

How do you solve a problem like Malaria?



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Disclosure

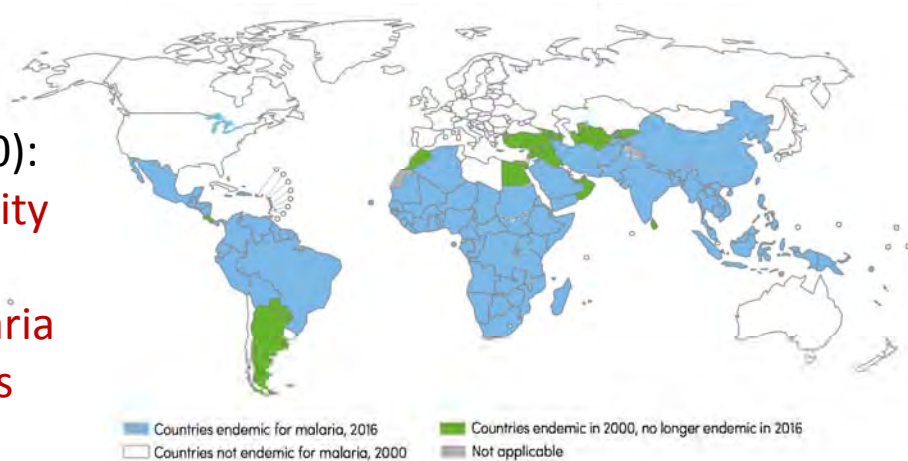
- We have no relevant financial relationships to disclose.

Objectives

- 1) Recall the classic signs and symptoms of uncomplicated malaria and contrast diagnostic measures
- 2) Review the approach to seizures in cases of malaria
