

**Guidelines for the Prevention and
Management of
Opportunistic Infections in Adults
and Children**

LaoPDR

FINAL DRAFT

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Acronyms and Abbreviations

ABC	Abacavir	IV	Intravenous
3TC	Lamivudine	Kg	Kilogram
AIDS	Acquired Immunodeficiency Syndrome	LPV LPV/r NRTI	lopinavir lopinavir/ritonavir Nucleoside reverse transcriptase inhibitor
AFB	Acid-Fast-Bacilli		Non-nucleoside reverse transcriptase inhibitor
ALC	Absolute lymphocyte count	NNRTI	Nelfinavir
ALT	Alanin transferase, serum	NFV	Nevirapine
AZT	Azidothymidine (zidovudine)	NVP od	Once daily
ART	Antiretroviral therapy	ORS	Oral Rehydration Salt
BAL	Broncho Alveolar Lavage	PCP	Pneumocystis carinii pneumonia
bid	Two time per day	PCR	Polymerase chain reaction
CBC count	Complete blood	PEP	Post exposure prophylaxis
CMV	Cytomegalovirus	PTB	Pulmonary tuberculosis
CNS	Central nervous system	PI	Protease inhibitor
CSF	Cerebrospinal fluid	PMTCT	Prevention of mother to child transmission
CT	Computerized tomography	PPE	Papular Pruritic Eruption
CTX	Cotrimoxazole	RIF	Rifampicin
CXR	Chest Xray	RH	Rifampicin/Isoniazid
d4T	Stavudine	RHE	Rifampicin/Isoniazid
ddC	Zalcitabine	RHZE	Rifampicin/Isoniazid Pyrazinamide/ Ethambutol
ddI	Didanosine		Ritonavir
EBV	Ebstein-Barr virus	RTV	Streptomycin/ Isoniazid/ Pyrazinamide/ Ethambutol
EIA	Enzyme immune assay	SRHZE	Sexually Transmitted Infection
ELISA	Enzyme linked immunosorbent assay		Saquinavir
ETH	Ethambutol		Tuberculosis
EFV	Efavirenz		Three times per day
GI	Gastrointestinal		Trimethoprim- Sulfamethoxazole
INH	Isoniazid	STI	Voluntary testing and counselling
HAART	Highly active antiretroviral therapy	SQV	Venereal disease research laboratory (syphilis)
HbsAg	Hepatitis B surface antigen	TB tid TMP/SMZ	Western Blot
HCV	Hepatitis C virus		White Blood Cell
HIV	Human Immunodeficiency Virus	VCT	World Health Organisation
HPV	Human Papilloma Virus	VDRL	
HSV	Herpes Simplex Virus	WB	
IM	Intra Muscular	WBC	
INH	Isoniazid	WHO	
IU	International Unit		

Cotrimoxazole prophylaxis

	CD4 not available	CD4 available
When to start primary cotrimoxazole (CTX) prophylaxis	WHO clinical stage 2, 3, 4, (including all patients with TB)	Any WHO clinical stage CD4 < 350 cells/mm ³
When to stop cotrimoxazole prophylaxis in patients on ART	Continue prophylaxis indefinitely	CD4 count > 350 cells/mm ³ for 6 months on ART

Table 1: When to start and stop cotrimoxazole prophylaxis

Doses of cotrimoxazole in adults and adolescents	960 mg (800 mg SMZ + 160 mg TMP) per day <ul style="list-style-type: none"> • 2 X 480mg /day or 1 x 960 mg/day • Dosing is the same for primary and secondary prophylaxis
Commencing secondary cotrimoxazole prophylaxis	Secondary prophylaxis is recommended for all patients who have completed successful treatment for PCP
Timing the initiation of cotrimoxazole in relation to initiating ART	Start cotrimoxazole prophylaxis first Start ART two weeks later if the individual is tolerating co-trimoxazole and has no symptoms of allergy (rash, hepatotoxicity) A two week separation will assist clinical management where the cause of the symptoms maybe either cotrimoxazole or ART (especially if starting nevirapine containing regimen)
Universal option	Countries may choose to adopt universal cotrimoxazole for everyone living with HIV and any CD4 count or clinical stage. This strategy may be considered in settings with high prevalence of HIV and limited health infrastructure
Cotrimoxazole in pregnant women	Women who fulfill the criteria for cotrimoxazole prophylaxis should continue on it throughout their pregnancy If a woman requires cotrimoxazole prophylaxis during pregnancy, it should be started regardless of the stage of pregnancy Breast feeding women should continue to receive prophylaxis
Patients allergic to sulpha-based medications	Dapsone 100mg per day, if available Cotrimoxazole desensitization may be attempted but not in patients with a previous severe reaction to CTX or other sulpha containing drugs.
Monitoring	No specific laboratory monitoring is required

Table 2: Additional notes on the use of cotrimoxazole

Toxicity	Clinical description	Recommendation
Grade 1	Erythema	Continue CTX with follow-up and antihistamines
Grade 2	Diffuse maculopapular rash, dry desquamation	Continue CTX with follow-up and antihistamines
Grade 3	Vesiculation, mucosal ulceration	Discontinue CTX for 2 weeks and restart CTX with desensitization
Grade 4	Exfoliative dermatitis, Stevens-Johnson Syndrome* or erythema multiform, moist desquamation	Discontinue CTX and never restart

Table 3: Cotrimoxazole toxicity grading scale for adults and adolescents

*Stevens-Johnson Syndrome (SJS) is similar to extensive burns. Treatment is most successful if SJS is recognized and treated early. All medication should be temporarily stopped until the patient is stable. Apart from intensive supportive therapy, no generally accepted specific treatment regimen exists. Treatment is symptomatic and may include IV fluids, electrolyte supplements and blood products. Skin care includes prompt treatment of secondary bacterial infections.

The use of systemic steroids is controversial. Corticosteroids may have some benefit early in the treatment and have no benefit late after presentation.

Co-trimoxazole desensitization

In cases of non life threatening adverse reactions, treatment should be stopped for two weeks, and the patient should then be rechallenged with cotrimoxazole in a gradually increasing dose (desensitization).

A. 1 ml cotrimoxazole suspension (40 mg TMP\ 200 mg SMX\5 ml) in 10 ml water.

- Day 1: 1 ml solution
- Day 2: 2 ml solution
- Day 3: 4 ml solution
- Day 4: 8 ml solution

B. Cotrimoxazole UNDILUTED suspension

- Day 5: 0,6 ml
- Day 6: 1,25 ml
- Day 7: 2,5 ml
- Day 8: 5 ml
- Day 9: 10 ml

C. Cotrimoxazole tablets (80 mg TPM- 400 mg SMX)

- Day 10: 1 CTX
- Day 11-17: 2 x 1 CTX\day
- Hereafter: 1 tablet 960 mg / day

Table 4: Example of desensitization scheme for cotrimoxazole

If desensitization fails, another regimen needs to be given. WHO recommends dapsone 100 mg once daily as the first alternative for prevention of PCP.

Toxoplasmosis prophylaxis

Primary prophylaxis	960 mg (800 mg SMZ + 160 mg TMP) per day (same as for PCP) (2 X 480mg or 1 X 960mg/day)
Secondary prophylaxis	

Antifungal prophylaxis

	When to start	What to start	When to stop
Primary prophylaxis	CD4 count < 100 cells OR WHO stage IV	Fluconazole 400mg once weekly	CD4 count > 100 for at least 6 months on ART If no CD4 count do not stop
Secondary prophylaxis	After success treatment of cryptococcal infection	Fluconazole 200mg once daily	

Table 4: When to start and stop fungal infection prophylaxis

Fluconazole prophylaxis should be provided to all women, including pregnant women, who need it based on medical criteria.

Tuberculosis prophylaxis

New text from TB department

Active TB must be excluded before giving isoniazid (INH) prophylaxis. If active TB cannot be active excluded, do not give INH prophylaxis. INH prophylaxis is 300mg per day for 9 months.

In Lao PDR, INH prophylaxis is recommended for children <5 years of age if a family member has active TB. The dose is 10 mg/kg/day for 6 months for HIV negative children and for 9 months in HIV positive children or children born to HIV positive mothers.

MAC Prophylaxis

- Primary prophylaxis not recommended
- Secondary prophylaxis is recommended after treatment of MAC until immune recovery on ART (CD4 >100 repeated twice 6 months apart stable on ART after 6 months).
 - Azithromycin 1,250 mg once weekly

Tuberculosis

Clinical Presentation

Even in HIV-infected patients, pulmonary TB is the commonest form of TB. In more advanced HIV infection, the typical TB chest X-ray findings of upper lobe infiltrates with cavitation are replaced by atypical findings of bilateral infiltrates (especially lower zones) with no cavitation. HIV infected patients are more likely to present with a miliary pattern on CXR and with hilar/mediastinal lymph node enlargement.

Features of PTB	Stage of HIV infection	
	EARLY	LATE
Clinical picture	Often resembles post-primary PTB	Often resembles primary PTB
Sputum smear result	Often positive	Often negative
Chest X-ray appearance	Often cavities	Often infiltrates with no cavities

Table 5: Early and late TB presentations

Diagnosis

Typical clinical presentation. Sputum examination for AFBs (which may be negative in immunosuppressed patients). WHO recommends 3 sputum samples. Chest X-ray may show typical or atypical findings

Treatment (Treat according to National Guidelines)

Short course therapy with an initially intensive phase of 4 drugs are usually advised: 2 months INH, RIF, PZA and EMB, followed by a four month continuation phase of INH and RIF.

TB Diagnostic Category	Patients
Category I	<ul style="list-style-type: none"> ▪ New smear-positive pulmonary TB ▪ New smear-negative pulmonary TB with extensive parenchymal involvement, concomitant HIV disease or severe forms of extrapulmonary TB
Category II	Previously treated sputum smear-positive pulmonary TB: <ul style="list-style-type: none"> -relapse -treatment after default -treatment failure
Category III	<ul style="list-style-type: none"> ▪ New smear-negative pulmonary TB (other than Category I) ▪ Less severe forms of extrapulmonary TB
Category IV	Chronic and MDR-TB (still sputum-positive after supervised re-treatment)

Table 6: TB diagnostic categories

Source: TB/HIV: A clinical manual, 2nd ed, World Health Organization WHO/HTM/TB/2004.329

TB Diagnostic Category	TB treatment regimens	
	Initial phase	Continuation phase
I	2HRZ	4HR or 6HE daily ^a
II	2HRZES or 1HRZE	5HRE
III	2HRZE	4HR or 6HE daily ^a
IV	Specially designed individualized cases (are suggested for this category)	

Table 7: Recommended treatment

Source: TB/HIV: A clinical manual, 2nd ed, World Health Organization WHO/HTM/TB/2004.329
H=Isoniazid, *R*=rifampicin, *Z*=Pyrazinamide, *E*=Ethambutol, *S*=streptomycin

a. This regimen may be associated with a higher rate of treatment failure and relapse compared to the 6-month regimen with rifampicin in the continuation phase

Case Definitions

- **Pulmonary TB (PTB)**
 - Smear-positive patient, M+ or PTBM+ (or BK+):
 - Patient with at least 2 sputum smear-positive samples,
 - Or patient with at least 1 sputum smear-positive sample and X-ray anomalies suggesting active pulmonary TB,
 - Or patient with at least 1 sputum smear-positive sample and 1 culture positive.
 - Smear-negative patient M- or PTBM- or (BK-):
 - Patient with 2 sets (taken at least 2 weeks apart) of at least 2 sputum smear –negative samples, X-ray anomalies suggesting active pulmonary TB, and no response to 2 different courses of broad-spectrum antibiotics,
 - Or patient with sputum smear-negative samples, whose culture is positive for M.tuberculosis,
 - Or when X-ray and cultures are not available, patient with 2 sets (taken at least 2 weeks apart) of at least 2 sputum smear-negative samples, and no response to 2 different courses of broad-spectrum antibiotics,
 - **In addition**, for whom a doctor prescribed a complete treatment of anti-TB chemotherapy.
- **Extra-pulmonary TB (EPTB)**
 - Patient with clinical signs and history corresponding to active extra-pulmonary TB
 - Or patient with at last one culture-positive non-pulmonary sample for M.tuberculosis
 - **In addition**, for whom a doctor prescribed a complete treatment of anti-TB chemotherapy.

Sputum smear microscopy should always be done and culture when possible. Patients presenting with TB pleural effusion, miliary TB or mediastinal lymphadenopathy without evidence of parenchymal localization are classified in this category. Any patient presenting with M+ pulmonary disease and an extra-pulmonary form at the same time is considered an M+ case for recording purposes.

- **New case**

TB in a patient who has never taken anti-TB drugs for over one month, in the past 5 years.

- **Retreatment**

Patients who received at least 1 month TB treatment in the past 5 years and return with a diagnosis of TB. They composed of:

- **Relapse:** a patient, who was classified as "cured" or "treatment completed" but who returns with a diagnosis of TB disease (smear-positive, or occasionally smear– or EP).
- **Failure:**
- **Without cultures:** a patient under treatment who remains positive 4 months or more after beginning of treatment **OR**
- Patients initially M- or EP with no significant clinical improvement and no significant gain of weight after 4 months of treatment and for whom diagnosis of failure is established by a doctor.
- **With cultures:** A patient presenting a positive culture at 4 months of treatment or later **or** Patients initially M- or EP with no significant clinical improvement and no significant gain of weight after 4 months of treatment and for whom the diagnosis of failure is established by a doctor.
- **Return after default:** a patient who interrupts treatment for over two months and who returns smear-positive.
- **Others:** patients who cannot be included in one of the above categories; for example, patients who have previously been treated via an erratic or unknown TB regimen. This group includes the chronic cases: patients presenting a failure to a re-treatment regimen and suspected of having developed MDR TB (Multi drug resistance TB).

- **Transferred in:** a patient who began treatment and had been registered in another TB program, and was then referred during treatment.

Treatment outcomes:

- **Cured patient:** Patient, initially M+, who completed treatment and has at least two negative bacteriological verifications: one at the end of treatment and the other in a previous occasion at least one month apart.
- **Patient having completed treatment:** Patient, initially M+, who has undergone a complete course of treatment but for whom there is no bacteriological verification available.
Patients initially M– and EP who have completed their treatment.
- **Death:** Patient who died during treatment, whatever the cause of death.
- **Treatment interrupted (default):** Patient who definitively interrupted treatment, at no matter what point, or patient who interrupted treatment for over two months.
- **Transfer out:** Patient transferred to another center.

Management of reactions to anti TB Drugs

A-Hypersensitivity (allergic) reactions

These rarely occur in the first week of treatment. They are commonest in the second to the fourth week. They are less frequent with isoniazid, rifampicin, and ethambutol than they are with streptomycin. Very rarely patients are become allergic to all three drugs in a regimen.

