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GLOBAL  
PROGRAMME  
ON  
**AIDS**

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GUIDELINES FOR THE CLINICAL MANAGEMENT  
OF HIV INFECTION IN ADULTS

DECEMBER 1991

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WORLD  
HEALTH  
ORGANIZATION

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## Preface

The number of people infected with the human immunodeficiency virus (HIV) continues to increase rapidly. The World Health Organization (WHO) estimates that over 10 million adults have already become infected and at least one million children have been born with the infection.

Most, if not all, of those infected with the virus are ultimately expected to develop AIDS - more than two million cases of AIDS have already occurred since the beginning of the pandemic. Progression from HIV infection to AIDS takes an average of ten years, so that AIDS cases will continue to develop from the existing pool of infected people for some time to come, no matter how successful our efforts to curb the further spread of HIV.

Infections and tumours are the paramount clinical problems confronting health care providers caring for patients with HIV-related disease. Treatment of these infections and tumours is of great importance as it decreases suffering and prolongs life in the absence of effective and non-toxic antiretroviral drugs or immunotherapy against HIV itself. However, clear treatment guidelines are lacking in many parts of the world and health care workers have often not received training in the management of HIV-related disease.

To respond to this situation, the WHO Global Programme on AIDS (GPA) has developed guidelines for the clinical management of HIV infection in adults. There are wide variations in the presentation of HIV-related diseases, availability of resources and health infrastructures. It is hoped that the guidelines will provide a model to assist all countries, but especially those in the developing world, to formulate national guidelines in accordance with their own particular needs and resources. Adaptation of these guidelines should take place through national/institutional workshops.

The guidelines represent the consensus of a number of clinical experts working in this area, and will be revised from time to time in the light of experience. Comments are welcome and should be sent to the Global Programme on AIDS, World Health Organization, 1211 Geneva 27, Switzerland.

## Acknowledgements

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## Introduction

When faced with a new clinical situation in which research is progressing rapidly, clinicians may find that accepted standards of diagnosis and treatment are unclear, changing or even lacking. HIV infection and AIDS pose such a problem. At present the lack of clear guidelines for clinical management may lead to inaccurate clinical diagnosis, inappropriate treatment, and unsuitable resource planning. These guidelines were developed in response to this lack of a consistent clinical management approach and are part of WHO's commitment to the overall care of people with HIV infection.

It is not possible to prepare guidelines that are universally applicable since this would assume worldwide uniformity in disease presentation, resource availability and health infrastructure. However, it is hoped that countries will use the guidelines presented here as a model when developing their own national guidelines. They are intended to serve the following purposes:

- to assist health care personnel in the diagnosis and clinical management of HIV-infected people;
- to reduce the economic burden of HIV infection by preventing excessive use of diagnostic tests and inappropriate treatment;
- to assist in assessing resource requirements for the HIV epidemic;
- to aid health professionals in the teaching and learning process.

The guidelines are mainly concerned with symptoms and diseases that can be easily identified clinically. They are not intended to replace the health care workers' own clinical judgement.

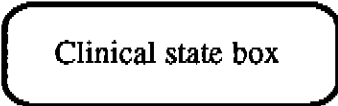
Because of the great variability in health care facilities throughout the world, the guidelines have been structured so as to apply to three different levels of care, based on diagnostic capabilities:

- Level A:** no laboratory or X-ray available, e.g. dispensary or primary health care clinic;
- Level B:** small laboratory available, chest X-ray and microscopy may be possible, e.g. district hospital;
- Level C:** laboratory and other diagnostic facilities of a major hospital, e.g. university teaching hospital.

## Introduction

Where appropriate the guidelines are presented in the form of flow-chart algorithms or decision maps, which read from top to bottom and from left to right. They contain three differently shaped boxes, which have the following functions:

**Clinical state or problem definition box:** This box defines the clinical state or problem. It has only one exit path and may or may not have an entry path. This type of box always appears at the beginning of an algorithm.



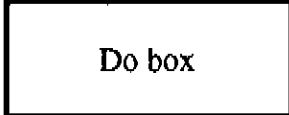
Clinical state box

**Decision box:** This box contains the information necessary for taking some sort of decision. It always has an entry path and two exit (yes and no) paths.



Decision box

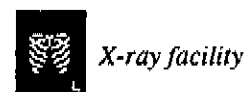
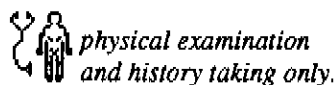
**Do box:** This box indicates an action, which may be either therapeutic or diagnostic.



Do box

Small letters in square brackets (e.g. [a]) within a box refer to the annotations or comments printed on the facing page. These are an essential part of the algorithm, since not all of the information needed to use it can be provided in graphic form or within the boxes. The boxes are also numbered for easy reference.

Each clinical algorithm starts with a clinical box describing the symptoms or problem for which the algorithm is appropriate. In chapters 3-8, this box is followed by initial steps which lead to a branching point. At this point the reader has to choose the appropriate level of care, A, B, or C. For each level the required facilities, indicated by the algorithm, are briefly described and illustrated by small pictures (icons). The choice of level then guides the reader to the corresponding page, where the algorithm continues.



The reader is advised to make use of the following techniques in studying the algorithms.

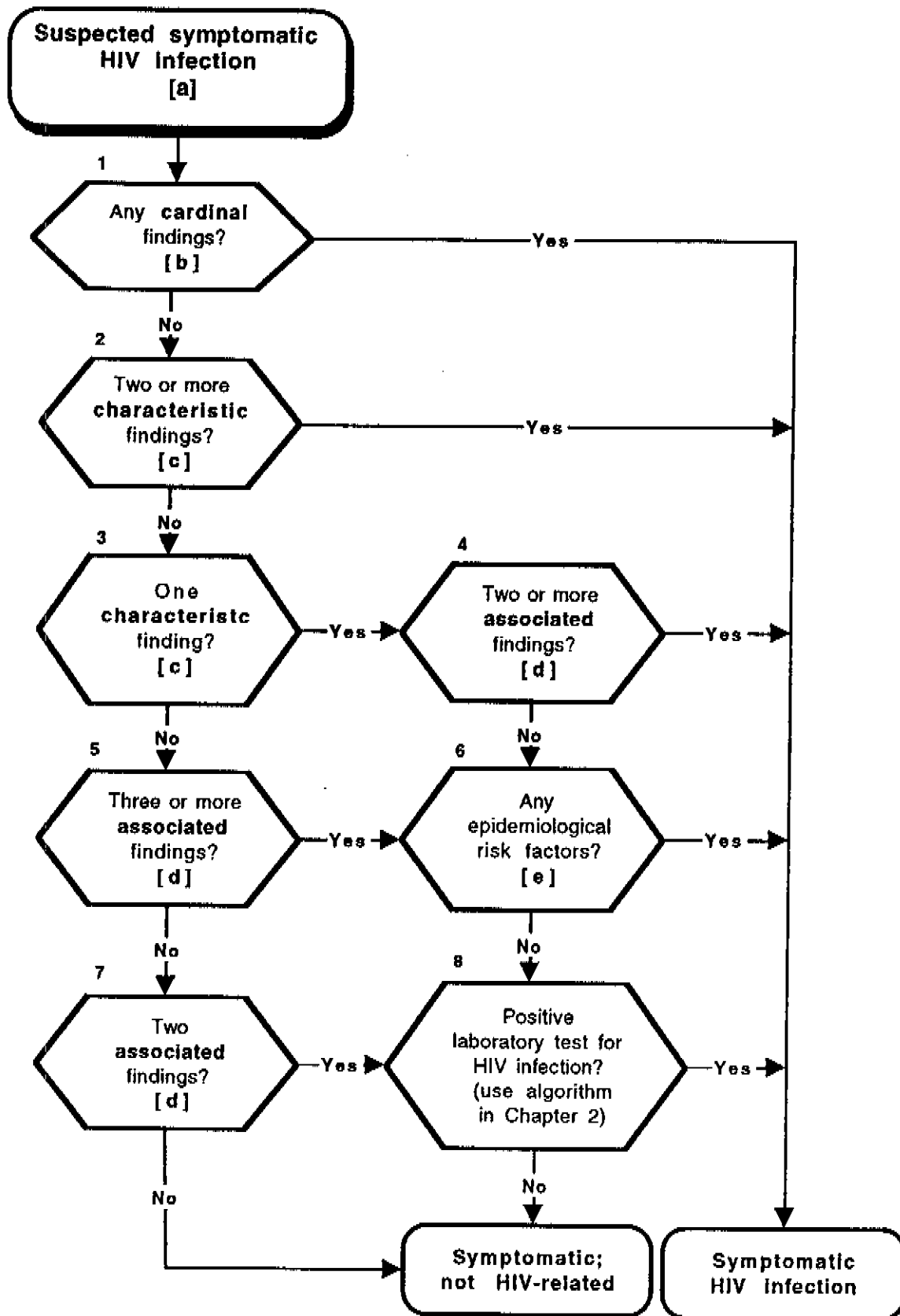
1. Read the algorithm through without reading the annotations, in order to understand the logic flow. A clinician experienced in managing HIV infection should not expect to agree with everything in the algorithm, as there are often more ways than one in which it can be written.
2. Read the algorithm again slowly, paying careful attention both to the annotations and the end-point of each branch. Do not hesitate to pencil in comments as you read, since it has been shown that one of the best ways to understand an algorithm is to rewrite it.
3. Imagine using the algorithm to manage several patients presenting with symptomatic HIV infection. The application of an algorithm to clinical data is a good way of testing it and of learning how it works.

A careful history should be taken and a physical examination always carried out before an algorithm is applied.

## **Chapter 1**

# **Recognition of Symptomatic HIV Infection**

# Recognition of Symptomatic HIV Infection



**Annotations:**

- a. The aim of this Chapter is to help the health care provider to recognize the patient with symptomatic HIV infection, as an aid to clinical management.

Although symptomatic HIV infection can be recognized without laboratory testing, wherever HIV testing is available and affordable it can be used to substantiate the clinical suspicion (see Chapter 2).

- b. Cardinal findings:

- Kaposi sarcoma<sup>1</sup>
- *Pneumocystis carinii* pneumonia
- *Toxoplasma* encephalitis
- oesophageal candidiasis
- cytomegalovirus retinitis.

- c. Characteristic findings:<sup>2</sup>

- oral thrush (in patient not taking antibiotics)
- hairy leukoplakia
- cryptococcal meningitis (may be a cardinal finding in Africa)
- miliary, extrapulmonary or noncavitary pulmonary tuberculosis<sup>3</sup>
- herpes zoster, present or past, particularly multidermatomal, age < 50 years
- severe prurigo
- Kaposi sarcoma (other than as cardinal finding)
- high-grade B-cell extranodal lymphoma.

- d. Associated findings:<sup>2</sup>

- weight loss (recent, unexplained) of more than 10% of baseline body weight, if assessable<sup>3</sup>
- fever (continuous or intermittent) for more than 1 month<sup>3</sup>
- diarrhoea (continuous or intermittent) for more than 1 month
- ulcers (genital or perianal) for more than 1 month
- cough for more than 1 month<sup>3</sup>
- neurological complaints or findings<sup>4</sup>
- generalized lymphadenopathy (extrainguinal)
- drug reactions (previously not seen), e.g. to thiacetazone or sulfonamides
- skin infections (severe or recurrent), e.g. warts, dermatophytes, folliculitis.

<sup>1</sup> Kaposi sarcoma is a cardinal finding only when: (1) intraoral lesions are present; (2) lesions are generalized; or (3) lesions are rapidly progressive or invasive.

<sup>2</sup> If no other obvious cause of immunosuppression is present.

<sup>3</sup> The combination of fever, weight loss and cough is characteristic of both tuberculosis and AIDS.

<sup>4</sup> Neurological complaints or findings associated with HIV infection include seizures (especially focal), peripheral neuropathy (motor or sensory), focal central motor or sensory deficits, dementia, and progressively worsening headache.

## Recognition of Symptomatic HIV Infection

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e. Epidemiological risk factors:

1. Present or past high-risk behaviour:

- drug injecting
- multiple sex partners
- sex partner(s) with known AIDS or HIV infection
- sex partner(s) with known epidemiological risk factor or from an area with a high prevalence of HIV infection
- males having penetrative sexual intercourse with males.

2. Recent history of genital ulcer disease.

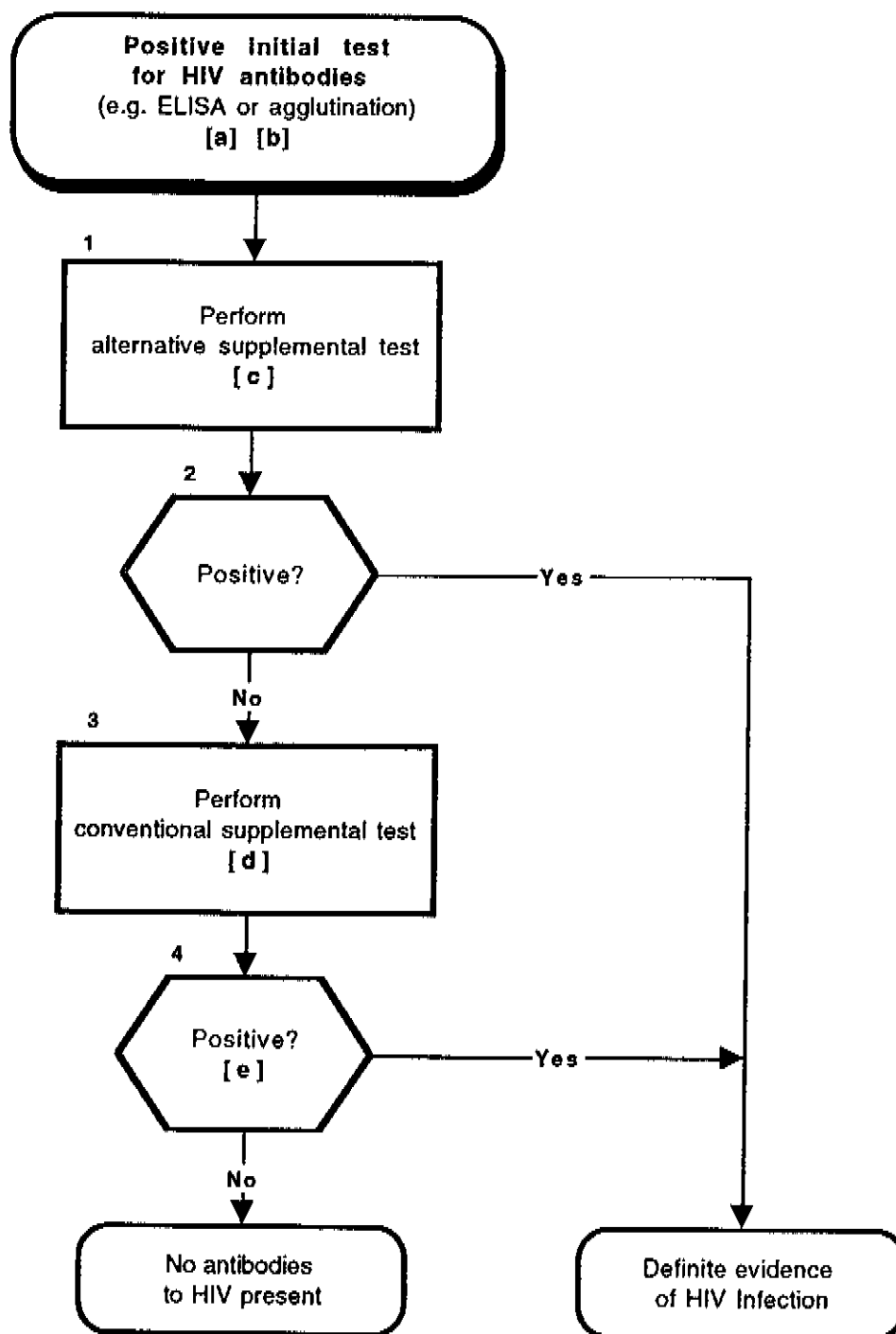
3. History of transfusion after 1975 of unscreened blood, plasma or clotting factor; or (even if screened) from an area with a high prevalence of HIV infection.

4. History of scarification, tattooing, ear piercing or circumcision using non-sterile instruments.

## **Chapter 2**

# **Laboratory Evidence of HIV Infection**

# Laboratory Evidence of HIV Infection



**Annotations:**

- a. The strategy for detecting antibodies to HIV is to undertake initial tests (sometimes referred to as screening tests) on a specimen of serum or plasma followed by supplemental tests (which have also been called confirmatory tests). Both tests and testing strategies should be evaluated under field conditions and in the regions where they are to be used prior to implementation.

It is important to take into consideration relevant clinical and epidemiological information when reporting laboratory results.

- b. Enzyme-linked immunosorbent assays (ELISAs) and particle agglutination are widely used as initial tests. Currently available test kits are highly sensitive and specific, and identify specimens with reactive antibodies. Specimens must be shown to be repeatedly reactive before they are considered positive in the initial test.
- c. The alternative supplemental test should preferably be of a different type (indirect rather than competitive) and use different antigen preparations (viral lysate versus recombinant polypeptides or synthetic polypeptides) to the initial test in order to minimize the occurrence of false positive results.
- d. Conventional supplemental tests include Western blot (WB), indirect immunofluorescence assays (IFAs) and radioimmunoprecipitation assays (RIPAs). A conventional supplemental test is needed only when the results of the initial test and the alternative supplemental test are different or when a borderline result is obtained from either test.

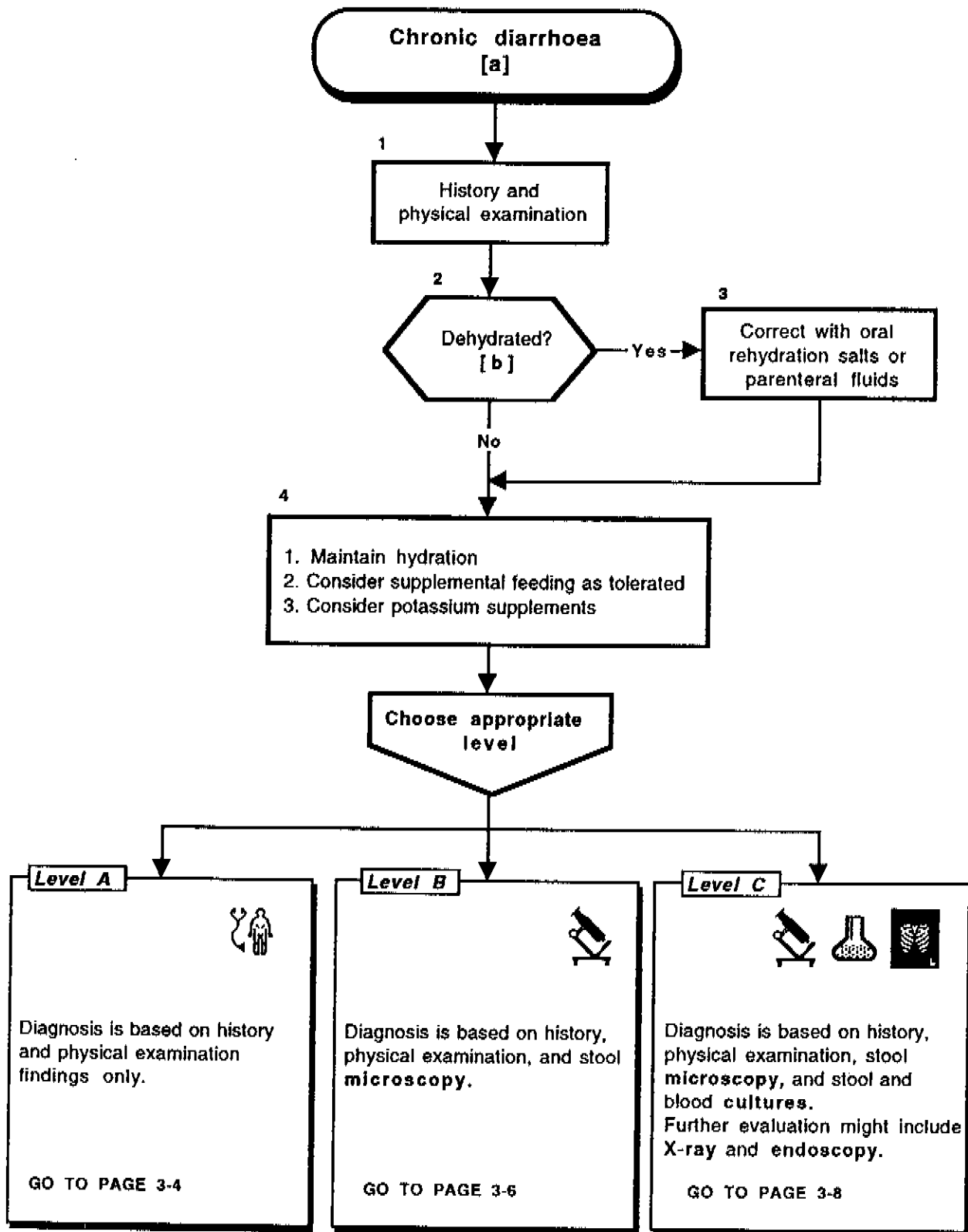
If a conventional supplemental test is not available, a second specimen should be obtained and tested 2 weeks after the first. The second specimen should be referred to a reference laboratory if the result is still inconclusive.

- e. An indeterminate pattern in a WB test may occur during the early stages of seroconversion. The same blood sample should be retested immediately. If the pattern is repeated, a second sample should be collected and tested 2 weeks after the first. If the pattern persists the person should be serially tested for at least 6 months. A person whose WB test results continue to be consistently indeterminate for 6 months – in the absence of epidemiological risk factors or clinical findings (see Chapter 1) – may be considered negative for antibodies to HIV.

## **Chapter 3**

# **Chronic Diarrhoea**

# Chronic Diarrhoea



**Annotations:**

- a. **Definition:** Liquid stools 3 or more times a day, continuously or episodically for more than one month, in a patient with symptomatic HIV infection.

Diarrhoea occurs at some point in the clinical course of most HIV infections. The management of acute diarrhoea should follow standard treatment guidelines (see document WHO/CDD/SER/80.2 REV.2, 1990).

