Neurocysticercosis in sub-Saharan Africa

Dr. Andrea-Sylvia Winkler, PhD
Department of Neurology
Technical University Munich

(Sero-)prevalence of cysticercosis (worldwide)

Worldwide 50 million people with cysticercosis (WHO 2005) = most frequent cerebral helminthosis

- Seroprevalences are highest in Mexico (44%) and India (24%).
- Community-based study (DANIDA) shows high seroprevalences of about 45% in Tanzania (rt-24h Ab-detecting ELISA).
- Antigen-ELISA was positive in about 17% of people.

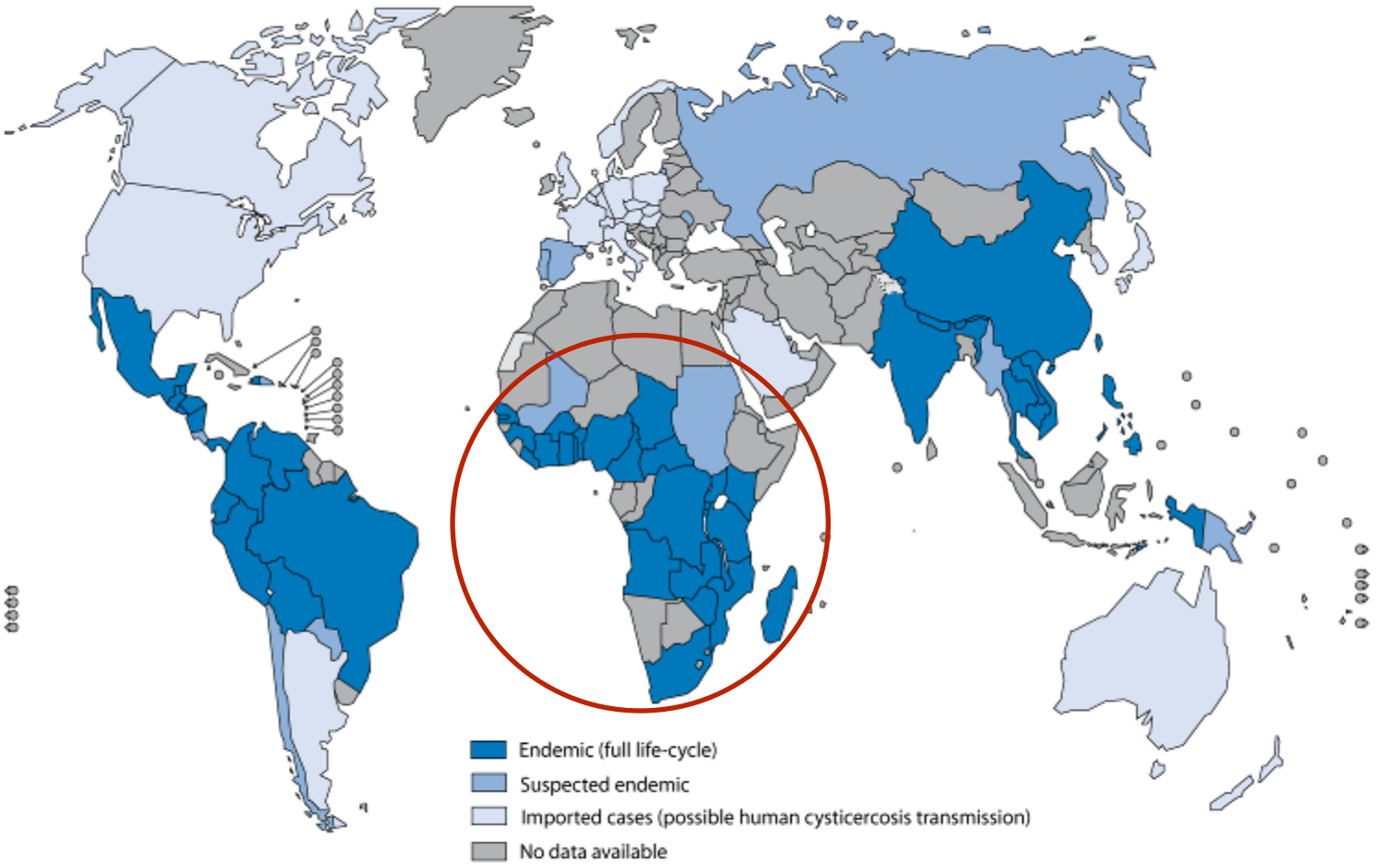
- Seroprevalence in California 1.8% - more than 1000 NCC cases/year in USA.
- Reports from within Europe, mainly Eastern Europe, indicate 10 NCC cases/year (many cases not reported – no seroprevalence studies)

Prevalence of neurocysticercosis (worldwide)

- Ecuador: 14% of normal population (CT confirmed)
- Peru: 52% of all children with partial epilepsy
- South Africa: 50% of incident epilpesy cases
- Tansania: 20% of prevalent epilepsy cases

- 30% of people with epilepsy in endemic areas have got NCC (*Ndimubanzi et al. 2010*).

Countries and areas at risk of cysticercosis, 2009



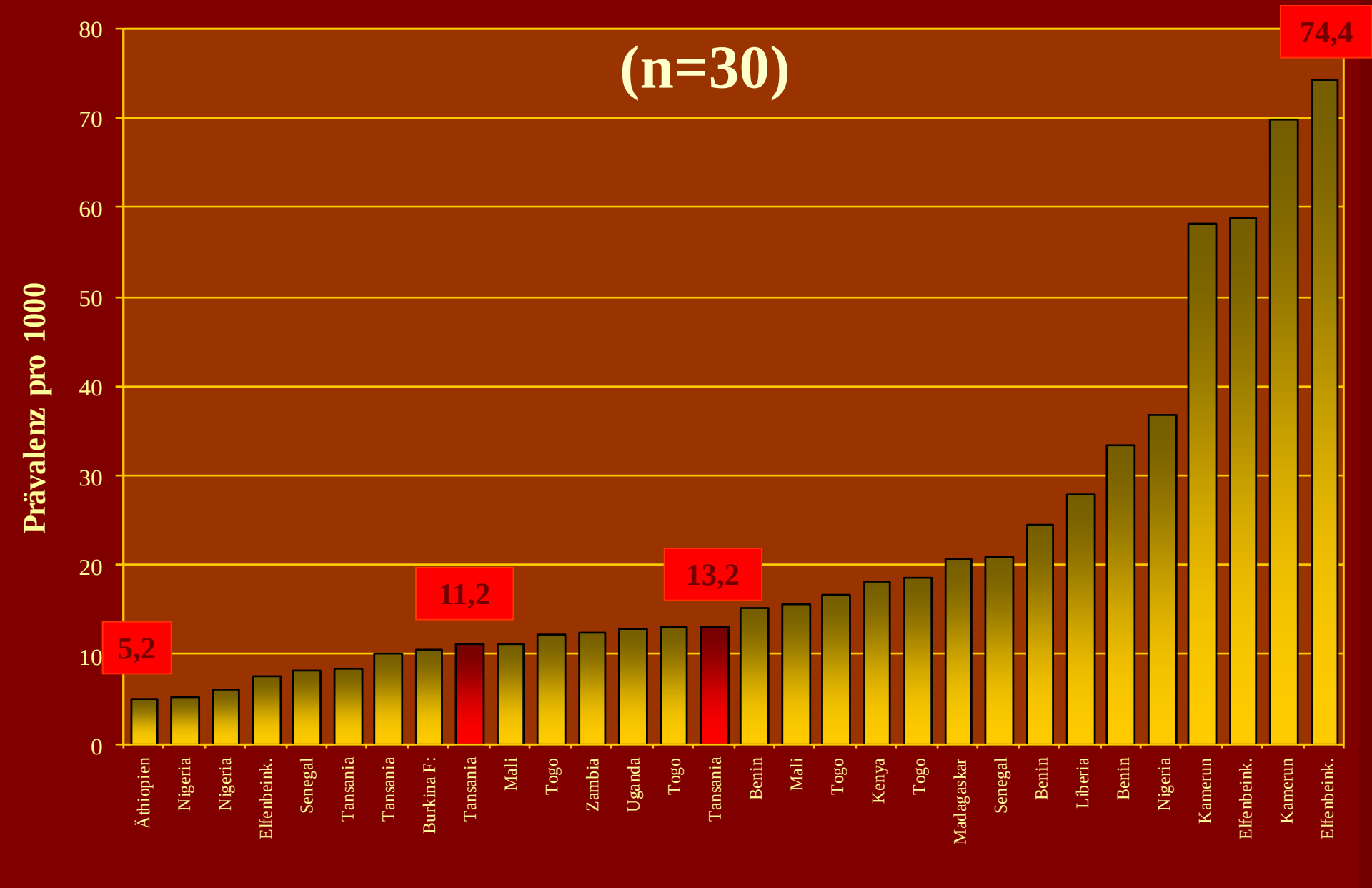
Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

Prevalence of neurocysticercosis (sub-Saharan Africa)

- Median prevalence of epilepsy in SSA is 15/1000 (*Preux and Druet-Cabanac 2005*).
- Real prevalence between 4 and 10/1000 (*Edwards et al. 2008, Winkler et al. 2009*).