- a- Mild: itching of the skin only: this is often the only sign of rifampicin allergy.
- b- Moderate: fever and rash. If severe the skin looks blistered and resembles urticaria.
- c- Severe: in addition to fever and rash there may be generalized swelling of lymph nodes, enlargement of liver and spleen, swelling round the eyes and swelling of the mucous membranes of the mouth and lips. High fever, a generalized blistering rash, and ulceration of the mucous membranes of the mouth, genitals, and eyes (Stevens-Johnson). This is a rare but dangerous reaction, particularly to patients with HIV infection. Very rarely, there may be chronic eczema involving the limbs occurring after the eighth week. This is almost always due to streptomycin.

Management

This is discussed in 2 parts: immediate and desensitization.

1. Immediate

If the only complaint is **mild itching**, usually continue drug treatment, as the patient desensitizes themselves (give anti histamine drug if available).

If there are **fever** and **rash** stop all drugs, give anti histamine drug.

If there is a **very severe reaction**, stop all drugs. Treat at the hospital with:

- Hydrocortisone 200 mg IV or IM then
- Dexamethasone 4 mg IV or IM until the patient can swallow, then
- Prednisolone 15 mg 3 times a day orally, reducing the dose gradually every 2 days depending upon the patient's response
- IV fluids if required.

Desensitization should **not** be attempted if **the** patient has had a very severe reaction.

2. Desensitization

This should not be begun until the hypersensitivity reaction has disappeared. Desensitization is best done at the hospital.

If possible give 2 anti Tb drugs, which the patient has not previously received while, you are carrying out desensitization.

Start giving test doses as shown in the following table:

Drugs	day 1	day2
Isoniazid	50 mg	300 mg
Rifampicin	75 mg	300 mg
Pyrazinamide	250 mg	1,0 g
Ethambutol	100 mg	500 mg
Streptomycin	125 mg	500 mg

Table 8: Challenge doses for hypersensitivity to anti TB drugs

If a reaction occurs with the first challenge dose drug, the patient is hypersensitive to that drug.

When starting to desensitize it is usually safe to begin with the tenth of the normal dose. then increase the dose by a tenth each day.

If he has a mild reaction to a dose, give the same dose (instead of a higher dose) next day. If there is no reaction, increase by a tenth each day. If the reaction is severe (which is unusual) go back to a lower dose and increase the doses gradually.

If the patient is in the hospital, or can attend at 12 hourly intervals, you can give the doses twice a day and save time. In most cases, you can complete the desensitization within 7 – 10 days.

As soon as desensitization to that drug is completed, begin giving it regularly but make sure that it's combined with at least one other drug (to which the patient is not sensitive) so as to prevent drug resistance.

Hepatitis B

All anti TB can cause damage to the liver and it is very difficult to decide whether hepatitis is due to the drugs or to infectious hepatitis.

Hepatitis as a side effect probably occurs in about 1 percent of treated patients, and is probably commonest with pyrazinamide.

Mild symptoms, less increase in serum enzymes are a common occurrence. This is not an indication to stop the drugs. If there is loss of appetite, jaundice, and liver enlargement, treatment should be stopped until the liver function has returned to normal. Strangely enough in most patients, the same drugs can be given again without return of hepatitis.

If the hepatitis has been severe, do not use Pyrazinamide or rifampicin for retreatment. Give streptomycin, isoniazid, and ethambutol

(2SHE\10 HE)

If the patient is severely ill with TB and might die without TB therapy, it is safest to give streptomycin and ethambutol (the least hepatotoxic drugs). When the hepatitis has settled restart standard chemotherapy unless the hepatitis has been very severe. if hepatitis has been severe, use **2 SHE\10 EH** .

Bacterial pneumonia

Bacterial pulmonary infections are common and severe in HIV disease. The most common causes are *Streptococcus pneumoniae* or *Haemophilus influenzae*. Other frequent bacterial pathogens include *S. aureus*, *Moraxella catarrhalis*, *Klebsiella pneumoniae* and *P.aeruginosa*.

The onset of symptoms is often abrupt with high fever, productive cough and pleuritic type chest pain. Infiltrates that are localised to one lobe most likely *S.pneumoniae*. More diffuse infiltrates are more likely to be due to *H.influenzae*.

Bilateral patchy consolidations in a critically ill patient suggests staphylococcal pneumonia. Upper lobe consolidation with cavitation has been observed in pulmonary *nocardiosis*, and can mimic tuberculosis. In nocardiosis there is often evidence of multiple abscesses (brain, lung, skin). A gram stain will show gram positive thin branching (mycelium like) filaments.

Diagnosis

The syndrome of fever, purulent sputum and localised infiltrate on the chest X-ray strongly suggests a bacterial pneumonia and additional diagnostic tests are often of little value.

Gram stain of sputum and culture yields the diagnosis in 75% of cases.

Treatment

1. **Amoxy-clavulanic acid** (Augmentin®) is active against *S.pneumoniae*, *Moraxella catarrhalis* and *H.influenzae*
2. **Second generation cephalosporines** (cefuroxime, cefaclor)
3. The recommended treatment for Nocardia is **TMP/SMX** 10/50 mg/kg x 2/day

The duration of the treatment varies from 6 weeks (for localised disease) to 6 months (disseminated disease). An alternative treatment for nocardiosis is minocycline 100 mg x 2/day combined with amikacin 15-25 mg/kg/day IV, once a day, or ceftriaxone 2 g/day combined with amikacin.

Seriously ill patients with a respiratory infection should receive a combination that contains a quinolone or chloramphenicol (or ceftriaxone if available) to cover for gram negative infections.

Treatment for severe life-threatening pneumonia could be: **ceftriaxone + amikacin** (gram negatives + gram positives, also staphylococcus), or **chloramphenicol + cloxacillin** (gram negatives + gram positives, including staphylococcus, atypical bacteria (chlamydia, mycoplasma)).

Pneumocystis Jiroveci Pneumonia (PCP)

A typical chest X-ray shows bilateral interstitial or alveolar infiltrates. Sometimes there are nodules or cavities, but the X-ray can be (at first presentation) misleadingly normal (25%). More than 80% of cases of pneumothorax in HIV-infected patients are due to PCP.

Diagnosis

In resource limited settings, the diagnosis is based on clinical presentation of dry cough, fever and shortness of breath and typical X- Ray. Induced sputum examination may be included in the diagnostic work up if available, but should not delay initiation of treatment based on clinical findings.

Treatment

1st choice	<p>Cotrimoxazole IV or high does orally if tolerated and not too unwell. (TMP 20 mg/kg/day and SMX 100 mg/kg/day divided over 4 doses.)</p> <p>Any patient who is hypoxic ($pO_2 < 70$ mmHg) should receive prednisolone.</p> <p>Prednisolone given orally.</p> <ul style="list-style-type: none">- 40 mg twice daily for 5 days- followed by 40 mg daily for 5 days- then 20 mg daily for 11 days (a total of 21 days together with TMP/SMX 21 days)
2nd choice	<p>Clindamycin intravenously IV 600 mg x 4/day and primaquine oral 15 mg/dag or Dapsone 100 mg/day and trimethoprim 20 mg/kg once a day. If the patient is unable to tolerate these regimens pentamidine 4 mg/kg/day intravenously can be used.</p>

Penicilliosis

Penicillium marneffeii is a common cause of opportunistic infection in HIV infected patients with late stage disease (CD4 < 100).

The most common clinical presentations are abrupt onset of fever, anaemia, skin lesions and weight loss. Respiratory complaints (cough, shortness of breath) are also common.

Chest X-ray shows diffuse nodular pulmonary infiltrates or cavitary disease. Less commonly, local or generalised lymphadenopathy, hepatomegaly or splenomegaly occur. Skin involvement occurs in patients with disseminated disease. The typical appearance is one of multiple papular lesions, often with central umbilication or ulceration, resembling molluscum contagiosum. The lesions are typically on the face, scalp and upper trunk. The differential diagnosis with TB and disseminated cryptococcal disease has to be made. If there are no skin lesions the diagnosis is difficult.

Diagnosis

The organism may be seen by microscopic examination of skin scrapings, touch preparations of skin biopsy or lymph node aspirate stained with Wright's stain, or cotton blue stain. Bone marrow aspirate is diagnostic in 100 % of cases. The diagnosis is confirmed by culturing the fungus from clinical specimens.

Treatment

Initial treatment should be with amphotericin B 0,6 mg/kg/day IV during two weeks, followed by itraconazole 200 mg twice daily for 10 weeks.

Secondary prophylaxis is with itraconazole 200 mg/day

Cryptococcal pneumonitis

Typically cryptococcal infection presents as meningitis but it can cause pneumonia.

Diagnosis is confirmed by sputum culture.

Treatment is with amphotericin B and fluconazole. (see Chapter 3: neurological disorders)

Toxoplasma pneumonitis

Sometimes it is difficult to distinguish from PCP.

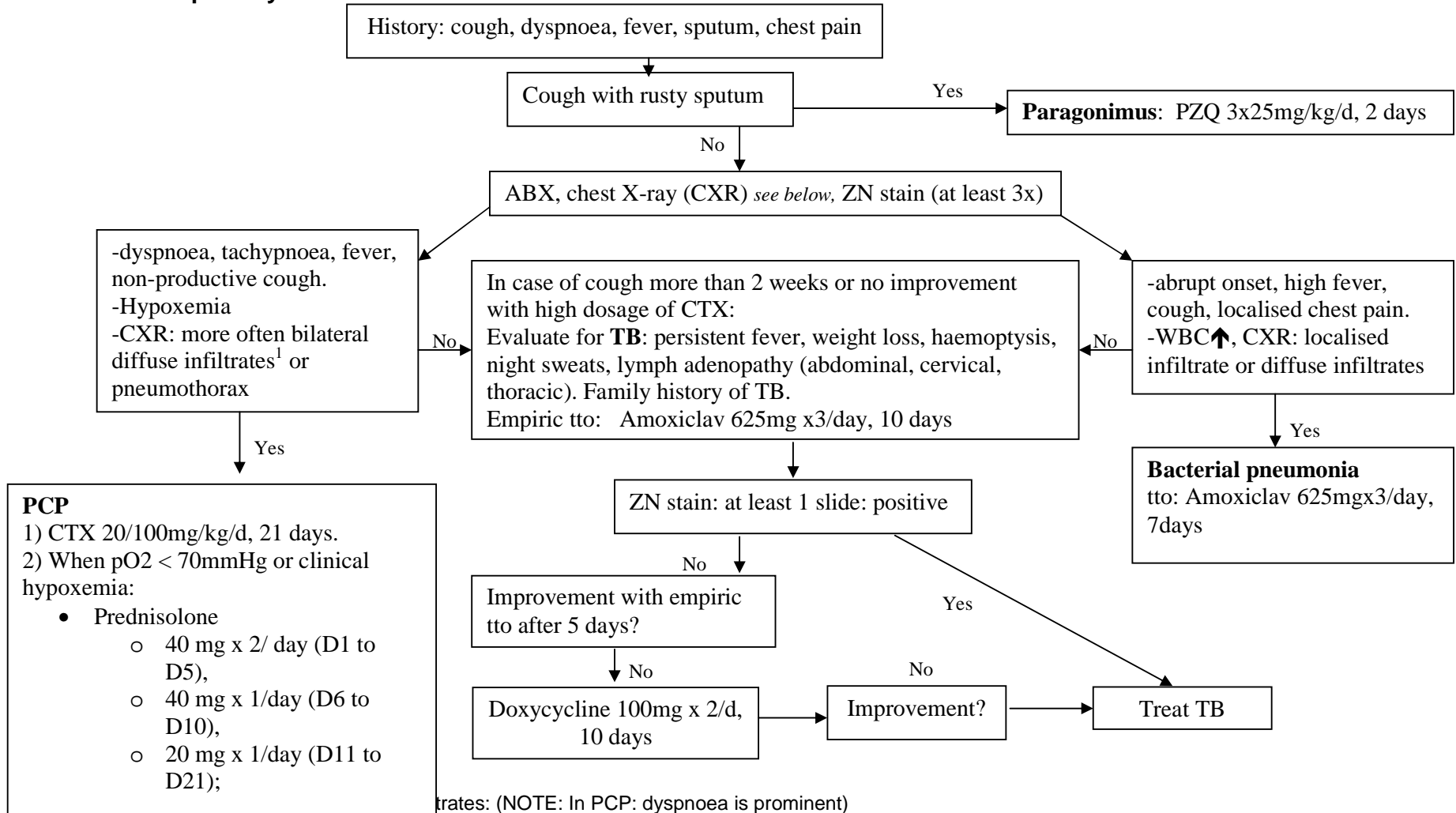
Diagnosis

Chest X-ray may show diffuse interstitial pattern or reticulonodular infiltrates.

Treatment

(See Chapter 3: Cerebral toxoplasmosis)

Flow chart - Respiratory conditions



- H. Influenza is treated by Amoxiclav = (amoxicillin-clavulanate)
- Atypical pneumonia (chlamydia, mycoplasma) treated by: Doxycycline
- TB or Extra pulmonary TB: miliary TB (see TB secftion for treatment)
- Strongyloides: diarrhea, ask for history of larva currens: Ivermectine or albendazole
- Fungal respiratory infections (cryptococcosis, histoplasmosis, penicilliose...): look for skin lesions, meningeal signs : Amphotericin.B.

Lung abscesses (air-fluid level, one or multiple)/ **cavitations**:

Bacterial: Amoxiclav.

TB

Cryptococcosis: Ampho.B

Nocardiosis: TMP/SMX 20/100mg/kg/d, 6 weeks-6 months

Strongyloides

Melioidosis: Amoxiclav = (amoxicillin-clavulanate)

Pleural effusion: thoracocentesis: Protein, cell count, differential count

TB:

Lymphocytic exudative effusion

Most frequent cause of unilateral pleural effusion → if thoracocentesis not possible → treat TB

Pericardial effusion: TB is the most likely treatable cause → treat TB

Eosinophilic pleural effusion:

Paragonimus: haemoptysis

pneumothorax, haemothorax

Neutrophilic exudative effusion:

Post- pneumonic effusion

Amoebic liver abscess

Introduction

Neurological manifestations are directly caused by HIV itself, by OI's or malignancy. Focal signs include seizures, paralysis, motor and sensory disturbances, and visual disturbance. Visual impairment is mostly due to CMV retinitis.

Meningitis can have different causes. Early in the course of the infection, it may be due to HIV itself. In advanced HIV infection, common OIs include cryptococcal meningitis, TB meningitis and bacterial meningitis (meningococcal and pneumococcal).

In South East Asia, fungal infections (cryptococcal meningitis and *Penicillium marneffe*) are more frequent than in other regions.

Conditions caused by HIV**Mononeuropathy and polyneuropathy**

The most common type is a distal, predominantly sensory neuropathy.

It can be caused by HIV itself or by other viral infections like herpes zoster and CMV.

Sometimes it is due to nutritional deficiencies responding to vitamin B.

It should be differentiated from syphilis and isoniazid (INH) toxicity, which can also cause painful neuropathies and myelopathies.

ARVs, especially nucleoside analogues are frequently responsible for peripheral neuropathy (Stavudine [d4T] 23%, DDI 13%).

Treatment

If no obvious cause is found (INH, syphilis) treatment with vitamin B complex and analgesics is given. If the pain is neuropathic and severe, carbamazepine can be effective.

