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Porto, Portugal, 11-17 July 2009**

**HIV/AIDS**

**Coinfection with HIV and Tropical Infectious Diseases**

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# **HIV/AIDS**

## **Coinfection with HIV and Tropical Infectious Diseases**

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- **Extreme poverty.**
- **Malnutrition.**
- **Life expectancy less than 47 years.**
- **One in four children die before 5 years old.**
- **Populations without access to clean water, basic sanitation and health education.**
- **Infectious diseases is constant threat (conflicts, migrations, refugees).**

# **HIV/AIDS**

## **Coinfection with HIV and Tropical Infectious Diseases**

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- **Landmines kill ~ 3000 persons each year and leave many others disabled.**
- **Mental health problems are frequent.**
- **Gender inequalities: women condition is bad, with violation of dignity, equality and humanity.**
- **In some areas of the world 90% of births are not assisted.**

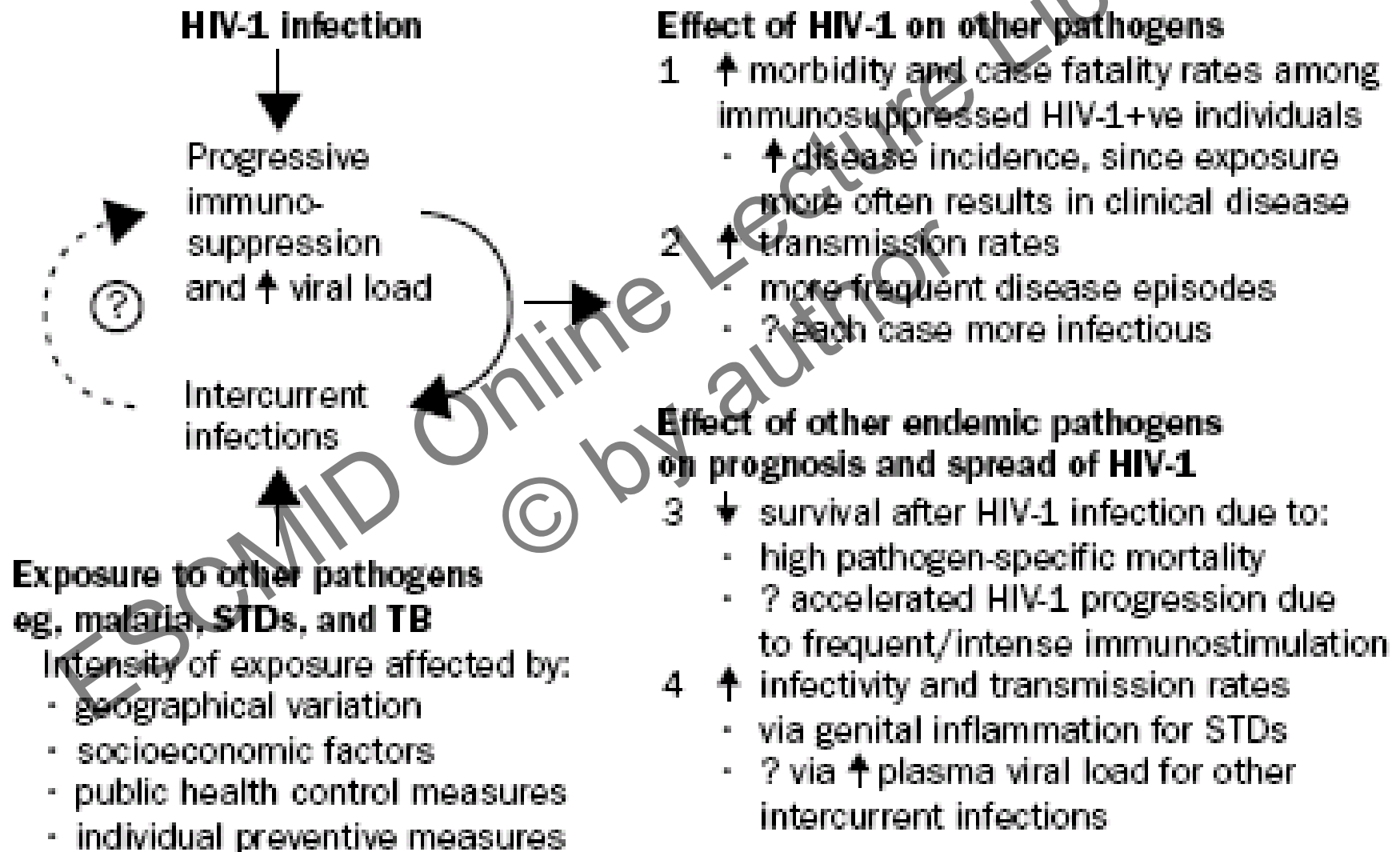
# **HIV/AIDS**

## **Coinfection with HIV and Tropical Infectious Diseases**

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- **The prevention strategies currently in use will not inflect HIV incidence among poorest populations, even though these prevention strategies have proven effective in settings from S. Francisco to Thailand or to Uganda and merits greater support.**
- **The risk to HIV stems less from ignorance and more from the precarious situations in which hundreds of millions live.**
- **Gender inequalities adds a special burden and is the main reason that, globally, HIV incidence is now higher among women than among men.**