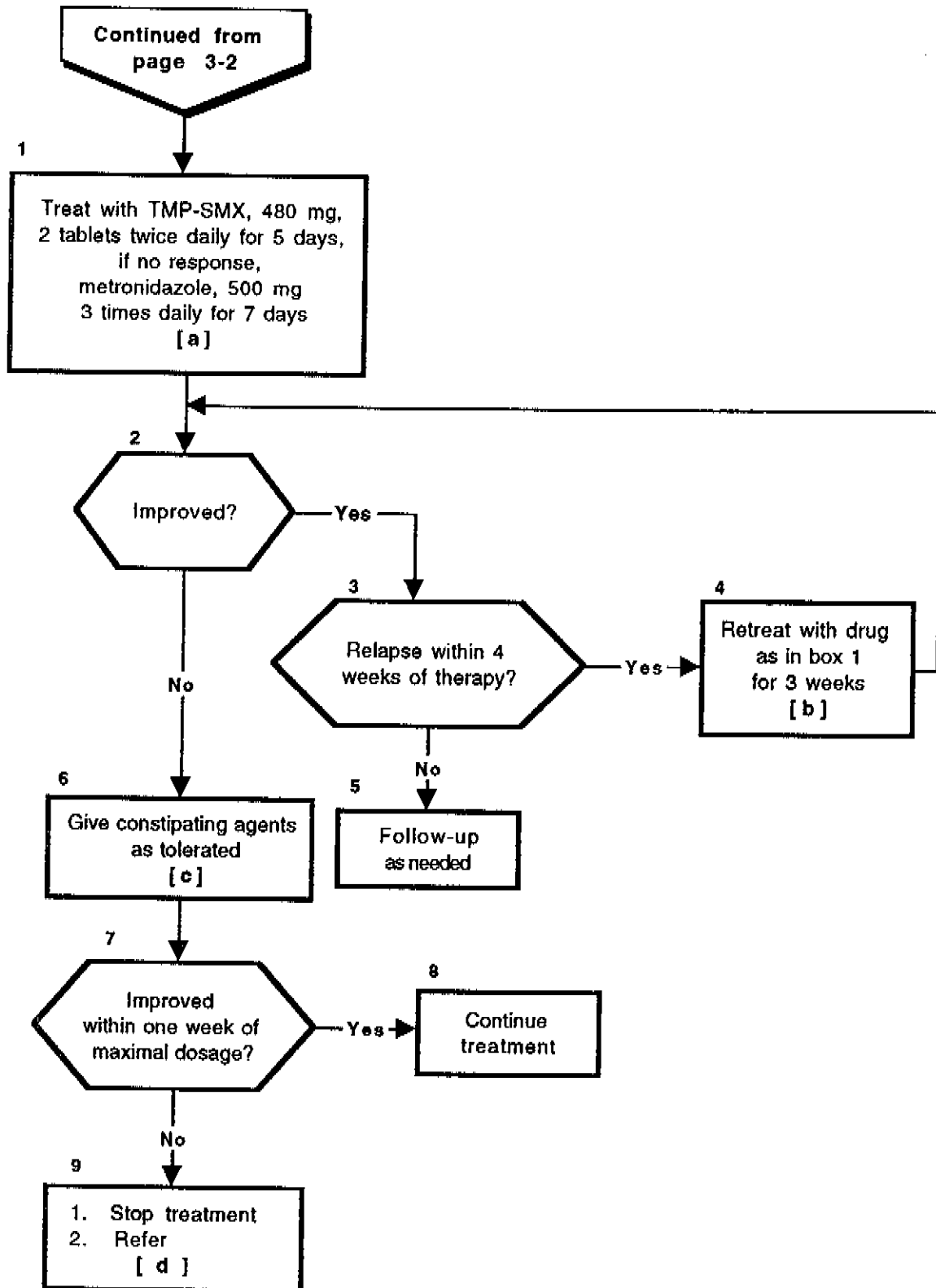
**Etiology:**

1. Infections:
  - cryptosporidiosis
  - *Isospora belli*
  - *Giardia lamblia*
  - *Salmonella* spp.
  - *Shigella flexneri*
  - *Campylobacter* spp.
  - *Entamoeba histolytica*
  - cytomegalovirus disease
  - *Strongyloides stercoralis*
  - *Mycobacterium avium* complex.
2. Malignancies:
  - Kaposi sarcoma
  - lymphoma.
3. Idiopathic (possibly HIV infection).

A list of the main causes in order of significance should be established in the light of available national or local information.

- b. Assessment of dehydration

Clinical features	Dehydration	
	Some	Severe
General appearance/condition	Restless, irritable	Usually conscious; apprehensive; cold, sweaty, cyanotic extremities
Pulse	Rapid	Rapid, feeble, sometimes impalpable
Respiration	Deep, may be rapid	Deep and rapid
Skin elasticity	Pinch retracts slowly	Pinch retracts very slowly (>2 seconds)
Eyes	Sunken	Deeply sunken
Mucous membranes	Dry	Very dry
Urine flow	Reduced amount and dark	None passed for 6 or more hours; empty bladder



Level A

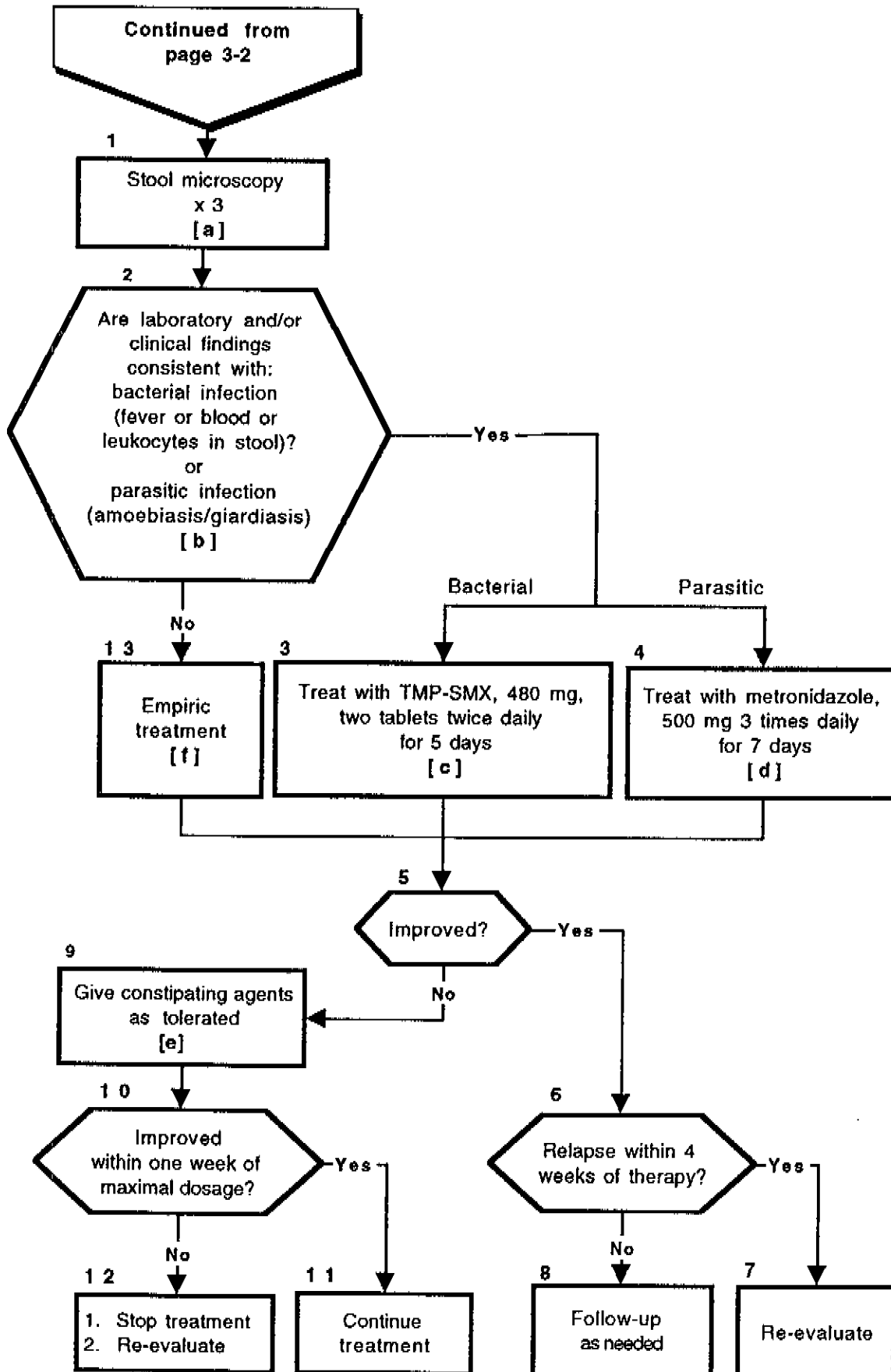
Annotations:

- a. TMP-SMX, trimethoprim-sulfamethoxazole. It is assumed that this treatment will eradicate possible bacterial or parasitic infections. Fever and bloody stools are more indicative of bacterial than parasitic infection.
- b. Relapse may be due to the short duration of the initial treatment. One prolonged course of treatment (for 3 weeks) is justified.
- c. For example, loperamide, 4 mg initially, followed by a further 2 mg after each unformed stool (maximal daily dosage 16 mg), diphenoxylate, 5 mg 4 times daily, or codeine 10 mg 3 times daily.

Before constipating agents are given, treatment of a potential helminthic infection can be tried, e.g. mebendazole, 100 mg 3 times daily for 7 days.

Constipating agents should not be used in patients with bloody diarrhoea, because of the risk of inducing toxic megacolon.

- d. If diarrhoea is disabling, refer to a centre with better care facilities.

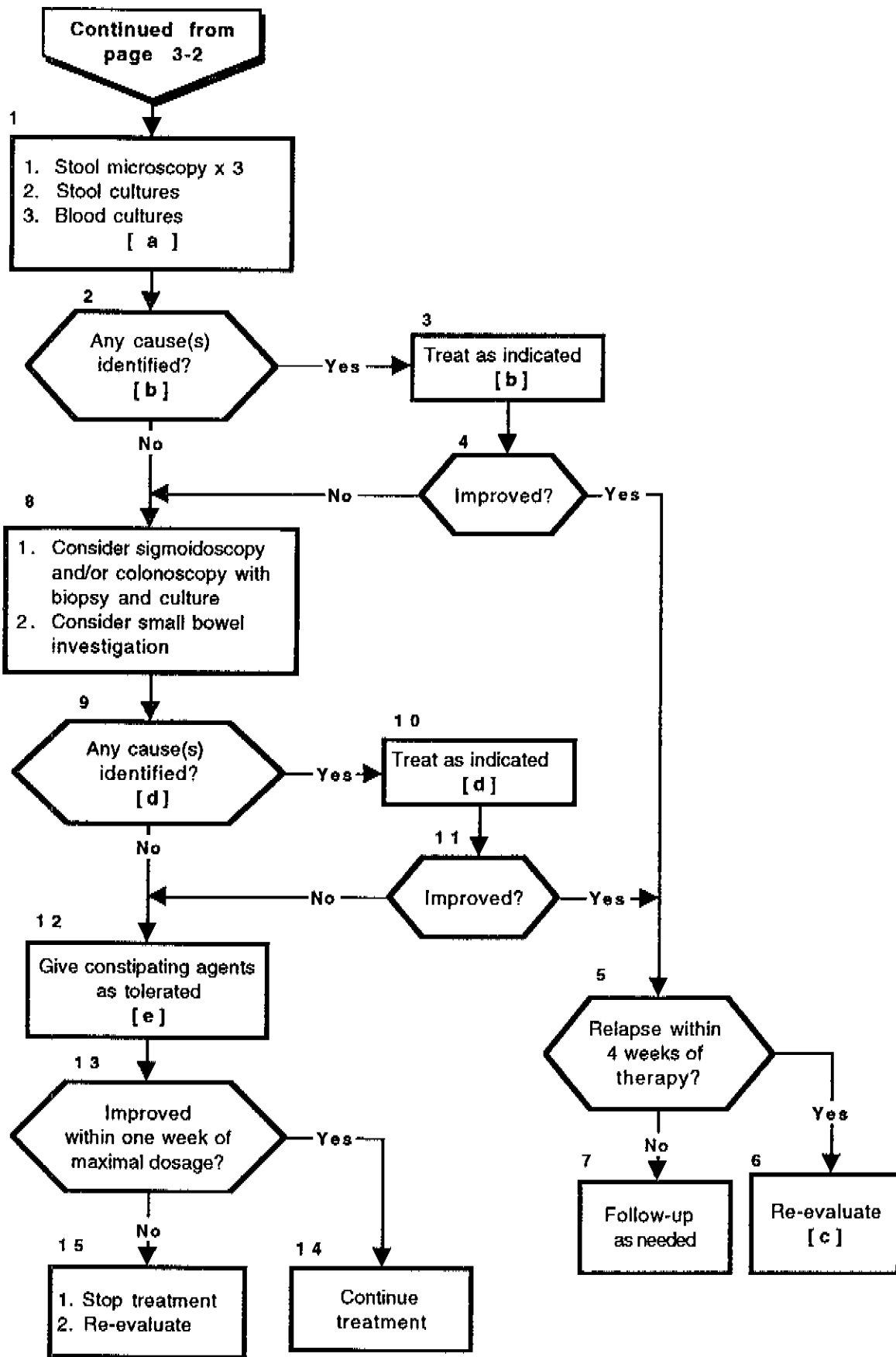


**Level B****Annotations:**

- a. Multiple stool examinations may increase the diagnostic yield of parasites.
- b. In the case of a helminthic infection, treat accordingly. Strongyloidiasis responds well to thiabendazole, 25 mg/kg 3 times daily for 3 days. Albendazole, 400 mg daily for 3 days, has been used more recently.
- c. If treatment for bacterial diarrhoea fails, treat empirically for parasites with metronidazole, 500 mg 3 times daily for 7 days. Metronidazole and trimethoprim-sulfamethoxazole (TMP-SMX) may be given simultaneously to the severely ill patient.
- d. If treatment for parasitic infection fails, consider TMP-SMX, 480 mg 2 tablets twice daily for 5 days, especially if fever and faecal blood or polymorphonuclear cells are found. In some countries treatment for amoebiasis may be followed by diloxanide, 500 mg 3 times daily for 10 days. Metronidazole and TMP-SMX may be given simultaneously to the severely ill patient.
- e. For example, loperamide, 4 mg initially, followed by a further 2 mg after each unformed stool (maximal daily dosage 16 mg), diphenoxylate, 5 mg 4 times daily, or codeine 10 mg 3 times daily.

Constipating agents should not be used in patients with bloody diarrhoea because of the risk of inducing toxic megacolon.

- f. If a microscopic examination does not identify a pathogen, empiric treatment should be tried prior to giving constipating agents. The choice of drug will depend on the pathogen of chronic diarrhoea locally prevalent.



## Level C

## Annotations:

- a. The identification of parasites in the stool is improved by multiple microscopic examinations. Stool culture is most valuable for salmonellosis, shigellosis and campylobacteriosis.

Blood culture should only be done if the patient is febrile or toxic. Salmonellosis, shigellosis and invasive *Mycobacterium avium* complex infections in HIV-infected patients are frequently bacteremic.

Assay for *Clostridium difficile* toxin should be considered in patients who are taking or have taken broad-spectrum antibiotics.

- b. Salmonellosis and shigellosis: e.g. trimethoprim-sulfamethoxazole (TMP-SMX), 480 mg, 2 tablets twice daily for 5 days.

*Campylobacter* spp.: e.g. erythromycin, 2 g daily for 5 days.

Giardiasis: e.g. metronidazole, 250 mg 3 times daily for 5 days.

*Entamoeba histolytica*: e.g. metronidazole, 500 mg 3 times daily for 7 days.

*Isospora belli*: e.g. TMP-SMX, 480 mg, 2 tablets 4 times daily for 10 days.

Strongyloidiasis: e.g. tiabendazole, 25 mg/kg 3 times daily for 3 days.

Cryptosporidiosis: there is currently no established effective treatment. Maintenance of fluid and electrolyte balance is of greatest importance, and constipating agents may also be useful.

*Mycobacterium avium* complex infection: this is resistant to standard antituberculous drugs (except ethambutol). Combination regimens including rifabutin, clofazimine, ethambutol, amikacin and others may assist individual patients but are not established as efficacious.

- c. Salmonellosis, shigellosis, campylobacteriosis and isosporiasis in HIV-infected patients often relapse. If relapse occurs after an initial course of antimicrobial therapy, a 6-12 week course of therapy should be administered.
- d. These include cytomegalovirus colitis, Kaposi sarcoma, lymphoma and *Mycobacterium avium* complex infection.

Disorders not associated with HIV infection, including colorectal carcinoma and inflammatory bowel disease, may also be detected.

The decision to treat any of the above-mentioned diseases will depend, among other things on the local circumstances and available expertise.

If the examinations fail to identify a pathogen and if no specific treatment has been given, a course of empiric antibiotic treatment should be tried prior to giving constipating agents.

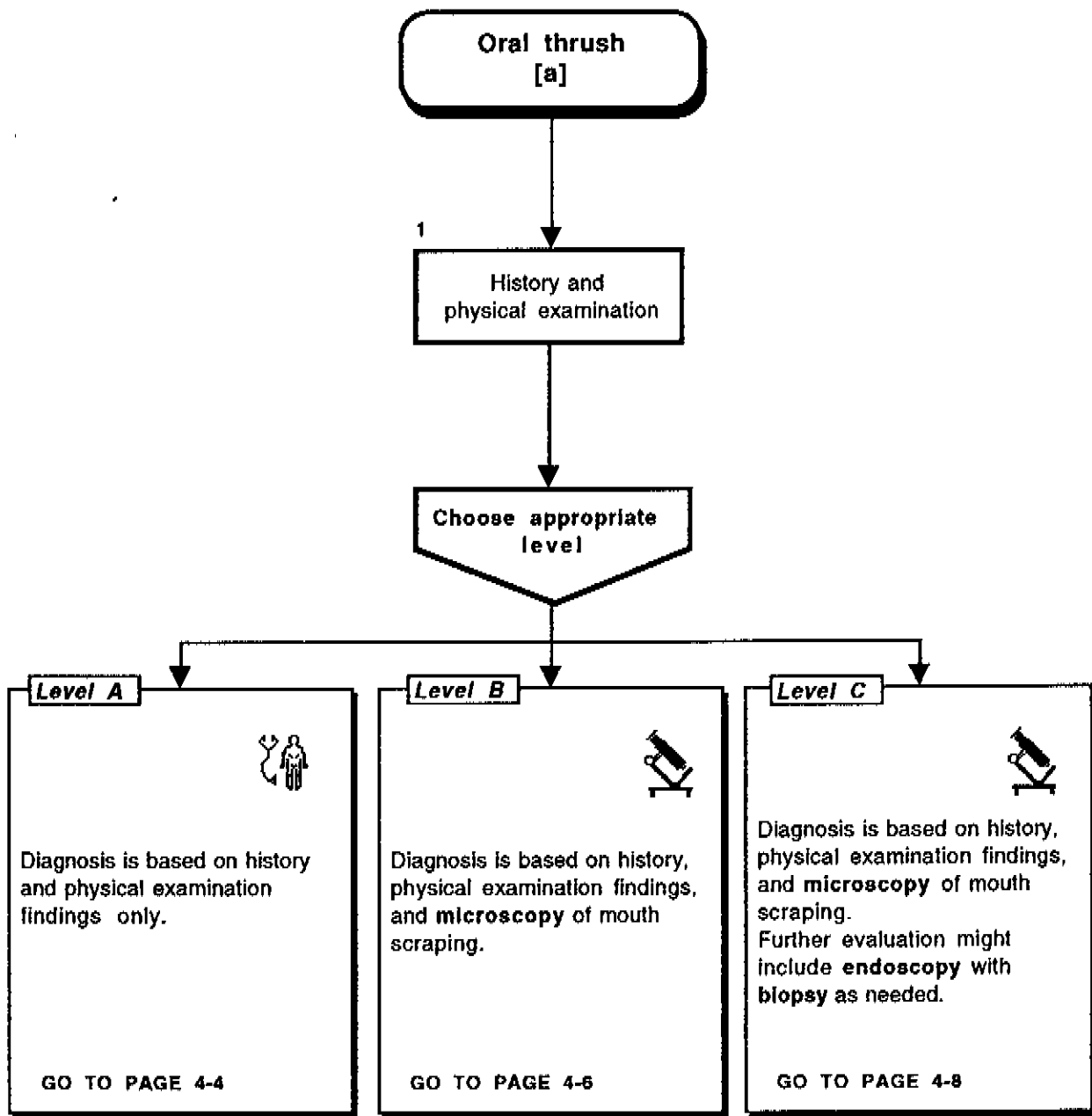
- e. For example, loperamide, 4 mg initially, followed by a further 2 mg after each unformed stool (maximal daily dosage 16 mg) or diphenoxylate, 5 mg 4 times daily.

Constipating agents should not be used in patients with bloody diarrhoea because of the risk of inducing toxic megacolon.

