AETC AIDS Education & Training Center Program Southeast

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Kentucky AIDS Education Training Center

Opportunistic Infections in HIV

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Faculty Disclosure

- I have no financial disclosure or conflicts of interest with the presented material in this presentation

Educational Need/Practice Gap

Gap = Healthcare providers do not always adequately screen HIV-positive patients for or recognize clinical evidence for possible opportunistic infections.

Need = Our healthcare providers need strategies to assist them in recognizing the OI using current guidelines for the prevention and treatment of OI in Adults and Adolescents with HIV.

Objectives

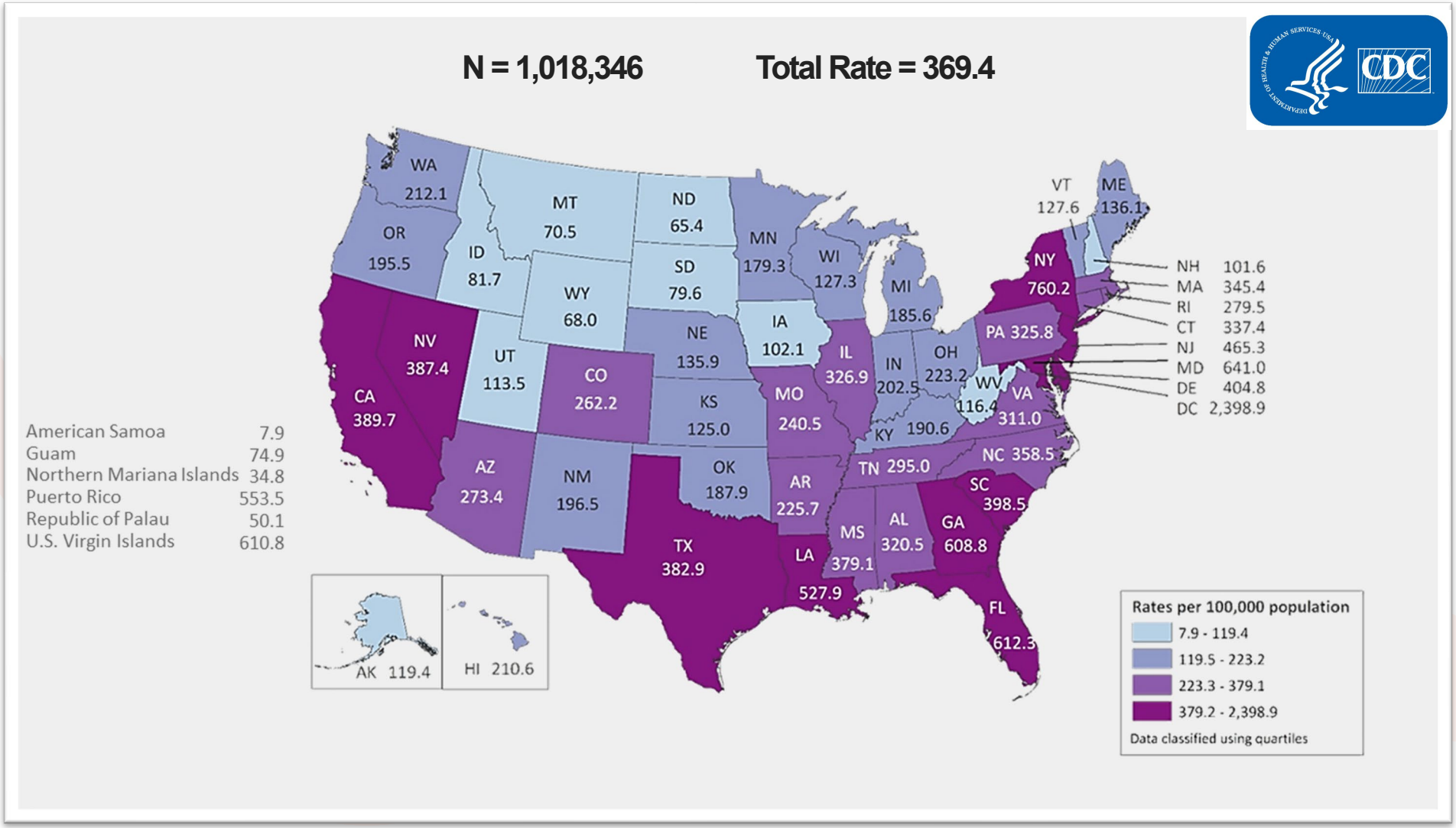
Upon completion of this educational activity, you will be able to:

- Recognize the clinical manifestations of common serious opportunistic infections (OI) that occur in persons with HIV
- Discuss recommendations for initiating and discontinuing primary prevention for OI in person with HIV
- Recognize potential adverse effects and contraindications for medications used as OI prevention

Expected Outcome

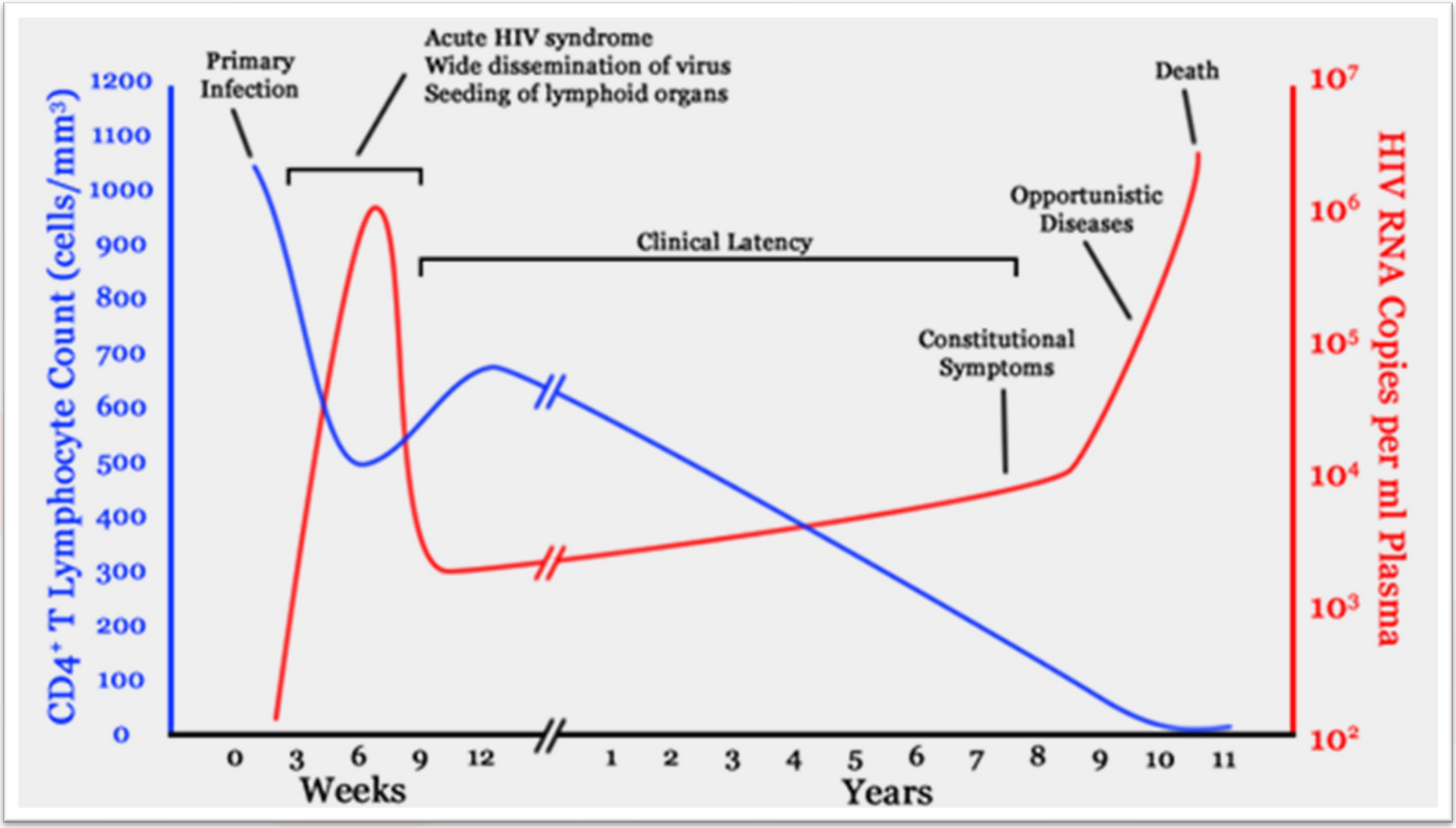
- As a result of this activity, learners should be better able to identify the signs/symptoms of OI in HIV-positive patients.

