

An approach to intracranial mass lesions in HIV-infected patients

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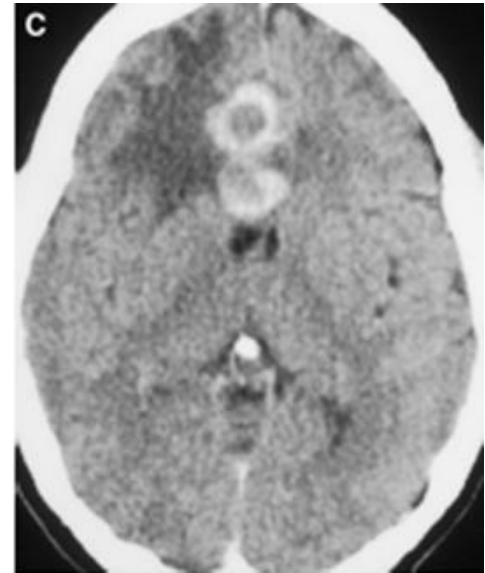
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Background:

- Neurological disease: Up to 2/3rds of HIV +
- Heralds onset of AIDS in 10-20%
- Intracranial mass lesions: up to 50% of these
- Presenting symptoms:
 - Seizures
 - Focal signs
 - Headaches
 - Altered mental state



Why are IML's difficult to manage?

- Significant morbidity and mortality
- Rely on ready access to CT-scan
- Lack of access to brain biopsy in LMICs and risk
 - 1209 diagnostic brain biopsies in HIV-infected patients: overall procedure related morbidity of 5.7% and mortality of 0.9%
- Very little robust or prospective evidence

Terminology

- Intracranial mass lesions (IML)
- Space occupying lesions
- Ring enhancing lesions
- Focal brain lesions

Aetiologies of IML in HIV infection

➤ Opportunistic infections:

- Parasites
 - Toxoplasma gondii
 - Neurocysticercosis
- Fungi
 - Cryptococcus neoformans
 - Candida albicans
 - Aspergillosis
 - Mucormycosis
- Bacteria
 - Mycobacterium tuberculosis
 - Mycobacterium avium-intracellulare
 - Nocardia
 - Listeria monocytogenes
 - Treponema pallidum

➤ Neoplasms:

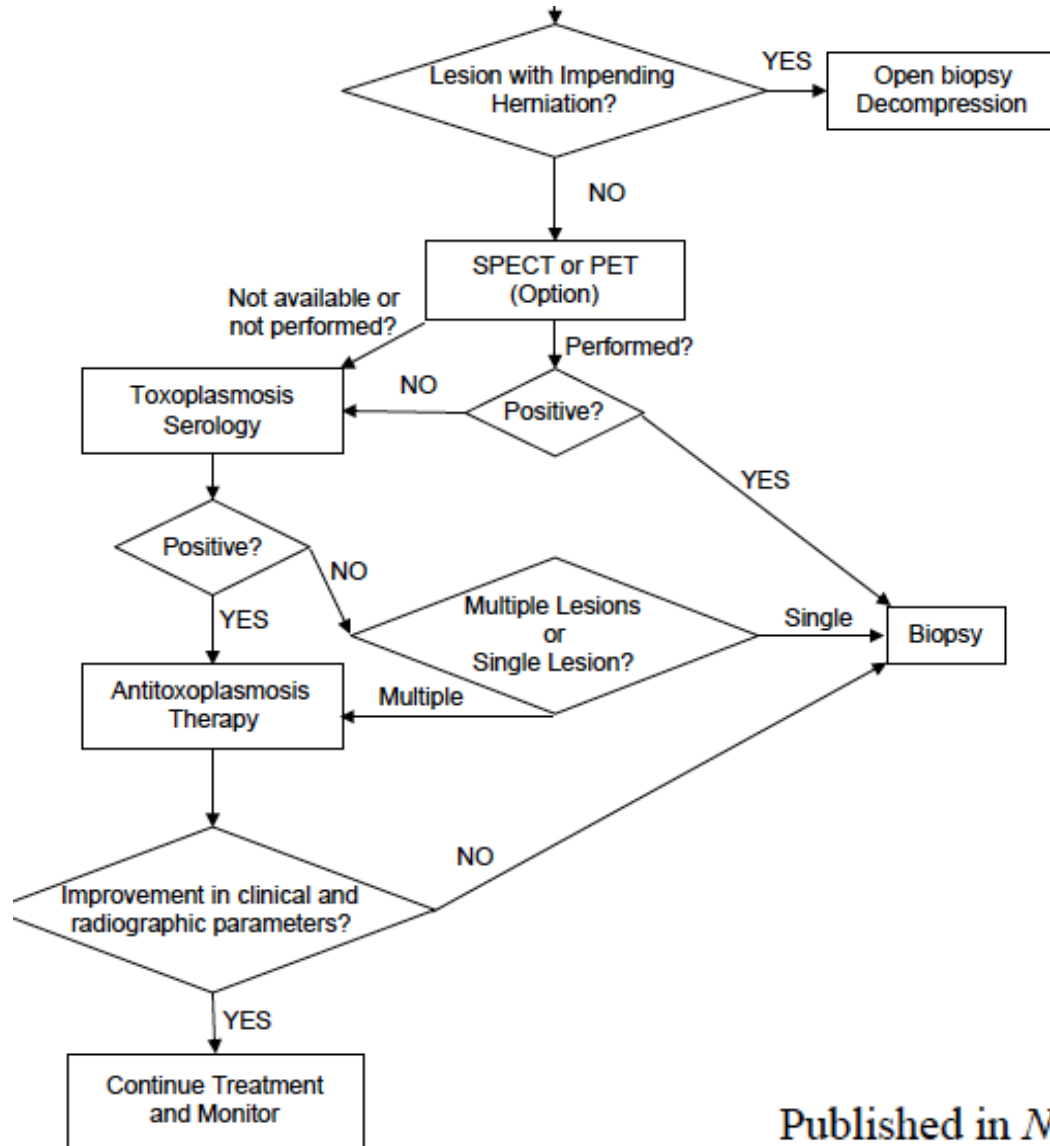
- Primary CNS lymphoma
- Glioma
- Kaposi sarcoma
- Metastatic neoplasm

