cough, haemoptysis
- Symptoms according to site of infection

Diagnostic tests

- Tuberculin skin test
  - Detection of TB infection
  - Delayed hypersensitivity reaction to tubercle bacillus
- Laboratory test
  - Sputum, urine for smear & culture
  - Tissue for histology
  - Tissue fluid e.g. CSF

NTEC Pharmacy Bulletin Issue
16 Apr 2004

Mantoux Test

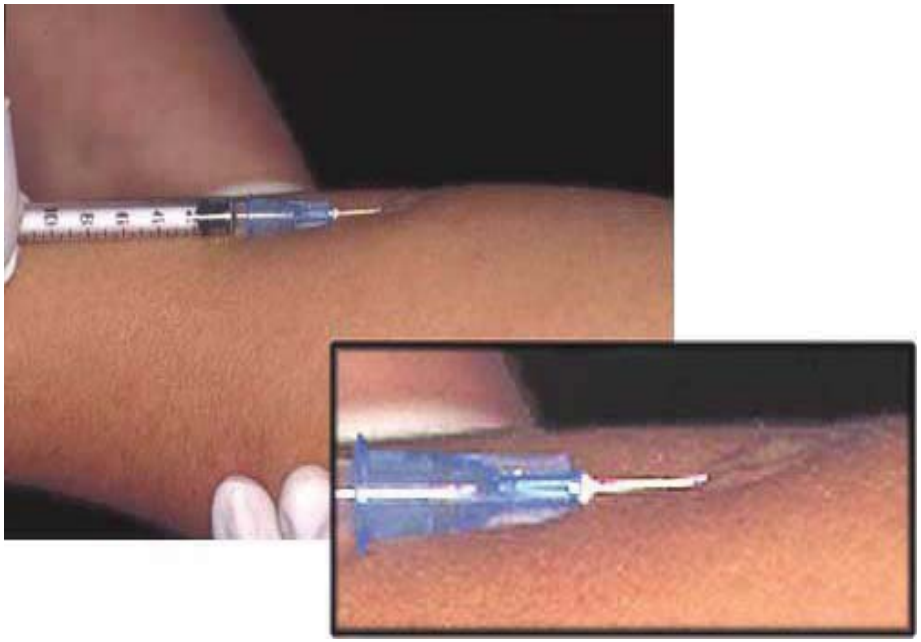
- PPD
  - Tuberculin purified protein derivative
  - Sterile preparation from precipitate of heat treated M Tuberculosis or bovis

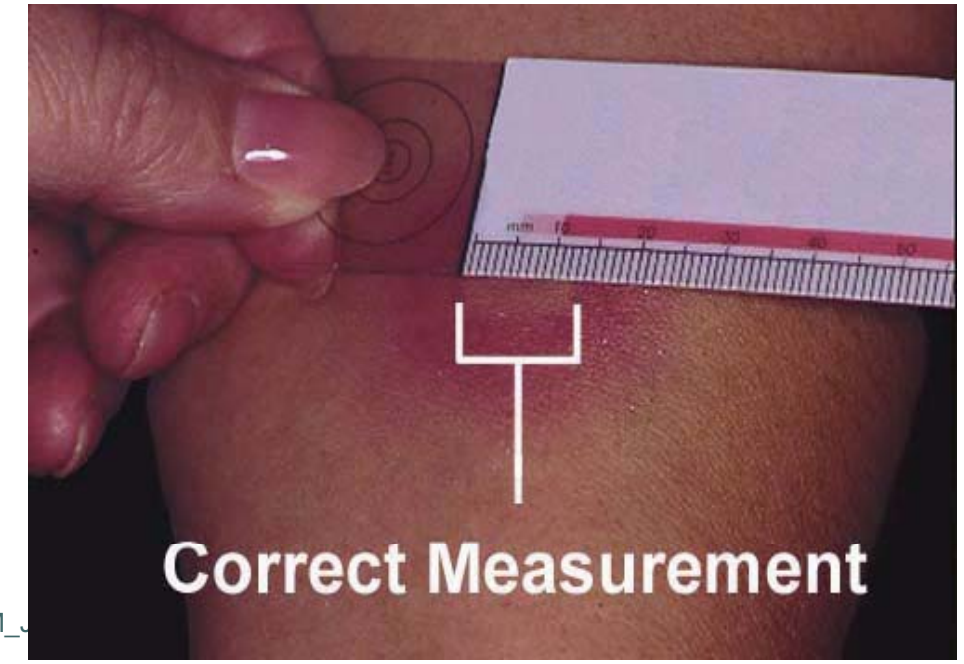
- *Previous infection with mycobacterium → delayed hypersensitivity reaction → reexposure to antigen (i.e PPD) → mount host immune system → skin induration*