## **Chapter 4**

### **Oral Thrush**

# Oral Thrush



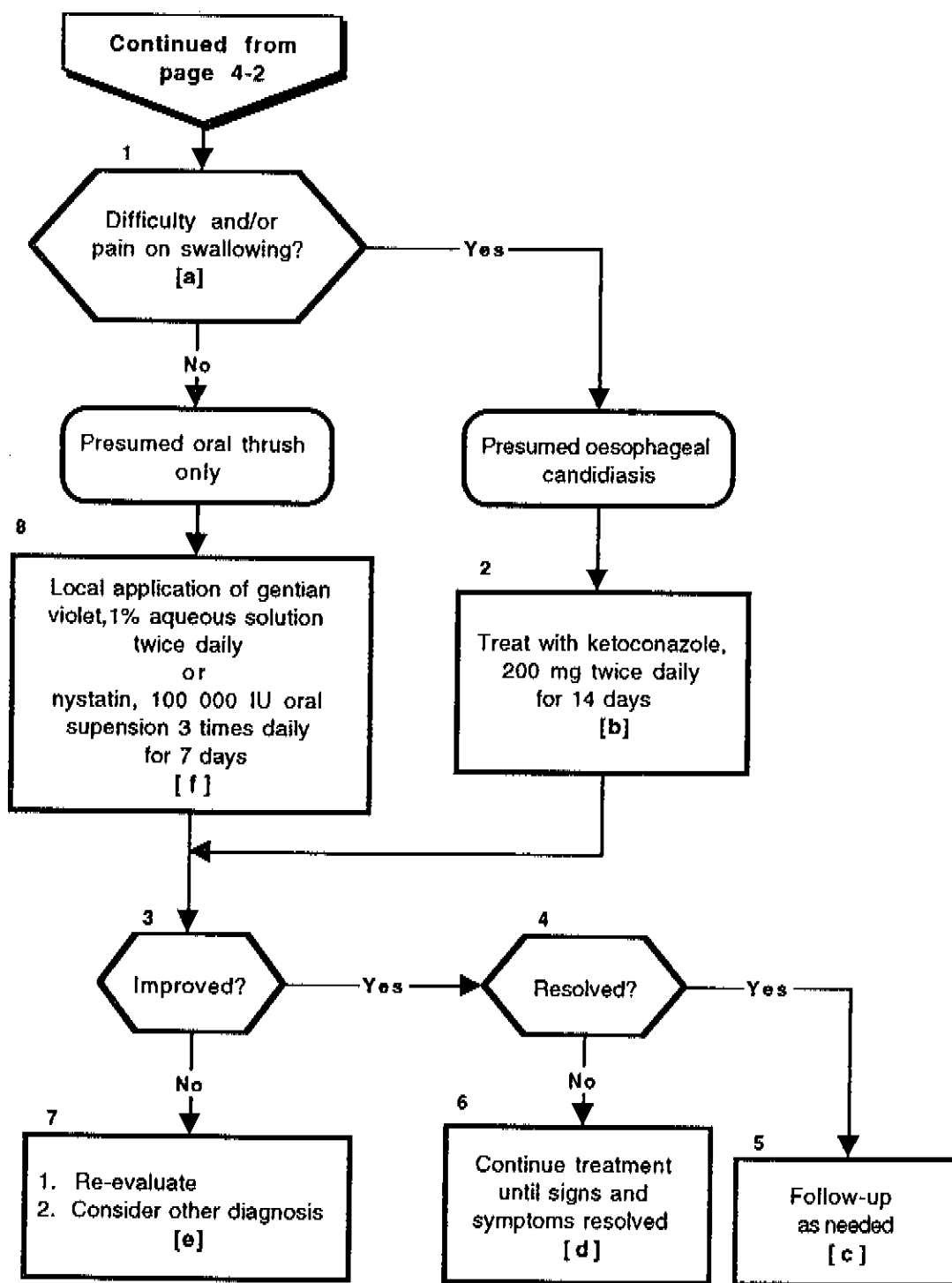
**Annotation:**

**a. Definition:**

**Presumptive:** The presence of whitish plaques on the oral mucosa. These plaques, usually located on the palatal or buccal mucosa, can be removed and then often reveal a bleeding surface.

**Definitive:** Microscopic demonstration of pseudohyphae and/or blastospores of *Candida albicans* from mouth scraping.

**Etiology:** *Candida albicans*.



**Level A****Annotations:**

- a. Candidiasis may extend into the oesophagus in HIV-infected patients with oral thrush and may cause difficulty (dysphagia) and/or pain (odynophagia) on swallowing. Other causes of oesophagitis are infections with cytomegalovirus and herpes simplex virus.

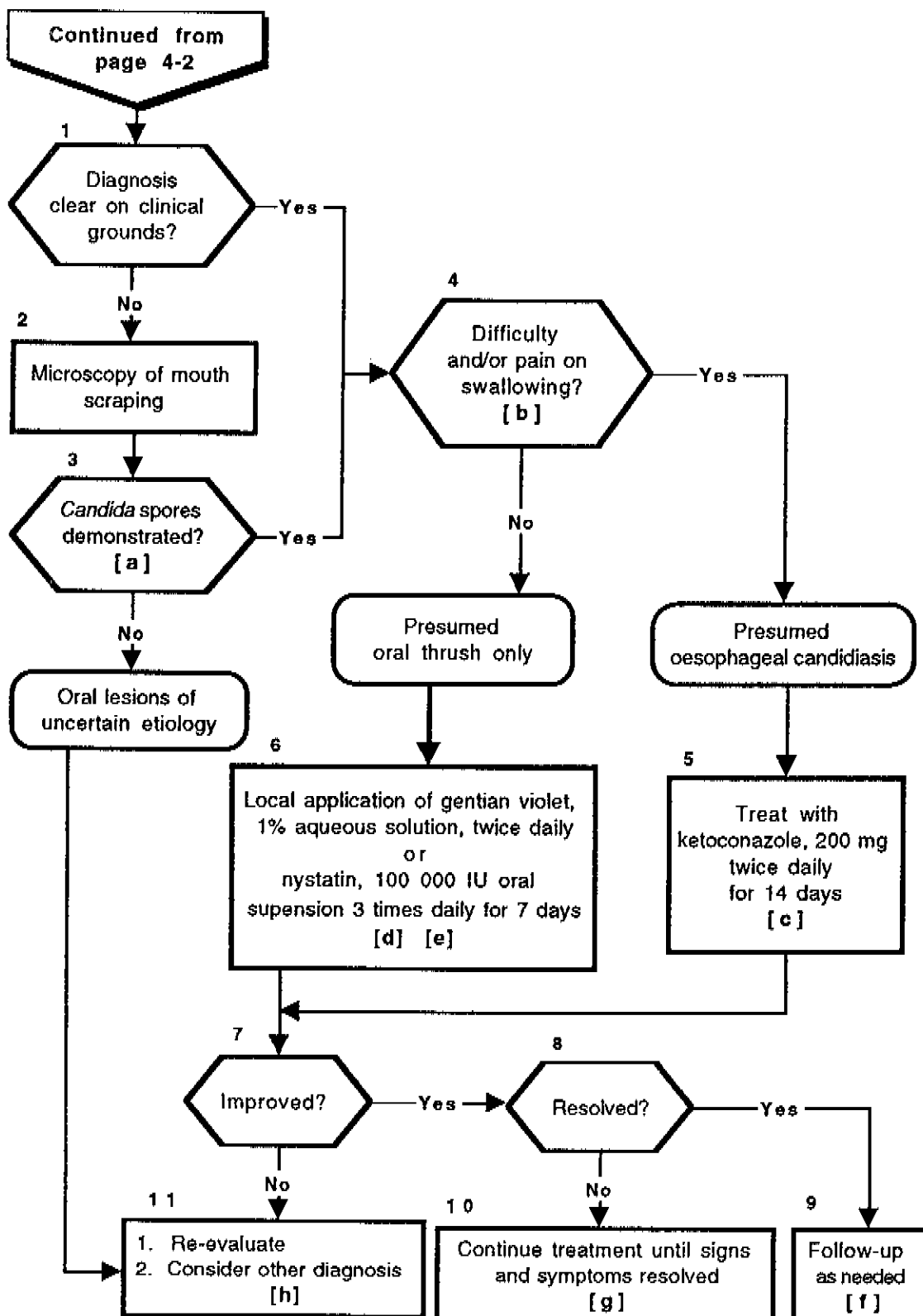
Rarely, these symptoms may be due to malignancy (Kaposi sarcoma, lymphoma, carcinoma) or ulceration owing to contact with oral tablets or acid reflux. Untreated oesophageal lesions, even if causing only mild discomfort, may alter eating habits and make already poor nutrition even worse.

- b. The use of ketoconazole should be avoided in the presence of active liver disease. If available new triazoles (e.g. fluconazole, 200 mg initial dose followed by 100 mg daily for 14 days) are alternatives.
- c. Oral thrush and oesophageal candidiasis have a high likelihood of recurrence and indicate a high risk of other opportunistic infections.
- d. Oesophageal lesions may resolve slowly although symptomatic response is usually prompt. Prolonged therapy until remission is often required.
- e. The presence of hairy leukoplakia may mimic oral thrush. For the differential diagnosis of oesophageal candidiasis, see annotation [a]. A patient with oral thrush who has received only local anti-infective treatment should receive a systemic antifungal drug prior to referral or should be referred for treatment.
- f. If oral suspension is not available, pessaries (100 000 IU, to be sucked every 4 hours) or tablets (500 000 IU, to be sucked every 6 hours) can be used.

Ketoconazole may be used initially for patients with severe thrush, particularly if extending into the pharynx, since this indicates a high likelihood of oesophageal candidiasis regardless of dysphagia.

# Oral Thrush

Level B



## Level B

## Annotations:

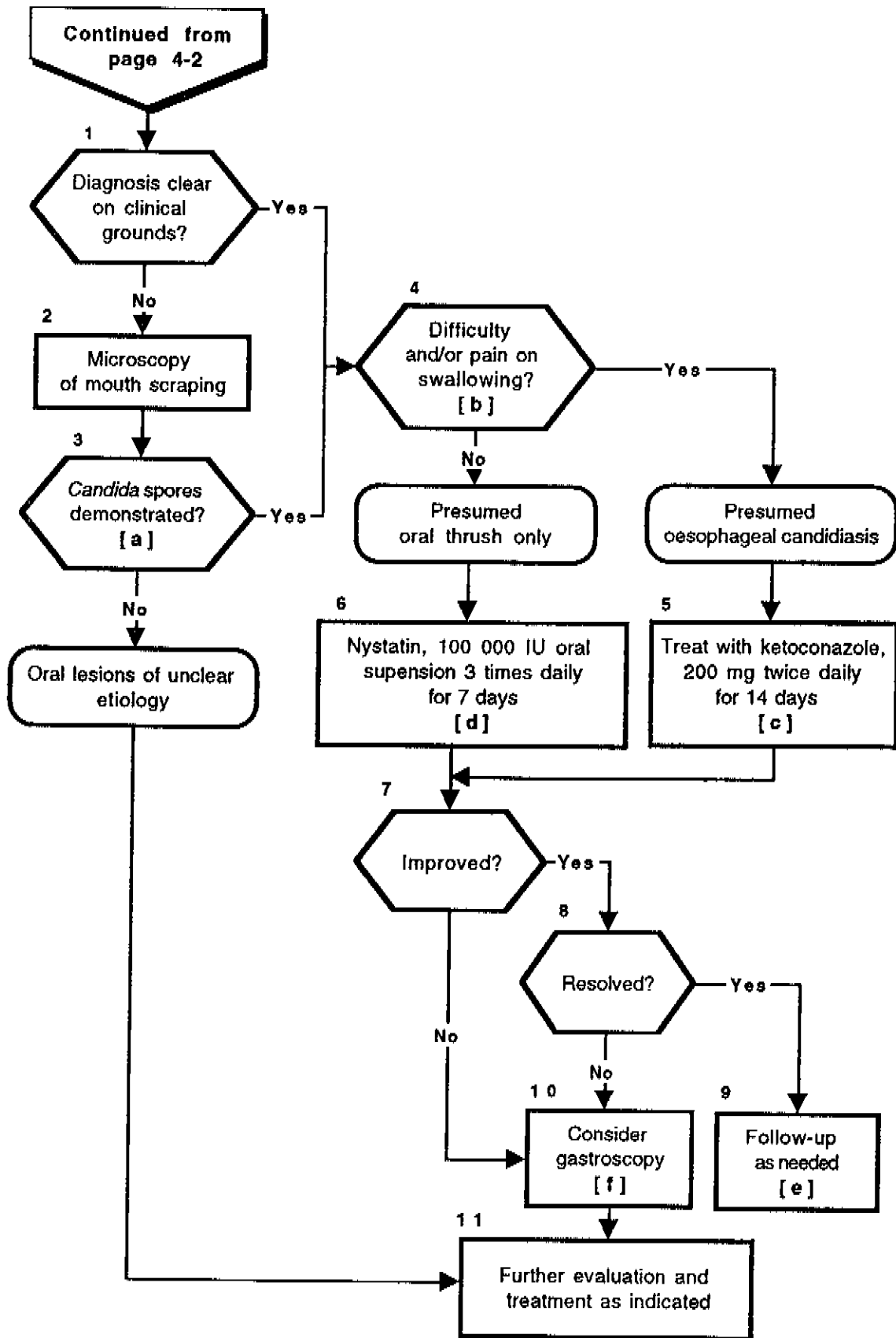
- a. The microscopic identification of pseudohyphae and/or blastospores of *Candida albicans* confirms the diagnosis.
- b. Candidiasis may extend into the oesophagus in HIV-infected patients with oral thrush and may cause difficulty (dysphagia) and/or pain (odynophagia) on swallowing. Other causes of oesophagitis are infections with cytomegalovirus and herpes simplex virus.

Rarely, these symptoms may be due to malignancy (Kaposi sarcoma, lymphoma, carcinoma) or ulceration owing to contact with oral tablets or acid reflux. Untreated oesophageal lesions even if causing only mild discomfort may alter eating habits and make already poor nutrition even worse.

- c. The use of ketoconazole should be avoided in the presence of active liver disease. If available, new triazoles (e.g. fluconazole, 200 mg initial dose followed by 100 mg daily for 14 days) are alternatives.
- d. If oral suspension is not available, pessaries (100 000 IU, to be sucked every 4 hours) or tablets (500 000 IU, to be sucked every 6 hours) can be used.

Alternative topical antifungal therapy is available, e.g. clotrimazole, 1% lozenges, miconazole, 2% gel, or amphotericin B, 10-mg lozenges.

- e. Ketoconazole may be used initially for patients with severe thrush, particularly if extending into the pharynx, since this indicates a high likelihood of oesophageal candidiasis regardless of dysphagia. Prolonged therapy for up to 14 days may be indicated. New triazoles (e.g. fluconazole, 200 mg initial dose followed by 100 mg daily for 14 days) may be more effective and less toxic.
- f. Oral thrush and oesophageal candidiasis have a high likelihood of recurrence and indicate a high risk of other opportunistic infections.
- g. Oesophageal lesions may resolve slowly, although symptomatic response is usually prompt. Prolonged therapy until remission is often required.
- h. The presence of hairy leukoplakia may mimic oral thrush. For the differential diagnosis of oesophageal candidiasis, see annotation [b]. A patient with oral thrush who has only received local anti-infective treatment should receive a systemic antifungal drug prior to referral or should be referred for treatment.



**Level C****Annotations:**

- a. The microscopic identification of pseudohyphae and/or blastospores of *Candida albicans* confirms the diagnosis.
- b. Candidiasis may extend into the oesophagus in HIV-infected patients with oral thrush and may cause difficulty (dysphagia) and/or pain (odynophagia) on swallowing. Other causes of oesophagitis are infections with cytomegalovirus and herpes simplex virus.

Rarely, these symptoms may be due to malignancy (Kaposi sarcoma, lymphoma, carcinoma) or ulceration owing to contact with oral tablets or acid reflux. Untreated oesophageal lesions, even if causing only mild discomfort may alter eating habits and make already poor nutrition even worse.

- c. The use of ketoconazole should be avoided in the presence of active liver disease. If available new triazoles (e.g. fluconazole, 200 mg initial dose followed by 100 mg daily for 14 days) are alternatives.
- d. Alternative topical antifungal therapy is available, e.g. clotrimazole, 1% lozenges, miconazole, 2% gel or amphotericin B, 10-mg lozenges.

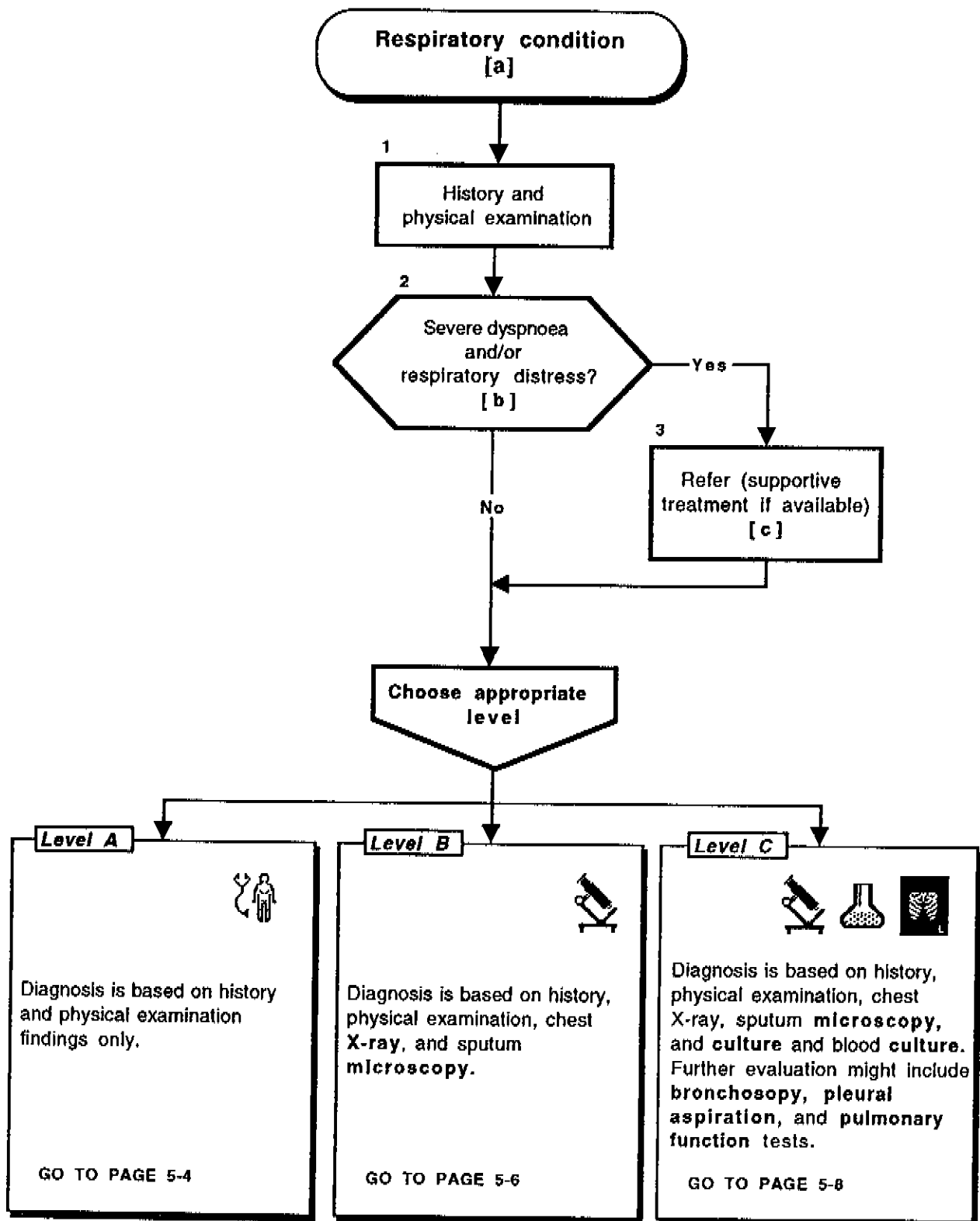
Ketoconazole may be used initially for patients with severe thrush, particularly if extending into the pharynx, since this indicates a high likelihood of oesophageal candidiasis regardless of dysphagia. New triazoles (e.g. fluconazole, 200 mg initial dose followed by 100 mg daily for 14 days) may be more effective and less toxic.

- e. Oral thrush and oesophageal candidiasis have a high likelihood of recurrence and indicate a high risk of other opportunistic infections. Antiretroviral therapy and primary prophylaxis for *Pneumocystis carinii* pneumonia (where this disease is known to occur frequently) should be considered.
- f. In the presence of oral candidiasis, gastroscopy is usually only performed after failure of adequate antifungal chemotherapy and in the presence of oesophageal symptoms. A biopsy is important to confirm tissue invasion by *Candida albicans* or to identify other causes (see annotation [b]).

## **Chapter 5**

# **Respiratory Conditions**

# Respiratory Conditions



**Annotations:**

- a. **Definition:** Persistence or worsening of cough and/or chest pain and/or dyspnoea in a patient with symptomatic HIV infection.

**Etiology:**

## 1. Pulmonary conditions:

## Infections:

- pyogenic bacteria
- *Mycobacterium tuberculosis*
- *Pneumocystis carinii* pneumonia
- fungal infection (cryptococcus, histoplasmosis coccidioidomycosis)
- atypical mycobacteria
- others: cytomegalovirus infection, toxoplasmosis.

## Malignancies:

- Kaposi sarcoma
- lymphoma.

## Others:

- lymphoid interstitial pneumonitis.

## 2. Other associated conditions:

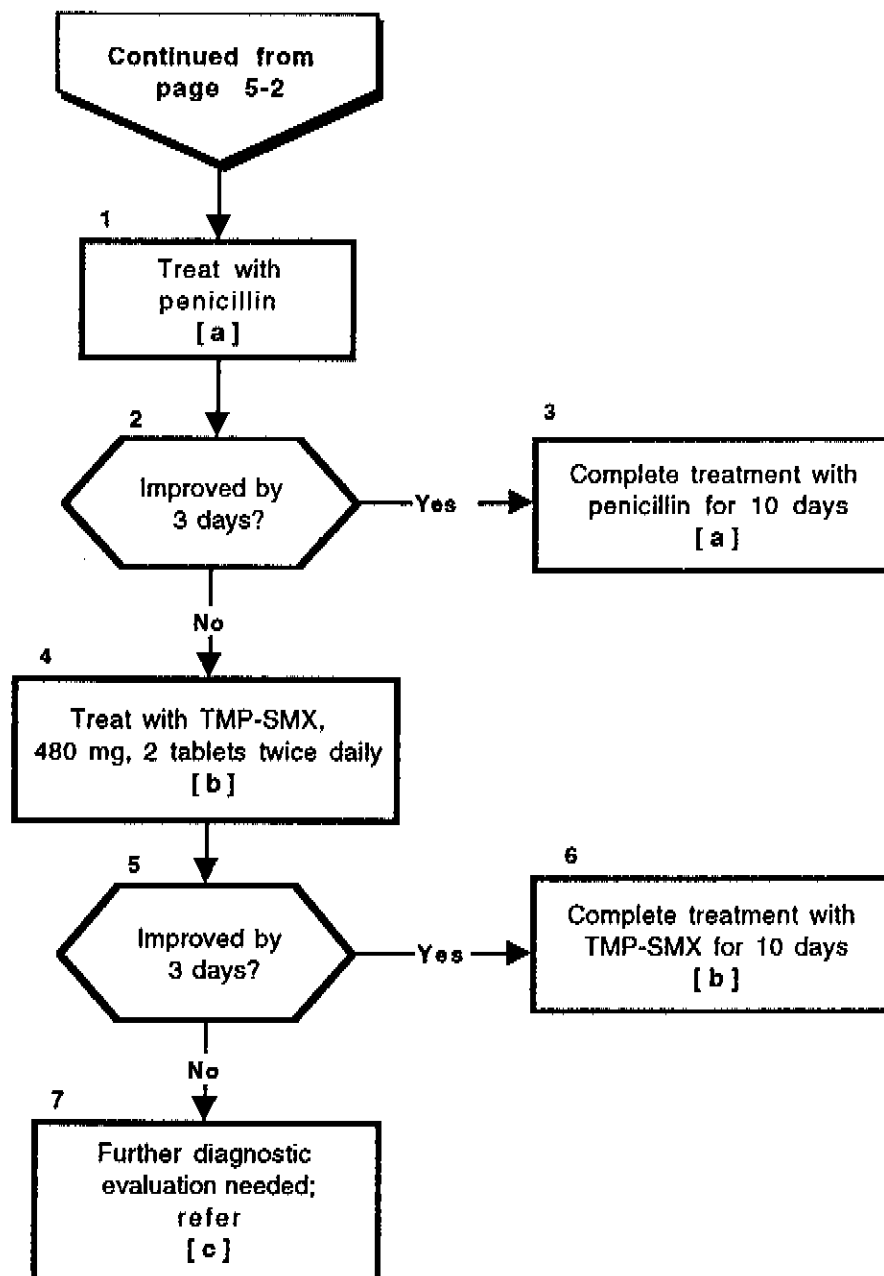
- pleural effusion/empyema (associated with tuberculosis, bacterial infection or cancer)
- pneumothorax (associated with tuberculosis, *Pneumocystis carinii* pneumonia or cancer)
- pericardial effusion (often associated with tuberculosis).