➤ Cerebrovascular disease

- Ischaemic disease
- Intracerebral hemorrhage

EVALUATION AND MANAGEMENT OF INTRACRANIAL MASS LESIONS IN AIDS

Report of the Quality Standards Subcommittee of the American Academy of Neurology



Toxoplasma encephalitis (TE)

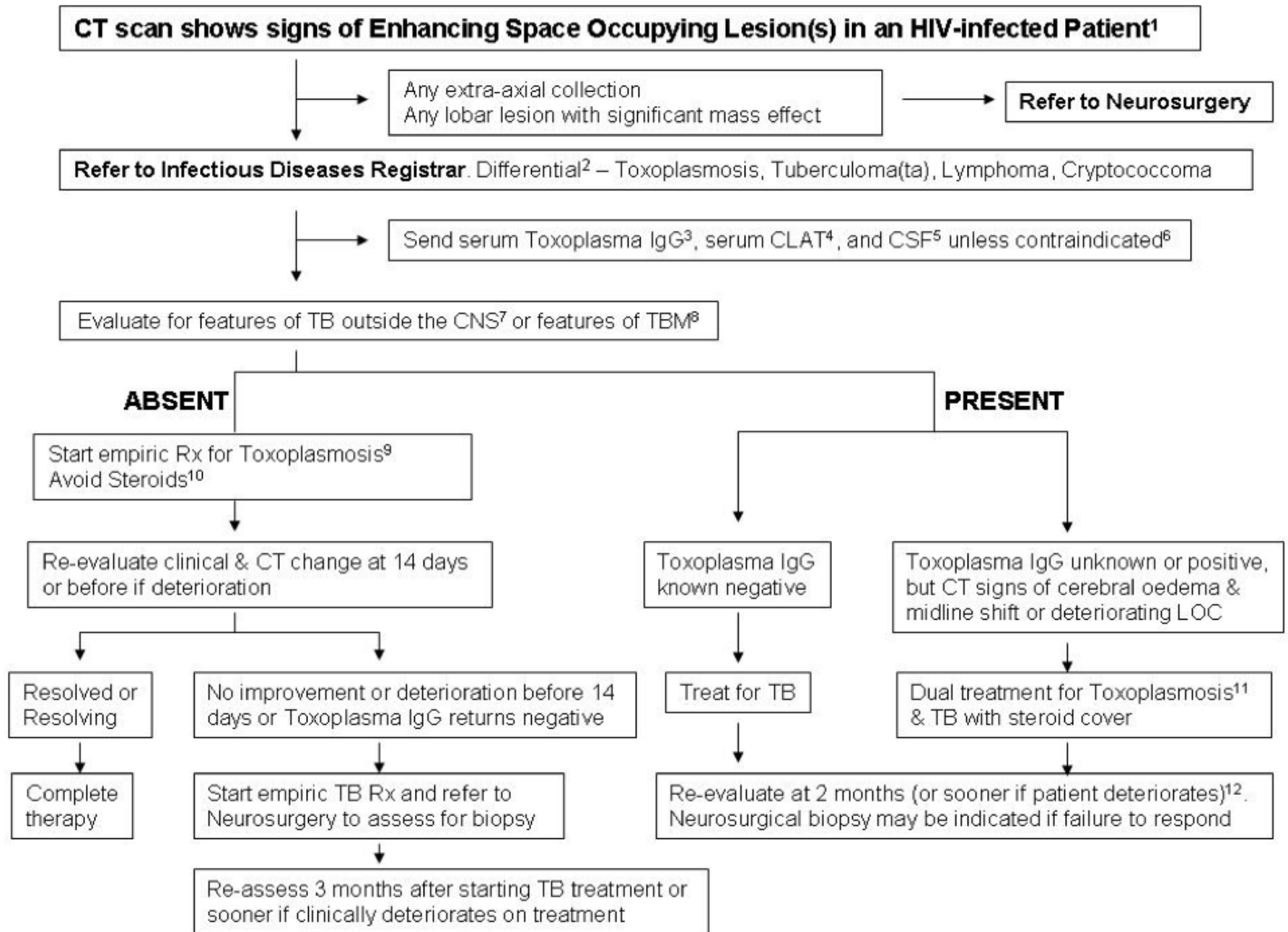
- Response to therapy
 - 74% by day 7
 - 91% by day 14 (median: 5 days)
- False negative serology?
 - 5 -22%
- SA HIV+ adult Toxo seropositivity rate: 8%
- 2 studies demonstrating higher titres with TE
 - OR 3.3 if >150 IU/ml
- Toxo PCR on CSF: 33-69% sensitive, 100% specific

