Professor PL Chiodni
FIS 2017

The JD Williams Lecture
in recognition of

Professor David Williams
1931 - 2005
In at the Deep End

Professor Peter L Chiodini
Hic jacet Raherus Primus Canonicus et Primus Prior hujus Ecclesiae
The lecture brief I received

“The lecture is intended for a senior and highly distinguished member of the profession to tell the audience about the highlights of their career and their wider thoughts and views”
Lived near Alexandra Palace, London
Leaving London 8 years old

- Father’s job relocated from London to a small provincial town
  - Only one book shop
  - “Sorry, we don’t stock those”…..“you’ll have to go to London for that”
  - Strong sense of desolation!

- Saved by Grammar School and parental encouragement +++
  - Father a machine operator

- University applications (UCCA).........
Headmaster

“I don’t like London, there are too many distractions”
Interesting Architecture
Stylish Fashion
BSc Zoology at King’s College London
• **1967** – Full-time student numbers 197,000
  • 0.36% of 54.94 million UK population
  • Under the 1962 Education Act, tuition fees for most students who secured a university place were paid by the state while relatively generous maintenance grants meant that student loans, bank overdrafts and credit card debts were largely unknown
  • There were also “Job fairs”!

• **2011** – Undergraduate student numbers 1.92 million
  • 3% of 63.26 million UK population
PhD at the Wellcome Foundation
Clinical Training at KCHMS
St George’s Hall, Liverpool
The Rotunda, Birmingham
Vellore, India
Then into the Deep End!
The Hospital for Tropical Diseases London

- Imported parasitic and infectious diseases
- From any part of the globe
- Tourists, refugees, migrants, business people etc
- 8,600,000 people in London
  - so a window on the world
- Important in sentinel surveillance
Malaria

First clinical trial of atovaquone in falciparum malaria

The road to atovaquone-proguanil [Malarone ®]
Malaria Rapid Diagnostic Tests

Appeared at ICOPA, Paris 1990

“Mixed” reception at first!

Peak of 320 million tests sold in 2013

Since then, decreasing sales in Asia

Sales in Africa have risen every year since 2008

http://apps.who.int/iris/bitstream/10665/255836/1/9789241512688-eng.pdf?ua=1
Figure 1: Mode of action of antigen-detecting malaria RDTs

Mode of action of common malaria RDT format:

(a) Dye-labelled antibody (Ab), specific for the target antigen, is present on the lower end of the nitrocellulose strip or in a well provided with the strip. Antibody, also specific for the target antigen, is bound to the strip in a thin (test) line, and either antibody specific for the labeled antibody, or antigen (Ag), is bound at the control line.

(b) Blood and buffer, which have been placed on the strip or in the well, are mixed with the labelled antibody and are drawn up the strip across the lines of bound antibody.

(c) If antigen is present, some labelled antibody will be trapped on the test line. Other labelled antibody is trapped on the control line.
ParaSight F

Marketed in 1995
Not commercially successful
Taken off the market in 2000

RDTs: Issues in practice

- **WHO**: Target sensitivity for RDTs
  95% at 100 parasites/μl

- Variation in performance
  - Between products
  - Between locations for same product
Caveat emptor

Buyer beware
WHO Product Testing

- 20 culture line *P. falciparum*
  - at 200 and 2000 parasites/µl

- 99 wild type *P. falciparum*
  - at 200 and 2000 or 5000 parasites/µl

- 35 wild type *P. vivax*
  - at 200 and 2000 or 5000 parasites/µl
WHO Specimen collection, characterisation and testing sites
# Malaria Negative Samples