A list of the main causes in order of significance should be established in the light of available national or local information.

- b. Dyspnoea is defined as subjective shortness of breath at rest or on minimal exertion.

Respiratory distress is defined as objective evidence of respiratory dysfunction including hypoxaemia, cyanosis, tachycardia and signs of ventilatory effort (intercostal indrawing, use of accessory muscles).

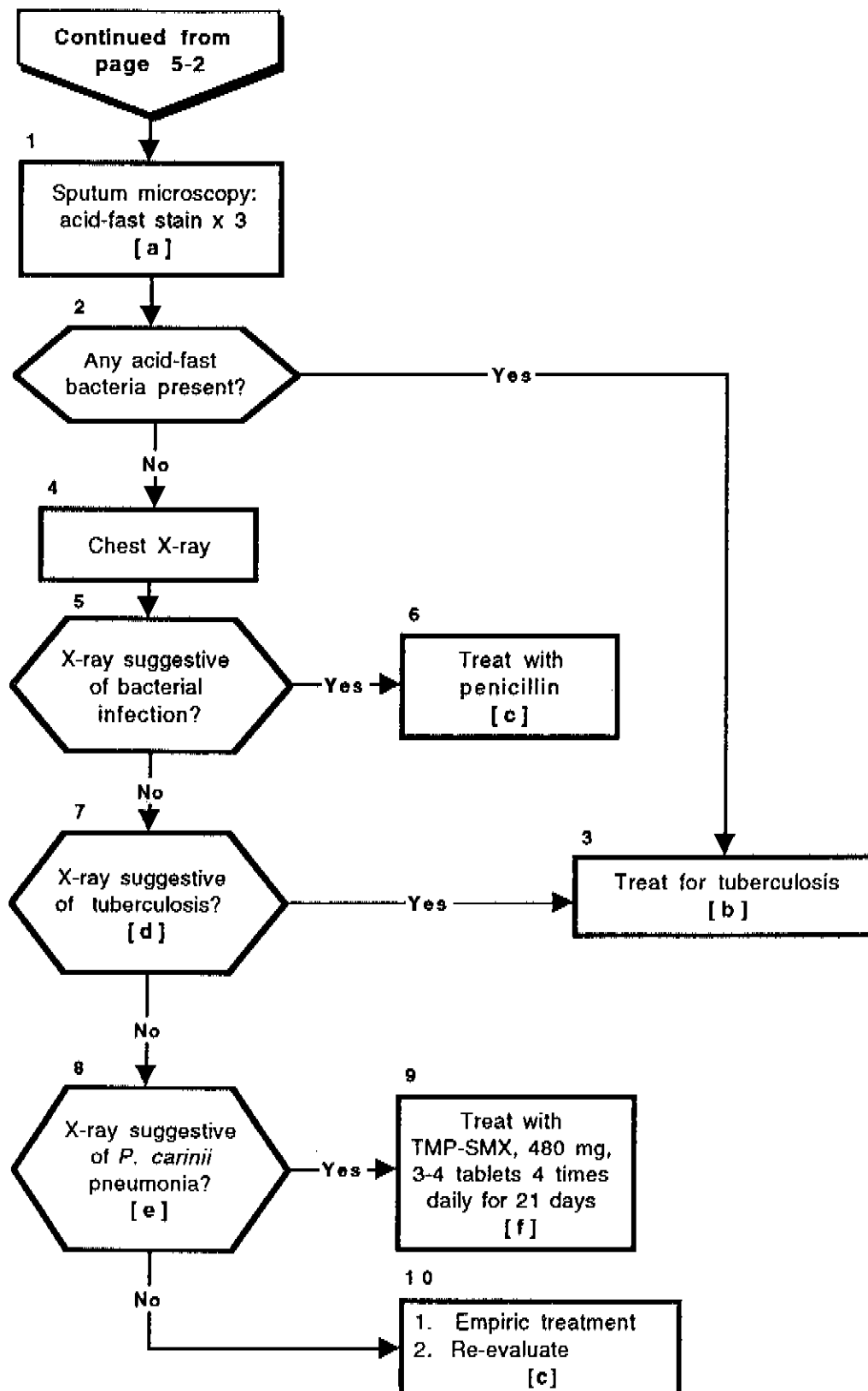
- c. Inspired oxygen therapy, where available, is indicated in the presence of hypoxaemia, diagnosed on clinical grounds (dyspnoea, cyanosis) or by measurement of blood oxygen concentration, where available. The use of assisted mechanical ventilation, where available, should depend on the criteria used in general medicine, although the outcome is often poorer in a person with HIV infection.



**Level A**

**Annotations:**

- a. In many countries, Gram-positive pyogenic bacteria will be the most probable cause of symptoms. The purpose of this algorithm is to provide guidance on the treatment of potential bacterial pneumonia. Response to penicillin (e.g. phenoxymethylpenicillin, 250 mg, 2 tablets 4 times daily, or ampicillin, 500 mg, 2 tablets twice daily) is likely to be prompt, allowing a short trial of empiric therapy.
- b. As no further diagnostic tools are available, a trial with a second antibiotic (e.g. trimethoprim-sulfamethoxazole (TMP-SMX), 480 mg, 2 tablets twice daily for 10 days) is justified. This will cover pyogenic infections not sensitive to penicillin.
- c. In many countries the exclusion of tuberculosis will be a high priority in patients not responding to antibiotic treatment.



## Level B

## Annotations:

- a. In countries with a high prevalence of tuberculosis, sputum examination for acid-fast bacteria is essential. If readily available, a chest X-ray should always be performed at presentation. A chest X-ray is also of value in assessing response to therapy. (For the purpose of clarity this algorithm shows a stepwise procedure, although sputum examination and chest X-ray are generally done simultaneously.)
- b. The highest priority is smear-positive pulmonary tuberculosis. Short-course therapy with an initial intensive phase is advised, e.g. for a patient of 51 kg or more, 2 months of daily treatment with isoniazid (H) and rifampicin (R), 2 tablets of a fixed combination (150 mg H and 300 mg R), pyrazinamide, 4 tablets of 500 mg, and ethambutol, 3 tablets of 400 mg, followed by a 4-month continuation phase of treatment 3 times weekly with isoniazid and rifampicin, 4 tablets of a fixed combination (100 mg H and 150 mg R) plus isoniazid, 1 tablet of 300 mg. If resources are scarce, a 6-month continuation phase of daily treatment with isoniazid, 300 mg, and ethambutol, 2 tablets of 400 mg can be given. Priority should be given to providing fully supervised treatment in the initial phase of treatment.

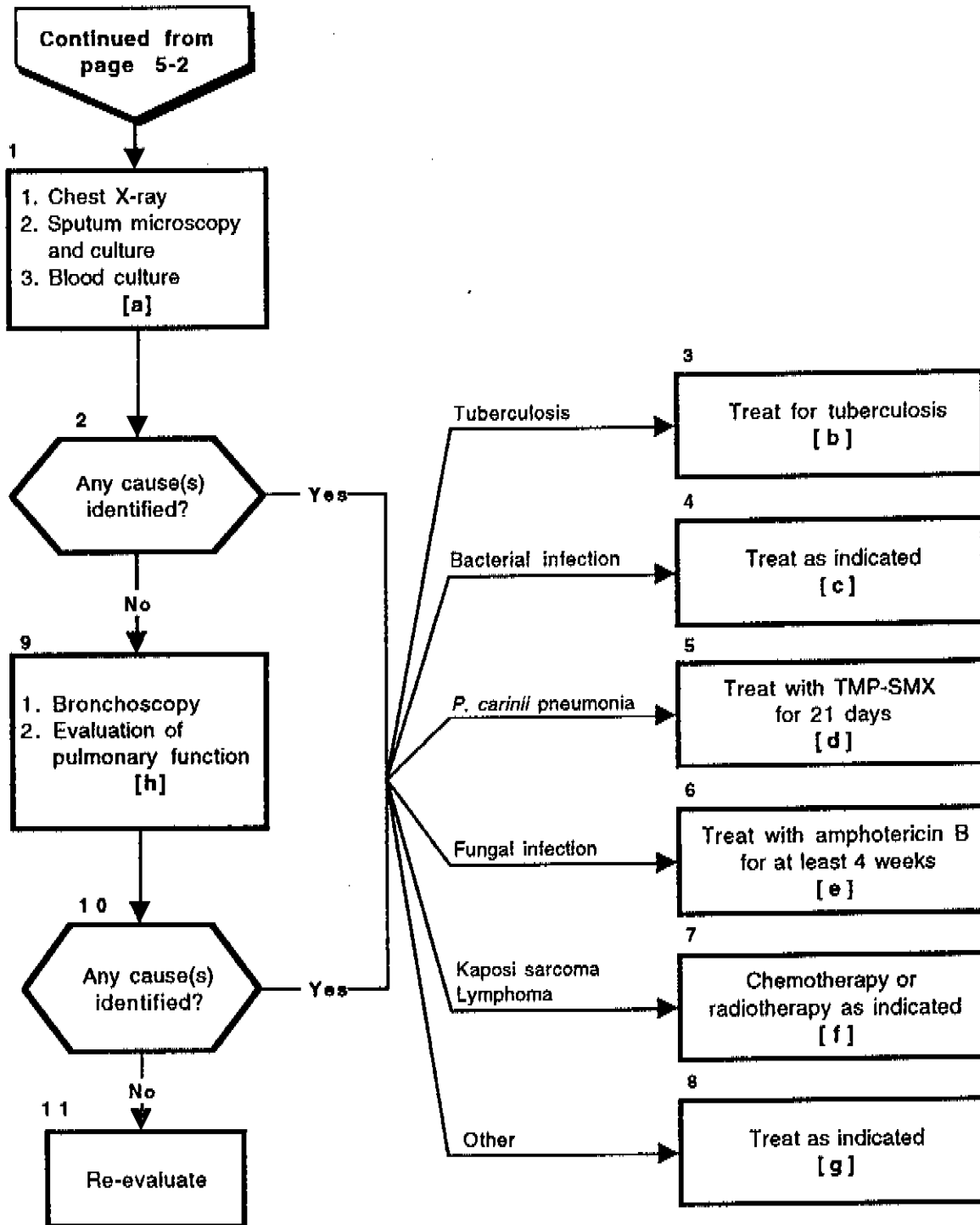
Thioacetazone should not be used in persons known to be or suspected of being infected with HIV, because of the occurrence of severe hypersensitivity reactions (see WHO guidelines in document WHO/TUB/91.161).

- c. In many countries, Gram-positive pyogenic bacteria will be the most probable cause of bacterial pneumonia. Response to penicillin (e.g. phenoxymethylpenicillin, 250 mg, 2 tablets 4 times daily, or ampicillin, 500 mg, 2 tablets twice daily for 10 days) is likely to be prompt. If there is no improvement within 3 days a different antibiotic, e.g. trimethoprim-sulfamethoxazole (TMP-SMX), 480 mg, 2 tablets twice daily for 10 days, should be given.
- d. In most HIV-infected patients with immune deficiency X-ray is consistent with primary rather than reactivated disease, with hilar and/or mediastinal adenopathy and localized middle or lower lung field infiltrates. Cavitation and apical infiltrates are uncommon. Pleural effusion is a prominent feature.

Pulmonary tuberculosis in a patient with a negative smear is defined as: radiographic abnormalities consistent with active pulmonary tuberculosis (i.e. a changing chest X-ray) and the decision by a physician to give a curative course of antituberculous chemotherapy.

- e. The chest X-ray is abnormal in more than 90% of documented cases of *Pneumocystis carinii* pneumonia, typically showing bilateral interstitial infiltrates.
- f. TMP-SMX, trimethoprim-sulfamethoxazole; see annotation [d], page 5-9.

Corticosteroids e.g. prednisone, 20 mg, 4 times daily, are recommended for the severely ill patient.





- e. A high level of suspicion is crucial to the diagnosis of fungal infection as the pulmonary presentation is non-specific.

Amphotericin B, 0.5-0.7 mg/kg daily by intravenous injection over 4-6 hours for 6 weeks if tolerated. Alternatively treat with fluconazole, 200-400 mg 4 times daily for 10 weeks (orally or by intravenous injection).

- f. Pulmonary Kaposi sarcoma is usually aggressive and rapidly fatal, justifying (in certain clinical settings) the use of immediate combined chemotherapy and/or radiotherapy. The approach to the management of lymphoma in HIV-infected patients is not altered by the presence of lung lesions.

- g. Cytomegalovirus pneumonitis is almost always an incidental diagnosis, resulting from bronchoscopy in a patient in whom other pulmonary pathogens are present. If there is clear evidence of invasive cytomegalovirus pneumonitis, a trial of ganciclovir, 5 mg/kg, twice daily by intravenous injection for 10 days, may be useful.

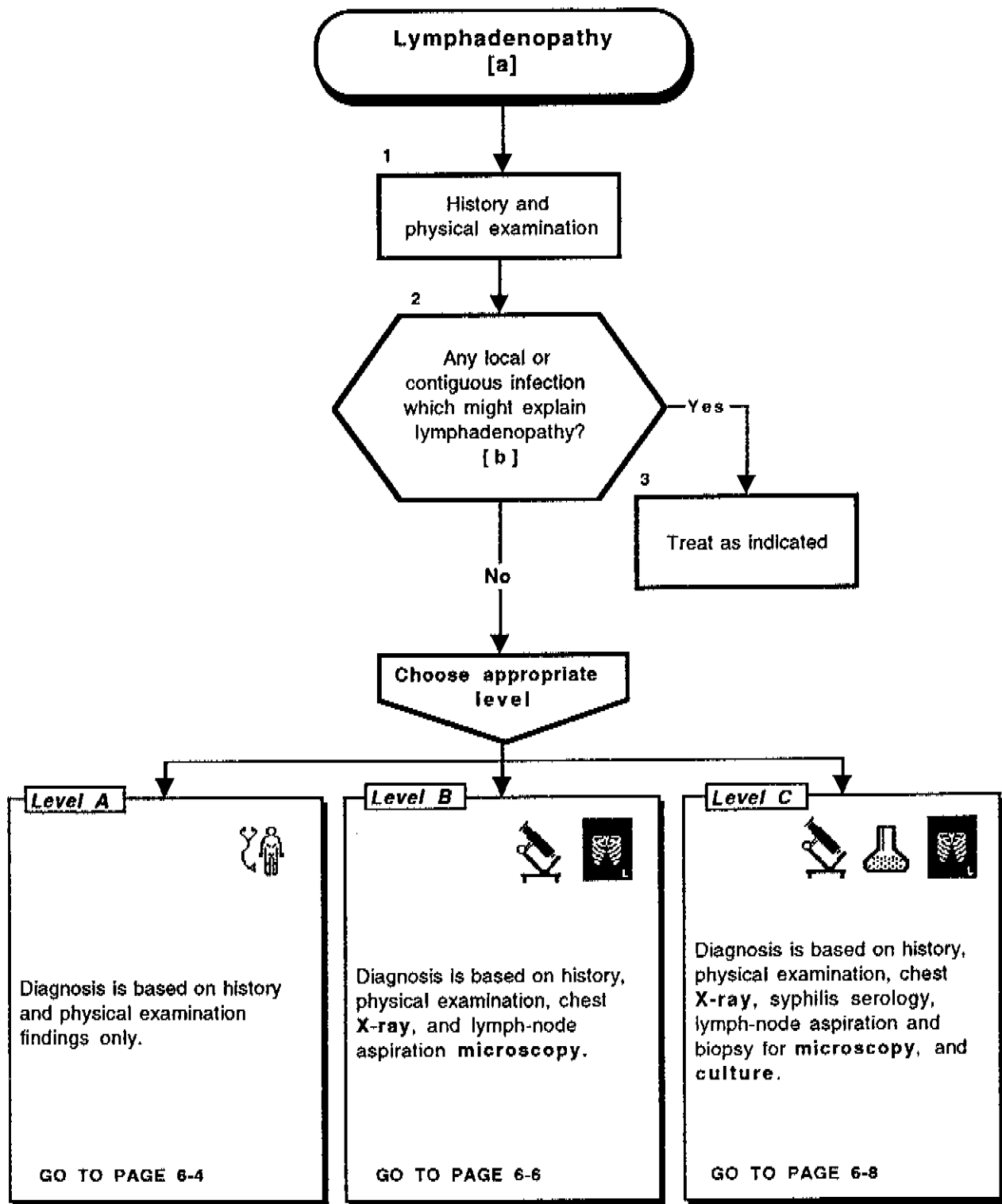
Lymphoid interstitial pneumonitis is seen mainly in children. When the patient is symptomatic, corticosteroids can be tried.

- h. Bronchoscopy is helpful in identifying an infectious (microscopy and culture) or tumorous (histology) etiology. For the diagnosis of *P. carinii* pneumonia, bronchoalveolar lavage can replace transbronchial biopsy.

## **Chapter 6**

# **Lymphadenopathy**

# Lymphadenopathy



**Annotations:**

- a. **Definition:** Lymph node enlargement in a patient with symptomatic HIV infection.

**Etiology:**

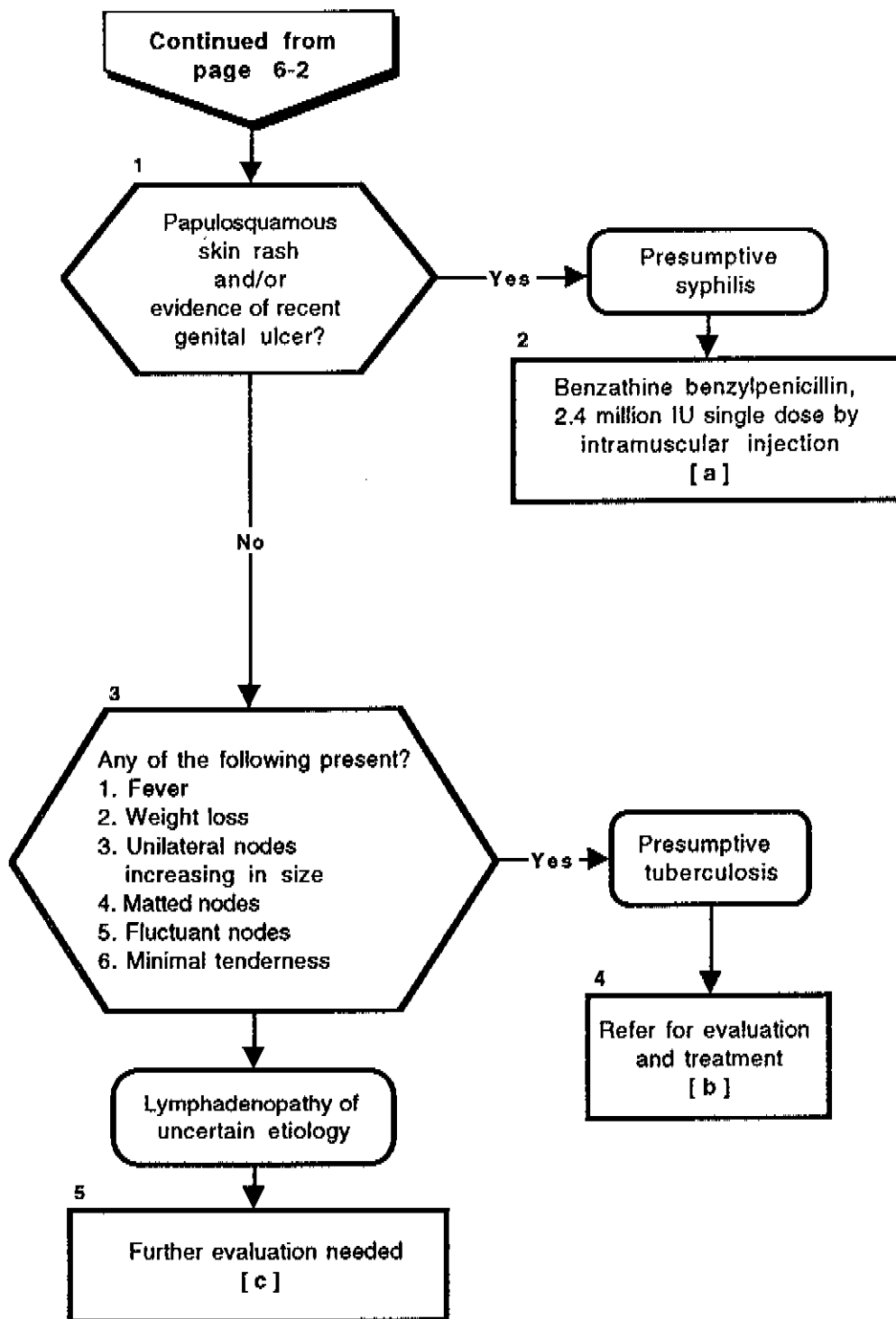
1. HIV infection itself.
2. Infections:
  - Bacterial**
    - tuberculosis
    - syphilis
  - Fungal**
    - histoplasmosis
  - Viral**
    - cytomegalovirus disease.
3. Malignancies:
  - lymphadenopathic Kaposi sarcoma (not necessarily associated with cutaneous Kaposi sarcoma)
  - lymphoma.
4. Dermatological conditions:
  - seborrhoeic dermatitis
  - chronic pyoderma.

