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TUBERCULOSIS
PROJECT
SOUTH AFRICA



health

Department:
Health
REPUBLIC OF SOUTH AFRICA

TB/HIV COLLABORATION

CLINICAL MANAGEMENT OF CONCOMITANT TB

URC

Learning Outcomes

- Explain how to diagnose TB in population with high HIV prevalence
- Understand the importance of screening of HIV+ clients for TB
- Discuss TB/HIV Indicators
- Management of Concomitant TB
- Describe Co-trimoxazole Preventive Therapy (CPT) or CTX
- Describe Isoniazid Preventive Therapy (IPT)

TB HIV Indicators

- % of TB patients counselled for HIV
- % of TB patients counselled, HIV tested
- % of TB patients tested, HIV positive
- % of TB/HIV patients started CPT

TB/HIV Indicators

- % of TB/HIV patients referred for HIV care
- % of TB/HIV patients started ART
- % HIV Positive patients amongst All TB cases

7. Proportion of HIV Positive cases amongst All TB cases

$$\frac{\text{The total number of HIV Positive cases} \\ \text{(newly tested + Known Positive cases)}}{\text{Total Number of TB cases started treatment for the} \\ \text{same period}} \times 100$$

TB/HIV Indicators Calculation

- **Example:**
- **Number of TB cases counselled for HIV**
- **Total Number of TB cases started treatment for the same period**

- **X 100**

- **These indicators are worked out in sequence.**
 - The first indicator is measured through the number of TB cases counselled for HIV, divided by the total number of TB cases started treatment for the same period.
 - The second indicator is measured through the number of TB cases that were tested for HIV, divided by the total number of TB cases that were counselled for HIV.
 - The third indicator is measured through the number of TB cases that tested HIV Positive, divided by the total number of TB cases that were tested for HIV
 - Etc.

National Data TB entry point 2006

- 32 % of TB patients had been tested for HIV
- 53% of TB patients were HIV-positive
- 98% of TB patients were receiving CPT

Status of HIV entry point in 2006

- TB screening of HIV patients was alarmingly low. (may be because there are no tools to collect this data)
- TB treatment for HIV patients was lower than expected
- IPT uptake was very low

HIV and TB dual epidemic

- TB is most common HIV-related opportunistic infection
- In South Africa an estimated 55.3% of TB patients co-infected with HIV
- Incidence of TB cases in South Africa rose with 276% (187 to 524/100 00 population)
- Progression of latent to active TB increased from 10% to 50%
- Risk of TB if HIV+ is 10% yearly versus 10% lifetime if HIV negative

Why TB/HIV Collaboration

- Reduce the burden of TB/HIV
- Prevent TB disease in HIV+
- Create an environment in which people choose to be tested for HIV

Why TB/HIV Collaboration

- provide a package of care for the dually infected
- build partnerships and strengthen collaboration
- to strengthen both programmes and make best use of resources

Three I's in the implementation of TB/HIV

- Intensified TB case finding
- Isoniazid preventive therapy
- Infection control (TB)

TB/HIV Interventions at Health Facilities

Interventions for TB/HIV can be done in both settings:

TB Clinics

- Offer HIV testing
- Refer for HIV evaluation
ART assessment
Cotrimoxazole
Diagnosis and treatment of
opportunistic infections

HIV Care Settings*

- Screen for TB symptoms
- Refer patients with symptoms for TB evaluation
- Refer all healthy HIV positive patients for IPT
- Develop TB infection control plan

Important Issues

- **HIV associated with 10% annual risk for active TB**
Result: Worsening TB epidemic
Need: Improved Case Finding and treatment
- **Latent tuberculosis progresses rapidly to active TB**
Result: Increased morbidity and mortality
Need: Isoniazid preventive therapy and antiretroviral therapy

Important Issues (2)

- **Patients with HIV and TB at high risk for other opportunistic infections**
Result: Increased morbidity and mortality
Need: Cotrimoxazole preventive therapy and ART
- **HIV-infected patients may show paradoxical worsening of TB when put on ART**
Result: Increased morbidity (and mortality)
Need: Recognition of immuno-reconstitution inflammatory syndrome (IRIS) and treatment with corticosteroids



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Diagnosis of TB in HIV



Exclusion of active PTB

- All HIV+ clients must be screened for TB
- Incidence of Extra Pulmonary TB increases in HIV+ clients
- All HIV+ clients must be asked about signs and symptoms of TB:
 - Cough > 2 weeks
 - Fever > 2 weeks
 - Night sweats
 - Weight loss >1.5kg in the past month
 - Other symptoms, like pleuritic chest pain and haemoptysis should prompt investigation for TB

