

Appendix A: Selected Significant Drug Interactions with Rifamycins

Type of drug	Comments
Anticonvulsants	Therapeutic drug monitoring recommended; may require anticonvulsant dose increase. Phenytoin: monitor serum phenytoin concentrations and seizure activity; increase dosage if needed.
Antipsychotics	Monitor clinical response; may need to increase haloperidol dose.
Antiretrovirals	APV, IDV, LPV/RTV, and NFV should not be used with R. EFV requires a dose increase to 800 mg/day when used with R.
Atovaquone	R reduces atovaquone levels by 50%; RFB probably has a similar effect. Consider alternative treatments for PCP.
Azole antifungal agents	Itraconazole, ketoconazole, and voriconazole concentrations may be subtherapeutic with any of the rifamycins and should be avoided if possible. Fluconazole has less reduction in serum concentrations vs. other azoles; monitor clinical response and increase fluconazole dose as needed.
Benzodiazepines	Monitor clinical response; may need to increase diazepam dose.
β-Adrenergic blocking agents	Monitor clinical response; increased propranolol hydrochloride or metoprolol dose may be needed.
Chloramphenicol	Monitor serum chloramphenicol concentrations; increased chloramphenicol dose may be needed; consider an alternative antibiotic.
Clarithromycin	RFB level increases by 56% and clarithromycin level decreases by 50%. Avoid R. Monitor signs and symptoms of infection; more study needed.
Corticosteroids	Monitor clinical response; may require two- to three-fold increase in corticosteroid dose.
Dapsone	Monitor clinical response, including potential hematologic toxic effects; increased dapsone dose may be necessary; additional study needed when used for PCP prophylaxis.
Digitoxin	Monitor arrhythmia control, signs and symptoms of heart failure, and serum digitoxin concentrations.
Digoxin (oral)	Monitor arrhythmia control, signs and symptoms of heart failure, and serum digoxin concentrations.

Type of drug	Comments
Doxycycline	Monitor clinical response; increase doxycycline dose if needed; consider an alternative antibiotic.
Hypoglycemics	Monitor blood glucose; may require hypoglycemic drug dose increase or change to an alternate hypoglycemic drug.
Hypolipidemics	For simvastatin and fluvastatin, monitor hypolipidemic effect; may require use of an alternate hypolipidemic drug. Concurrent use of atorvastatin or pravastatin with rifamycins appears safe.
Levothyroxine sodium	Monitor thyrotropin level; increased dose of levothyroxine sodium likely needed (based on case reports).
Mefloquine	Consider an alternative malaria prophylaxis/treatment.
Methadone hydrochloride	Increase methadone dose with concomitant R therapy; monitor and control withdrawal symptoms.
Metronidazole	Monitor for decreased clinical response; increase metronidazole dose if needed; use another agent if possible.
Oral anticoagulants	Monitor international normalized ratio; increased anticoagulant dose will likely be needed.
Oral contraceptives	Use alternative form(s) of birth control, as rifamycins decrease levels of oral contraceptives.
Theophylline	Monitor serum theophylline concentrations; increase theophylline dose if needed.
TMP/SMX	Increased levels of TMP/SMX but not considered clinically significant. Can use standard doses safely.
Tricyclic antidepressants	Therapeutic drug monitoring recommended; may require dose increase or change to alternative agent.

Sources: American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America. Treatment of tuberculosis. *Am J Respir Crit Care Med* 2003;167:603–62. Bartlett JG, Gallant JE. *Medical management of HIV infection*. Baltimore, MD: Johns Hopkins University, 2005. Finch CK, Chrisman CR, Baciewicz AM, Self TH. Rifampin and rifabutin drug interactions: an update. *Arch Intern Med* 2002;162:985–92. Gilbert DN, Moellering RC, Eliopoulos GM, Sande MA. *The Sanford guide to antimicrobial therapy 2006*. 36th ed. Sperryville, VA: Antimicrobial Therapy, Inc., 2006.

This is a partial list of significant drug interactions and the reader is advised to check the drug insert information before prescribing any medications in conjunction with rifamycins.

Appendix B: WHO Staging System for HIV Infection and Disease in Adults and Adolescents

Adult Clinical Stage I:

1. Asymptomatic
 2. Generalized lymphadenopathy
- Performance scale 1: asymptomatic, normal activity

Adult Clinical Stage II:

1. Weight loss <10% of body weight
 2. Minor mucocutaneous manifestations (seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
 3. Herpes zoster within the last five years
 4. Recurrent upper respiratory tract infections (i.e., bacterial sinusitis)
- And/or performance scale 2: symptomatic, normal activity

Adult Clinical Stage III:

1. Weight loss >10% of body weight
 2. Unexplained chronic diarrhea >1 month
 3. Unexplained prolonged fever (intermittent or constant) >1 month
 4. Oral candidiasis
 5. Oral hairy leukopenia
 6. Pulmonary tuberculosis
 7. Severe bacterial infections (i.e. pneumonia, pyomyositis, *S. typhi*)
- And/or performance scale 3: bedridden <50% of the day during last month

Adult Clinical Stage IV:

1. HIV wasting syndrome^a
 2. *Pneumocystis carinii* pneumonia or subacute dyspnea with exam or x-ray consistent with PCP
 3. Seizures or focal neurological findings
 4. Toxoplasmosis of the brain
 5. Cryptosporidiosis with diarrhea >1 month
 6. Cryptococcosis, extrapulmonary
 7. Cytomegalovirus disease of an organ other than liver, spleen, or lymph node (e.g., retinitis)
 8. Herpes simplex virus infection, mucocutaneous (>1 month) or visceral
 9. Progressive multifocal leukoencephalopathy
 10. Any disseminated endemic mycosis (i.e., histoplasmosis, coccidioidomycosis)
 11. Candidiasis of esophagus, trachea, bronchi
 12. Atypical mycobacteriosis, disseminated or pulmonary
 13. Non-typhoid *Salmonella septicaemia*
 14. Extrapulmonary tuberculosis
 15. Lymphoma
 16. Kaposi's sarcoma
 17. HIV encephalopathy^b
 18. Subacute meningitis consistent with cryptococcus or tuberculosis
- And/or performance scale 4: bedridden >50% of the day during last month

Adapted from: World Health Organization. *Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach*. Geneva: World Health Organization, 2004:61. (Accessed July 9, 2006 at: http://www.who.int/3by5/publications/documents/arv_guidelines/en/index.html.)