NTEC Pharmacy Bulletin Issue
16 Apr 2004

Mantoux test

- Intradermal injection of 0.1 ml PPD
- To volar side of forearm
- Look for a round wheal 8-10mm diameter
- Read at 48 to 72 hours (96hrs for elderly)
- Positive reaction→ induration ≥ 10mm





Results

- Interpret as Positive if patient has:
  - Large TST reaction
  - BCG long time ago
  - From area with high prevalence of TB
  - Known TB contact

TST reaction

Size of induration	>=5mm	>=10mm	>=15mm
Consider positive for	○HIV ○Close contacts ○Hx of TB	○Foreigner ○Low income ○Residential facilities ○Immuno-compromised ○< 4 years old	○People with no risk factors for TB

Interpretation

- False Positive
- Infection with non-tuberculous mycobacteria
- Vaccination with BCG

Interpretation

- False negative
  - 15-20%
  - Test error/anergy
  - Old age, high fever, steroid, immunosuppressant, hematological disease, HIV, recent viral infection, immature immune system (< 6mths)

Treatment

Pulmonary tuberculosis	Treatment
Uncomplicated	2HRZ + (E or S) →4HR
Retreatment	3(4)HRZES → 6(5)HR +/-E

H, isoniazid; R, rifampicin; S, streptomycin, E, ethambutol; Z, pyrazinamide

Extrapulmonary TB	Treatment
TBM	3HRZE+/-S → 9HR+/-E
Miliary	3HRZ + (E or S)→ 9HR+/-E
Bone & joints	2HRZ + (E or S)→10HR
Lymphendenitis (cervical)	2HRZ + (E or S) →4HR
Pericarditis, peritonitis, GU tract	Same as uncomplicated PTB Total 9 months

Paradoxical reaction

- Temporary exacerbation of TB symptoms and lesions after treatment
- At least 2 weeks after treatment
- Initially shown improvement to treatment
- More common in
  - Extrapulmonary TB
  - Disseminated TB

Multidrug resistant TB

- MDR-TB
- Resistance to at least both isoniazid & rifampicin in vitro
- 3.2% of world new TB cases
- 1% in HK
- Inadequate drug prescribed
- Poor drug compliance

Risk factor

- High index of suspicions
- Hx of incomplete treatment
- Close contact with MDR-TB patients
- Endemic area

Treatment

- According to drug sensitivity
- 5-6 drugs for 6 months
- Followed by 3-4 drugs
- Total duration 18 months

- Quinolones/ aminoglycosides

Extensively drug resistance TB

- XDR-TB
- Resistance to 1st line & some 2nd line drug
  - 1st line : at least isoniazid & rifampicin
  - 2nd line: any fluroquinolones and any 1 of the 3 injectable (capreomycin, kanamycin, and amikacin),

XDR-TB

- Speed of transmission probably no difference to all forms of TB
- Incidence is rare at this stage
- Variable treatment outcome
  - Depends on drug resistance
  - Disease severity
  - Own immune system

Infectious Control Measures

- NTEC guidelines, June 2007
- HA task force in Infection Control
- TB in HCW : 29-57 cases per year (DH figure)

Suspected TB case

- Airborne infection isolation room
- Continue airborne isolation (CDC 2006)
  - Till 3 consecutive negative AFB sputum smears collected
  - Or another diagnosis is made

Confirmed TB disease

- Smear positive PTB
- Airborne isolation until
  - Received anti-TB drug for minimum 2 weeks AND
  - Demonstrated clinical improvement
- MDR-TB
  - Till sputum smear show seroconversion

Non-infectiousness

- Smear –ve/ extrapulmonary TB
  - Non-infectious
- Smear +ve
  - Complete 2 weeks of chemotherapy + clinical improvement
- MDR-TB
  - Sputum smear conversion

Tuberculosis Manual,

Tuberculosis and Chest Service

Public Health Services Branch

Staff Precautions

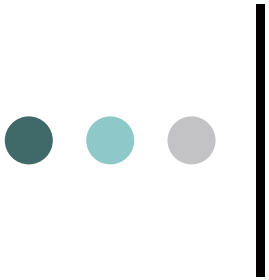
- High risk procedure → N95 mask
- On chemotherapy and improving --> Surgical mask
- Wear gloves when handling infectious material e.g. sputum
- Patients utilizing investigation facilities e.g. to x-ray should wear surgical mask

Contact tracing

- Patients
  - Required of HIV positive
  - < 1 year old with contact with infectious case > 8 hours in same ward
  - Expose to patient with strong smear +ve
- Staff
  - FU needed if carried out high risk procedure without airborne precautions

HCW with Significant Contact

- Monitor symptoms
- FU CXR annually for 2 yrs
- Limited role in Terbeculin skin test → high background positive rate



Thank You