Rates of Adults and Adolescents Living with Diagnosed HIV Infection
Year-end 2017—United States and 6 Dependent Areas



Note. Data are based on address of residence as of December 31, 2017 (i.e., most recent known address).

HIV disease progression

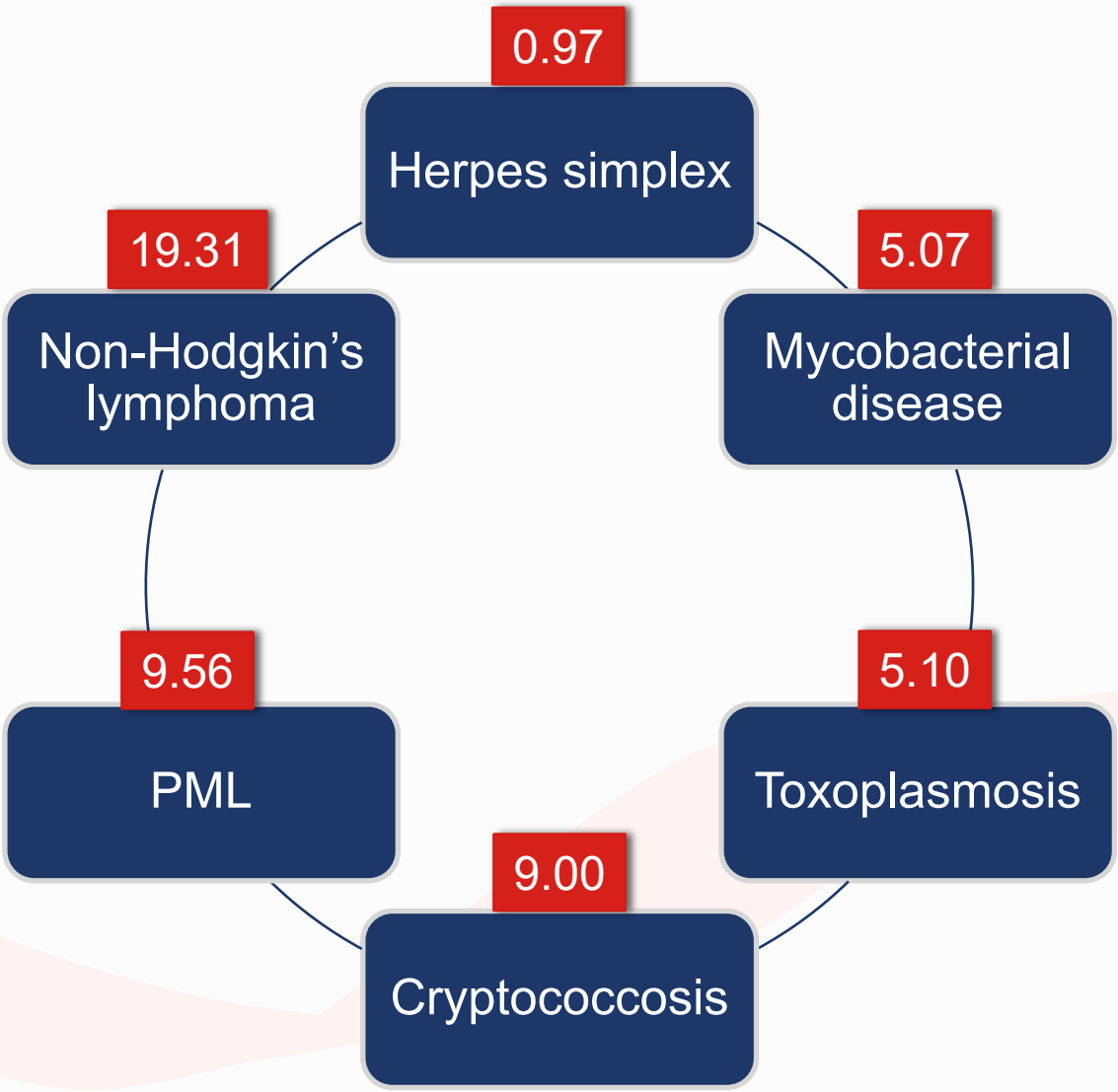


Opportunistic Infections and Malignancies Included in the 1982 Definition to Establish Diagnosis of Acquired Immunodeficiency Syndrome by the Centers for Disease Control and Prevention