# Coinfection with HIV and Tropical Infectious Diseases Potential Interactions



# Coinfection with HIV and Tropical Infectious Diseases

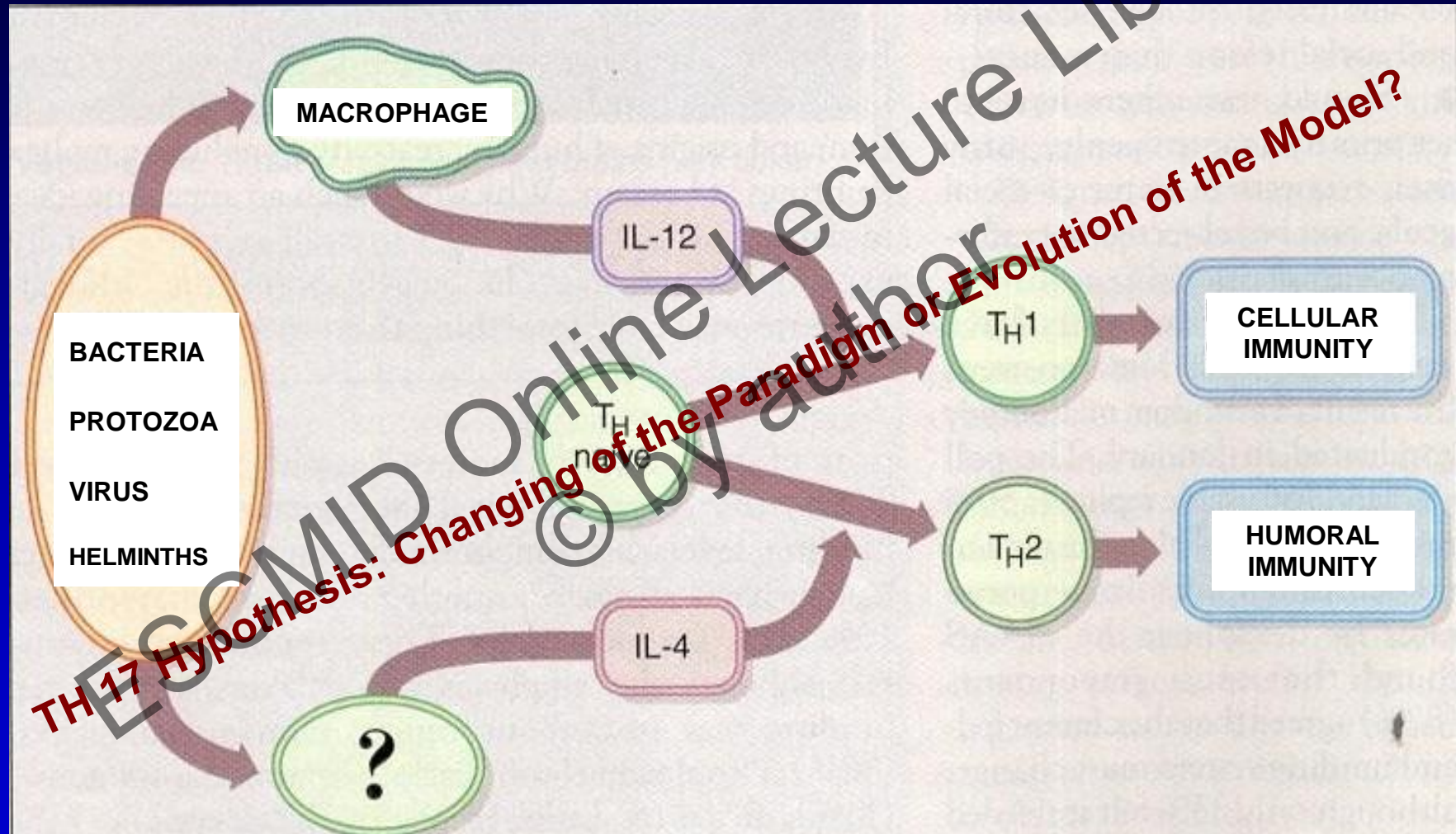
## Potential Interactions

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- High prevalence of parasitic infections in the tropics
- Geographic overlapping between HIV infection and parasitic diseases, suggesting bidirectional interactions between both entities.
- AIDS, malaria and tuberculosis are responsible for more than five million cases of disease and for more than 6 million death each year.
- When death from diarrhoeal disease and respiratory infections (5,8 million) are added, these five diseases alone are responsible for approximately 78% of the total infectious diseases burden.

