What’s new in malaria retinopathy?

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Presented at the University of British Columbia Department of Ophthalmology May 4, 2018
Acknowledgements to others

- Terrie E Taylor
- Nicholas A Beare
- Malcolm E Molyneux
- Valerie White
- Simon Glover
- Rachel Bronzan
- Simon Harding
- Nick Sargeant
- Jeanette Lindley
- Jane Gardiner
- Kevin Wade
- Brian Hoar
- Andrew McCormick

The Blantyre Malaria Project
Malaria: why is it important?

- 200-500 million cases per year
- Kills over 1 million/year
- African children bear 90% of the burden of mortality from malaria.
- Over $2 billion per year to the Africa economy alone
• Only *Plasmodium falciparum* causes life-threatening infection.
• *P. falciparum* infection causes red cells to become “sticky” and adhere to vessel walls, especially in brain.
Cerebral malaria (CM) is the most severe syndrome. Dx can be difficult.

- Clinical features are variable and not specific: broad DDx
- Other diseases may co-exist with malaria
- 25-75% population may have asymptomatic infection in disease-endemic areas
What’s OLD in Malarial retinopathy?
Life in Malawi 1990-94
25+ years later…

- Documented findings (before digital cameras!)
- Described histopathologic correlates
- Demonstrated clinical significance
- Change thinking of malaria researchers
White centered hemorrhages
Retinal Whitening  (mild perifoveal)
Retinal whitening (severe perifoveal)
Retinal whitening (peripheral severe)
Retinal whitening (peripheral severe)
Retinal whitening = capillary dropout = hypoxic retina
Photomicrograph of a flat section of retina showing vessels with an irregular distribution of parasitised RBCs

Segment with relatively more parasites and less haemoglobin

Segment with relatively less parasites and more haemoglobin
Photomicrograph of larger retinal vessel (H+E stain)

Central core of well haemoglobinised RBCs

Peripheral parasitised RBCs containing schizont stages and little haemoglobin
Clinical significance

Developed a grading scale for severity of each feature of malaria retinopathy

• Retinal signs associated with risk of death
• More severe signs = higher risk of death
• Retinal signs associated with specific clinical & laboratory indictors (e.g., Hct, platelets, lactate, respiratory distress, hours in coma)
Case-fatality Rates: children with clinical CM

44% (25.3-63.1)
Malarial retinopathy

36% (26.9-46.6)
Papilloedema

7% (4.2-9.8)
normal

15% (11.6-18.4)
Group R
“retinopathy positive CM”

- CM retinopathy- hemorrhages, abnormal vessels, or ret whitening (± papilledema)
  - Mortality rate 19%
  - Autopsies show cerebral sequestration of parasitized RBCs, hemorrhages, and fibrin thrombi
  - coagulopathy and local areas of tissue hypoxia secondary to hypoperfusion and anemia
Group N- “retinopathy negative”

- Most survive and wake up quickly
  - “mild” case of CM? prolonged post-ictal state?
- Among the 7% who die
  - autopsied cases have non malarial causes of death & incidental parasitemia.
- Almost 25% of children with clinical diagnosis of CM did NOT have CM (no cerebral sequestration) at autopsy
Group P- false CM

- Papilloedema alone (no CM retinopathy)
  - Mortality is 44%. Small group with multiple pathologies
  - Autopsied cases have NO sequestration of parasitized RBCs
  - Various other causes of death found
  - incidental parasitemia
Summary

- Children with clinical “CM” are a heterogeneous group best differentiated by fundus signs.
- Older studies (Rx or pathophysiology) did not take this into account leading to conflicting, unreproducible results.
- Requiring the fundus signs as a criteria for case definition allowed us (in 2015) to demonstrate with MRI that brain swelling is the key predictor of death in CM.
- Current research will focus on treating brain swelling to reduce mortality.
How can we ensure that fundus signs are used for accurate diagnosis when ophthalmologists are not available? (and non ophthalmologists can’t or won’t learn to examine the fundus!)

What’s new?
Automated Detection of Malarial Retinopathy in Digital Fundus Images for Improved Diagnosis in Malawian Children with Clinically Defined Cerebral Malaria

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• Algorithm Detection
• Specificity 100% Sensitivity 95%
Topcon desktop camera for imaging
and computer based processing
Portable camera (Pictor-plus) transmits images wirelessly to a tablet to generate patient records and results.
Current efforts

Smartphone-based retinal camera (iNview)

ASPIRE (Autodetection Software for Plasmodium Infection in Retinal Exams) software to be implemented on the smartphone
Take home message

• Malarial retinopathy (MR) is a unique entity consisting of 3 retinal signs
• It is the best way to accurately diagnose CM and the best predictor of outcome in patients with CM
• New imaging techniques allow non ophthalmologists to identify MR. This will enhance research aimed at understanding CM and determining the most effective treatments.