Aetiology of HIV-IML in South Africa

Aetiology	Bhigjee et al (n=38) %	Modi et al (n=32) %
Tuberculosis	11	53
Toxoplasmosis	39	3
Primary CNS lymphoma	0	3
Cryptococcoma	5	14
Brain abscess	16	0
Neurocysticercosis	0	19

(Bhigjee et al. *SAMJ*. 1999; Modi M, et al. *Q J Med*. 2004)

Groote Schuur HIV-IML clinical algorithm (2008)



Methods

- Retrospective folder review 2008-2013
- Intracranial mass lesions in HIV-infected adults
- 90 cases: 4 folders missing - 86 included
- UCT HREC approval 604/2013

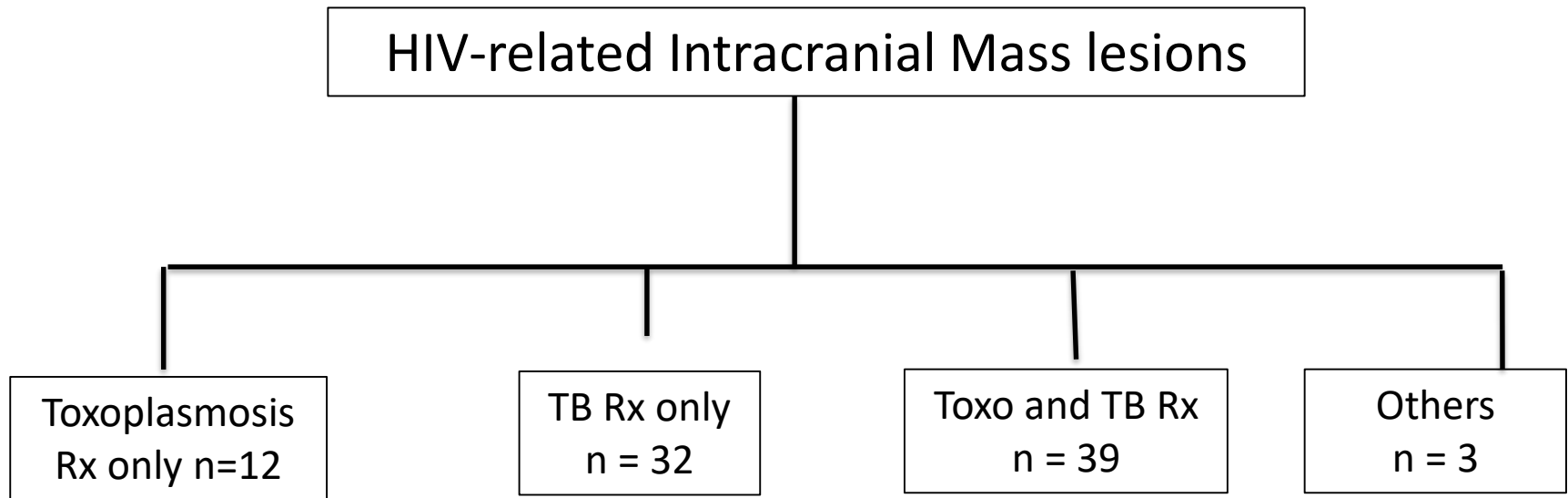
Case definitions

- **Confirmed TB:**
 - brain biopsy Ziehl-Neelsen (ZN), culture or PCR-positive for *Mycobacterium tuberculosis* (MTB), or CSF culture or PCR-positive for MTB.
- **Probable TB:**
 - radiological response of lesions in response to TB therapy alone and/or evidence of TB elsewhere
- **Probable cerebral toxoplasmosis:**
 - a positive toxoplasmosis serology, together with a clinical and radiological response to TMX therapy alone.
- **TB/toxoplasmosis or both:**
 - These patients were placed on TMX and anti-TB therapy, had positive toxoplasmosis serology, and were not differentiated due to a rapid early response suggestive of toxoplasmosis.
- **Cryptococcus:**
 - confirmed: positive culture of a brain biopsy,
 - probable: by virtue of a positive CLAT, gram stain, India-ink stain, or culture of CSF, together with a clinical and radiological response to antifungal therapy.
- **Others:** biopsy confirmed diagnoses.