<table>
<thead>
<tr>
<th>Nature of negative sample</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy volunteers</td>
<td>50</td>
</tr>
<tr>
<td>ANA positive</td>
<td>13</td>
</tr>
<tr>
<td>Anti mouse antibody</td>
<td>3</td>
</tr>
<tr>
<td>Rheumatoid factor positive</td>
<td>4</td>
</tr>
<tr>
<td>RPR positive</td>
<td>9</td>
</tr>
<tr>
<td>Chagas antibody positive</td>
<td>2</td>
</tr>
<tr>
<td>Dengue antibody positive</td>
<td>4</td>
</tr>
<tr>
<td>Leishmaniasis antibody positive</td>
<td>5</td>
</tr>
<tr>
<td>Schistosomiasis antibody positive</td>
<td>10</td>
</tr>
</tbody>
</table>
Wild-type *P. falciparum* (WHO 2017)

http://apps.who.int/iris/bitstream/10665/258597/1/9789241512916-eng.pdf?ua=1
Wild-type *P. vivax* (WHO 2017)

http://apps.who.int/iris/bitstream/10665/258597/1/9789241512916-eng.pdf?ua=1
Malaria diagnosis in the field no longer has to rely on guess-work.
Guidelines for malaria prevention in travellers from the UK: 2017

National Blood Service

- SACTTI Parasite Committee

- First non-endemic country to screen at-risk blood donors for Chagas disease

- Formulation and evolution of malaria donor screening
World Health Organization

- Malaria RDTs
- Guidelines for the management of Neurocysticercosis
- WHO Informal Working Group on Echinococcosis
- Chagas disease in non-endemic countries initiative
Changing case mix
Reacting to a changing case mix (1)
Chagas disease in Latin American migrants

- No systematic screening except blood/tissue and organ donors
- No established antenatal screening of at-risk mothers, despite the recommendations of the Migrant Health Guide
Reacting to a changing case mix (2)
Neurocysticercosis
Reacting to a changing case mix (3)

Cystic Echinococcosis (CE)
(or Cystic Hydatid Disease)
Life cycle

*Echinococcus granulosus* causes hydatid disease.

Intermediate host: Sheep, cattle etc. and other herbivores

Cyst in offal, esp. liver

Definitive host: Dog and other canines

Ovum 30–37 µm

Length 3–8 mm

Adult

30–36 hooks in two rows

4 suckers

Immature

Mature

Proglottids
Global distribution
Zoonotic *E. granulosus*
Budke et al (2006) EID 12(2) 296-303
HTD, London 2006 to 2016
160 new referrals (155 CE; 5 AE)
Omental cyst
WHO CE staging

Figure 1. A land planarian, *Bipalium kewense* Moseley. Photograph by P. M. Choate, University of Florida.
Regeneration

- Cut an *Ascaris* worm in half and it will die

- Cut a planarian in half lengthwise or transversely

- It will regenerate and produce two whole flatworms!

- Leave behind one protoscolex of hydatid and it will eventually form a new cyst.......
Current Management of Cystic Echinococcosis; a survey of specialist practice
### WHO-IWGE Expert Consensus

<table>
<thead>
<tr>
<th>Stage</th>
<th>Viability</th>
<th>Image</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE1</td>
<td>Viable</td>
<td>![Image]</td>
<td>&lt;5cm· albendazole alone 3-6 months &gt;5cm PAIR and albendazole</td>
</tr>
<tr>
<td>CE2</td>
<td>Viable</td>
<td>![Image]</td>
<td>Surgery or other percutaneous procedure with albendazole</td>
</tr>
<tr>
<td>CE3A</td>
<td>Transitional</td>
<td>![Image]</td>
<td>&lt;5cm· albendazole alone 3-6 months &gt;5cm· PAIR and albendazole</td>
</tr>
<tr>
<td>CE3B</td>
<td>Transitional</td>
<td>![Image]</td>
<td>Surgery or other percutaneous procedure with albendazole</td>
</tr>
<tr>
<td>CE4</td>
<td>Inactive</td>
<td>![Image]</td>
<td>Watch and wait</td>
</tr>
<tr>
<td>CE5</td>
<td>Inactive</td>
<td>![Image]</td>
<td>Watch and wait</td>
</tr>
</tbody>
</table>

# Current Management of Cystic Echinococcosis: A Survey of Specialist Practice

Laura Eve Nabarro, Zahir Amin, and Peter L. Chiodini

1The Hospital for Tropical Diseases, 2Department of Imaging, University College London Hospitals, and 3London School of Hygiene and Tropical Medicine, United Kingdom