# Coinfection with HIV and Tropical Infectious Diseases

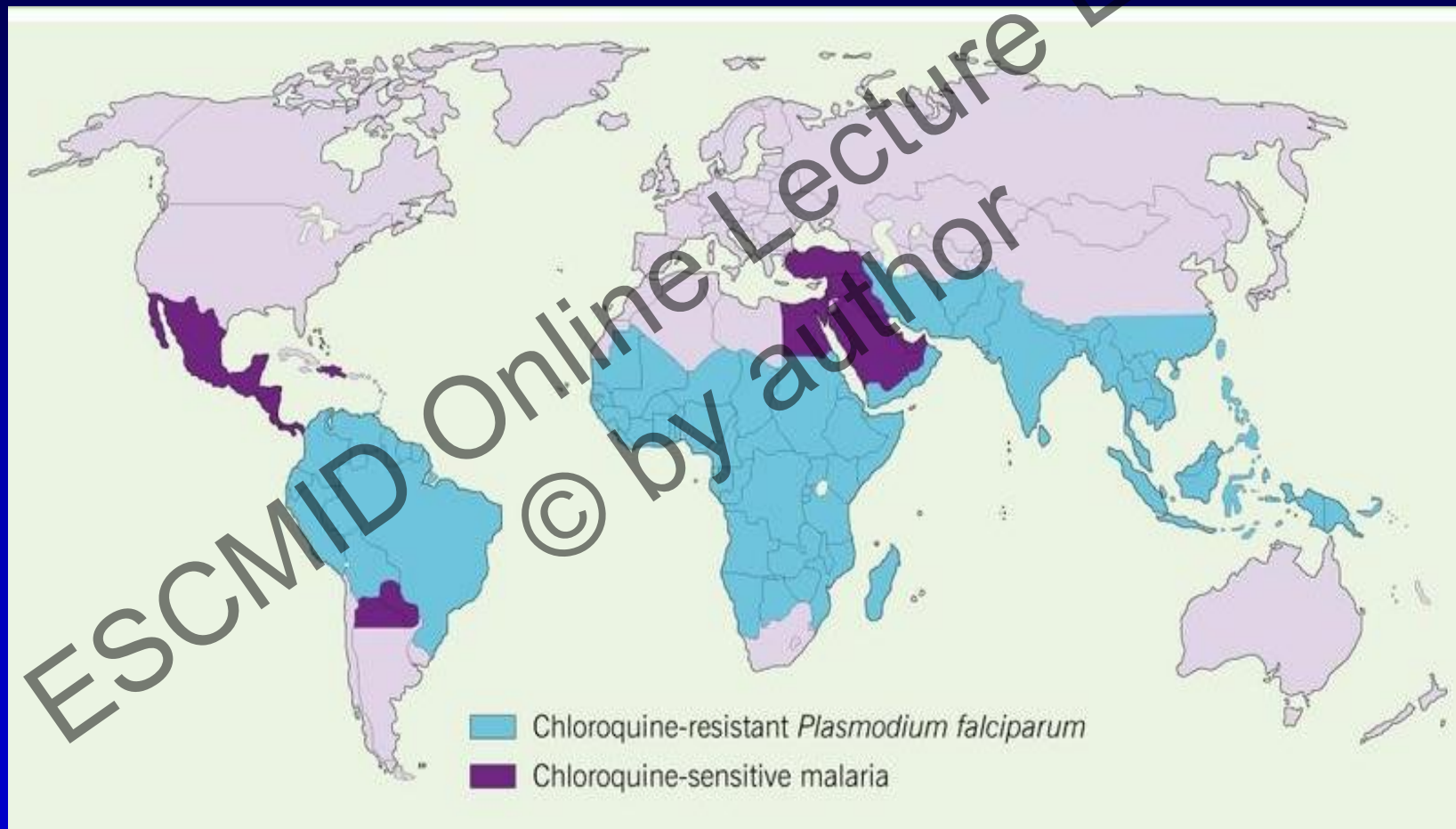
## Citokine-driven T Helper cell differentiation



# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Malaria

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# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Malaria

	Parasitaemia		
	N/total (%)	Odds ratio* (95% CI)	p
<b>HIV-1 status</b>			
HIV negative	231/3688 (6.3%)	1.0	
HIV positive	328/2788 (11.8%)	1.81 (1.43–2.29)	<0.0001
<b>Nearest CD4-cell count† (cells/μL)</b>			
≥500	115/1064 (10.8%)	1.0	
200–499	84/625 (13.4%)	1.37 (0.93–2.00)	
<200	35/259 (13.5%)	1.48 (0.80–2.43)	0.089
<b>WHO stage†</b>			
Stage 1	102/959 (10.6%)	1.0	
Stage 2	97/595 (16.3%)	1.76 (1.14–2.70)	
Stage 3	96/957 (10.0%)	1.05 (0.75–1.48)	
Stage 4	33/277 (11.9%)	1.34 (0.81–2.21)	0.56

\*Adjusted for age, sex, and pregnancy status. †HIV-positive individuals only.

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# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Malaria

	Clinical malaria		
	N/total (%)	Odds ratio* (95% CI)	p
<b>HIV-1 status</b>			
HIV negative	26/3688 (0.7%)	1.0	
HIV positive	55/2788 (2.0%)	2.56 (1.53-4.29)	0.0003
<b>Nearest CD4-cell count† (cells/<math>\mu</math>L)</b>			
$\geq$ 500	9/1064 (0.8%)	1.0	
200-499	15/625 (2.4%)	3.23 (1.32-7.94)	
<200	11/259 (4.2%)	6.12 (2.14-17.49)	0.0002
<b>WHO stage†</b>			
Stage 1	5/959 (0.5%)	1.0	
Stage 2	23/595 (3.9%)	8.59 (3.08-23.97)	
Stage 3	15/957 (1.6%)	3.63 (1.18-11.17)	
Stage 4	12/277 (4.3%)	9.34 (3.07-28.42)	0.0024

