

# HOW TO DO THE PERFECT FNA (AND BRING JOY INTO PATHOLOGISTS LIVES)

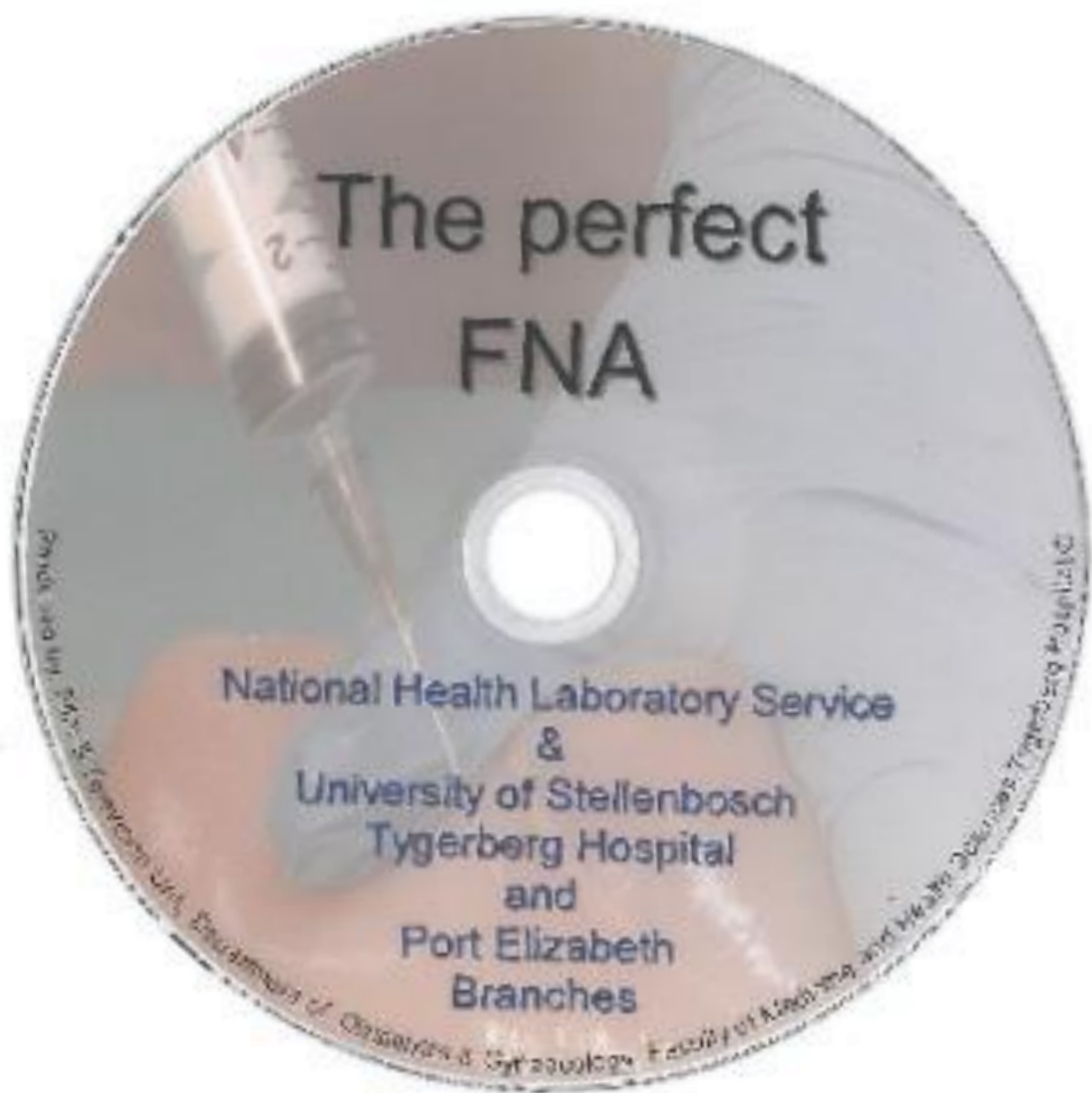
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# The perfect FNA

National Health Laboratory Service  
&  
University of Stellenbosch  
Tygerberg Hospital  
and  
Port Elizabeth  
Branches

Department of Parasitology & Mycology Faculty of Medicine and Health Sciences Tygerberg Hospital

1930 first series reported Memorial Hospital NY  
1960's practiced and published in Scandinavia  
1980's interest returned in USA and Europe

**High income  
countries**

**Low income  
countries**

% countries publishing  
articles on FNA

52.8%

29.7%

Top topics in publications

Breast

Sm round cell tumours

Pancreatic disease

**Infectious disease**

Mechanism for collection of material for diagnostic tests e.g..

Culture, ZN, PCR

Diagnostic modality in its own right ( cytopathology)

Triage

Facilitation of appropriate ancillary investigations





# TUBERCULOSIS

1/3 of the world population infected with TB

2 billion patients affected

9 million *new* cases TB each year (8.6 in 2012)

Annually 1.8 million TB related deaths world wide – more than **5000 per day**

90% these occur in the developing world

In the USA – 10-15 million people TB-infected

# TB LYMPHADENITIS

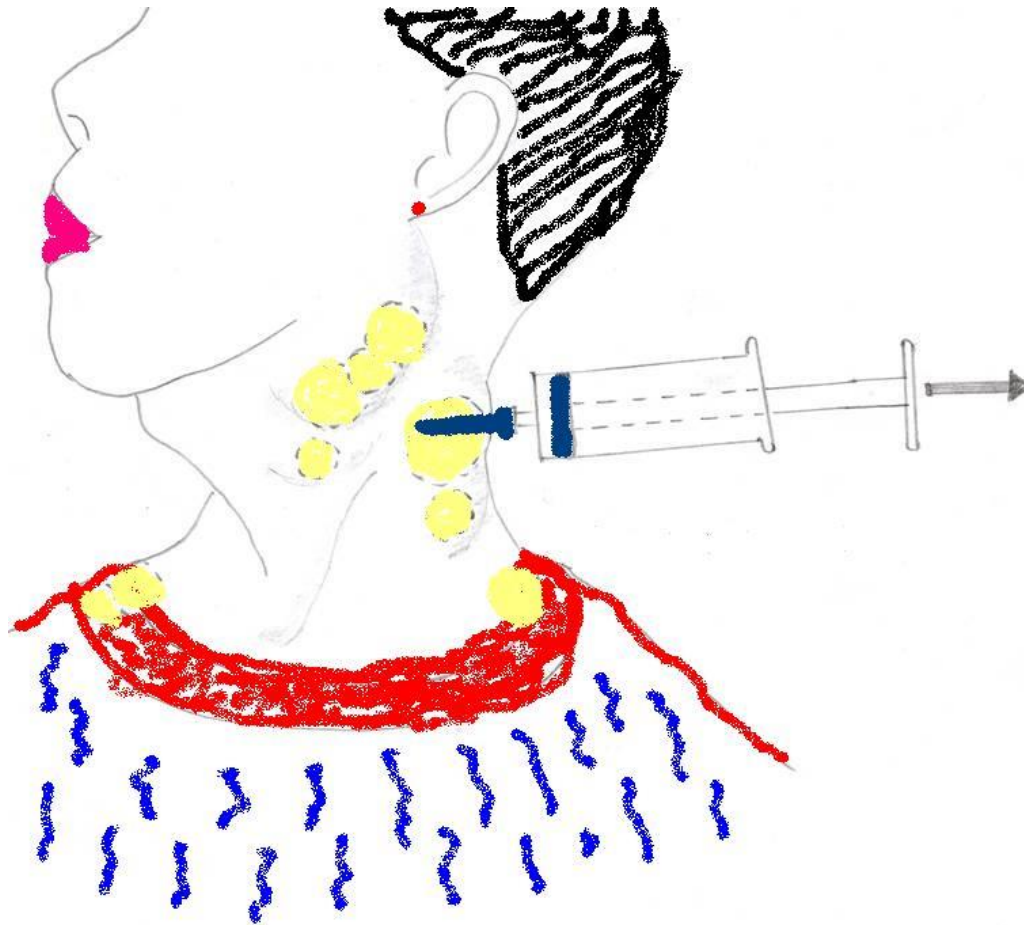
10-30% children with pulmonary TB have extra thoracic manifestations of disease

In endemic areas, TB lymphadenitis is the commonest of these (up to 50%)

TB lymphadenitis is the most common (22-48%) cause of persistent cervical LAD in endemic areas