Stop d4T/ddl if suspected to be the cause.

HIV encephalopathy

AIDS dementia complex occurs relatively late in the course of HIV infection, when immunosuppression is more severe. The initial manifestations are loss of memory and abnormal behaviour. Other symptoms include incontinence and gait disturbances with ataxia. When available, AZT may be useful in treating HIV-associated dementia.⁷

Opportunistic infections

- Protozoal infection: *Toxoplasma gondii*
- Fungal infection: *Cryptococcus neoformans*, *Candida* species
- Mycobacterial infection: *M. tuberculosis*, MAC
- Viral infections: Cytomegalovirus, herpes simplex virus, varicella zoster virus, JC virus (the virus causing progressive multifocal leukoencephalopathy -PML)

Cryptococcus neoformans

Cryptococcus neoformans is the most common life-threatening fungal infection. It occurs most often in HIV-positive patients with CD4 counts < 50. It presents as meningitis, with fever and headache and neck stiffness the main symptoms.

Diagnosis

Lumbar puncture: increased opening pressure, sometimes only slightly elevated WBC count (predominantly lymphocytes)

Staining: India Ink and direct microscopic examination: positive in most cases

Cryptococcal Ag on CSF (latex agglutination): this test has a sensitivity of 92% but is expensive.

Treatment

- 1st choice: Amphotericin B (IV) 0,7 mg/kg/day (2 weeks) followed by fluconazole 400 mg once a day for 8 weeks, reduced to 200 mg once a day as a maintenance therapy to be taken life long or until immune recovery on ART.
- 2nd choice: Fluconazole oral throughout (400 mg once a day for 8 weeks, followed by 200 mg once a day)

Primary prophylaxis

Fluconazole 400 mg once weekly

Secondary prophylaxis

Fluconazole 200 mg once daily

Additional notes on the preparation and use of amphotericin B

(Source: Clinical HIV-AIDS Care Guidelines, Savannakhet Provincial Hospital, Setthathirath University Hospital, Lao PDR, August 2007)

1- Take history

- Nausea, vomiting
- Diarrhea
- Anorexia
- Severe muscle cramping
- Weakness
- Chest pain
- Palpitations
- Lethargy, sleepiness
- Decrease urination
- Black stool or easy bruising\bleeding
- Pain at previous IV site.

2- Laboratory (if indicated)

- Routine monitoring: potassium, creatinine, urea, ABX, glucose (day 1,7,14)
- If not available, the most important thing is to observe the patient well. Give enough food and supplements of potassium and magnesium.

3- Premeditation 30-60 minutes before Ampho B infusion:

- Paracetamol 1 GM PO plus promethazine 25 mg PO.
- Hydrocortisone 100 mg IV if severe rigor or chills occurred on previous infusion.

4- Record vital signs (initially and when needed during the infusion) :

- Temperature
- Heart rate
- Respiratory rate
- Blood pressure

5- Hydrate with normal saline 1000 ml (over 2 hours) to avoid nephrotoxicity before ampho B infusion

6- Infuse amphotericin B over 4 to 6 hours.

- Starting dose: Day 1: 0,4 mg\kg in 500 ml of dextrose 5%
- Full dose: day 2 to day 14: 0,7 mg\kg in 500 of dextrose 5 %.
- Adjusted dose: if decline in renal function during therapy, or significant adverse reactions, physician may reduce dose by half.
- The total cumulative dose should remain the same when dose is adjusted.
- If rigor or chills give Hydrocortisone 100 mg.
- Regular lumbar puncture (daily if needed) as long as the patient reports severe headache.

7- Review instructions to the patient.

- Drink 2-3 liters of fluids per day.

- Small frequent meals plus supplementation with oral magnesium, one tablet daily, and potassium chloride 600 mg twice daily (caution with potassium replacement if significant preexisting renal failure).

8- For seizures

- Diazepam 10 to 20 mg IV orrectally, then load with phenitoin. If seizures do not recur, the phenitoin may be interrupted during the maintenance phase.

9- Begin fluconazole after 14 days amphotericin B

- 800 mg per day for 3 days.
- Then, 400 mg/day for 8 weeks.
- Then, 200 mg/day until CD4 are over 100,at least ,6 months under ARVs.

Remark: In case the CRAG (antigen crypto test) result is positive in the blood AND the Indian ink stain (or CRAG) in the CSF result is negative, the patient is considered to be having an extra-pulmonary cryptococcosis (other than meningeal cryptococcosis), and therefore, he will be treated as followed:

- Fluconazole 800 mg per day for 3 days.
- Then, 400 mg/day for 8 weeks.
- Then, 200 mg/day until CD4 > 100 and at least 6 months on ARVs.

Toxoplasmosis encephalitis

Symptoms

Most common signs and symptoms are focal signs (motor and sensory loss), headache and fever. Sizures and come may occur. Meningeal irritation is infrequent.

Diagnosis

CSF findings are non specific or normal.

A CT scan is not necessary to make the diagnosis of toxoplasma brain abscess. *Toxoplasma gondii* is in many countries the most common cause of focal brain disease in HIV patients., Empiricla treatment for Toxoplasmosis shoud be givne to any HIV positive patient presenting with headache, fever and focal neurological signs, and who has normal CSF findings. If the diagnosis of toxoplasmosis is correct the patient should improve within 7 days. Response to empirical therapy is currently being considered as a diagnostic criterion.

Initial Treatment ¹²

1st choice High dose cotrimoxazole (10/50 mg/kg/day) in two divided doses per day for 4 weeks

2nd choice Sulfadiazine and pyrimethamine for 6-8 weeks
 Pyrimethamine 100 mg loading dose, followed by 50 mg/day
 Sulfadiazine 1-2g x 4/day (100 mg/kg/day)
 Folinic Acid 10 mg per day

In case of intracranial hypertension: papilloedema, vomiting: corticosteroids: 4 x 40 mg prednisolone or dexamethasone 4 mg x 4/day.

Anti-epileptic treatment in case of seizures: phenytoin 2-3 x100 mg/day (after a loading dose of 15 mg/kg/day the first day).

Primary treatment should be continued for four (TMP/SMX) to 6 (sulfadiazine, clindamycin) weeks. After this the doses are reduced and patients should remain on this maintenance therapy for life.

Secondary prophylaxis

Cotrimoxazole 960mg/day (2 X 480mg /day or 1 x 960 mg/day)

Tuberculous meningitis

Symptoms

Headache, fever and decreased consciousness.
Neck stiffness and positive Kernig's sign.

Diagnosis

Lumbar puncture: CSF may look cloudy. WBC: 500/mm³; lymphocytes (early in the course: granulocytes)
High protein level (40 mg/dl-100 mg/dl)
Low glucose level (<20 mg/dl)
CSF microscopy positive for AFBs.
Always exclude cryptococcal meningitis by CSF microscopy (Indian ink stain).

Treatment

Follow the National TB program's protocols.
A 7 month continuation phase with daily isoniazid and rifampicin (7HR) is recommended for category 1 patients with the following forms of TB: TB meningitis, miliary TB, spinal TB with neurological signs. In case of severe neurologic signs (cranial nerve lesions, drowsiness, coma) the use of steroids (prednisone 1 mg/kg during 2-4 weeks, then tapered over 4-6 weeks) is recommended.
Patients treated with steroids have more rapid symptomatic relief and less neurological sequelae. Repeated LP if opening pressure is high opening pressure. This may be necessary daily.

Cytomegalovirus (CMV)

50% of CMV disease is retinitis. Other neurological manifestations include myelopathy and encephalitis.
Induction therapy with IV Ganciclovir effectively treats retinitis in 70-90% of patients. The drug is expensive and beyond the reach of most developing countries.

Diagnosis of CMV Retinitis

The diagnosis of CMV retinitis is by ophthalmoscopic examination (fundoscopy) of the retina through a dilated pupil by a skilled clinician. Dilation of the pupil is critical because CMV retinitis can occur anywhere in the retina and without a dilated pupil only a fraction of the retina can be examined.[1]
Diagnosis of CMV retinitis does not require laboratory tests or eye tests.[2]
CMV retinitis is characterized by dense retinal whitening, which can vary in appearance from "cotton wool spots" to "dry and granular." Hemorrhage is frequently present but may be absent. The retinitis tends to follow vessels, with central clearing where the retina has already been destroyed.[1] All patients with CD4 count <50 cells/ml must have retinal screening examination.
CMV retinitis is a sign of disseminated CMV infection which can be fatal without adequate treatment.

Systematic Retinal Screening

CMV retinitis does not cause pain or redness. Typical symptoms are floaters, scotoma and blurred vision but may go unnoticed.[3] Routine ophthalmoscopic examination meets accepted criteria for appropriate screening interventions: the disease is common, treatable, and easy to diagnose at an early stage, and the consequences of untreated CMV retinitis are loss of vision and blindness.[1]

Treatment

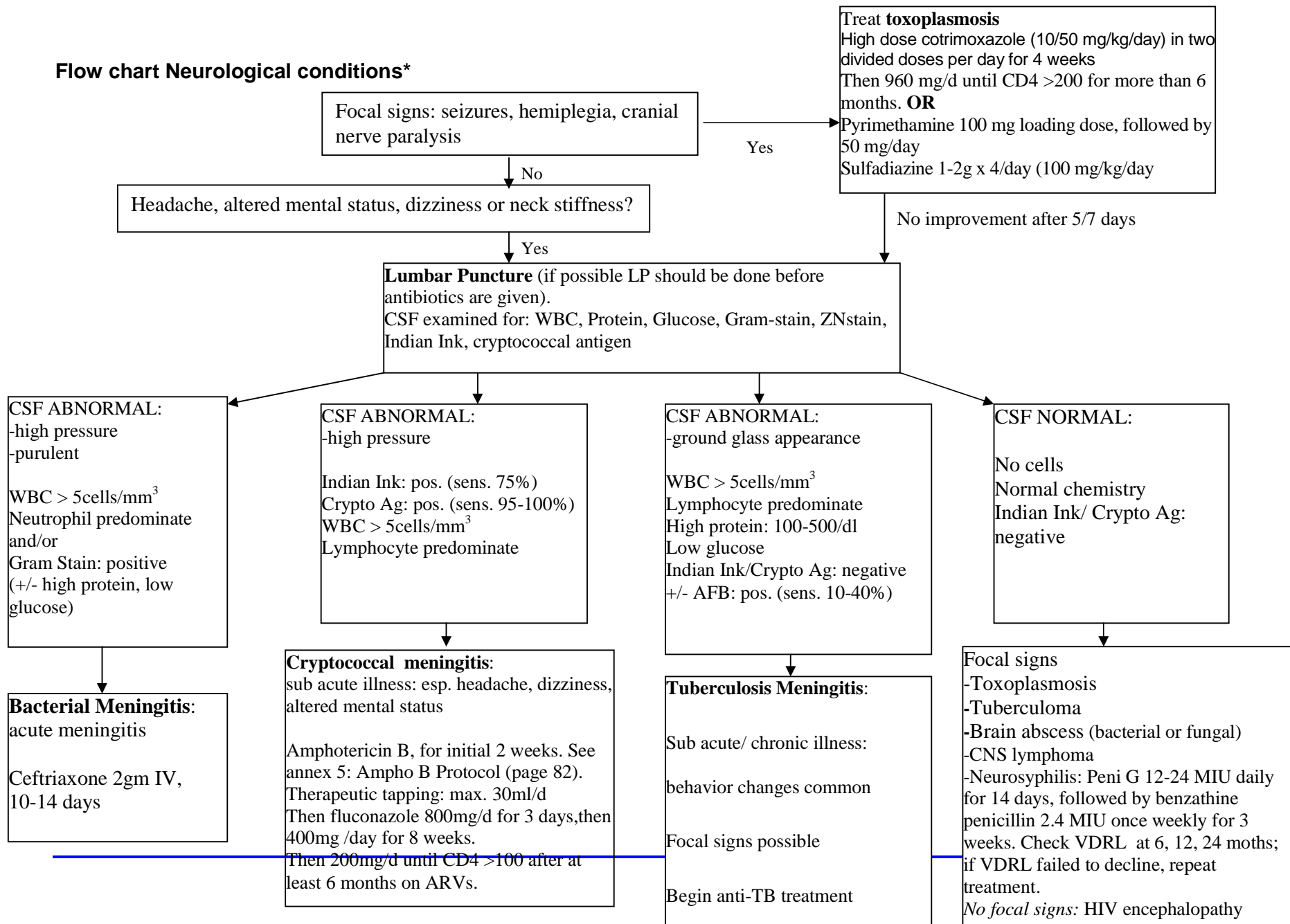
Specific CMV treatment	Antiretroviral therapy
Intraocular ganciclovir Oral valganciclovir 900 mg twice daily for 21 days, then 900 mg as maintenance therapy until CD4 >100	Commence and continue antiretrovirals indefinitely Reactivation of CMV retinitis is unlikely if CD4 count >100 cells/ml

- [1] Heiden D, Ford N, Wilson D, Rodriguez WR, Margolis T, Janssens B, et al. Cytomegalovirus retinitis: the neglected disease of the AIDS pandemic. PLoS medicine. 2007 Dec;4(12):e334.
- [2] Meer Jvd. Summary of the International Consensus Symposium on advances in the Diagnosis, Treatment and Prophylaxis of Cytomegalovirus infection. Antiviral Res. 1996 32:119-40.
- [3] Wei LL, Park SS, Skiest DJ. Prevalence of visual symptoms among patients with newly diagnosed cytomegalovirus retinitis. Retina (Philadelphia, Pa. 2002 Jun;22(3):278-82.