Prevalences of epilepsy from rural Africa



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- Assume that 850 million people live in SSA (*World bank 2011*).
- Assume a global prevalence of NCC in PWE of almost 30% of PWE (*Ndimubanzi et al. 2010*).

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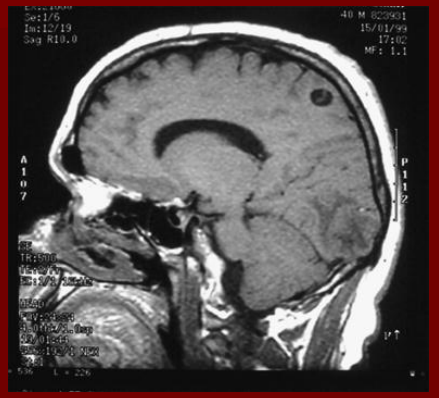
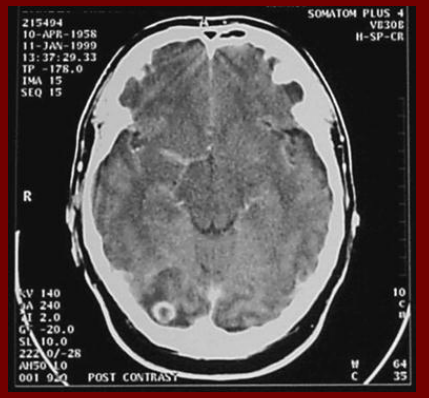
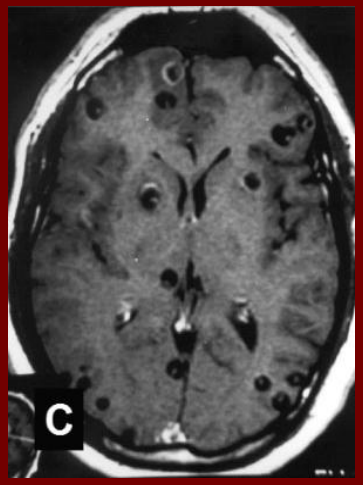
- *1.02-2.5 million people with NCC based on epilepsy*
- *3 million people with NCC based on all neurological symptoms*
- *In addition, 2.4 million people with latent NCC*

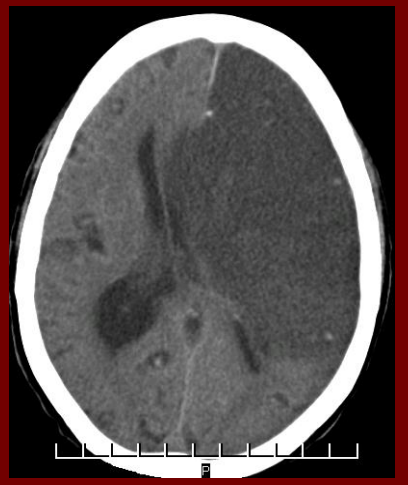
Pathology of NCC

- Focal lesions (with and without inflammation)
- Encephalitis (rarely Meningitis < 10% of all cases)
- Infarcts
- Vasculitis
- Hydrocephalus
- Myelopathy





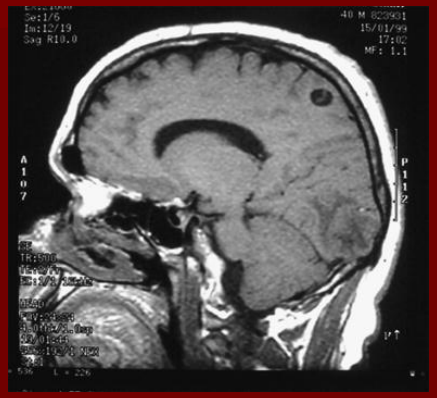


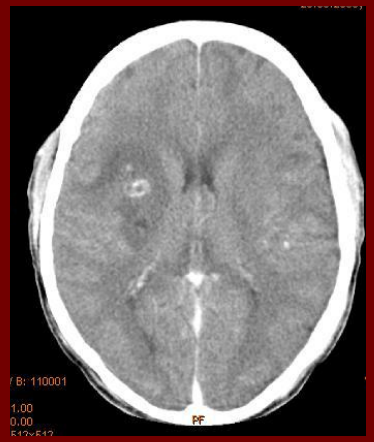


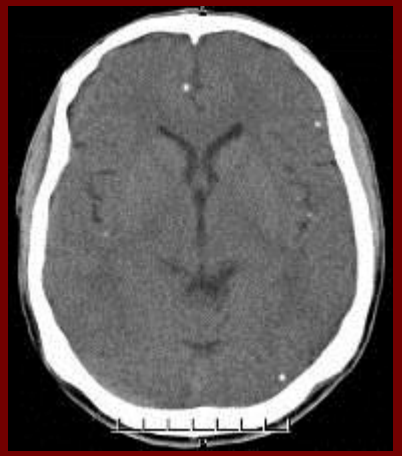
Classification of NCC

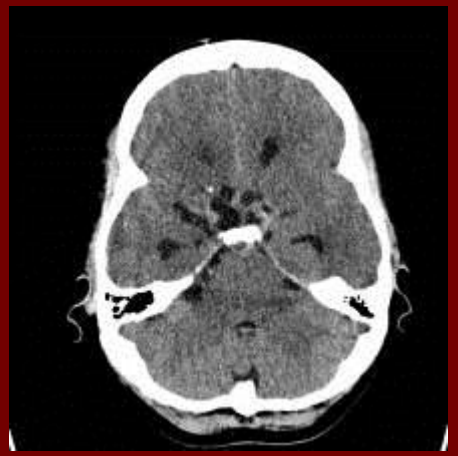
- Active (cysts)
- Transitional (granuloma and ring enhancing lesions)
- Inactive (calcifications)

- Parenchymal NCC
- Extraparenchymal NCC (ventricle, subarachnoid space)





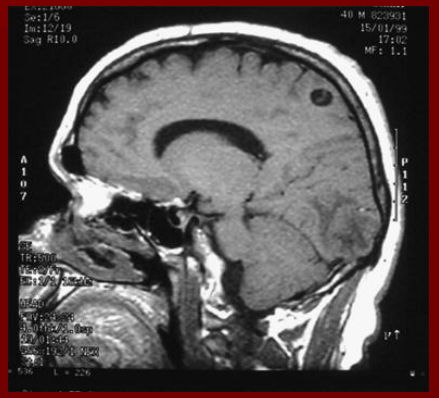


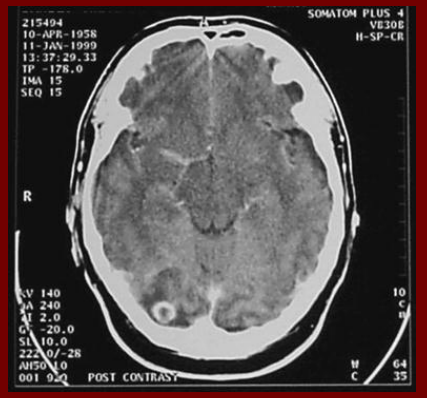


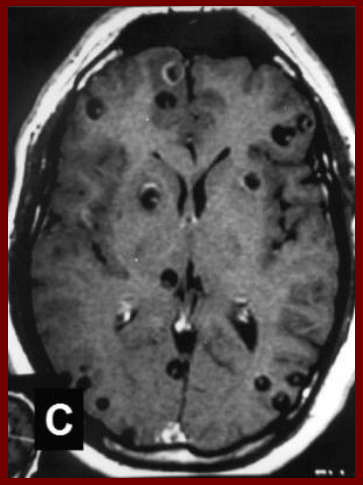
Symptoms of NCC

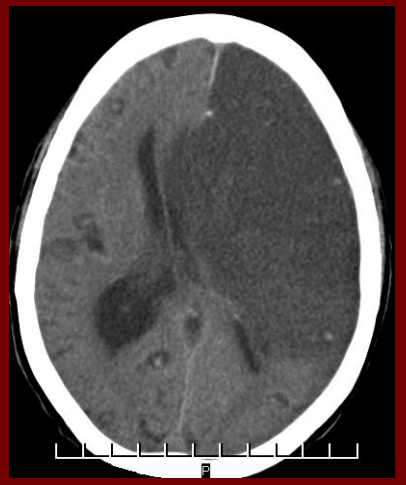
- **Symptomatic seizures**
- **Epilepsy**
- Headache
- Increased i.c. pressure
- Focal neurological signs
- Psychiatric problems
- Learning difficulties

- Very sick patient with encephalitis!