Children may contribute up to 40% of the case load in TB endemic areas and if 5 -10% of these have peripheral lymphadenopathy, FNAB may be an invaluable diagnostic aid

# FINE NEEDLE ASPIRATION BIOPSY





**Table 2 Comparison of different superficial mass lesion sample collection methods to achieve a definitive tissue diagnosis**

	<b>Open surgical biopsy</b>	<b>Core needle biopsy</b>	<b>Standard Needle Aspiration (greater than 22G)</b>	<b>Fine Needle Aspiration Biopsy (22G or smaller)</b>
<b>Suitable for small lesions (1x1cm)</b>	Yes	No	Yes	Yes
<b>Entire mass sampled</b>	Yes, if excision	No	No	Yes
<b>Complications</b>	Risk of anaesthesia, hospitalization, sinus formation, infection	Sinus formation, infection	Rare	Extremely rare
<b>Cost</b>	Hospitalization, theatre time	High cost of needle	Minimal	Minimal
<b>Hospitalisation</b>	Yes	No	No	No
<b>Anaesthetic required</b>	General	Local	Local	None
<b>Time for entire procedure</b>	1-2 days	30 minutes	30 minutes	10 minutes
<b>Tissue diagnosis</b>	Yes	Yes	No	Yes
<b>Microscopy for organism</b>	Yes	Yes	Yes	Yes
<b>Culture</b>	Yes	Yes	Yes	Yes
<b>Time for initial result</b>	1-2 days	1-2 days	12-24 hours (Possible in <1 hr)	12-24 hours (Possible in <1hr)

**Table 3** Comparison of methods to confirm a mycobacterial diagnosis in children

Method	Hospitalization required	Suitable ages	Local/general anaesthetic	Equipment / infrastructure
<b>FNAB</b>	No	All	No	None
<b>Gastric aspirates</b>	Yes	All	No	None
<b>Induced sputum</b>	Yes	All	No	Nebulizer, suction, saturation monitor
<b>Sputum</b>	No	>7-8yrs only	No	None
<b>Surgical biopsy</b>	Yes	All	Yes	Full theatre

# FINE NEEDLE ASPIRATION IN NODAL TB

Rapid and inexpensive

Cytomorphology

Classical

Atypical, in immune compromised patients

Not specific

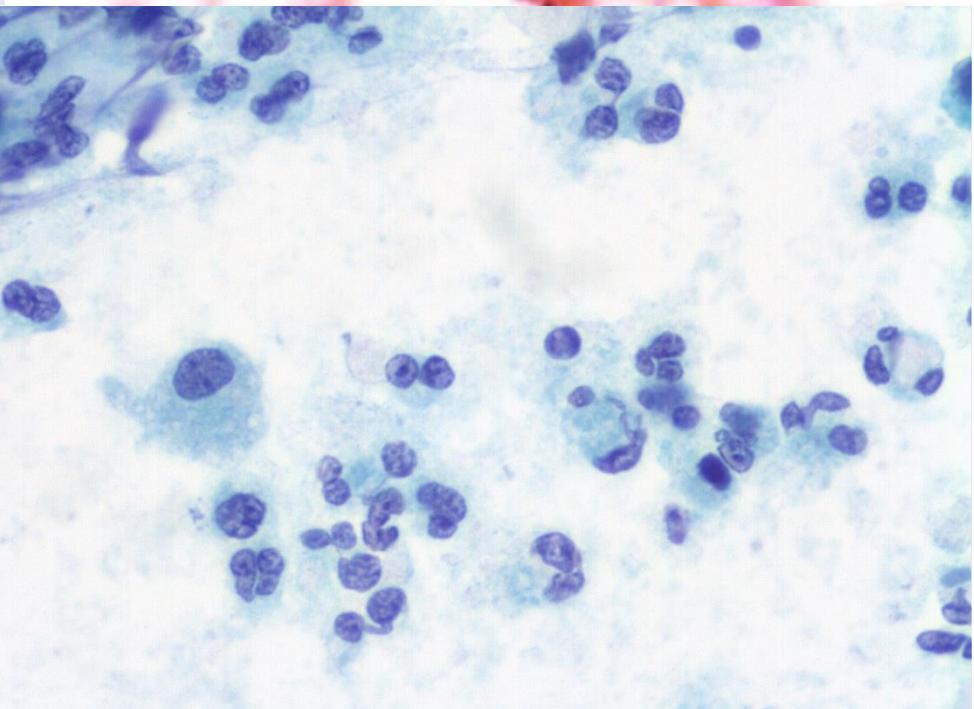
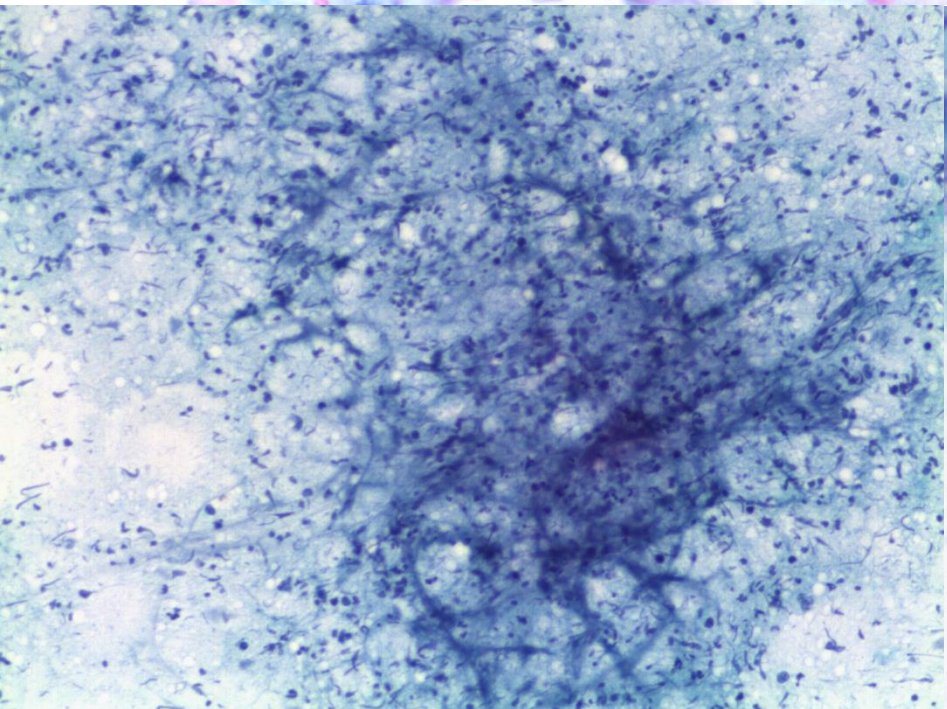
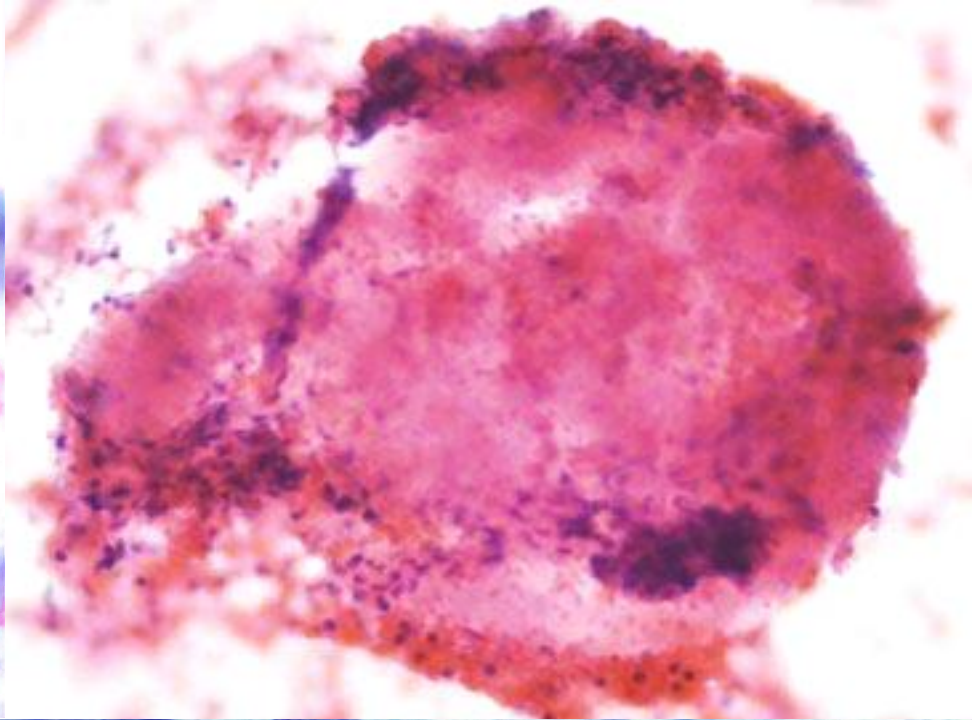
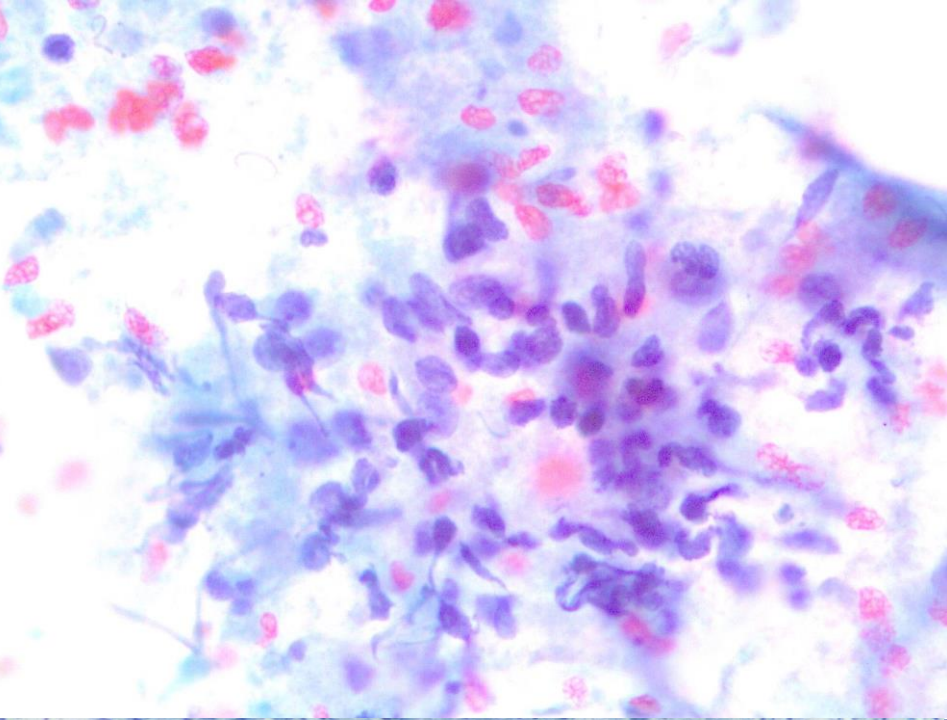
Identification of organism (Overall sens 20 – 70 %)