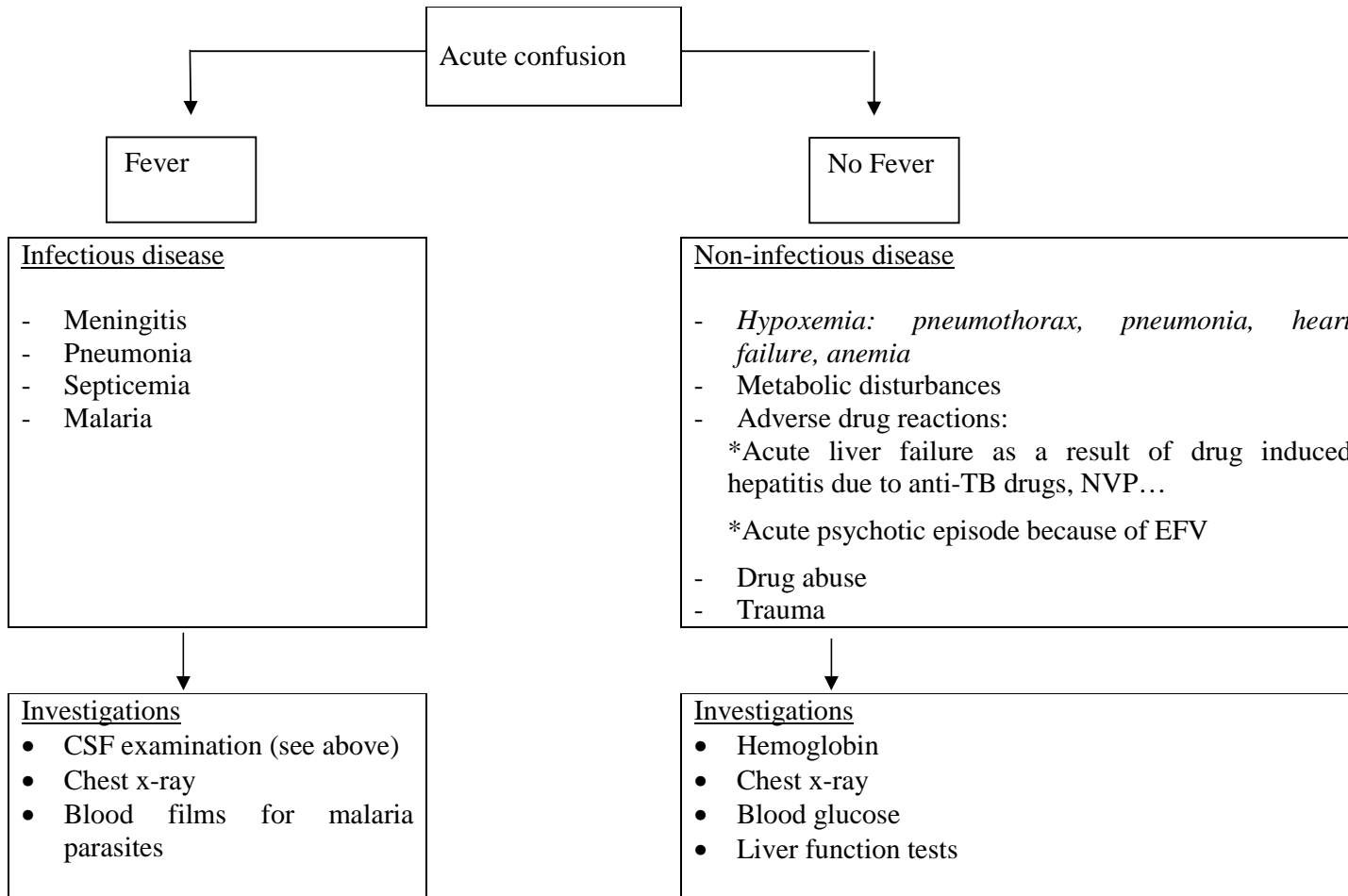
Malignancies

If signs and symptoms of a mass lesion/focal lesion of the brain does not respond to empirical treatment against toxoplasmosis, lymphoma is another possible diagnosis. Kaposi's sarcoma of the brain occurs rarely.

Flow chart Neurological conditions*



Flow chart-Acute Confusion



Notes

(A). Headache in patient with symptomatic HIV infection, often persistent and severe and rapidly increasing or not responding to common drugs used for pain relief. It can be with or without fever.

Infections

- Tuberculosis meningitis
- Cryptococcal meningitis
- Toxoplasma meningo-encephalitis
- Neuro-syphilis
- CMV encephalitis
- HIV meningitis
- PML
- HIV encephalopathy
- Chagas meningo-encephalitis

Malignancy

- Lymphoma; Kaposi's sarcoma

Drugs

- AZT related headache: Almost half of the patients taking AZT have headache. This occurs mainly in the first week of treatment and can be treated with analgesics. In case the headache is severe always, bear in mind that patient may have underlying OI. If headache is not improving with analgesics, the patient may have problems to stay compliant with his treatment and a switch might be considered.

(B). Causes of headache not related to HIV infection: **migraine, toothache, hypertension**, etc. should be identified and treated. Other causes, such as **tension headache**, may be produced by anxiety related to the diagnosis of HIV.

Sinusitis is a frequent HIV-related cause of headache and should be treated as usual. Infectious diseases that can lead to headache, e.g. malaria, trypanosomiasis, typhoid fever, dengue fever, yellow fever, rickettsiosis should be considered.

Notes on TB meningitis

Diagnostic rules developed for diagnosis of TB meningitis are hampered by lack of sensitivity and specificity, therapy is usually started in an empirical way, and therefore simple diagnostic algorithms are useful to standardize clinical practice in a given setting with a high TB prevalence. A group in Vietnam has studied a diagnostic index (DI) system based on age (<36 years old), CSF cell count (>900/ μ l), and duration of illness (<6 days) and % of neutrophils (>75%) to distinguish between bacterial or tuberculosis meningitis in patients who have a CSF: blood glucose ratio of less than 50%.

In their setting (high TB prevalence, low HIV prevalence) they used a score of 4 or less as a diagnostic threshold for TB meningitis see table below. This diagnostic index had a sensitivity of 97% and a specificity of 91%.

	Diagnostic index
Age \geq 36 years	2
Age <36 years	0
Blood WBC \geq 15,000/mm ³	4
Blood WBC < 15,000/mm ³	0
Sick \geq 6 days	-5
Sick < 6 days	0
CSF WBC count \geq 900	3
CSF WBC count < 900	0
CSF % neutrophils \geq 75%	4
CSF % neutrophils < 75%	0
TOTAL SCORE	X

Always exclude cryptococcal meningitis by CSF microscopy (Indian ink stain)

Causes of diarrhoea in patients with HIV infection

An infectious agent can be identified in about 50% of patients with HIV-associated diarrhoea.

Bacterial infection: Campylobacter, Shigella, and Salmonella species
Protozoal infection: Cryptosporidium species, Giardia lamblia, Isospora belli, Entamoeba histolytica, microsporidium species.
Toxin induced: E. Coli and Clostridium difficile
Mycobacterial infection: M. avium complex, Mycobacterium tuberculosis
Helminthic infection: Strongyloides stercoralis
Fungal infection: Candida species (seldom a cause of diarrhoea)
Viral infection: Cytomegalovirus, herpes simplex virus.
Non-infectious disorders: Kaposi's sarcoma, lymphoma,
AIDS enteropathy: direct cytopathic effect of HIV disease

Table 10: Common causes of diarrhoea

Treatment of Bacterial Gastroenteritis

strongyloides stercoralis	Ivermectine 0,2 mg/kg/d, 2 days and to be repeated after 2 weeks
giardia lamblia	Metronidazole 3 x 500mg, 5 days
isospora belli, cyclospora	cotimoxazole 480 mg, 4x2 tab /day, 10 days followed by 2x2 tab/day, 3 weeks (if cotimoxazole intolerance: ciproxine 500mg bid for 7 days (slightly less effective) followed by cotimoxazole prophylaxis)
entamoeba histolytica	Metronidazole 3 x 750mg, 10 d
clostridium difficile	Metronidazole 3 x 500mg, 10 days
quinolone resistant campylobacter	Erythromycine 2 x 500mg/d, 5 days
trichuris trichiura	Albendazol 2 x 400mg, 3 d

Table 11: Treatment of common causes of diarrhoea

Mycobacterium Avium Complex**Clinical presentation**

The most common findings are fever, severe anaemia, weight loss and fatigue. More than 70% of patients have gastrointestinal or hepatobiliary symptoms: diarrhoea, abdominal pain, hepatomegaly, and increased ALT. It occurs mostly when CD4 count is <50

Diagnosis

Typical clinical picture and MTB excluded as much as is possible in a resource limited setting.

Treatment

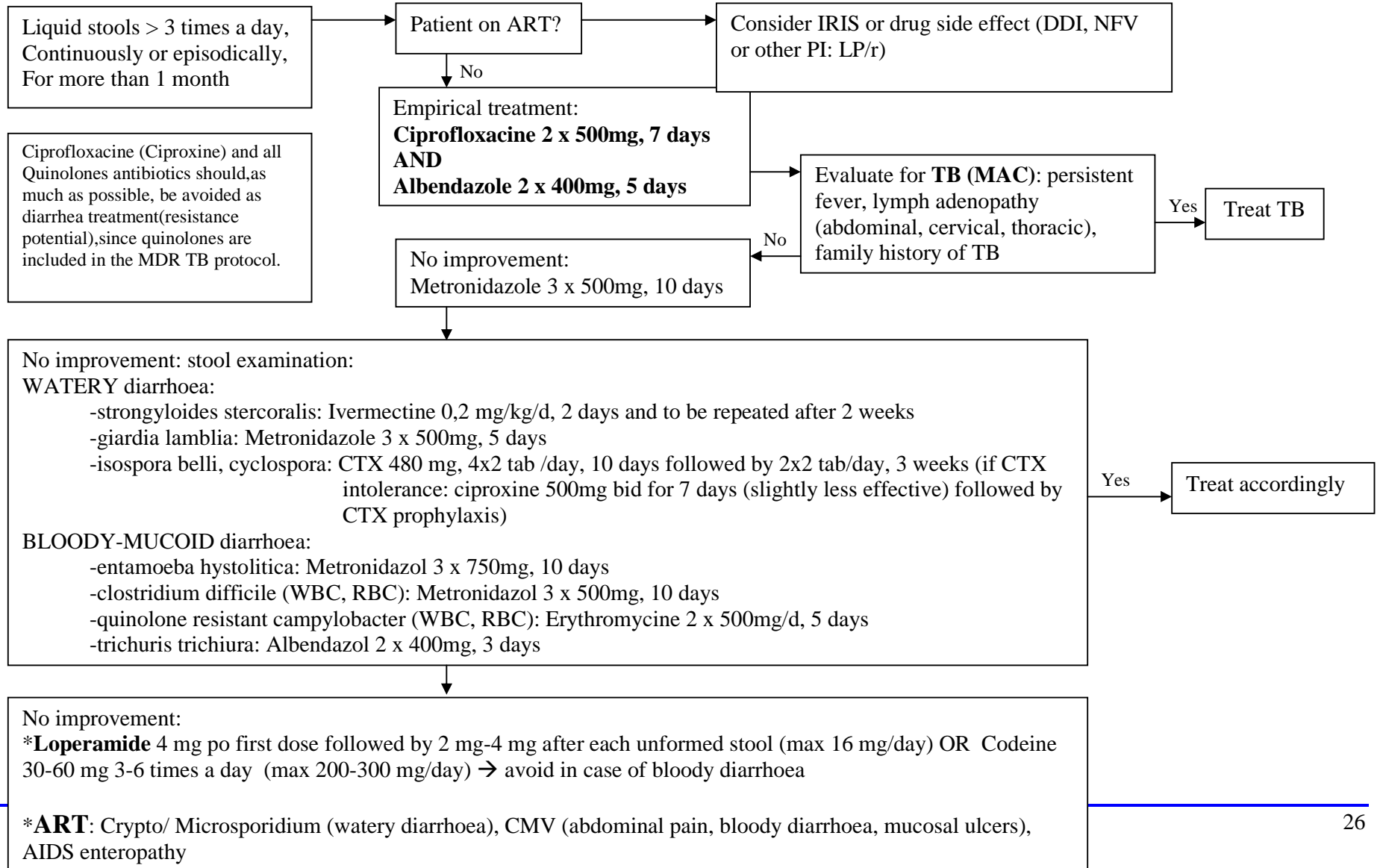
Azithromycin (500-600mg once a day) or clarithromycin (500mg twice a day) plus ethambutol (15mg/kg/day) plus rifampicin (300mg once a day)

ART may resolve the condition

Secondary prophylaxis

Azithromycin 1,250 mg weekly until CD4 >100 for 3-6 months on ART

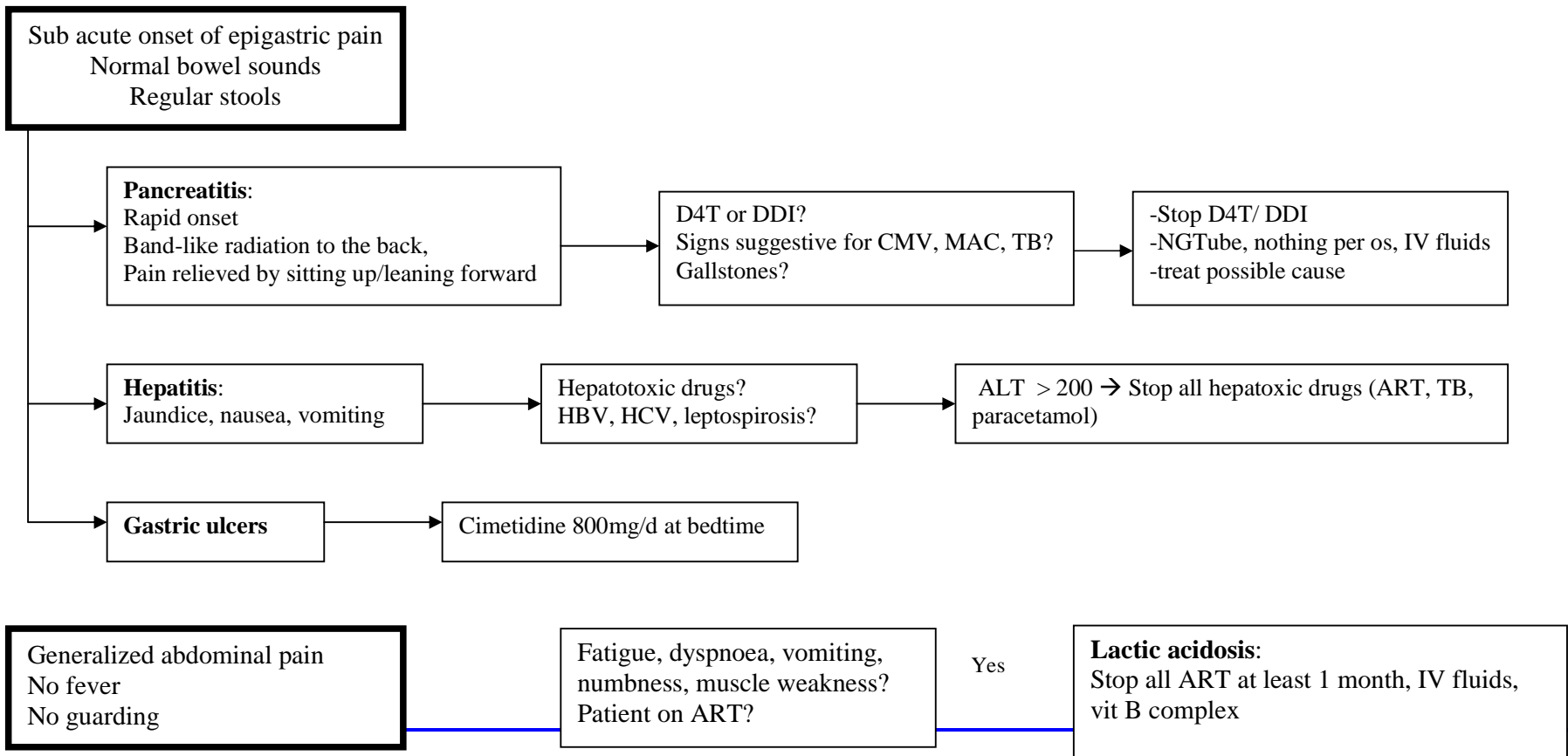
Flow chart -chronic diarrhea



Flow chart-abdominal pain

Most frequent causes of abdominal pain:

- Disseminated TB
 - Bacterial infections: salmonella, shigella, campylobacter, clostridium difficile, staphylococcal
 - Parasites and protozoan infections: micro/ cryptosporidium, isospora belli, strongyloides (see flow chart diarrhea)
 - Malignancies: lymphoma, Kaposi sarcoma
- In patients on ART: drug-induced hepatitis / pancreatitis, IRIS (see flow chart IRIS), lactic acidosis
 → In patients with CD4 < 50/mm³: consider disseminated MAC, CMV



Oral hairy leukoplakia

Presents like non removable white plaques with vertical folds, mostly on the lateral surface of the tongue, and is caused by the Epstein-Barr Virus (EBV). It does not need any treatment. However it is a sign of immune suppression.