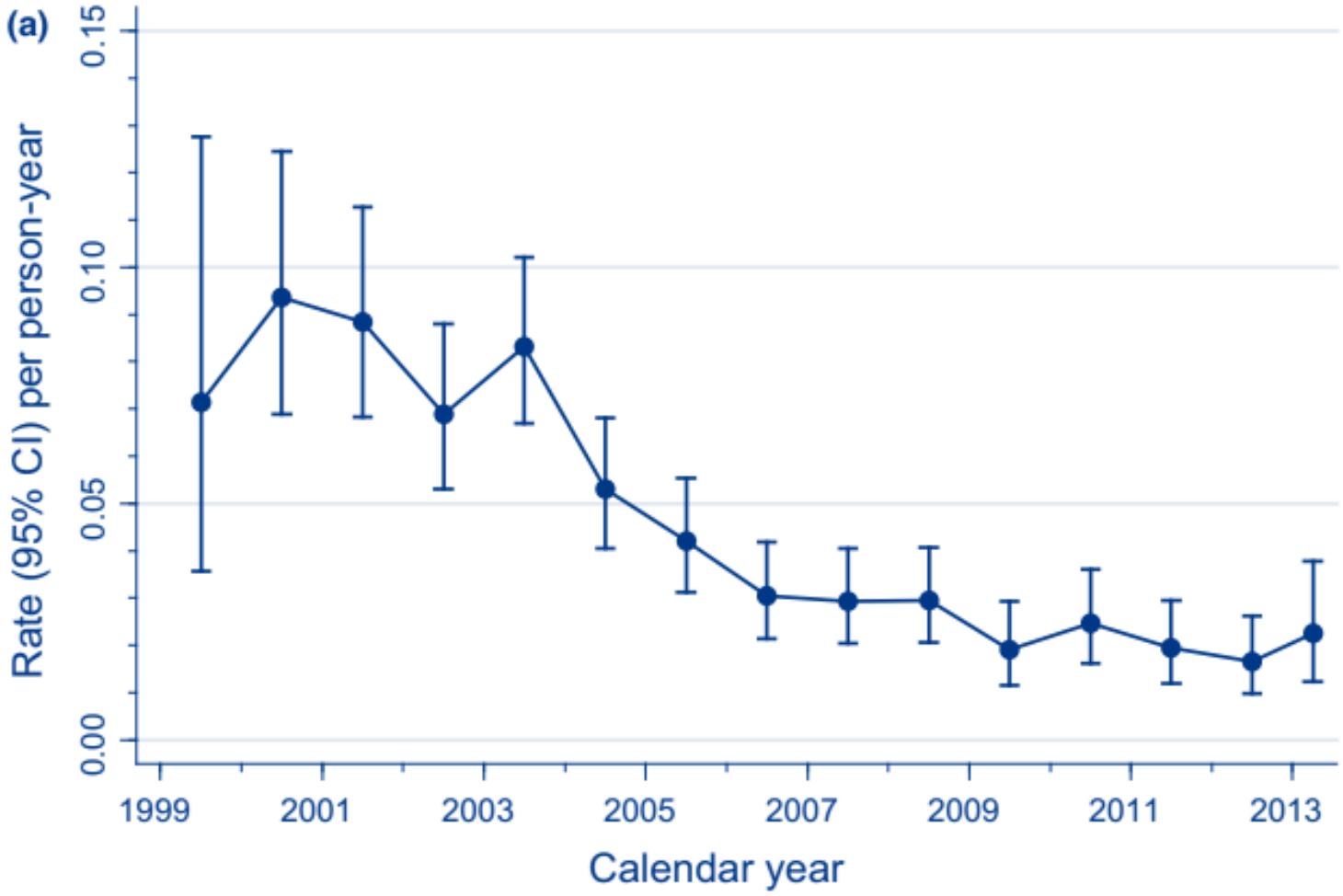
Infections
Atypical mycobacteria
Toxoplasmosis
Cryptosporidiosis
Strongyloidosis
Pneumocystis jirovecii
Candidiasis
Cryptococcus neoformans
Cytomegalovirus
Herpes simplex virus
Progressive multifocal leukoencephalopathy (John Cunningham virus-associated)
Malignancies
Kaposi sarcoma
Primary brain lymphoma

[a] Data derived from Selik et al,[4] Appendix.

Risk of Death Associated with ADEs Adjusted Hazard Ratio



Mocroft A, and ART Cohort Collaboration CROI 2007# 80

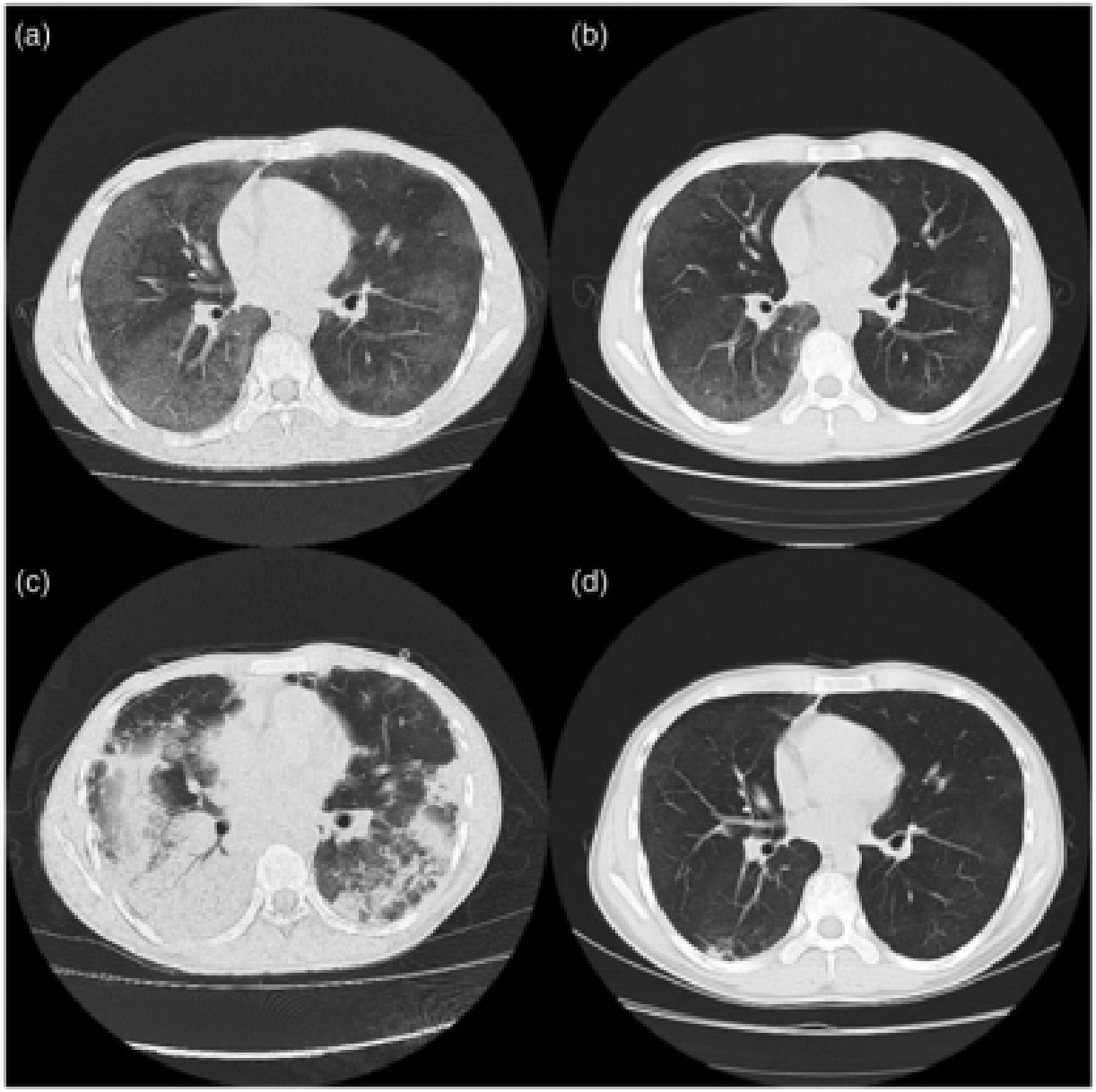

(a)
Rate (95% CI) per person-year
0.00
0.05
0.10
0.15
1999
2001
2003
2005
2007
2009
2011
2013
Calendar year

Case 1

- A 21-year-old man was referred to ED with a 20-day history of dyspnea and productive cough.
- He started empirical antibiotic treatment but the symptoms were not relieved.