ZN/Kinyoun

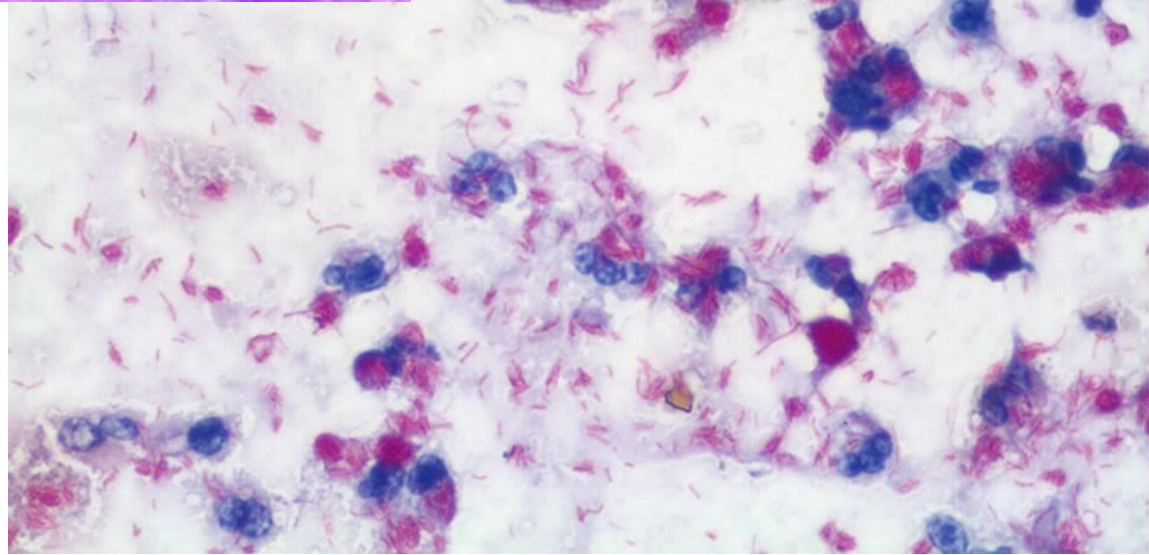
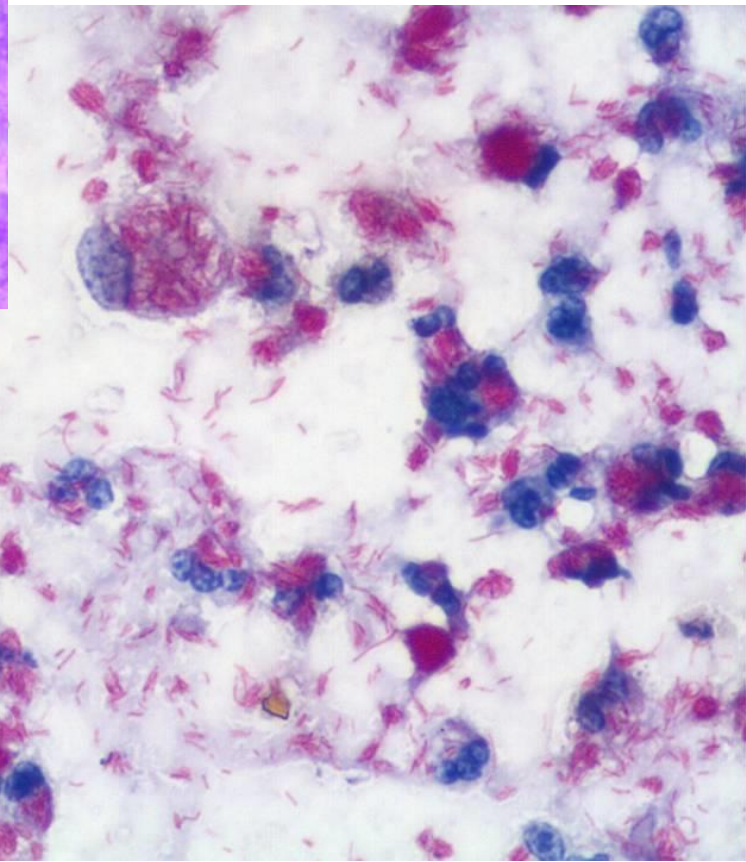
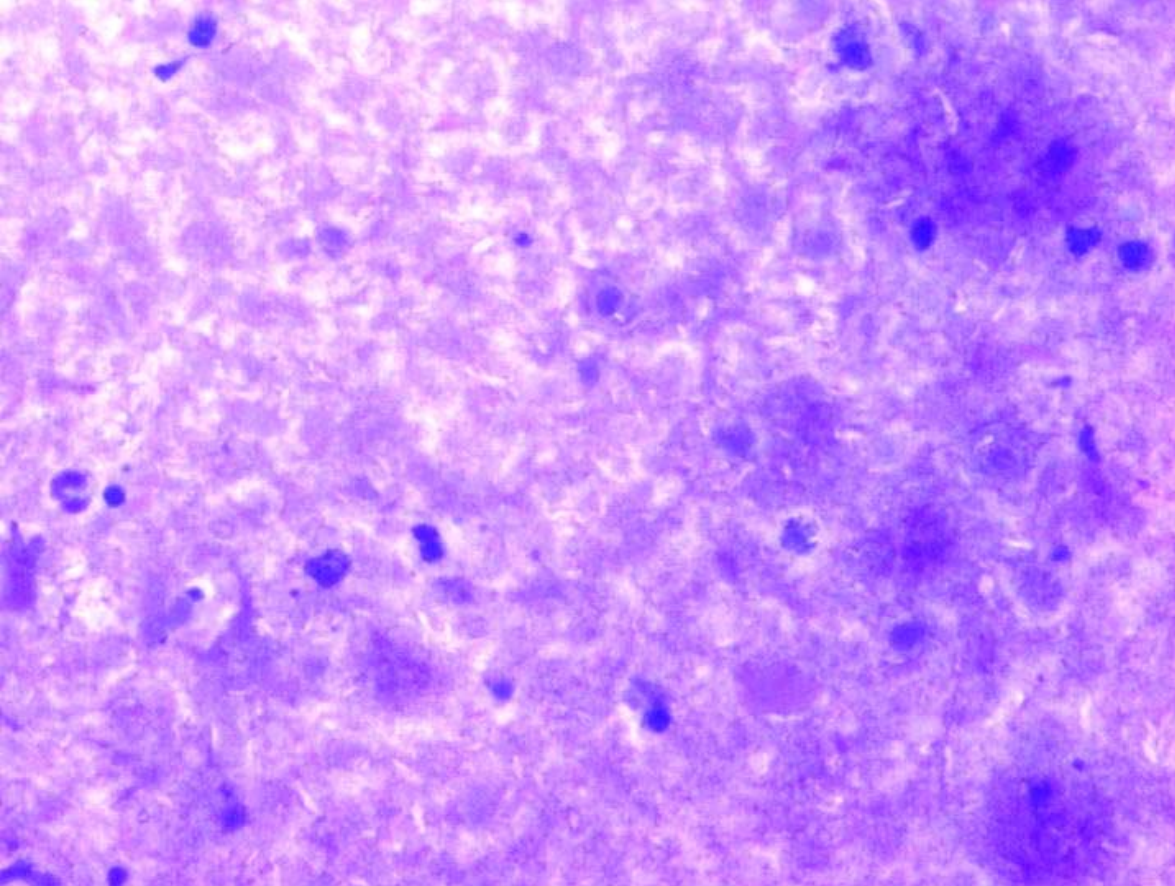
Fluorescence

