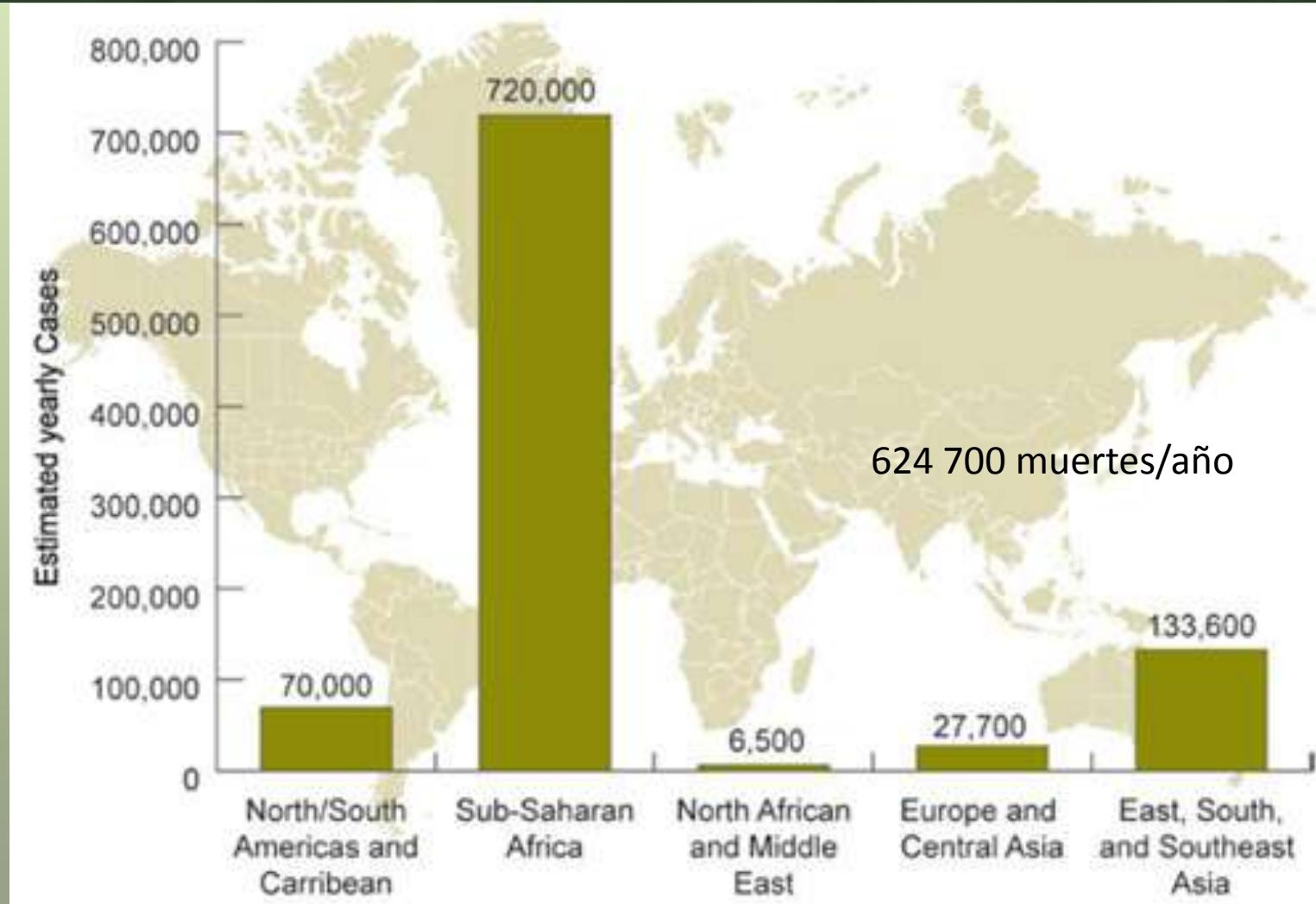


# **“Cryptococcus y Criptococcosis: el despertar del gigante”**

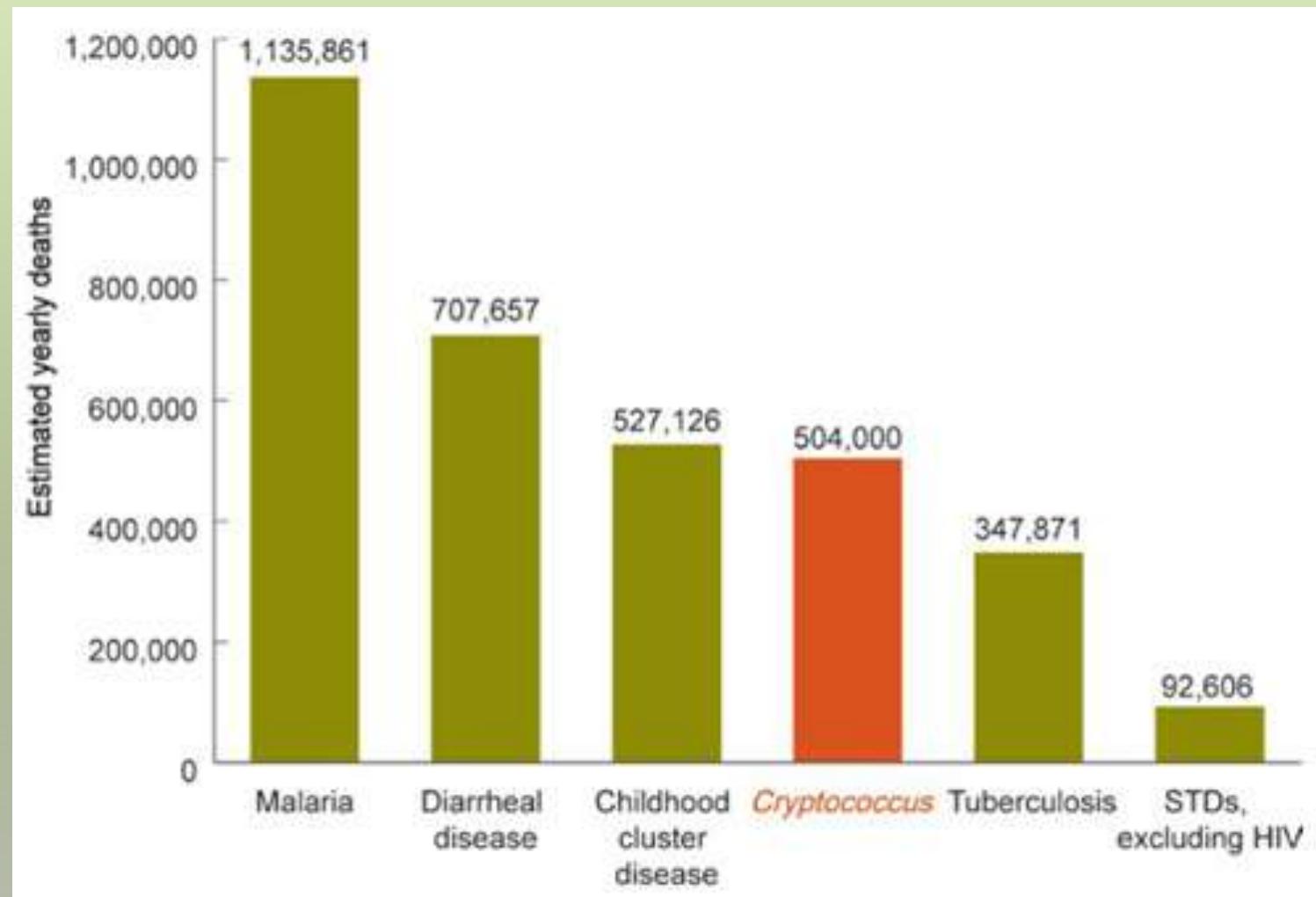
**Dr. Juan Villalobos V.**  
**Servicio Infectología**  
**Hospital México-CCSS**  
**Costa Rica**

# Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS

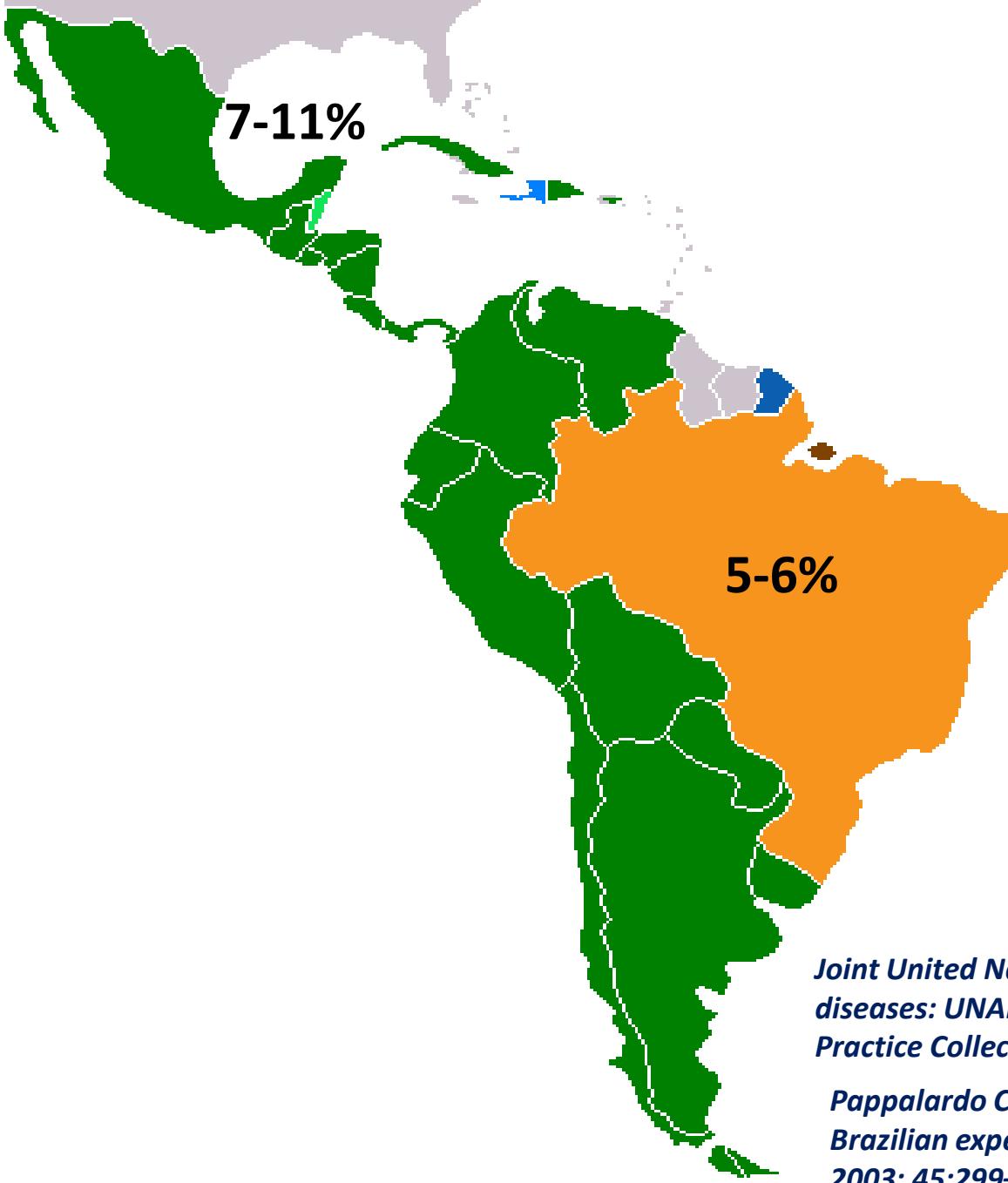


*BJ Park et al. Estimation of the global burden of cryptococcal meningitis among persons living with HIV/AIDS AIDS 2009; 23:525-530.*

# Comparation of deaths in sub-Saharan Africa due to HIV related cryptococcosis



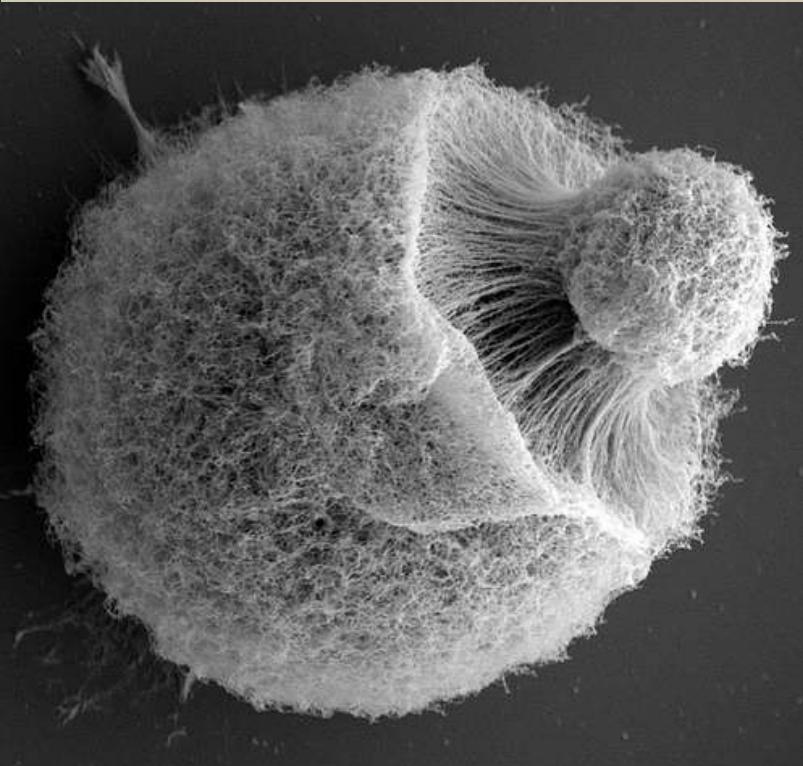
*BJ Park et al. Estimation of the global burden of cryptococcal meningitis among persons living with HIV/AIDS AIDS 2009; 23:525-530.*



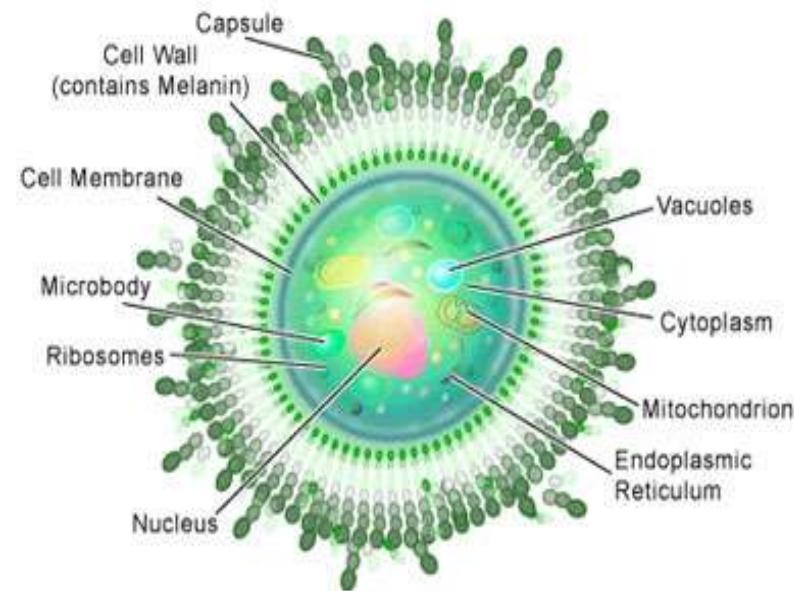
## Incidencia de Criptococcosis en pacientes con VIH/SIDA en Latinoamérica

*Joint United Nations Programme on HIV/AIDS. HIV-related opportunistic diseases: UNAIDS technical update. UNAIDS Web site 1998 October; Best Practice Collection:1–9. <http://www.unaids.org>. Accessed 11 June 2008.*

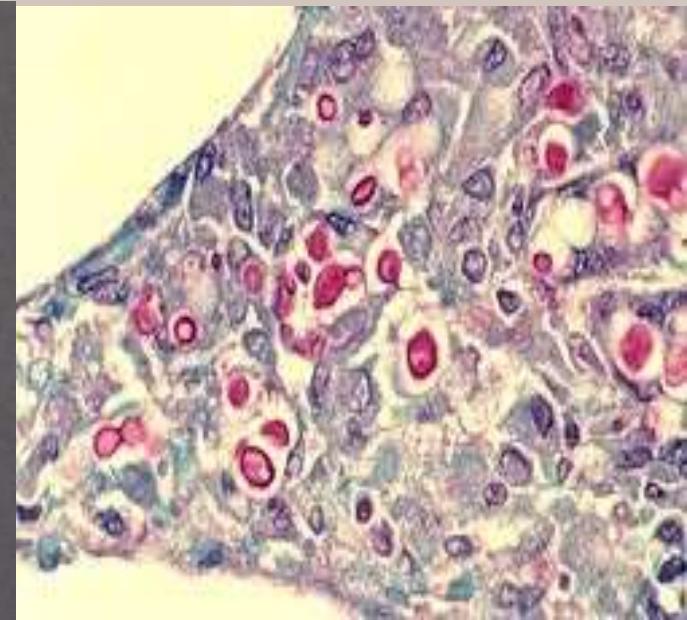
*Pappalardo CSM, Melhem MSC. Cryptococcosis: a review of the Brazilian experience for the disease. Rev Inst Med Trop Sao Paulo 2003; 45:299–305.*



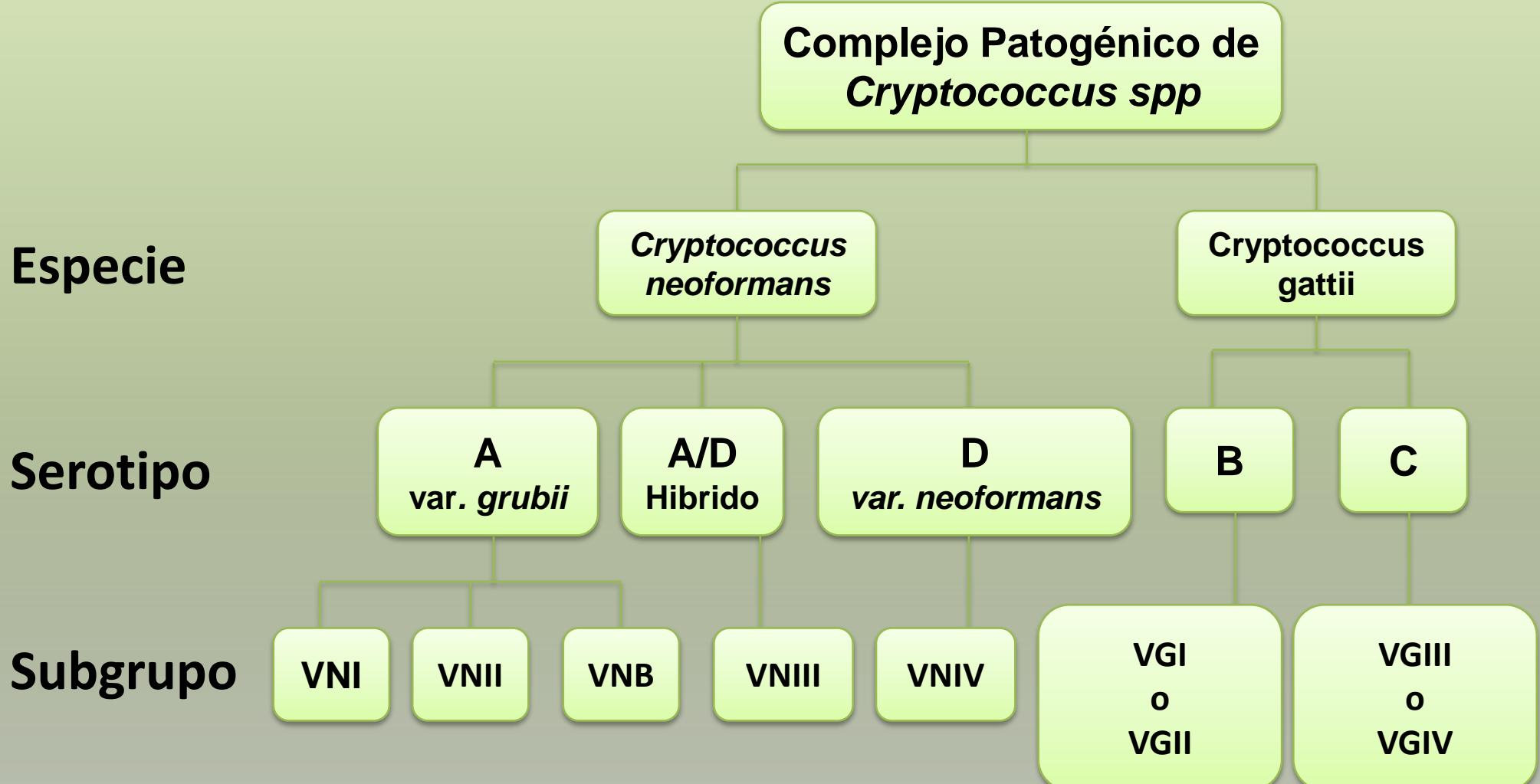
Las levaduras de *Cryptococcus* son esféricas u ovaladas, con 5–10 µm de diámetro, poseen una prominente capsula de polisacáridos que es su mas importante factor de virulencia.