Locally adapted classification for epilepsy

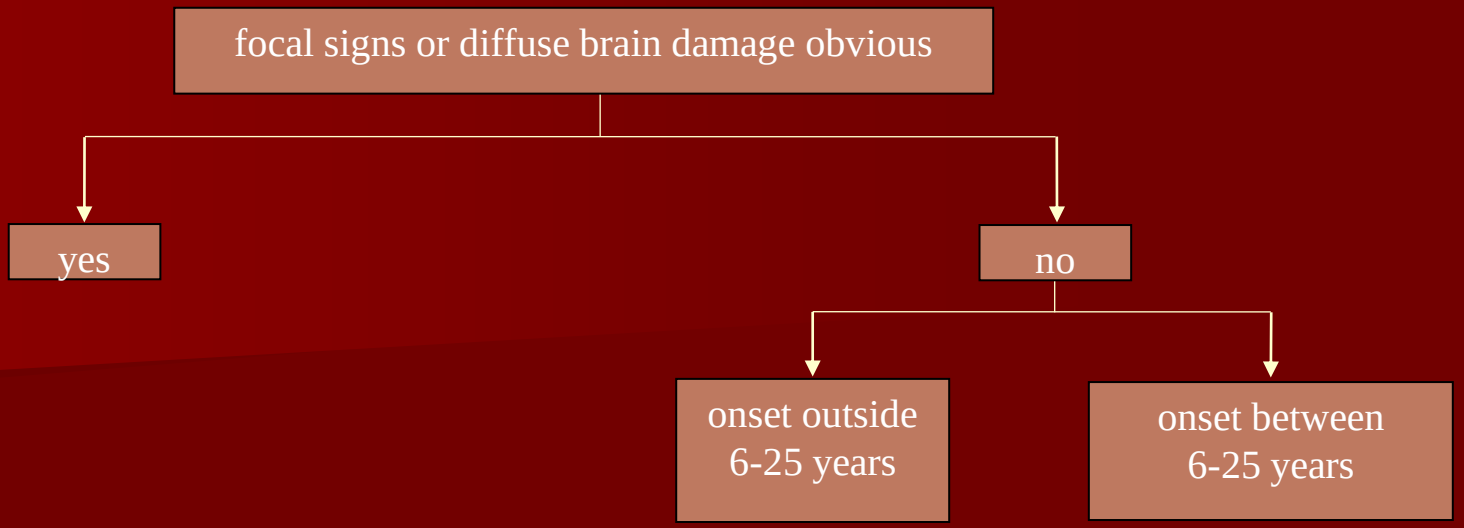
- Causes are different (e.g. infection, perinatal brain damage)
- Limited diagnostic possibilities (no EEG, MRT)
- Few specialized clinics
- Few trained personnel
- Limited medication

Epilepsy study in northern Tanzania

- Haydom Lutheran Hospital, northern Tanzania
- Recruitment of 346 people with epilepsy
- Recruitment phase 25 months (August 2002-September 2004)
- Screening of all patients with standardized questionnaires

ILAE classification of epileptic seizures (ICES)

I. Partial seizures (Seizures with a focal origin)
1. Simple partial seizures (consciousness not impaired)
2. Complex partial seizures (consciousness not impaired)
3. Secondary generalized seizures
II. Generalized seizures
1. Absences
2. Myoclonic seizures
3. Clonic seizures
4. Tonic seizures
5. Tonic-clonic seizures (Grand-mal)
6. Atonic seizures
III. Unclassified epileptic seizures