- 3) Apply treatment principles for severe malaria based on guidelines and evidence-based medicine
- 4) Identify prognostic factors to predict outcomes in cases of malaria

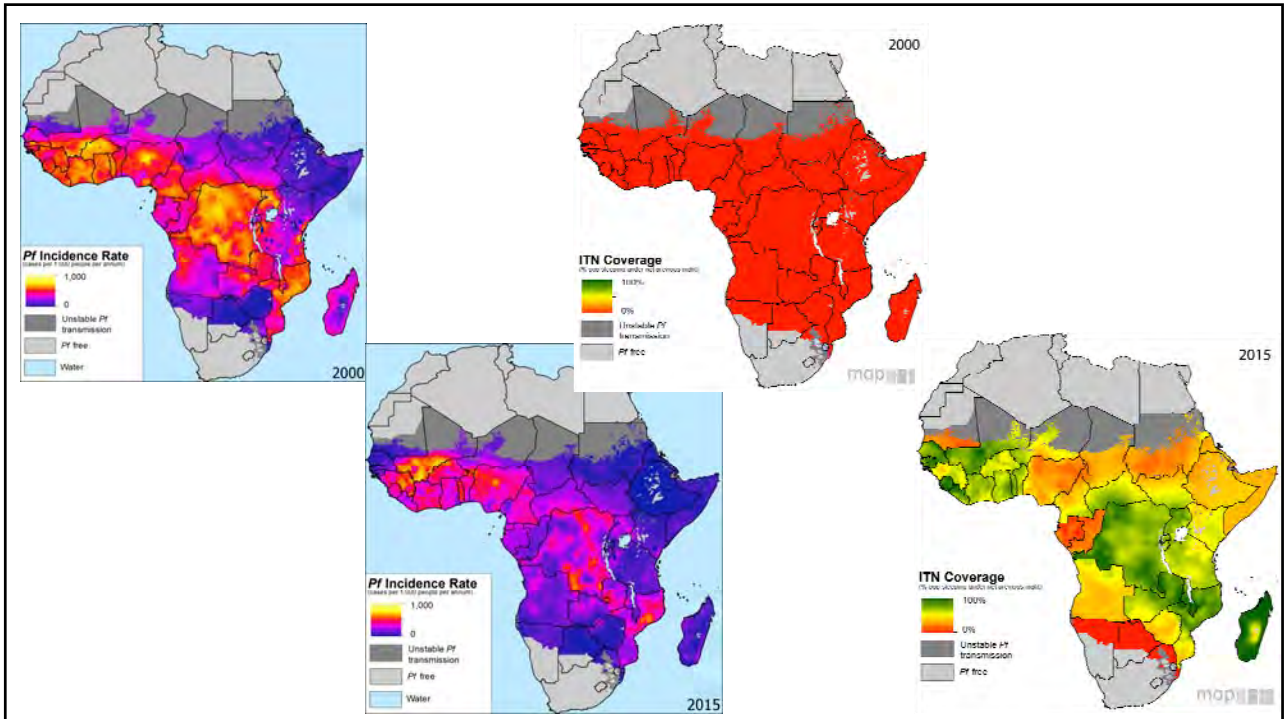
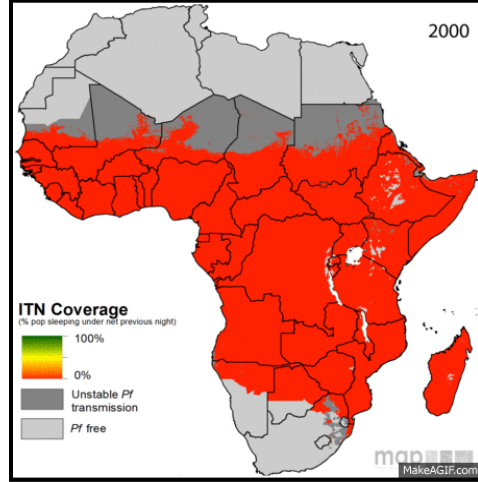
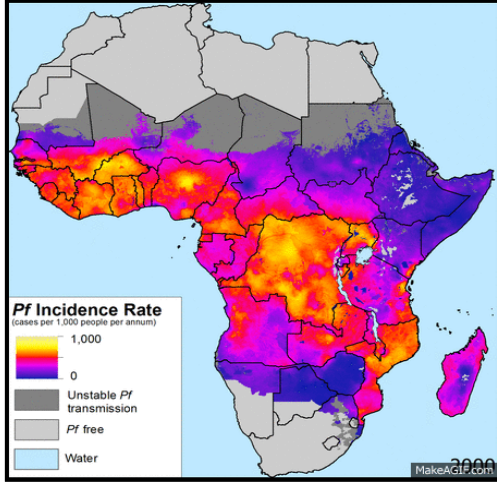
Global Targets (GTS 2016-2030):

