

APPENDICES

Appendix 1: World Health Organisation Adults HIV and AIDS Staging System

Stage I

1. Asymptomatic
2. Persistent generalised lymphadenopathy (PGL)
3. Acute retroviral infection (sero-conversion illness) and/or performance Scale 1: asymptomatic, normal activity.

Stage II

4. Unintentional weight loss <10% of body weight
5. Minor mucocutaneous (e.g. seborrhoea, prurigo, fungal nail infections, oral ulcers, angular cheilitis)
6. Herpes zoster within the last five years
7. Recurrent upper respiratory tract infection (e.g. bacterial sinusitis) (URTI) and/or performance Scale 2: symptomatic, normal activity.

Stage III

8. Unintentional weight loss >10% of body weight
9. Chronic diarrhoea >one month
10. Prolonged fever >one month
11. Oral candidiasis
12. Oral hairy leukoplakia
13. Pulmonary TB within the last year (PTB)
14. Severe bacterial infections (pneumonia, pyomyositis)
15. Vulvovaginal candidiasis >one month / poor response to therapy and/or performance Scale 3: bedridden <50% of the day during the last month.

Stage IV

16. HIV wasting (8+9 or 10)
17. *Pneumocystis carinii* pneumonia (PCP)
18. CNS toxoplasmosis (Toxo)
19. Cryptosporidiosis plus diarrhoea >one month
20. Isosporiasis plus diarrhoea
21. Cryptococcosis – non pulmonary
22. Cytomegalovirus infection other than liver, spleen or lymph node (CMV)
23. Herpes simplex infection; visceral or >one month mucocutaneous (HSV)
24. Progressive multifocal leucoencephalopathy (PML)
25. Disseminated mycosis (i.e. histoplasmosis, coccidiomycosis)
26. *Candida* oesophageal/tracheal/pulmonary
27. Atypical mycobacteriosis disseminated (MOTT)
28. Non-typhoidal *Salmonella* septicaemia
29. Extra-pulmonary tuberculosis (ETB)
30. Lymphoma
31. Kaposi's sarcoma (KS)
32. HIV encephalopathy (ADC)
33. Invasive cervical carcinoma and/or performance Scale 4: bedridden >50% of the day during the last month

Appendix 2: Modified WHO clinical staging Paediatric HIV & AIDS classification

Please note: The South African National Paediatric HIV Consensus Team have modified the original WHO Clinical Staging Guidelines for practical reasons. WHO intends updating these in 2004, and the guidelines in this document will be updated to conform to the WHO modifications when they appear.

Stage I

- Asymptomatic
- Generalised lymphadenopathy
- Hepatomegaly
- Splenomegaly
- Parotomegaly
- Chronic suppurative OM
- Eczema/ seborrhoeic dermatitis

Stage II

- Unexplained chronic diarrhoea (≥ 2 weeks)
- Failure to thrive
 - 60 - 80% expected body weight
 - Not responding to nutritional rehabilitation or anti-TB therapy (if clinically indicated). Other correctable causes excluded.
- Recurrent or severe bacterial infection (≥ 2 episodes pneumonia or 1 episode meningitis)
- Oral candidiasis beyond neonatal period
 - Severe persistent or recurrent, not responding to topical therapy
- Haematological
 - Thrombocytopenia (platelet count $< 40\,000 \times 10^9/l$) not responding to prednisone 2 mg/kg/day after 2 weeks
 - Neutropenia (neutrophil count $< 500 \times 10^9/l$) not responding to switch from co-trimoxazole to dapsone

- Severe lymphoid interstitial pneumonitis:
 - Persistent hypoxia $< 90\%$ in the absence of acute infection and/OR
 - Persistent tachypnoea in the absence of acute infection and/OR
 - Easy fatiguability on exertion and/OR
 - Evidence of bronchiectasis and/OR
 - Cor pulmonale
- ≥ 2 episodes zoster or severe herpetic disease