NAATs

Culture







# PAPANICOLAOU INDUCED FLUORESCENCE

Inexpensive, rapid

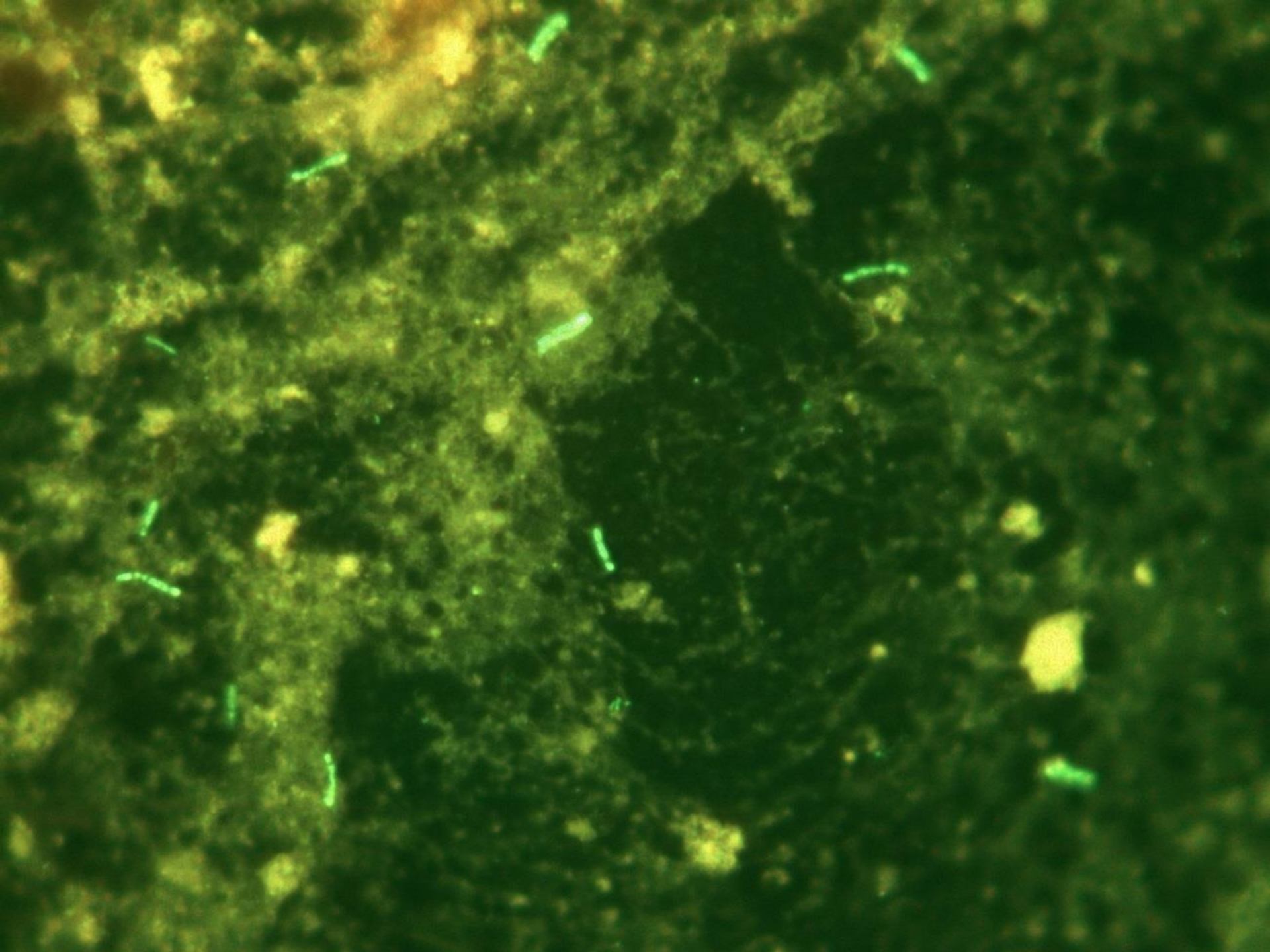
No toxic, carcinogenic substances

**No additional stains**

Mycobacteriae, Gram-negative bacteria, Fungi,  
Pneumocystis

Lymph node aspirates – no normal microbial  
colonisation





# THE VALUE OF LED FLUORESCENCE MICROSCOPY IN FNAB OF PAEDIATRIC LYMPH NODES

182 FNAB smears from 121 children

Mycobacterial cultures were positive in 84 (69%) children

	Sensitivity	Specificity
LED (mains powered)	48.2%	78.4%
LED (rechargeable battery )	50.0%	86.7%
MVL	51.8%	78.4%



# DIAGNOSTIC YIELD OF FNAB IN HIV-INFECTED ADULTS WITH SUSPECTED MYCOBACTERIAL LYMPHADENITIS

5 year, retrospective, descriptive, laboratory-based study

All patients of ages 14 years and above

Referred to the Tygerberg Hospital FNAB clinic for aspiration of cervical lymph nodes for suspected TB LAD

Specimens sent for cytology and mycobacterial culture

A total of 368 patients

HIV positive - 226 (61.4%)

HIV negative - 25 (6.8%)

HIV unknown - 117 (31.8%)

Mycobacterial lymphadenitis diagnosed in 293 (79.6%) patients

# RESULTS

Diagnostic yield in the HIV-positive and -negative populations  
84% v. 52% ( $p < 0.001$ )

Sputum sample submitted in 84/368 patients (34.5%)

226 *Mycobacterium tuberculosis*,

1 *M. avium-intracellulare*

1 *M. szulgai*

These results justify XPERT as the initial diagnostic modality  
in HIV infected patients

# DIAGNOSING MYCOBACTERIAL LYMPHADENITIS IN CHILDREN USING FINE NEEDLE ASPIRATION BIOPSY

Prospective study Tygerberg hospital, Cape Town

Jan 03- June 05

Children under 13 years

175 aspirates entered into study



# CULTURE AS GOLD STANDARD ?

However, culture can also be false negative

Detects 85-90% of cases of cavitating pulmonary TB

Pilot study 8/21 negative cultures false negative

“New” gold standard

**Positive culture +/- cytology + evidence of organism on special stains (bacteriological confirmation)**

May correlate with

Patients on TB treatment prior to FNA

Radiological evidence of disease

Response to treatment

	<b>CYTOLOGY</b>	<b>FLUOR</b>	<b>ZN</b>	<b>CULTURE</b>
<b>SENS</b>	78%	67%	62%	75%
<b>SPEC</b>	91%	97%	97%	100%
<b>PPV</b>	93%	97%	97%	100%
<b>NPV</b>	73%	66%	63%	72%
<b>EFF</b>	83%	79%	76%	84%

SHOULD FNAB BE THE FIRST LINE DIAGNOSTIC  
PROCEDURE IN PAEDIATRIC TUBERCULOSIS  
SUSPECTS WITH PERIPHERAL  
LYMPHADENOPATHY?