- ^a HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).
- ^b HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition, other than HIV infection, which could explain the findings.

Appendix C: WHO Staging System for HIV Infection and Disease in Children

Pediatric Clinical Stage I:

1. Asymptomatic
2. Generalized lymphadenopathy

Pediatric Clinical Stage II:

1. Chronic diarrhea >30 days duration in absence of known etiology
2. Severe persistent or recurrent candidiasis outside the neonatal period
3. Weight loss or failure to thrive in the absence of known etiology
4. Persistent fever >30 days duration in the absence of known etiology
5. Recurrent severe bacterial infections other than septicemia or meningitis (e.g., osteomyelitis, bacterial (non-TB) pneumonia, abscesses)

Pediatric Clinical Stage III:

1. AIDS-defining opportunistic infections
2. Severe failure to thrive (wasting) in the absence of known etiology^a
3. Progressive encephalopathy
4. Malignancy
5. Recurrent septicemia or meningitis

Source: World Health Organization. *Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach*. Geneva: World Health Organization, 2004:62. (Accessed July 9, 2006 at: http://www.who.int/3by5/publications/documents/arv_guidelines/en/index.html.)

^a Persistent weight loss >10% of baseline or less than 5th percentile on weight for height chart on two consecutive measurements more than one month apart in the absence of another etiology or concurrent illness.

Appendix D: Adult Dosing Guidelines for Selected Antiretroviral Drugs

Drug	Adult dosing	Important side effects; comments
Nucleoside reverse transcriptase inhibitors (NRTIs)		
Abacavir (ABC)	300 mg 2x/day	<ul style="list-style-type: none"> • Hypersensitivity in 2-5% of patients • Alcohol increases ABC levels by 40%
Didanosine (ddI)	<p><60 kg, 125 mg 2x/day or 250 mg/day; 100 mg 2x/day if combined with TDF</p> <p>≥60 kg, 200 mg 2x/day; 125 mg 2x/day if combined with TDF</p>	<ul style="list-style-type: none"> • Chills or fever, headache, nausea, vomiting, peripheral neuropathy, pancreatitis, lipodystrophy, weakness, abdominal pain, diarrhea, retinal changes, optic neuritis, fat redistribution/accumulation, rash, lactic acidosis, severe hepatomegaly with steatosis • Take on empty stomach • Increased toxicity with d4T • Avoid during pregnancy • Alcohol increases risk of pancreatitis • Adjust dose with renal failure
Emtricitabine (FTC)	200 mg/day	<ul style="list-style-type: none"> • Generally well-tolerated • Headache, decreased appetite, nausea, vomiting, rash, lactic acidosis, hepatomegaly, skin hyperpigmentation • Related chemically to 3TC, but more potent
Lamivudine (3TC)	150 mg 2x/day or 300 mg/day	<ul style="list-style-type: none"> • Generally well-tolerated • Headache, decreased appetite, nausea, diarrhea, vomiting, lactic acidosis, hepatomegaly, pancreatitis (especially in children)

Drug	Adult dosing	Important side effects; comments
Stavudine (d4T)	Immediate-release: <60 kg, 30 mg 2x/day; ≥60 kg, 40 mg 2x/day Extended-release: <60 kg, 75 mg/day; ≥60 kg, 100 mg/day	<ul style="list-style-type: none"> • Peripheral neuropathy, lipodystrophy, lactic acidosis, hepatomegaly with steatosis, pancreatitis, hyperlipidemia • Fatal pancreatitis has been reported when used with ddI • Avoid during pregnancy • Do not use with AZT
Zidovudine (AZT)	300 mg 2x/day Perinatal HIV transmission prevention: <ul style="list-style-type: none"> • For mother: 100 mg 5x/day or 200 mg 3x/day or 300 mg 2x/day starting at the 14th week of gestation until labor, then 2 mg/kg IV over 1 hour followed by 1 mg/kg/hour IV until umbilical cord clamping • Alternative: 2 mg/kg IV over 1 hour followed by 1 mg/kg/hour until delivery + single-dose NVP 200 mg orally at onset of labor 	<ul style="list-style-type: none"> • Anemia, headache, insomnia, malaise, anorexia, constipation, nausea, vomiting, lactic acidosis, hepatomegaly with steatosis, leukopenia, myopathy, neuropathy • Do not use with d4T • See Protocol 2.4 for appropriate management of infants born to mothers treated with this regimen
Nucleotide reverse transcriptase inhibitor (NRTI)		
Tenofovir (TDF)	300 mg/day	<ul style="list-style-type: none"> • Nephrotoxicity, including Fanconi syndrome • Take with food

Drug	Adult dosing	Important side effects; comments
Nonnucleoside reverse transcriptase inhibitors (NNRTIs)		
Efavirenz (EFV)	600 mg/day If used concurrently with R, 800 mg/day	<ul style="list-style-type: none"> • Dizziness, agitation, vivid dreams, hepatitis, lipodystrophy, depression, hallucinations, impaired concentration, insomnia, somnolence, rash (very common, especially in children), hyperglycemia, hyperlipidemia and fat redistribution (less common) • Administer at bedtime without food (at least 2 hours after a meal) • Avoid during pregnancy. • Decreases effectiveness of oral contraceptives
Nevirapine (NVP)	200 mg/day for 14 days, then 200 mg 2x/day Perinatal HIV transmission prevention: for women with no prior ART, single-dose NVP 200 mg orally at onset of labor, followed by 4 mg/kg administered to the newborn within 48-72 hours of birth	<ul style="list-style-type: none"> • Headache, fatigue, diarrhea, nausea, rash (most common), fat redistribution (less common), hepatitis (generally within 12 weeks of initiation), hepatic failure (severe, life-threatening hepatotoxicity, some fatal cases), severe skin reactions (Stevens-Johnson syndrome) • Women with CD4 >250 cells/mm³, including pregnant women, are especially vulnerable for fatal hepatotoxicity
Protease inhibitors (PIs)		
Amprenavir (APV)	1200 mg 2x/day If with RTV: 600 mg 2x/day + 100 mg RTV 2x/day	<ul style="list-style-type: none"> • Nausea, vomiting, diarrhea, rash, Stevens-Johnson syndrome, lipodystrophy • Avoid taking with high-fat meal • Decrease dose in liver failure to 300 mg • Decreases effectiveness of oral contraceptives • Avoid during pregnancy