Stage III

- Severe failure to thrive
 - $< 60\%$ expected body weight
 - Not responding to nutritional rehabilitation or TB therapy if clinically indicated
- Encephalopathy
- Recurrent septicaemia (≥ 2 episodes)
- Bronchiectasis
- Cardiomyopathy
- Progressive nephropathy
- Candidiasis (oesophageal or pulmonary)
- Disseminated fungal infection (Coccidioidomycosis, Cryptococcosis, Histoplasmosis)
- Disseminated mycobacterial infection (M. tuberculosis, BCG, avium-intracellulare, Kansasi)
- CMV disease with onset at age > 1 month (at site other than lymph nodes, spleen, liver)
- HSV causing mucocutaneous ulcer persisting > 1 month, or oesophagitis, pneumonitis, oesophagitis in a child older > 1 month
- Pneumocystis carinii pneumonia (PCP)
- Progressive multifocal leukoencephalopathy
- Cerebral toxoplasmosis with onset > 1 month of age
- Recurrent/persistent salmonella ESBL
- Malignancies

Appendix 3: Paediatric dosing schedule

Method 1:	Method 2:
<p>The body surface area of a child can be determined using the nomogram for infants and young children as stated in the Handbook of Paediatrics, 5th edition or on page 297 of the Paediatric Standard Treatment Guidelines 1998 (purple book)</p>	<p>Use the following formula:</p> $BSA = \sqrt{\frac{Hgt(cm) \times Wgt(kg)}{3600}} \text{ m}^2$ <p>For example: Height: 80 cm Weight: 12 kg</p> $BSA = \sqrt{\frac{80(cm) \times 12(kg)}{3600}} \text{ m}^2$ <p>Use your calculator in the following way: Step 1: Press: 80 x 12 and = Step 2: Press: ÷ 3600 and = Step 3: Press: square root button Your answer = 0.52 m²</p>

Appendix 4: TB prophylaxis

Guidelines for tuberculosis (TB) preventive therapy among HIV-infected patients

Background

The dramatic spread of the HIV epidemic throughout sub-Saharan Africa in the past decades has been accompanied by up to a fourfold increase in the number of TB cases registered by the national TB programmes. Strategies to control TB must now include interventions to reduce HIV infection.

On the other hand, it is estimated that around 50% of new adult cases of TB in South Africa are co-infected with HIV. TB is the commonest

cause of morbidity and mortality among HIV-infected population in South Africa. Studies have shown that TB does accelerate HIV-disease progression. Therefore, preventive TB therapy should be offered in the package of care for people living with HIV. While it is not likely to reduce the incidence of TB in the community, it can provide real benefits to the individuals.

TB preventive therapy is the use of one or more anti-tuberculosis drugs given to individuals with latent infection with *M. tuberculosis* in order to prevent the progression to active TB disease.

Trials have shown that maximum benefits from TB preventive therapy are achieved in HIV-infected patients with evidence of TB infection as assessed by a positive tuberculin skin test. In these patients, the risk of developing TB is reduced by 60%, and their survival is also prolonged. However, some benefit is also shown in HIV-positive groups in general, regardless of the tuberculin test result.

TB preventive therapy and health services

TB preventive therapy is an intervention that should be part of the package of care for people living with HIV. It should only be offered in the following situations (pre-requisites):

- If quality voluntary counselling and rapid testing for HIV is available.
- If there is effective screening for active TB before initiating TB preventive therapy.
- If there is capacity for monthly follow-up and monitoring of patients to encourage adherence, address eventual side-effects and exclude active TB disease.
- If the local HIV/AIDS programme takes responsibility for implementation of preventive therapy.
- If there is strong collaboration between HIV/AIDS and TB programmes.

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

Exclusion of active TB

It is essential to exclude active TB in every patient prior to starting preventive therapy. This is critical in order to avoid giving one drug to patients with TB disease who require the full regimen.

Patients interested in TB preventive therapy should be specifically asked about signs and symptoms of TB:

- Cough >2 weeks
- Fever >2 weeks
- Night sweats
- Other symptoms, like pleuritic chest pains, haemoptysis should also prompt investigations for TB
- Weight loss of >1.5 kg in the past 4 weeks: weight should be measured at each clinic visit to allow documented evidence of weight loss. A weight loss of >1.5 kg should be considered a positive screen indicator.