A list of the main causes in order of significance should be established in the light of available national or local information.

- b. A careful physical examination should identify any local or contiguous infection that might explain the lymphadenopathy. Infections prevalent in the region concerned, e.g. trypanosomiasis or *Paracoccidioides brasiliensis* infection should also be considered.

Persistent generalized lymphadenopathy is common in HIV-infected patients and is often due to HIV alone. It is defined as follows:

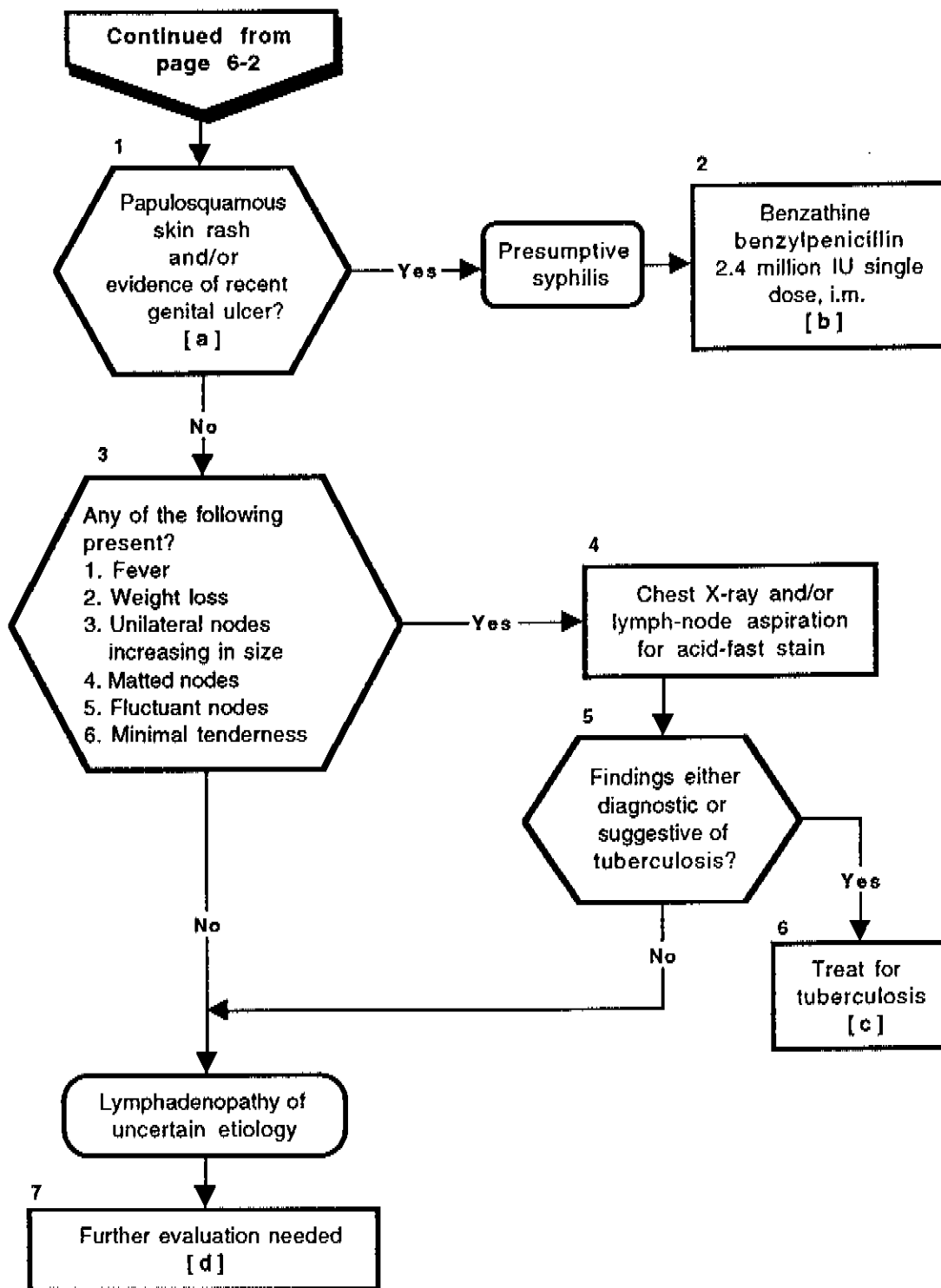
1. More than 3 separate lymph node groups affected.
2. At least 2 nodes more than 1.5 cm in diameter at each site.
3. Duration of more than 1 month.
4. No local or contiguous infection that might explain the adenopathy.



**Level A****Annotations:**

- a. Alternative treatment: if long-acting penicillin is not available or for non-pregnant patients allergic to penicillin, tetracycline, 500 mg 4 times daily for 15 days (see WHO guidelines in document WHO/VDT/89.447).
- b. Tuberculosis in HIV-infected individuals is frequently extrapulmonary with peripheral lymph nodes frequently involved and showing one or more of the features listed in box 1.
- c. Persistent generalized lymphadenopathy is common in HIV-infected patients. The purpose of this algorithm is to identify tuberculosis or syphilis.

In an asymptomatic patient no further investigation or treatment is required. However, in patients with recently symptomatic lymphadenopathy, rapidly enlarging nodes, marked nodal asymmetry, and constitutional symptoms, referral for biopsy should be considered. The same is true for patients not responding to empiric therapy. A biopsy is useful for excluding lymphoma, lymphadenopathic Kaposi sarcoma and infiltrative fungal or mycobacterial disease.



**Level B****Annotations:**

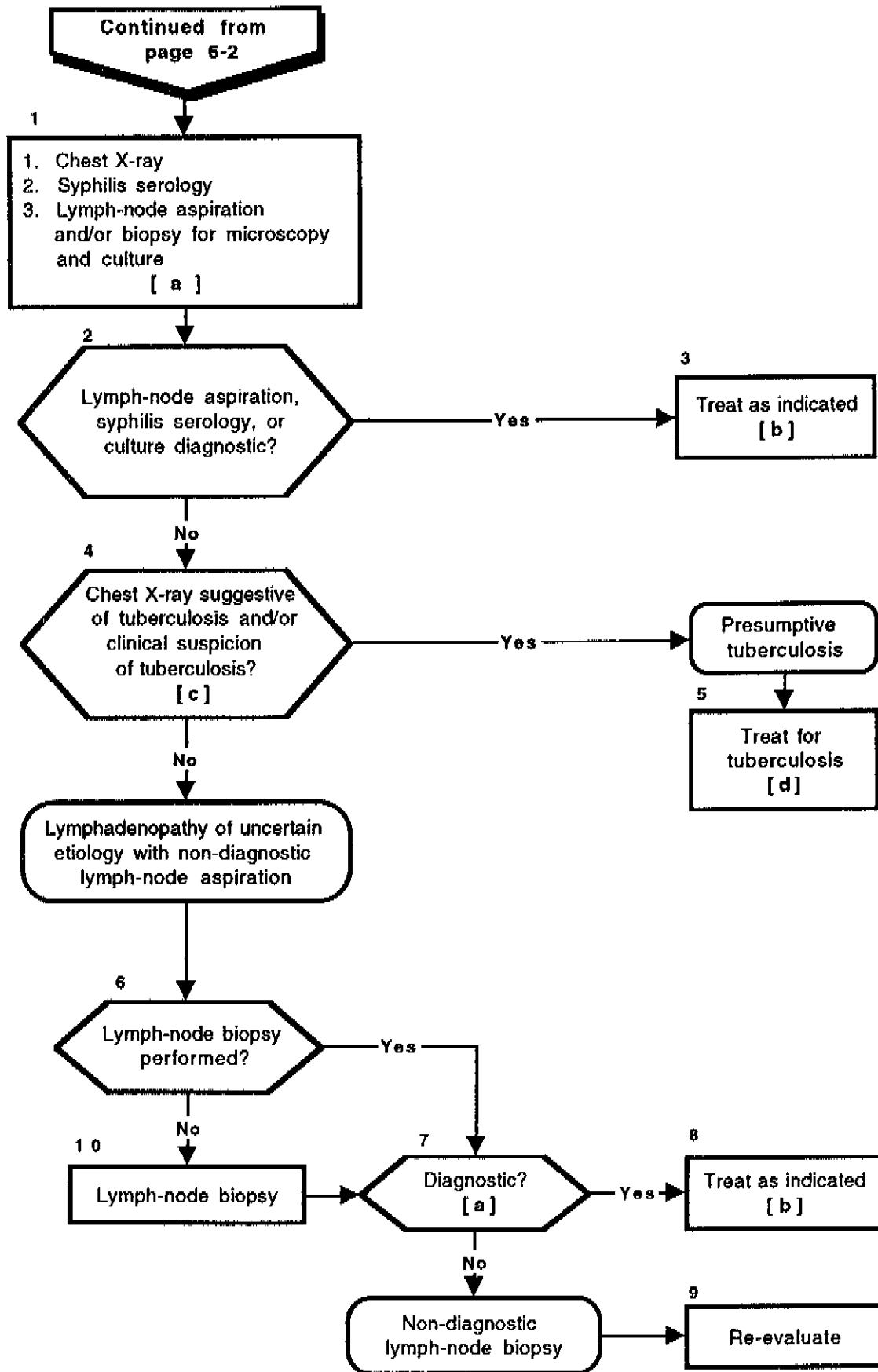
- a. Where available, serological testing (Venereal Disease Research Laboratories test, *Treponema pallidum* haemagglutination assay) is of additional benefit in substantiating the diagnosis of syphilis.
- b. Alternative treatment: if long-acting penicillin is not available or for non-pregnant patients allergic to penicillin, tetracycline, 500 mg 4 times daily for 15 days (see WHO guidelines in document WHO/VDT/89.447).
- c. Tuberculosis in HIV-infected individuals is frequently extrapulmonary with peripheral lymph nodes frequently involved and showing one or more of the features listed in box 5. For the treatment of pulmonary tuberculosis see page 5-7.

Lymph node tuberculosis: e.g. for a patient of 51 kg or more, a 2-month initial phase of daily treatment with isoniazid (H) and rifampicin (R), 2 tablets of a fixed combination (150 mg H and 300 mg R), and pyrazinamide, 4 tablets of 500 mg, followed by a 2-month continuation phase of treatment 3 times weekly with isoniazid and rifampicin, 4 tablets of a fixed combination (100 mg H and 150 mg R) plus isoniazid, 1 tablet of 300 mg. Where resources are scarce, a 6-month continuation phase of daily treatment with isoniazid, 300 mg, and ethambutol, 2 tablets of 400 mg can be given.

Thioacetazone should not be used in persons known to be or suspected of being infected with HIV, because of the occurrence of severe hypersensitivity reactions (see WHO guidelines in document WHO/TUB/91.161).

- d. Persistent generalized lymphadenopathy is common in HIV-infected patients. The purpose of this algorithm is to identify tuberculosis or syphilis.

In an asymptomatic patient no further investigation or treatment is required. However, in patients with recently symptomatic lymphadenopathy, rapidly enlarging nodes, marked nodal asymmetry, and constitutional symptoms referral for biopsy should be considered. The same is true for patients not responding to empiric therapy. A biopsy is useful for excluding lymphoma, lymphadenopathic Kaposi sarcoma and infiltrative fungal or mycobacterial disease.



**Level C**
**Annotations:**

- a. Value of investigations used in the patient with symptomatic HIV infection and lymphadenopathy:

Etiology	Chest X-ray	Serology	Lymph-node culture	Microscopy
Tuberculosis	+	-	+	+
Syphilis	-	+	-	+
Fungal infection	+/-	+/-	+/-	+
Kaposi sarcoma	-	-	-	+
Lymphoma	+	-	-	+

Key: + useful; - not useful; +/- may be useful

A positive (single) serological test for toxoplasmosis is not diagnostic of the disease; a negative test can be used to exclude toxoplasmosis.

- b. Syphilis: benzathine benzylpenicillin 2.4 million IU single dose by intramuscular injection.

Alternative treatment: if long-acting penicillin is not available or for non-pregnant patients allergic to penicillin, tetracycline, 500 mg 4 times daily for 15 days (see WHO guidelines in document WHO/VDT/89.447).

Histoplasmosis: investigate for infection elsewhere. Initial treatment with amphotericin B, followed by chronic suppressive therapy with ketoconazole, 100 mg daily, or itraconazole, 400 mg daily.

Kaposi sarcoma: the treatment depends on the extent of disease elsewhere and the severity of the symptoms. Bulky adenopathy or lymphoedema can be relieved with radiotherapy (see also page 9-10).

Lymphoma: combination chemotherapy.

Benign follicular hyperplasia: no treatment and not of prognostic significance.

- c. Clinical suspicion of tuberculosis is raised by the following signs and symptoms: fever, weight loss, unilateral nodes increasing in size, matted nodes, fluctuant nodes, minimal tenderness.
- d. For the treatment of pulmonary tuberculosis see page 5-7.

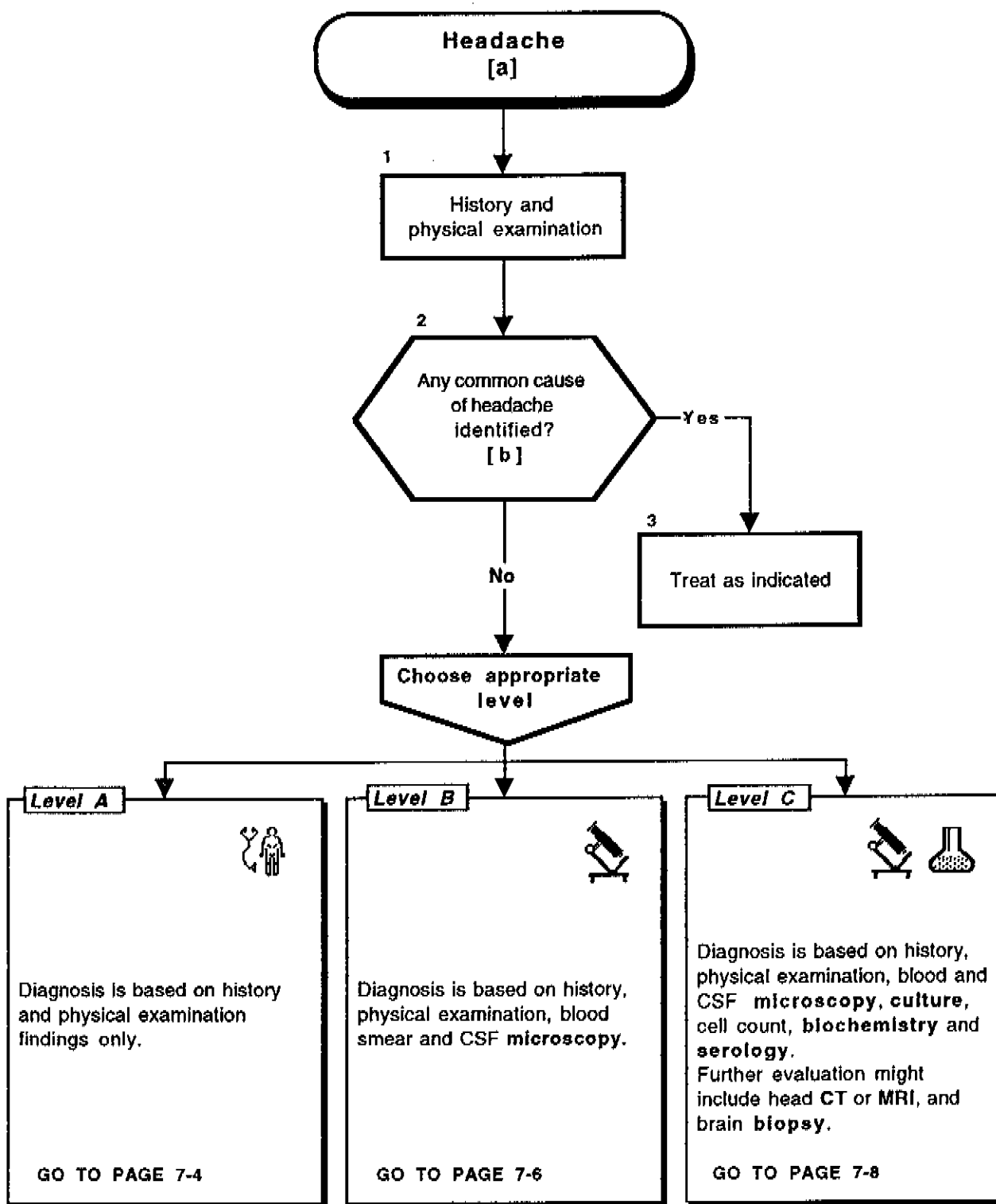
Lymph node tuberculosis: e.g. for a patient of 51 kg or more, a 2-month initial phase of daily treatment with isoniazid (H) and rifampicin (R), 2 tablets of a fixed combination (150 mg H and 300 mg R), and pyrazinamide, 4 tablets of 500 mg, followed by a 2-month continuation phase of treatment 3 times weekly with isoniazid and rifampicin, 4 tablets of a fixed combination (100 mg H and 150 mg R) plus isoniazid, 1 tablet of 300 mg. Where resources are scarce, a 6-month continuation phase of daily treatment with isoniazid, 300 mg, and ethambutol, 2 tablets of 400 mg can be given.

Thioacetazone should not be used in persons known to be or suspected of being infected with HIV, because of the occurrence of severe hypersensitivity reactions (see WHO guidelines in document WHO/TUB/91.161).

## **Chapter 7**

### **Headache**

# Headache



**Annotations:**

- a. **Definition:** Headache in a patient with symptomatic HIV infection, often persistent or severe and rapidly increasing or not responding to common drugs used for pain relief. It can be with or without fever.

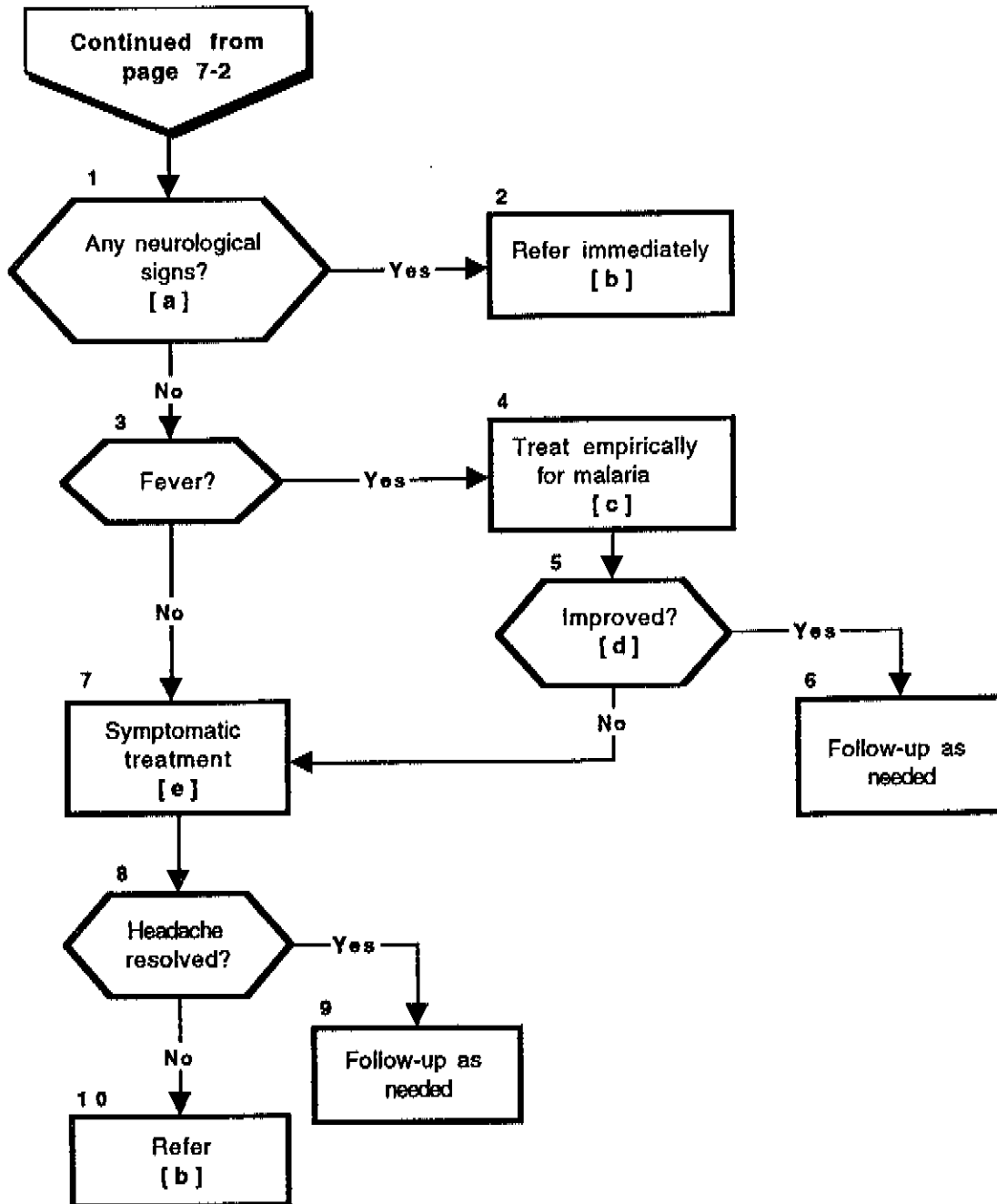
**Etiology:**

1. **Infections:**
  - tuberculous meningitis
  - cryptococcal meningitis
  - *Toxoplasma* meningoencephalitis
  - neurosyphilis
  - viral meningoencephalitis (e.g. due to cytomegalovirus)
  - chronic HIV meningitis
  - progressive multifocal leukoencephalopathy.
2. **Malignancy:**
  - lymphoma.
3. **Drug side effect:**
  - zidovudine.