Drug	Adult dosing	Important side effects; comments
Atazanavir (AZV)	400 mg/day	<ul style="list-style-type: none"> • Take with food
Indinavir (IDV)	800 mg 3x/day	<ul style="list-style-type: none"> • Abdominal pain, nausea, vomiting, asymptomatic hyperbilirubinemia, back pain, acute hemolytic anemia, hyperglycemia (including cases of new onset diabetes mellitus), hepatitis (rare), nephrolithiasis, lipodystrophy • Take with plenty of water to avoid nephrolithiasis • Take on empty stomach • If boosted with RTV 100 mg, can be dosed 800 mg 2x/day and taken with food
Lopinavir/ Ritonavir (LPV/ RTV)	400/100 mg 2x/day 533/133 mg 2x/day when combined with EFV, APV, NFV, or NVP	<ul style="list-style-type: none"> • Diarrhea, lipodystrophy, nausea • Refrigeration required • Take with food
Nelfinavir (NFV)	1250 mg 2x/day	<ul style="list-style-type: none"> • Secretory diarrhea, nausea, vomiting, lipodystrophy • Take with food
Ritonavir (RTV)	Start at 300 mg 2x/day and escalate to 600 mg 2x/day over 2 weeks	<ul style="list-style-type: none"> • Hepatitis, lipodystrophy • Refrigeration required • Poorly tolerated when used alone at 600 mg 2x/day; best used to boost levels of other PIs

Source: Bartlett JG, Gallant JE. *Medical management of HIV infection*. Baltimore, MD: Johns Hopkins University, 2005.

Appendix E: Pediatric Dosing Guidelines for Selected Antiretroviral Drugs

Drug	Pediatric dose Maximum dose	Commonly available formulations
Nucleoside reverse transcriptase inhibitors (NRTIs)		
Zidovudine (AZT)	8-15 mg/kg (180-300 mg/m ²) 2x/day Postpartum prophylaxis: 4 mg/kg 2x/day for 1-6 weeks ^a Max 300 mg 2x/day	Syrup: 10 mg/ml Capsule: 100 mg Tablet: 300 mg
Lamivudine (3TC)	4 mg/kg 2x/day Max 150 mg 2x/day	Syrup: 10 mg/ml Tablet: 150 mg
Stavudine (d4T)	1 mg/kg 2x/day Max 40 mg 2x/day	Syrup: 1 mg/ml Capsule: 30 mg, 40 mg
Abacavir (ABC)	8 mg/kg 2x/day Max 300 mg 2x/day	Syrup: 20 mg/ml Tablet: 300 mg
Nonnucleoside reverse transcriptase inhibitors (NNRTIs)		
Nevirapine (NVP)	Induction dose (14 days): 4 mg/kg/day (200 mg/m ²) Maintenance dose, <8 years: 7 mg/kg 2x/day Maintenance dose, ≥8 years: 4 mg/kg 2x/day Postpartum prophylaxis: 4 mg/kg for 6 weeks ^b Max 200 mg 2x/day	Syrup: 10 mg/ml
Efavirenz (EFV)	~15 (10-20) mg/kg/day Max 600 mg/day	Capsule: 200 mg Tablet: 600 mg
Protease inhibitors (PIs)		
Lopinavir/ Ritonavir (LPV/RTV)	<15 kg 12/3 mg/kg 2x/day; ≥15 kg 10/2.5 mg/kg Max 400/100 mg 2x/day	Capsule: 133.33/33.33 mg Tablet: 200/50 mg
Nelfinavir (NFV)	55 mg/kg 2x/day Max 1250 mg 2x/day	Tablet: 250 mg

Fixed-Dose Combinations

Formulations	Pediatric dose Maximum dose
AZT 300 mg + 3TC 150 mg	2x/day Max 1 tablet 2x/day
3TC 150 mg + d4T 30 mg	
3TC 150 mg + d4T 40 mg	
3TC 150 mg + d4T 30 mg + NVP 200 mg	

^a AZT can be used alone or in combination with NVP for HIV-exposed infants postpartum, depending on what treatment the mother has received (see Protocol 2.4).

^b NVP is used in combination with AZT for HIV-exposed infants postpartum (see Protocol 2.4).

Appendix F: HIV-Related Complications of the Skin, Lymph Nodes, and Mucous Membranes

Disease	Etiology and presentation	Treatment
Enlarged lymph nodes, nodules, or masses		
Generalized lymphadenopathy	May be HIV-related or result of OIs such as TB, atypical mycobacteria, histoplasmosis, coccidioidomycosis, lymphoma, Kaposi's sarcoma, Epstein-Barr virus, toxoplasma, tularemia, CMV, or Castleman's disease; also seen in immune reconstitution syndrome (see Section 3.9.7 and Protocol 3.26); less often lymphoma.	Treatment should be directed at the specific OI. If no OI can be identified, consider initiating ART.
Kaposi's sarcoma	Firm subcutaneous brown-black or purple nodules at any cutaneous site, especially face, chest, genitals, and extremities.	May resolve with ART. Surgical excision, intralesion or systemic chemotherapy, radiation, cryotherapy, or laser therapy in specialist centers may be successful if the sarcoma is extensive and widespread.
Lymphoma	Increased risk in patients with HIV. Often in body cavities or CNS. Hard, painless lymph nodes are typical. May be associated with fever.	If specialized care centers are available, consider biopsy and treatment based on definitive diagnosis.
Salivary gland enlargement	Enlargement of submandibular, parotid, and other glands; may be mistaken for lymphadenopathy. Should rule out abscess and lymphoma. If parotid swelling, consider mumps in differential diagnosis.	Usually resolves or improves with ART. If evidence of pus or infection present, consider drainage and treatment with dicloxacillin 250-500 mg orally 4x/day for 10-14 days or clindamycin 150-300 mg orally 4x/day for 10-14 days. Promote good oral hygiene

