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Central nervous system histoplasmosis in AIDS: a case-series in French Guiana

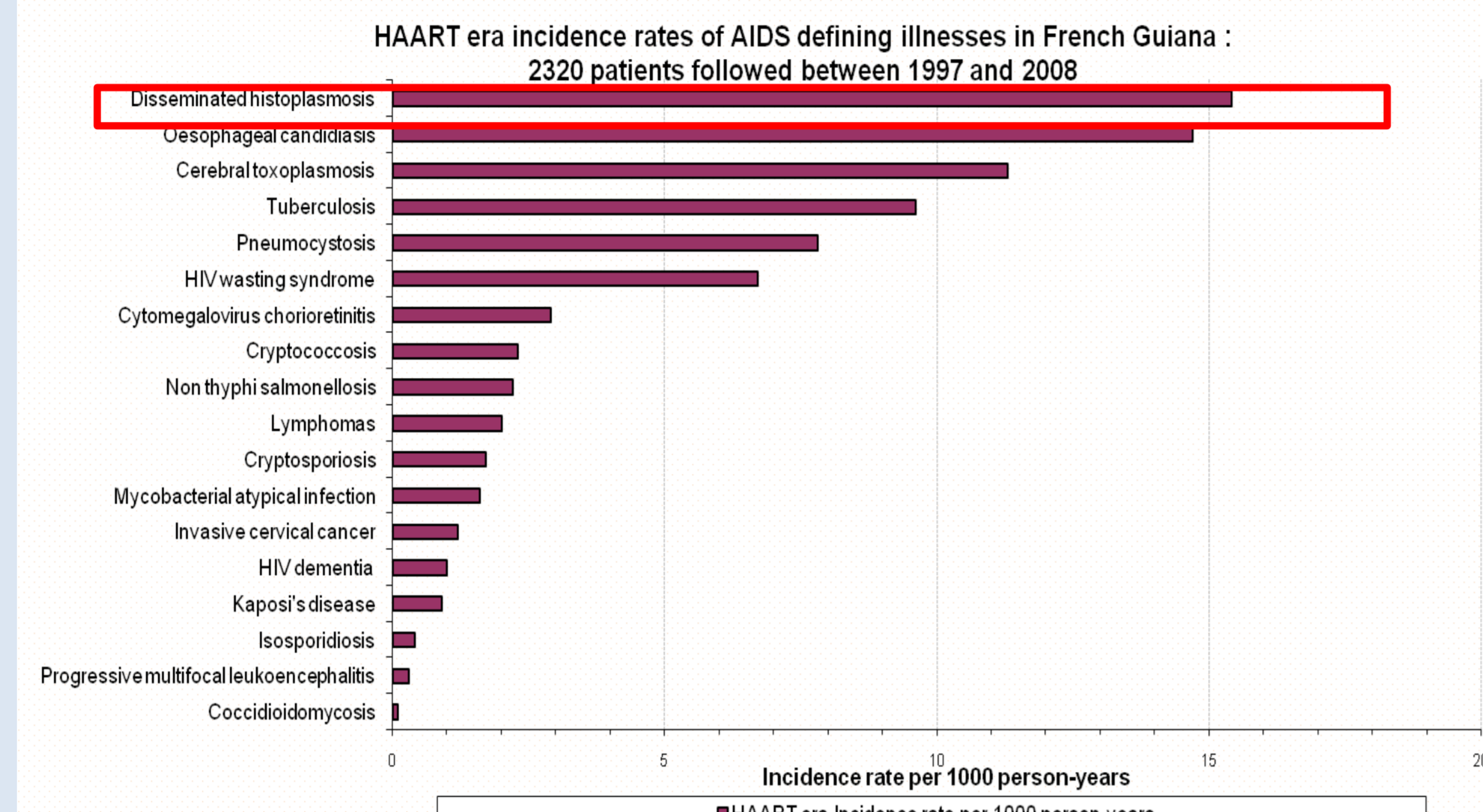
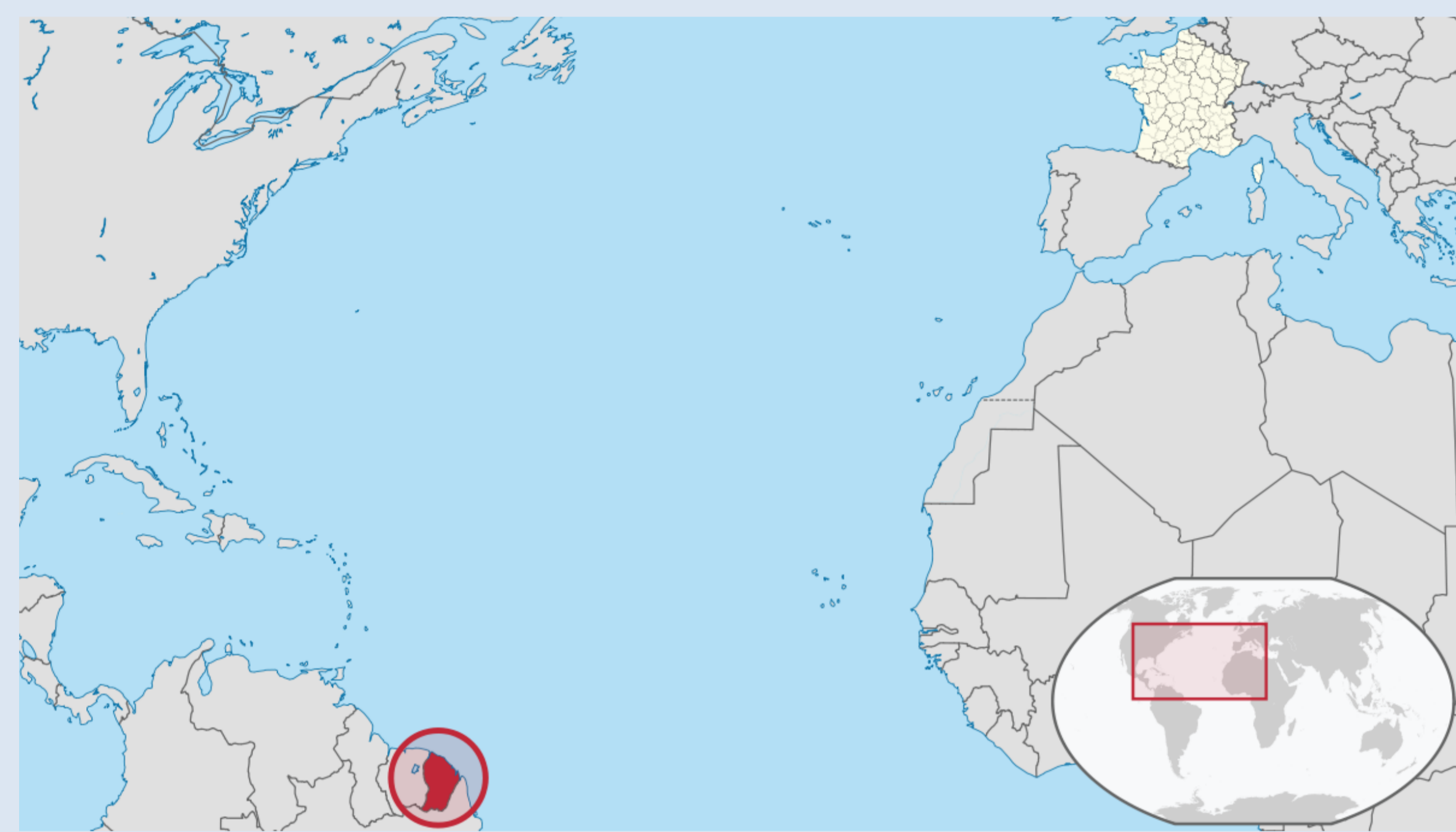
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BACKGROUND