- Reduce mortality by >90%
- Eliminate malaria in >35 countries



Incidence

ITN



Case

- You are working in a hospital in sub-Saharan Africa.
- A 5-year-old girl presents with fever, chills and malaise x 2 days. This morning she woke up and vomited once, and her father witnessed a 2-minute generalized tonic-clonic seizure.
- He brings her to the nearest hospital. On arrival she is alert and is tired but generally well- appearing.




You suspect which of the following?

- A. Complicated malaria
- B. Uncomplicated malaria
- C. Influenza
- D. Shigella gastroenteritis
- E. Not enough information to answer


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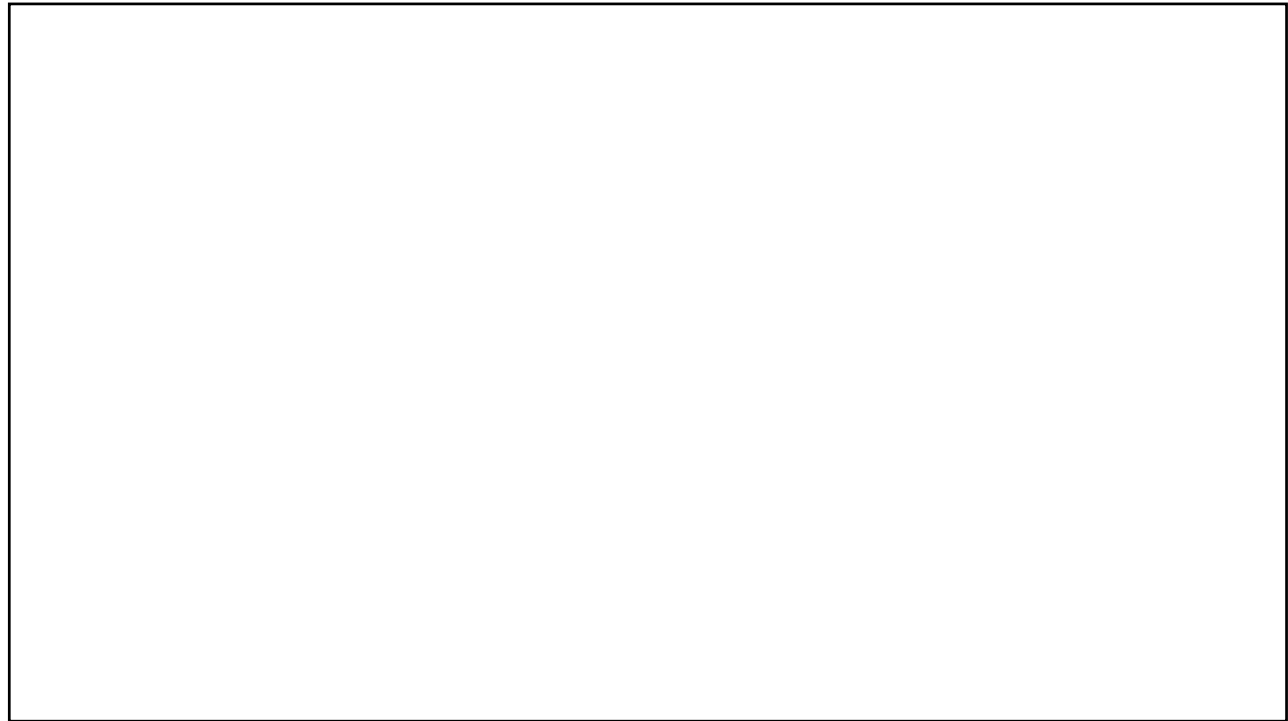
**Uncomplicated
Malaria**

- Fever
- Fatigue & Lassitude
- Nausea and vomiting
- Muscle and joint pain
- Cough
- Diarrhea



Given that you are in a malaria endemic area you think uncomplicated malaria is likely. Your options for malaria testing include:

- A. Thick and thin film microscopy
- B. Only thick film microscopy
- C. Immunochromatographic Rapid Diagnostic Tests (RDTs)
- D. Nucleic acid PCR
- E. Malaria Binding Protein Assay (MBPA)



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Suspected malaria: Nonspecific Sx's

∴ whenever possible parasite testing should be done
Do not rely on clinical diagnosis

Where malaria transmission is HIGH, test when:

- Hx of fever or T>37.5 w/o other obvious cause
- Children with "pallor" or Hgb<8

Where malaria transmission is LOW :

- More discretion should be used prior to parasitological diagnosis

	Thick Film Microscopy	Thin Film Microscopy	RDTs	Nucleic acid PCR
Sensitivity	+++	+	+/- *	+++
Specificity	++	++	++	+++
Identification	+	+++	+/-*	+++
Quantification	-	+++	-	-
Other	Most sensitive method routinely available	Allows quantification and identification	<ul style="list-style-type: none"> • Easy • Minimal training • Improves time to treatment • No electricity required! 	<ul style="list-style-type: none"> • Detection of drug resistance patterns. • Not available rapidly or in most LMICs

* Depending on they type of RDT some only detect p.f.



Case

- You are working in a hospital in sub-Saharan Africa.
- A 5-year-old girl presents with fever, chills and malaise x 2 days. This morning she woke up and vomited once and her father witnessed a 2-minute generalized tonic-clonic seizure.
- He brings her to the nearest hospital. On arrival she is sleepy and hypotonic.



Differential Dx?

- Idiopathic
- Febrile Seizure
- Hypoglycemia
- Malaria
- Uremia?
- Meningitis?

Seizures

- Most common neurological complication of acute *P falciparum* malaria
 - simple tonic-clonic
 - partial convulsive episodes
 - clinically silent electrical status
 - excess salivation
 - irregular respiratory pattern



Definitions

Definitions

- Neuro
- Resp
- CVS
- Metabolic
- Heme
- Renal
- ID

Definitions

- **Neuro**
 - ALOC: GCS < 11 (adults) / BCS < 3 (children)
 - Prostration
 - Seizures: >2 in 24h
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- Pulmonary edema: CXR / O₂sat < 92% with RR > 30

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- Shock: CRT > 3 sec / SBP < 70 (decomp)