<table>
<thead>
<tr>
<th>Case</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>34-year-old man with abdominal pain. 10-cm CE2 cyst. Expert Consensus suggests surgery or other percutaneous procedure with ABZ for 1 day before and 1 month afterward</td>
</tr>
<tr>
<td>Case 2</td>
<td>Inoperable disseminated disease. Expert Consensus suggests medical treatment maintained indefinitely</td>
</tr>
<tr>
<td>Case 3</td>
<td>Fever and abdominal pain. Type 3A cyst involving diaphragm and lung base. No specific guidance in Expert Consensus. Watch-wait, drug therapy, OPC and PAIR contraindicated. ABZ 1 day pre- and 1 month postsurgery</td>
</tr>
<tr>
<td>Case 4</td>
<td>76, male. 2 previous surgeries for hepatic CE. Hepatitis on ABZ. Recurrent 3B cyst with biliary communication. Expert Consensus suggests surgery for 3B cysts. Do not use scolicidal agent in cysts communicating with biliary tree. If hepatitis on ABZ, measure plasma ABZ sulfoxide levels and consider switching to mebendazole</td>
</tr>
<tr>
<td>Case 5</td>
<td>61-year-old man with cough. Pulmonary CE1 cyst (7x6 cm) and hepatic CE1 cyst (8x6 cm). Expert Consensus suggests surgery. Avoid preoperative ABZ. 1 month post-operative ABZ</td>
</tr>
</tbody>
</table>
Survey of Specialist Practice

- 41 clinicians
- 23 countries
- 5 continents
Patient A

34 year old M
Abdominal pain
9x9x10cm hepatic cyst
ALT 197, ALP257, EO 2
Hydatid IgG positive
# Patient A

34 year old M  
Abdominal pain  
9x9x10cm hepatic cyst  
ALT 197, ALP257, EO 2  
Hydatid IgG positive  

## Issues
- PAIR for type 2  
- Length of drug Rx

**Most use ABZ, 5% ABZ/PZQ**

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>% used</th>
<th>Pre procedure BMZ therapy</th>
<th>Post procedure BMZ therapy</th>
<th>Expert consensus guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watch and wait</td>
<td>2.5</td>
<td></td>
<td></td>
<td>Contraindicated (progression)</td>
</tr>
<tr>
<td>Drug therapy alone</td>
<td>0</td>
<td></td>
<td></td>
<td>Contraindicated (failure)</td>
</tr>
<tr>
<td>PAIR</td>
<td>12.5</td>
<td>4d to 6 months</td>
<td>3 weeks to 6 months</td>
<td>Contraindicated (recurrence)</td>
</tr>
<tr>
<td>Other percutaneous intervention (PEVAC)</td>
<td>10</td>
<td>1 week to 1 month</td>
<td>1 month to 6 months</td>
<td>With drug cover (length not specified)</td>
</tr>
<tr>
<td>Surgery</td>
<td>62.5</td>
<td>0-6 months</td>
<td>1 month to 1 year</td>
<td>With drug cover (1 day pre to 1month post)</td>
</tr>
<tr>
<td>Other</td>
<td>12.5</td>
<td>Further investigation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Current lack of harmonization

- Practices used but known to be ineffectual
  - PAIR in type 2 cysts
  - Cyclical courses of albendazole
    - A clinical governance issue

- Practices used but known to be unsafe
  - Scolicidal agents in cysts in continuity with the biliary tree
    - A clinical governance issue

- Areas where there is no definitive evidence
  - Length of albendazole treatment
  - Precise role of praziquantel
  - Length of albendazole treatment in disseminated disease
What can we do?