Disease	Etiology and presentation	Treatment
Sexually transmitted infections	May present with inguinal mass or adenopathy.	See Section 2.6.
Tuberculosis	Typically a single swollen lymph node, most commonly in the cervical chain; may be generalized. Lymph nodes initially firm and small can become large and fluctuant. Suppuration with drainage and chronic fistulization may occur. Diagnosis can be confirmed on biopsy or aspirate.	See Section 2.4.
Infected skin lesions (lesions that are red, tender, warm, pustular, or crusty)		
Abscess or folliculitis	Most commonly caused by <i>Staphylococcus aureus</i> .	Incise and drain fluctuant abscesses with sterile technique. Start dicloxacillin 50-500 mg orally 4x/day or cephalexin 500 mg orally 4x/day or clindamycin 150-400 mg orally 4x/day. Treat for 7-14 days or until resolved. Follow-up in 1-2 days to confirm improvement.
Impetigo	Red, tender, warm papules, often with a honey-colored crust. Frequently on the face (around the mouth), trunk, and groin of adults. Contagious. May appear as ulcerating lesions.	Dicloxacillin 250-500 mg orally 4x/day or cloxacillin 250-500 mg orally 4x/day or erythromycin 250-500 mg orally 4x/day or clindamycin 150-400 mg orally 4x/day.
Other lesions	Eczema, psoriasis, contact dermatitis, prurigo nodularis, and other lesions can mimic infection.	See sections on eczema, psoriasis, contact dermatitis, and prurigo nodularis in this table. Generally do not require antibiotics unless superinfection is present.

Disease	Etiology and presentation	Treatment
Cellulitis	Skin is red and warm; patient may be systemically unwell with fever. May progress to more severe soft tissue infection.	Start dicloxacillin or cephalexin 500 mg orally 4x/day for 7-14 days or until resolved.
Severe soft tissue infection	Rapidly progressing skin infection, may involve subcutaneous fascia, pyomyositis, systemic toxicity. May be life- or limb-threatening.	Start benzathine benzylpenicillin 4 MU IV 6x/day. Add clindamycin 600 mg IV or orally 3x/day. If IV not available, start dicloxacillin and clindamycin orally. May need hospitalization and possibly specialist care or surgery.
Skin conditions that present as blisters or vesicles		
Adverse drug reactions	Some drug reactions can cause generalized blistering or small bumps. A peeling rash involving the eyes or mouth can represent a very serious drug reaction causing Stevens-Johnson syndrome.	Stop all medications. Administer oral antihistamines. If Stevens-Johnson syndrome is suspected, hospitalize for supportive care. If reaction is severe, give prednisone 1-2 mg/kg orally, tapering 5-10 mg every 1-3 days. If patient was on ABC, do not reintroduce (may be fatal). See Protocol 3.7.
Contact dermatitis	Typically limited to the area in contact with the causative agent.	Hydrocortisone 1% cream or ointment 3x/day. If severe, with blisters or edema, consider prednisone 1 mg/kg/day orally, tapering 5-10 mg/day over 7-10 days.
Herpes simplex	Vesicles with an erythematous base. Usually oral, genital, or peri-rectal. Generally in clusters. May have a history of recurrence.	If first episode or severe reaction, administer acyclovir 400 mg orally 5x/day for 10 days. See Protocol 3.21.

Disease	Etiology and presentation	Treatment
Herpes zoster	Vesicles with an erythematous base in a dermatomal distribution. Lesions in more than one dermatome or lesions in eye are considered to be disseminated (or complicated) disease.	All patients with HIV should be treated with antiviral therapy regardless of timing of lesion onset. Administer acyclovir 10 mg/kg IV over 1 hour 3x/day for 7 days. Administer analgesia as required. See Protocol 3.21.
Skin conditions that present as generalized or itching rashes		
Adverse drug reactions	Generalized widespread red rash with small papules, usually on trunk. Blistering or a peeling rash involving the eyes or mouth can represent a very serious drug reaction leading to Stevens-Johnson syndrome.	Stop all medications. Administer oral antihistamines. If Stevens-Johnson syndrome is suspected, hospitalize for supportive care. If reaction is severe, give prednisone 1-2 mg/kg orally, tapering 5-10 mg every 1-3 days. If patient was on ABC, do not reintroduce (may be fatal). See Protocol 3.7.
Eosinophilic folliculitis	Itchy papules and pustules most commonly on the head, trunk, and upper part of extremities. Difficult to differentiate from infective folliculitis; a biopsy will reveal eosinophilic infiltrate in the follicular epithelium. May occur with immune reconstitution.	Usually resolves once ART is initiated. Permethrin cream and topical steroid creams can help; antihistamines for pruritis.
Scabies (also head and body lice)	Rash and excoriations on the torso. Burrows can often be seen in the web space between the fingers and on the wrist. The face is usually not affected. Itching can persist for two weeks after treatment.	Permethrin cream 5% (preferred): apply from chin to toes. Wash hair if involved. Leave on for 8-10 hours, then wash. Repeat in one week. Safe for children >2 months of age. Alternative: lindane 1%, same usage as permethrin. Seizures can occur from coverage of broad areas. Do not use in children or pregnant women. Trim fingernails, wash clothes and bedding.