French Guiana is a French region located on the Northeastern coast of South America. Its surface is covered of more than 98% of rainy Amazonian rain forest



Histoplasmosis is a fungal infection due to *Histoplasma capsulatum*

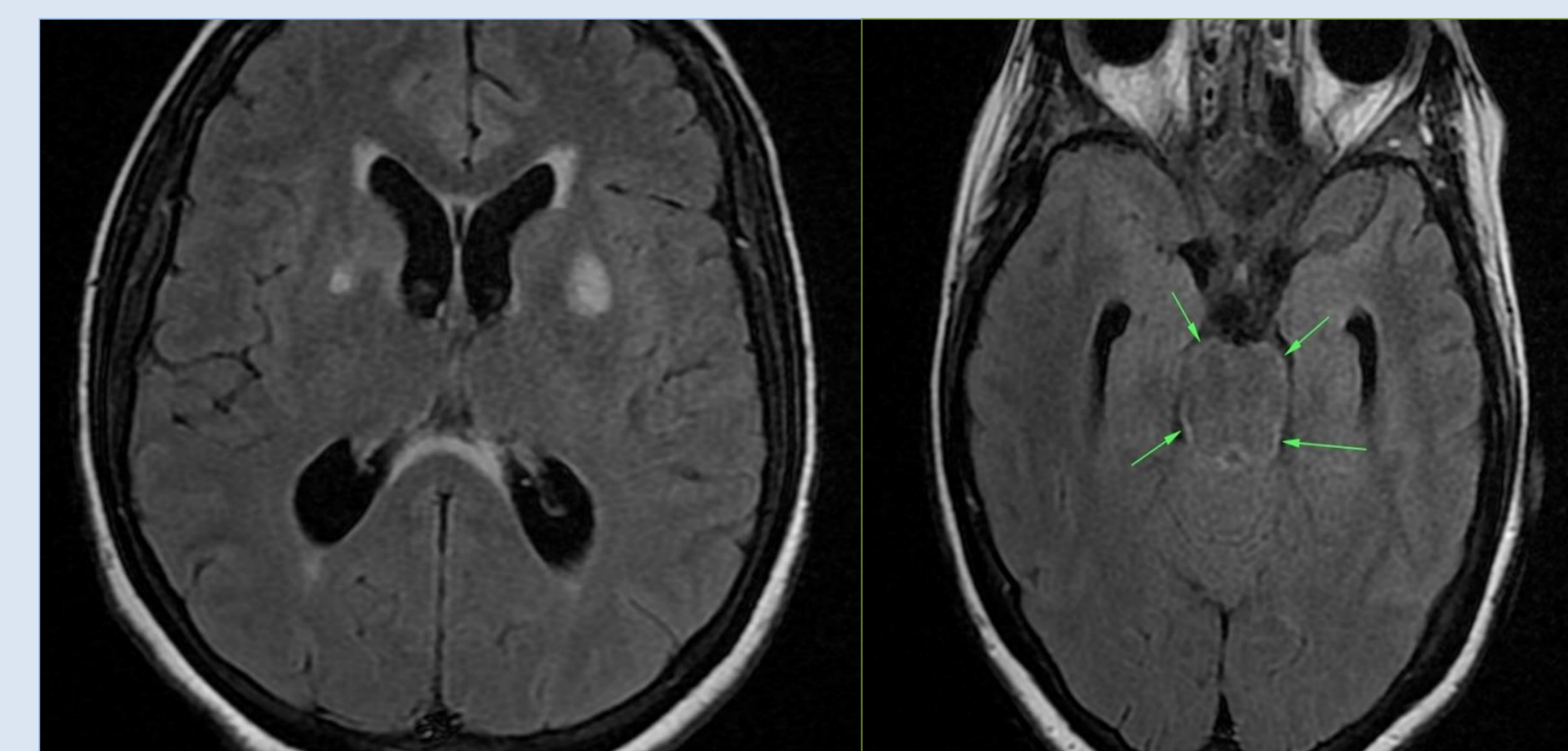
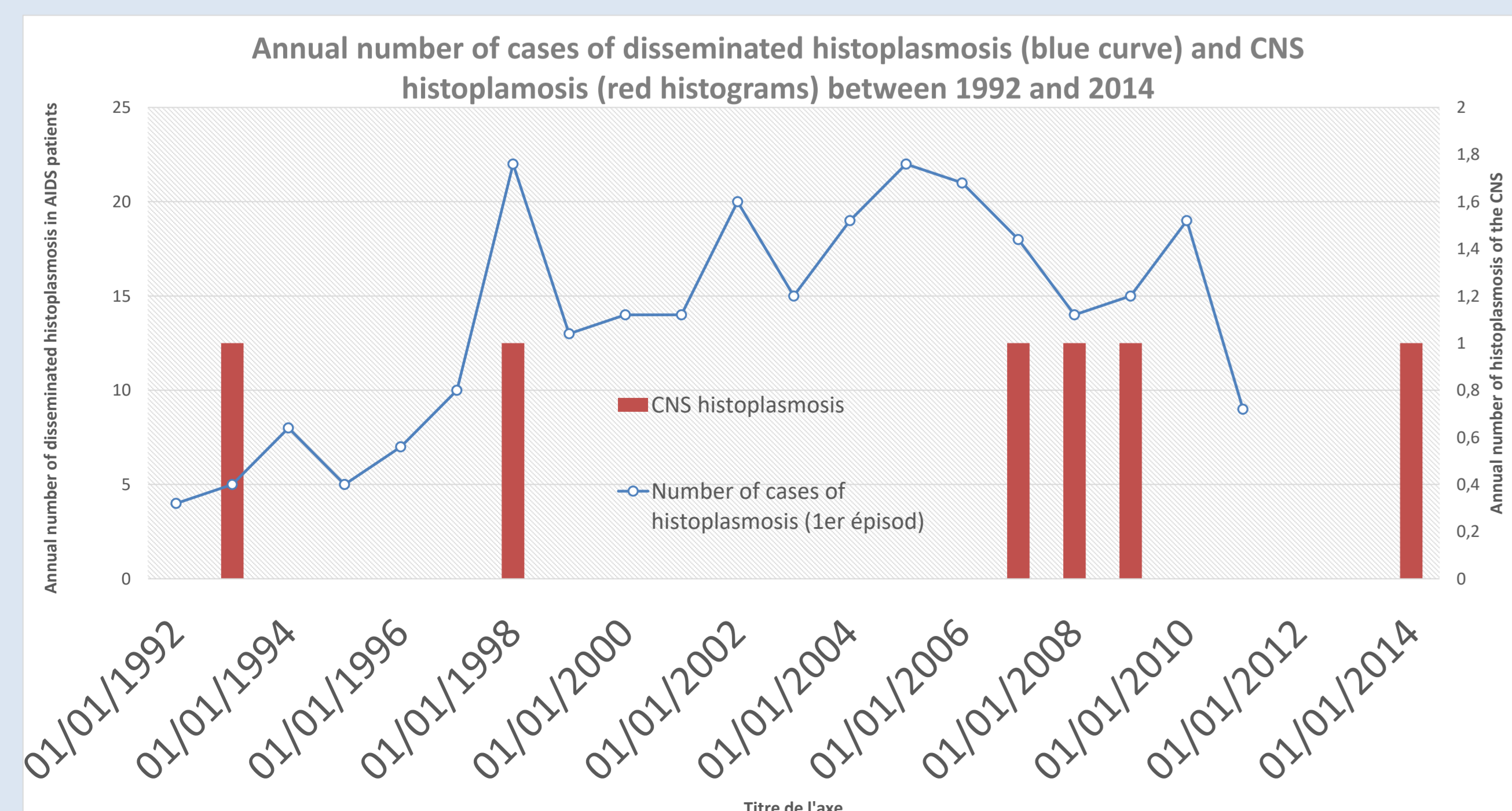
It is the main opportunistic infection reported in patients with AIDS in French Guiana. which is responsible of disseminated severe infection in immunosuppressed patients