focal signs or diffuse brain damage obvious
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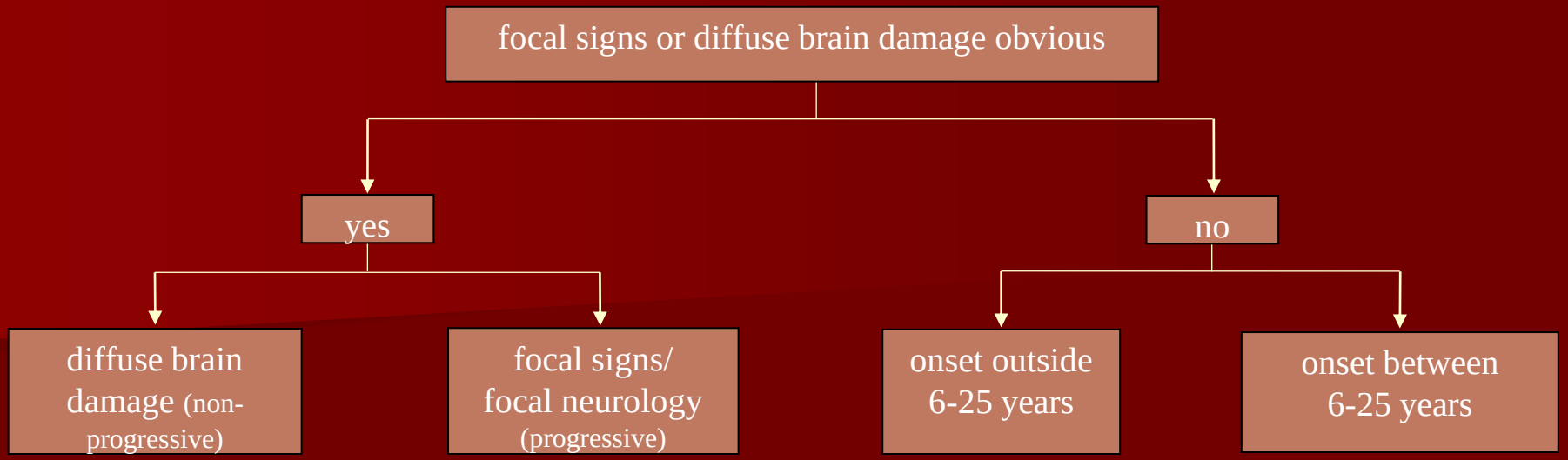
no
onset outside 6-25 years
onset between 6-25 years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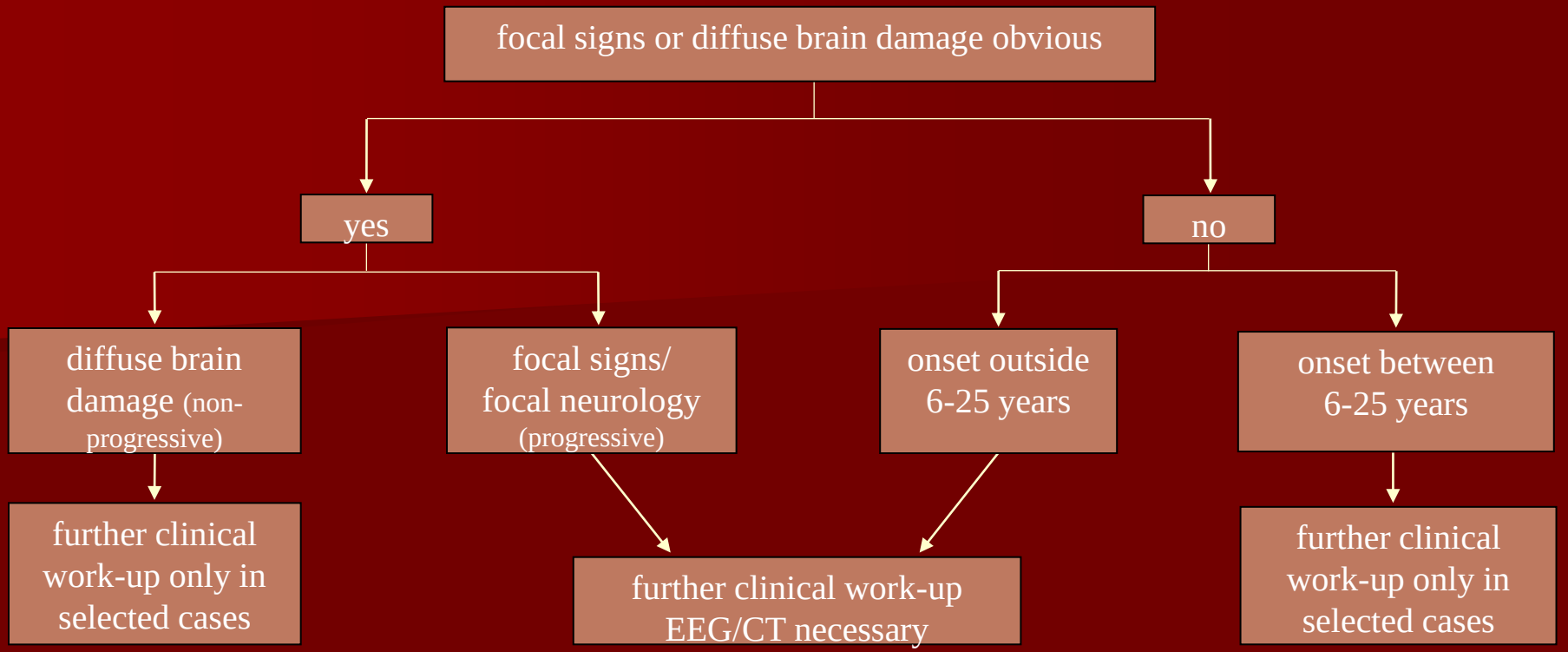
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further clinical work-up only in selected cases
further clinical work-up EEG/CT necessary
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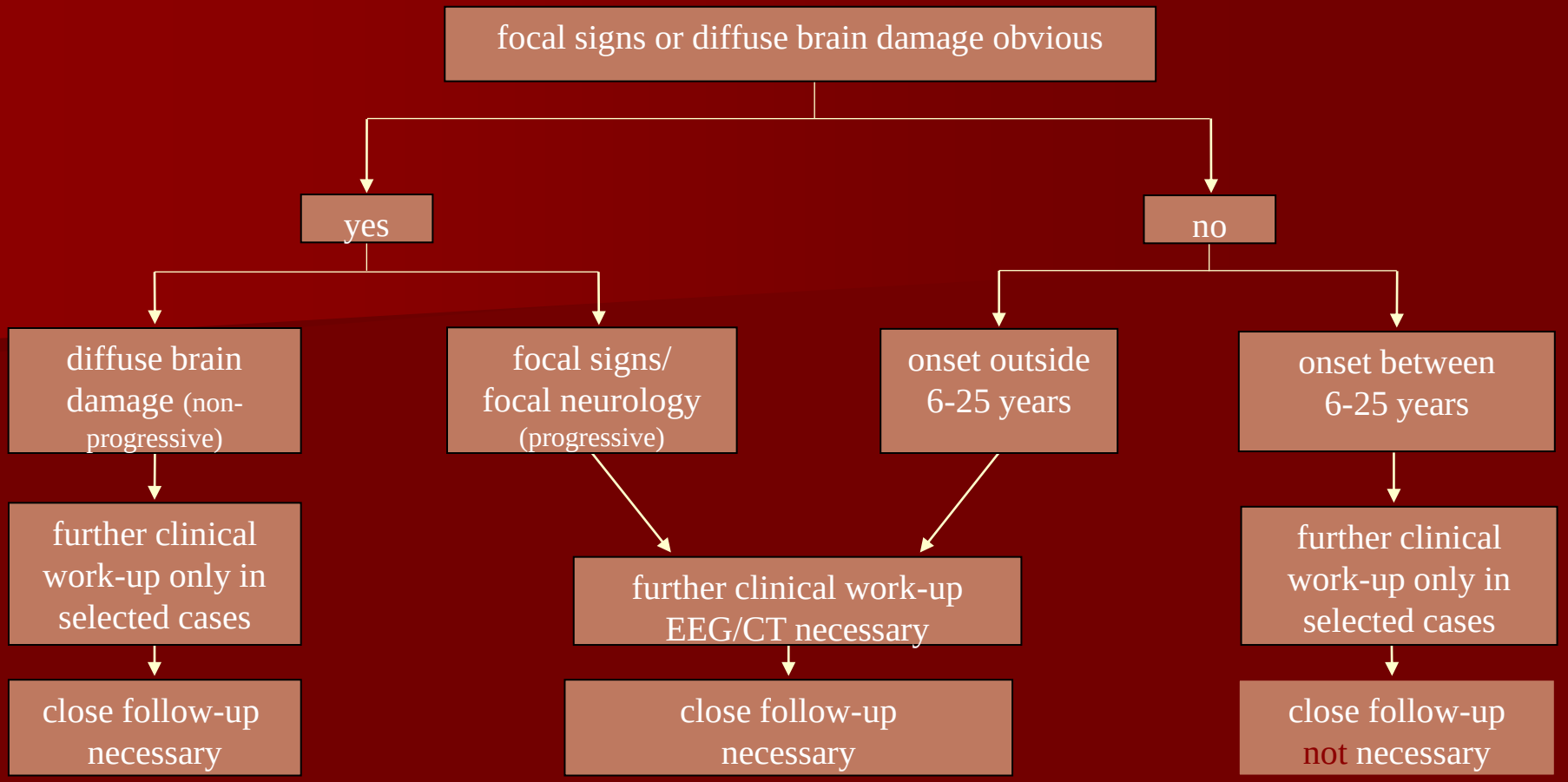
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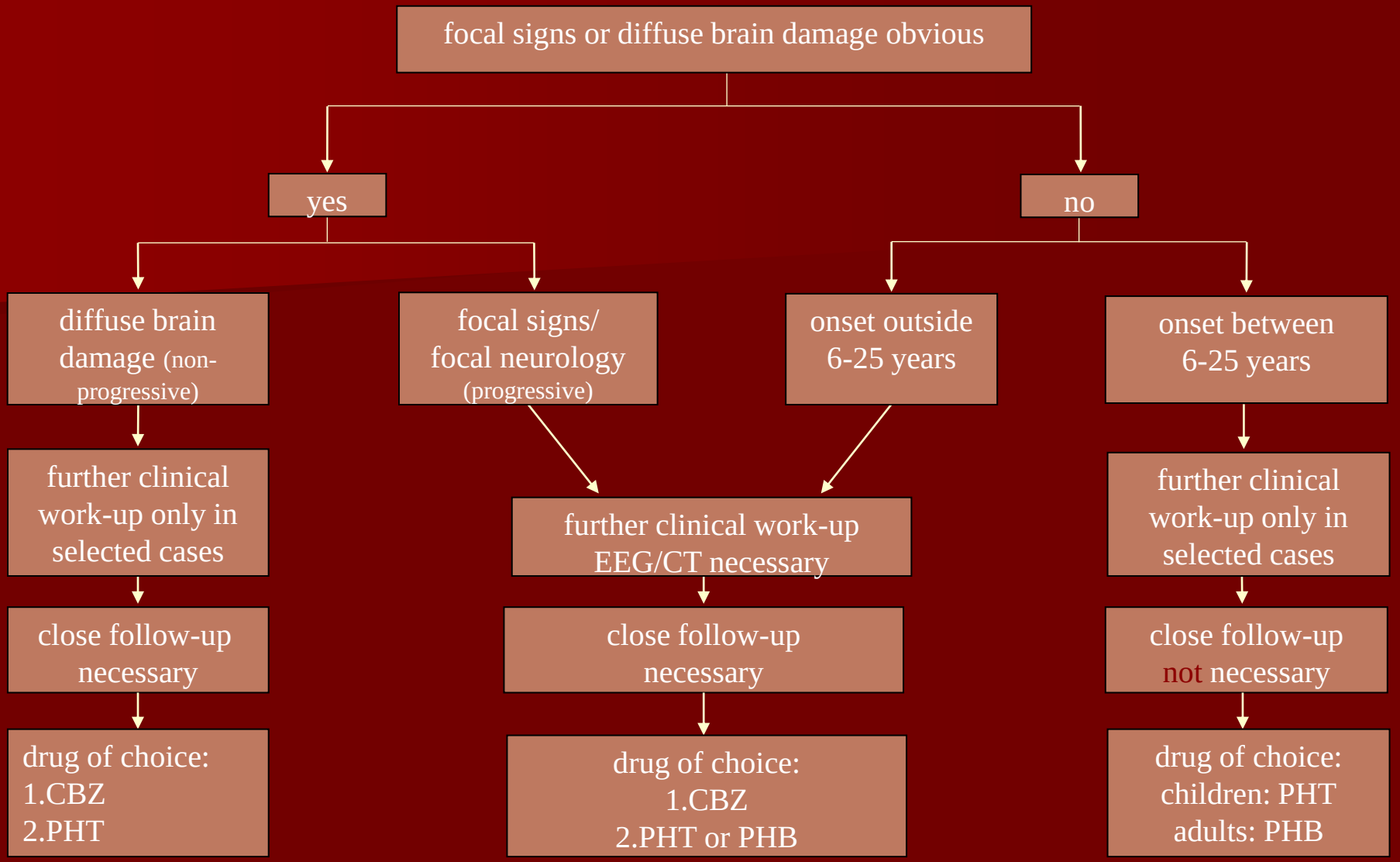
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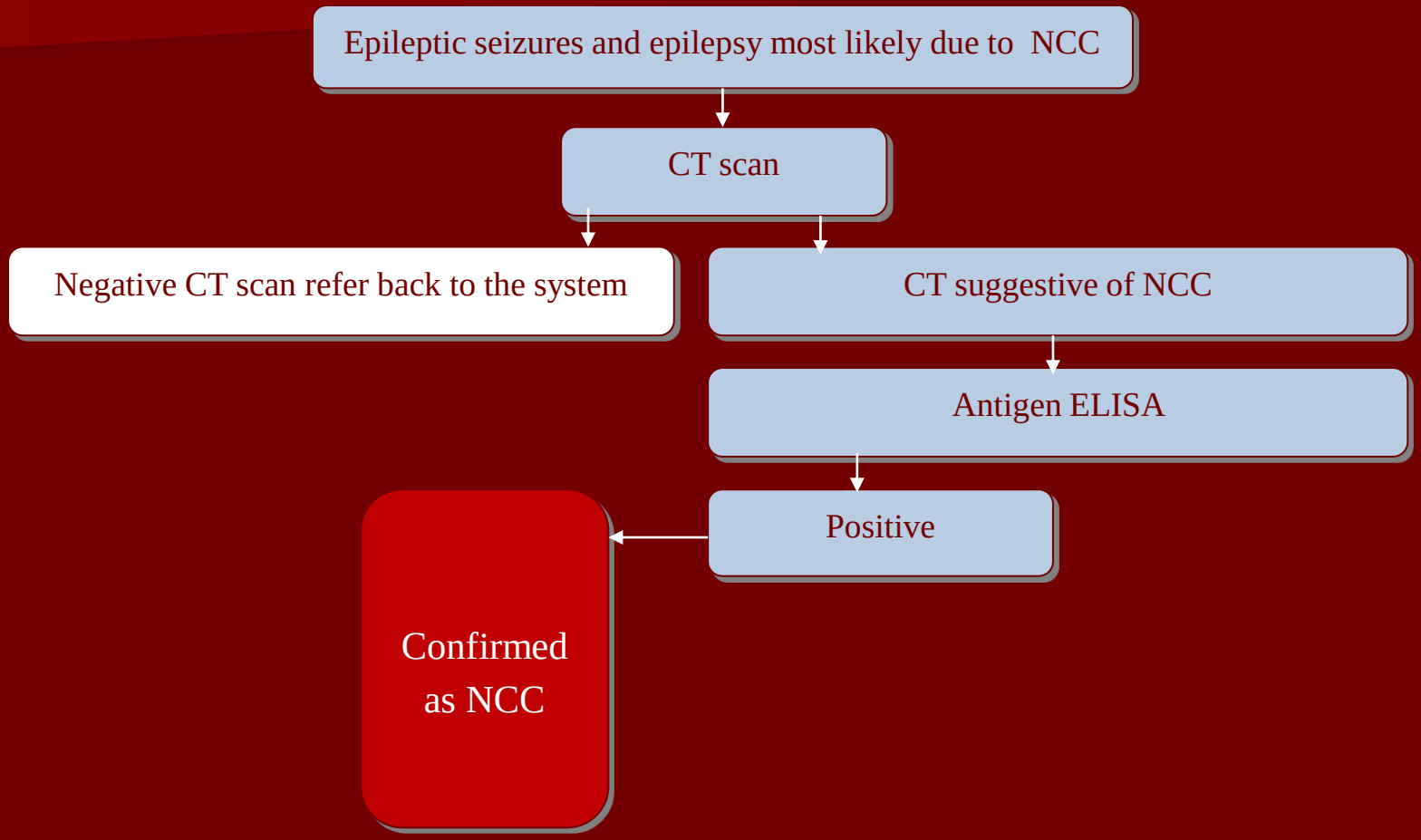
drug of choice: 1.CBZ 2.PHT
drug of choice: 1.CBZ 2.PHT or PHB
drug of choice: children: PHT adults: PHB