Disease	Etiology and presentation	Treatment
Norwegian scabies (<i>Scabies crustosa</i>)	Usually in advanced immunosuppression (CD4 <100 cells/mm ³). Can mimic psoriasis. Itching may be absent. Extensive crusting.	Permethrin cream 5%: leave on for 24 hours; 6% sulfur on days 2-7. Repeat for several weeks. Single-dose ivermectin 200 mcg/kg reported to be effective.
Prurigo nodularis	Hyperpigmented, hyperkeratotic, often excoriated papules and nodules up to 1 cm. May be due to insect bites. Scratching results in worsening pruritis.	Give oral antihistamines. Insecticides and bed-netting may be effective in preventing new lesions. Topical corticosteroid cream may help; can use high-potency steroid creams under an occlusive dressing. Aim to break the itch-scratch cycle, which may take several weeks or months. Condition may also improve with ART.
Early secondary syphilis	Macular rash on trunk palms and soles.	Single-dose benzathine benzylpenicillin 2.4 MU IM.
Oral and skin lesions caused by fungal infections		
Candidiasis (skin)	In children: causes a diaper-rash-type rash involving the trunk and extremities. In adults: causes flat or slightly raised red lesions; also common in the mouth (see section on oral lesions elsewhere in this table).	Topical ketconazole, miconazole, clotrimazole, econazole, or nystatin, all 2x/day.

Disease	Etiology and presentation	Treatment
Dermatophytic fungi	Red, often itchy lesions; may cause changes in skin pigment. Lesions can occur in the groin (<i>T. cruris</i>), on the feet (<i>T. pedis</i>), or on the body (<i>T. corporis</i>). <i>T. capitis</i> (ringworm) causes pale round scaling patches on scalp or round patches with thick reddish edges on the body or web of the feet. It is harder to treat than the aforementioned fungal infections.	Topical ketoconazole, miconazole, clotrimazole, econazole, or nystatin, all 2x/day, or single-dose fluconazole 150 mg orally or 150 mg/week orally for 2-4 weeks. Ringworm: topical ketoconazole 2x/day may be sufficient if lesions are few or small. If extensive, consider fluconazole 150 mg/week orally for 2-4 weeks or griseofulvin 500 mg/day orally for 4-6 weeks. In children: griseofulvin 10-20 mg/kg/day until hair regrows, usually 6-8 weeks.
Seborrhea	Very common in HIV-infected individuals. Can present as mild dandruff or patches of scaly areas with indistinct borders. Common in the scalp, hairline, central face; also seen in body folds and chest. Usual etiology is <i>Malassezia</i> species.	Ketoconazole (1% or 2%) shampoo or lotion. If severe, consider corticosteroid cream and ketoconazole. Often resolves or improves with ART.
Tinea versicolor	Typically causes areas of hypopigmentation. May be confused with vitiligo, which is not an infectious disease and will not respond to antifungal agents.	Usually resistant to topical agents. Administer single-dose ketoconazole 200 mg or 400 mg orally for 7 days, or single-dose fluconazole 400 mg orally.
Other skin lesions		
Dry skin (xerosis)	Often very itchy; antihistamines do not provide much relief.	Apply humectants or moisturizing creams.

Disease	Etiology and presentation	Treatment
Eczema	Red rash, often itchy, flaking lesions that may have whitish patches or scaling; may become superinfected. Often on the groin and face (especially in children), under the arms, on the elbows, and elsewhere. Can be confused with contact dermatitis or psoriasis.	Apply topical corticosteroid creams. Treat itching with antihistamines. Dry the skin gently and avoid harsh or perfumed soaps.
Insect bites	Fleas: lower legs. Mosquitoes and other biting insects: arms and legs.	Fleas: wash clothes and bedding; do not allow pets and other animals in the house. Mosquitoes and other biting insects: use bed nets with insecticide; use topical insect repellent as needed; give antihistamines for itching. Monitor for signs of superinfection.
Leprosy	Skin patches with no sensation to soft touch, heat, or pain; not itchy. Can occur in any location of the body. Hypopigmented, pale or reddish; flat, raised, or nodular. Chronic (>6 months).	If never treated in the past, treat with multidrug therapy per WHO guidelines.
Longitudinal pigmented nail beds	Seen in almost 50% of persons on AZT; more common in dark-skinned patients. Occurs 4-8 weeks after initiating treatment.	No treatment necessary.
Molluscum contagiosum	Pearly white or flesh-colored papules with central umbilication; most common on the face and genitals. Diagnosis is usually made by clinical appearance.	Usually no treatment needed. Lesions will disappear in patients responding to ART.
Psoriasis	Thick, red, scaling patches with distinct margins. Often on elbows, knees, scalp, hairline, and lower back. May be itchy.	Coal tar ointment 5% in salicylic acid 2%.

Disease	Etiology and presentation	Treatment
Warts (human papilloma virus)	Flesh-colored papules or raised areas of skin; common in genital or perianal area.	Topical treatment with cryotherapy or topical podofilox 0.5%.
Lesions of the mucous membranes		
Angular cheilitis	Sores at the corners of the mouth. Most often caused by candidiasis but can also be present with malnutrition and vitamin B deficiency.	Consider empiric fluconazole 100 mg/day orally for 10-14 days; provide nutritional supplementation.
Aphthous ulcer	Cause is unknown; however, HIV, HSV, CMV, and drug reactions can also cause ulcers of the mouth.	Topical lidocaine or triamcinolone hexacetonide in orabase; if severe and refractory, consider prednisone 40 mg/day orally for 1-2 weeks.
Gingivitis/periodontitis	Redness or dead tissue around teeth and gum line; receding gum line; painful chewing. Can become necrotizing and cause loss of teeth.	Metronidazole 500 mg orally 2x/day for 7-10 days. Promote good oral hygiene. If necrotizing, may need dental consultation for debridement and teeth extraction.
Oral hairy leukopenia	Whitish or grayish, feathery, irregular-appearing lesions, usually at base of tongue or gums.	Usually improves or resolves with ART.
Thrush (candida)	White plaques on an inflamed base on tongue, palate, buccal mucosa, or oropharynx.	Fluconazole 200-400 mg/day orally for 10-14 days; see Section 3.9.4 and Protocol 3.22 on candidal infections.

Sources: Bartlett JG. *The Johns Hopkins Hospital 2005-6 guide to medical care of patients with HIV infection*. Baltimore, MD: Johns Hopkins University, 2005; Sande MA, Gilbert DN, Moellering RC. *The Sanford Guide to HIV/AIDS Therapy*. Hyde Park, VT: Antimicrobial Therapy, 2005.