Oral candidiasis

White sloughs covering areas of superficial ulceration on the gums, palate and tongue. In severe cases these lesions extend into the lower pharynx and oesophagus to cause dysphagia, nausea and epigastric pain. Oral candidiasis usually occurs in patients with CD4 < 300. Candidiasis may present atypical with erythematous lesions, with atrophic ulcers or as angular cheilitis with localised disease at the corners of the mouth.

Topical antifungals

GENTIAN VIOLET	Local application of Gentian Violet 1% aqueous solution twice daily for 1 week is effective. However the acceptability of this treatment may be low in adults.
MICONAZOLE ORAL GEL	Miconazole oral gel (4 x 60 mg/day)

Systemic therapy

FLUCONAZOLE	200mg per day for 10 days
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Oesophageal candidiasis

Pain or difficulty with swallowing often associated with oral candida. Treatment is with fluconazole 200mg.day for 7 days. Recurrence is common unless immune recovery occurs on ART. Other causes of oesophagitis are HSV, CMV and HIV

Aphthous ulcers

Aphthous ulcers are often self limiting. Topical steroids (Kenalog in Orabase) are useful. Steroids are very effective for deep ulcers of unknown origin (1week prednisolone 40 mg daily).

Necrotizing gingivitis

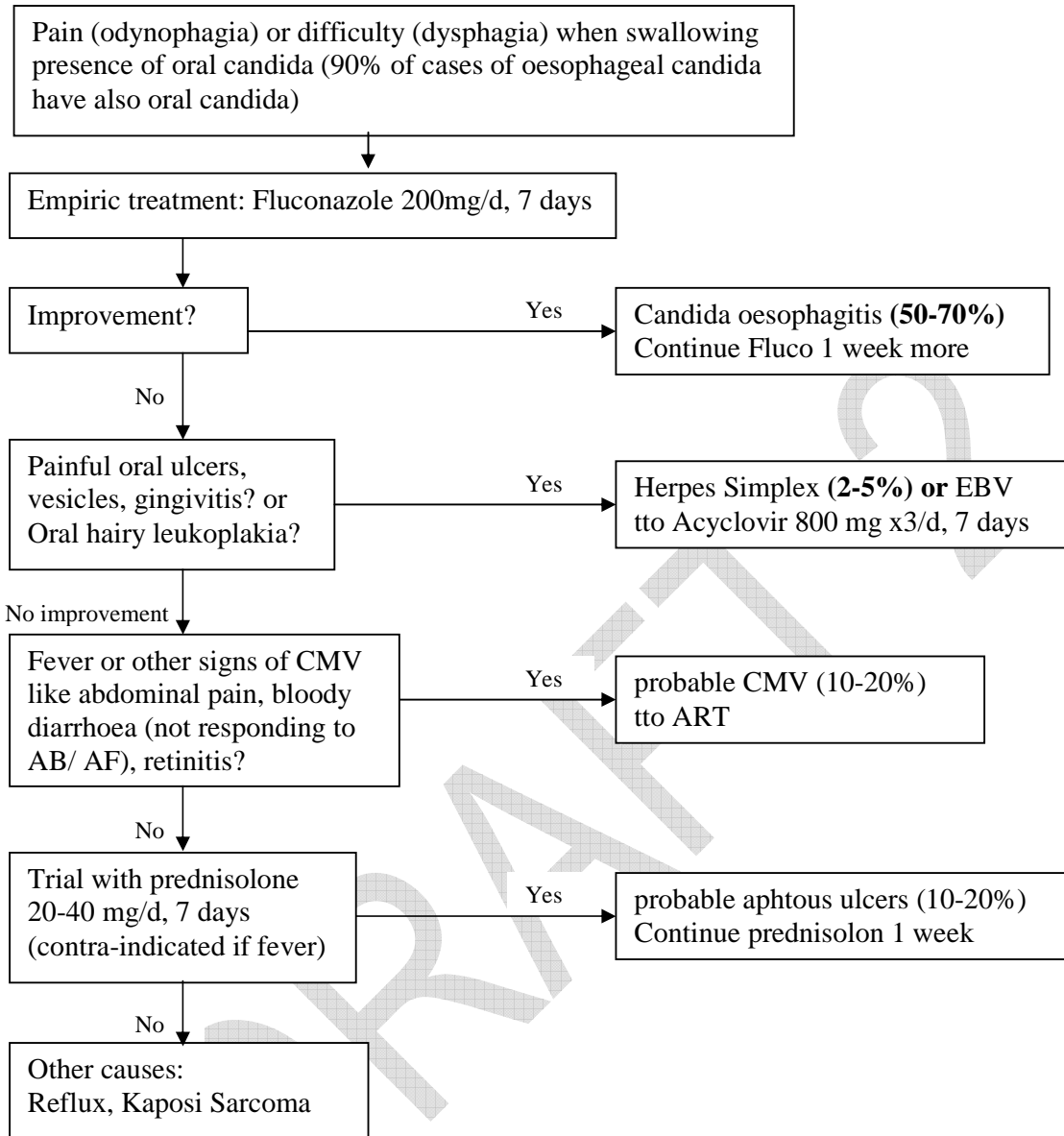
Gum inflammation caused by bacteria of the oral flora and responds frequently to oral hygiene, antiseptic mouth washes and antibiotics, which are effective against anaerobic infections:

- Metronidazole 500 mg, 3 times daily for 7 days. or
- Penicillin V 500 mg, 4 times daily for 7 days.

Herpes simplex stomatitis

Herpes simplex virus 1 and 2 (HSV) are common in HIV positive patients. Treatment consists of topical antiseptics to avoid secondary infection and oral acyclovir (200 mg, 5 times daily, if no response increase the dose to 400 mg, 5 times daily for 1 week)

Flow chart- oesophageal conditions



Pathogens and Treatments**INFECTIOUS**➤ **BACTERIA**

- Folliculitis
- Impetigo
- Ectyoma
- Abscess
- Cellulitis

Pathogen: pyogenous *Streptococcus* (A, C, G), *Staphylococcus aureus*, rarely *Pseudomonas aeruginosa*

CD4 count: any

Diagnosis: clinical

Treatment

- ✓ local antiseptic with gentian violet or polyvidone iodine tid
- ✓ antibiotherapy if ectyoma, abscess, cellulitis: oxacillin (adult: 1 gr tid; children 50mg/kg/day qid) for 7-10 days; surgery (drainage) if abscess

• **Syphilis**

Pathogen: *Treponema pallidum*

CD4 count: any

Lesion: indurated genital ulcer (chancre); maculo-papular rash with palms and soles involvement

Diagnosis: serology (TPHA-VDRL); direct examination of clinical specimen (ulceration scrap) with black-field microscope

Treatment: benzathine penicilline 2.4 millions UI IM 1 dose + treat sexual contacts

• **Bacillary angiomatosis**

Pathogen: *Bartonella henselae*, *Bartonella quintana*

CD4 count: <50/mm³

Lesion: red papules, 1-5cm in diameter, resembling Kaposi sarcoma, which bleed if traumatized; nodules in the subcutaneous tissue

Diagnosis: histopathologic examination of tissue biopsy specimens (vascular proliferative histopathology, with bacilli on modified silver stain).

Treatment: doxycycline 200mg od for 8 weeks if isolated skin involvement (8-16 weeks if disseminated disease).

➤ **MYCOBACTERIA**

Pathogen: *Mycobacterium avium intracellulare*, *M. tuberculosis*

CD4 count: <100/mm³

Lesion: chronic ulcers, nodules, abscess

Diagnosis: skin biopsy= presence of acid-fast bacilli

Treatment: If failure consider MAC treatment *cf* (see Diarrhoea: chapter 4)

➤ **VIRUS**• **Herpes simplex**

Pathogen: herpes simplex virus (HSV)

Lesion: chronic, multiple, confluent ulcerations of skin and mucosa; frequent genito-anal or extremities (oral, face, hands, legs) localizations

CD4 count: any; risk increases if low CD4 count

Diagnosis: clinical= “Any chronic skin ulceration in an HIV-positive patient is HSV unless proven otherwise”

Treatment

- ✓ local antiseptic with gentian violet or polyvidone iodine
 - ✓ acyclovir: po 400mg q8h (adults), 5mg/kg 5 times/day (children) for 7-10 days
- If extensive or oral lesions, consider IV acyclovir 5mg per kg q8h (adults and children) for 7 days.
In case of frequent recurrences, consider long-term suppressive therapy with acyclovir (400mg bid for adults).

- **Herpes zoster (shingles) and chicken-pox (varicella)**

Pathogen: varicella zoster virus (VZV)

Lesion: vesiculous lesions, usually with unilateral metameric topography in herpes zoster

CD4 count: any; higher risk of multimeric and necrotizing lesions with low CD4 count

Diagnosis: clinical

Treatment

- ✓ local antiseptic with gentian violet or polyvidone iodine
- ✓ acyclovir p.o. 800mg 5 times per day (adults), 10mg/kg q8h (children) for 7 days
- ✓ IV acyclovir 10mg/kg q8h (adults) or 1500g/sq.m/day in 3 divided doses (children) for 7 days if disseminated herpes zoster, ophtalmic herpes zoster, diarrhea, malabsorption
- ✓ Acyclovir ophtalmic ointment if ophtalmic herpes zoster

- **HIV primary infection**

Lesion: maculo-papulous rash similar to secondary syphilis, mucous involvement, associated with flu-like illness; occurs about 15 days after contamination and usually resolve after 10 days

CD4 count: any

Diagnosis: clinical

Treatment: symptomatic (antihistaminic)

- **Molluscum contagiosum**

Pathogen: poxvirus

CD4 count: usually <200/mm³

Lesion: small umbilicated papules, in groups of 1 to 10 elements, usually on face or pubis

Diagnosis: clinical; biopsy of the lesion with mycological culture can be useful as the lesions are similar to the lesions seen in histoplasmosis, cryptococcosis and penicilliosis.

Treatment: local (liquid nitrogen therapy or extraction)

- **Warts**

Pathogen: papillomavirus

CD4 count: any but risk increases if low CD4 count

Lesion: chronic keratotic papules, usually on face, hands, feet; genital warts present as papillomatous genital tumours and are associated with dysplasia and genital and rectal cancer.

Diagnosis: clinical

Treatment: podophyllin 20% solution 1-2 times per week, electrocautery or liquid nitrogen

➤ **FUNGI**

- **Cryptococcosis**

Pathogen: *Cryptococcus neoformans* var. *neoformans*

CD4 count: <100/mm³

Lesion: papule, nodule, umbilicated papule, ulceration

Diagnosis: mycological direct examination (capsulated yeast) and culture of skin biopsy or lesion swab

Treatment: if no neurological involvement (CSF negative for *Cryptococcus*), fluconazole 400mg od for 10 weeks, followed by maintenance therapy with fluconazole 200mg od.

- **Penicilliosis**

Pathogen: *Penicillium marneffe*

CD4 level: <100/mm³

Lesion: umbilicated papules, small ulcers, nodules

Diagnosis: mycological direct examination and culture of skin biopsy or lesion swab

Treatment: if no disseminated disease (chest Xray, blood culture, no hepatomegaly) itraconazole 400mg od for 8-10 weeks, followed by maintenance therapy with itraconazole 200mg od. (Same as above)

- **Histoplasmosis**

Pathogen: *Histoplasma capsulatum*, *Histoplasma duboisii*

CD4 count: <100/mm³

Lesion: oral or skin ulcerations, nodules, folliculitis- or cellulitis-like lesions, umbilicated papules

Diagnosis: mycological direct examination and culture of skin biopsy or lesion swab

Treatment: fluconazole 400mg od for 10 weeks, followed by maintenance therapy with fluconazole 200mg od

- **Candidiasis (thrush)**

Pathogen: *Candida albicans*, *Candida glabrata*

CD4 count: any

Lesion

- ✓ oral candidiasis: painless, creamy white, plaque-like lesions of the buccal or oropharyngeal mucosa or tongue surface, which can be easily scraped off; erythematous patches on the anterior or posterior upper palate or diffusely on the tongue; angular cheilitis.
- ✓ vulvovaginitis characterized by a creamy to yellow-white adherent vaginal discharge associated with mucosal burning and itching.

Diagnosis: clinical

Treatment

- ✓ oral candidiasis: local lesion care with nystatin or miconazole 1% cream or oral patch, 7-10 days; if severe, treatment with fluconazole 200mg bid (adults)
- ✓ genital candidiasis: topical miconazole for 3-7 days; topical nystatin 100,000 units daily for 14 days; or oral fluconazole 200mg for 1 dose. Complicated vaginitis (prolonged or refractory episodes) requires antimycotic therapy for >7 days

- **Dermatophytosis**

Pathogen: *Trichophyton sp*

CD4 count: any; more frequent if CD4<100/mm³

Lesion: onychomycosis, intertrigo (feet, groin), scalp and skin with squamous rash

Diagnosis: clinical

Treatment: Miconazole cream bid for 4-8 weeks

- **Parasites**

- **Scabies**

Pathogen: *Sarcoptes scabiei*

CD4 count: any

Lesion: often atypical; pruritic, erythematous-squamous or papulo-squamous hyperkeratotic lesions of knees, elbows, chest

Diagnosis: clinical; parasitological analysis of skin scraping if available

Treatment

- ✓ adults: 25% benzylbenzoate solution. Apply the lotion on the whole body, except the head. The application is left on the skin to dry and then repeated the next day. Treatment should be repeated weekly until all lesions clear. In severe cases, ivermectin 200mcg/kg as a SINGLE oral dose.
- ✓ older children: 0.3% gamma benzene hexachloride applied from neck down to toe for 12 hours followed by bath.
- ✓ neonate or infant : topical 5-10% sulfur cream applied overnight for at least 5 days.

Household contacts should be treated. Antihistamines to relieve severe itching may be required. Bedding and clothing should be decontaminated. .

- **Demodicidosis**

Pathogen: *Demodex follicularum*

CD4 count: any

Lesion: peri-ocular pruritic and papules

Diagnosis: clinical; skin scraping if available

Treatment: local application of permethrin

NON-INFECTIOUS

- **Cancer**

- **Kaposi sarcoma**

Lesion: flat or papular painless skin or mucous (palate, inner side of cheeks) lesions of reddish, blue or purple color (brown or black patches on dark-skinned people).

Kaposi sarcoma is a vascular proliferation induced by Human-herpes Virus 8 (HHV8), usually occurring with CD4 count <200/mm³.