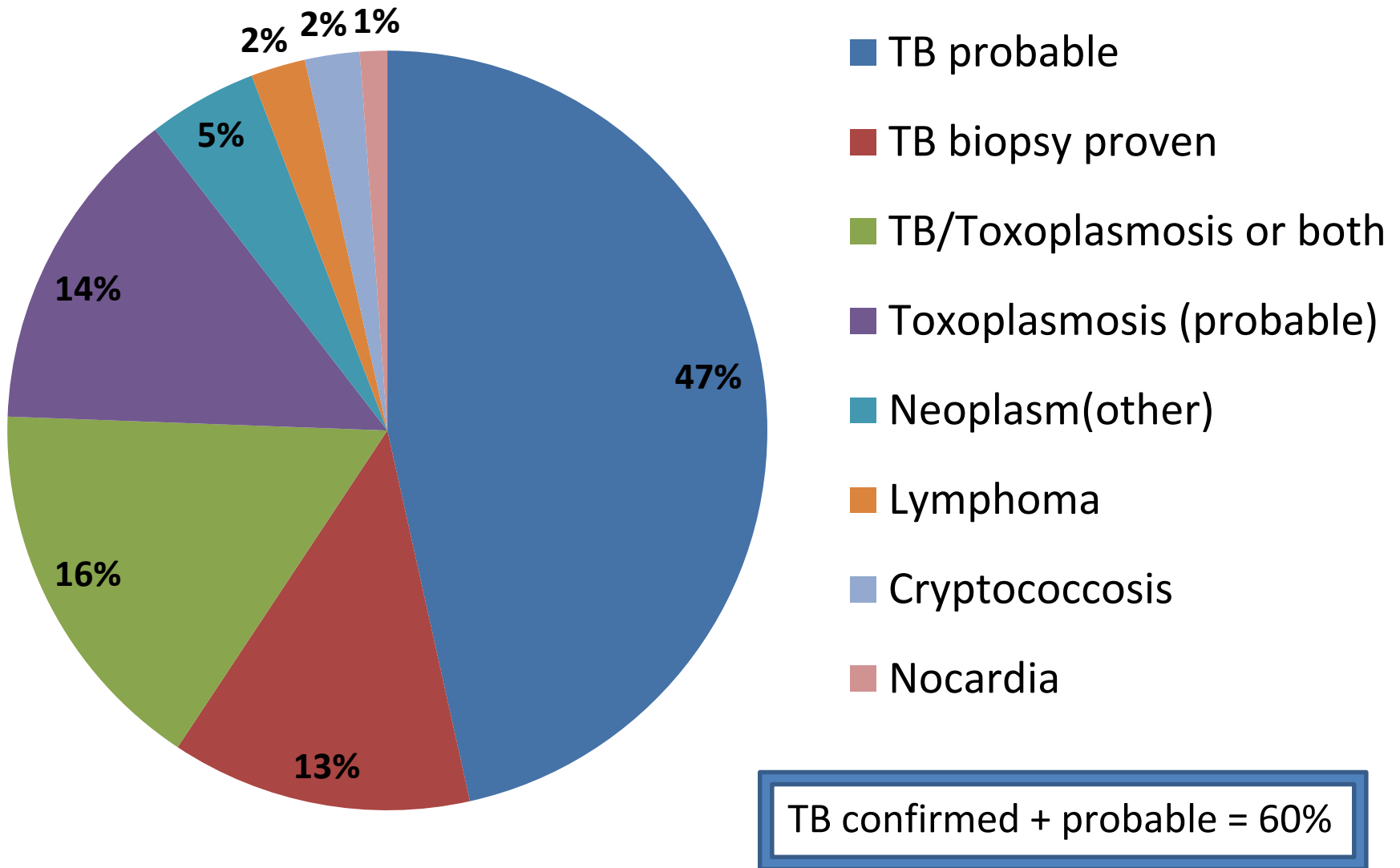
Baseline characteristics

	Total n = 86
Male (%)	59 (69)
Age, median (IQR)	36 (29-40)
CD4, median (IQR)	70 (19-139)
On ART (%)	37 (43)
On TB therapy (%)	32 (37)