- On admission, his vital signs were normal: temperature 36.5C; respiration rate 15 breaths/minute; pulse 70 beats/minute; and blood pressure 105/60 mmHg. Breath sounds in the bilateral lungs were rough without rales

- Chest computed tomography (CT) on the day of admission showed ground-glass opacities in the bilateral lungs.



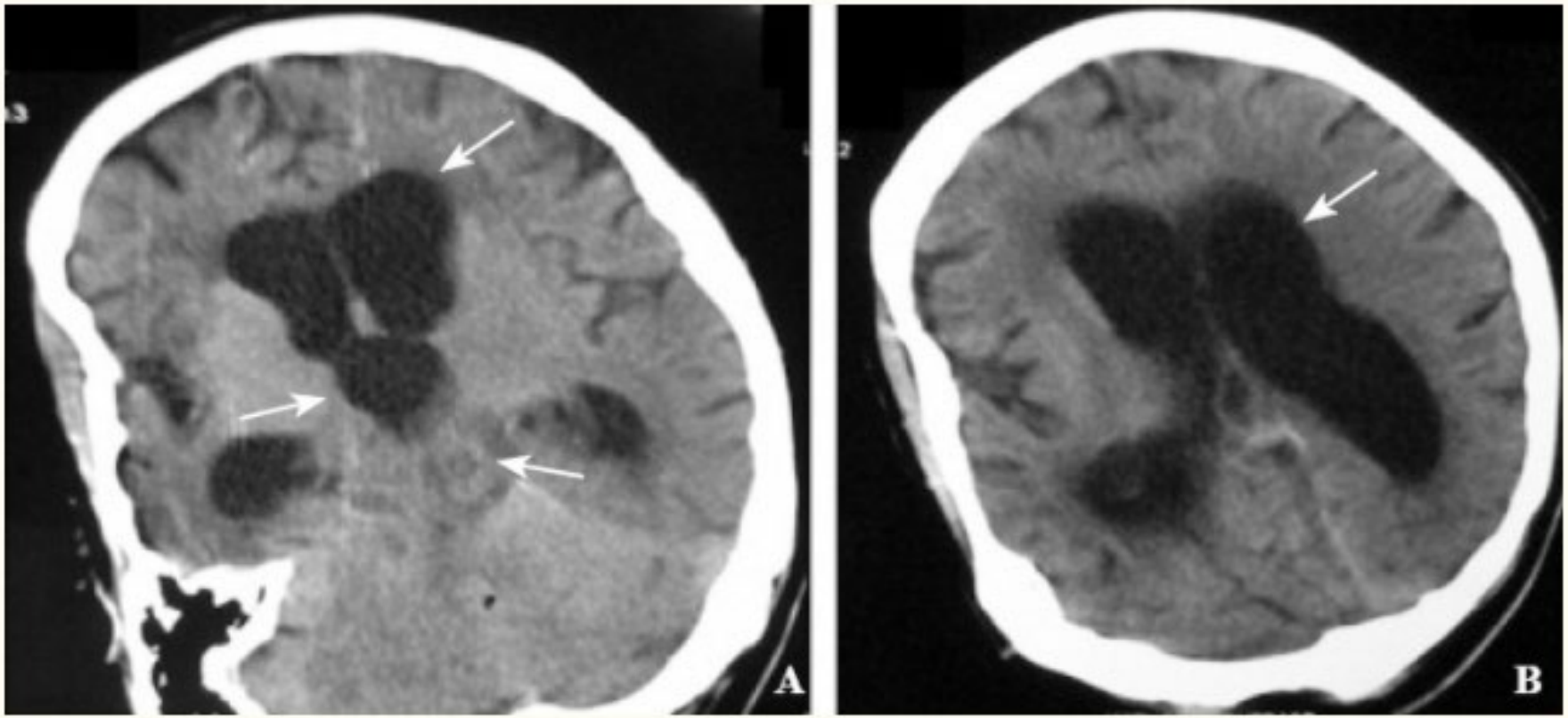
PNEUMOCYSTIS JIROVECII

- *Pneumocystis* pneumonia is caused by *Pneumocystis jirovecii*, a ubiquitous organism that has been classified as a fungus.
- Before the use of effective antiretroviral therapy and *Pneumocystis* pneumonia prophylaxis, PCP occurred in up to 80% of patients with AIDS.
- *Pneumocystis jirovecii* is most likely transmitted via the airborne route and disease occurs by acquisition of new infection or by reactivation of latent infection.
- The risk of developing *Pneumocystis* pneumonia increases markedly with advanced immunosuppression and approximately 90% of individuals with PCP have a CD4 count less than 200 cells/mm^3

Case 2

- 34-year-old man admitted to the emergency department with fever and altered mental status progressing for two days.
- His complaints began 7 days before with mild headache; after that he experienced progressive confusion, vomiting and a generalized tonic clonic seizure.

- On physical examination the patient was lethargic and quite ill. Upon admission to the emergency department, his body temperature was 38.5 ºC, blood pressure 110/70 mmHg, heart rate 102 beats/minute, respiratory rate 22/minute and oxygen saturation of 94% on room air. Bedside serum glucose level was 98 mg/dL.



Axial brain CT scan without IV contrast. (A, B) An ill-defined hypodense lesion is seen in left side of the midbrain extending to tectum (thick arrow), which causes an obstructive supratentorial hydrocephalus (thin arrows).