All patients with 1 or more signs and symptoms must be investigated further for TB. They are not immediately eligible for TB preventive therapy. Sputum specimens must be collected for the following investigations:

- 2 sputum samples for microscopy
- 1 sputum for culture

Trials have shown that a chest x-ray does not improve case detection, and is an additional barrier for people to access the intervention. Emphasis is on sputum samples and, where appropriate, on identification of extrapulmonary TB.

Chest x-ray is not recommended in the screening for TB preventive therapy, but still has a role in those who are TB suspects with negative sputum smears, as per the national TB guidelines.

Eligibility for TB preventive therapy

Clinical trials have shown that the benefit of TB preventive therapy is greater in HIV-positive people with positive tuberculin skin test.

All HIV-positive people, with no signs and symptoms suggestive of active TB, with positive tuberculin skin test, are eligible for TB preventive therapy.

- Particular attention should be given to the following populations: miners, prisoners, TB contacts and health care workers.
- Patients with signs and symptoms suggestive of TB must be investigated for TB (see flowchart, page 88). If they are not confirmed with TB (smear and culture are both negative), and they recover from their illness, they can be re-assessed after 3 months for TB preventive therapy.
- HIV-positive people, with no symptoms, but with negative tuberculin skin test, should not be offered TB preventive therapy.
- Tuberculin skin test should be offered to all HIV-infected people. Staff should be trained to provide quality tuberculin skin test using the Mantoux technique.

Tuberculin skin test

The tuberculin skin test measures the body's immune response to an injection of tuberculin purified protein derivative (PPD). The Mantoux test is the recommended technique that injects a known amount of PPD between the layers of the skin (intradermally). The injection must go into the skin and not under the skin. The reaction is measured at the site of injection 48-72 hours later.

The induration (not the eventual erythema) must be measured accurately: measure the diameter of the reaction at the widest points of the raised, thickened area. Record the result in millimetres. To help measure accurately, mark the edges of the induration at the widest point with a pen (two point pen method). Then measure the exact distance between the two points.

Positive tuberculin skin test results:

Tuberculin test	Previous BCG	NO previous BCG	HIV positive
Mantoux	≥15 mm	≥10 mm	>4 mm

What does a positive tuberculin skin test mean?

A positive test indicates infection with TB, but not necessarily TB disease. A positive reaction occurs after BCG immunisation and remains positive for several years thereafter. This reaction is usually weaker than the reaction to natural infection with *M. tuberculosis*.

Conditions that may reduce or suppress the tuberculin skin test include:

- HIV infection
- malnutrition
- severe viral infections (e.g. measles, chicken pox)
- cancer
- immuno-suppressive drugs (e.g. steroids)
- severe disseminated TB

Who is not eligible for TB preventive therapy?

- Patients with active liver disease or active alcohol abuse should not be offered TB preventive therapy. This is because of potential hepatotoxicity of the drug used for preventive therapy.
- Patients with history of TB treatment:
 - Any patient who had active TB in the past 2 years, should not be offered TB preventive therapy.
 - Any patient who was treated for TB more than 2 years ago, may be offered TB preventive therapy. The curative effect of TB treatment and prophylactic effect of INH lessens over time, and thus re-infection is common.
- Patients on ART should not be offered TB preventive therapy, as 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 ART is started. This is because there is no interaction between isoniazid and the current ART regimen used.

Recommended regimen

The standard regimen for TB preventive therapy is: Isoniazid (INH) daily.
The dose is: 5 mg/kg/day (maximum 300 mg per day).
The recommended duration is: 6 months.

Additional Vitamin B6 (Pyridoxine) is part of the vitamin complex that HIV-infected patients receive in sufficient dosage to prevent the eventual occurrence of peripheral neuropathy.

At this stage the intervention should be given once only and the protective effect is expected to last for 18 months.