Table 2

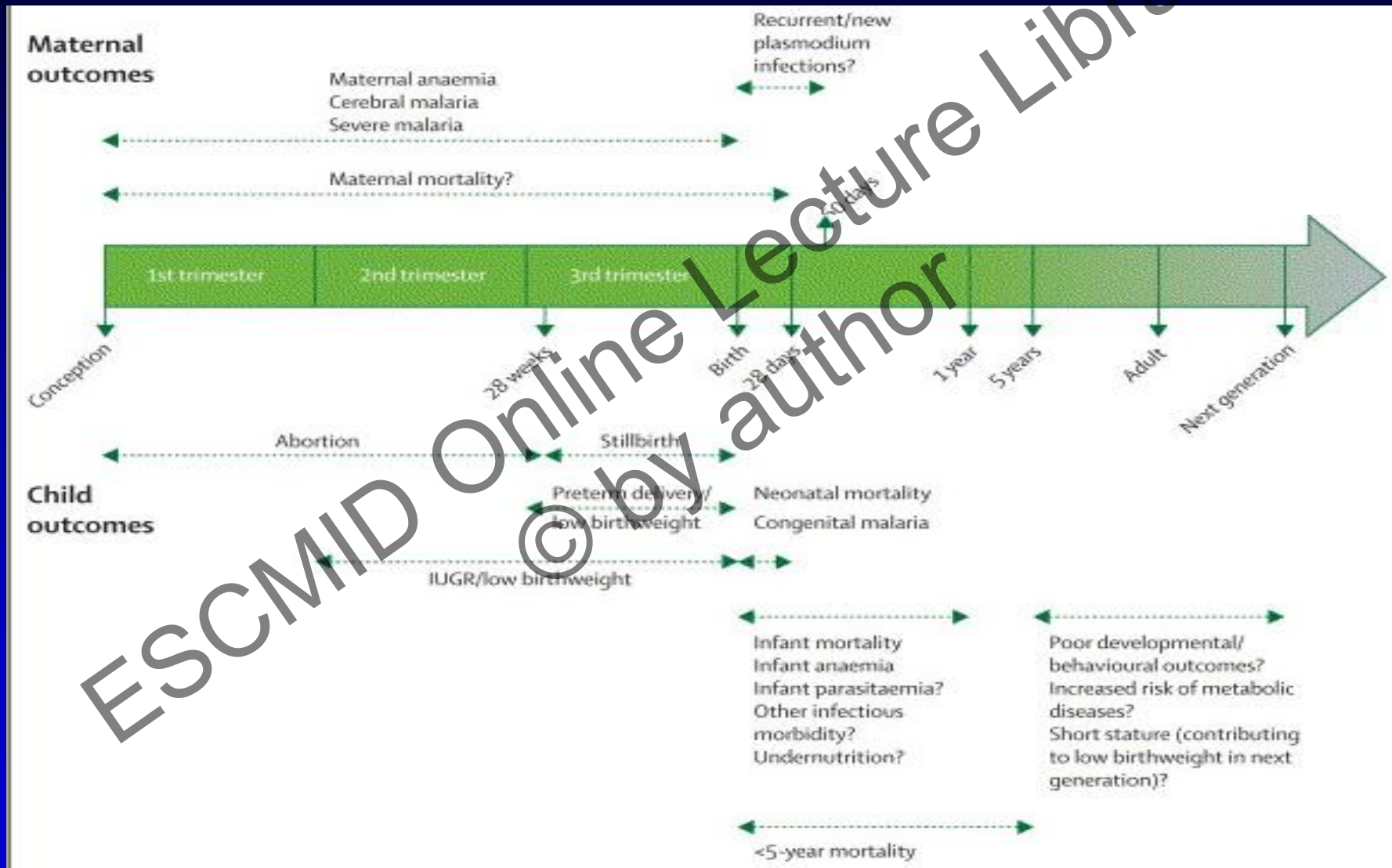
# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Malaria

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- It has been shown that malaria antigen immune activation of peripheral mononuclear cells of normal donors up-regulates HIV replication by 10-100 fold.
- Persons with malaria have a higher HIV-1 plasma viral load than individuals without malaria.
- A significant viral load decrease is achieved after antimalarial therapy.

# Coinfection with HIV and Tropical Infectious Diseases Malaria and Pregnancy



# Coinfection with HIV and Tropical Infectious Diseases

## HIV, Malaria and Pregnancy

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- In non-HIV infected women placental parasitaemia has been associated with:
  - Low birth weight;
  - Increased infant mortality in primigravidae.
- Immune responses do inhibit the parasite, however, and the effectiveness of uteroplacental immunity increases in subsequent pregnancies under the pressure of continued exposure to malaria.
- The beneficial effects (maternal, placental and neonatal) of parity on the control of malaria during pregnancy are attenuated/eliminated in the face of HIV coinfection.
- Placental malarial infection and maternal HIV infection appear to have a synergistic effect on infant mortality.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Malaria: treatment of uncomplicated malaria

### RECOMMENDATIONS

The treatment of choice for uncomplicated falciparum malaria is a combination of two or more antimalarials with different mechanisms of action.

ACTs are the recommended treatments for uncomplicated falciparum malaria.

The following ACTs are currently recommended:

- artemether-lumefantrine, artesunate + amodiaquine, artesunate + mefloquine, artesunate + sulfadoxine-pyrimethamine.

The choice of ACT in a country or region will be based on the level of resistance of the partner medicine in the combination:

- in areas of multidrug resistance (South-East Asia), artesunate + mefloquine or artemether-lumefantrine
- in Africa, artemether-lumefantrine, artesunate + amodiaquine; artesunate + sulfadoxine-pyrimethamine.

The artemisinin derivative components of the combination must be given for at least 3 days for an optimum effect.

Artemether-lumefantrine should be used with a 6-dose regimen.

Amodiaquine + sulfadoxine-pyrimethamine may be considered as an interim option in situations where ACTs cannot be made available.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Malaria: treatment of uncomplicated malaria in pregnancy

