

# Porto 2018 - 18<sup>th</sup> TropNet Workshop

Thursday, 17/05/2018

## 1. Welcome and Introduction (Sandra Xara, Mario Joao Goncalves)

## 2. Report of steering committee and coordinator (Christoph Hatz)

### Overview on the current network status

- 75 member sites, including 3 new member sites (Brussels, Vicenza, Bern)

### Network coordination & rotation issues of steering & research committee members

- Steering committee: Leo Visser (replaced 2018), Guido Calleri, Thomas Zoller, Anu Kantele, Jose Munoz, Camilla Rothe, Federico Gobbi, Jill Dixon (replaced 2018)
  - suggested replacements: Olivia Veit (Basel/Zürich), Victoria Johnson (London), Matthias Schmidt (Newcastle)
  - **elected on the 18.05.2018:** Olivia Veit, Matthias Schmidt
- Research committee: Thomas Zoller, Anu Kantele, Jan Clerinx, Philipp Zanger, Guido Calleri, Andrea Angheben, Mirjam Schunk, Camilla Rothe, Philipp Zanger, Silja Bühler, Matthieu Mechain
  - suggested replacements: Juan Cuadros (Alcala de Henares-Madrid), Emmanuel Bottieau (Belgium), Kristine Morch (Norway)
  - **elected on the 18.05.2018:** Juan Cuadros, Emmanuel Bottieau
- Coordinator until 2019: Christoph Hatz
  - suggested replacements: Negrar/Verona, Berlin
  - potential coordinators can put themselves forward until summer 2018
  - election will take place in autumn 2018, in order to assure a smooth handing over process from Basel to the new coordination team and site.

Matthias Schmidt: It would make sense to elect a new coordinator before 2019

Vote on this suggestion: 33 in favour, 3 against it

Christoph Hatz: problem -> it was not announced, some people are not here

Anu Kantele: vote in a few months

Thomas Zoller: to be a president-elect you have to have an agenda and you have to set up support at your home institution → the decision should be postponed

Christoph Hatz: it could be done like in ISTM: people interested put together a dossier which is then sent around and members can vote on it (deadline: September 2018)

Vote on this suggestion: no vote on this subject -> Coordinator cannot be elected today as the issue has not been scheduled

***o add-on 15.10.2018 (Hatz): a silent vote including 23 responding members has opted for Negrar/Verona, the only applicant. The Steering Committee had previously decided that there should be a silent vote and not a general vote by mail or at the next meeting because Negrar/Verona was the only applicant despite renewed calls to apply, and because the application of Negrar/Verona was considered to be excellent.***

- Steering committee function: several meetings a year
- projects (mandatory):
  - define one or two projects that every site should/must contribute
  - XX: what is the definition of a mandatory project?
    - CH: it should be a topic which is seen by all/most of the sites, the project would then be suggested and then there will be a vote on it
  - make national guidelines available
  - annual surveys of the sites
- active and associated members?
  - Camilla Rothe: re-assess which of the members are still interested in being a member; do we bother if a member is active/inactive?
  - Blaise Genton: there is no real advantage in having different member status

- Thomas Zoller: since we don't have regular activities, it is difficult to define active/associated members -> but dedication of member sites should be assessed (i.e. minimal contribution: annual survey)
- Jose Munoz: somehow the connection between the member sites has to be kept up between the annual meetings
- Kristine Morch: meeting face-to-face is very important, especially in smaller centres
- Zeno Bisoffi: there should be a minimal "entry ticket" to the network like filling the annual survey
- Andreas Neumayr: 1) the whole communication is network based -> if your email address does no longer work, you are no longer reachable; 2) the forum is set up initiate projects → it is not up to coordination centre to define activities, if a member wants a project to happen, this centre should take the initiative

#### Proposals for the venue of the next TropNet meeting in 2019

- Basel, Berlin, Lausanne, London, Torino

**Venue of next TropNet meeting:** Torino, 28<sup>th</sup> and 29<sup>th</sup> March 2019. The meeting will be organized by the local site, together with the present coordinator. The new coordination team will be involved in the process.