# RESPIRATORY SPECIMENS IN CHILDREN POOR MICROBIOLOGY STANDARD

	Adult	Child
Culture sensitivity (sputum/ GA)	80%	20-50%
Smear microscopy (sputum/ GA)	<75%	<10%

Difficult to obtain representative specimen  
Paucibacillary disease  
Acid pH of gastric contents  
High rates of EPTB

Evaluate the **diagnostic yield** and **time to diagnosis** of (FNAB) versus routine respiratory specimens

Children (< 13 years) with a palpable peripheral lymph node mass symptoms suspicious of tuberculosis.

Any other mycobacterial specimens (within 30 days of the FNAB) during the 4-year period January 2003 to January 2007.

If the patient had 3 gastric washings and 1 induced sputum, and **any** one of these was positive, for the comparative analysis this was regarded as a positive result

Retrospective review laboratory records of the Cytology Unit at Tygerberg Hospital



**Table 3** Specimen type, yield and organisms cultured in 95 patients

Specimen type	Number of specimens	Consecutive specimens collected No (% specimen type)			Culture pos No (% specimens)	TB No. (%)	M. bovis BCG No. (%)	NTM No. (%)
		1st	2nd	3rd				
<b>FNAB</b>	95				<b>51 (54)</b>	36 (71)	15 (30)	0
<b>Gastric aspirates</b>	143	80	52(65)	<b>11 (14)</b>	<b>39 (27)</b>	30 (77)	8 (21)	1 (3)
<b>Induced sputum</b>	15	10	5 (50)	0	<b>6 (60)</b>	6 (100)	0	0
<b>Sputum</b>	11	7	3(43)	1(14)	<b>5 (71)</b>	5 (100)	0	0
<b>Nasopharyngeal aspirates</b>	10	7	3 (43)	0	<b>5 (71)</b>	4 (80)	1 (20)	0
<b>Non-respiratory specimens</b>	26 <sup>a</sup>				<b>3 (12)</b>	2(8) (CSF)	1(4)(pus swab)	0

**Table 4** Diagnostic yield of Fine Needle Aspiration Biopsy (FNAB) compared to standard respiratory specimens (*M bovis* BCG excluded)

Standard respiratory specimens	FNAB negative	FNAB positive	Total
All gastric aspirates negative	25(37%)	19(28%)	44(65%)
Any gastric aspirate positive	3(4%)	21(31%)	24(35%)
<b>Total</b>	28(41%)	40(59%)	68(100%)
All other respiratory specimens negative	2(17%)	4(33%)	6(50%)
Any other respiratory specimen positive	0	6(50%)	6(50%)
<b>Total</b>	2(17%)	10(83%)	12(100%)
All respiratory specimens negative	26(35%)	19(26%)	45(61%)
Any respiratory specimen positive	3(4%)	26(35%)	29(39%)
<b>Total</b>	29(39%)	45(61%)	74(100%)

# SUMMARY

95 children from whom 95 FNAB's, 143 gastric aspirates, 36 other respiratory specimens and 26 non-respiratory specimens were obtained.

Mycobacterial infection was diagnosed in **70/95 (73.3%)** patients.

Cases without respiratory specimens (6) and cases with *M bovis BCG* (15) were **excluded** from comparative analysis.

In the remainder, **FNAB** was positive in 45/74 (**60.8%**) cases, and **any respiratory** specimen in 29/74 (**39.2%**) cases ( $p < 0.001$ ).

Mean time to bacteriologic diagnosis with **FNAB** was **7.1 days** (95% CI 4.1-10.1) compared to **22.4 days** (95% CI 15.8-29.1) for any **respiratory** specimen ( $p < .001$ )

In this study **FNAB showed a better yield than respiratory specimens** (gastric aspirates and/or other respiratory specimens), even when all these specimens were combined as a single test.

# MYCOBACTERIAL TRANSPORT MEDIUM FOR ROUTINE CULTURE OF FNAB

We compared **mycobacterial yield**  
and **time to positive culture** following  
bedside culture into **standard MGIT**  
**tubes**

vs.

inoculation into an inexpensive “in –  
house” liquid transport medium  
followed by immediate and delayed  
laboratory inoculation into MGIT  
tubes

Cost comparison  
MGIT tube R34  
TB transport bottle R8



Results were **concordant** in 142/150 (**94.7%**) bedside and laboratory inoculation pairs.

57/150 (38%) cultured Mycobacterium tuberculosis complex

Similar results were obtained even after the “in house” transport bottle was kept at room temperature for 7 days before culturing for mycobacteria to mimic long transit time to laboratory.

There was **no significant difference in time to positive culture** between the bedside and laboratory inoculation tubes (**16.2 days** S.D. 0.87 versus **17.1 days** S.D. 0.85).

The use of inexpensive “in house” liquid growth medium transport bottles, combined with practical tuition in FNAB, will improve cost effective diagnosis of TB at primary health care level.

# XPERT<sup>®</sup> MTB/RIF

48/50 patients referred for FNAB at Tygerberg Hospital, South Africa, suspected mycobacterial lymphadenitis.

Positive cytomorphology with direct visualization of the organism and/or positive tuberculosis culture served as the reference standard.

30 (62.5%) were diagnosed with tuberculosis (TB)

# XPERT<sup>®</sup> MTB/RIF

Xpert<sup>®</sup> MTB/RIF identified 29/30 cases laboratory proven TB

Sensitivity      96.7% (29/30)

Specificity      88.9% (16/18)

6/6 (100%) of the smear negative culture positive cases.

Xpert<sup>®</sup> MTB/RIF correctly identified rifampin resistance in 1/2 cases

# XPERT<sup>®</sup> MTB/RIF CHILDREN

Tygerberg hospital, Western Cape and Dora Nginza hospital,  
Eastern Cape, South Africa

September 2011 to December 2012.

Combined reference standard

- 32 positive on Xpert<sup>®</sup> MTB/RIF
- 36 positive on cytology
- 25 Positive on culture for M. tuberculosis complex.

## Xpert<sup>®</sup> MTB/RIF

Sensitivity 80%

Specificity 93.8%



There can be no keener revelation  
of a society's soul  
than the way in which  
it treats its children

Nelson Mandela, 1996



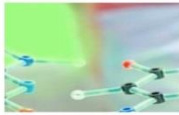
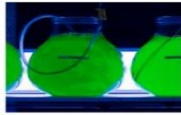
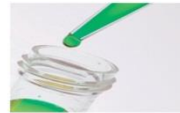
*“Semper aliquid novi  
Africam adferre”*