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### RECOMMENDATIONS

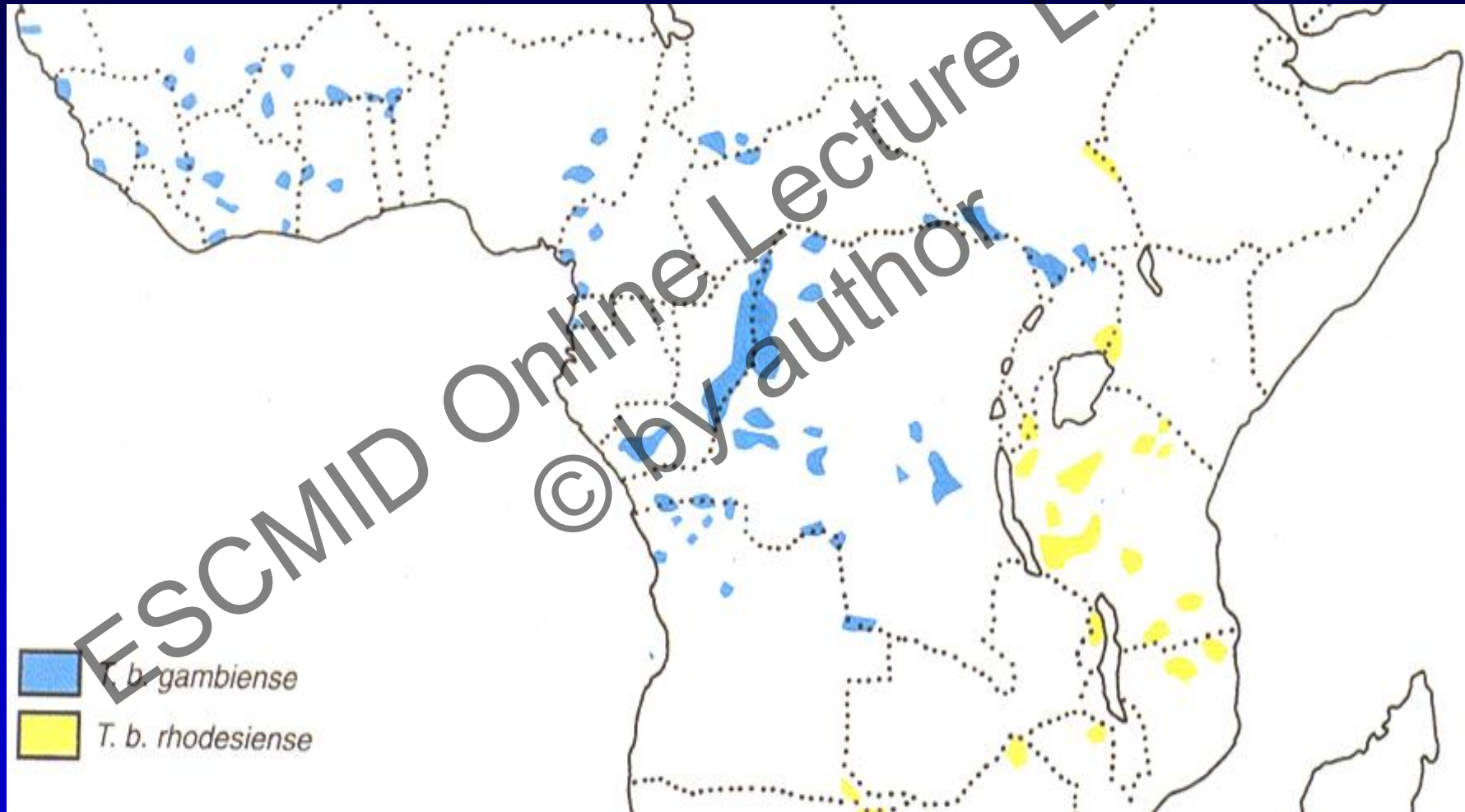
First trimester: quinine + clindamycin<sup>3</sup> to be given for 7 days.  
ACT should be used if it is the only effective treatment available.

Second and third trimesters: ACT known to be effective in the country/region or artesunate + clindamycin to be given for 7 days or quinine + clindamycin to be given for 7 days.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Human African Trypanosomiasis

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# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Human African Trypanosomiasis

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- Sleeping sickness caused by *Trypanosoma brucei gambiense* and *T. b. rhodesiense* and transmitted by the tsetse fly, puts ~ 60 million people at risk of infection in 36 countries of sub-Saharan Africa.
- An estimated 300 000 cases have been reported annually in the past years.
- *Trypanosoma brucei gambiense*: infections occur in limited foci and are sporadic.
- *Trypanosoma brucei rhodesiense*: sleeping sickness occurs in epidemics.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Human African Trypanosomiasis

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- Interaction between human african trypanosomiasis (HAT) is biologically plausible, since cell-mediated immunity is important in the host response to HAT.
- In cross-sectional studies no associations between HIV infection and *T. b. gambiense* infection was found.
- However, in one study, HIV-1 positive patients were significantly more likely to relapse after treatment with Eflornitine (DFMO), indicating that HIV positive persons may be at a higher risk for treatment failure than HIV seronegatives.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Chagas' disease

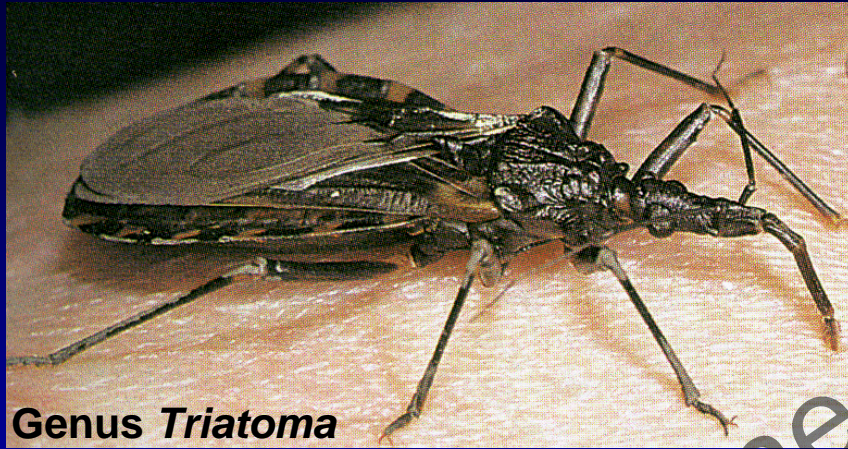
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*in Tropical Medicine and Parasitology. Mosby, 5 th edition 2002*

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Chagas' disease



The deep cracks in the mud walls provide ideal harbourage for large populations of *Rhodnius*, *Triatoma* or *Panstrongylus*

The disease is characterized by two phases: acute phase with high parasitaemia of *T. cruzi* and a chronic phase usually without detectable parasitaemia.

While CNS involvement is never observed in chronic Chagas' disease, it occurs in immunocompromised persons, as a result of reactivation of dormant *T. cruzi* infection acquired years earlier.