C



# Relación y nomenclatura de las especies patógenas de *Cryptococcus*

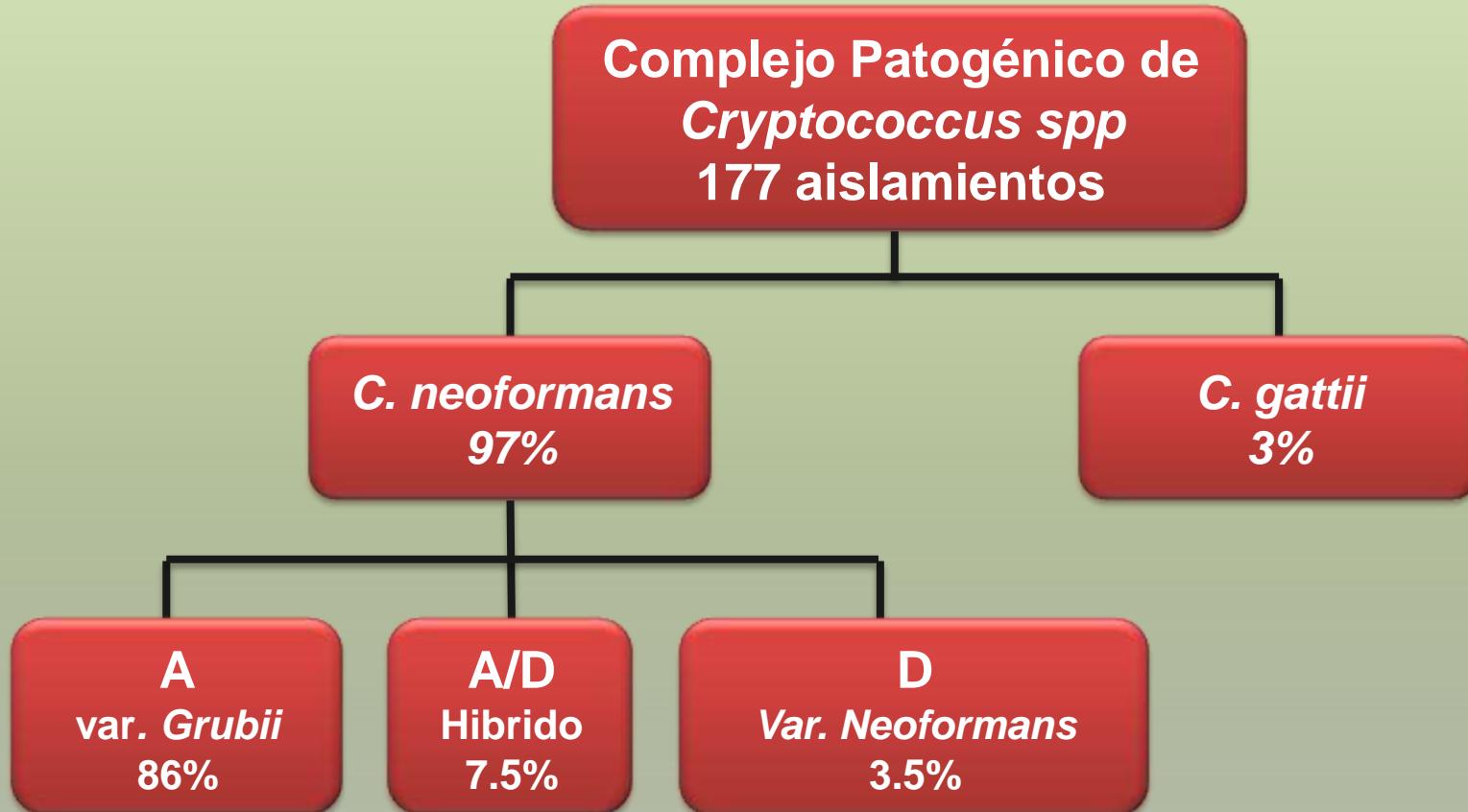


# Especies y Serotipos predominantes en Latinoamérica



Meyer W, Castaneda A, Jackson S, Huynh M, Castaneda  
E. Molecular typing of IberoAmerican *Cryptococcus*  
*neoformans* isolates. *Emerg Infect Dis* 2003; 9:189–195.

# Especies y Serotipos predominantes en Latinoamérica

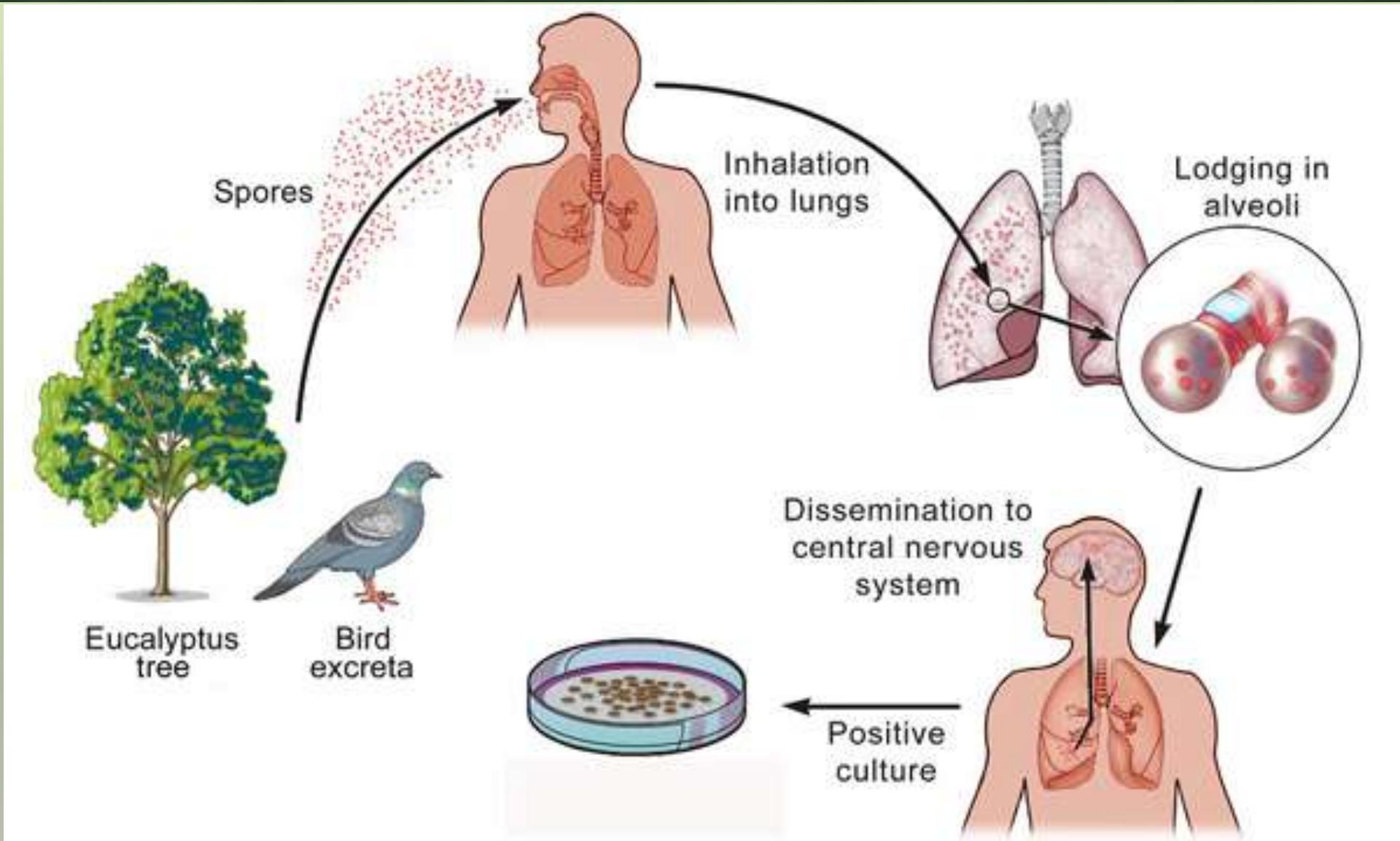


Meyer W, Castaneda A, Jackson S, Huynh M, Castaneda E. Molecular typing of IberoAmerican *Cryptococcus neoformans* isolates. *Emerg Infect Dis* 2003; 9:189–195.