Toxoplasmosis IgG positive (%)	38/68 (56)

Initial treatment approaches



Final Aetiology of Intracranial Mass Lesions



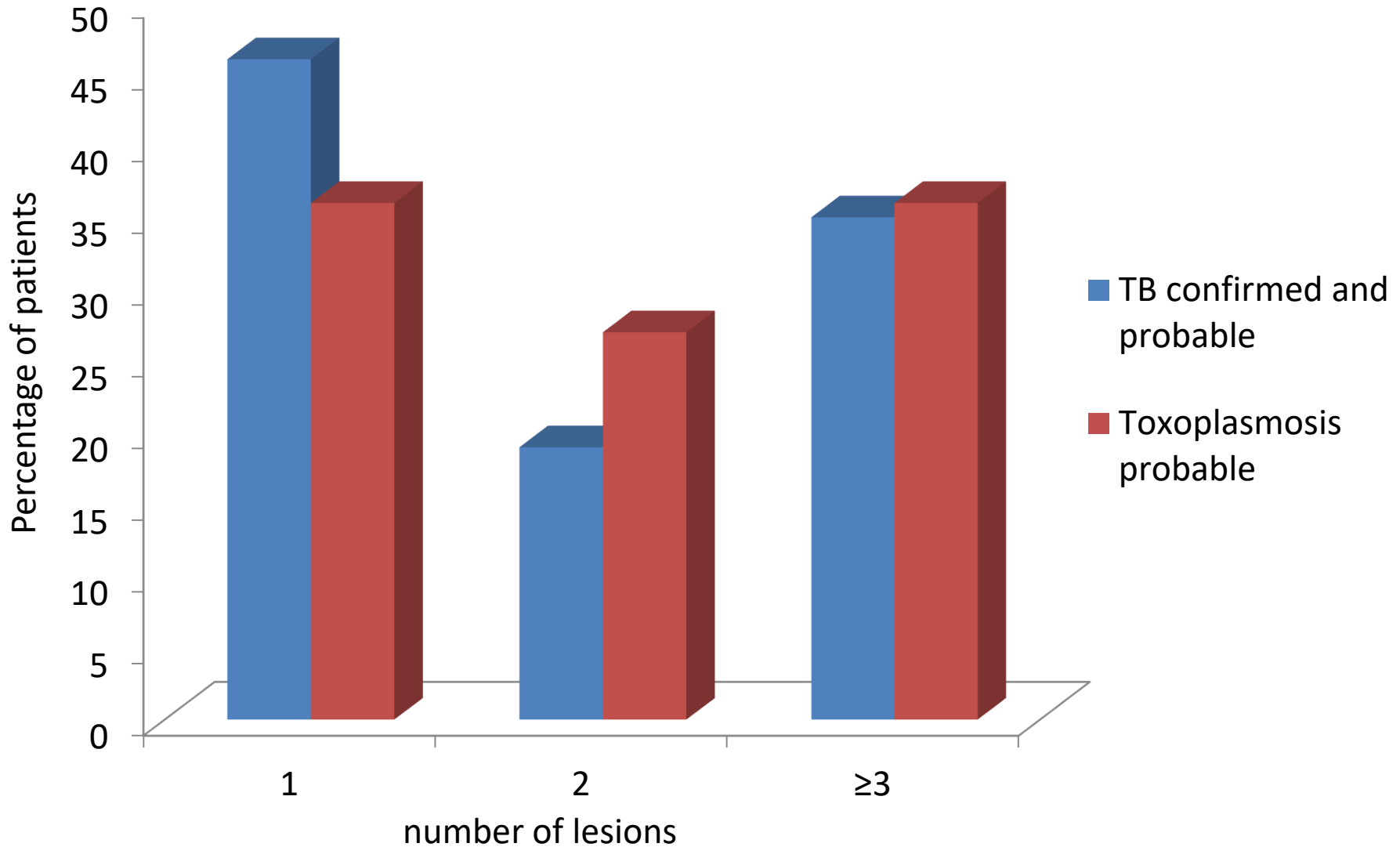
What can help us distinguish TB from
Toxoplasmosis at the outset?