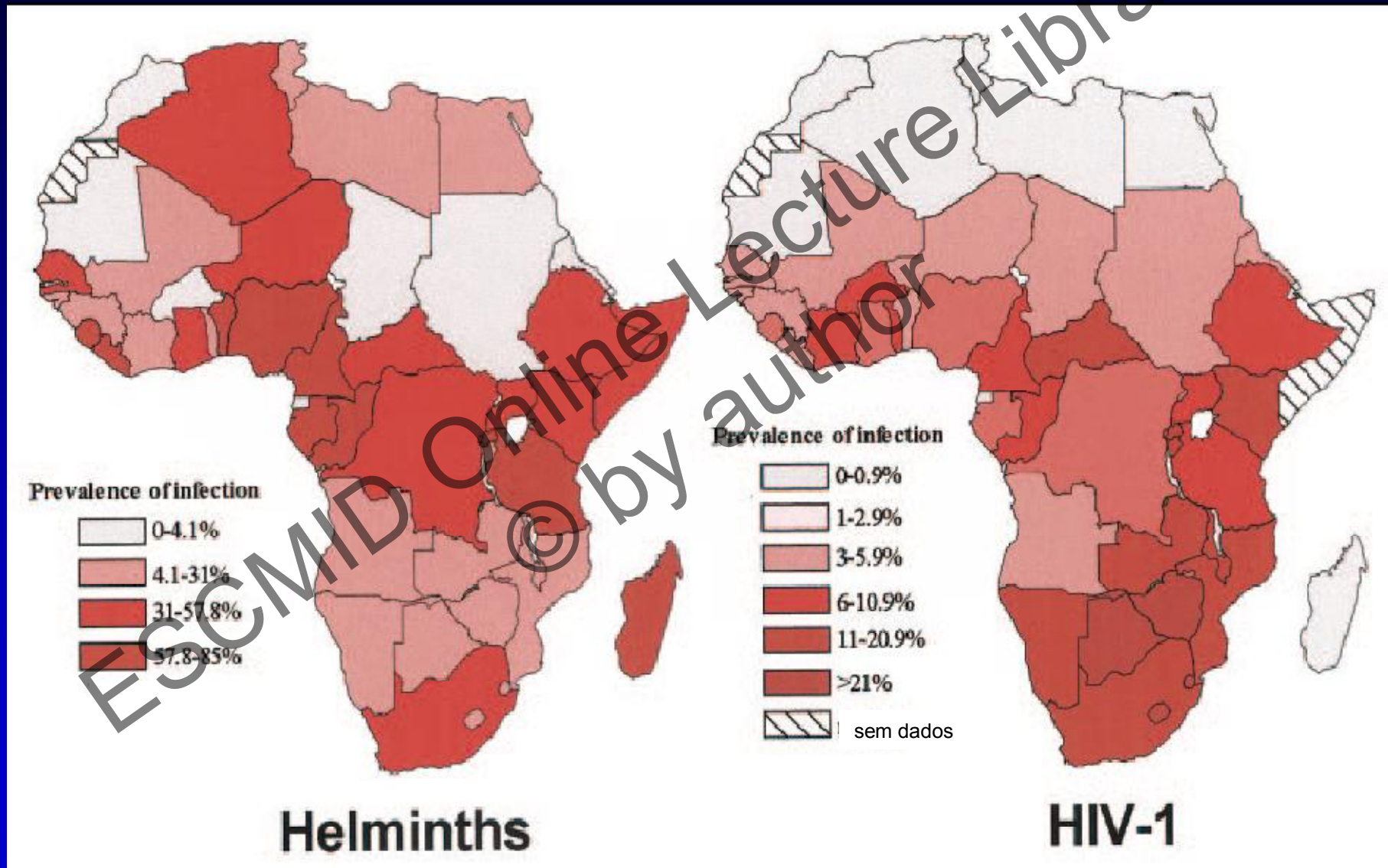
CNS manifestations include:

- Acute fatal meningoencephalitis;
- Tumoral lesions or a granulomatous encephalitis – brain chagoma.

Heart disease as the main clinical manifestation of *T. cruzi* reactivation with or without simultaneous CNS involvement has also been described.

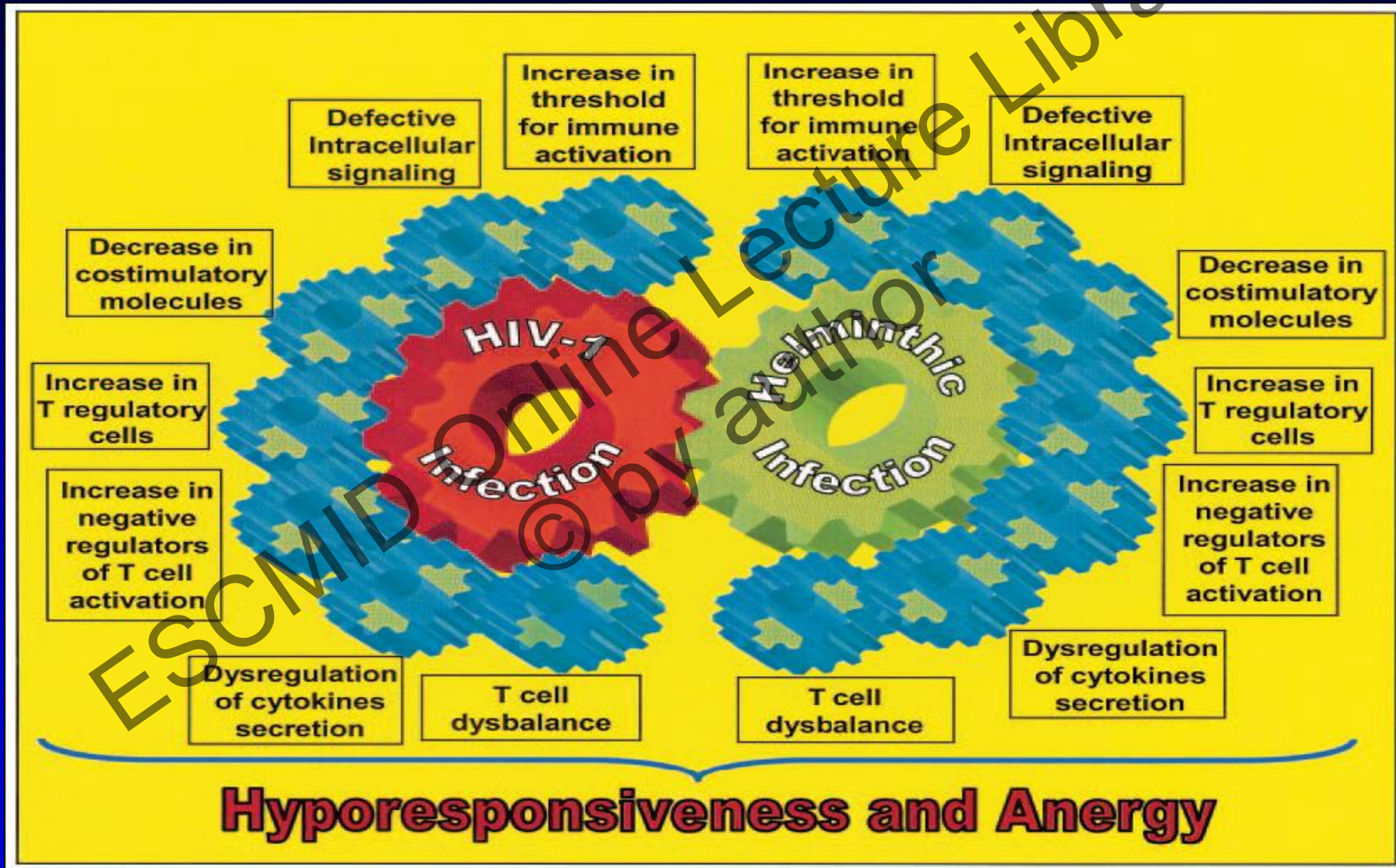
# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Intestinal Helminths: Africa