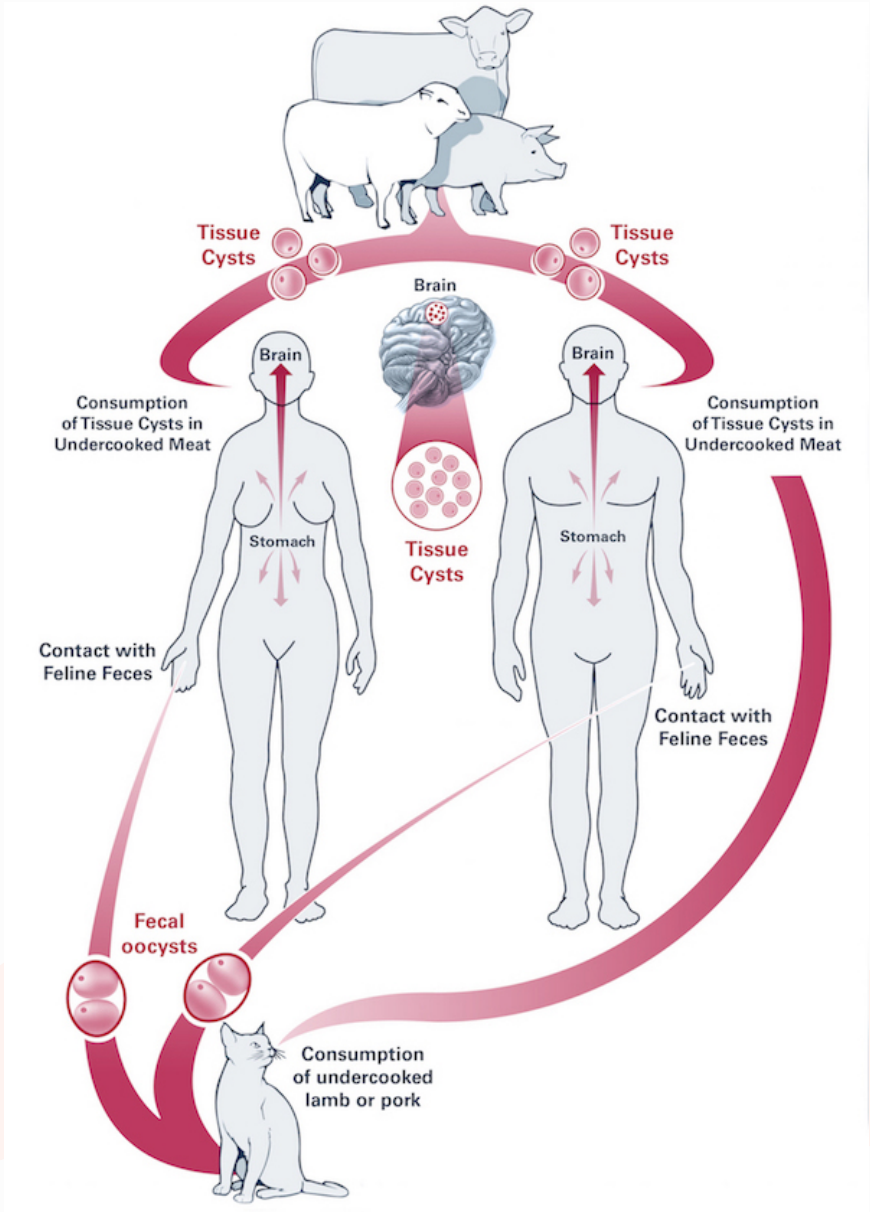
TOXOPLASMOSIS

- Most common cause of intracerebral lesions in persons with HIV.
- 15-30% of US population is seropositive.
- MRI shows that around 70% of cerebral toxoplasmosis lesions are multifocal. Although considered rare, single lesion may be present in 14% to 17% of AIDS patients.

Toxoplasmosis

- *Toxoplasma gondii* is a protozoan parasite that can infect humans and cause encephalitis and more rarely, retinitis, pneumonitis, and disseminated disease.

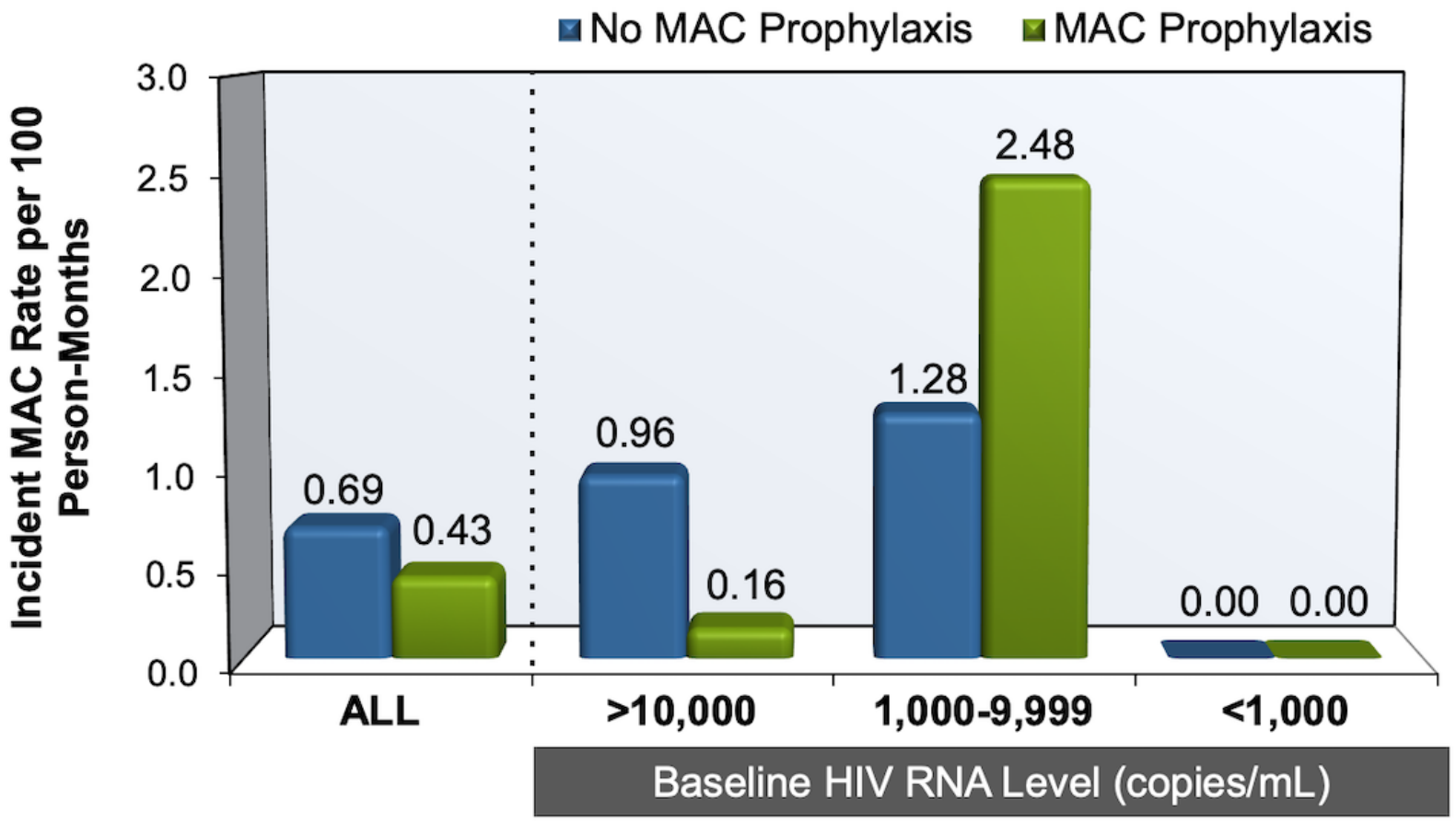
- Most cases of toxoplasmosis in persons with HIV result from reactivation of latent *T. gondii* cysts as immunity wanes.