Diagnostic approach

- Currently the protocol for diagnosis of TB follows NTCP principles, irrespective of HIV status
- In HIV+ patients a higher degree of attention will be required
- Diagnosis of TB in HIV+ persons more difficult
 - increased frequency of sputum smear negative disease (pulmonary or extra-pulmonary)
 - increased atypical radiology

Clinical features

Depend on degree of immunodeficiency

- In earlier stages of HIV clinical presentation similar to HIV negative individuals
- As CD4 count drops TB more atypical and increased risk for extra-pulmonary disease

Clinical Features (2)

- Prominent weight loss
- Prominent night sweats
- Less massive haemoptysis

Sputum Collection

Sensitivity of microscopy depends on:

- quality of sputum
- quality of laboratory processing and
- Quality of staining and microscopy

If a patient is unable to produce adequate sputum, nebulisation with sterile 5% saline may be indicated and the service of a physiotherapist may be helpful

Diagnosis of PTB

- All patients with 1 or more signs and symptoms must be investigated further for TB
- Sputum specimens must be collected for the following investigation:
 - 2 sputa samples for microscopy
 - 1 sputum for culture
- Increased proportion of smear negative PTB in HIV (pulmonary & extra-pulmonary)

Diagnosis of PTB (2)

- Chest x-ray **does not** improve case detection
- It is an additional barrier for people to access intervention and treatment
- Emphasis is on sputum sample
- Chest X-ray is not recommended in the screening for TB preventive therapy, but still have a role in those who are TB suspects with negative sputum smears, as per NTCP guidelines

Case definition for smear negative PTB

- 2x negative smears
- No response to antibiotics
- Positive Sputum culture

Management of Concomitant TB



HAART in patients with TB

- Very common situation as TB is the **commonest cause** of morbidity and mortality in HIV-infected patients
- Complex **drug-drug interactions**
- Shared **toxicity**
- Paradoxical **deterioration** of TB due to immune reconstitution

Concomitant TB in adults

- TB is a common co-morbid illness with HIV.
- If an HIV infected patient has symptoms suggestive of TB, 2 sputa for AFB and 1 for culture
- If TB is diagnosed there are 2 scenarios to consider

Scenario 1

The patient develops TB while on HAART

- All patients on HAART should be **monitored** for **development of TB**
- If TB is diagnosed patient should be **referred to doctor** for assessment and treatment
- **HAART should be continued** throughout TB treatment, with changes to regimens and monitoring
- Patients must be monitored for: **drug interaction, toxicity and Immune reconstitution**

Scenario 2

Patient develops TB before commencing HAART

- **TB** treatment always comes **first!**
- CD4+ > 200 – commence **ART after** TB treatment has been completed.
- CD4+ < 50 – initiate ART as soon as TB medication is tolerated
- CD4+ 50 - 200 – delay ART until **after intensive phase** of TB treatment has been completed *unless patient very ill*

HAART in HIV patients with TB

<i>Situation</i>	<i>Recommendations</i>
PTB and CD4 > 200 / μ l	Treat TB, monitor CD4 count 3 –6 monthly Defer ART
PTB and CD4 50-200 / μ l	Start TB Rx and repeat CD4 count after 2/12. Initiate HAART after 2 week wash-out ✓ Efavirenz (EFV) ✓ d4T/3TC (or AZT/3TC or AZT/ddI) ✓ For second line treatment ritonavir / lopinavir
PTB and CD4 < 200 / μ l or EPTB	Start TB Rx and HAART as soon as TB Rx tolerated (2 weeks)

Common shared toxicity of antiretroviral and antituberculous therapy

<i>TOXICITY</i>	<i>TB DRUG/S</i>	<i>ART</i>
Peripheral neuropathy	INH	Stavudine (d4T) Zalcitabine Didanosine (ddl)
Rash	RIF INH PZA	NNRTI's
Nausea	PZA	Didanosine (ddl,Videx) Zidovudine (AZT) Protease inhibitors
Hepatitis	RIF INH PZA	NNRTI's

Points to remember

Patients should be counseled on

- Treatment for TB together with ART involves taking a large number of tablets. (*Patients may struggle with adherence*)
- When ART is commenced, the patient's TB symptoms may temporarily worsen as part of immune reconstitution (*Patients may stop taking treatment*)