Appendix G: Treatment and Prophylaxis for Common Infections in HIV-Positive Patients

Disease Likely CD4 count at occurrence	Preferred treatment regimen(s)	Preferred prophylactic regimen(s)
Candidiasis, esophageal CD4 <200 cells/mm ³	Fluconazole 400 mg/day orally for 14-21 days	No prophylaxis
Candidiasis, oropharyngeal CD4 <200 cells/mm ³	Fluconazole 200 mg/day orally for 10-14 days	No prophylaxis
Herpes simplex, genital (first episode)	Acyclovir 400 mg orally 5x/day for 10 days	No prophylaxis
Herpes, uncomplicated varicella-zoster	Acyclovir 800 mg orally 5x/day for 10 days	No prophylaxis
Herpes, disseminated (or complicated) varicella-zoster	Acyclovir 10 mg/kg IV over 1 hour 3x/day for 7 days; max dose 20 mg/kg 3x/day	No prophylaxis
Malaria, chloroquine-sensitive	Chloroquine 1 g (600 mg base) followed by 500 mg in 6 hours then 500 mg/day for 2 days Alternative: quinine 640 mg 3x/day orally or IV + doxycycline 100 mg 2x/day orally for 7 days	Consider prophylaxis based on local resistance patterns for pregnant women in endemic areas
Malaria, chloroquine-resistant	Quinine 650 mg 3x/day orally or IV + doxycycline 100 mg 2x/day orally for 7 days	Consider prophylaxis based on local resistance patterns for pregnant women in endemic areas
Meningitis, cryptococcal CD4 <100 cells/mm ³	Amphotericin B 1 mg/kg/day IV + flucytosine 25 mg/kg orally if available for 14 days, followed by fluconazole 400 mg/day orally or IV for 8-10 weeks	Secondary prophylaxis after treatment: fluconazole 200 mg/day orally

Disease Likely CD4 count at occurrence	Preferred treatment regimen(s)	Preferred prophylactic regimen(s)
<i>Mycobacterium avium</i> complex CD4 <50 cells/mm ³	Clarithromycin 500 mg orally 2x/day + E 15 mg/kg/day + RFB 300 mg/day Alternative: azithromycin 600 mg/day orally + E 15 mg/kg/day + RFB 300 mg/day	Primary prophylaxis if CD4 <50 cells/mm ³ : azithromycin 1200 mg/week orally Alternative: clarithromycin 500 mg 2x/day orally
<i>Pneumocystis carinii</i> pneumonia CD4 <200 cells/mm ³	TMP/SMX 2 DS tablets 3x/day for 21 days Alternatives: atovaquone 750 mg 2x/day orally for 21 days or clindamycin 300-450 mg 4x/day orally + primaquine 30 mg/day orally for 21 days	Primary and secondary lifelong prophylaxis: TMP/SMX 1 DS tablet/day or 3x/week Alternatives: dapsone 100 mg/day orally or atovaquone 750 mg/day orally
Syphilis , early or less than one year	Single-dose benzathine benzylpenicillin 2.4 MU IM Alternative: doxycycline 100 mg 2x/day orally for 15 days	No prophylaxis
Syphilis , latent or more than one year	Benzathine benzylpenicillin 2.4 MU/week IM for 3 weeks Alternative: doxycycline 100 mg 2x/day orally for 30 days	No prophylaxis
Syphilis , neurosyphilis	Benzathine benzylpenicillin 3-4 MU IV 6x/day for 10-14 days Alternative: procaine-penicillin G 2.4 MU/day IM + probenecid 0.5 g orally 4x/day for 10 days	No prophylaxis

Disease Likely CD4 count at occurrence	Preferred treatment regimen(s)	Preferred prophylactic regimen(s)
Toxoplasmosis CD4 <100 cells/mm ³	<p>Preferred: pyrimethamine 100 mg orally first day, then 50-100 mg/day + sulfadiazine 0.5-2 g 4x/day + folinic acid 10 mg/day for at least six weeks, then life-long prophylaxis</p> <p>Alternatives: TMP 10 mg/kg/day divided 2x/day (not first-line therapy) for at least 6 weeks, followed by suppression regimen; or pyrimethamine 200 mg loading dose orally followed by 75 mg/day + sulfadiazine 6-8 g/day orally in 4 divided doses</p>	<p>Primary prophylaxis if CD4 <200 cells/mm³: TMP/SMX 1 DS tablet/day</p> <p>Secondary prophylaxis: pyrimethamine 25-50 mg/day + sulfadiazine 0.5-1 g 4x/day + folinic acid 10 mg/day</p>
Tuberculosis	See Tables 2.1 and 2.2	Primary prophylaxis if PPD >5 mm: H 300 mg/day + pyridoxine 50 mg/day for 9 months
Typhoid fever , less severe cases	<p>Ciprofloxacin 500 mg orally 2x/day for 10 days</p> <p>Alternatives: TMP/SMX 1 DS tablet 2x/day for 10 days or cefixime 10-15 mg/kg orally 2x/day for 10 days</p>	No prophylaxis
Typhoid fever , severe cases	Ceftriaxone 50 mg/kg/day IV for 14 days (max dose 2 g/day)	No prophylaxis

Appendix H: Examples of Information Systems to Support HIV Treatment and Program Scale-up in Resource-Poor Settings

Stand-alone databases

Mosoriot medical record, Kenya^a

Microsoft Access[®] data are entered from a paper record. Used for general medical care in one hospital for more than two years and was extended to support HIV treatment at Moi University. This is now being superseded by a system built on the OpenMRS architecture.^b

Children's Hospital, Lilongwe, Malawi^c

Microsoft SQL Server[®] and Visual Basic[®] now converted to open source software (Linux and MySQL) and extended to collect information on HIV patients. Physicians, nurses, and other staff perform all data entry, including medication orders. Has made heavy use of a touch-screen medical record system for more than two years.

Ministry of Health database, Cuba

Includes extensive clinical data on the approximately 1,200 patients in the country who require ART.

Department of Health and Human Services, United States

Careware system (using Microsoft Access[®]) provides comprehensive tools for tracking HIV patients and their treatment. Currently used in more than 300 health centers and hospitals in the U.S. Deployed in Uganda in October 2003. An Internet-accessible version has now been deployed in the US and several African countries. Careware is closed source but available free of charge at <http://hab.hrsa.gov/careware>.