Kaposi can be disseminated with pulmonary and extensive gastro-intestinal involvement.

Diagnosis: clinical or skin-biopsy

Treatment: start ARV treatment.

- **Epidermoid carcinoma**

Higher risk of oral, anal and uterine cervix epidermoid carcinoma in HIV-infected patients.

➤ **Seborrheic dermatitis**

Lesion: chronic erythematous-squamous lesions of face (nose, eyebrows) and scalp, more frequent if low CD4 count.

Diagnosis: clinical

Treatment: Miconazole cream or ketoconazole shampoo OD

➤ **Pruritic Papular Eruption**

CD4 count: any; more frequent if low CD4 count

Lesion: pruritic with diffuse, symmetrical papulo-vesicular lesions followed by cutaneous erosion, and associated with pruritic lesions

Diagnosis: clinical

Treatment: topical steroids, anti-histaminic and skin moisturizing can help relieve symptoms. The best treatment is the control of HIV-infection and immune recovery on ARV treatment.

➤ **Aphthous stomatitis**

Lesion: painful oral ulcers

Diagnosis: clinical, usually after failure of empirical herpes treatment

Treatment: local steroids; ARV treatment

➤ **Oral Hairy Leukoplakia**

Lesion: white, corrugated (rough), non painful lesion that normally appears on the lateral borders of the tongue and will not "wipe away". OHL is related to the Epstein-Barr virus.

Treatment: usually not necessary. Improves under ARV treatment.

➤ **Toxicoderma**

Lesion: drug-related maculopapular rash, associated with pruritic, sometimes fever and mucous involvement if severe.

Drugs involved: cotrimoxazole, isoniazide, rifampicin, penicillins... On first exposition to the drug, the rash will usually appear after day 8 of treatment.

Treatment: Discontinue drug. Local care with moisturizing cream. Symptomatic treatment with anti-histaminic.

DEFINITIONS

Abcess

Localized accumulation of polymorphonuclear leukocytes (pus) with tissue necrosis involving the dermis and subcutaneous tissue.

Cellulitis

Deep subcutaneous infection of the skin typically by bacteria that results in a localized area of erythema and inflammation.

Chelosis

Cracking or fissuring at the corner of the mouth.

Ecthyma

Ulcerative lesion of the skin that usually arises on the lower extremities and is caused by group A beta-hemolytic streptococci (in the tropics) and *S. aureus* (in urban settings and temperate climates). Because ecthyma extends into the dermis, it is often referred to as a deeper form of impetigo.

Erythema

Blanchable redness of the skin that can be localized or generalized and is caused by dilation of superficial blood vessels and capillaries near the skin's surface.

Folliculitis

Pustules and/or papules centered upon hair follicles.

Impetigo

Flaccid pustules, which rupture to form a thick honey-colored to brown crust.

Intertrigo

superficial skin disorder involving any area of the body where opposing skin surfaces may touch and rub, such as the creases of the neck, the skin folds of the groin, armpit, breast and between the toes. It presents as skin reddening (erythema), maceration (softening and deterioration), burning, and itching. There may also be erosions, fissures (cracks) and exudation (oozing) and secondary infections.

Macule

A circumscribed flat area (< 1 cm) of discoloration without elevation or depression of surface relative to surrounding skin.

Nodule

A palpable, solid lesion, less than 1 cm in diameter. These are usually found in the dermal or subcutaneous tissue, and the lesion may be above, level with, or below the skin surface. A nodule extends deeper than a papule.

Papilloma (papillomatous lesion)

benign epithelial tumor projecting from the surrounding surface

Papule

A well-circumscribed, elevated, solid lesion, less than 1 cm. Usually dome shaped.

Pustule

A small inflamed skin swelling that is filled with pus, similar to a blister or pimple.

Onychomycosis

Chronic fungal infection of the nails causing chronically thickened, splitting, rough, discolored nails.

Squamous lesion

Lesion covered with or formed of scales

Ulcer

Lesion with greater than 50% surface area ulceration.

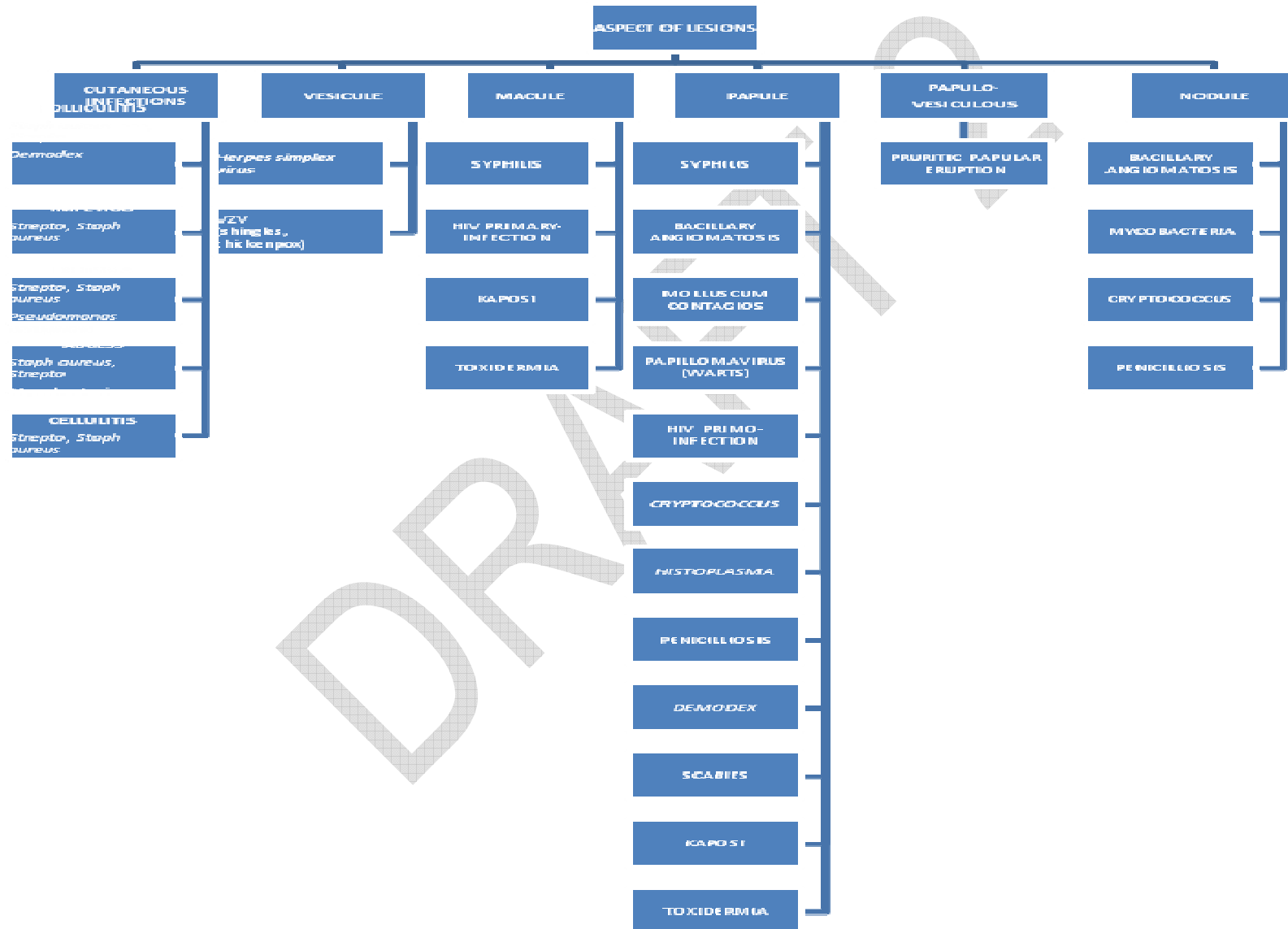
Ulceration

Localized defect in the skin of irregular size and shape where epidermis and some dermis have been lost. Leaves a concavity in the skin.

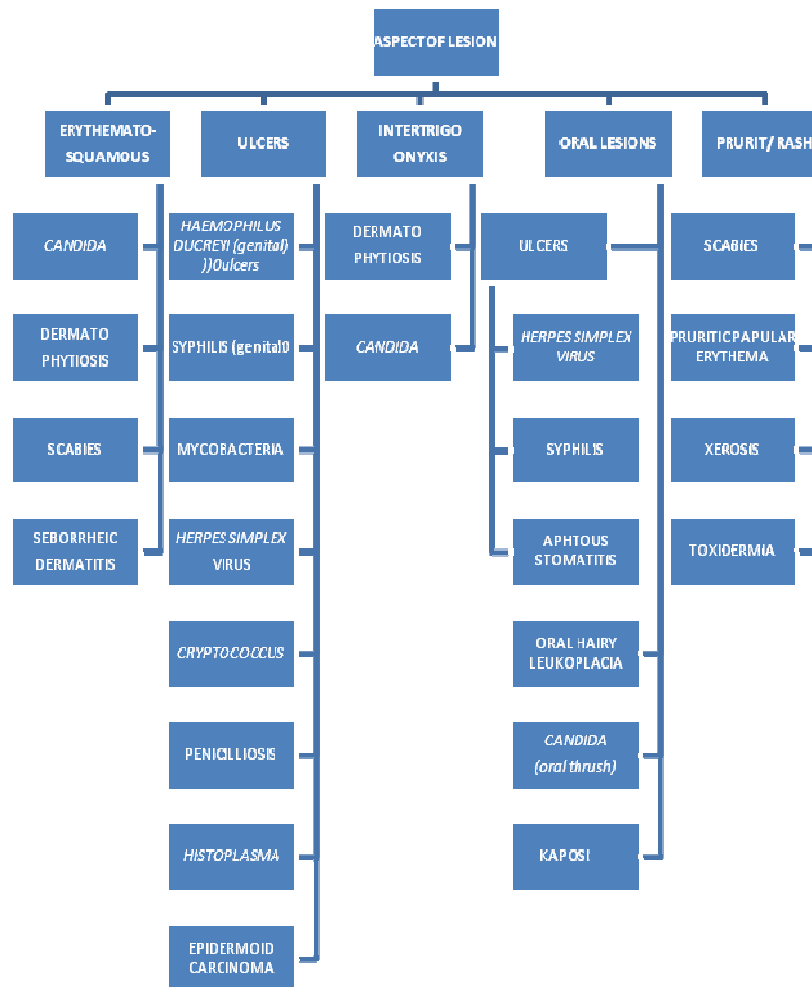
Vesicle

A small, superficial, circumscribed elevation of the skin, less than 1 cm, which contains serous fluid.

Flow charts - Skin conditions
DIAGNOSIS (I)

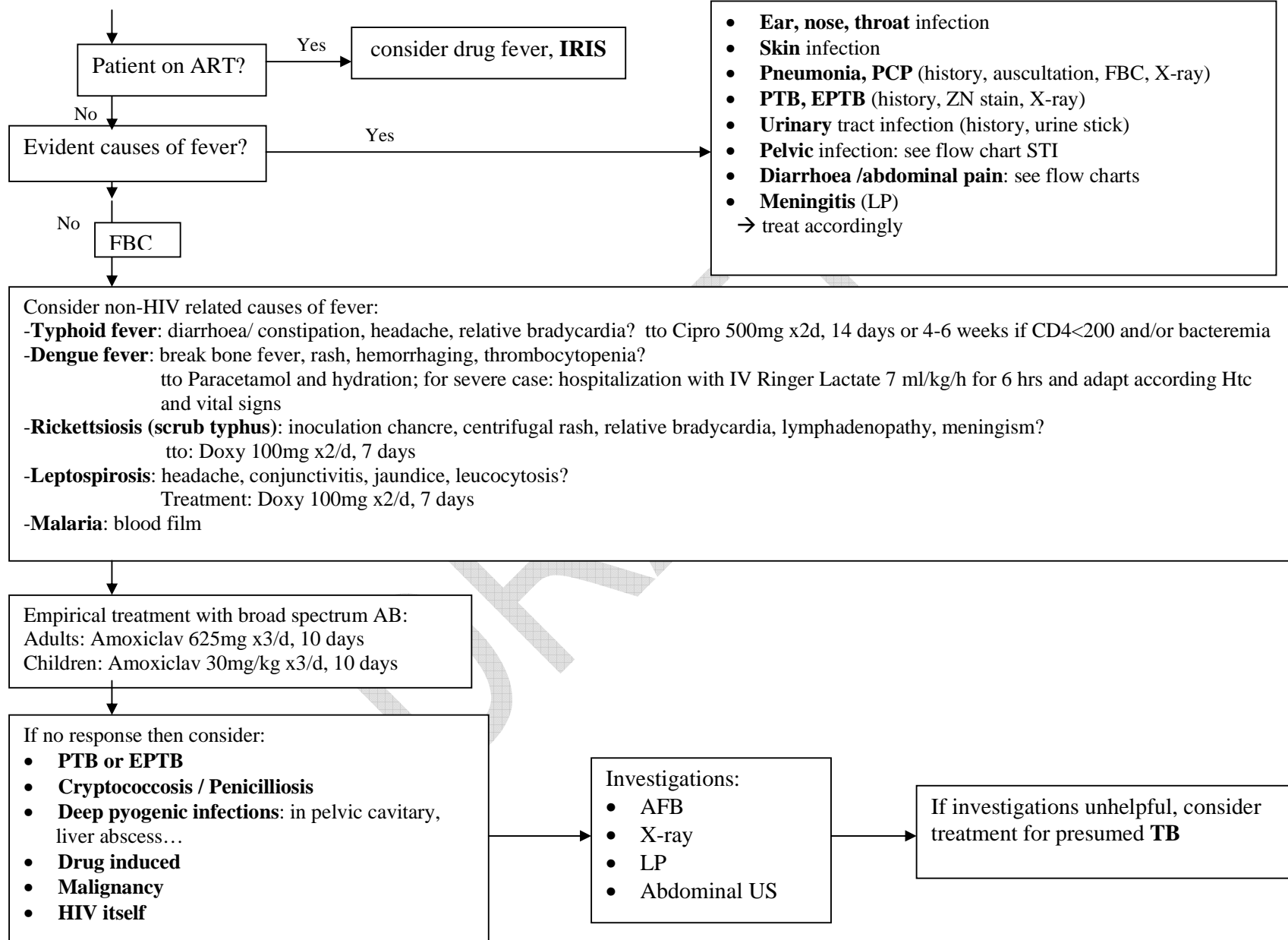


DIAGNOSIS (II)