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- Acidosis: BD > 8 / HCO₃ < 15 / Lactate > 5
- Hypoglycemia: <40

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- **Heme**

- Anemia: Hgb < 5 / Hct < 15
- Jaundice: Tbili > 3
- Bleeding

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 - Renal impairment: Creat > 3 / BUN > 20
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 - Hyperparasitemia: P falciparum > 10%

ALOC


Blantyre Coma Scale		Score
Tracking (“eyes”)	Watches/follows	1
	Fails to watch/follow	0
Verbal (“mouth”)	Cries appropriately/speaks	2
	Abnormal cry/moans	1
	No vocal response to pain	0
Withdrawal (“motor”)	Localizes pain	2
	Withdraws from pain	1
	No response	0

The patient’s smear is positive for malaria.
What is your next step?

- A. Obtain rapid diagnostic test to confirm smear results
- B. Give normal saline bolus 20 mL/kg
- C. Obtain lumbar puncture
- D. Start parenteral antimalarial
- E. Intubate


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Work-up

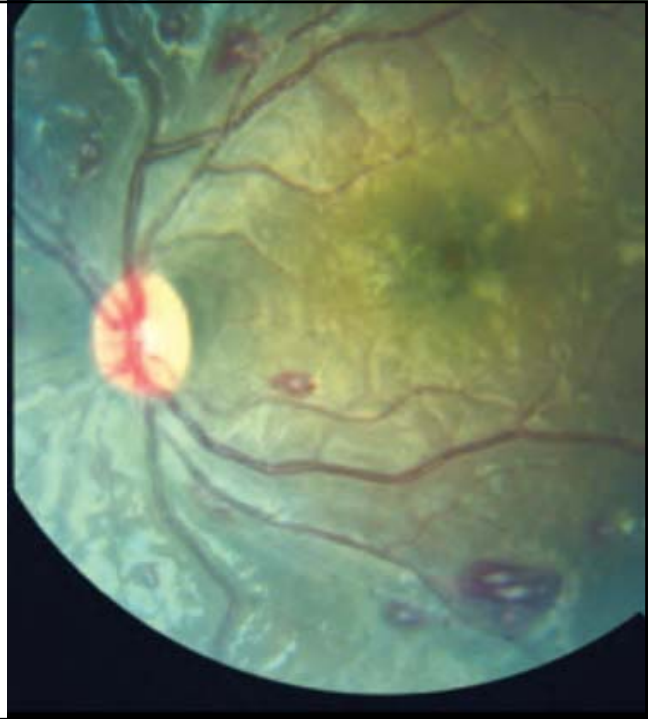
- CBC
- Blood culture
- Chem panel
- Type and cross
- Smear
- LP

Work-up

- CBC ✓
- Blood culture?
- ~~Chem panel~~
- Type and cross ✓
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- LP???

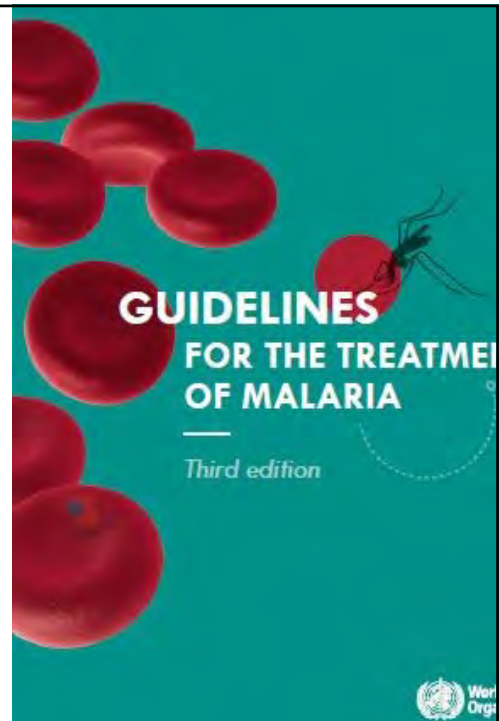
Cerebral Malaria

- Clinical dx considerably improved by ophthalmoscopy
 - retinal whitening
 - vessel changes
 - retinal hemorrhages
 - papilledema