FUCHIA (Follow-Up of Clinical HIV Infection and AIDS Guide for Users)

Microsoft Access[®] and the Delphi programming language. Developed by Epicentre, the epidemiology group of Médecins Sans Frontières, to support their HIV treatment projects. It supports clinical care and long-term follow-up of patients, including scheduling of visits, and includes data on medications and certain investigations and generates some reports. Available free of charge at <http://www.epicentre.msf.org>.

Internet-based medical record systems

PIH-EMR, Peru^d

Supports clinical care, logistics such as assessment of drug requirements, and research studies on drug-resistant tuberculosis. In heavy use for over four years. Most data are entered from paper forms, with nurse order entry of medications now implemented. Extensions link TB laboratories to clinics and allow data collection with personal digital assistants. It uses the Linux operating system, Apache web server, Tomcat Java Servlet engine, and an Oracle[®] database.

Web-based collaboration and telemedicine systems (not specifically for HIV)
RAFT^a

Supports remote collaboration, case discussion, and data sharing over low bandwidth networks between Geneva University Hospitals and Bamako, Mali. The collaboration is being extended to other West African Francophone countries. Uses Linux and other open source software.

IPATH^f

A Web-based tool for image sharing in pathology and radiology. In use in South Africa, Switzerland, and the Pacific. Available free of charge at <http://www.sourceforge.net>.

TeleMedMail^g


Java and open source software. A secure e-mail and Web-based based telemedicine system under evaluation in South Africa and Peru. Available free of charge at <http://www.sourceforge.net>.

SatelLife

Local healthcare workers collect data on PalmPilots[®] and download information onto cell phones that transfer the data to a central database. More information at <http://pda.healthnet.org/>.

- ^a Rotich JK, Hannan TJ, Smith FE, et al. Installing and implementing a computer-based patient record system in sub-Saharan Africa: the Mosoriot Medical Record System. *J Am Med Inform Assoc* 2003;10:295-303.
- ^b Mamlin B, Biondich, PG, Wolfe B, et al. Cooking up an open source EMR for developing countries: OpenMRS - a recipe for successful collaboration. *Proc AMIA Symp* 2006; in press.
- ^c Douglas G. The Lilongwe Central Hospital patient management information system: a success in computer-based order entry where one might least expect. *Proc AMIA Symp* 2003:833.
- ^d Fraser H, Jazayeri D, Mitnick C, et al. Informatics tools to monitor progress and outcomes of patients with drug resistant tuberculosis in Peru. *Proc AMIA Symp* 2003:270-4.
- ^e Geissbuhler A, Ly O, Lovis C, L'Haire J. Telemedicine in western Africa: lessons learned from a pilot project in Mali, perspectives and recommendations. *Proc AMIA Symp* 2003:249-53.
- ^f Oberholzer M, Christen H, Haroske G, et al. Modern telepathology: a distributed system with open standards. *Curr Probl Dermatol* 2003;32:102-14.
- ^g Fraser HS, Jazayeri D, Bannach L, et al. TeleMedMail: free software to facilitate telemedicine in developing countries. *Proc MedInfo* 2001;10:815-9.

Appendix I: Example of Comprehensive Paper Form for Intake Visit

	Zanmi Lasante Programme TB / VIH	No. DEM: _____	DONNÉES DE BASE
Information démographique			
1. Date (jour/mois/année): ____/____/____			
2. Nom: _____		Prénom: _____ Prénom 2: _____	
3. No. d'identification dans le DEM: _____ 4. No. dossier: _____			
5. Sexe: <input type="checkbox"/> F <input type="checkbox"/> M		6. (a) Date de naissance: ____/____/____ (b) Age: ____ ans ____ mois	
7. Nom de la mère: _____		Prénom de la mère: _____	
8. Lieu de naissance: _____			
9. Pour les enfants, (a) Personne responsable: Nom: _____ Prénom: _____ Prénom 2: _____			
(b) No. dossier personne responsable: _____ (c) Lien avec le patient: _____			
10. Résidence actuelle: _____			
11. Agent/Compagnateur: _____			
12. Clinique: <input type="checkbox"/> Belladères <input type="checkbox"/> Boucan-Carré <input type="checkbox"/> Cange <input type="checkbox"/> Cerca-la-Source <input type="checkbox"/> Hinche <input type="checkbox"/> Lascahobas <input type="checkbox"/> Saint-Marc <input type="checkbox"/> Thomonde <input type="checkbox"/> Autre: _____			
Sérologie VIH			
13. TR: <input type="checkbox"/> non-réactif <input type="checkbox"/> réactif <input type="checkbox"/> indéterminé Date du diagnostic: ____/____/____			
14. Est-ce que le patient a reçu l'assistance-conseil en post-test? <input type="checkbox"/> non <input type="checkbox"/> oui			
15. Est-ce que le partenaire du patient a été référé pour un TR? <input type="checkbox"/> non <input type="checkbox"/> oui			
16. Encointe: <input type="checkbox"/> non <input type="checkbox"/> oui, DDR: ____/____/____ DPA: ____/____/____			
Enquête sur la tuberculose			
17. (a) Tuberculose active? <input type="checkbox"/> non <input type="checkbox"/> oui, date du diagnostic: ____/____/____			
(b) Extra-pulmonaire? <input type="checkbox"/> non <input type="checkbox"/> oui			
(c) Chimiorésistance connue? <input type="checkbox"/> non <input type="checkbox"/> oui, antibiogramme: _____			
Revue fonctionnelle des appareils			
18.			
	Durée (jour/semaines/mois)		Durée (jour/semaines/mois)
Toux (>3 semaines)	<input type="checkbox"/> _____	Prurigo	<input type="checkbox"/> _____
Fièvre (sans frêt)	<input type="checkbox"/> _____	Eruption	<input type="checkbox"/> _____
Sueurs nocturnes	<input type="checkbox"/> _____	Convulsions	<input type="checkbox"/> _____
Perte de poids (>10%)	<input type="checkbox"/> _____	Déficit neurologique focal	<input type="checkbox"/> _____
Hémoptysie	<input type="checkbox"/> _____	Confusion	<input type="checkbox"/> _____
Diarrhée (≥1 mois)	<input type="checkbox"/> _____	Neuropathie	<input type="checkbox"/> _____
Diarrhée (<1 mois)	<input type="checkbox"/> _____	Nausée	<input type="checkbox"/> _____
Dyspnée	<input type="checkbox"/> _____	Vomissement	<input type="checkbox"/> _____
Dysphagie	<input type="checkbox"/> _____	Ictère	<input type="checkbox"/> _____
Céphalée	<input type="checkbox"/> _____	Fatigue	<input type="checkbox"/> _____
Trouble visuel	<input type="checkbox"/> _____		
<input type="checkbox"/> Autres (spécifier): _____			
<input type="checkbox"/> Autres 2 (spécifier): _____			