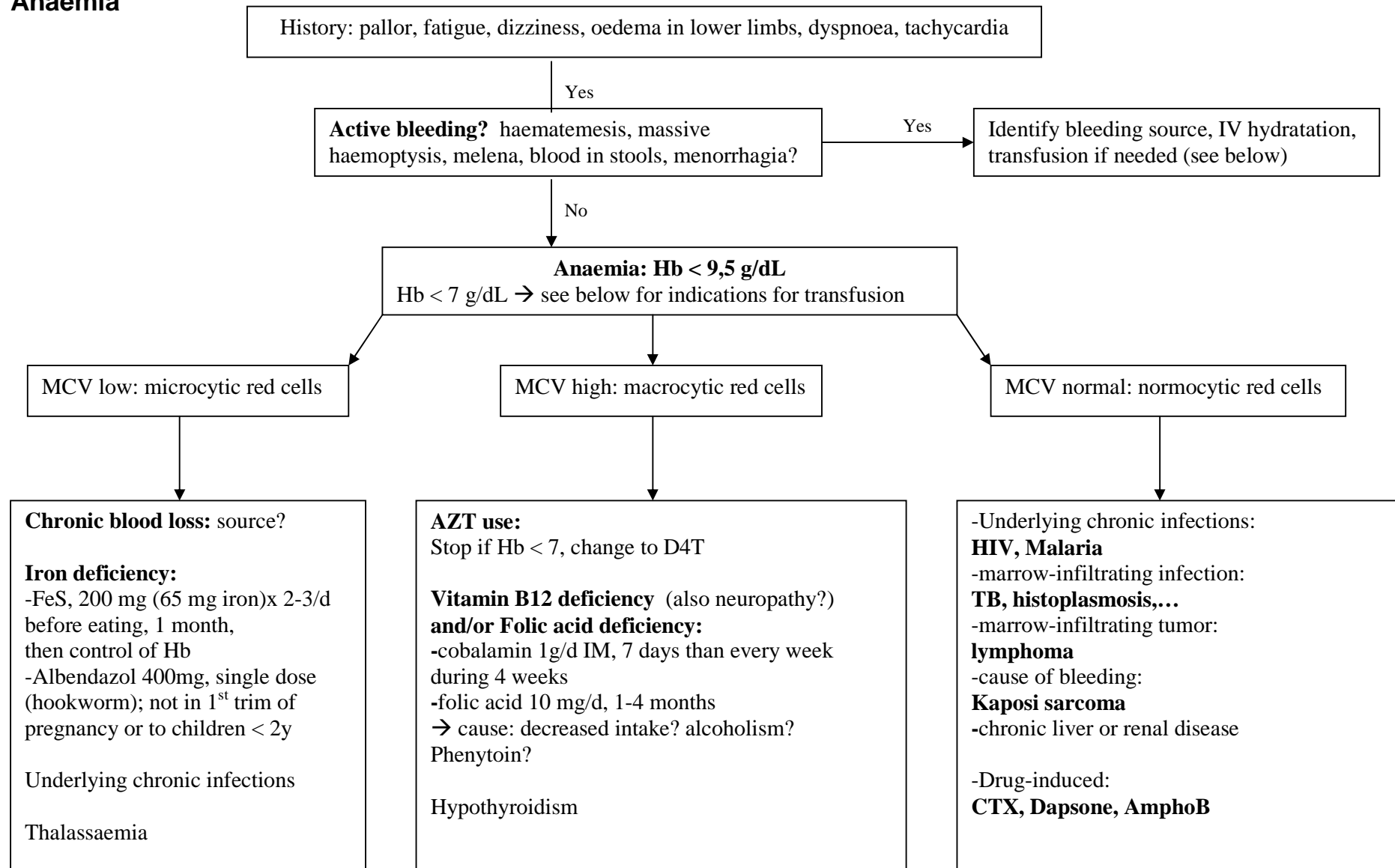


Flow chart-Fever

THINK ALWAYS TB



Flow chart Anaemia



Immediately life threatening anemia: indications for transfusion

Signs of severe anemia: sweating, thirst, cold extremities, tachycardia, and dyspnoea, shock

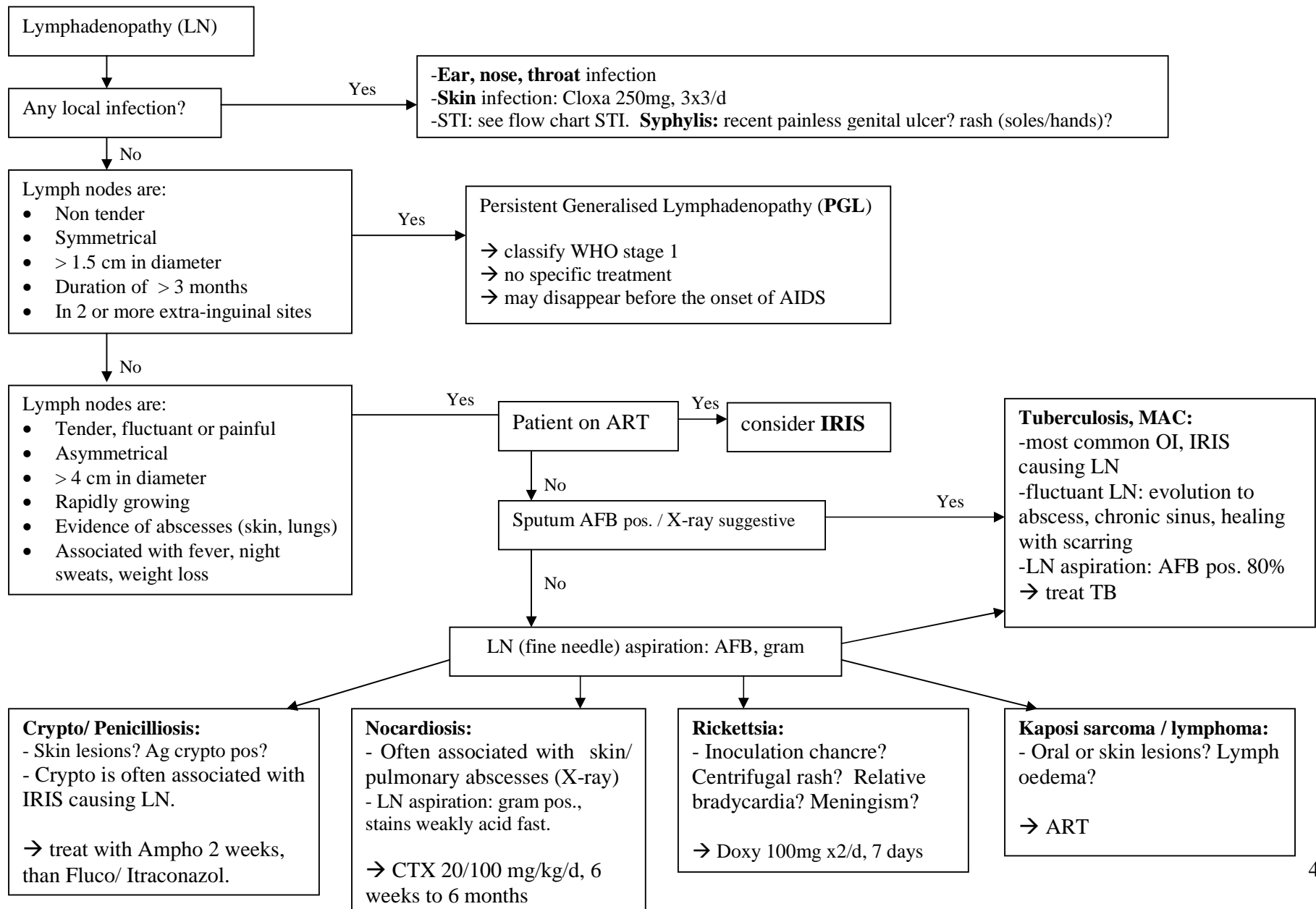
1. Oxygen therapy
2. ***Ensure that the blood of the donor has been tested negative for HIV, HBV, HBC, and syphilis.***
3. Calculate the volume of whole blood to be transfused

Adult

Volume = Desired Hb – Patient HB x 6 x Patient weight	i.e.: Desired Hb = 7 g/dl Patient Hb = 4 g/dl Patient weight = 50 kg Volume = (7-4) x 6 x 50 = 900 ml
Debit of transfusion: (1 ml whole blood = 15 drops)	i.e.: 900 ml to be transfused in 3 hours 900 (ml) / 180 (minutes) = 5 ml/min 5 (ml) x 15 (drops) = 75 drops / minute

<p>1. Not pregnant</p> <p>2. Pregnant: > 36 weeks</p> <p> < 36 weeks</p>	<p>Hb < 7g/dl AND respiratory distress → 500ml whole blood over 3-4 hours. Hb < 7g/dl AND asymptomatic → no transfusion.</p> <p>Hb < 7g/dl, even if asymptomatic → transfusion.</p> <p>Hb < 7g/dl AND respiratory distress → 500ml whole blood over 4-6 hours, 1mg/kg furosemide IV halfway the transfusion to reduce risk of fluid overload.</p>
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Flow chart - Lymphadenopathy



Significance of low BMI	BMI < 18 significant independent predictor of mortality in Africa. BMI < 16 increases the risk of disease progression by fivefold.
Causes of malnutrition: Reduced food intake (food insecurity, nausea, anorexia, dysphagia, depression) Intestinal malabsorption Metabolism deregulation, cytokines-mediated	Reduced calorie intake and frequency of diarrhea associated with wasting.
HIV-related:	OI: chronic diarrhea, TB, Paragonimus... HIV Malignancy (lymphoma...)
Non- HIV-related:	Tropical endemic non-opportunistic intestinal parasite infections: <i>Opisthorchis</i> : Prevalence: study in 2004 in Lao PDR among pts with chronic diarrhea: 29,8% / study in 2003 among schoolchildren: 10,9% <i>Schistosoma mekongi</i> : Prevalence: 2 studies among schoolchildren in 1998 and 2003 in Lao PDR: 1,5% and 1,7% Diabetes Thyrotoxicosis → Rule out / treat
Treatment HIV-related:	Treat OI : treat chronic diarrhea according to flow chart, TB treatment and paragonimus tto if suspicion Albendazole 400mg, 2x1/d, 5days: (hookworms, ascaris, giardia, strongyloides, microsporidium, trichuris) → Systematic to every patient PZQ 600mg, 3x25mg/d, 1 day: → BMI < 17: empiric PZQ ARV
Nutritional intervention	Multivitamins Peanuts contain high quantity of glutamine Supplementary or therapeutic feeding (if available)

Management of opportunistic infections in children

For HIV-infected children, comprehensive care involves support for the child and family with appropriate measures to prevent, diagnose and treat opportunistic infections and the use of antiretroviral therapy.

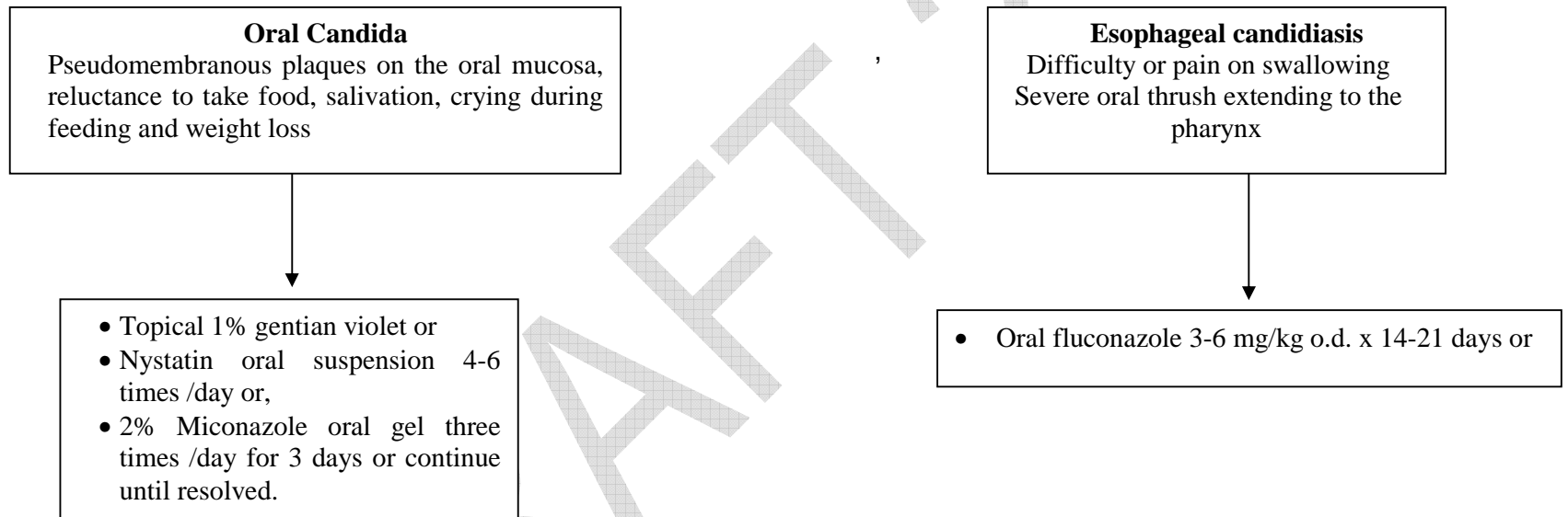
Prophylaxis for opportunistic infections

- All children born to HIV-infected mothers should receive primary PCP prophylaxis irrespective of clinical evidence of HIV disease, starting at 4-6 weeks of age.(annex 5)
- All children with confirmed HIV infection should receive primary cotrimoxazole prophylaxis.
- Give cotrimoxazole 6 mg/kg/day (of the TMP component) as single once every day.
- Give dapsone 2 mg/kg/day as a single dose (max. 100 mg/day) for children who cannot tolerate cotrimoxazole. Dapsone can induce haemolytic anaemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. G6PD deficiency is common in Myanmar (approximately 12% of the population). Dapsone should be given with caution to people with G6PD deficiency.
- Secondary prophylaxis is the same as primary prophylaxis
- Prophylaxis for PCP can be stopped if the child is confirmed HIV negative or if CD4 levels are above age adjusted levels for three months on ART.