When and how to start

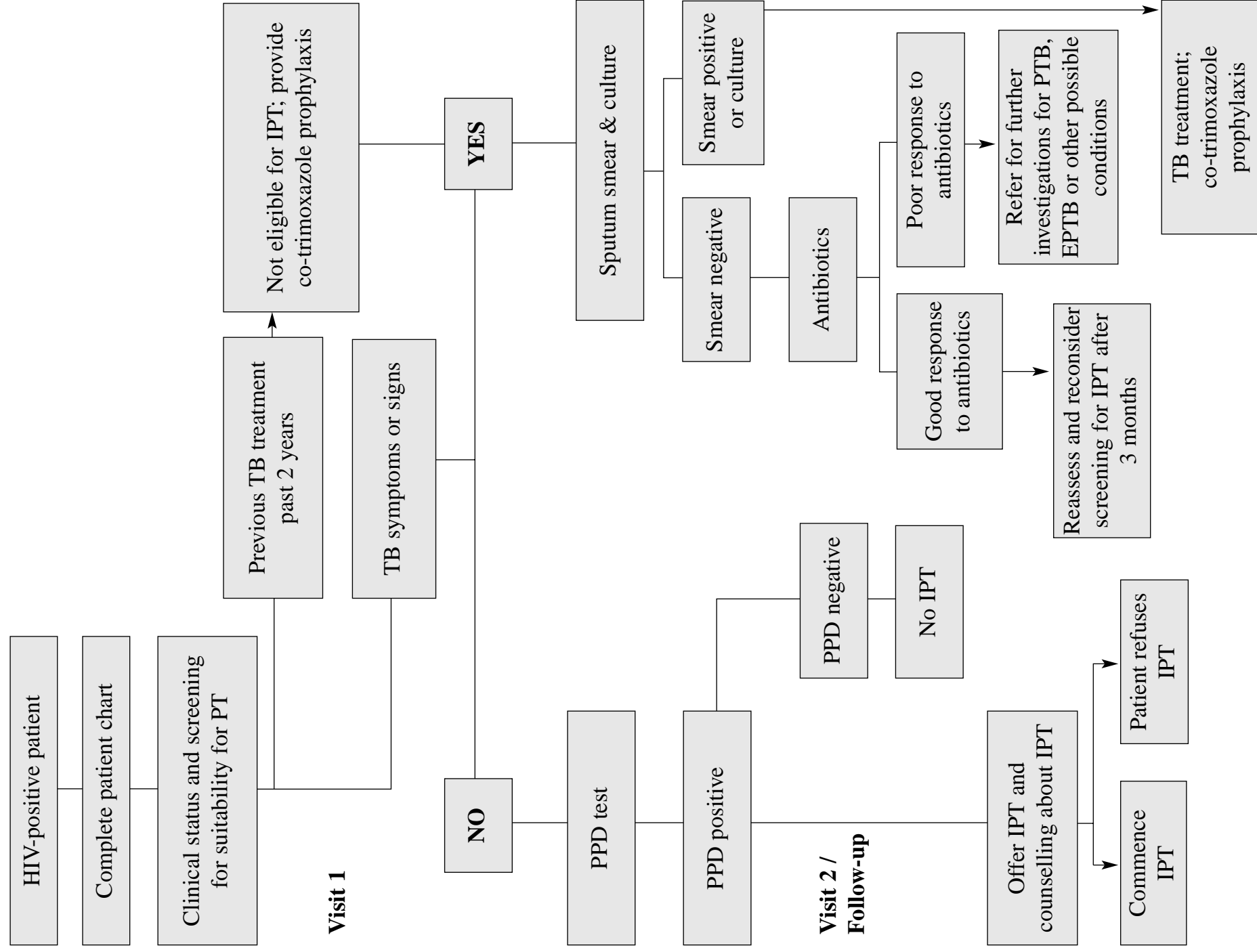
Information about TB, including preventive therapy, should be made available to all people living with HIV/AIDS. Experiences from trials and operational research have stressed the importance of relevant information for the patients including the issue of adherence. TB preventive therapy must be discussed and adequately planned to ensure full understanding and adherence by the patients. During the post-test counselling, the patient is informed about the possibility of TB preventive therapy, and is told to come if she/he is interested. It is not recommended to offer TB preventive therapy immediately after breaking the HIV result to the patients.

For people who know their HIV status for one month or longer, a two-visit schedule is recommended as follows:

First visit

- The known HIV-infected patient is offered TB screening (symptomatic). This screening is essential to exclude any active TB that would require full treatment.
- The health worker must systematically enquire on the existence of the signs and symptoms discussed above and investigate as appropriate.
- It is only when the patient is free of the above symptoms that she/he is offered the tuberculin skin test.