Its location in the central nervous system (CNS) is rarely described.

The main objective of this study was to estimate the incidence of CNS impairment in an endemic area for AIDS-related histoplasmosis and the secondary objective was to describe the clinical and paraclinical characteristics.

MATERIALS/METHODS

An observational, prospective, multicentric study was conducted from January 1st, 1990 to December 31st, 2014, on people living with HIV (PLHIV) admitted for an incident case of histoplasmosis in one of the three main hospitals of French Guiana. All histoplasmosis cases were confirmed according to the EORTC-MSG criteria and a written consent was obtained.



FLAIR sequence highlighting bilateral hypersignal of predominantly left lenticular nuclei and hydrocephalus

RESULTS

Among the 345 PLHIV with a diagnosis of histoplasmosis during the 25 years study period, six (1.7%) had a cerebro-spinal fluid (CSF) positive for *Histoplasma capsulatum* in culture and PCR (5) or PCR only (1).

Sex ratio M/F 0.5, 4 women and 2 men had ; mean age of 40 years. The CD4 count ranged from 7-65/mm³ (mean 41/mm³).

5/6 patients had neurological signs, meningoencephalitis, meningeal syndrome, febrile headache, focal deficit, psychomotor retardation, ataxia, and/or confusion. Anemia, neutropenia and an increased CRP were associated with CNS involvement. CNS imaging was abnormal for 50% patients. 2/3 patients treated with antifungal therapy received itraconazole. 2 died within one month after admission (33%).

CASE	1	2	3	4	5	6
Age (years) and gender	33 F	36 F	47 M	35 M	48 F	39 F
Time before diagnosis (days)	18	69	1	7	28	39
CD4 count (/mm ³)	29	62	29	7	65	56
HIV RNA (copies/μl)	NA	NA	NA	687 000	59 894	147 615
HAART at Presentation	No	No	No	Yes but not observant (Ritonavir, Fosamprenavir, Abacavir, Lamivudine)	Yes but not observant (Lamivudine, Zidovudine, Lopinavir, Ritonavir)	Tenofovir, Lamivudine, Efavirenz
Co-infection	VHC	VHC	No	No	No	No
Opportunistic diseases	No	No	Toxo and TB	Esophageal candidiasis	EBV	CMV, TB
Non neurological symptoms (duration)	fever, diarrhea, short breath (12 weeks)	fever, splenomegalie (2 weeks)	weight lost, cough, lymphadenopathies (cervical, axillary, subclavian) (12 weeks)	weight lost, fever, abdominal pain, vomiting (12 weeks)	weight lost, dyspnea, cough, expectoration, otomastoiditis	fever, abdominal pain, nausea, vomiting, diarrhea, cough
Neurological symptoms (duration)	Meningo-encephalitis	meningeal syndrome, headaches (2 weeks)	headaches, ideomotor slowdown, focal deficit	no	Ataxie	Headaches, acute confusional state, meningeal syndrome, Dysarthria,
Imaging	Chest X-RAY = interstitial syndrom, Ab echo =normal Brain CT scan =none	Chest X-RAY = right upper lobe opacity sequelae of tuberculosis, Ab echo= splenomegaly and lymphadenopathies, Brain CT scan = hydrocephalus	Brain CT scan = edema and parenchymatous lesions in cockade	Brain CT scan =normal	Brain CT scan = normal	Brain CT scan =hypodense gap, ventricular dilatation MRI= FLAIR and T1 Hypersignal of the basal ganglia
CSF analysis	unknown	leukocytes: 71 , PR: 0,98g/l, Glu: 2,2 mmol/l	leukocytes: 20 (% P: 5,L:95,M: 0) PR : 1,4g/l, Glu:2,9 mmmol/l	leukocytes: 1 PR 0,3g/l Glu: 2,8 mmol/l	WBC: 44 (%P:25,L:75), PR: 1,7g/l, Glu: unknown	leukocytes :11 PR:0,72g/l, Glu 1,2mM
Mycological diagnosis	Culture	Culture	PCR	Culture	Culture	Culture
Treatment	Amphotericine B	Itraconazole	Liposomal Amphotericine B 7 days then Itraconazole	Itraconazole	Amphotericine B liposomal	Amphotericine B only 1 day, then Itraconazole
HAART	Zidovudine	No	No	Ritonavir, Fosamprenavir, Abacavir, Lamivudine	Didanosine, Zidovudine, Lopinavir, Ritonavir	Efavirenz, Emtricitabine, Tenofovir, disoproxil
Outcome in months (still alive)	1 (no)	88 (no)	96 (yes)	53 (no)	0 (no)	12 (yes)

Figure 4: Clinical, biological, radiological and outcome characteristics of each patient

NA = not available; Toxo= toxoplasmosis, TB= tuberculosis, Ca= candidosis, CMV=cytomegalovirus, EBV= Ebstein Baar virus, MRI=Magnetic resonance imagin, Echo ab= abdominal echographie, WBC =White Blood Cells, PR= Protein, Glu= Glucose CSF, PCR= Protein Chain Reaction

CONCLUSION

The diagnostic was difficult in deeply immunocompromised PLHIV presenting with a non-specific clinical and paraclinical picture. The main differential diagnosis is CNS tuberculosis. It raised the importance of fungal screening in any PLHIV presenting with a neurological impairment and returning from an endemic area.