Diagnosis and treatment of opportunistic infections

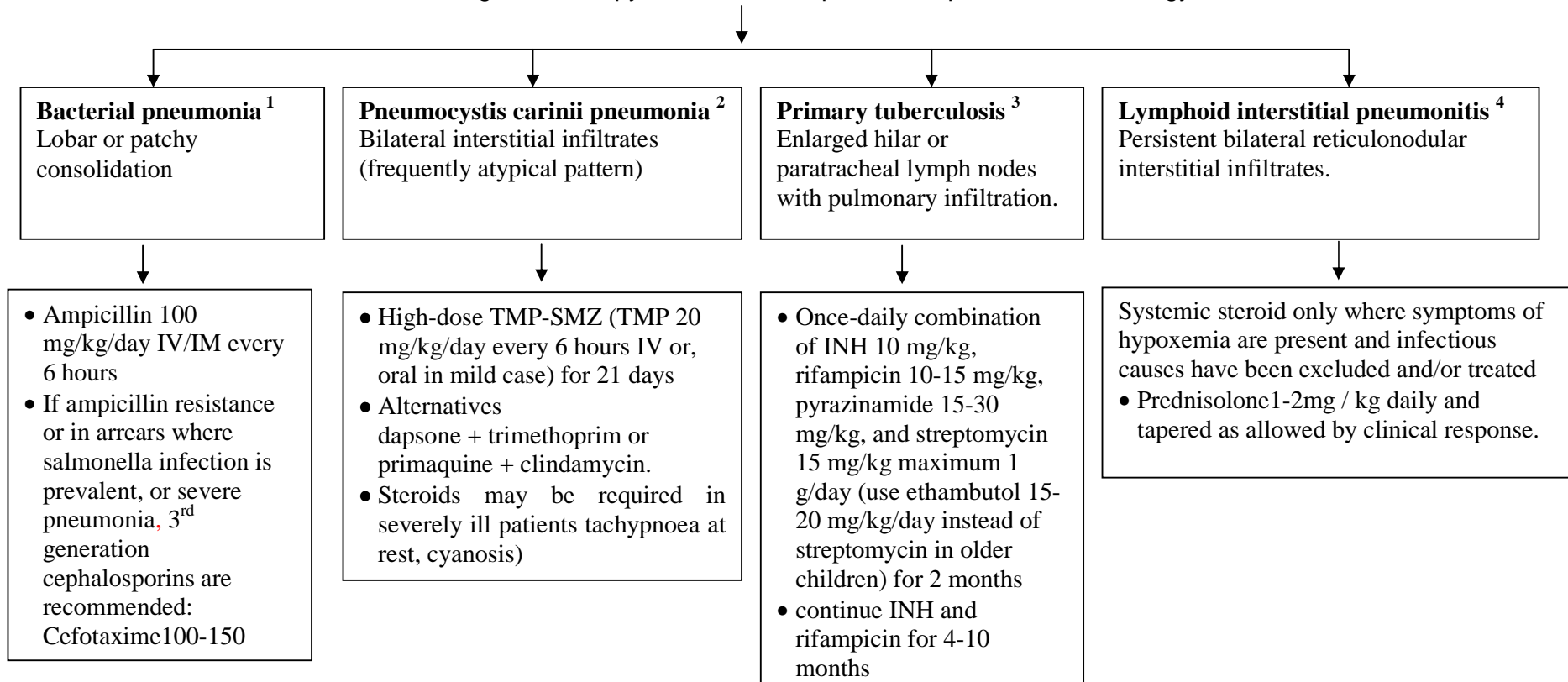
- oral thrush
- respiratory infections
- chronic diarrhoea
- persistent or recurrent fever
- neurological abnormalities
- failure to thrive
- HIV-associated skin diseases in children

Oral and Oesophageal Conditions



Respiratory conditions

Diagnosis is made on the basis of clinical presentation, CXR, other investigations
e.g., microscopy and culture of sputum and pleural fluid, histology



NOTES ON RESPIRATORY CONDITIONS

Several pathogens can be present at the same time.

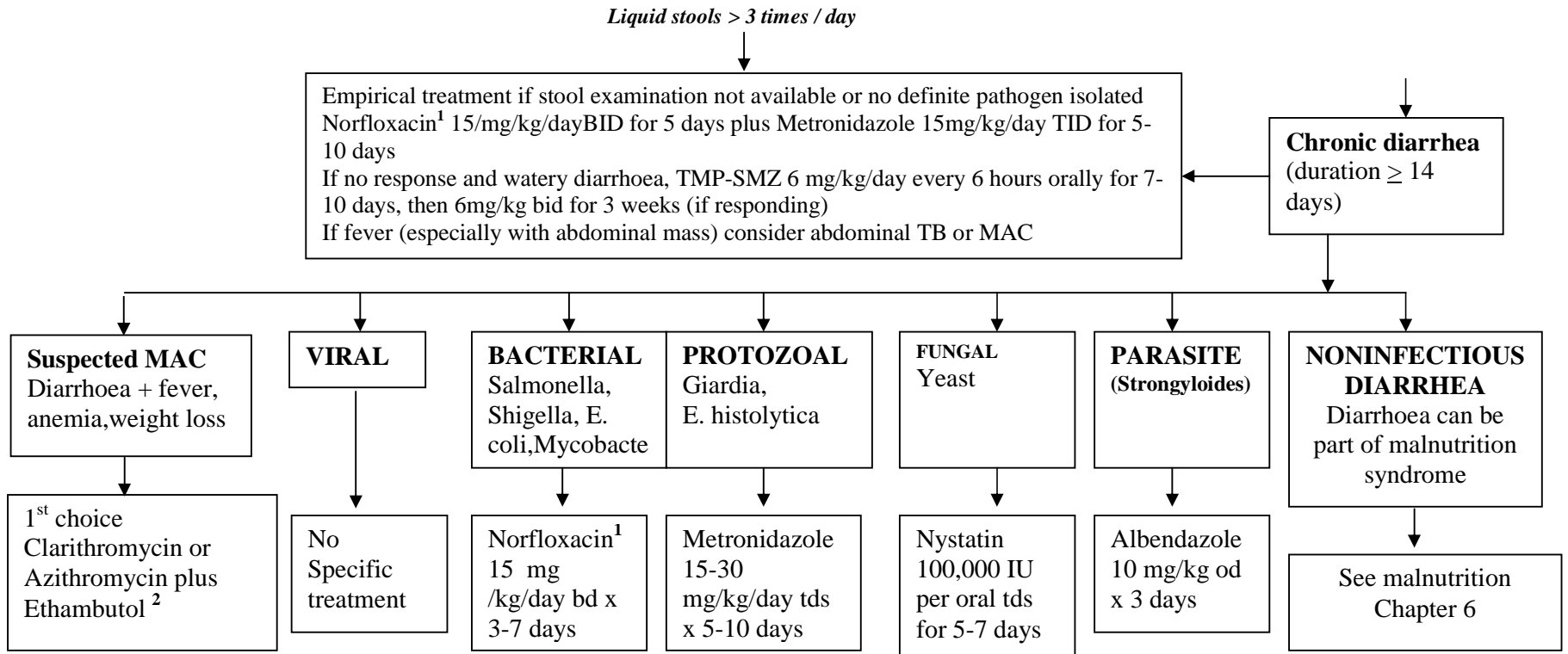
CXR is often is non-specific and interpretation can be difficult. Clinical assessment is also required.

	1. Bacterial pneumonia	2. Pneumocystis carinii pneumonia	3. Primary tuberculosis	4. Lymphoid interstitial pneumonitis
Chest Ray	Lobar or patchy consolidation	Bilateral interstitial infiltrates (frequently atypical pattern)	Enlarged hilar or paratracheal lymph nodes with pulmonary infiltration.	Persistent bilateral reticulonodular interstitial infiltrates.
Clinical signs	Acute onset, productive cough, abnormal chest auscultation, toxic signs	Acute or sub acute onset of symptoms, prominent dyspnoea and tachypnoea, wheezes and rhonchi, progressive fever, dry cough, usually normal chest auscultation Organism- Silver stain from BAL, biopsy, gastric fluid aspirate	Gradual onset, prominent wasting and fever, usually normal chest auscultation, family contact with TB may be present.	Gradual chronic progressive onset, afebrile, cough, wheezing, dyspnoea, signs of chronic respiratory insufficiency. Auscultatory findings are rare in early stage, lymphadenopathy, clubbing, Consider in children with no response to antibiotics <u>and</u> to empirical anti-TB therapy

Note on LIP

LIP is a chronic lung disorder of unknown cause that affects up to 40% to 50% of perinatally acquired HIV-infected children. Chest X-ray shows a bilateral diffuse, interstitial, reticulonodular infiltrates. Clinically, there is a wide spectrum of severity, from asymptomatic to and oxygen dependency. LIP may also remit spontaneously. A presumptive diagnosis may be made on the basis of suggestive x-ray changes that persist for months, are unresponsive to antimicrobial therapy, and are not the result of other specific infectious pathogens. PCP can co-exist with LIP.

Chronic Diarrhoea



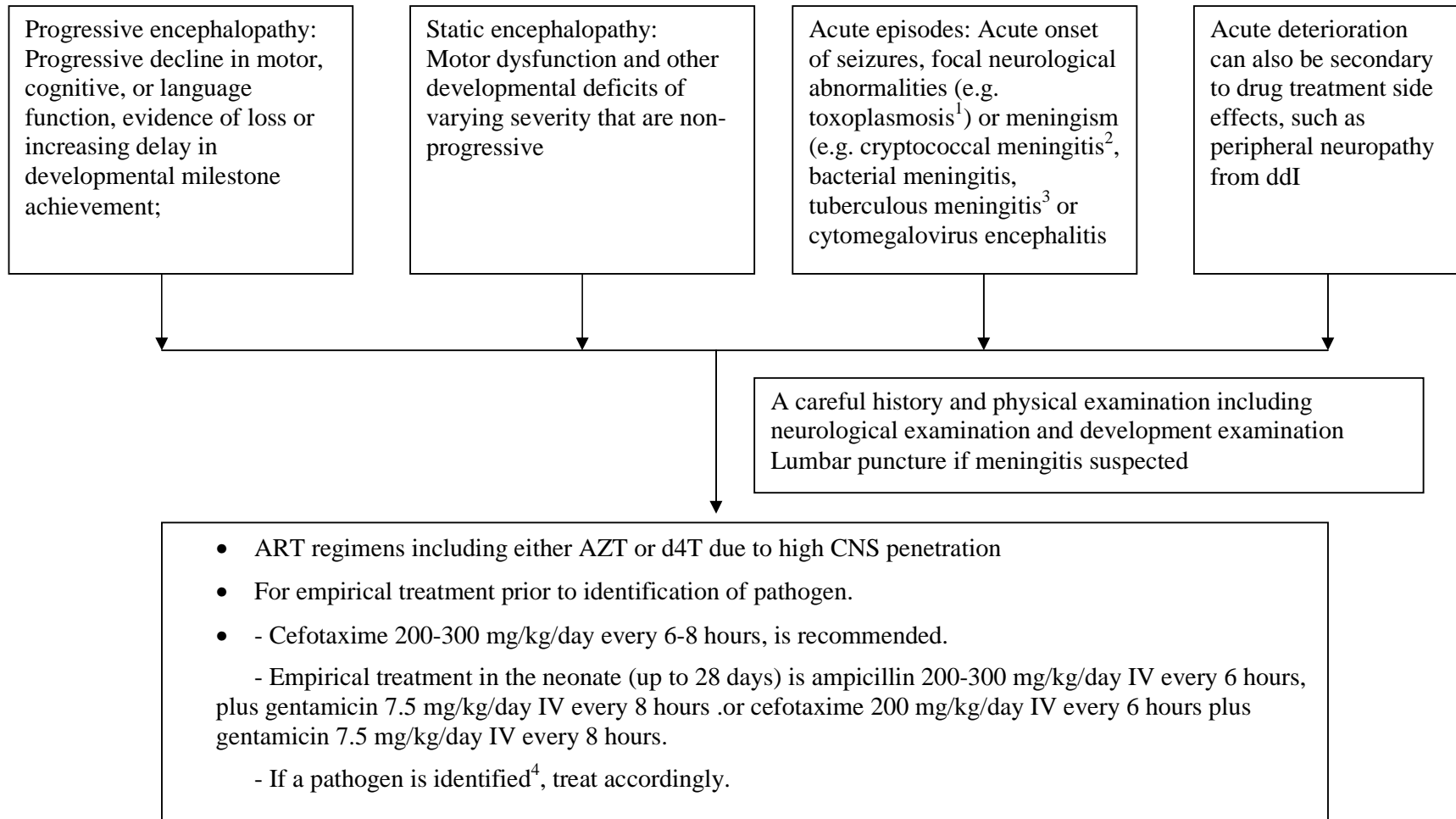
1. The safety of norfloxacin in prepubertal children has not been established.

Arthropathy has been reported in immature animals.

2. Doses of MAC drugs in children

Clarithromycin	15 mg/kg/day PO BD (max 500 mg/day)
Azithromycin	20 mg/kg/day PO weekly (max 1.25 gm/day)
Ethambutol	15-20 mg/kg/day PO OD (max 1.5 gm/day)
Rifabutin	5-10 mg/kg/day PO OD (max 300 mg/day)
Ciprofloxacin	20-30 mg/kg/day PO/IV OD/BD (max 1.5 gm/day)

Neurological abnormalities



Annotations

1. Toxoplasma encephalitis

- Fever, focal neurological deficit (2 ring enhancing lesions on MRI)
- Positive anti-Toxoplasmosis gondii IgG

Focal neurological signs: start presumptive treatment for toxoplasmosis (improvement should be seen within 7-10 days if diagnosis is correct). Toxoplasmosis treatment: Pyramethamine loading dose 2mg/Kg/day BID for two days, then 1mg/kg once daily for 6 weeks plus Sulphadiazine 120mg/kg/day QID for 6 weeks plus folinic acid 5mg (if available) every 2-3 days.

If signs of raised intracranial pressure are present: add prednisolone 2 mg/kg qid; after 5 days (or when signs of improvement), taper dose with 0.5 mg/kg every 5 days.

2. Cryptococcal Meningitis

- Fever, headache, meningism, usually sub acute
- Vesicular or popular skin lesions may be present
- Pneumonitis may be present
- Positive CSF, stain (positive serum cryptococcal Ag)

For patients without neurological signs, lumbar puncture should be performed.

Cryptococcal meningitis treatment: Amphotericin B 0.5-1mg/kg/day IVI once daily over 4-6 hours for 2 weeks, followed by fluconazole 12mg/kg/day every 12-24 hours for 8 weeks.

3. Treatment of tuberculous meningitis (Follow National tuberculosis treatment guidelines)

4. CMV encephalitis

- Rapidly progressing delirium, cranial nerve defects, ataxia, nystagmus
- CSF-protein, mononuclear pleocytosis
- MRI- Periventricular enhancement
- CMV by PCR in CSF or brain

Skin conditions

Viral		Bacterial		Fungal		Parasitic		Other dermatosis	
Cause	Treatment	Cause	Treatment	Cause	Treatment	Cause	Treatment	<p>Pruritic Papular Eruption (PPE) moderate topical steroids oral antihistamine</p> <p>Seborrheic dermatitis, psoriasis, malnutrition dermatosis Treatment is the same as in nonimmuno-compromised hosts</p>	
Herpes simplex	Acyclovir 5 mg/kg/dose every 8 hrs. IV for 7-10 days or oral acyclovir 5 mg/ kg/dose 5 times a day	Impetigo Ecthyma Folliculitis Furunculosis	Cloxacillin 50 mg/kg/day q.i.d orally for 7-10 days or until lesions healed Alternatives: Erythromycin First generation cephalosporin	Candidiasis	Topical imidazole miconazole for 2 weeks or longer or	Scabies	In older children, 0.3% gammaben benzene hexachloride applied from neck down to toe for 12 hours followed by bath.		
Herpes zoster or chickenpox	Acyclovir 10 mg/kg/dose every 8 hrs. or 1500 g/sq.m./day in 3 divided doses IV for 7days			Ringworm	clotrimazole cream twice daily for 4-6 weeks	In neonate or infant scabies, topical 5-10% sulfur cream applied overnight for at least 5 days.			
Molluscum contagiosum	Surgical extraction , Cryotherapy			Tinea capitis	Griseofulvin 10-15 mg/kg daily for 8-12 weeks				
Condyloma acuminata	10-25% podophyllin applied topically once weekly by provider or Cryotherapy								