Immune reconstitution

- Affects up to 25% patients starting ART
- First weeks sees a worsening of conditions (*Pulmonary infiltrates, cough, persistent fever, sweats, lost of weight, decreasing visual acuity*)
- TB most common reason for IRIS
- Do not stop ART drugs
- Treat with high doses corticosteroids (1 mg/kg) for 2 weeks

Concomitant TB

- Patients on 2nd line treatment : need to add ritonavir which is only stopped 1 month after completion of TB treatment
- If TB infection is present before starting ART
 - Time of initiation of ARVs depends on CD4 count and clinical condition
 - Use efavirenz instead of nevirapine

Concomitant TB and pregnancy

If TB develops while on ART

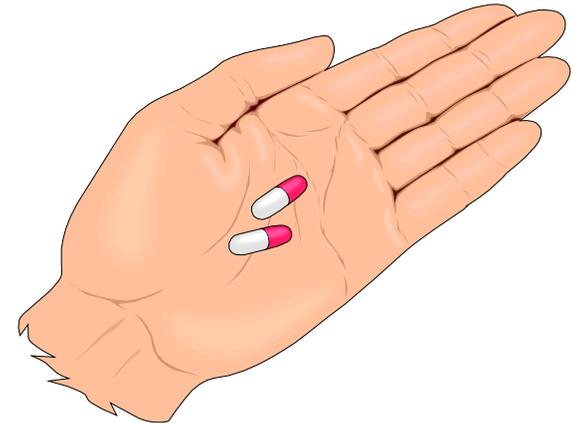
- Continue ARV therapy throughout TB treatment
- Patients on 1st line therapy containing nevirapine need to be swapped to efavirenz
- Pregnant patients on 1st line therapy containing nevirapine or efavirenz need to be swapped to kaletra and ritonavir during 1st and 2nd trimester (EFV acceptable in 3rd trimester)

Cotrimoxazole Preventive Therapy (CPT)



Indication for CPT

- CD4 count < 200
- Co-existent TB
- Any AIDS defining illness (irrespective of CD4 count)
- Unexplained weight loss (>10% BW)
- Chronic diarrhoea
- Oral hairy leukoplakia
- Oral thrush



Cotrimoxazole hypersensitivity

- **Permanently discontinue if severe**
 - Stevens-Johnson
 - Fixed drug eruption
- Antihistamines and/or steroids & continue
 - If no improvement discontinue CTX
- Dapsone if rash recurs (unless Stevens-Johnson)

J Infect Dis. 2001;184:992-7.

Isoniazid Preventive Therapy (IPT)



IPT preventive therapy

- Benefits HIV infected individuals
- Does not aim to control TB on a public health scale
- Is not an alternative to the DOTS strategy for controlling TB
- Very effective intervention for HIV infected individuals prior to starting ARV

Eligibility for IPT

All HIV positive clients, with no signs and symptoms suggestive of TB, with a positive tuberculin skin test (TST), who has not had active TB in the last 2 years, are eligible for IPT