Africa always brings [us]  
something new

*Pliny. Historia Naturalis bk. 8, sect. 42 )*

*You can't depend on your  
eyes when your  
imagination is out of focus*

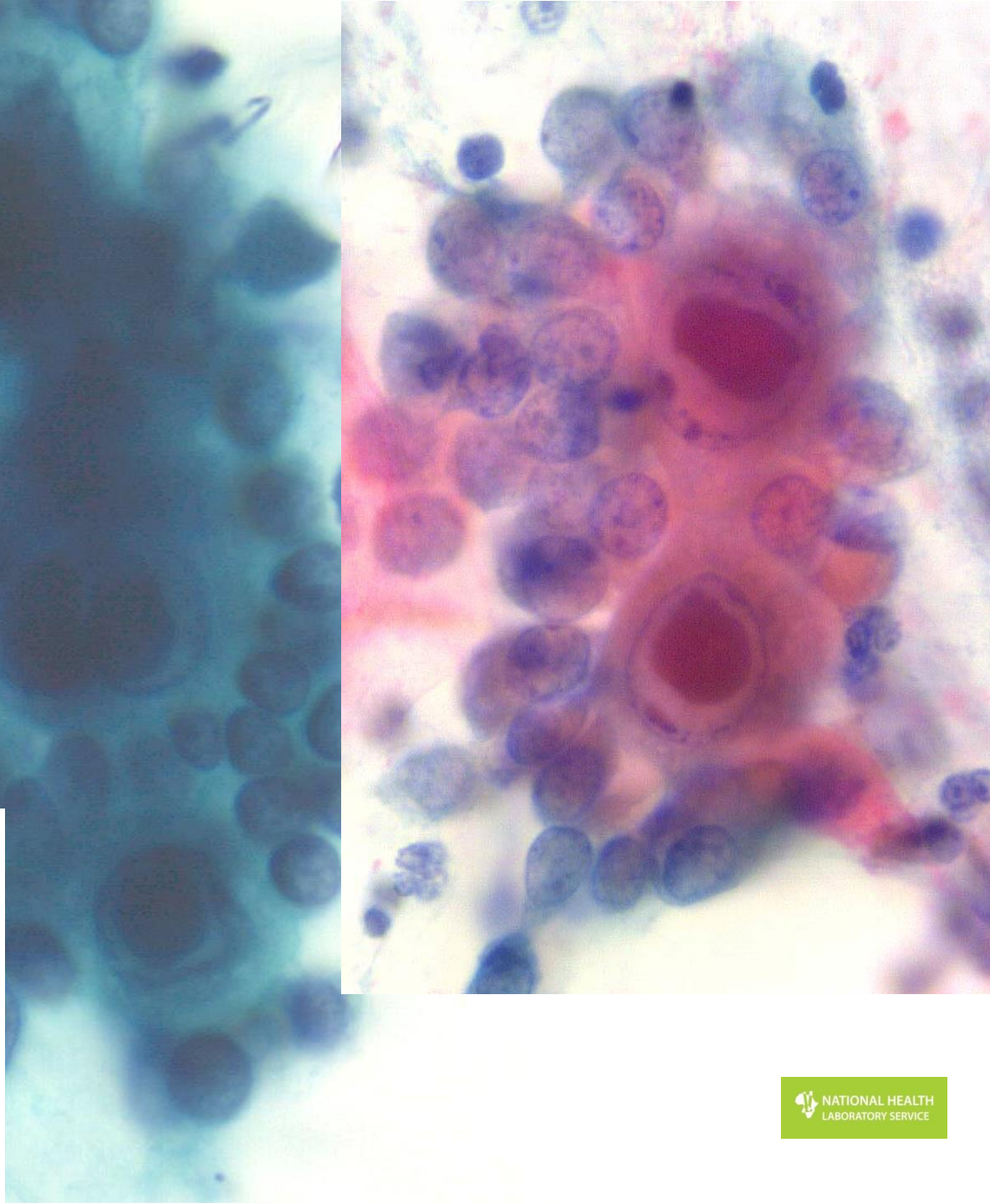
*Mark Twain*

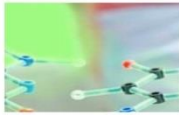
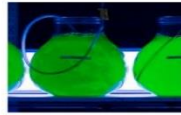
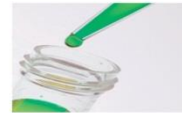


# VIRAL INFECTIONS



5 month old baby,  
HIV+  
Ill defined mass left  
angle of jaw,  
FNAB performed

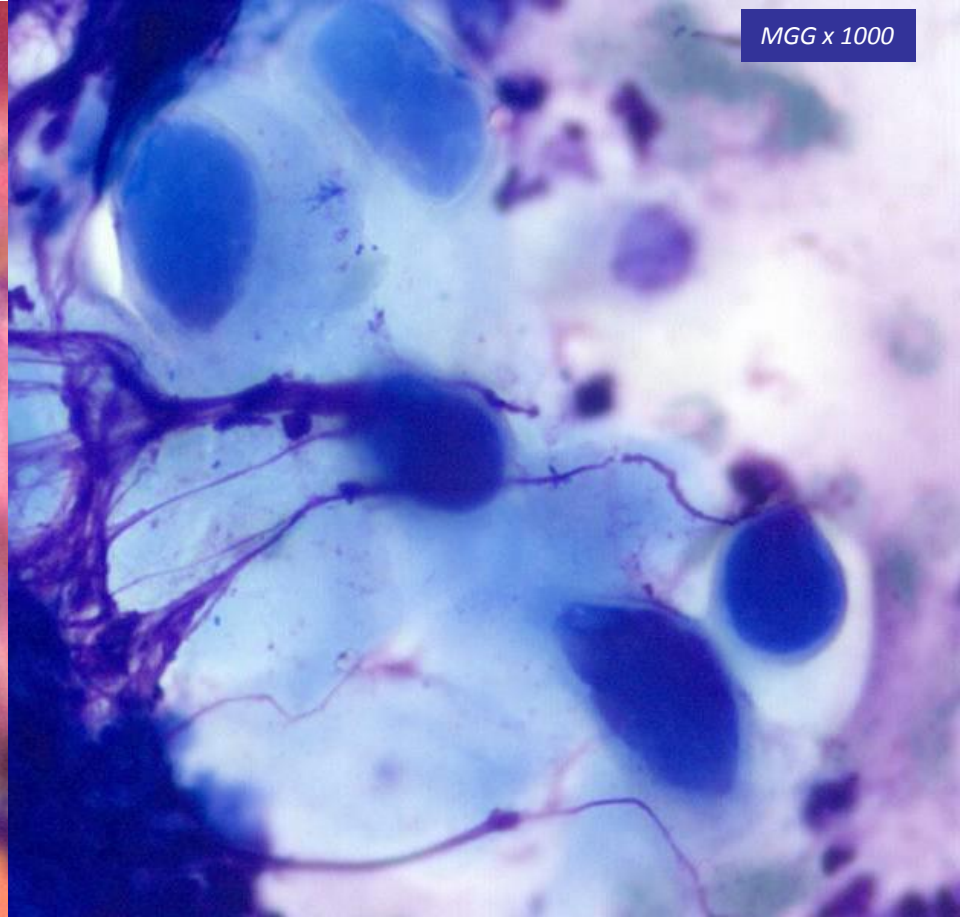
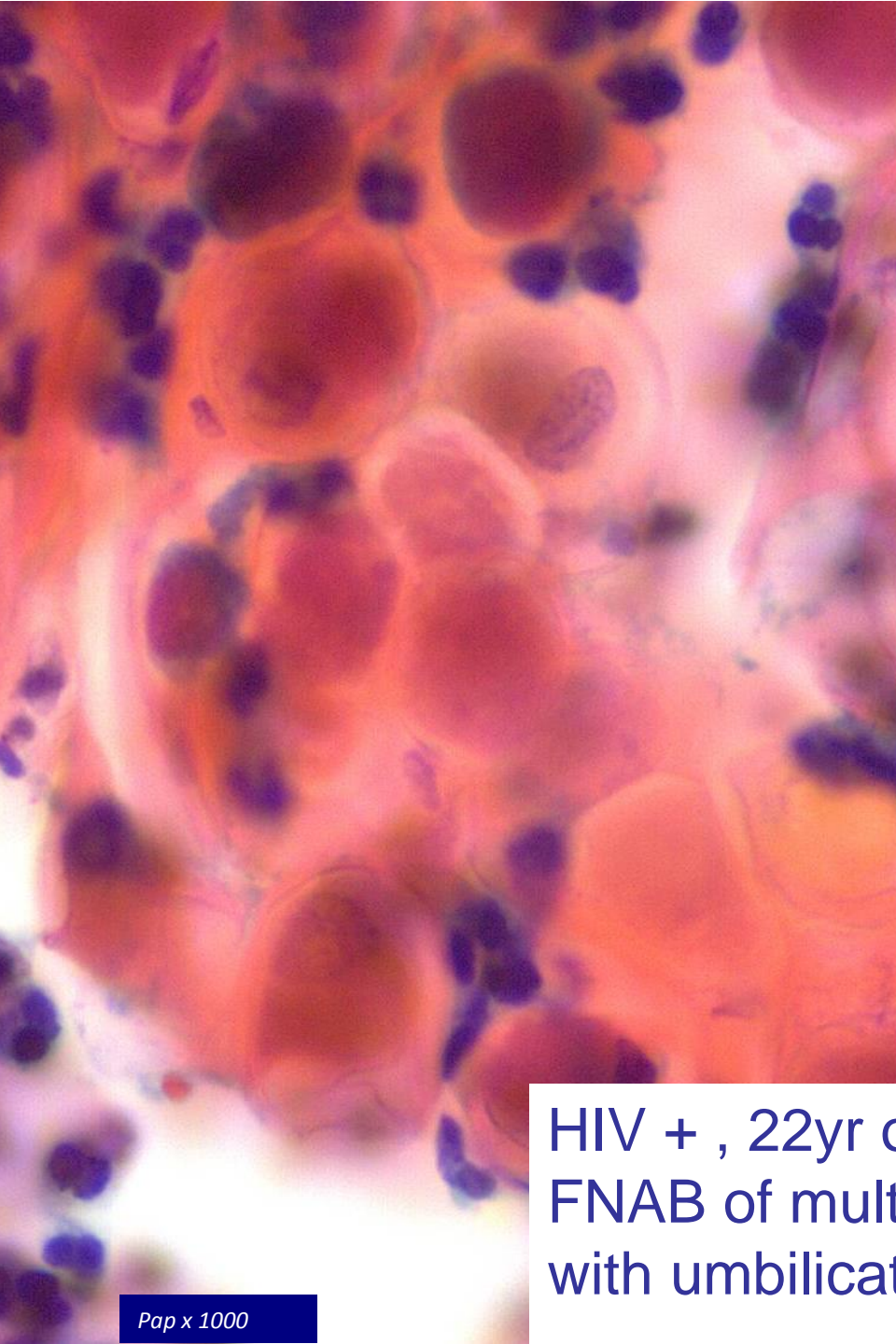




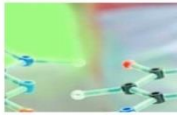
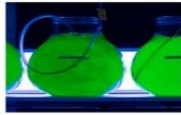
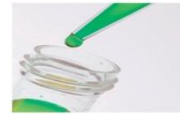
# CYTOMEGALOVIRUS INFECTION





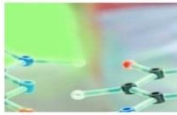
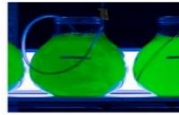
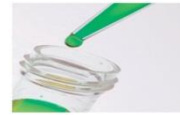


HIV + , 22yr old female  
FNAB of multiple 1cm skin nodules  
with umbilicated centres.