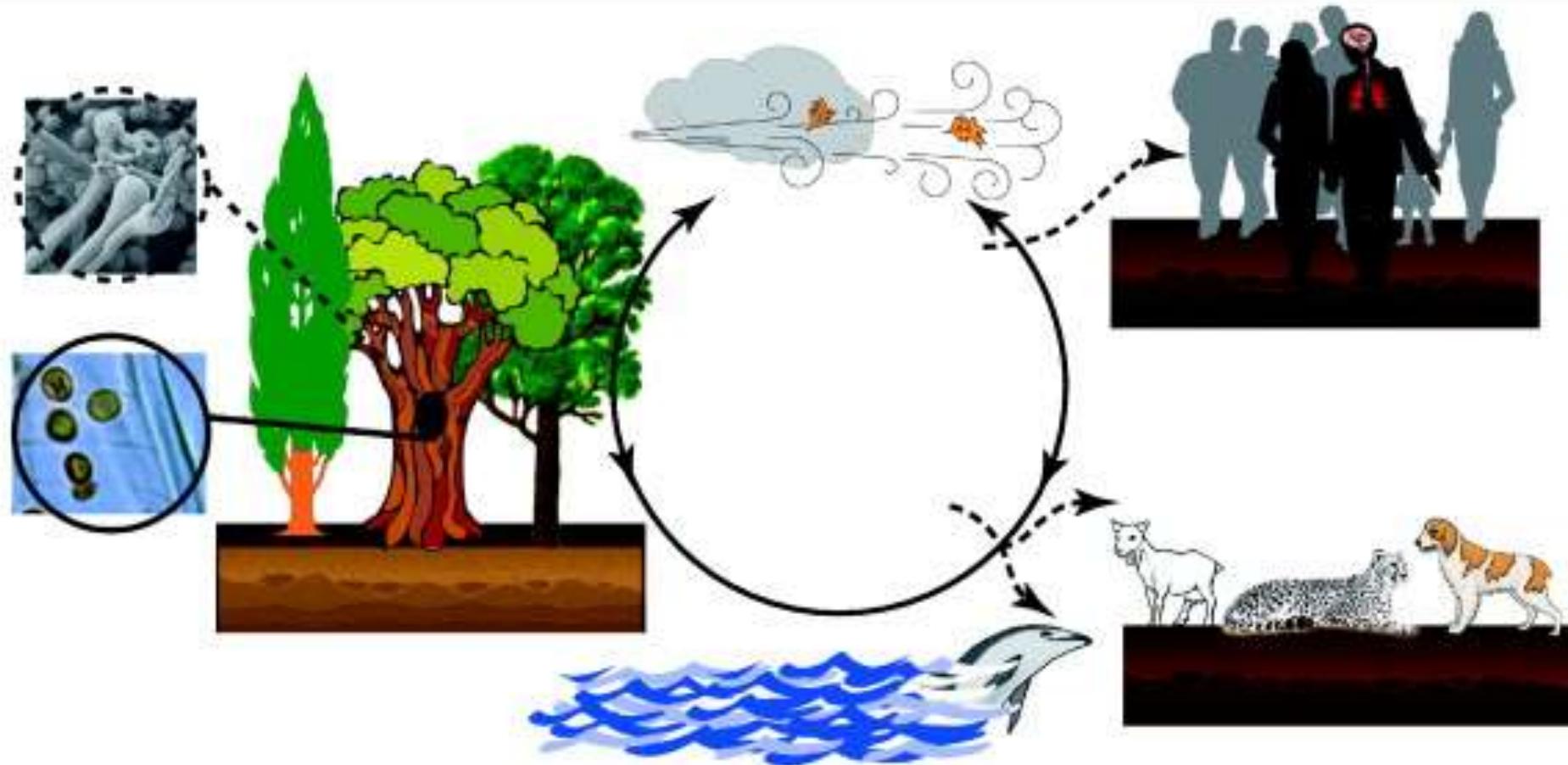
# Especies de Criptococcus aisladas de muestras clínicas Costa Rica - 2012



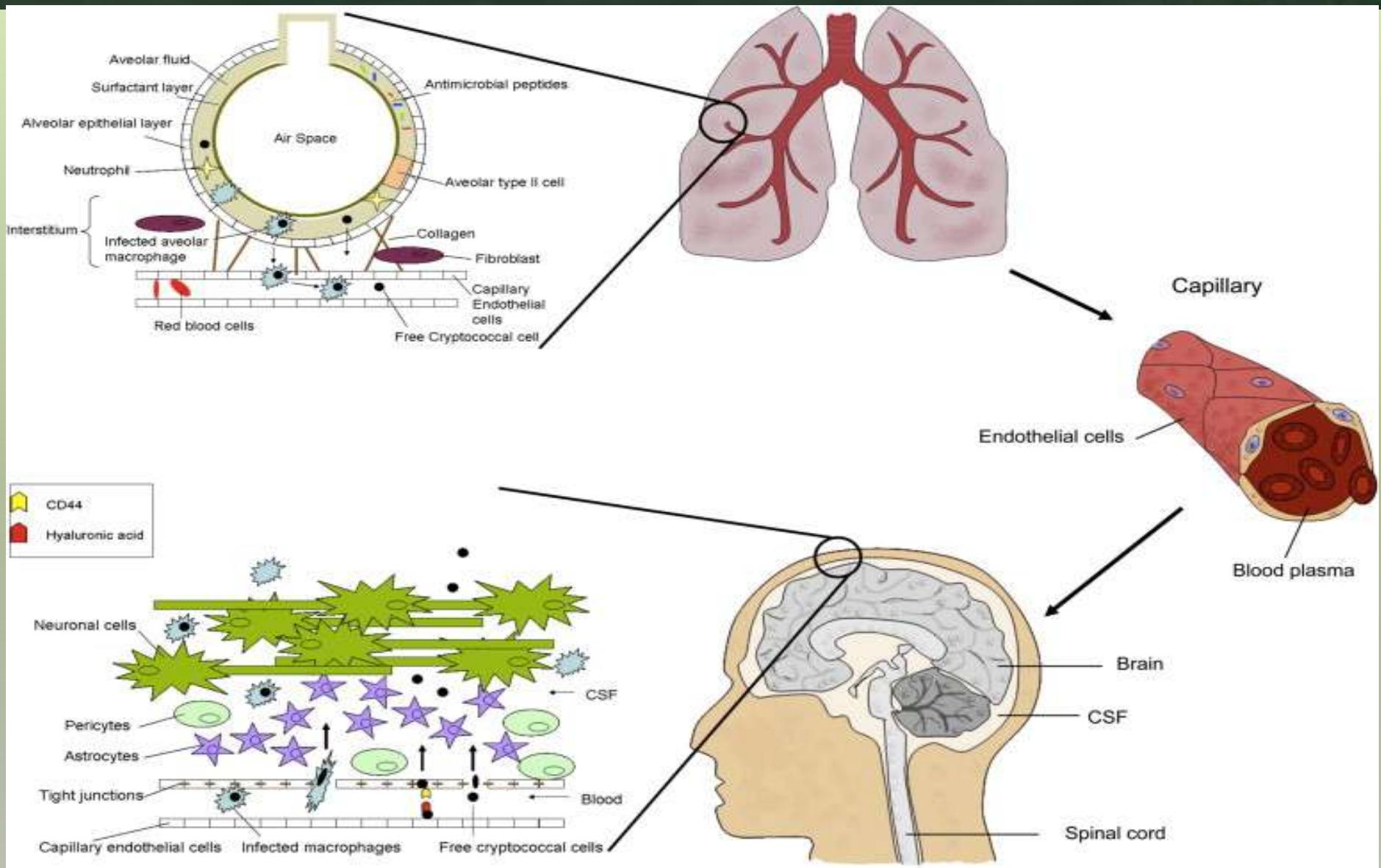
# Infección por *Cryptococcus spp*



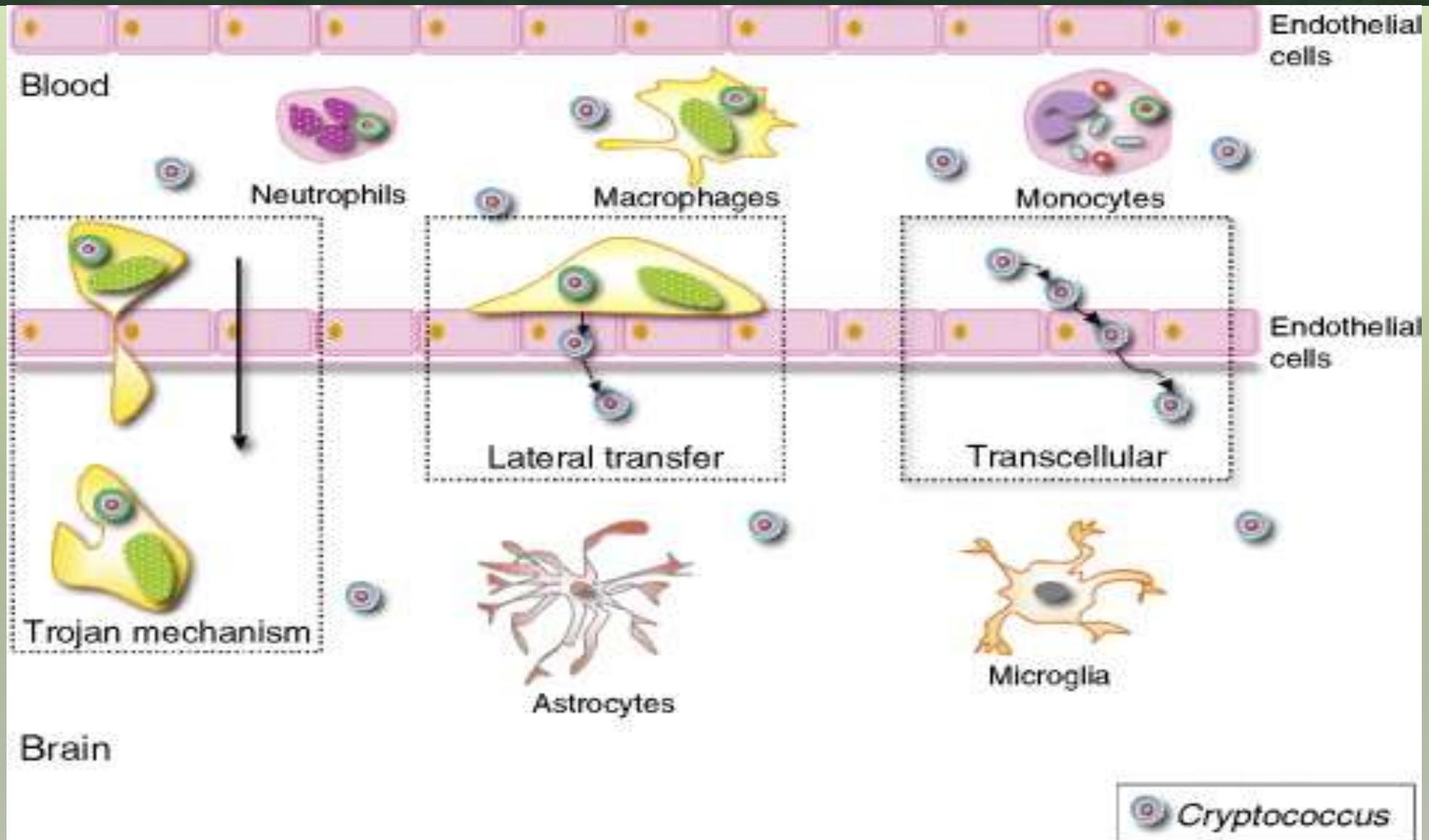
# Infección por *Cryptococcus gattii* (VGII)