# Coinfection with HIV and Tropical Infectious Diseases

## Possible interference of helminthic and/or HIV-1 infection on the capacity of host immune response



# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Intestinal Helminths

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- The assumption that immune dysregulation associated with chronic helminthic infections alters the natural history of HIV infection in an unfavourable manner is sustained by results from a field study in Ethiopia:
  - HIV viral load is significantly higher in individuals with various helminthic infections than in individuals without helminths;
  - HIV infection correlated positively with the parasite load;
  - The viral load decreased after elimination of the worms by antiparasitic treatment.

## Coinfection with HIV and Tropical Infectious Diseases

### HIV and Intestinal Nematodes: *Strongyloides stercoralis*

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- Although strongyloidiasis has traditionally been considered a tropical disease, increased worldwide travel and migration challenge this view.
- *Strongyloides stercoralis* is the only nematode that has been implicated as the cause of an HIV-related opportunistic infection.
- Individuals can acquire the infection, usually at a younger age through skin penetration by the infective larvae from the soil and remain infected into adulthood. An internal autoinfestation cycle allows the parasite to reside within the asymptomatic host for years.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Intestinal Helminths: *Strongyloides stercoralis*

Host	Common signs and symptoms	Eosinophilia	Treatment
Normal immune system	<p>Gastrointestinal (most common): progressive weight loss, diarrhea, abdominal pain, vomiting</p> <p>Dermatologic: larva currens (perianal, rapidly moving and pruritic linear eruption due to migration of larvae); this symptom is pathognomonic of strongyloidiasis</p>	Usually present in ~70% of cases	Single drug: albendazole 400 mg twice daily × 7 d <i>OR</i> ivermectin 200 µg/kg daily × 1–2 d
Immunosuppressed	<p>Same as host with normal immune system</p> <p>Respiratory (most common outside the gastrointestinal tract): dyspnea, wheezing, hemoptysis, cough, respiratory distress</p> <p>Fever</p> <p>Gram-negative/polymicrobial bacteremia due to migration of larvae through the bowel wall</p>	Often absent	<p>Combination therapy: albendazole 400 mg twice daily × 7 d <i>AND</i> ivermectin 200 µg/kg daily × 1–2 d</p> <p>In cases of disseminated strongyloidiasis, albendazole and ivermectin are continued until there is evidence that the parasite is cleared</p>

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Intestinal Helminths: *Strongyloides stercoralis*

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### Box 1: Risk factors for disseminated strongyloidiasis

#### Major risk factors

Immunosuppressive therapy (particularly corticosteroids)