# MOLLUSCUM CONTAGIOSUM



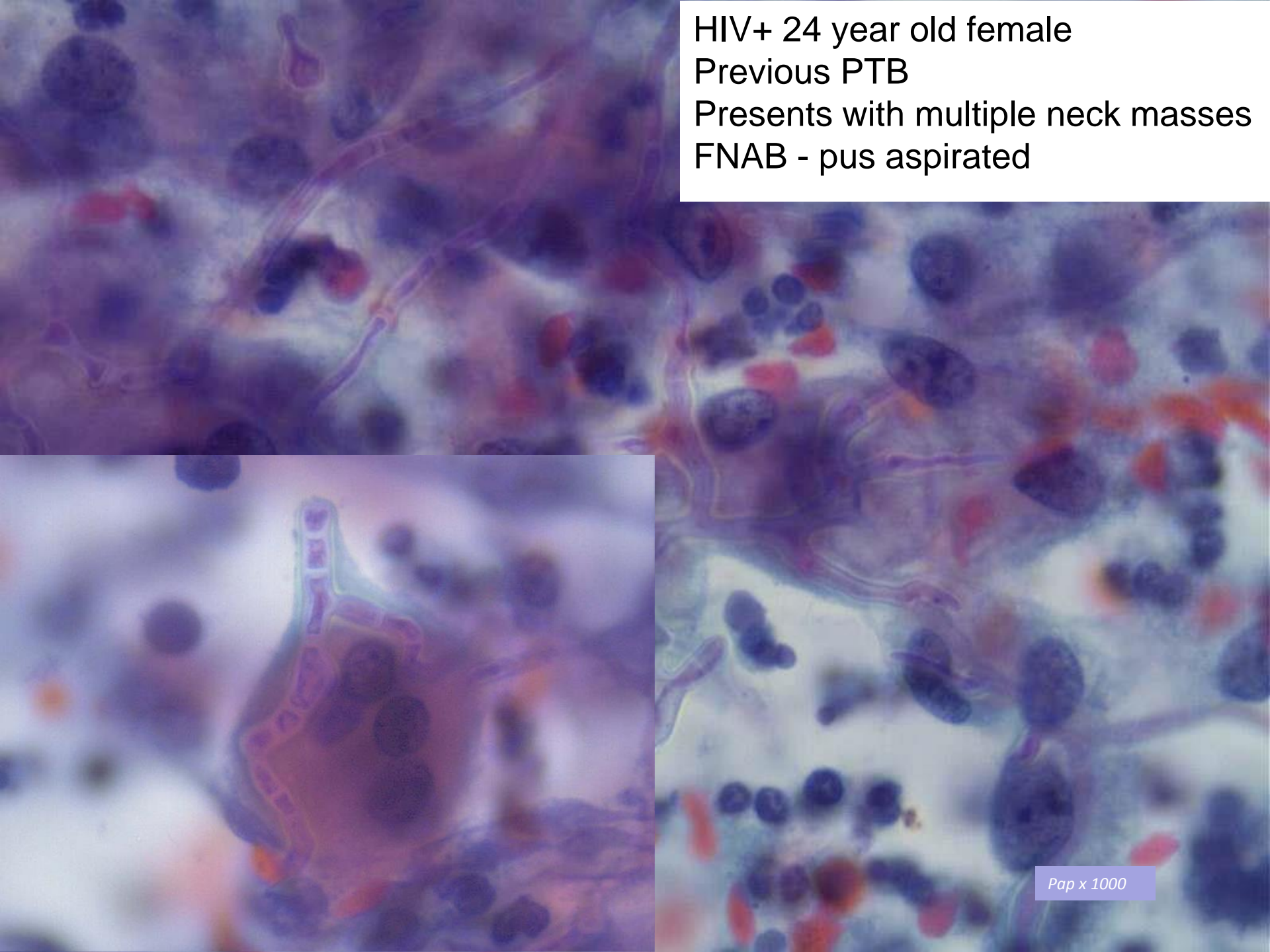


# FUNGAL INFECTIONS





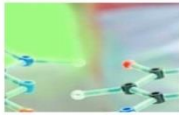
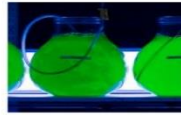
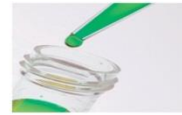
HIV+ 24 year old female  
Previous PTB  
Presents with multiple neck masses  
FNAB - pus aspirated





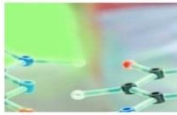
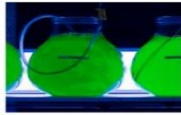
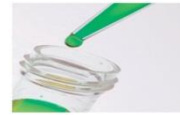