• For harmonization we will need
  • Clarity in our advice on:
    • Length and pattern of albendazole treatment
    • Role of praziquantel
  • Revision of the WHO-IWGE guidelines
    • Making better use of the evidence we have
    • Making them more prescriptive
      • Vagueness in the current version can spawn variation in clinical practice
“As is your pathology, so is your practice”

Flynn F (1985)
## NEQAS Parasitology Schemes

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Date started</th>
<th>Number of participants</th>
<th>Number of countries</th>
<th>No of countries outside Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faecal parasitology</td>
<td>1986</td>
<td>590</td>
<td>40</td>
<td>12</td>
</tr>
<tr>
<td>Blood parasitology</td>
<td>1986</td>
<td>272</td>
<td>34</td>
<td>7</td>
</tr>
<tr>
<td>Toxoplasma serology</td>
<td>1993</td>
<td>322</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Parasite serology</td>
<td>2005</td>
<td>63</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Malaria RDTs</td>
<td>2010</td>
<td>123</td>
<td>23</td>
<td>4</td>
</tr>
</tbody>
</table>
Effects of EQA: Blood film microscopy

UKNEQAS Blood Parasitology
Participants subscribing since the start of the scheme

Participants' scores expressed as a percentage
Establishment of the 1st World Health Organization International Standard for Plasmodium falciparum DNA for nucleic acid amplification technique (NAT)-based assays
David J Padley*, Alan B Heath1, Colin Sutherland2, Peter L Chiodini2, Sally A Baylis1 and the Collaborative Study Group

Address: 1National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 3QG, UK and 2Hospital for Tropical Disease, Mortimer Market, Off Tottenham Court Road, London, WC1E 6AJ, UK

Email: David J Padley* - dpadley@nibsc.ac.uk; Alan B Heath - ah Heath@nibsc.ac.uk; Colin Sutherland - Colin.Sutherland@lshtm.ac.uk; Peter L Chiodini - peter.chiodini@uclh.org; Sally A Baylis - baysa@pci.de; the Collaborative Study Group - dpadley@nibsc.ac.uk
* Corresponding author

Published: 24 July 2008
Received: 29 November 2007
Accepted: 24 July 2008
Malaria Molecular EQA Scheme

The UK NEQAS Scheme for Molecular Diagnosis of Malaria entered the pre-pilot stage in 2014

Pilot Scheme in 2015

Full Scheme in 2016
Participants

- **Pre-Pilot:** Two distributions each containing eight (8) specimens. 25 participants returned results.

- **Pilot:** Two distributions each containing eight (8) specimens. 28 labs returned results.

- **Live:** Four distributions each year; each containing four (4) specimens. 53 labs returned results.

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**EQA Scheme for the detection of Malaria nucleic acid**

- Austria
- Belgium
- Chile
- Denmark
- Finland
- Greece
- Hong Kong
- Italy
- Kenya
- Germany
- Ireland
- Brazil
- Netherlands
- India
- Norway
- Slovenia
- Sweden
- Thailand
- United Kingdom
- Portugal
Freeze-dried samples for distribution
Medical Leadership

- Six years as Clinical Director
- Another deep end!
- Relocated HTD from the workhouse of St Pancras to University College London Hospitals
Medical Leadership
Dean of the Faculty of Travel Medicine
Royal College of Physicians and Surgeons of Glasgow
The Next Generation of Medical Students

Diverse?
Representative of the general population?
With insight into “ordinary”/ “day to day”/ “routine” life?
Are those who wish to compete and gain access to medical training able to do so whatever their background?
A concerning report

State of the Nation 2017: Social Mobility in Great Britain

November 2017
“The Social Mobility Foundation (SMF) is a charity which aims to make a practical improvement in social mobility for young people from low-income backgrounds..... in order to provide opportunities and networks of support for 16-17 year olds who are unable to get them from their schools or families.”

http://www.socialmobility.org.uk/about-us
• **Background Criteria:**

  • Are personally eligible for Free School Meals (household income is below £16,190 if in England/Wales/Northern Ireland or £16,105 if in Scotland) during secondary schooling

  • OR

  • Are the first generation in their family to attend university in the UK AND attend a school on [this list (List B)]:

*List B: Schools with 20% or more students eligible for Free School Meals

http://www.socialmobility.org.uk/criteria-programmes/