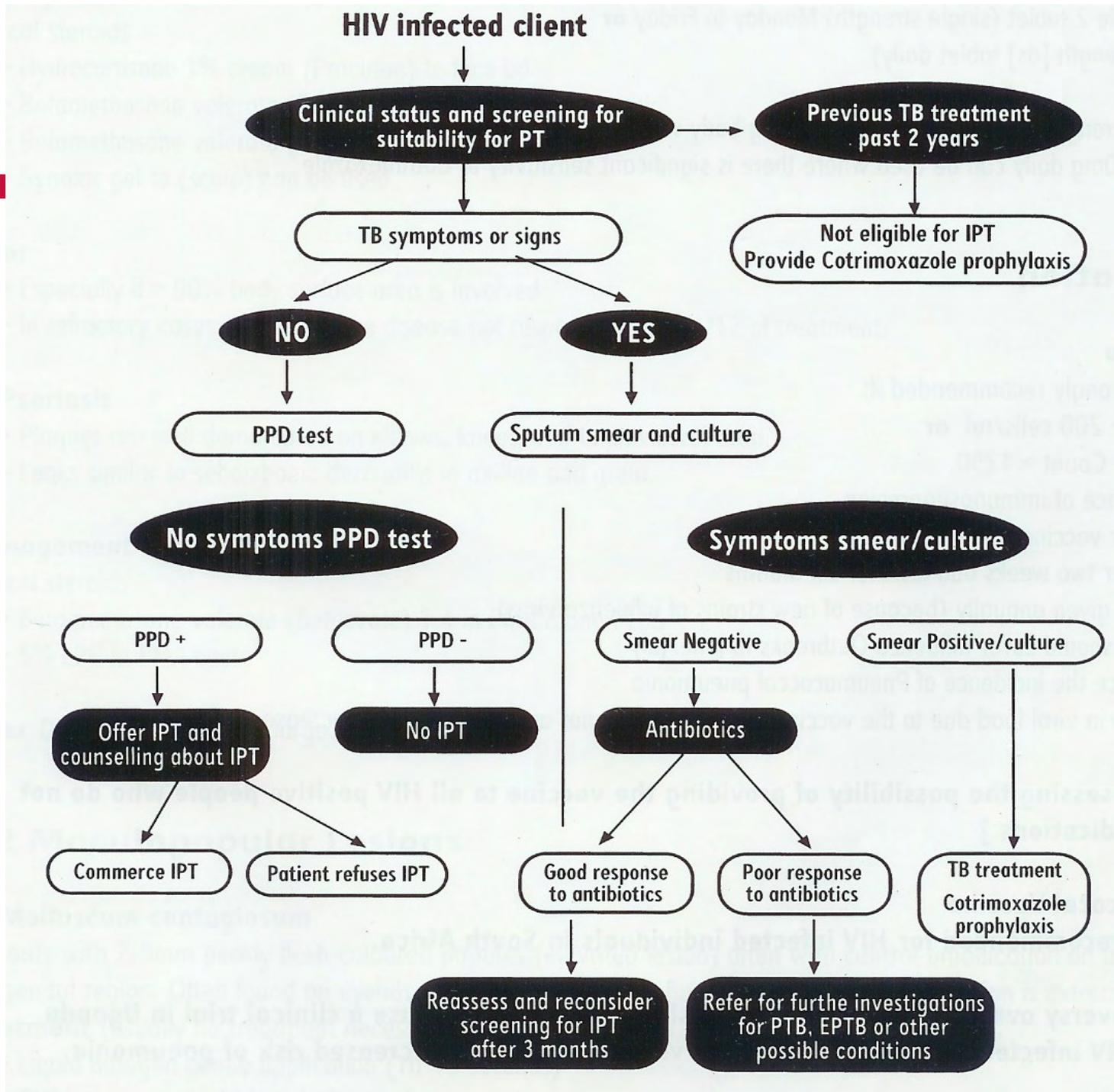
Significance of TST

- Mantoux test recommended technique
- Injecting a known amount of PPD intradermally
- Reaction is measured 48-72 hours later
- Induration (not erythema) must be measured
- Diameter at widest points of the raised area (mm)
- Positive tuberculin skin test results:

<i>Tuberculin test</i>	<i>Previous BCG</i>	<i>NO previous BCG</i>	<i>HIV+</i>
Mantoux	≥ 15 mm	≥ 10 mm	> 4 mm

Who is not eligible for IPT

- HIV negative patients
- HIV+ patients with active liver disease or active alcohol abuse
- HIV+ patients who had active TB in past 2 years should not be considered
- HIV+ patients who had IPT before
- Patients on ART



What about ART and IPT?

- In patients on ART there is currently no evidence of added benefit
- Patients who receive TB preventive therapy and who require to start ART can complete their TB preventive therapy even if the ARV treatment is started

Recommended regimen

- INH: 5 mg/kg/day (maximum 300 mg per day) for 6 months
- Additional Pyridoxine to prevent peripheral neuropathy (50 mg od)
- The intervention should be given once only

TB prophylaxis duration of benefit

- **INH 300mg daily for 6 months**
 - lost significance after 12 months
- **RIF + INH/PZA daily for 3 months**
 - remained significant at 3 years