Advantages of the SSA classification

- Easy to use also for untrained personnel
- No need of EEG and imaging
- Transferrable to the ILAE classification
- Quick therapeutic triage
- Choice of right antiepileptic medication
- Approximate prognostic estimation

Diagnostic algorithm for suspected NCC in SSA?



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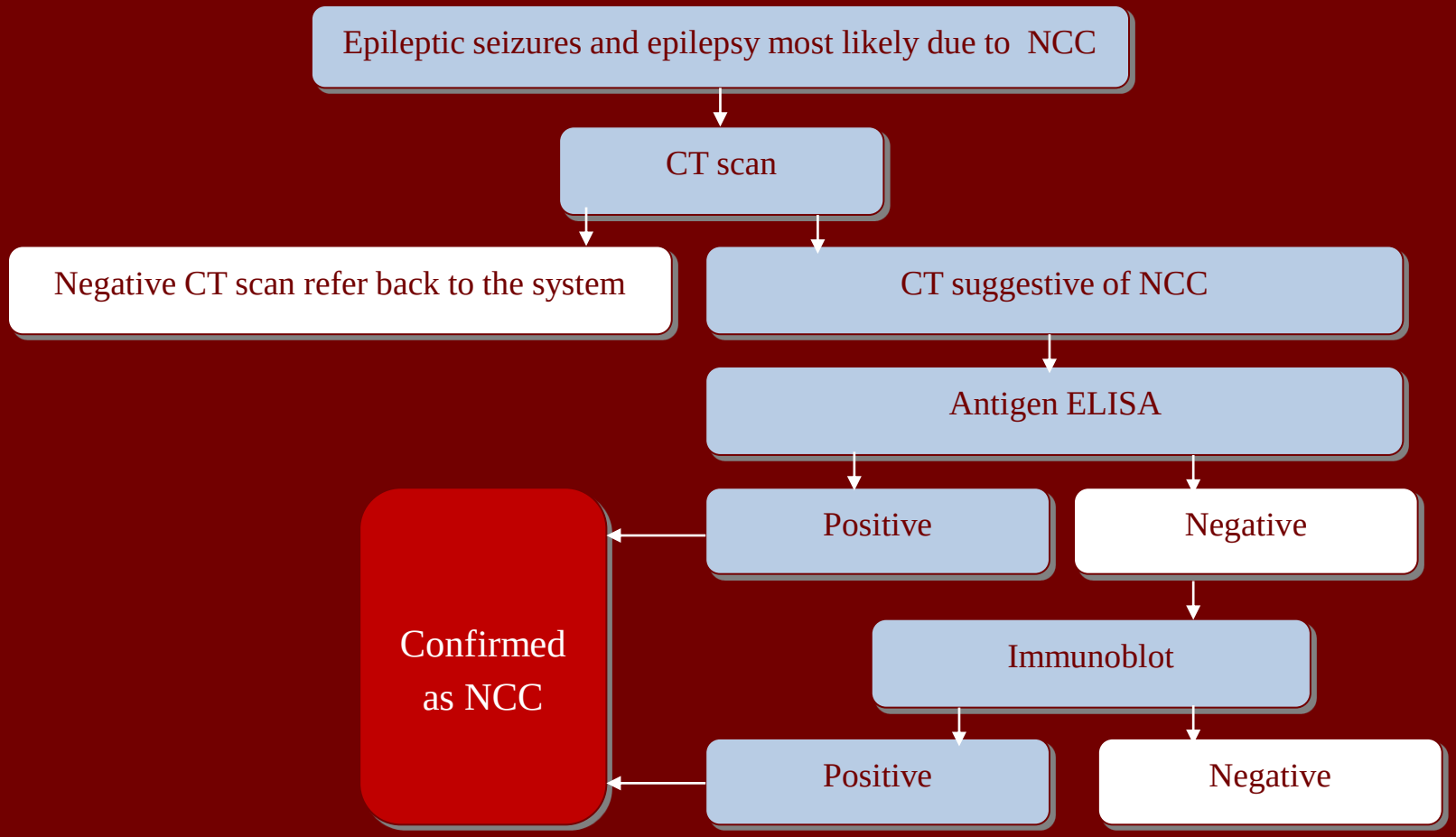


CT scan in SSA - why so important?

- Within a few weeks or months the situation in the brain can change for better or for worse.
- HIV status of the patients may play a role.
- If the number of cysts has increased, antihelminthic treatment may harm the patient seriously.
- If the number of cysts has decreased, antihelminthic treatment may be unnecessary altogether.
- Triaging of patients suitable for neurosurgery or those that would require special treatment regimes (subarachnoid/ventricular forms)

Therapy – when?

Factors that determine therapeutic approach in general:

- Localisation of cysts (intra- extraparenchymal)
- Stage of cysts (active, transitional, inactive)
- Number and size of cysts (single lesion – many lesions)
- Inflammatory response (contained – widespread)
- Severity of clinical symptoms
- Potential risk of future complications

Sentences to be retained when it comes to therapy?