DISSEMINATED *MYCOBACTERIUM AVIUM* COMPLEX

- *Mycobacterium avium* complex represents a group of nontuberculous mycobacteria that are ubiquitous in the environment.
- The mode of transmission is thought to occur via inhalation, ingestion, or inoculation via the respiratory or gastrointestinal tract. Most persons with HIV who are diagnosed with disseminated MAC have a CD4 count less than 50 cells/mm^3

Mycobacterium avium Complex Infection Rate in the HIV Outpatient Study, 1996-2007



CRYPTOCOCCAL MENINGITIS

- The global disease burden is high, with an estimated 223,100 cases of cryptococcal meningitis occurring in 2014, mostly in sub-Saharan Africa; this estimated number of cases is significantly lower than the 957,900 cases per year estimated in 2008.
- Caused by *Cryptococcus neoformans*
- Adult and Adolescent Opportunistic Infection Guidelines
  - *Recommend routine serum cryptococcal antigen (CrAg) testing on all patients with a CD4 count less than 100 cells/mm^3*

CYTOMEGALOVIRUS

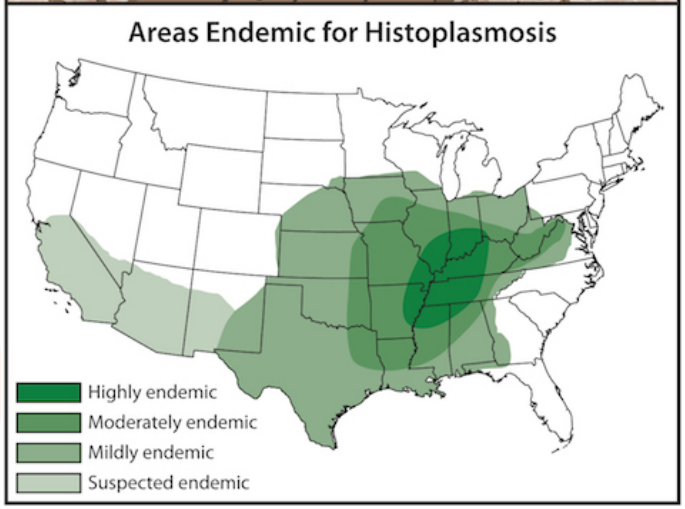
- Cytomegalovirus (CMV) is a double-stranded DNA herpes virus that can cause invasive disease in persons with HIV, including CMV retinitis, colitis, esophagitis, and neurologic disease.

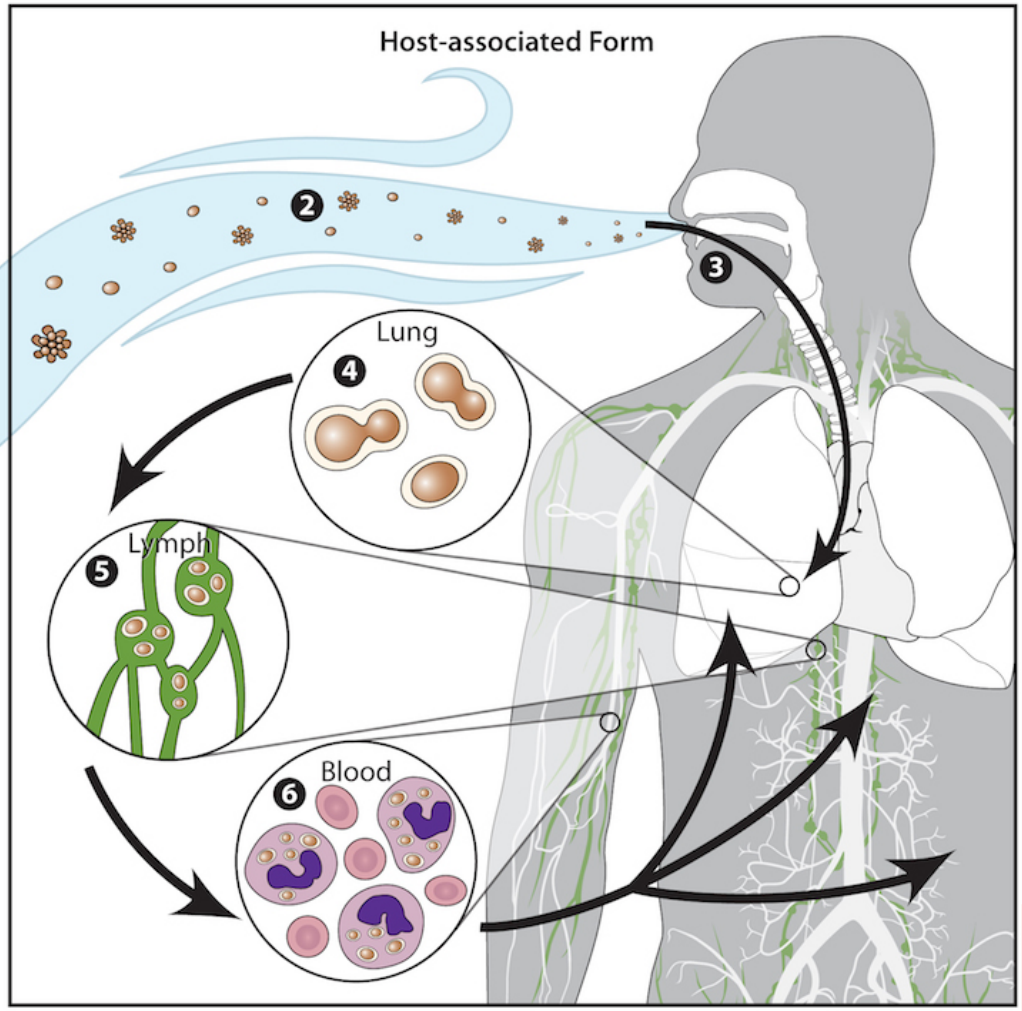
- Risk factors for the development of clinical CMV disease include previous opportunistic infections, a high HIV RNA level (greater than 100,000 copies/mL) and a high level of CMV viremia.

HISTOPLASMOSIS

- Histoplasmosis is a fungal infection caused by *Histoplasma capsulatum*, which is the most common endemic mycosis in the United States.
- Most cases of histoplasmosis in persons with HIV result from reactivation of latent *Histoplasma* infection after the CD4 count has declined to less than 150 cells/mm^{3}.