Objectives of Tx

- Primary: prevent death (!)
 - Mortality 100% without treatment, 10-20% with
- Secondary:
 - Prevent disability
 - Prevent recrudescence of infection
 - Prevent spread of infection



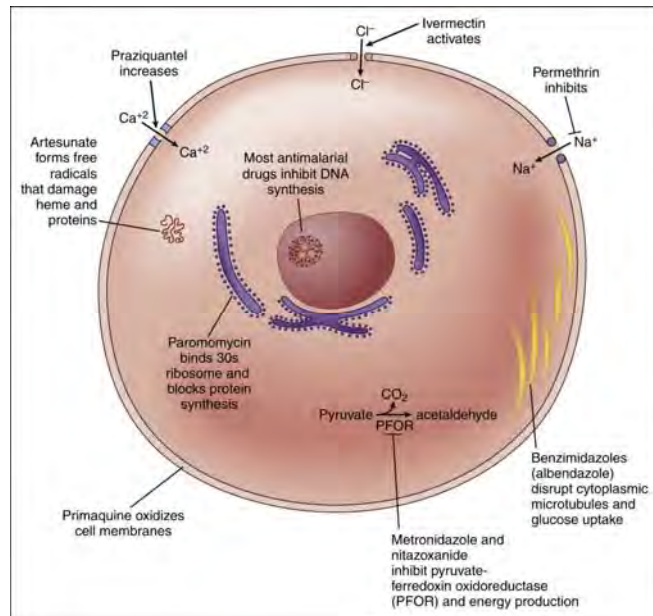
First steps

- A
 - Control airway in unconscious patient
- B
 - Supplemental oxygen
 - Respiratory support
- C
 - IV access
- D
 - Coma score
 - Glucose level



Anti-malarials

- Initial - Parenteral
 - Artesunate IV/IM/PR
 - Artemether IM
 - Quinine IV/IM
- Follow-on – PO
 - ACT

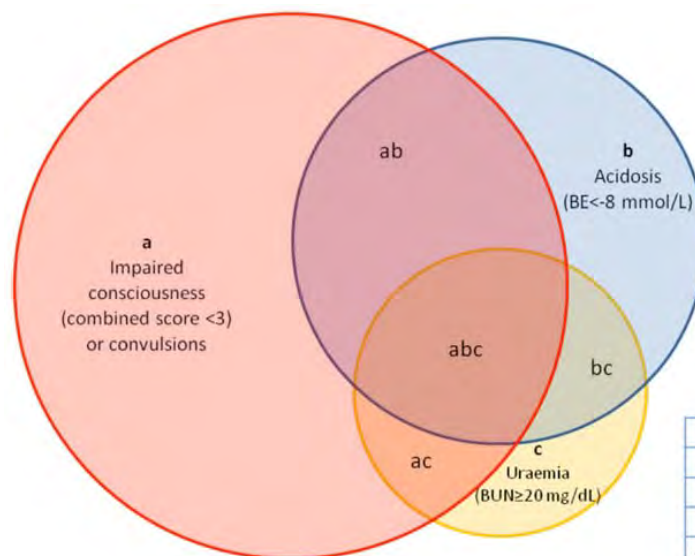


Additional aspects

- Fluid Therapy
 - Boluses are contraindicated (!)
- Blood transfusion
- Antibiotics
 - Indicated in areas of moderate/high transmission
- Anticonvulsants
 - Respiratory support is essential

Outcomes

- 2 *clinical* features, impaired consciousness (defined as coma or prostration) and respiratory distress (a clinical sign of metabolic acidosis), identified 84% of fatal cases [Marsh, *NEJM* 1995]
- 4 parameters (out of 20 indicators of severity) independently associated with fatality [von Seidlein, *Clin Inf Dis* 2012]:
 - base deficit (>8 mmol/L)
 - coma
 - elevated blood urea nitrogen (BUN, >20 mg/dL)
 - underlying chronic illness