Comparative baseline characteristics of TB vs Toxoplasmosis

	TB total n = 51	Toxo n = 12
Male, %	53	58
Age, median (IQR)	32 (27-39)	40 (31-41)
CD4, median (IQR)	102 (30-108)	24 (8-34)
On ART, %	45	25
Toxoplasmosis IgG positive (%)	17/42 (42)	12/12 (100)

CD4 <100 cells/mm³ for cerebral toxoplasmosis demonstrated an odds ratio (OR)=11, p-value=0.027 (95% confidence interval: 1.31-91.72)

Number of CT brain lesions

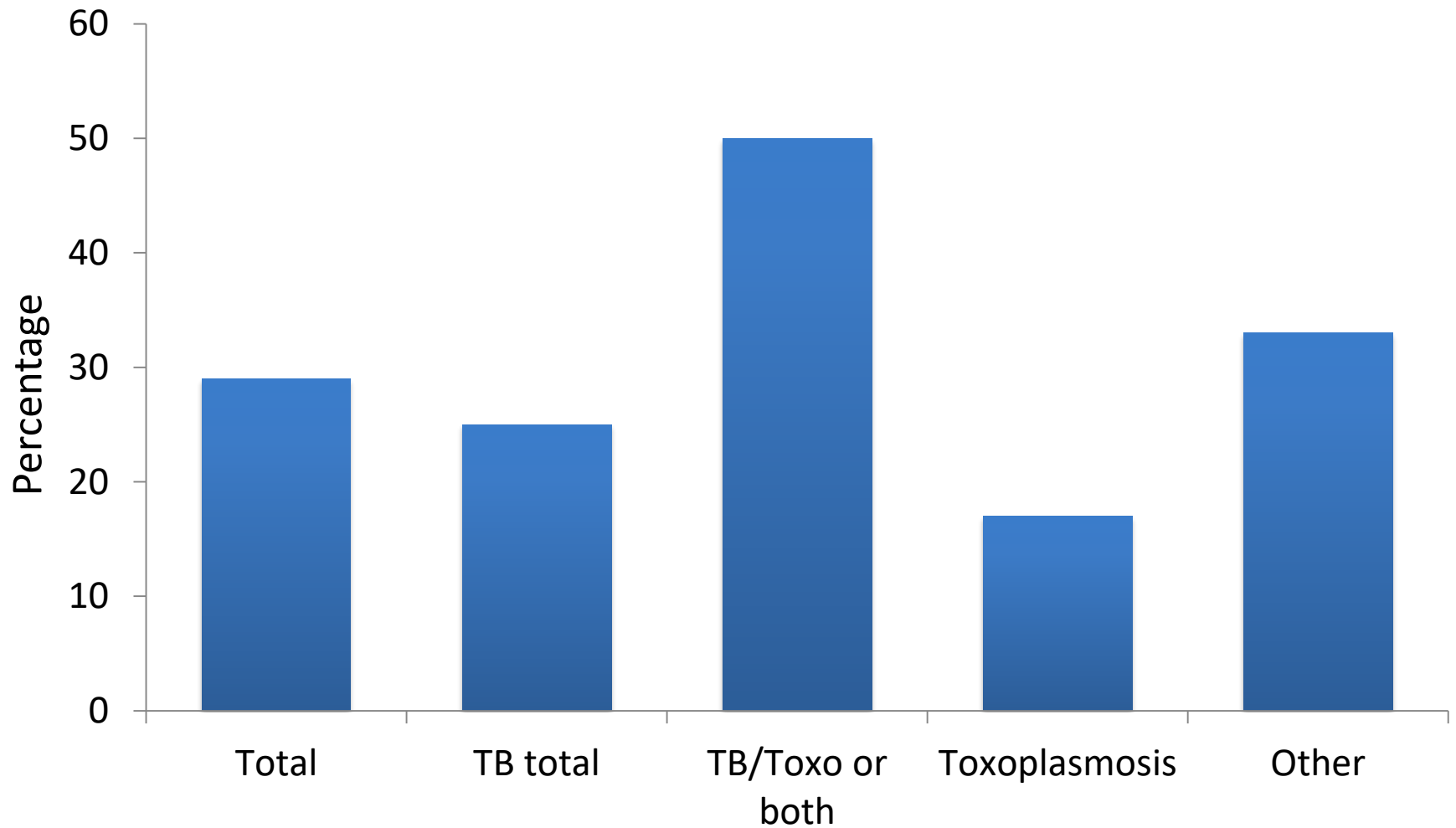


Brain biopsy findings

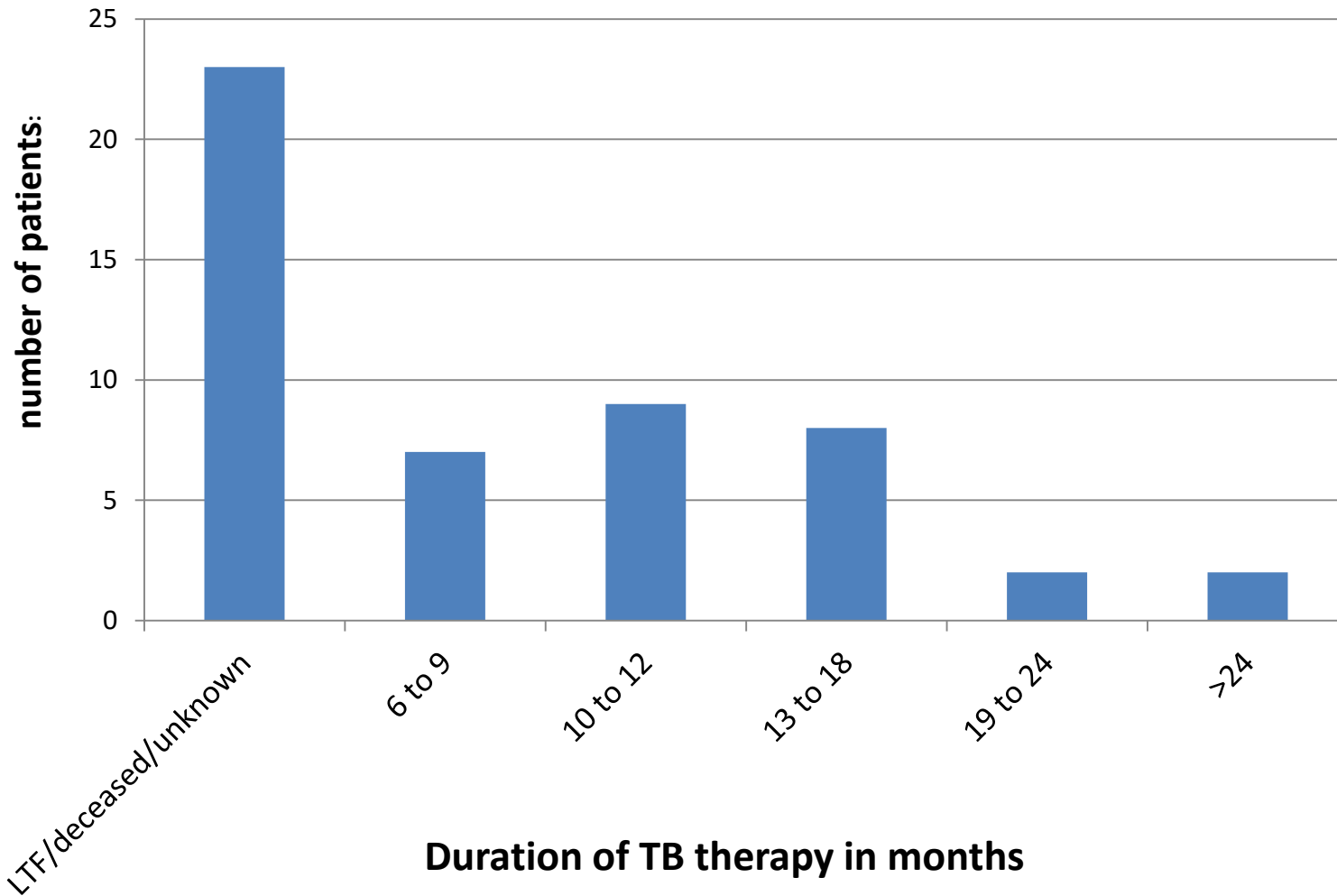
17 performed (20%)