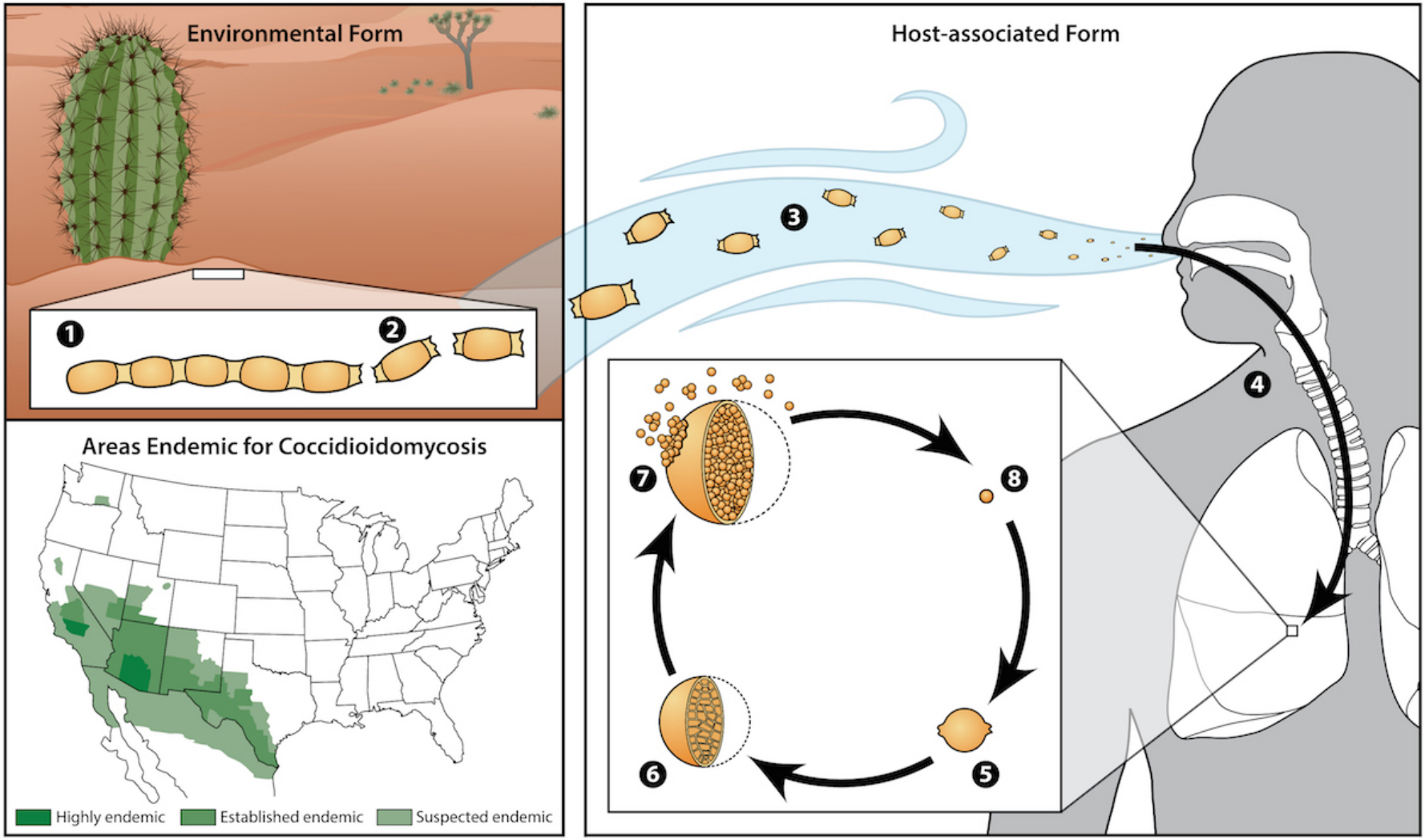

Environmental Form
1


Areas Endemic for Histoplasmosis
Highly endemic
Moderately endemic
Mildly endemic
Suspected endemic


Host-associated Form
2
3
Lung
4
Lymph
5
Blood
6

COCCIDIOIDOMYCOSIS

- Coccidioidomycosis is caused by a soil-dwelling fungus, *Coccidioides immitis*, and encompasses a wide spectrum of clinical disease among individuals with HIV.
- The risk of developing symptomatic coccidioidomycosis is significantly increased in persons with HIV who have a CD4 count less than 250 cells/mm^3 and live (or have lived) in a region endemic for coccidioidomycosis.

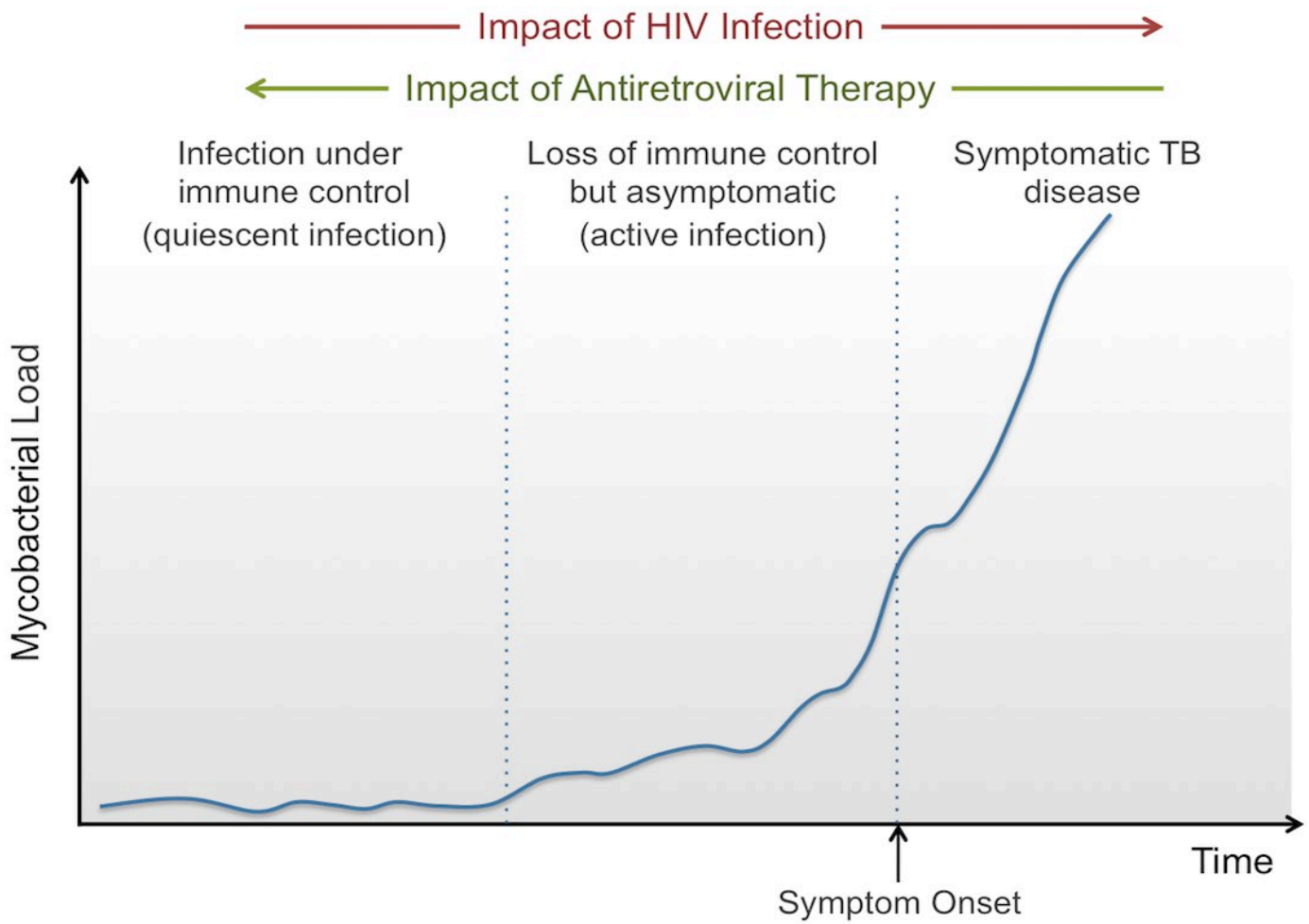

Environmental Form
1
2
Areas Endemic for Coccidioidomycosis
Highly endemic
Established endemic
Suspected endemic
Host-associated Form
3
4
5
6
7
8