- Do not treat asymptomatic cysts.
- Do not treat inactive lesions with antihelminthic drugs.
- Do not treat transitional lesion with antihelminthic drugs.
- Never use antihelminthic drugs in widespread inflammation.
- Never use antihelminthic drugs if cysts are scattered throughout the brain (encephalitis!).
- Subarachnoid and ventricular forms need special treatment considerations.

Symptomatic treatment

- Analgesics
- Steroids
- Antiepileptic drugs

Steroids

- Prednisolone: 1mg/kg/day p.o. or Dexamethasone 10-20 mg/d
- Length of treatment variable, according to symptoms

- At once and without antihelminthics in cases with cerebral oedema, signs of increased intracranial pressure, vasculitis, compression of the brainstem, spine or optic nerve.

- Antihelminthics may be given at a later point.

- In most parenchymal NCC together with antihelminthics; pre-treatment may be required; in subarachnoid forms high doses of both drugs and long treatment.

- Increased metabolism by antiepileptic medication

Antiepileptic medication

- Phenytoin, Phenobarbitone, Carbamazepine (usually well controlled with monotherapy on standard dosage)
- Therapy may be lifelong if calcifications are present.
- In active NCC after successful treatment for at least one year (no calcifications!) trial of tapering
- Additional antihelminthic medication reduces severity but not frequency of epileptic seizures (*Garcia et al. 2004*).

Antihelminthics (active NCC)

- Albendazole: 15 mg/kg per day x 8-15 days
- Praziquantel: 50 mg/kg per day x 8-15 days; short course: 100 mg/kg for one day!

- Albendazole is more effective than Praziquantel (better penetration into CNS)

- Increased metabolism by steroids and antiepileptic drugs (Praziquantel > Albendazole)

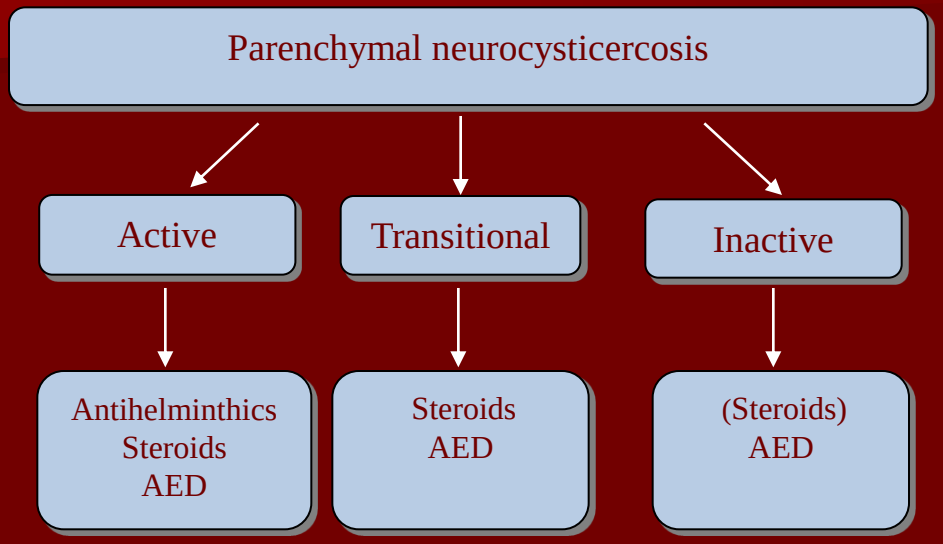
- Only in active NCC; be aware of sudden increased intracranial pressure with „sudden death“; Combination with steroids and control-CTs are essential!

- Contraindicated in encephalitis, increased intracranial pressure and ophthalmological cysticercosis

Surgery

- Ventricular form (endoscopically)
- Hydrocephalus shunting (mainly ventricular and subarachnoid form – prognosis in SSA poor)
- Accessible cysts with mass effect (e.g. Sylvian fissure)
- Potential danger of dissemination of cyst material
- Potential danger of hydrocephalus post-OP
- Perioperative risks (high in SSA)

Treatment algorithm for NCC



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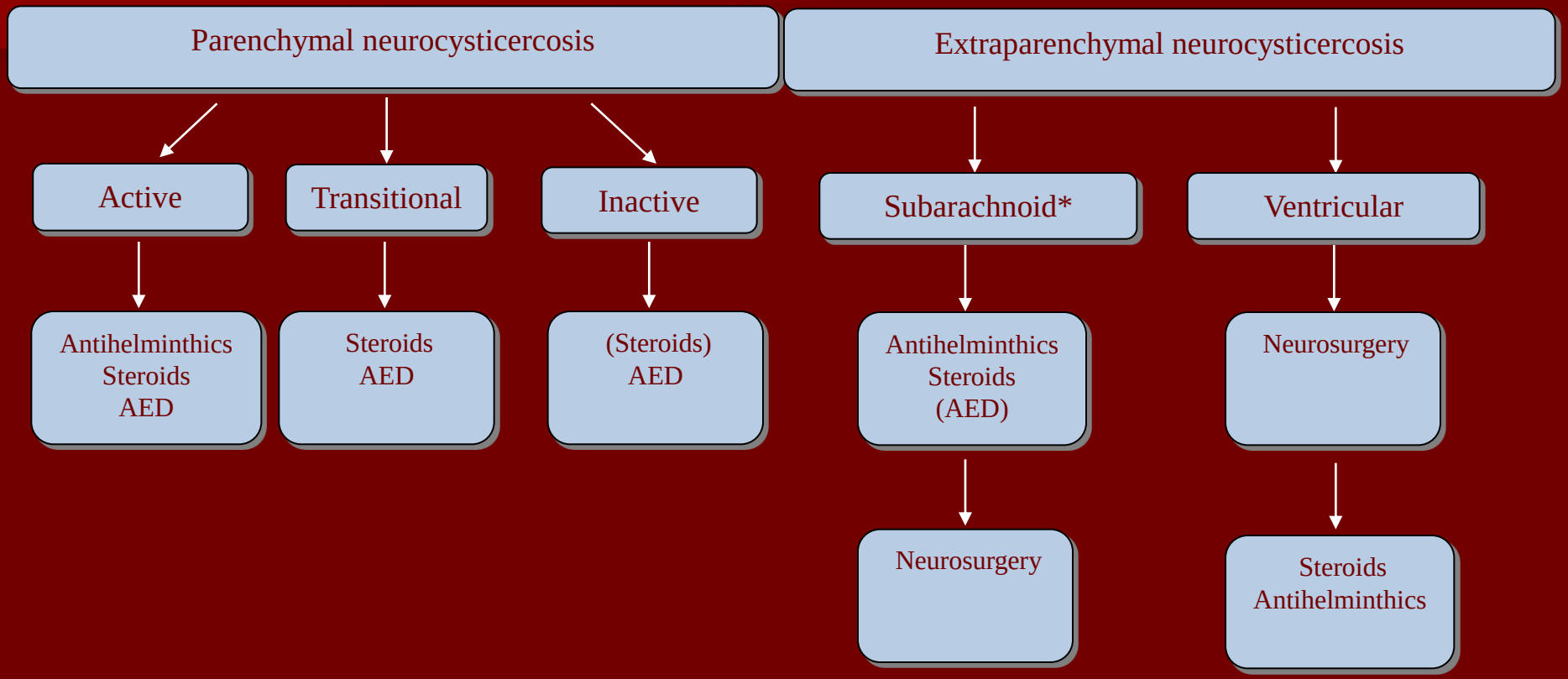
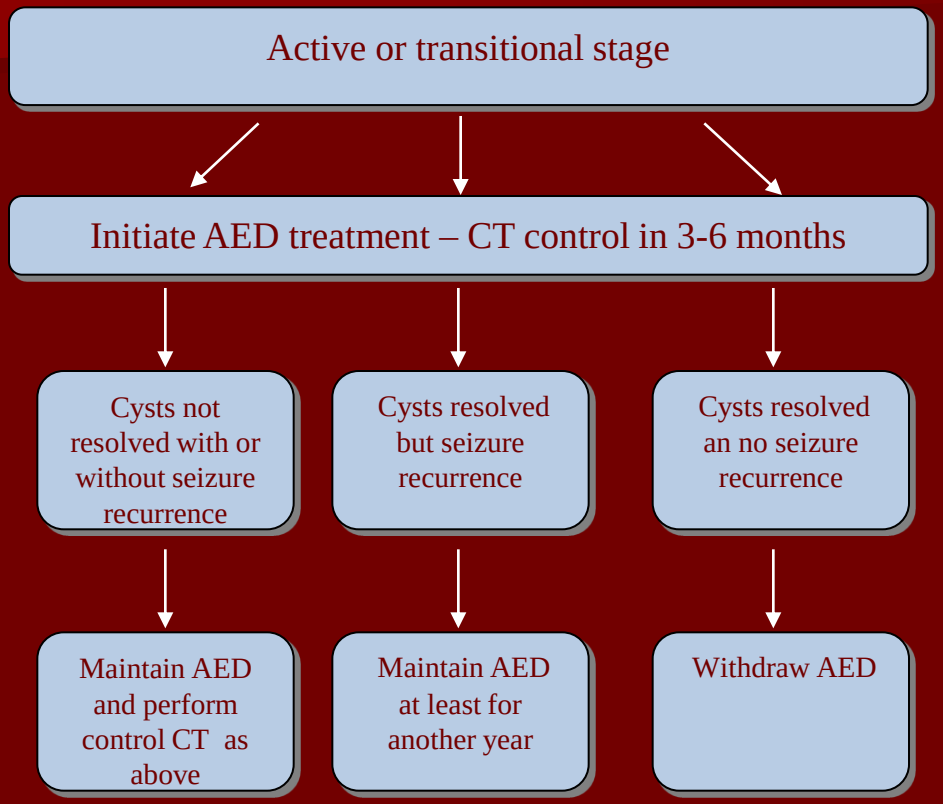