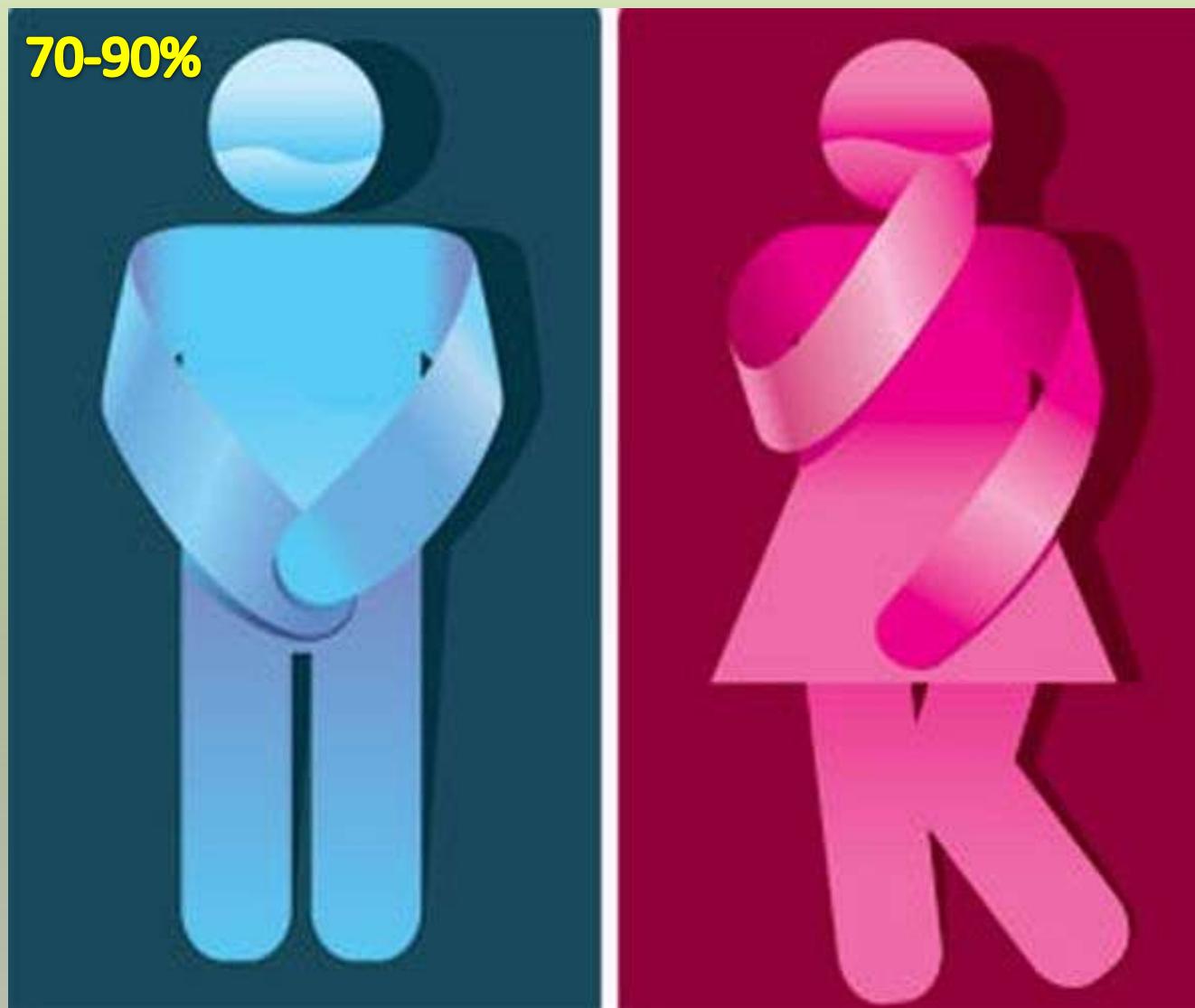
# Diseminación del *Cryptococcus*



# Invasión al Sistema Nervioso Central



# Distribución por Genero



Infección por VIH responsable del 70-90% de los casos

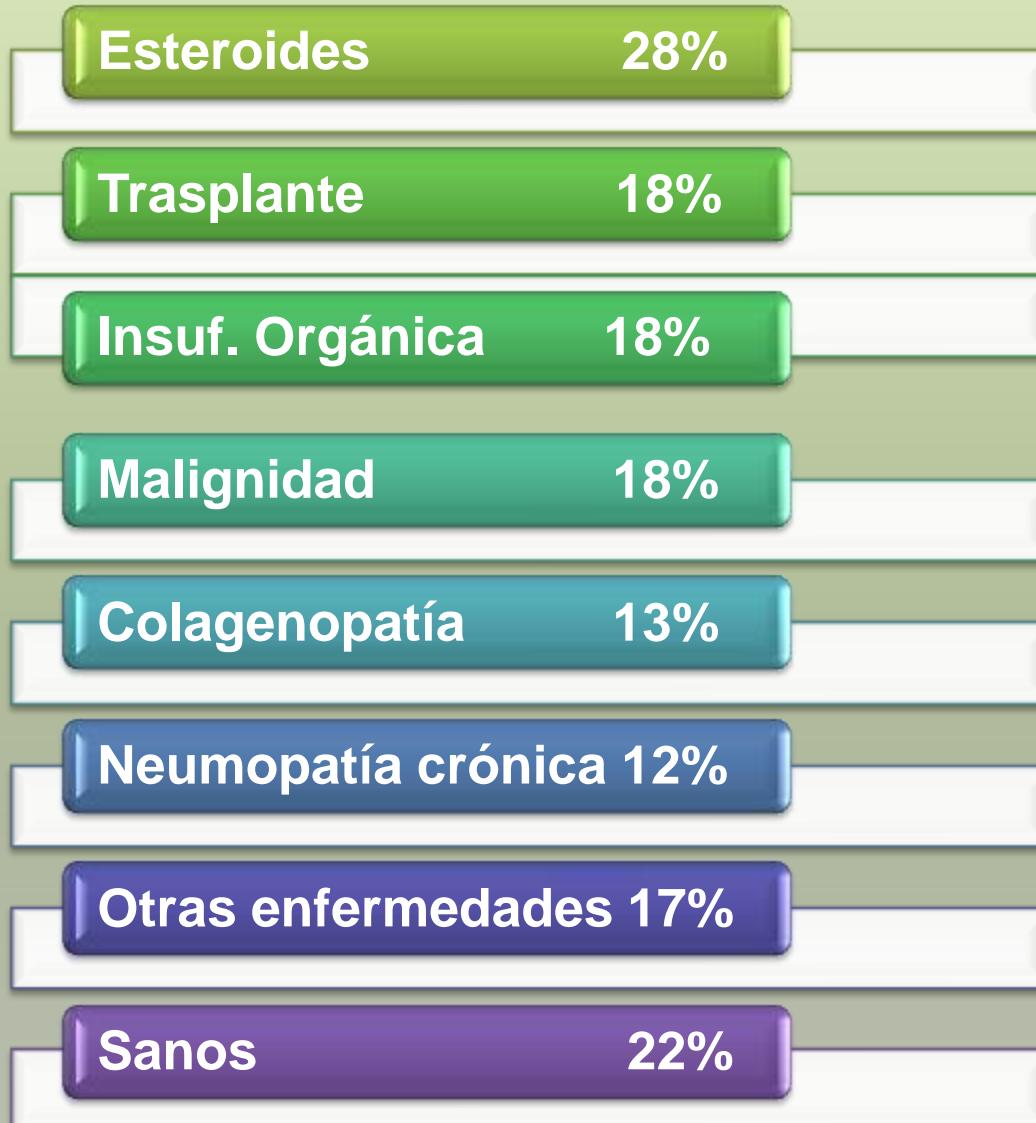


Pappas PG et al. *Cryptococcosis in human immunodeficiency virus-negative patients in the era of effective azole therapy*. Clin Infect Dis 2001, 33, 690–699.