Figure 9: Screening for tuberculosis preventive therapy flowchart among HIV-infected patients



Second visit

- Three days (48-72 hrs) later, the patient is seen for reading the result.
- If the skin test is positive, the patient is offered TB preventive therapy, with adequate provision of information.
- If the test is negative, TB preventive therapy is not offered, and the patient may be given a subsequent appointment to review the condition, the clinical staging and CD4 status accordingly (see ART guidelines).
- During on-going counselling sessions, the patients will be informed about:
 - HIV
 - symptoms of side-effects of isoniazid (particularly hepatitis)
 - the importance of adherence
 - the symptoms of active TB
 - the importance of seeking care, if they develop an illness
- Patients starting TB preventive therapy should be given one-month supply at a time. They are expected to cover the 6 months therapy within a period of 9 months.

Monitoring

Isoniazid 5 mg/kg daily is to be given for 6 months. Patients are requested to collect their supplies on a monthly basis. This visit is the opportunity for:

- on-going counselling
- identification of side-effects (minor: peripheral neuropathy; major: jaundice, vomiting and confusion, due to hepatitis)
- early detection of active TB

Patients should come for review if any symptoms occur.

- If the patient develops active TB, stop the preventive therapy and start the full TB treatment regimen.
- In case of peripheral neuropathy, prescribe 100 mg pyridoxine (Vitamin B6) daily until symptoms disappear.
- If the patient develops signs and symptoms suggestive of hepatitis, stop INH preventive therapy immediately, and refer to a medical officer.
- If the patient interrupts therapy, enquire about the possible reasons for interrupting. Counsel on the importance of adherence appropriately. Restart the therapy after assessing the reasons for bad adherence. Ensure that the 6 months therapy is taken within a 9-month period. If the patient interrupts for the second time, consider stopping the therapy.

Preventive therapy has shown to benefit HIV-infected patients. It does not aim to control TB on a public health scale, and it is not an alternative to the DOTS strategy for controlling TB. It is a very effective intervention for HIV-infected patients prior to starting ART.

These TB preventive guidelines may be reviewed upon evidence of new developments.

ACRONYMS AND ABBREVIATIONS

3TC	Lamivudine	M&E	Monitoring and Evaluation
ACTG	AIDS Clinical Trials Group	MCC	Medicines Control Council
AIDS	Acquired Immune Deficiency Syndrome	NGO	Non-governmental Organisation
ALT	Alanine Amino Transferase	NNRTI	Non-nucleoside Reverse Transcriptase Inhibitors
ANC	Antenatal care	NRTI	Nucleoside Reverse Transcriptase Inhibitors
ART	Antiretroviral treatment	NVP	Nevirapine
ARV	Antiretroviral	OI	Opportunistic Infection
AZT	Zidovudine	PACTG	Paediatric AIDS Clinical Trials Group
CBO	Community Based Organisation	PCR	Polymerase Chain Reaction
CHBC	Community Home Based Care	PEP	Post-exposure Prophylaxis
CHW	Community Health Worker	PI	Protease Inhibitors
CoC	Continuum of Care	PLWHA	People Living with HIV/AIDS
D4T	Stavudine	PMTCT	Prevention of Mother-to-child Transmission
ddI	Didanosine	RTV	Ritonavir
DOTS	Directly Observed Therapy, short course	STI	Sexually Transmitted Infection
EDL	Essential Drugs List	TB	Tuberculosis
EFV	Efavirenz	THP	Traditional Health Practitioners
EPI	Expanded Programme on Immunisation	TLC	Total Lymphocyte Count
HBC	Home Based Care	VCT	Voluntary Counselling and Testing
HIV	Human Immunodeficiency Virus	VL	Viral Load
INH	Isoniazid		
IPT	Isoniazid Preventive Therapy		
LPV	Lopinavir		

RESOURCES

AIDS Helpline:	0800 012 322
Circles of Support Information Hotline:	0860 222 777
Red Ribbon Resource Centre (for free booklets on ART):	(011) 880-0405
National Association of People with AIDS (National office):	(011) 873-0325
Department of Health (HIV/AIDS and STIs Directorate):	(012) 312-0121
Department of Social Development (National HIV/AIDS Co-ordinator):	(012) 312-7500

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