This is the first page of a comprehensive intake form that is currently being finalized. Subsequent sections of this form collect information on the results of clinical, laboratory, and radiographic investigations; previous diagnoses; previous treatment with ART or anti-TB drugs; previous adverse effects; known allergies; and social history and socioeconomic status, including living conditions, employment, education, mode and ease of transport to the clinic, and activities of daily living. A different form is used for follow-up visits and collects information on treatment status, adherence issues, adverse events from medications, and any changes to the treatment regimen. Both forms will be available at <http://www.pih.org>.

Appendix J: Screenshot of Treatment Plan Section of EMR Intake Form

Conduite à tenir	
11. <input type="checkbox"/> Prophylaxie:	<input type="checkbox"/> INH <input type="checkbox"/> fluconazole 200 mg pour muguet non-invasif <input type="checkbox"/> TMP/SMX
<input type="checkbox"/> Autre prophylaxie pour infections opportunistes (spécifier):	<input type="text"/>
<input type="checkbox"/> Traitement antirétroviral	
<input type="checkbox"/> Traitement antituberculeux:	<input type="text"/> <input type="button" value="v"/> (si autres, spécifier: <input type="text"/>)
<input type="checkbox"/> Autres traitements pour infections opportunistes	
<input type="checkbox"/> fluconazole 400 mg pour œsophagite (spécifier dose):	<input type="text"/>
<input type="checkbox"/> amphotéricine B pour méningite cryptococcose (3-5 mg/kg/jour):	<input type="text"/>
<input type="checkbox"/> TMP/SMX pour PCP ou toxoplasmose (15 mg/kg/jour q6h):	<input type="text"/>
<input type="checkbox"/> chloroquine (spécifier dose):	<input type="text"/>
<input type="checkbox"/> autres (spécifier):	<input type="text"/>
<input type="checkbox"/> Planification familiale:	<input type="text"/>

Appendix K: Screenshot of ART Initiation Section of EMR Intake Form

Résumé antirétroviral

42. (a) Ce patient nécessite-t-il le traitement antirétroviral? oui non traitement en cours

Si le patient doit commencer les ARVs aujourd'hui ou reçoit déjà les ARVs, compléter alors le tableau ci-dessous.

Indiquez les ARVs. *Vous allez spécifier la dose complete dans une page suivante.*

(b) Médicament et préparation

Date du début du traitement (jour/mois/année)

NRTI NRTI NNRTI/PI j, m, 2006 a

43. Est-ce que le patient débute les ARVs pour PTME? non oui
44. Est-ce que le patient débute les ARVs pour prophylaxie? non oui
- Si oui,

Appendix L: Example of EMR Decision Support: Automatic Warnings

Traitement

Regime contre VIH:

Date du debut: 16 j juil m, 2006 a

d4T + NRTI + NNRTI/PI

<https://www.hiv-emr.org>



Vous ne pouvez pas prescrire la meme NRTI deux fois.

OK

- Prophylaxie pour exposition au sang
- Prophylaxie pour rapport sexuel avec quelqu'un VIH+
- Aucun

Appendix M: Suggested Indicators for Program Evaluation

Minimum Data Set

1. **Percentage of people with advanced HIV infection receiving ART**
 - Numerator: Number of people receiving ART according to UNAIDS/WHO standards at the start of the year + number of people who started treatment in the last 12 months – number of people for whom treatment was stopped (including those who died)
 - Denominator: Number of people with advanced HIV disease (often estimated to be 15 percent of total number with HIV infection)
2. **Number of drug regimens distributed each month**
3. **12-month program retention rate**
 - Numerator: Number of individuals who are still on treatment 12 months after beginning therapy
 - Denominator: All patients who are started on therapy over a given period of time
4. **Percentage of adults on treatment who gain weight**
 - Numerator: Percentage of adults who gain at least 10 percent body weight at month six after initiation of ART
 - Denominator: All patients who were started on ART who presented with weight loss or cachexia
 - Note: This number uses weight gain as a rough indicator for therapeutic success. As treatment is made available earlier in the course of disease this parameter may become less helpful. It also has less utility in centers where CD4 cell counts are available.

5. Survival rate
 - Numerator: Number of people still alive at 6 months, 12 months, and 24 months after initiation of ART
 - Denominator: Total number of individuals in treatment
6. Prevention of mother-to-child transmission
 - Numerator: Number of HIV-positive pregnant women who received ART for pMTCT
 - Denominator: Number of HIV-positive pregnant women who are offered ART

Additional useful programmatic data

1. Number of patients who are offered VCT
2. Percentage of patients who accept HIV testing
3. Proportion of HIV tests that are positive
4. Mean increase in CD4 cell count in patients on therapy
5. Percentage of HIV infected patients who are screened for STIs and TB, and number who complete treatment
6. Percentage of patients receiving social support (e.g., educational and nutritional assistance)
7. Number of HIV-positive patients receiving prophylaxis for opportunistic infections
8. Toxicities of ART
9. Number of patients switched from first-line therapy and reasons for change
10. Percentage of patients who have significant increase in CD4 cell count six months after initiation of therapy
11. Percentage of children who have a definitive diagnosis of HIV infection among all children whose mother received ART