*MethAg x 400*



# TRICHOPHYTON VIOLACEUM



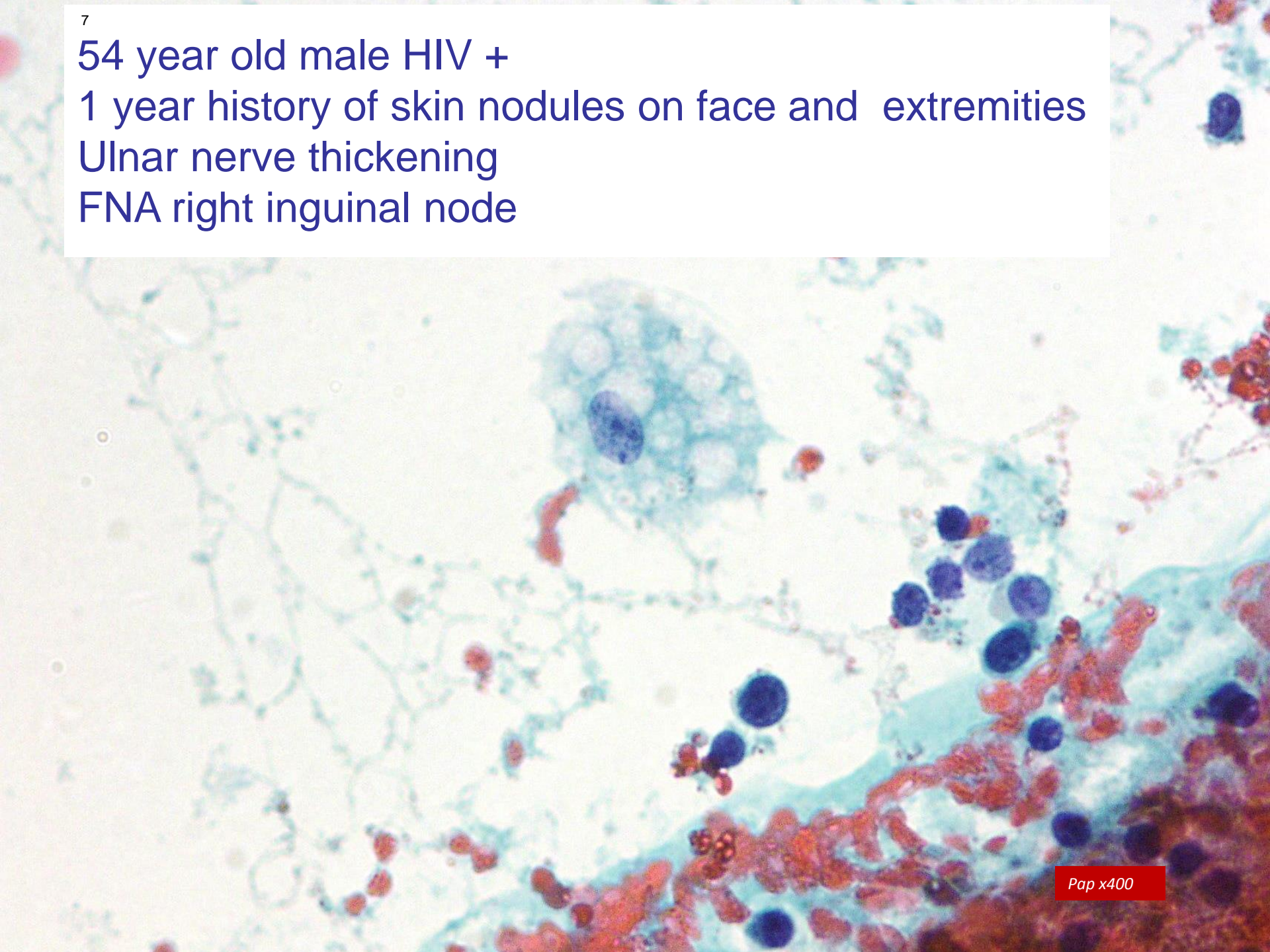


# BACTERIAL INFECTIONS

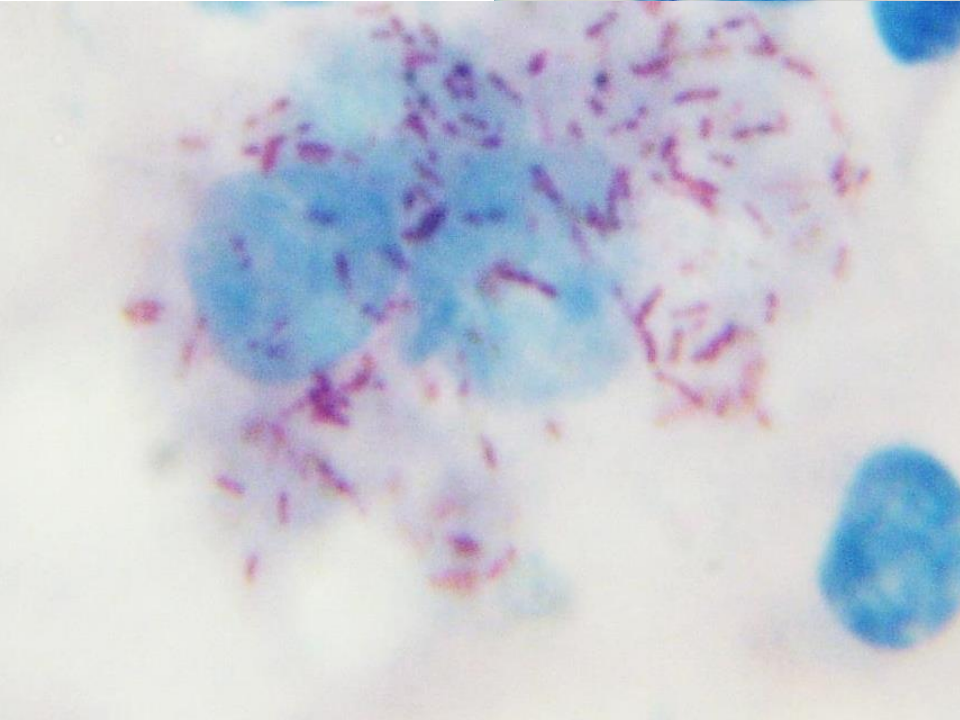




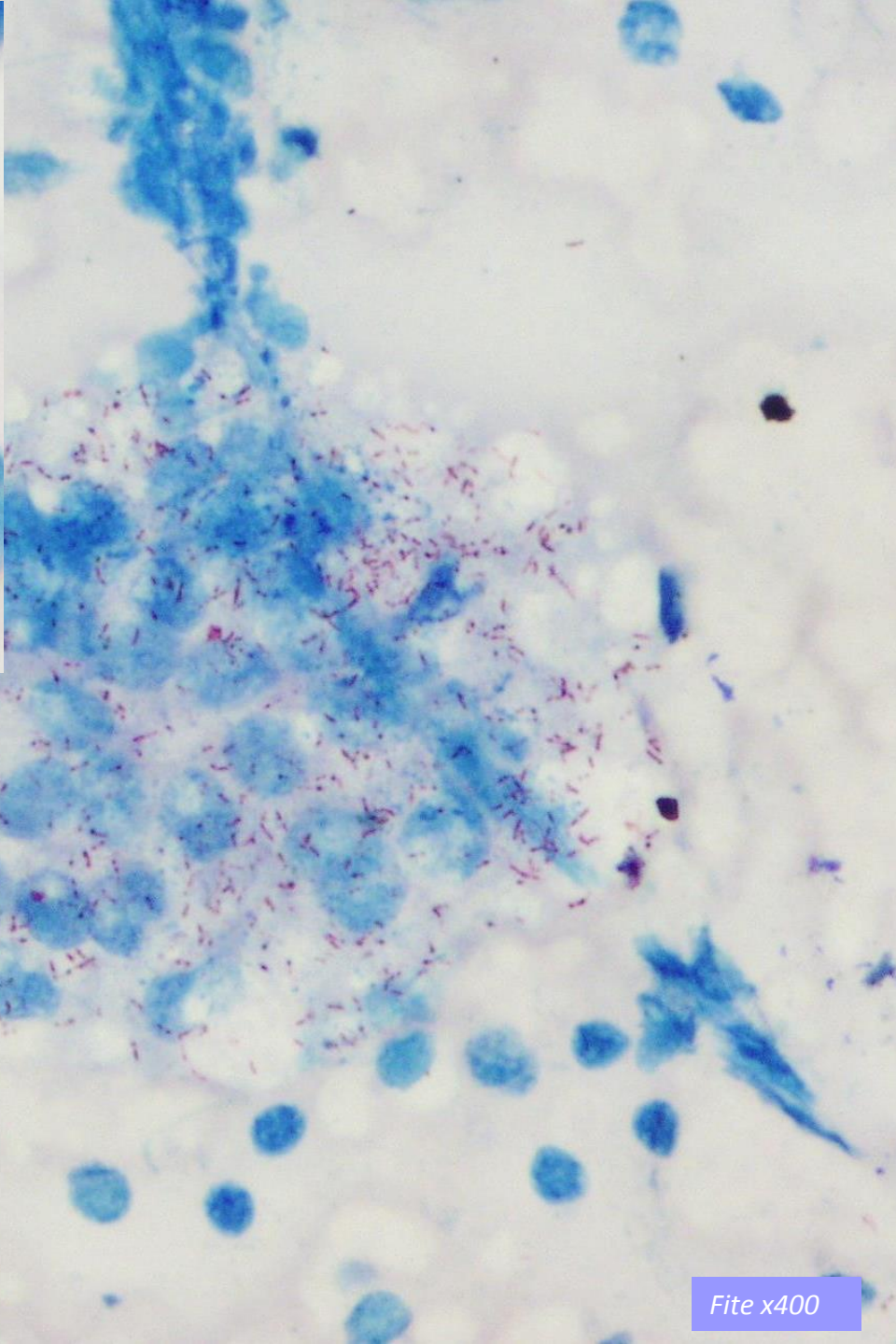
54 year old male HIV +  
1 year history of skin nodules on face and extremities  
Ulnar nerve thickening  
FNA right inguinal node



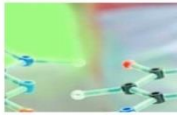
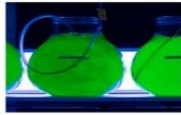
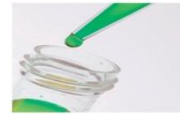




Fite x1000



Fite x400

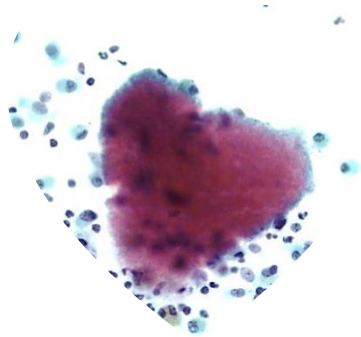


# *MYCOBACTERIUM LEPRO*





What counts in life is not the mere fact that we have lived. It is what difference we have made to the lives of others that will determine the significance of the life we lead



NELSON MANDELA (18 May 2002)