A list of the main causes in order of significance should be established in the light of available national or local information.

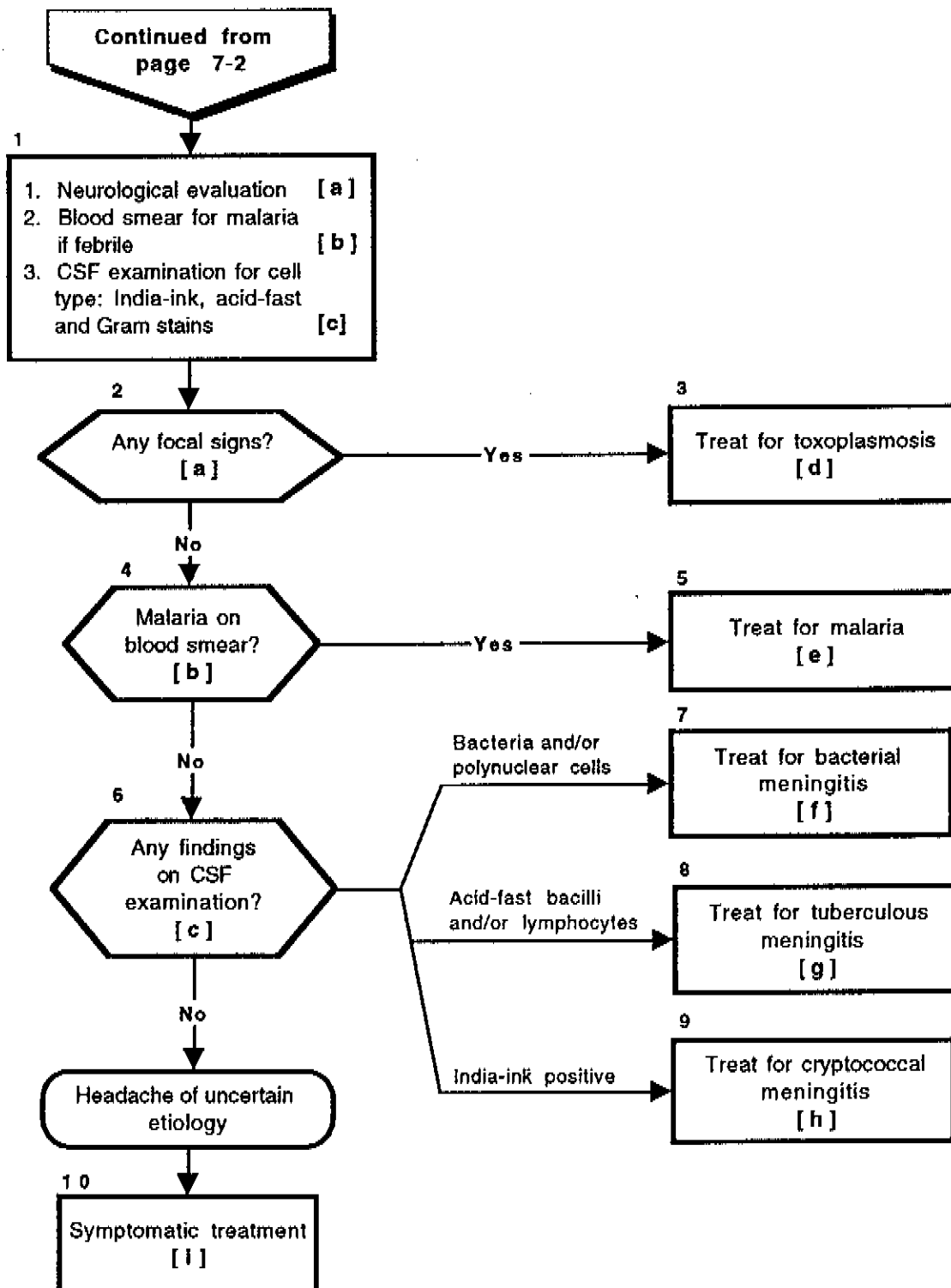
- b. Causes of headache not related to HIV infection, e.g. migraine, tension, sinusitis, refractive disorders, dental disease, anaemia, hypertension, drugs (e.g. indometacin), should be identified and treated.

Infectious diseases prevalent in the region concerned that can lead to headache, e.g. malaria, African trypanosomiasis, typhoid fever, dengue fever, yellow fever, and rickettsiosis, should also be considered and treated, if possible.



**Level A****Annotations:**

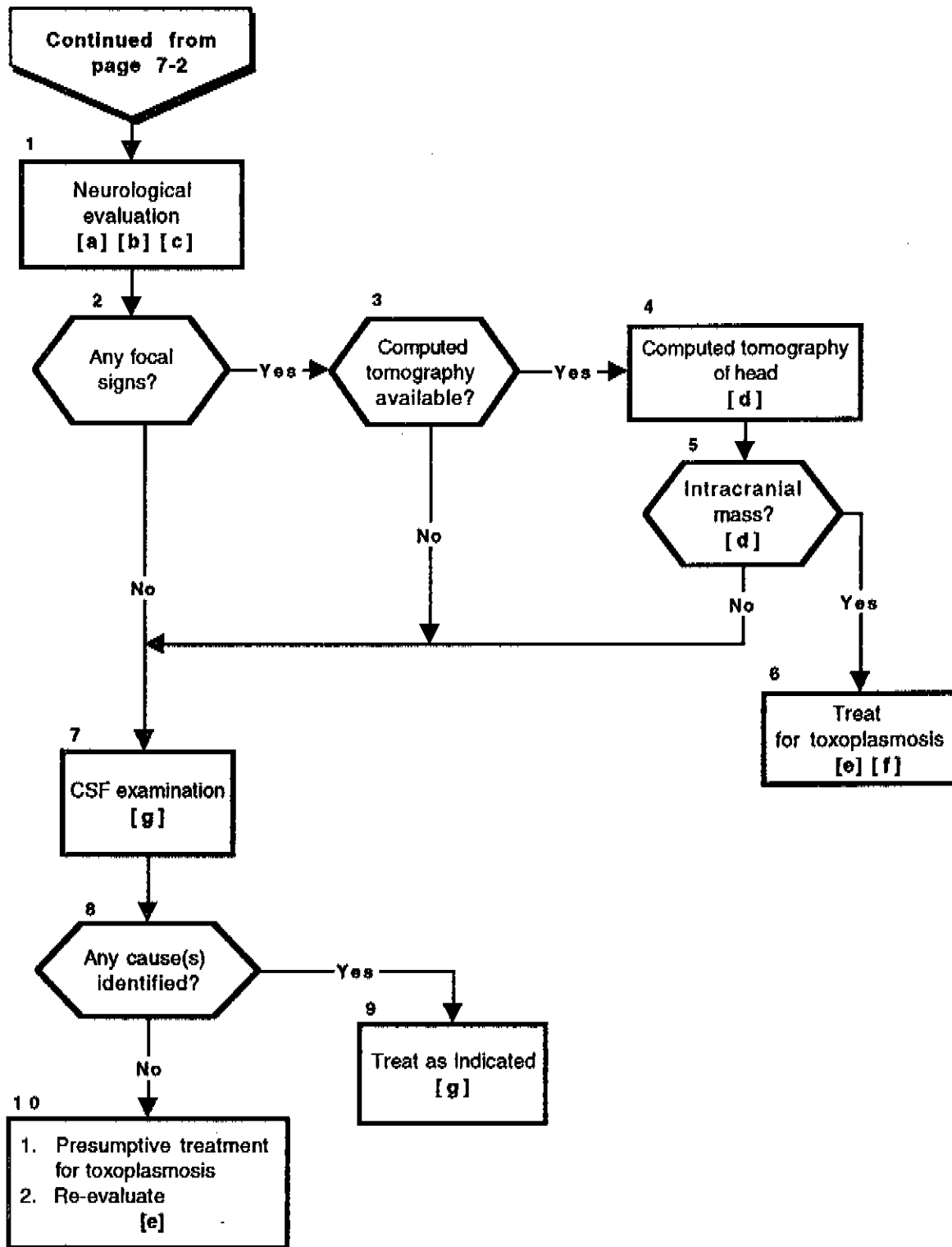
- a. These include:
  1. Changes in mental state (may be subtle) including loss of concentration, personality change (mild to psychotic), confusion, cognitive impairment, dementia.
  2. Focal neurological deficits including paresis, cranial nerve palsies, movement disorders, ataxia, aphasia.
  3. Seizures.
  4. Evidence of meningeal irritation or raised intracranial pressure (neck stiffness, high blood pressure and slow pulse in the presence of fever).
- b. Wherever possible, further evaluation of headache, particularly in a patient with symptomatic HIV infection showing neurological signs, should be pursued to identify treatable conditions. Cerebral malaria can lead to mental changes. In areas where malaria is prevalent, empiric treatment may be indicated.
- c. See national guidelines on malaria.
- d. Cryptococcal meningitis may present with fever and headache only. Referral for further evaluation may be indicated.
- e. As in patients without HIV infection; commence with a simple analgesic such as paracetamol and increase to compound analgesics containing narcotics of varying strength as needed and available. In palliative treatment, optimal relief is essential.



**Level B****Annotations:**

- a. This should cover:
  1. Changes in mental state (may be subtle) including loss of concentration, personality change (mild to psychotic), confusion, cognitive impairment, and dementia.
  2. Focal neurological deficits including paresis, cranial nerve palsies, movement disorders, ataxia, and aphasia.
  3. Seizures.
  4. Evidence of meningeal irritation or raised intracranial pressure, (neck stiffness, high blood pressure, and slow pulse in the presence of fever).
- b. A blood smear for malaria parasites should be carried out in areas where the disease is endemic or when there is a history of recent travel to such an area.
- c. Examination of cerebrospinal fluid (CSF) is valuable for confirming the diagnosis of major causes of headache treatable at a Level B facility (tuberculosis; cryptococcal meningitis; bacterial meningitis).
- d. Toxoplasmosis is the most probable cause of focal signs. It usually responds promptly and well to treatment and this response can be used to support the diagnosis. There is a high rate of recurrence on cessation of therapy. Primary therapy is given for 6 weeks: pyrimethamine loading dose 75-100 mg, then 25-50 mg daily plus sulfadiazine, 6-8 g daily in 4 doses. If the response is good, lifelong chronic suppressive therapy is advisable: pyrimethamine, 25 mg daily plus sulfadiazine, 2-4 g daily. If there is no response to primary therapy, a diagnosis of cerebral toxoplasmosis is unlikely.
- e. See national guidelines on malaria.
- f. For example, benzylpenicillin 12-24 million IU daily by intravenous injection in divided doses every 4 hours or chloramphenicol 2-4 g daily by intravenous injection in divided doses every 4 hours. Treat for a minimum of 7 days or for 4-5 days after the patient becomes afebrile.
- g. See annotation [h] on page 7-10.
- h. Amphotericin B, 0.5-0.7 mg/kg daily by intravenous injection for 6 weeks, if tolerated. Alternatively treat with fluconazole, 200-400 mg daily for 12 weeks (orally or by intravenous injection). Maintenance therapy e.g. fluconazole 200 mg daily or amphotericin B, 1 mg/kg weekly by intravenous injection is indicated as relapses are common.
- i. As in patients without HIV infection; commence with a simple analgesic such as paracetamol and increase to compound analgesics containing narcotics of varying strength as needed and available. In palliative treatment, optimal relief is essential.

If headache is not resolved consider referral.



## Level C

## Annotations.

- a. This should cover:
1. Changes in mental state (may be subtle) including loss of concentration, personality change (mild to psychotic), confusion, cognitive impairment, and dementia.
  2. Focal neurological deficits including paresis, cranial nerve palsies, movement disorders, ataxia, and aphasia.
  3. Seizures.
  4. Evidence of meningeal irritation or raised intracranial pressure, (neck stiffness, high blood pressure, and slow pulse in the presence of fever).
- b. A blood smear for malaria parasites should be carried out in areas where the disease is endemic or when there is a history of recent travel to such an area.
- c. Examination of cerebrospinal fluid (CSF) is delayed until a mass has been ruled out. Computed tomography (CT) of the head is therefore advised before lumbar puncture in the presence of focal signs in view of the risk of raised intracerebral pressure and the high probability that the CT will contribute more to the diagnosis than CSF analysis (toxoplasmosis, lymphoma).
- d. A combination of focal signs and multiple enhancing lesions on CT is virtually diagnostic for toxoplasmosis. Magnetic resonance imaging (MRI), if available, is more sensitive but the practical advantage is small except when the CT is normal or shows a single non-enhancing lesion in the patient with focal findings. A single non-enhancing lesion suggests an alternative diagnosis (lymphoma, tuberculoma, fungal abscess, rarely Kaposi sarcoma). Both CT and MRI are valuable in assessing the response to treatment.
- e. Toxoplasmosis usually responds well and promptly to treatment and this response can be used to support the diagnosis (especially where the signs are not typical). The rate of recurrence on cessation of therapy is high. The optimal duration of treatment in HIV-infected persons has not been established. However, many authorities recommend 6 weeks for primary therapy: pyrimethamine, loading dose 75-100 mg, then 25-50 mg daily plus sulfadiazine, 6-8 g daily in 4 doses. If the response is good, lifelong chronic suppressive therapy is advisable: pyrimethamine, 25 mg daily, plus sulfadiazine, 2-4 g daily.
- Alternative primary treatment: pyrimethamine (as above) plus clindamycin, 300-600 mg 4 times daily. If there is no response to primary therapy, a diagnosis of cerebral toxoplasmosis is unlikely. The absence of IgG antibodies to *Toxoplasma gondii* in the blood decreases the likelihood of toxoplasma infection.
- f. If CT and/or MRI are not diagnostic for toxoplasmosis but for another disease, this should be treated, if possible.

A brain biopsy is usually limited to patients with atypical features and/or accessible (usually

single) lesions or lesions not responsive to therapy for toxoplasmosis when there is a commitment to therapy for the probable diagnosis (malignancy, lymphoma, Kaposi sarcoma; infection, including tuberculosis, fungal abscess, progressive multifocal leukoencephalopathy, cytomegalovirus).

g. Value of CSF examination in the patient with symptomatic HIV-infection and headache

Etiology	Microscopy	Culture	Cell count	Serology	Biochemistry
Pyogenic bacteria	+	+	+	-	-
<i>Cryptococcus neoformans</i>	+	+	-	+	-
<i>Mycobacterium tuberculosis</i>	+	+	-	-	+/-
<i>Treponema pallidum</i>	+/-	-	+	+	+

Key: + useful; - not useful; +/- may be useful.

Pyogenic meningitis: e.g. benzylpenicillin 12-24 million IU daily by intravenous injection in divided doses every 4 hours for 14 days (see document WHO/VDT/89.447).

Cryptococcal meningitis: amphotericin B, 0.5-0.7 mg/kg daily by intravenous injection over 4-6 hours for 6 weeks if tolerated. Alternatively treat with fluconazole, 200-400 mg daily for 12 weeks (orally or by intravenous injection). Maintenance therapy e.g. fluconazole 200 mg daily or amphotericin B, 1 mg/kg weekly by intravenous injection is indicated as relapses are common.

Neurosyphilis: benzylpenicillin 12-24 million IU daily by intravenous injection in divided doses every 4 hours for 14 days (see WHO/VDT/89.447).

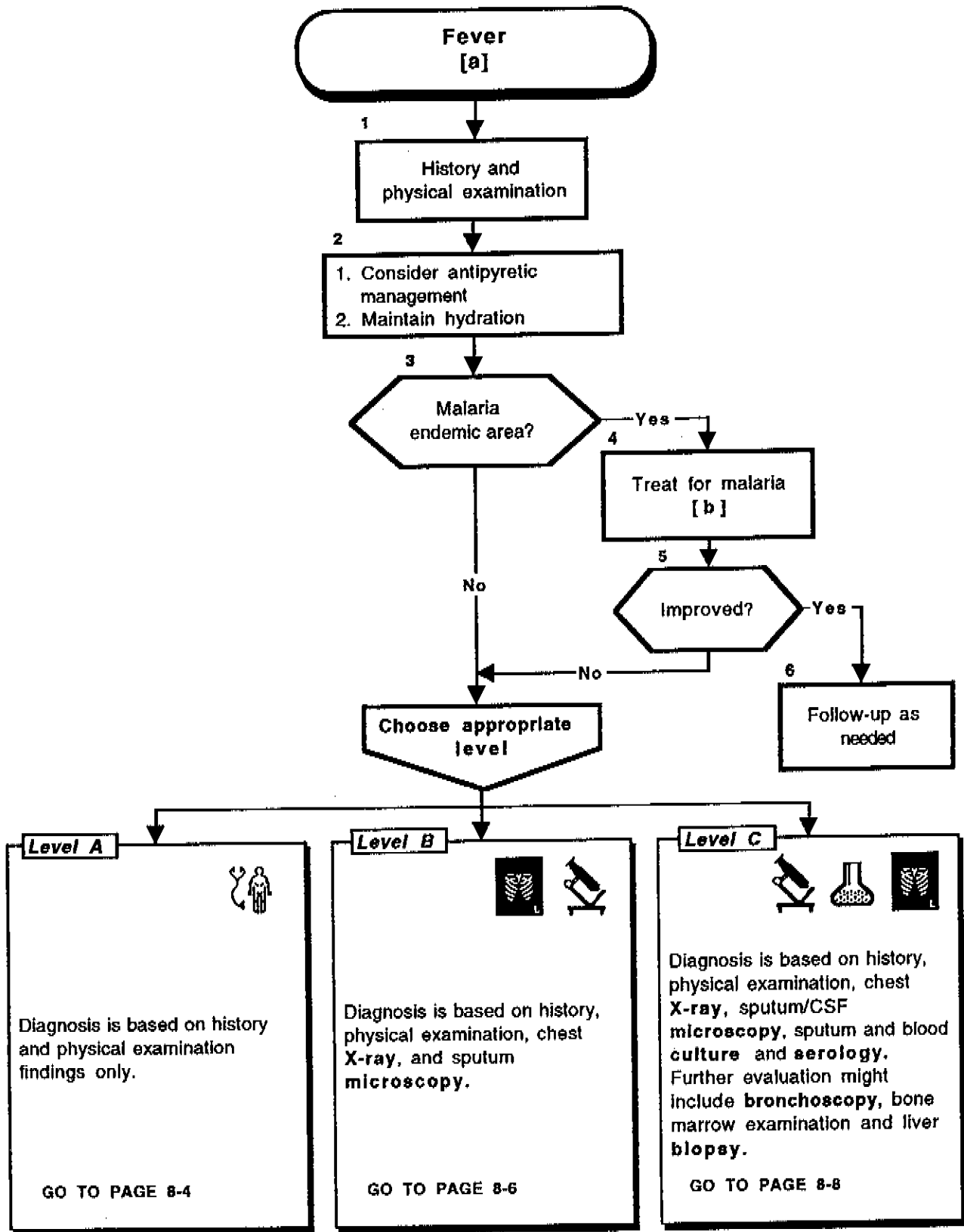
Tuberculous meningitis: e.g. for a patient of 51 kg or more, 2 months of daily treatment with isoniazid (H) and rifampicin (R), 2 tablets of a fixed combination (150 mg H and 300 mg R), pyrazinamide, 4 tablets of 500 mg, and ethambutol, 3 tablets of 400 mg, followed by a 4-month continuation of phase of treatment 3 times weekly with isoniazid and rifampicin, 4 tablets of a fixed combination (100 mg H and 150 mg R) plus isoniazid, 1 tablet of 300 mg. If resources are scarce, a 6-month continuation phase of daily treatment with isoniazid, 300 mg, and ethambutol, 2 tablets of 400 mg can be given.

Thioacetazone should not be used in persons known to be or suspected of being infected with HIV, because of the occurrence of severe hypersensitivity reactions (see WHO guidelines in document WHO/TUB/91.161).

## **Chapter 8**

### **Fever**

# Fever



**Annotations:**

- a. **Definition:** Fever with a duration of more than 2 weeks as the only clinical presentation
- in a patient with a prior history of symptomatic HIV infection;
  - in a known HIV-positive patient with an asymptomatic prior history;

Where fever is defined as a body temperature of  $> 38.0^{\circ}\text{C}$  continuously for more than 24 hours or intermittently for more than 24 hours in any 72-hour period.

**Etiology:**

## 1. Infections:

## Mycobacterial

- *Mycobacterium tuberculosis*, *M. avium* complex

## Fungal

- cryptococcosis

## Bacterial

- bacteremia due to *Salmonella* spp., *Streptococcus pneumoniae*, *Haemophilus influenzae*

## Viral

- cytomegalovirus, Epstein-Barr virus

## Protozoal

- *Pneumocystis carinii*, *Toxoplasma gondii*

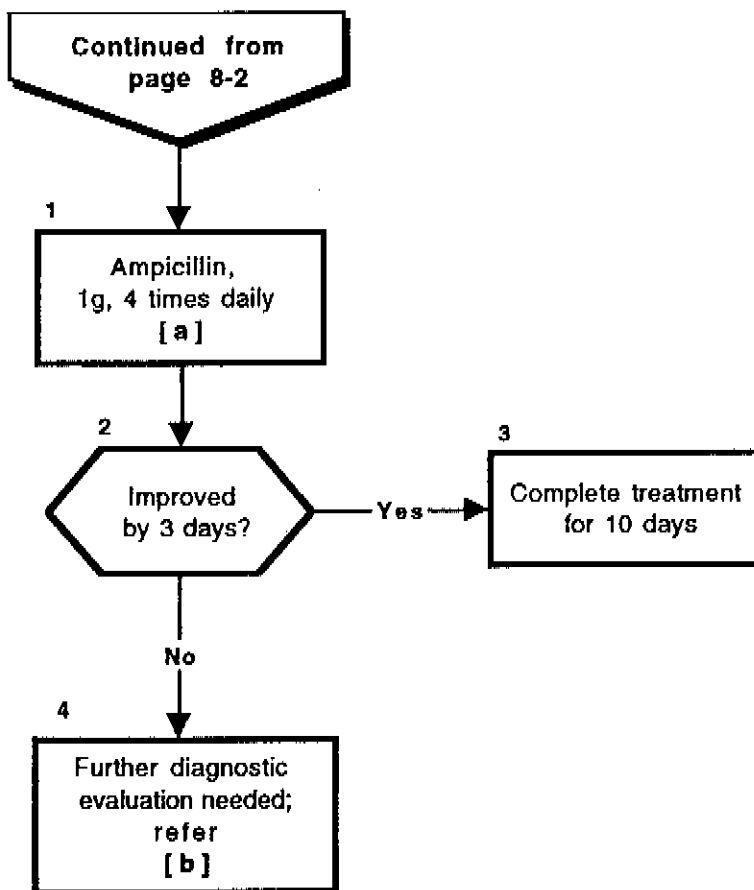
HIV infection itself.