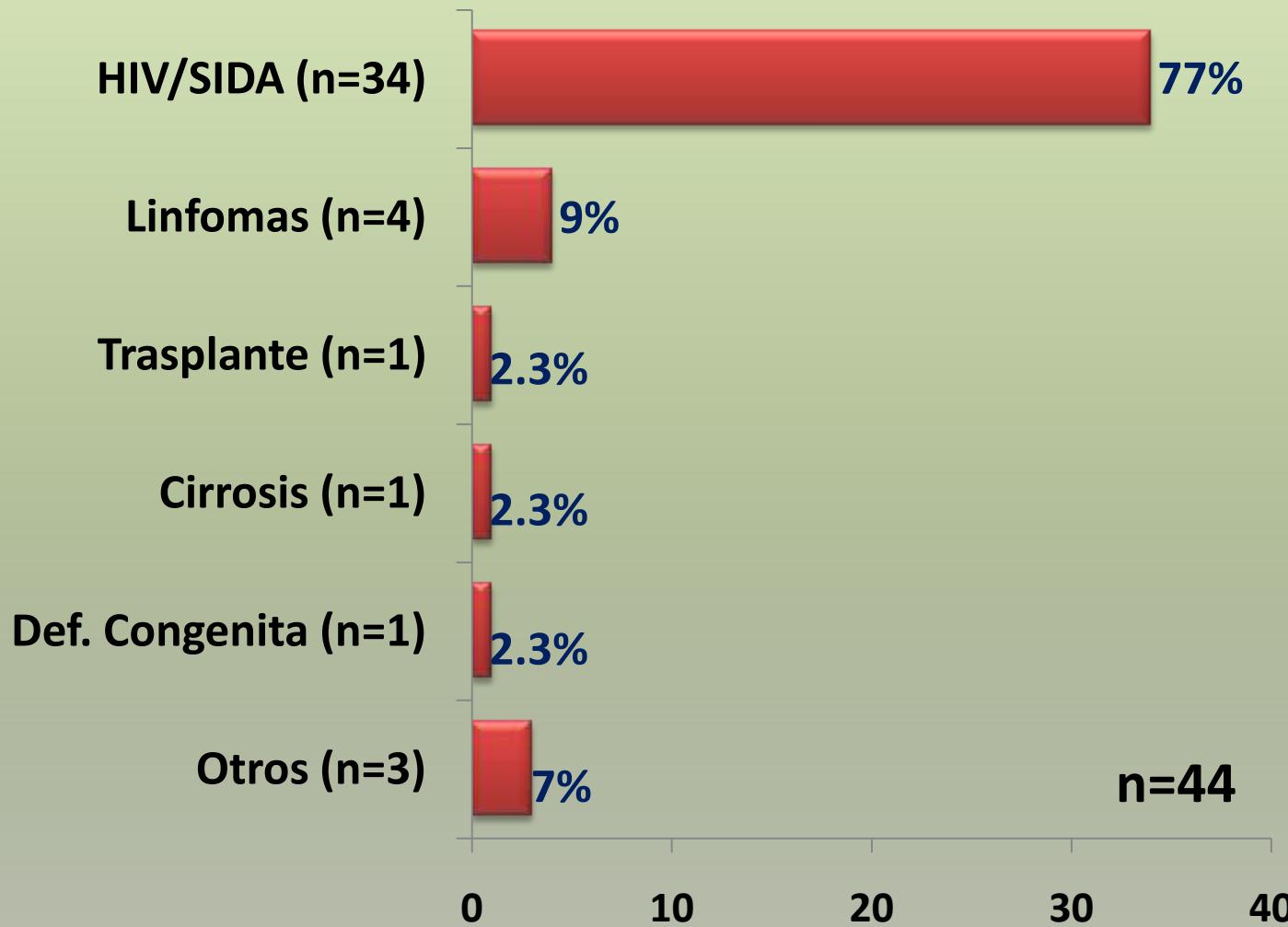
**306 pacientes**

**sin infección**

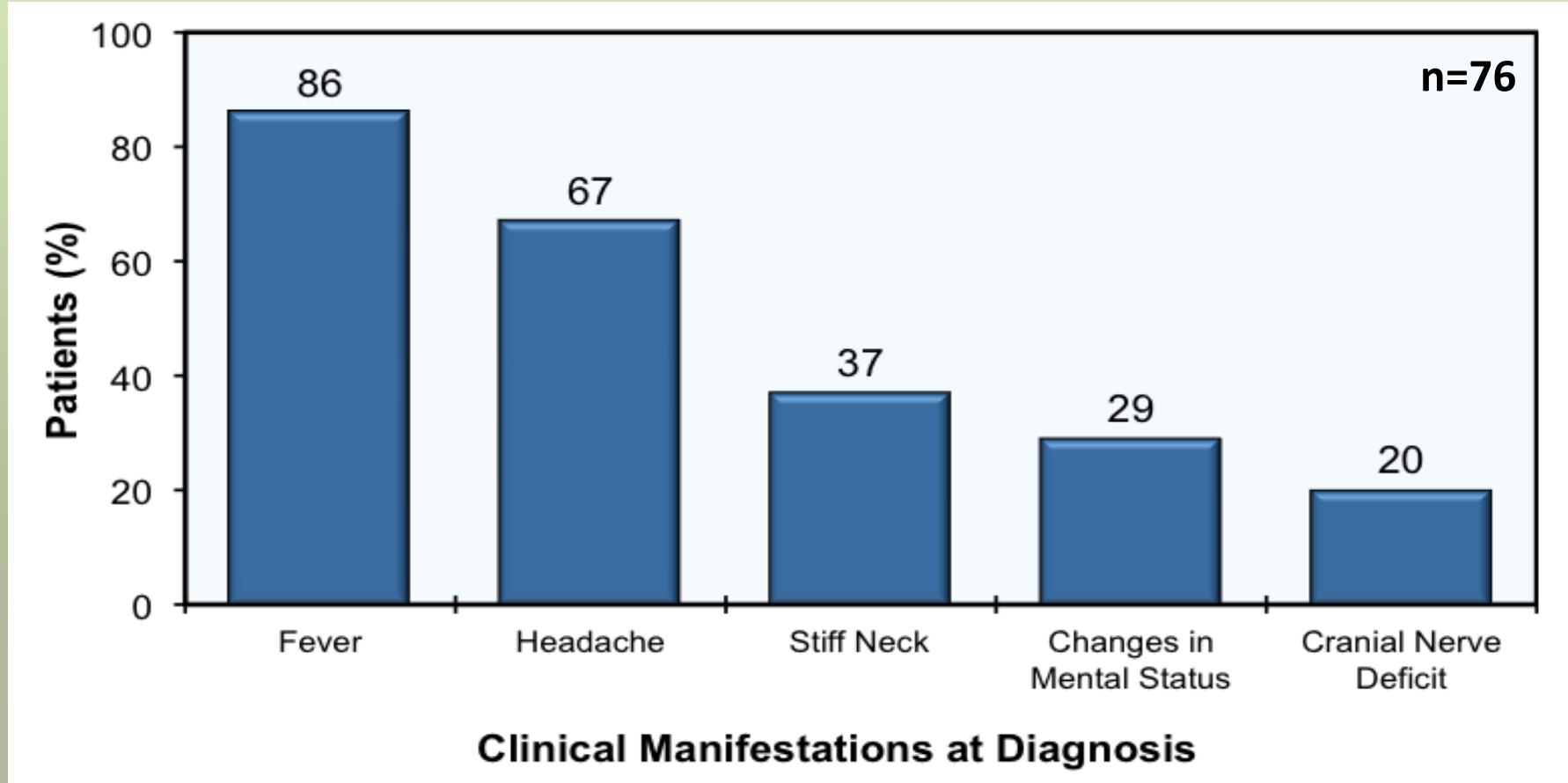
**por el VIH**



# Distribución porcentual de las co-morbilidades en los pacientes con Criptococosis Hospital México - 2007 a 2011



# Manifestaciones Clínicas en el Paciente Infectado con el VIH



Darras-Joly C, Chevret S, Wolff M, et al. Cryptococcus neoformans infection in France: epidemiologic features of and early prognostic parameters for 76 patients who were infected with human immunodeficiency virus. Clin Infect Dis. 1996; 23:369-76.

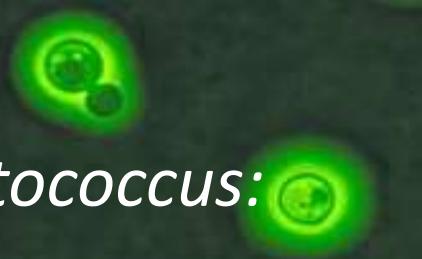
# Características Clínicas de la Criptococosis según hospedero

	HIV	Trasplantado	Inmunocompetente
Curso Clínico	Agudo	Subagudo	Crónico
Forma Clínica	Diseminada	Diseminada	SNC, Pulmón
Presión (cm H2O)	14-70	9-70	15 - >55
Leucocitos (mm3)	0-35	33-188	108
Glucosa (mg/dL)	47	36-52	27-38
Proteínas mg/dL)	65	74-83	161
Antígeno Capsular	93-100%	98-100%	≥87%
Tinta China	79-85%	50-80%	50-62%
Cultivo (+) LCR	98%	73-93%	-
Antígeno en suero	93%	88-91%	-
Hemocultivo (+)	57-62%	33-39%	≤10%