AIDS 2001;15:2137

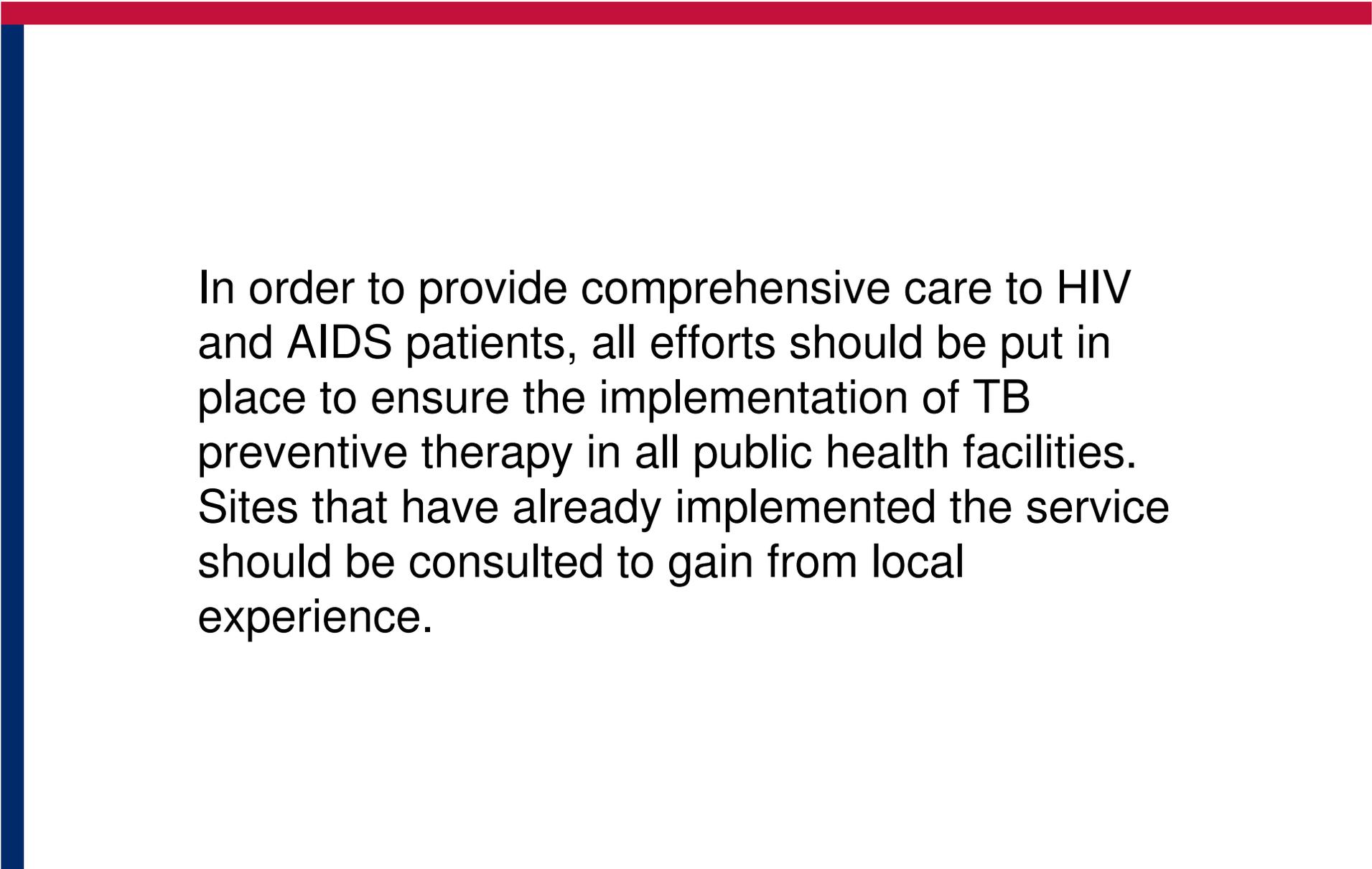
Practicalities of IPT

Second visit:

- Three days (48-72 hrs) later to read TST:
 - If TST +, the patient is offered preventive therapy and informed about symptoms of side effects of INH and the symptoms of active TB
 - If TST negative, preventive therapy is not offered
- Patients should be given one-month supply at a time
- Expected to cover the 6 months therapy within a period of 9 months.

IPT and health services

- IPT should be part of the package of care for all PLWHA
- It should be offered in the following situations:
 - Quality HIV counselling and testing is available
 - Effective TB screening is available
 - Capacity for monthly follow-up and monitoring
 - Presence of a strong collaboration between HIV and AIDS and TB programmes
 - Presence of a functioning HAST committee in the district/sub-district



In order to provide comprehensive care to HIV and AIDS patients, all efforts should be put in place to ensure the implementation of TB preventive therapy in all public health facilities. Sites that have already implemented the service should be consulted to gain from local experience.