## 2. Malignancy:

- lymphoma.

A list of the main causes in order of significance should be established in the light of available national or local information.

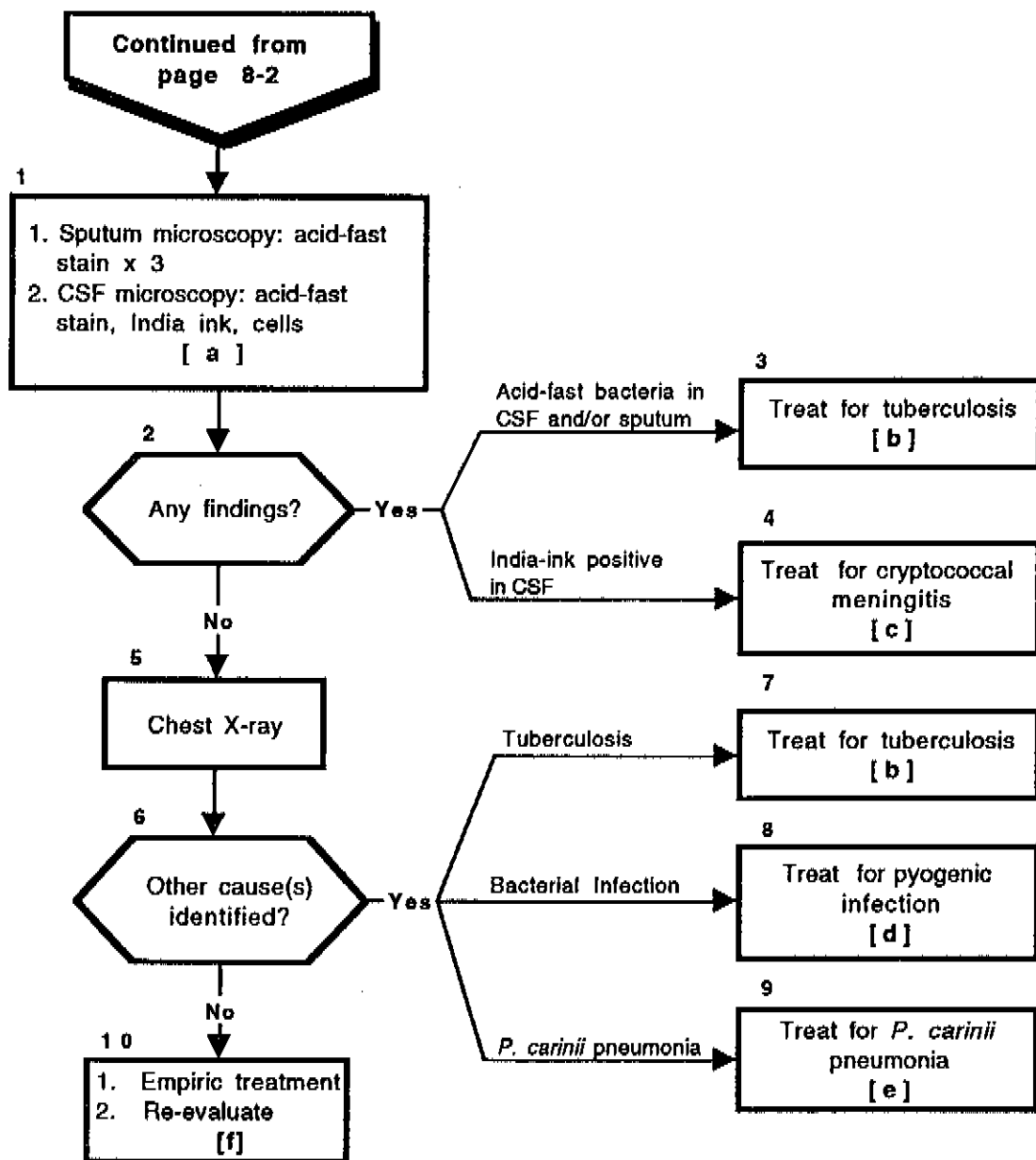
- b. In endemic areas a febrile patient must be given antimalarial treatment prior to further diagnostic investigations (refer to national guidelines on malaria).



**Level A**

**Annotations:**

- a. Use a broad-spectrum antibiotic, e.g. ampicillin, 1g 4 times daily for 10 days, which will treat the pathogens most frequently responsible for bacterial fevers. Alternatively, use chloramphenicol, 500 mg 3 times daily for 10 days.
- b. Referral is particularly helpful in identifying treatable diseases such as tuberculosis or *Pneumocystis carinii* pneumonia or cryptococcal meningitis.



**Level B****Annotations:**

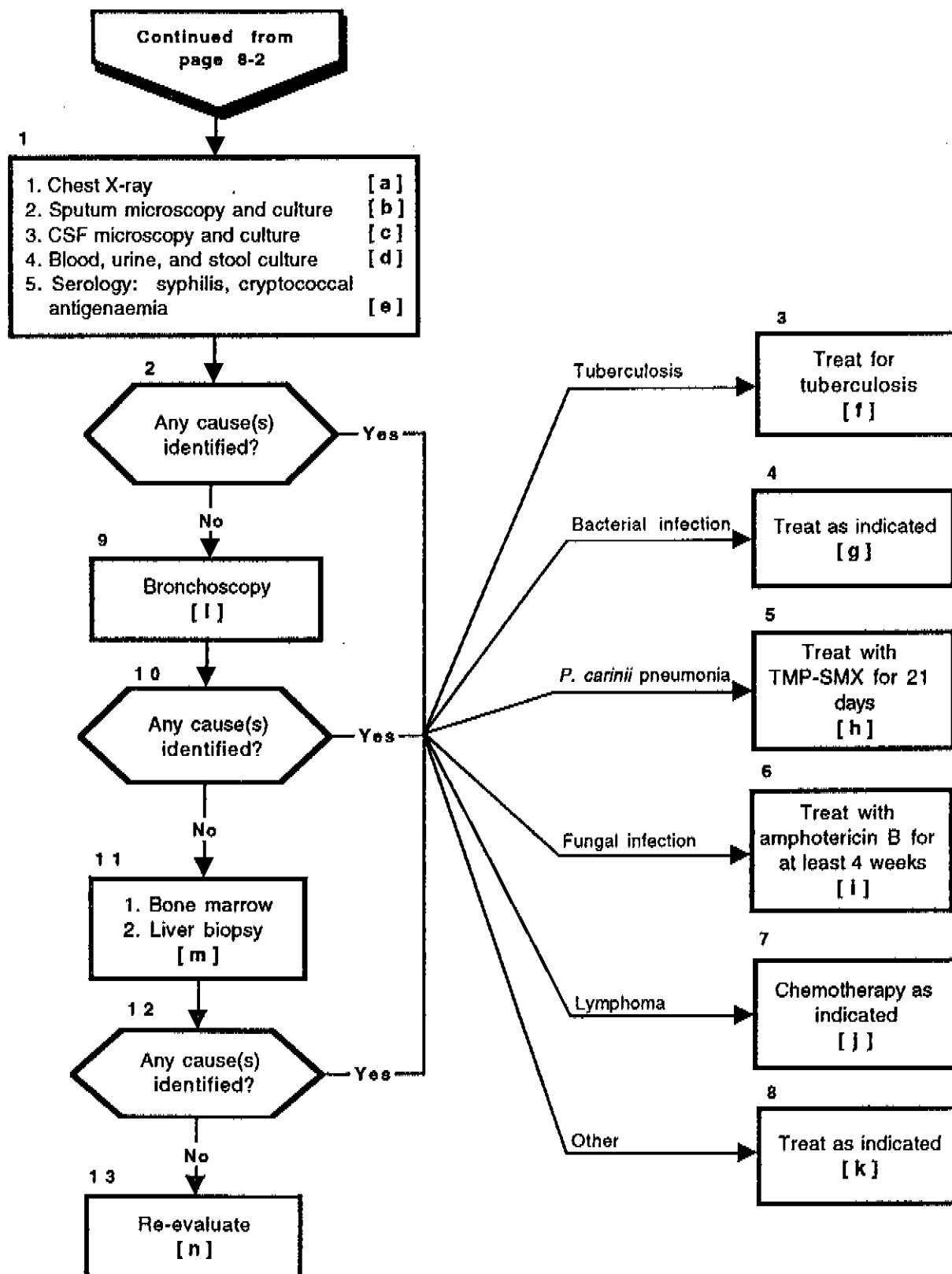
- a. In countries with a high prevalence of tuberculosis, examination of sputum and cerebrospinal fluid (CSF) for acid-fast bacteria is essential. If readily available, a chest X-ray should also always be performed at presentation. A chest X-ray is also of value in assessing response to therapy. (For the sake of clarity, this algorithm shows a stepwise procedure, although sputum examination and chest X-ray are usually done simultaneously.)
- b. The highest priority is smear-positive pulmonary tuberculosis. Short-course therapy with an initial intensive phase is advised, e.g. for a patient of 51 kg or more, 2 months of daily treatment with isoniazid (H) and rifampicin (R), 2 tablets of a fixed combination (150 mg H and 300 mg R), pyrazinamide, 4 tablets of 500 mg, and ethambutol 3 tablets of 400 mg, followed by a 4-month continuation phase of treatment 3 times weekly with isoniazid and rifampicin, 4 tablets of a fixed combination (100 mg H and 150 mg R) plus isoniazid, 1 tablet of 300 mg. If resources are scarce, a 6-month continuation phase of daily treatment with isoniazid, 300 mg, and ethambutol, 2 tablets of 400 mg can be given.

Thioacetazone should not be used in persons known to be or suspected of being infected with HIV, because of the occurrence of severe hypersensitivity reactions (see WHO guidelines in document WHO/TUB/91.161).

- c. Amphotericin B, 0.5-0.7 mg/kg daily by intravenous injection over 4-6 hours for 6 weeks, if tolerated. Alternatively treat with fluconazole, 200-400 mg daily for 12 weeks (orally or by intravenous injection). Maintenance therapy, e.g. fluconazole 200 mg daily or amphotericin B, 1 mg/kg weekly by intravenous injection is indicated as relapses are common.
- d. In many countries, Gram-positive pyogenic bacteria will be the most probable cause of bacterial pneumonia. Response to penicillin (e.g. phenoxymethylpenicillin, 250 mg, 2 tablets 4 times daily, or ampicillin, 500 mg, 2 tablets twice daily for 10 days) is likely to be prompt. If there is no improvement within 3 days a different antibiotic, e.g. trimethoprim-sulfamethoxazole, 480 mg, 2 tablets twice daily for 10 days, should be given.
- e. TMP-SMX, trimethoprim-sulfamethoxazole; see annotation [h], page 8-9.

Corticosteroids, e.g. prednisone, 20 mg 4 times daily, are recommended for the severely ill patient.

- f. In the absence of any suggestive laboratory or radiological findings, treat empirically with a broad-spectrum antibiotic, e.g. ampicillin or chloramphenicol.



## Level C

## Annotations:

- a. If the chest X-ray is suggestive of a pleural effusion, a pleural aspiration should be performed.
- b. Sputum should be stained with Gram and acid-fast stains, India ink and KOH, and cultured for bacterial, fungal and viral infection. Staining of induced sputum is a highly sensitive method of identifying *Pneumocystis carinii* pneumonia (stain with modified Giemsa or toluidine blue).
- c. Lymphocytic meningitis without any other finding is highly predictive of a tuberculous meningitis: treat empirically for tuberculosis. If no response within 3 weeks, re-evaluate.
- d. Cultures (using appropriate media) are performed to identify bacteria, mycobacteria and fungi.
- e. Cryptococcal antigenaemia indicates a cryptococcal infection which may be extraneurological and asymptomatic.
- f. The highest priority is smear-positive pulmonary tuberculosis. Short-course therapy with an initial intensive phase is advised, e.g. for a patient of 51 kg or more, 2 months of daily treatment with isoniazid (H) and rifampicin (R), 2 tablets of a fixed combination (150 mg H and 300 mg R), pyrazinamide, 4 tablets of 500 mg, and ethambutol 3 tablets of 400 mg, followed by a 4-month continuation phase of treatment 3 times weekly with isoniazid and rifampicin, 4 tablets of a fixed combination (100 mg H and 150 mg R) plus isoniazid, 1 tablet of 300 mg. If resources are scarce, a 6-month continuation phase of daily treatment with isoniazid, 300 mg, and ethambutol, 2 tablets of 400 mg can be given.

Thioacetazone should not be used in persons known to be or suspected of being infected with HIV, because of the occurrence of severe hypersensitivity reactions (see WHO guidelines in document WHO/TUB/91.161).

- g. The selection of the antibiotic will depend on the organism identified and the result of sensitivity testing.
- h. Oral or intravenous trimethoprim-sulfamethoxazole (TMP-SMX): TMP, 15 mg/kg daily plus SMX, 75 mg/kg daily in 4 divided doses, e.g. for a patient of 64 kg body weight, TMP-SMX, 480 mg, 3 tablets orally 4 times daily. Assessment of benefit requires at least 7 days as *Pneumocystis carinii* pneumonia may initially worsen. If the patient responds, continue for at least 14 and preferably 21 days in the absence of side-effects. If the patient is unable to tolerate the full course, change to pentamidine isothionate 4 mg/kg daily by intravenous injection, if available. The risk of recurrence is high and can be reduced by prophylaxis. Commonly used regimens include TMP-SMX, 480 mg, 2 tablets twice daily, dapsone, 100 mg daily and aerosolized pentamidine.

Corticosteroids e.g. prednisone, 20 mg, 4 times daily, are recommended for the severely ill patient.

- i. Systemic candidiasis is rare in HIV-infected people.

Amphotericin B, 0.5-0.7 mg/kg daily by intravenous injection over 4-6 hours for 6 weeks if tolerated. Alternatively treat with fluconazole, 200-400 mg daily for 12 weeks (orally or by intravenous injection). Maintenance therapy e.g. fluconazole 200 mg daily or amphotericin B, 1 mg/kg weekly by intravenous injection is indicated as relapses are common.

- j. The approach to the management of lymphoma in HIV-infected patients is not altered by the presence of lung lesions.

- k. Leishmaniasis: e.g. sodium stibogluconate injection (1ml = 100 mg antimony), 6 ml daily by intravenous or intramuscular injection.

Syphilis: e.g. benzathine benzylpenicillin, 2.4 million IU, single dose by intramuscular injection. Alternative treatment: if long-acting penicillin is not available or for non-pregnant patients allergic to penicillin, tetracycline, 500 mg 4 times daily for 15 days (see WHO guidelines in document WHO/VDT/89.447).

- l. Bronchoscopy is helpful in detecting an infectious (microscopy and culture) or tumorous (histology) etiology. For the diagnosis of *Pneumocystis carinii* pneumonia, bronchoalveolar lavage (BAL) can replace transbronchial biopsy.

- m. Liver biopsy for histological examination and culture.

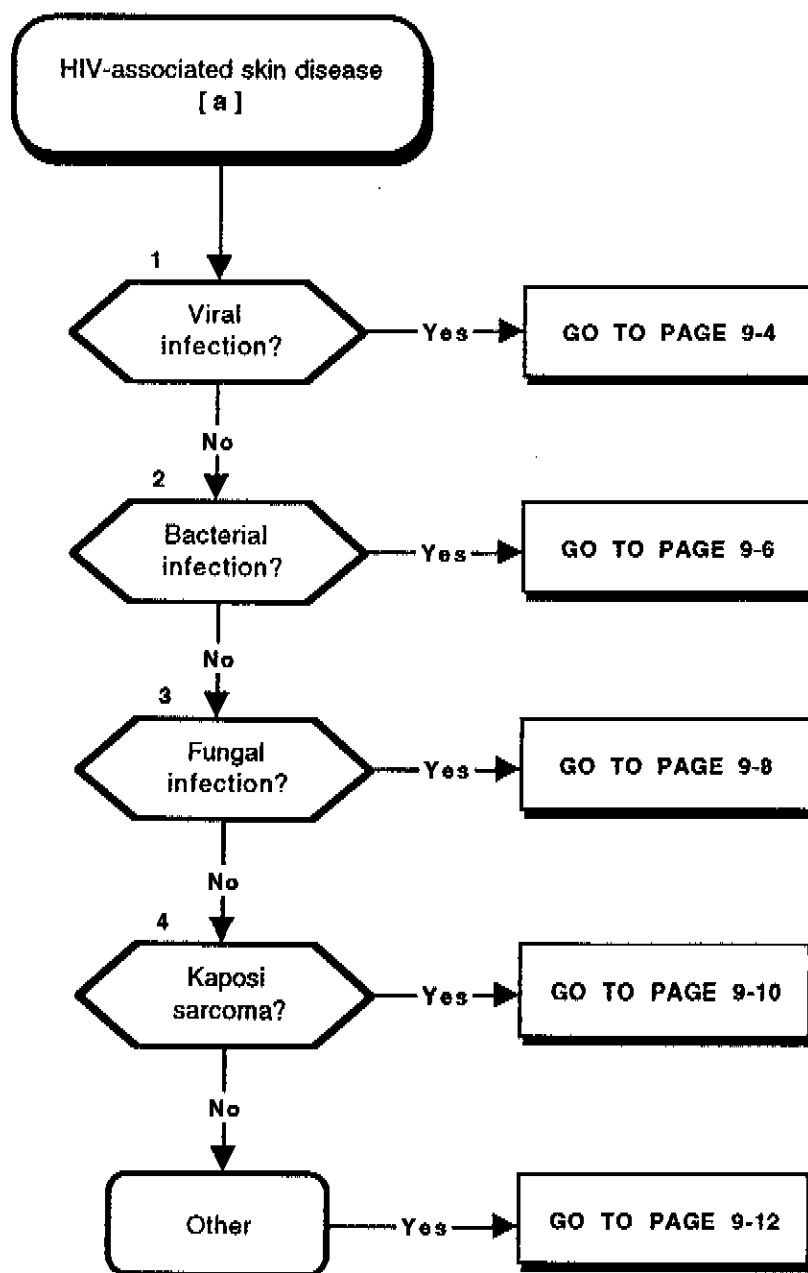
- n. Ampicillin, 1g 4 times daily for 10 days, as an empirical treatment. If this treatment fails some further investigations may be useful:

- computed tomography scan of head to look for cerebral toxoplasmosis;
- sigmoidoscopy including rectal biopsy to look for bacteria, mycobacteria, cytomegalovirus;
- gastroscopy to look for gastrointestinal lymphoma.

## **Chapter 9**

# **HIV-Associated Skin Diseases**

# HIV-Associated Skin Diseases



**Annotations:**

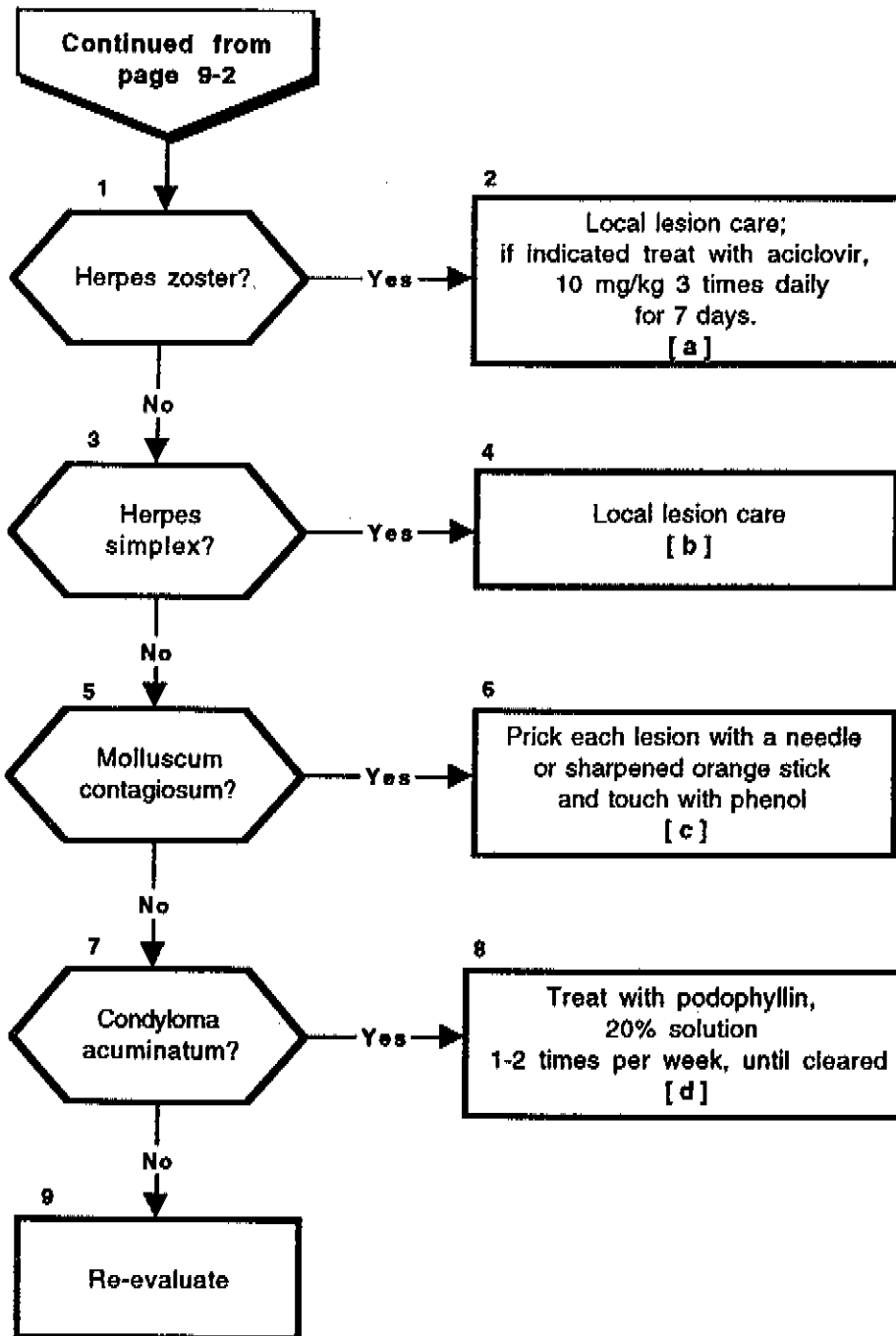
- a. **Definition:** The presence of a dermatosis in a patient with symptomatic HIV infection.