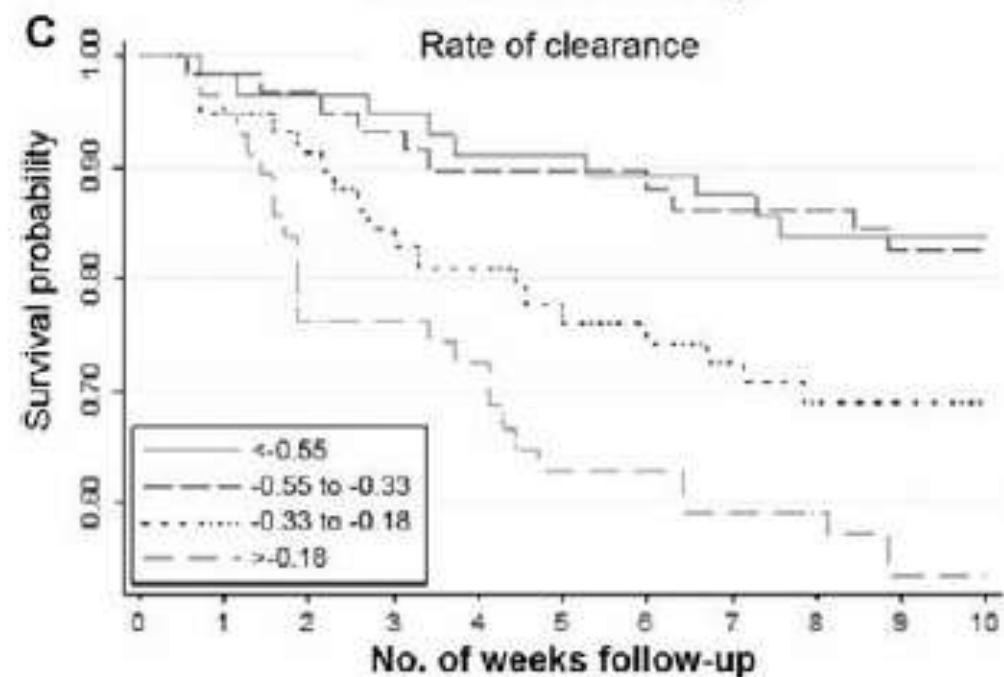
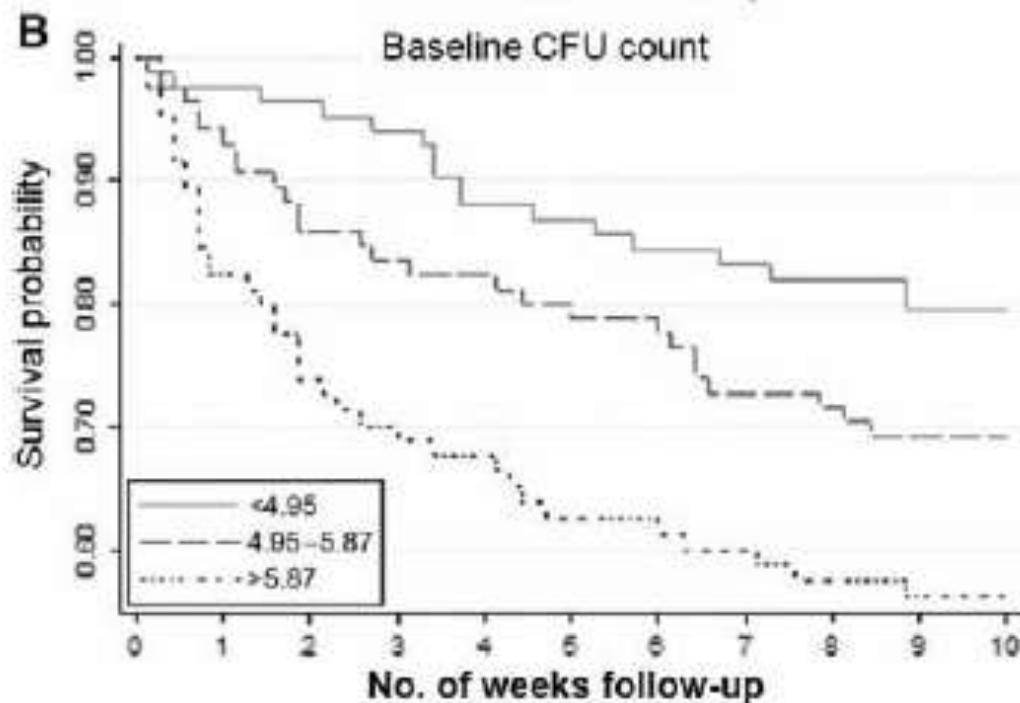
# Principios del tratamiento de la meningitis por *Cryptococcus*:

- 1. Inducción:** 2 - 4 semanas
  - *fungicida, rápida y potente*
- 2. Consolidación:** 8 semanas
  - *fungistática potente*
- 3. Mantenimiento:** 6 m - 1 año
  - *fungistática, prolongada*

# Principios del tratamiento de la meningitis por *Cryptococcus*:

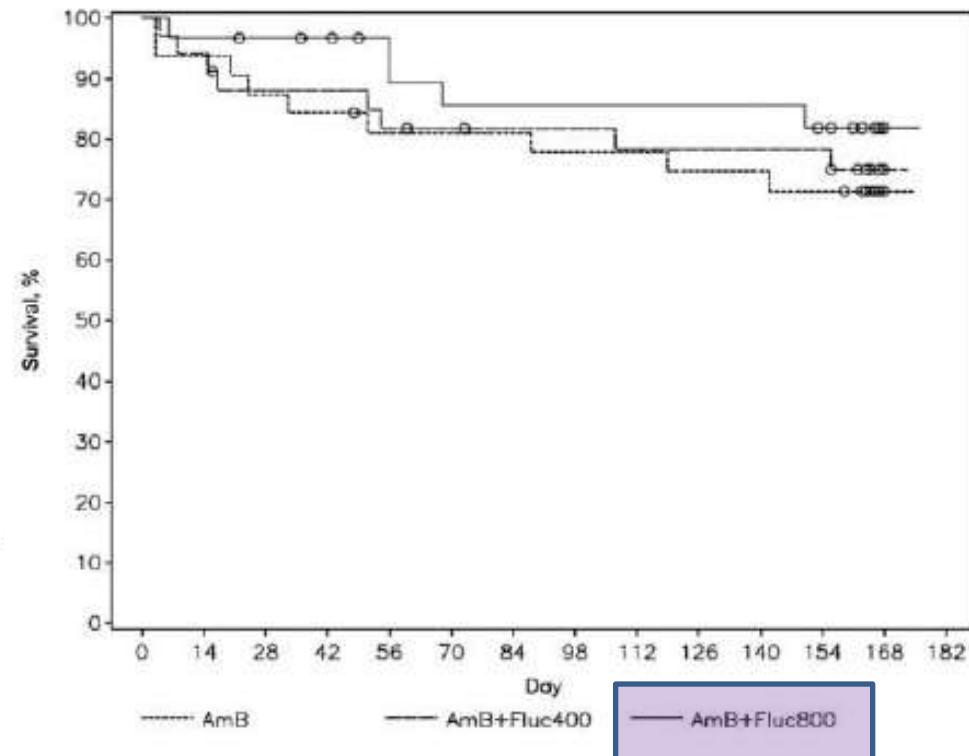
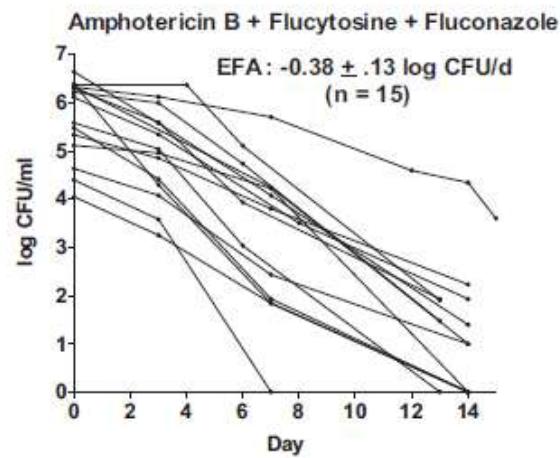
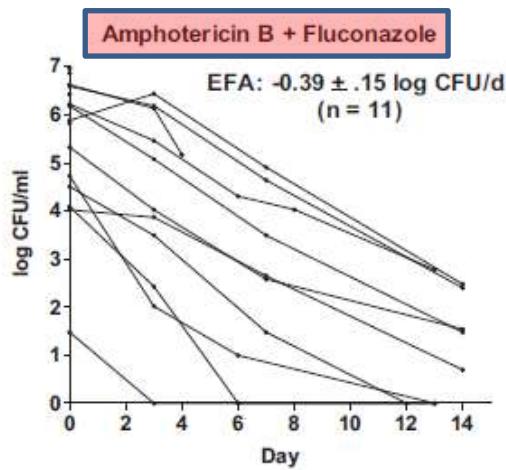
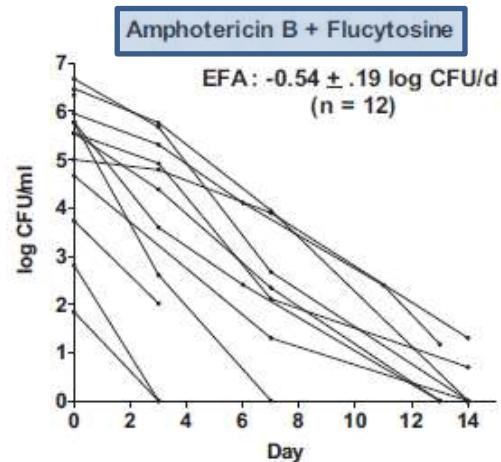
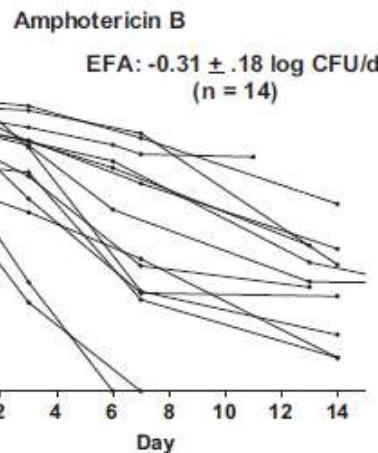
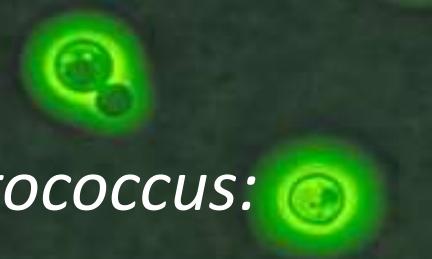


## Carga Fúngica: reducción de la población



*Bicanic T, Murooza C, Brouwer A, et al. Independent association between rate of clearance of infection and outcome of HIV-associated cryptococcal meningitis: analysis of a combined cohort of 262 patients. Clin Infect Dis 2009; 49:702–709*

# Principios del Tratamiento de la meningitis por *Cryptococcus*:



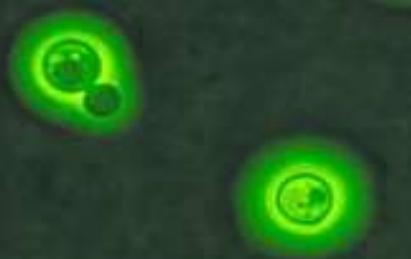
Brouwer AE, Rajanuwong A, Chierakul W et al. Combination antifungal therapies for HIV-associated cryptococcal meningitis: a randomised trial. Lancet 2004; 363, 1764–767.