Transplantation

Hematologic malignant disease

Human T-lymphotropic virus-1 infection

#### Additional risk factors

Malnutrition

Diabetes mellitus

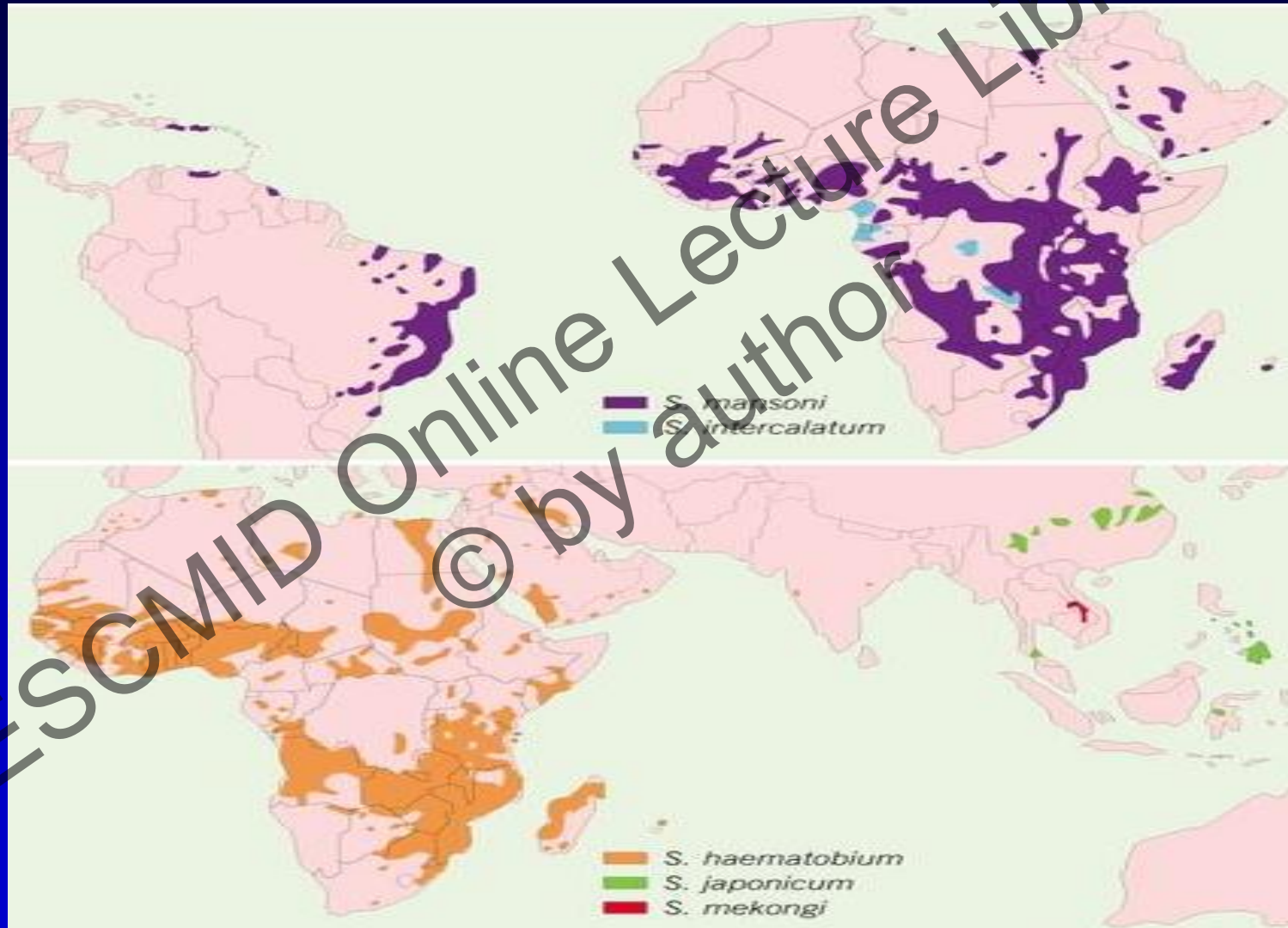
Chronic renal failure

Chronic alcohol consumption

Note: Some cases may have no identifiable risk factors for immunodeficiency.

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Intestinal Trematododes: *Schistosomiasis*



In Infectious Diseases, Mosby, 1st edition, 1999

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and Intestinal Trematododes: *Schistosomiasis*

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- To date there is no convincing evidence that any trematode infection is more frequent, severe or difficult to treat in the presence of HIV coinfection.
- Suppression of egg excretion is found in *Schistosoma mansoni* infected HIV seropositive individuals in Kenya, although the clinical and epidemiological significance of this observation remains unclear. In fact, egg excretion rates were significantly correlated with CD4 levels.
- There is pathophysiological, immunological and epidemiological evidence suggesting that genital schistosomiasis, a special form of *S. haematobium* infection, is a risk factor for the transmission of HIV, both in women and men, and presumably alters the natural history of HIV infection in a deleterious way.
- In women, genital schistosomiasis occurs in 60% of individuals infected with *S. haematobium*, involving the vulva, vagina and the cervix as well as upper genital organs and result in a pathology similar to that observed in some sexually transmitted infections.

Am J Trop Med Hyg 1997;56:515-521  
Intern J STD and AIDS 1994;5:368-72  
Lancet 2000;355:117-18

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and ectoparasites: *Sarcoptes scabiei* var *hominis*

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# Coinfection with HIV and Tropical Infectious Diseases

## HIV and *Mycobacterium leprae*



- Leprosy: infection of the skin and peripheral nerves by *M. leprae*.
- It continues to be a public health problem with ~410 000 new cases registered in 2004.
- India, Brazil, Congo, Nepal, Tanzania and Mozambique have the highest number of cases.
- There is little or no evidence on the possible interactions between HIV/AIDS and leprosy, although multibacillary disease may be overrepresented in those with concurrent HIV infection.

Clin Infect Dis 1999;28:947-65  
Lancet Infect Dis 2006;6:350-360  
*In Color Atlas and Synopsis of Clinical Dermatology*. McGraw-Hill, 1997

# Coinfection with HIV and Tropical Infectious Diseases

## HIV and *Mycobacterium leprae*

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- The published epidemiologic data are limited in quality but show neither an increased HIV prevalence among leprosy cases nor an alteration in clinical spectrum of leprosy among coinfecting patients.
- Leprosy has been reported presenting as immune reconstitution disease among patients commencing combined antiretroviral treatment.
- Observations suggest that cell-mediated immune responses to *M. leprae* are preserved at the site of disease despite evidence that these responses are abrogated systemically by contrast with tuberculosis, in which the host granulomatous response is impaired by HIV coinfection.
- These paradox may relate to differences between the activation state and rates of turnover within leprosy and tuberculosis granulomas that differentially affect the susceptibility of the granulomas to HIV.

## Coinfection with HIV and Tropical Infectious Diseases HIV and *Mycobacterium ulcerans*

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- Many other nontuberculosis mycobacteria have been demonstrated to cause opportunistic disease in HIV-1 infected patients.
- HIV does not appear to exacerbate disease due to *M. ulcerans*, the causative agent of Buruli ulcer in Africa.



*In Cabo Verde viagem pela história das ilhas. Edição Caminho 2003*