**Etiology:**

1. **Viral infections:**
  - herpes zoster
  - herpes simplex
  - molluscum contagiosum
  - condyloma acuminatum.
  
2. **Bacterial infections:**
  - furunculosis
  - impetigo and pyoderma (staphylococci, streptococci)
  - hidradenitis suppurativa
  - pyomyositis (often with discharging sinuses).
  
3. **Fungal infections:**
  - candidiasis
  - dermatophytosis.
  
4. **Malignancy:**
  - Kaposi sarcoma.
  
5. **Other dermatoses:**
  - drug eruptions
  - chronic prurigo or urticaria (blood parasites or other common etiologies excluded)
  - severe seborrhoeic dermatoses
  - generalized erythroderma
  - severe psoriasis
  - Scabies.

Some sexually transmitted diseases occur with increased frequency or altered expression and the management needs to be reviewed (see national guidelines).

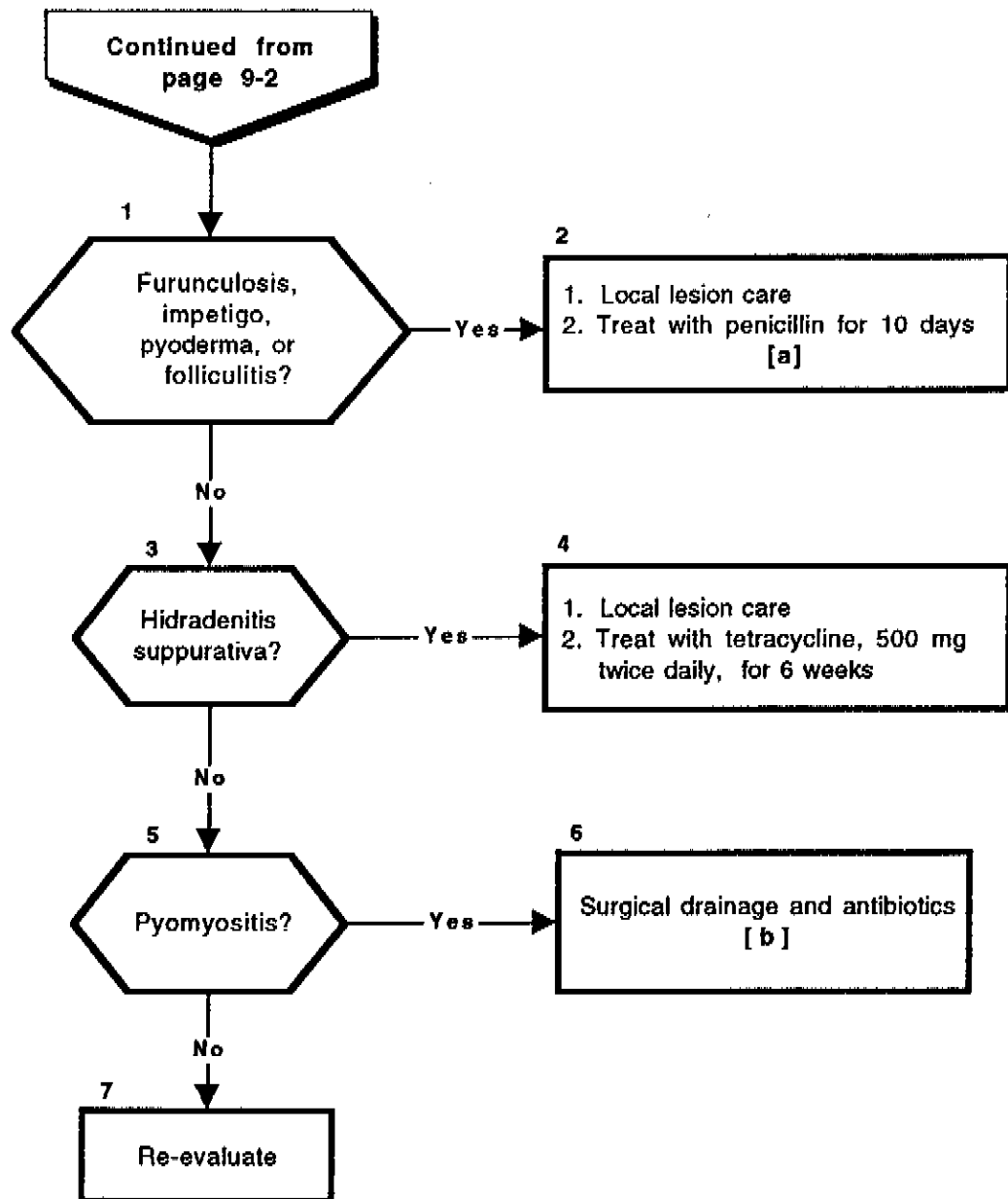
A list of the main causes in order of significance should be established in the light of available national or local information.



**Viral infection**

**Annotations:**

- a. The greatest benefit of aciclovir is seen in patients with ophthalmic or disseminated zoster. Treatment should be commenced within 5 days of presentation and should continue until new lesions have stopped forming or old lesions have scabbed. Post-herpetic neuralgia is uncommon; if present, pain-modifying agents are considered useful, e.g. phenytoin (100 mg daily slowly increasing to 250-300 mg daily) or carbamazepine (100 mg daily increasing to 400 mg daily in 10 days).
- b. Ulcers which are persistent and very painful may be treated with oral aciclovir, 200 mg 5 times daily, until healed. Where available, chemosuppression with oral aciclovir, 200-400 mg twice daily, should be administered.
- c. Alternatively, where available, cryotherapy with liquid nitrogen is recommended. The recurrence rate is high.
- d. Alternatively, glacial trichloroacetic acid may be applied 1-2 times per week until the lesion has cleared. Where available, cryotherapy with liquid nitrogen is recommended. The recurrence rate is high.



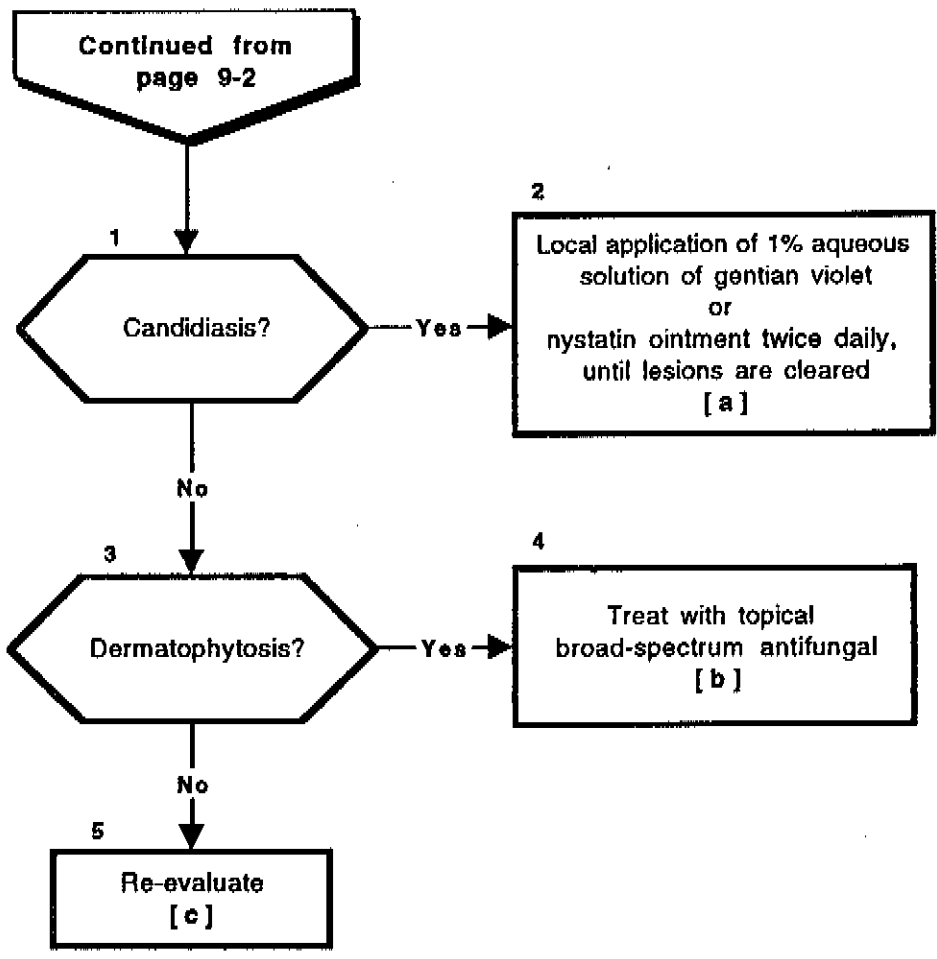
**Bacterial infection**

**Annotations:**

- a. For example, phenoxymethylpenicillin, 250-mg tablets 4 times daily for 10 days. In case of treatment failure, penicillinase-resistant penicillin, e.g. cloxacillin, should be given. In severe cases the patient may require intravenous treatment with penicillinase-resistant penicillin or cephalosporins because of the risk of systemic spread.
- b. Where facilities are available to determine the sensitivity of the organism identified, the treatment should be in accordance with the findings.

# HIV-Associated Skin Diseases

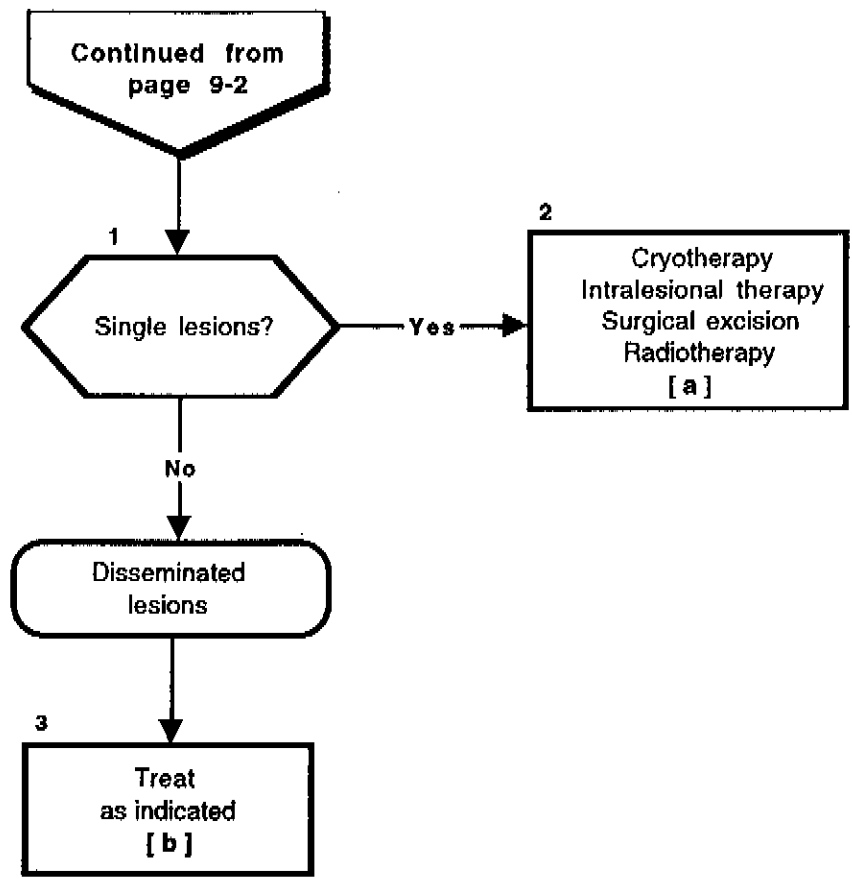
## Fungal infection



**Fungal infection**

**Annotations:**

- a. If there is no response to therapy, try other topical antifungal drugs, e.g. clotrimazole, 1% cream. In severe cases systemic therapy, e.g. ketoconazole, 200 mg twice daily may be required.
- b. Widespread dermatophytosis may necessitate systemic treatment with griseofulvin, 500 mg twice daily, where available.
- c. Cutaneous lesions of systemic cryptococcosis or disseminated histoplasmosis are rare, but respond well to antifungal chemotherapy.



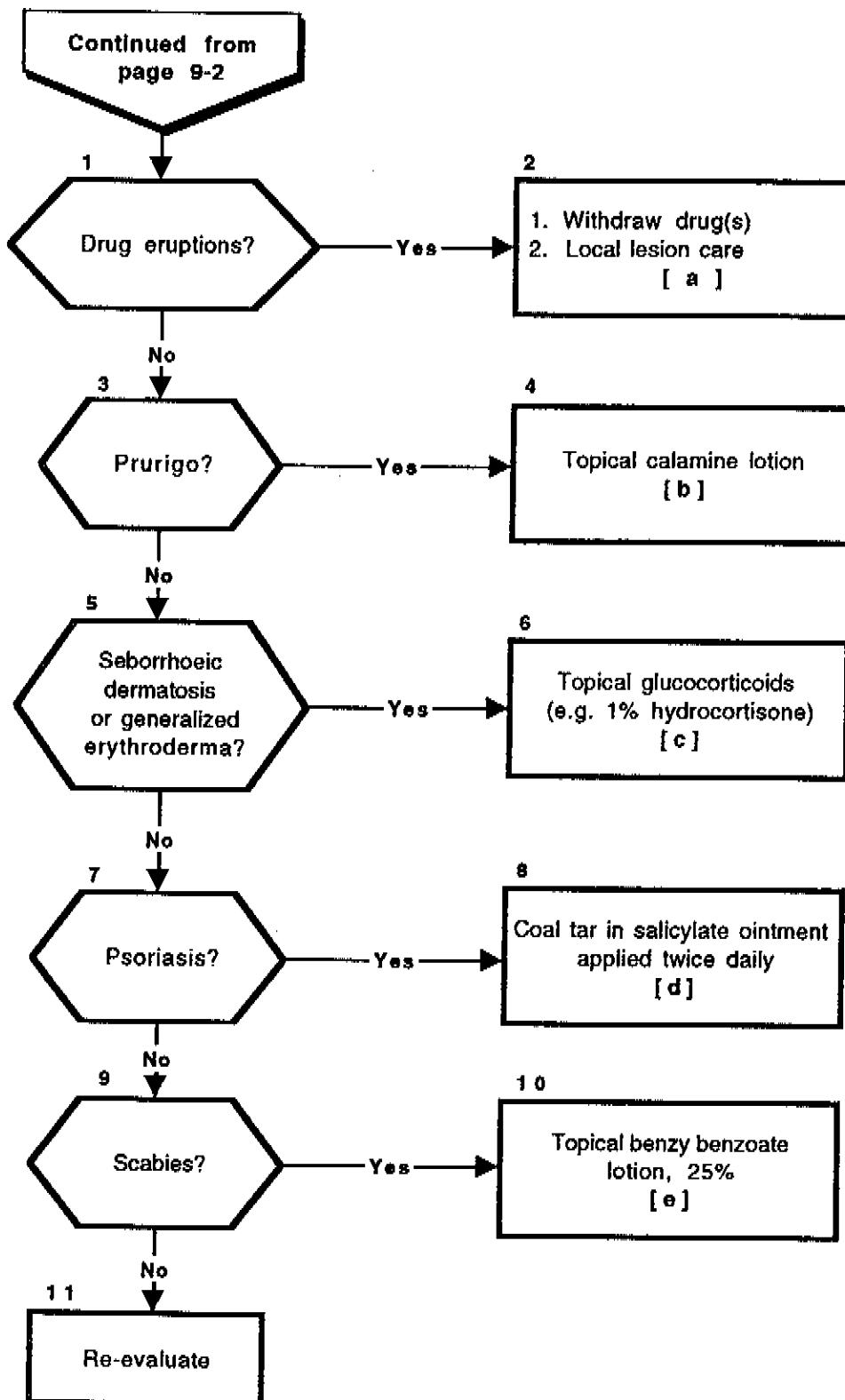
**Kaposi sarcoma****Annotations:**

- a. Lesions of the face or exposed parts of the body may be treated locally. Palliative treatments for cutaneous Kaposi sarcoma (KS) include cryotherapy (topical liquid nitrogen) intralesional therapy with either vinblastine or alpha interferon and surgical excision. Radiotherapy is used for intraoral or pharyngeal KS, painful cutaneous KS, and lymphoedema of the face and extremities. In single lesions the results with any of the treatment choices mentioned are promising.
- b. For the treatment of systemic KS, alpha interferon alone (or in combination with zidovudine) has been used in patients with severe immune depression. The treatment may benefit up to half of the patients but only temporarily.

For rapidly progressive and/or disseminated mucocutaneous disease, or when the tumour compromises the function of vital organs, chemotherapy may effect rapid tumour regression and be life saving. Among the drugs reported to be effective as single agents or as part of a combination regimen are bleomycin, doxorubicin, etoposide, vinblastine, and vincristine.

# HIV-Associated Skin Diseases

*Other dermatoses*



**Other dermatoses**

**Annotations:**

- a. Trimethoprim-sulfamethoxazole, sulfadiazine, pentamidine and aciclovir are the drugs most often associated with drug eruptions. Thioacetazone has also been incriminated. Corticosteroids should only be given in life-threatening situations.
- b. Prurigo can be very disabling. Sometimes antihistamines, e.g. diphenhydramine, 50-mg tablets every 6 hours may be helpful.
- c. Topical coal tar is also helpful. In severe cases with coexistent candidiasis, topical ketoconazole is beneficial.
- d. Severe psoriasis may respond to topical corticosteroids.
- e. The application is left on the skin to dry and then repeated the next day. Avoid contact with the eyes.

## **Chapter 10**

# **Management of the HIV-Infected Asymptomatic Person**

The management of HIV-infected people who are asymptomatic consists of counselling and medical follow-up. This publication deals only with clinical management - for guidance on counselling please refer to appropriate documents, for example, *Guidelines for counselling about HIV infection and disease*, Geneva, World Health Organization, 1990 (WHO AIDS Series, No. 8).

The medical management of asymptomatic HIV-infected persons aims at: (1) early detection of HIV-associated disease and treatment; (2) primary prophylaxis when indicated; and (3) determination of the appropriate time to start antiretroviral therapy.

Where resources are scarce, priority should be given to regular clinical follow-up with only minimal laboratory investigations (e.g. haemoglobin and total lymphocyte count). Many authorities recommend follow-up every 6 months.

Knowledge of the degree of immune deficiency (particularly CD4 count) assists with decision-making in: (1) interpretation of symptoms; (2) primary prophylaxis, e.g. for *Pneumocystis carinii* pneumonia; and (3) commencement of antiretroviral therapy. The frequency of visits should increase as the CD4 count falls.

## 1. History Taking and Physical Examination

History taking and physical examination can be done at all levels and are essential for classifying the patient as asymptomatic or detecting onset of disease.

### *History taking*

Look for symptoms of HIV infection such as fever, night sweats, weight loss, anorexia, diarrhoea, cough, worsening headache, visual symptoms, seizures, diffuse lymphadenopathy, pruritis, genital ulcers, skin rash or itching, difficulty on swallowing (dysphagia) or pain on swallowing (odynophagia). Ask specifically about current medication.

### *Physical examination*

This should cover the following:

- general: weight loss, fever
- neurological examination: peripheral neuropathy, cognitive disorders
- skin changes: herpes zoster, herpes simplex, folliculitis, tinea, Kaposi sarcoma, prurigo, seborrhoeic dermatitis, severe psoriasis
- oral cavity: thrush, hairy leukoplakia, gingivitis, Kaposi sarcoma, lymphoma
- eyes: funduscopy (less useful than in symptomatic patients)
- lymph nodes: focal or diffuse enlargement
- lungs: pneumonia, pleural effusion
- abdominal examination: hepatosplenomegaly

- genitalia: chancre/ulcers
- anus: ulcers, warts.

## 2. Laboratory Examination and X-ray

Regular laboratory testing should be limited where resources are scarce (see above). Where available, some of the investigations to be performed include:

Tests to assess the degree of immune deficiency and evolution of HIV infection; use best available test(s):

- total lymphocyte count
- CD4 lymphocyte count and percentage
- $\beta$ 2-microglobulin
- neopterin (urine or serum)
- p24 antigen.

Tests to assess potential infection:

- serology: toxoplasmosis<sup>1</sup>, cytomegalovirus, syphilis, hepatitis B
- tuberculin skin test
- complete blood count, erythrocyte sedimentation rate
- liver function tests
- chest X-ray.

The tuberculin skin test is of limited value in establishing a diagnosis of tuberculosis, because of the high level of anergy found in HIV-infected persons. Reactivity is reasonably preserved in less immunocompromised individuals and suppressed in persons with advanced stages of HIV infection and AIDS.

## 3. Drugs

There is evidence that both primary prophylaxis (for *Pneumocystis carinii* pneumonia) and antiretroviral therapy (using zidovudine) are beneficial for certain subgroups of asymptomatic HIV infected-persons. Research is going on to identify better those subgroups and to determine the appropriate dosage of the drugs currently used and other drugs.

<sup>1</sup> Antitoxoplasma IgG is detectable in the serum of many HIV-infected people who do not have toxoplasmosis. Absence of IgG antibodies is strong evidence against *Toxoplasma gondii* infection.

## Management of the HIV-Infected Asymptomatic Person

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Isoniazid prophylaxis has been shown to be beneficial in preventing tuberculosis in people who are not HIV-infected. Efficacy and feasibility studies are presently under way to determine the usefulness of isoniazid prophylaxis in asymptomatic individuals with dual infection (tuberculosis and HIV).

#### 4. Immunization

The antibody response to many antigens, including vaccines, is diminished in patients infected with HIV. Immune responses to vaccines tend to be better in persons in the early stages of HIV infection. There is no increase in the rate of vaccine adverse reactions. Inactivated vaccines should be administered to persons with HIV infection where indicated. Live vaccines are not usually given to immunocompromised individuals; for more information, see document WHO/GPA/INF/89.6.

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