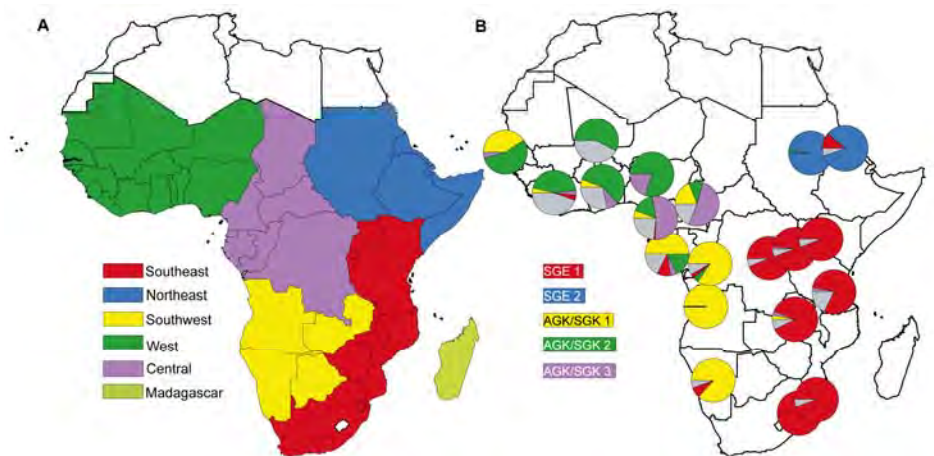
	Total	Died	%
a	1123	64	6%
b	658	39	6%
c	185	12	7%
abc	312	133	43%
ab	438	100	23%
ac	183	34	19%
bc	329	41	13%

von Seidlein, *Clin Inf Dis* 2012

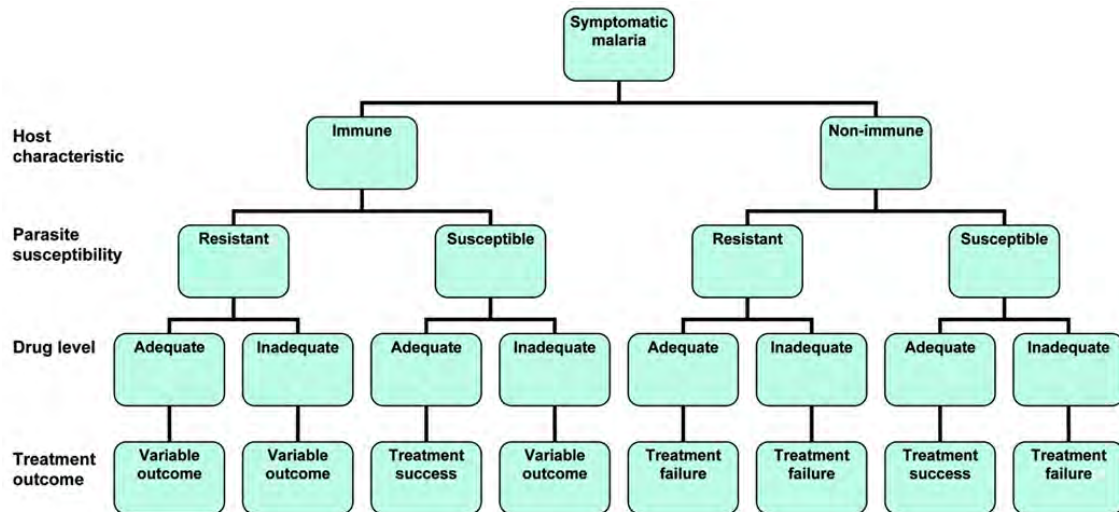
Outcomes (2)

- Outcomes for cerebral malaria remain poor, with high in-hospital mortality and neurological sequelae in survivors
- Greatest mortality were children with coma (19.6%) [Dondorp, *Lancet* 2010]
- Sequelae occurred in approximately 11% [Newton, *Pharm Ther* 1998]
 - ataxia (43%)
 - hemiplegia (39%)
 - speech disorders (39%)
 - blindness (30%)
 - cognitive and behavioral abnormalities

Antimalarial Drug Resistance Patterns



Mechanisms of drug resistance



New hope

ABUZZ PROJECT



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Take home points

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1. For diagnosis, thick smear is gold standard ... but RDT less dependent on technique, and can diagnose pre-treated cases
2. Seizures in children with malaria may be multifactorial ... maintain a broad differential to detect all possible causes
3. In a child with coma in RLS, treat empirically with parenteral antimalarials ... without waiting for diagnostic results
4. Familiarize yourself with local resistance patterns AND guidelines ... as local healthcare providers may not have access to similar information



Thank you