	Number
Confirmed TB	9
Probable TB	2
Nocardia	1
Cryptococcus	1
inconclusive	4

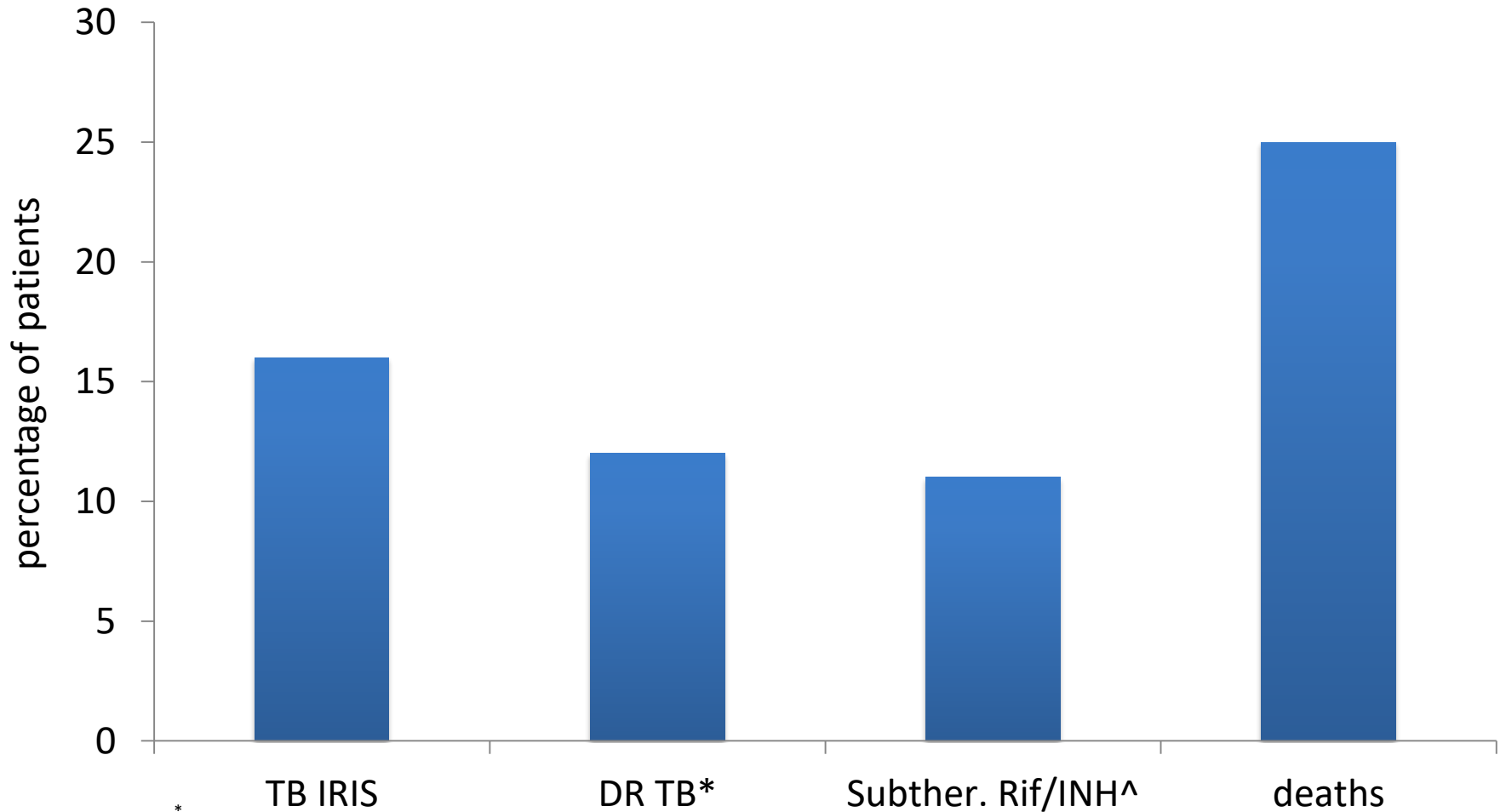
Mortality by final diagnoses



Duration of TB therapy for probable & proven TB cases:



Complications in TB patients (n=51)



*Drug resistant TB (rif, inh or both)

^Subtherapeutic rif or inh serum levels

Drug resistant TB IMLs

- 5/6 died, other LTF
- NB is CSF penetration of drugs
- Low penetration of some new short course drugs:
 - Bedaquiline
 - Clofazimine

Study conclusions

- TB caused 59% of IML in HIV-infected patients at GSH
 - Greater than 1/3 already on TB therapy
 - 16% of TB cases presented as, or developed TB-IRIS
- Toxoplasmosis occurred exclusively at low CD4 counts
 - And was associated with better outcome
- PCNSL is rare in our setting in the ART era
- Brain biopsy is useful for non-responsive lesions

How then to manage a case in 2018?

- Q is whether we shouldn't just put all on empiric TB & Toxo Rx?
 - Risk is of severe drug reaction (1 fatal SJS)
- Try LP if safe
 - CSF Xpert Ultra, CLAT, Toxoplasmosis PCR?, EBV PCR
- Consider Toxo likelihood into CD4/serology
- Thorough w/u for TB elsewhere
- Close, specialist follow up as available
- Biopsy any non-responders

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