* The racemose NCC form is a malignant version of the subarachnoid form.

Treatment algorithm for epileptic seizures



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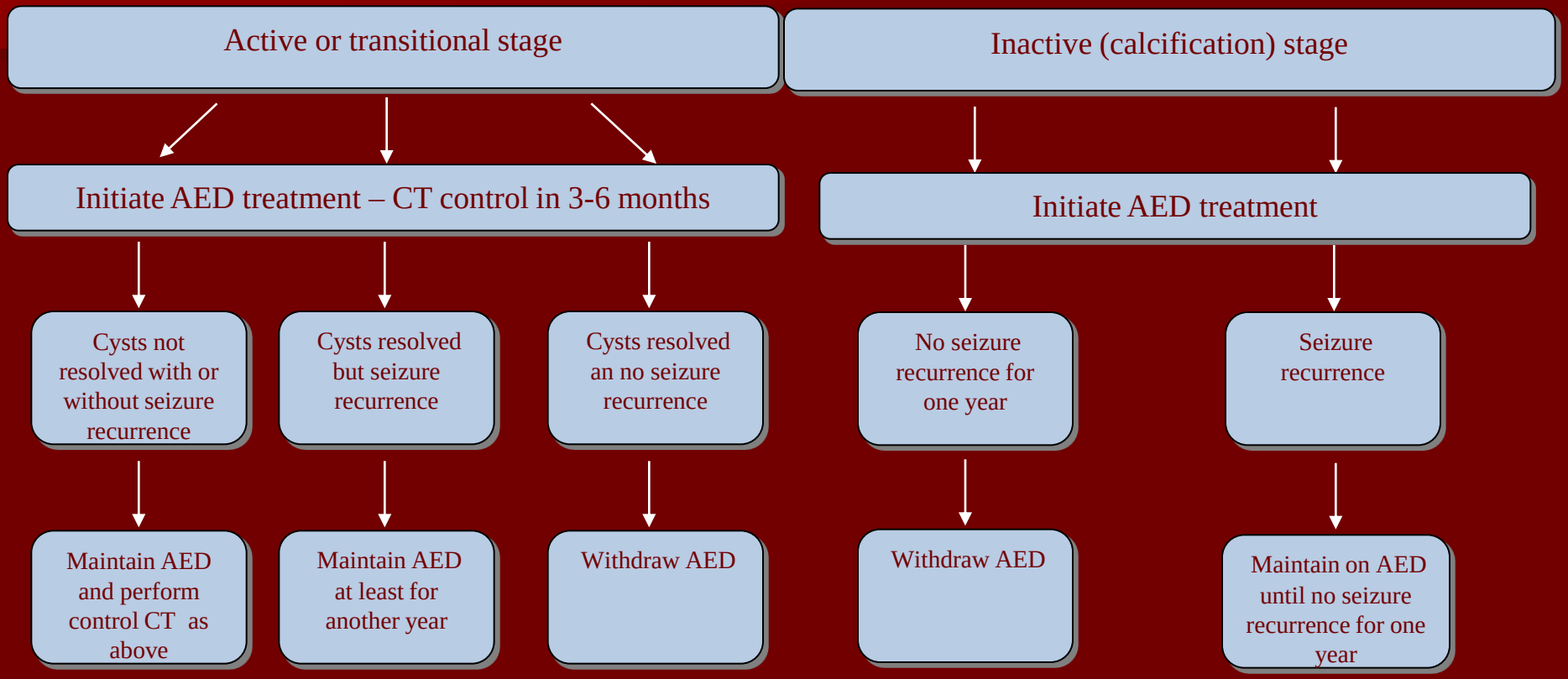
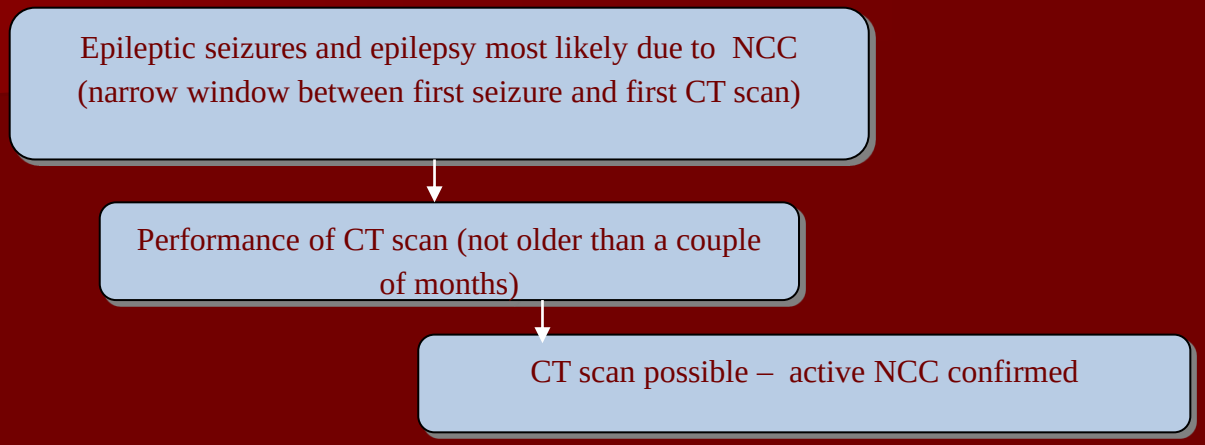


Carpio and Ross 2012 http://emedicine.medscape.com/article/1168784-overview#a0199

Treatment algorithm for SSA according to availability of CT scans



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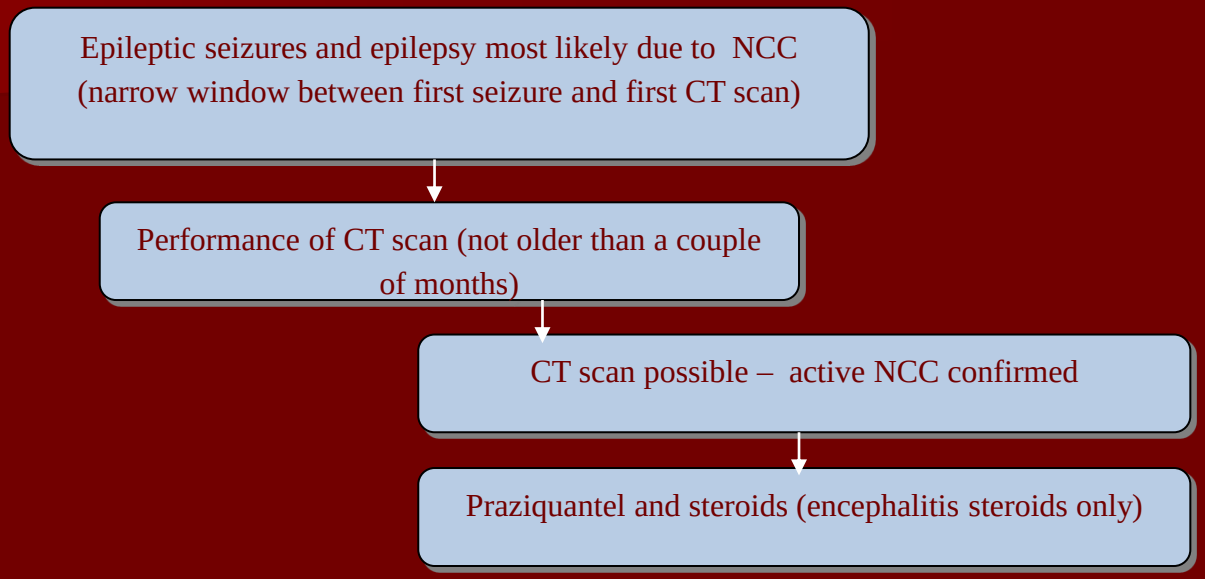