Pappas PG et al. A Phase II Randomized Trial of Amphotericin B Alone or Combined with Fluconazole in the Treatment of HIV-Associated Cryptococcal Meningitis. Clinical Infectious Diseases 2009; 48:1775–83

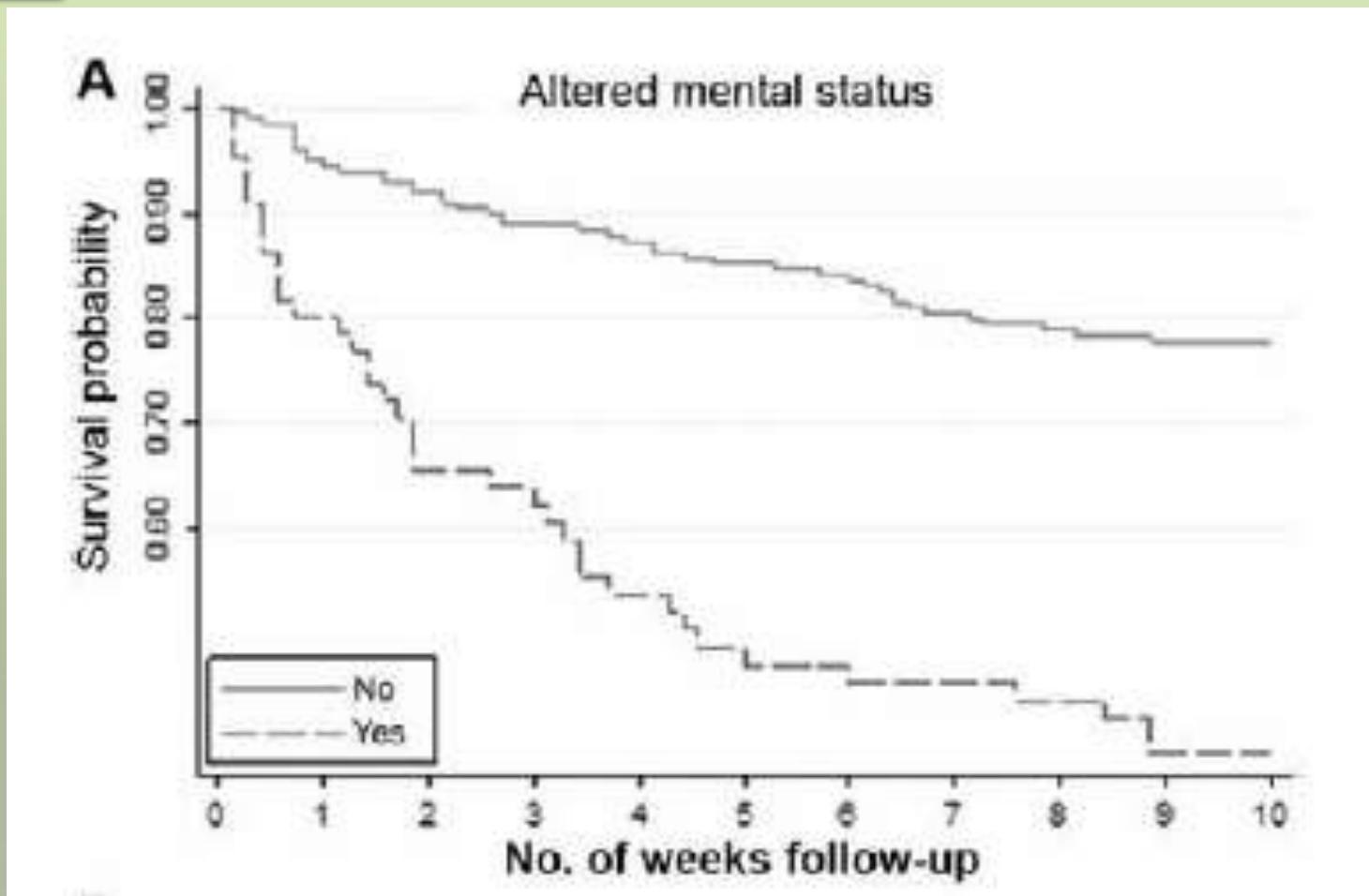
Combinación + dosis altas

# Principios del Tratamiento de la meningitis por *Cryptococcus*:

- Reducción de la inmunosupresión
- Manejo de Hipertensión Endocraneana
- Síndrome de Reconstitución Inmunológica



## Kaplan-Meier survival curves by *altered mental status* at presentation (yes or no).



Bicanic T, Murooza C, Brouwer A, et al. Independent association between rate of clearance of infection and outcome of HIV-associated cryptococcal meningitis: analysis of a combined cohort of 262 patients. *Clin Infect Dis* 2009; 49:702–709



# Síndrome de Reconstitución Inmunológica

## Respuesta paradójica

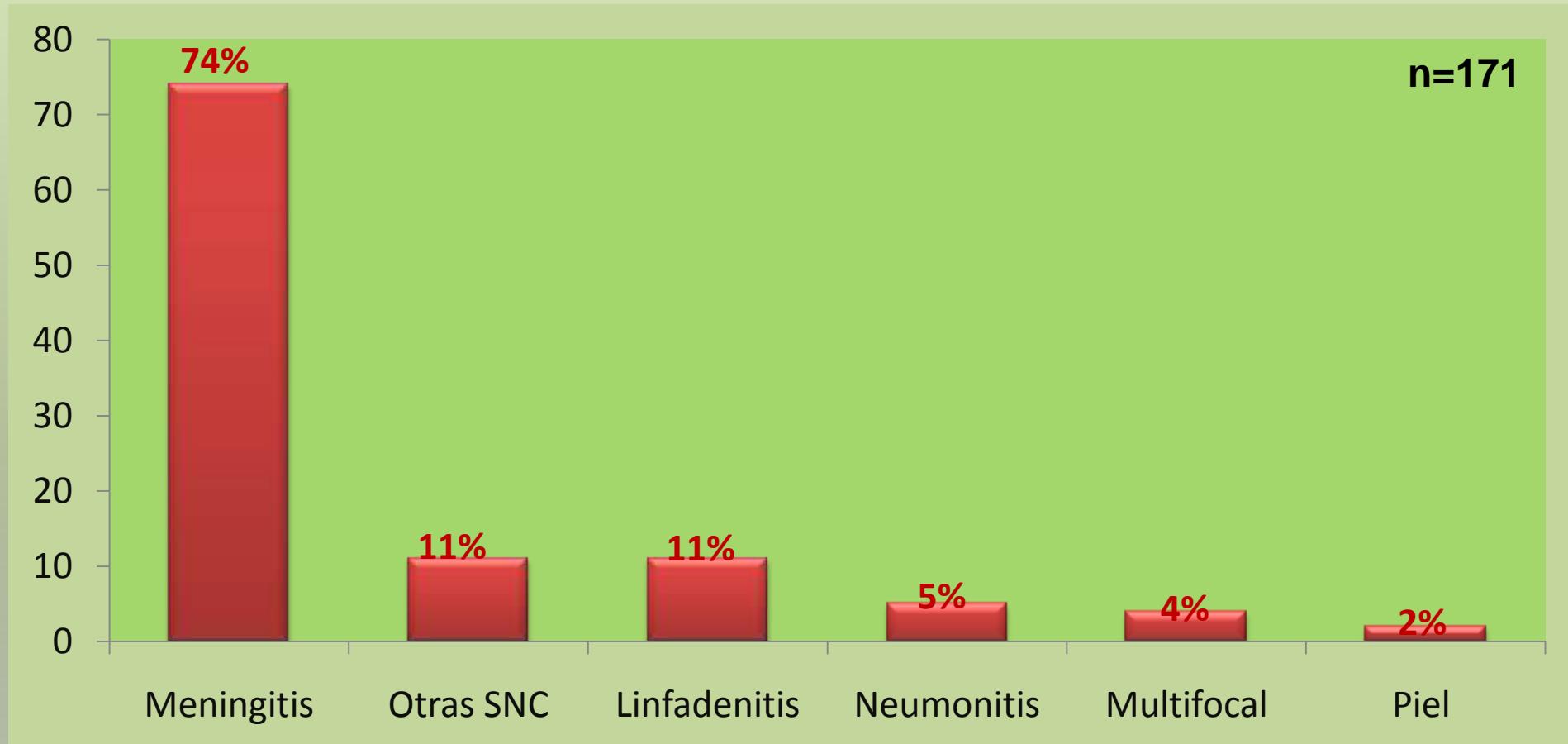
**Panel 1: Case definition for paradoxical cryptococcal immune reconstitution inflammatory syndrome in patients HIV-1**

### Antecedent requirements

- Taking antiretroviral therapy
- Cryptococcal disease diagnosed before ART by positive culture or typical clinical features plus positive India ink staining or antigen detection
- Initial clinical response to antifungal therapy with partial or complete resolution of symptoms or signs, fever, or other lesions, or reduction in CSF cryptococcal antigen concentration or quantitative culture

*Haddow LJ. Cryptococcal immune reconstitution inflammatory syndrome in HIV-1-infected individuals: proposed clinical case definitions. Lancet Infect Dis 2010; 10: 791–802.*

# Síndrome de Reconstitución Inmunológica



*Haddow LJ. Cryptococcal immune reconstitution inflammatory syndrome in HIV-1-infected individuals: proposed clinical case definitions. Lancet Infect Dis 2010; 10: 791–802.*

# Síndrome de Reconstitución Inmunológica

## **Panel 1: Case definition for paradoxical cryptococcal immune reconstitution**

### **Other explanations for clinical deterioration to be excluded**

- Non-adherence or suboptimum antifungal therapy, indicated by an increase in quantitative culture or antigen titre, or any positive cryptococcal culture after 3 months of antifungal therapy
- Alternative infection or malignant disease in the affected site
- Failure of ART excluded if possible (eg, failure to achieve  $\geq 1 \log_{10}$  copies/mL decrease in viral load by 8 weeks of ART)

*Haddow LJ. Cryptococcal immune reconstitution inflammatory syndrome in HIV-1-infected individuals: proposed clinical case definitions. Lancet Infect Dis 2010; 10: 791–802.*