Criteria for Starting, Discontinuing, and Restarting Opportunistic Infection Prophylaxis for Adults with HIV

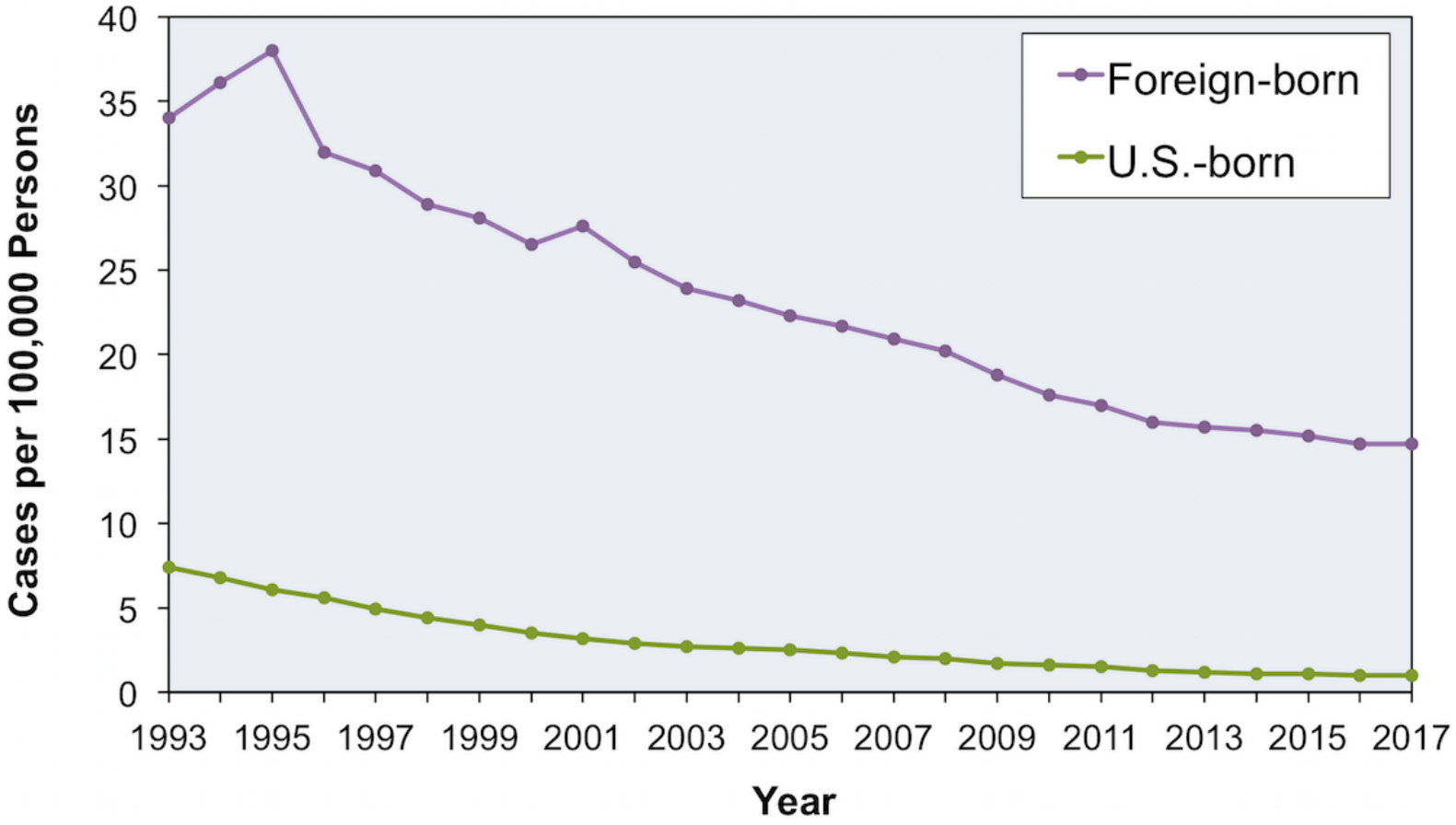
OI	Criteria for Initiating Primary Prophylaxis	Criteria for Discontinuing Primary Prophylaxis	Criteria for Restarting Primary Prophylaxis	Criteria for Initiating Secondary Prophylaxis	Criteria for Discontinuing Secondary Prophylaxis	Criteria for Restarting Secondary Prophylaxis
PCP	CD4 < 200 or oral candidasis	CD4 > 200 for 3 mos	CD4 < 200	Prior PCP	CD4 > 200 for 3 mos	CD4 < 200
Toxoplasmosis	+ serum IgG CD4 < 100	CD4 > 200 for 3 mos	CD4 < 100 – 200	Prior toxoplasmic encephalitis	CD4 > 200 sustained and completed initial therapy and is asymptomatic	CD4 < 200
MAC	CD4 < 50	CD4 > 100 for 3 mos	CD < 50 – 100	Documented disseminated disease	CD4 > 100 sustained and completed 12 mos of MAC tx and asymptomatic	CD4 < 100
Cryptococcosis	none	n/a	n/a	Documented disease	CD4 > 100 – 200 sustained and completed initial therapy and asymptomatic	CD4 < 100 - 200
Histoplasmosis	none	n/a	n/a	Documented disease	No criteria recommended for stopping	n/a
CMV	none	n/a	n/a	Documented end-organ disease	CD4 > 100 – 150 sustained and no evidence of active disease and regular exams	CD4 < 100 - 150

Latent Tuberculosis Infection

Host Immune Control in Person with LTBI



Tuberculosis Case Rates per 100,000 Population by Origin of Birth—United States, 1993–2017



LTBI TESTING IN PERSONS WITH HIV*

- All persons with HIV should undergo testing for LTBI at the time of HIV diagnosis, regardless of their epidemiological risk of TB exposure.
- The tuberculin skin test or IGRA can be used as the screening method for LTBI.
- Annual testing for LTBI is recommended for persons with HIV who are at high risk for repeated or ongoing exposure to persons with active TB.
- Persons with HIV and advanced immunosuppression (CD4 count less than 200 cells/mm^3) who have negative tuberculin skin test result should undergo repeat testing for latent tuberculosis infection after they start on antiretroviral therapy and have an increase in CD4 count to 200 cells/mm^3 or greater.
- The routine use of both tuberculin skin test and IGRAs to screen for LTBI is not recommended in the United States.
- All persons with a positive tuberculin skin test or IGRA should be evaluated for the possibility of active TB disease.

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