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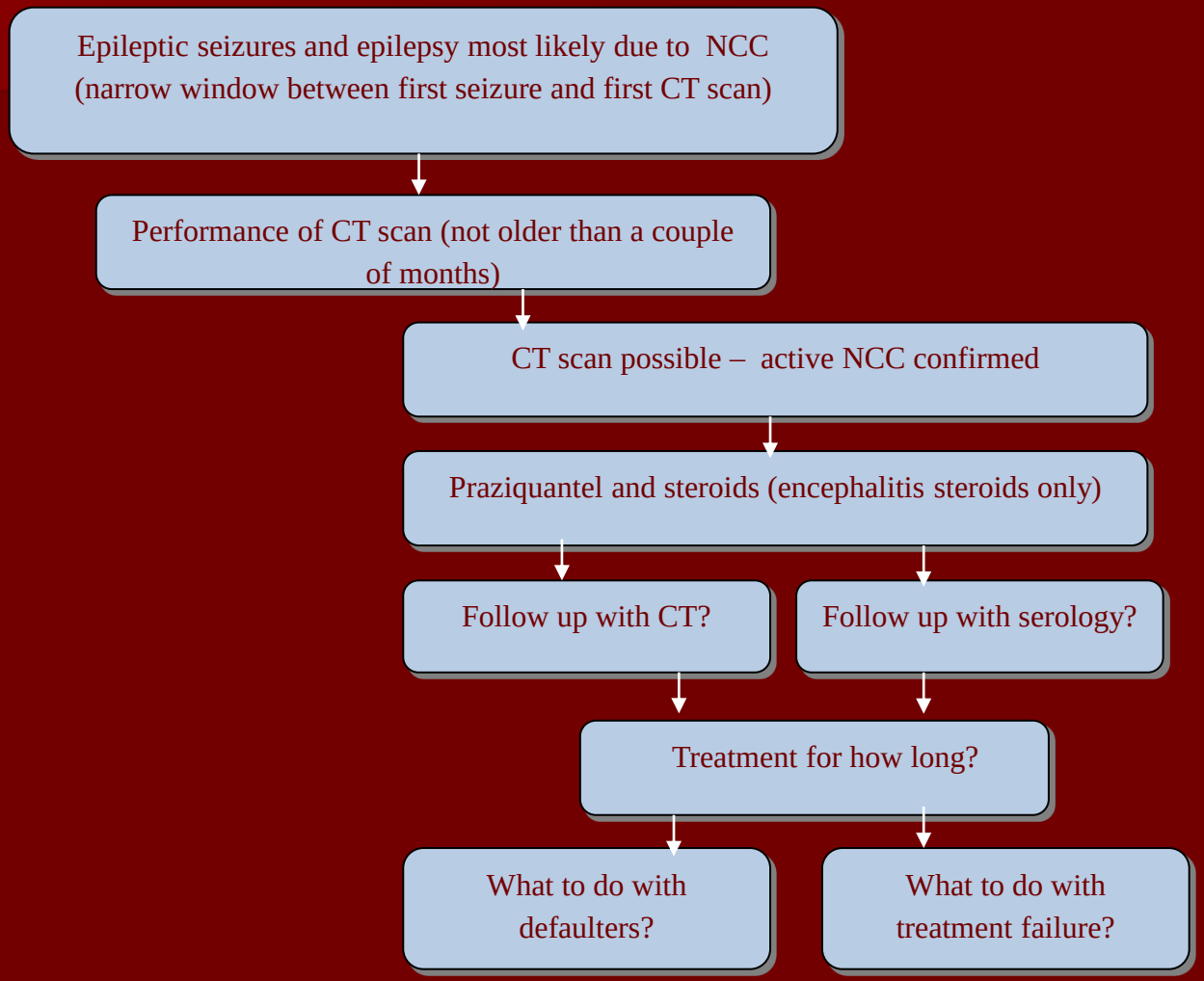

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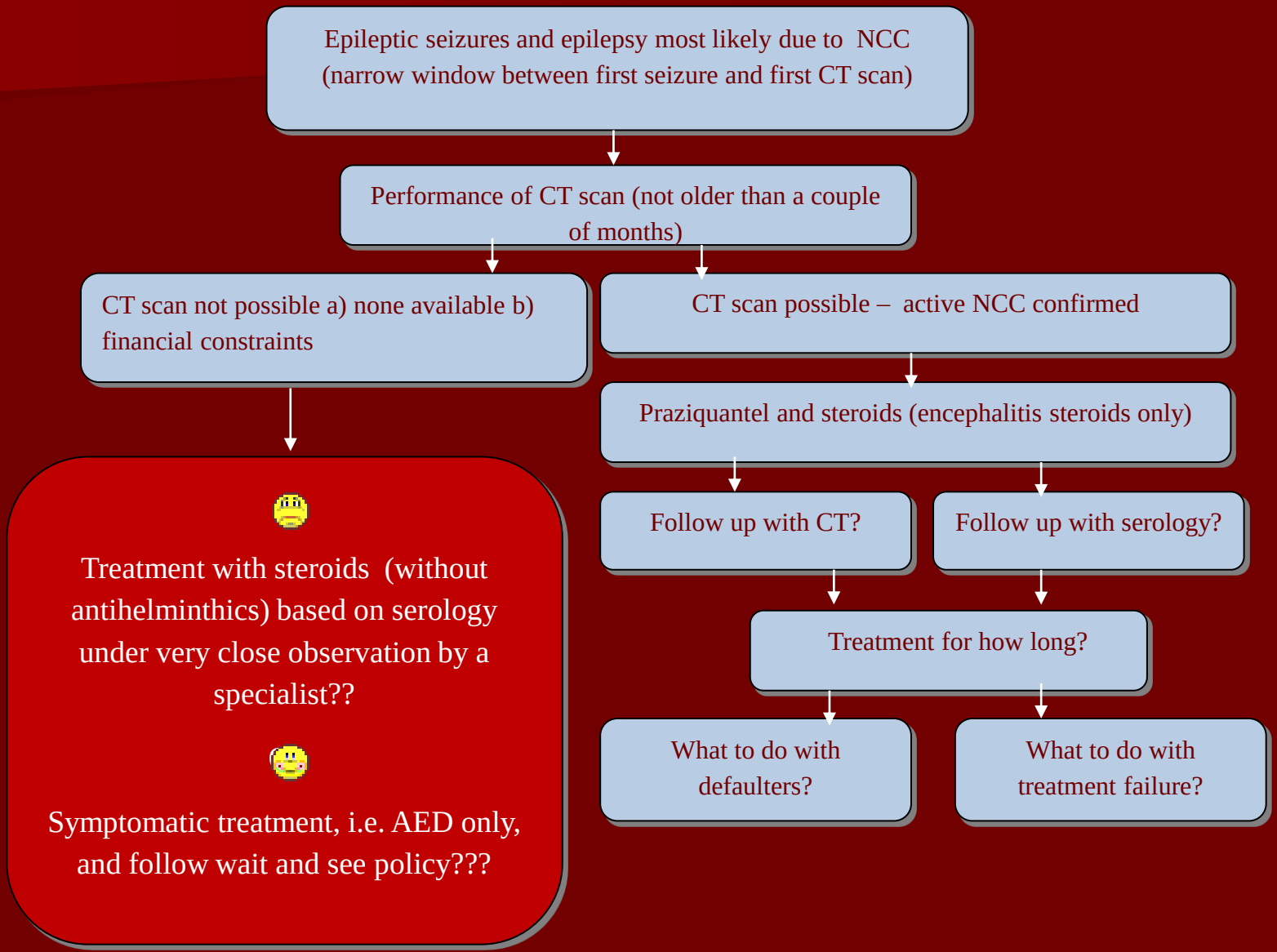

Future?

Five important 80:20 rules

- Most people with NCC are asymptomatic: Symptomatic cases account for between 10% and 40% of all NCC cases (Carpio & Ross 2012 (medscape)).
- 20% of symptomatic cases will be due to active NCC (cysts etc); 80% due to calcifications.
- If symptomatic, seizures present in approx 80% (78%; *Carabin et al. 2011*).
- 30% of people with epilepsy in endemic areas have got NCC (*Ndimubanzi et al. 2010).*
- 80-90% have intraparenchymal forms and 20-10% have extraparenchymal forms.