#### Review of the TropNet platforms

- 6 platforms (research, policy development, teaching & training, surveillance/reporting, network resources, public)
- regarding surveillance/reporting: alarm cases/unusual cases should also be communicate to Geosentinel/EuroTravnet, but basic data is not going to be collected
- teaching and training: it is up to the different centres what courses they want to set up in the name of TropNet
- Annual survey:
  - 2017 25 centres contributed
  - P. knowlesi malaria went up
- TropNet Forum: the tool to
  - Communicate outbreaks & emerging diseases
  - Discuss suspicious syndromes & unusual presentations
- List of orphan drugs is updated

#### News on the International Expert Committee for Travel Medicine

- Switzerland, UK, Italy, Spain
- ECTM as a Travel Medicine "Think Tank"
  - Consensus on rational, risk based recommendations for travel medicine
  - Optimizing pre- and post-travel health advice
- Andrea Angheben: if ECTM is a TropNet action, all TropNet members should agree on this to be a TropNet action, even if they cannot participate
- Christoph Hatz: the set up should become more democratic in the future, with more active involvement of the centres

### **3. Report on closed/ongoing TropNet studies & studies with TropNet participation**

Eurartesim: update on TropNet - SigmaTau study on the treatment of uncomplicated *P. vivax* malaria (Andreas Neumayr)

- Study is closed. N = 18 from 12 sites.

LeishMan: update on ongoing activities (Andreas Neumayr)

- 8 countries (17 institutions)
- still collecting data
- database currently in a transition period regarding organization and funding
- Leo Visser: one of the aspects that makes this group successful is that they meet regularly face-to-face

GiardiaTREAT & GiardiaREF: update on the ongoing studies on first- & second-line treatment of giardiasis  
(Andreas Neumayr)

- GiardiaTREAT: not enough centres are participating -> not going on
- GiardiaREF:
  - compare efficacy of quinacrine with albendazole/chloroquine as a second-line drug
  - endpoints: parasitological cure and/or clinical cure
  - results: cure rate in albendazole/chloroquine arm is low but numbers are too low
  - Jan Clerinx: quinacrine has more side effects and is more expensive than it used to be
    - AN: no difference regarding side effect in this study so far
- it is clearly decided that the study should go on

TropNet Research Committee Report (Thomas Zoller)

- Review process:
  - new studies submitted to research committee
  - cover letter, protocol, if available ethical review
  - review by RC within 4 weeks
  - feedback by RC: scientific quality, ethical considerations, technical feasibility, partners involved, recommendations for amendments
  - final recommendation
  - coordinator: final decision for implementation
  - support by RC
- Studies can also include partners outside TropNet
  - DH: if Geosentinel should be involved, it is better to go through the coordinator; the coordinator can assess for which centres the study would fit
- it should be clearly stated in the protocol what qualifies you as an author

Update on severe malaria study & Artemisinin safety studies: HAEMO-ART & SMPS-Update (Thomas Zoller)

- HAEMO-ART:
- primary outcome: delayed haemolysis (LDH/Hapto) at day 14
  - 40% of patients with uncomplicated *P. falciparum* malaria showed hemolysis
  - sites: Berlin, Rostock, Hamburg, Wien, Negar
  - target: 100 fully evaluable patients
  - final results expected by end 2018

SMPS (severe malaria pharmacovigilance system (artesunate case register):

- observational study in patients treated with i.v. artesunate
- aim > 250 patients
- data collection: electronic questionnaire, takes 10 minutes
- current status: 195 patients, 16 reporting sites

Prospective comparative multi-centre study on imported *P. ovale wallikeri* and *P. ovale curtisi* infections: final results (Gerardo Rojo Marcos)

- 96 samples, 17 excluded
- 79 correctly genotyped
  - 35 *P. curtisi*
  - 44 *P. wallikeri*
- Conclusion:
  - *P. wallikeri* more frequent in males and Caucasian patients, more thrombocytopenia, higher INR, shorter latency → *P. wallikeri* might be more pathogenic than *P. curtisi*
  - Clinical evolution with treatment good; chemoprophylaxis less effective than in *P. falciparum*; DM might be a risk factor for *P. ovale* infection

Loiasis: comparison of different drug regimens for the treatment of loiasis – results of the study and proposal of management at TropNet centres (Federico Gobbi)

- ivermectin alone, albendazole alone, albendazole + ivermectin, dec + ivermectin, dec + albendazole
- data on 165 patients
- Outcomes:

- DEC: cure 69%
- IVM cure: 52%
- ALB cure: 50%,
- IVM & Dec cure: 71%
- DEC & ALB cure: 100%
- ALB & IVM cure: 93%
- Two new study proposals:
  - Similar study for Mansonella perstans -> cases are welcome
  - To obtain more clinical information on Loa loa and M. perstans
- **Contact details:** federico.gobbi@sacrocuore.it

TropNet-ZikaPLAN WP: Zika virus infection in European travellers (Andreas Neumayr)

- set up a biobank of blood, urine and semen of Zika patients
- current status: 21 patients enrolled (problem: epidemic is over)
- new idea: setting up a biobank with negative samples and samples of travellers vaccinated against JE, FSME etc to evaluate future Zika tests
- linked studies:
  - persistence and infectivity of zika in semen
  - proof-of-concept study evaluating baited-filter paper for virological sentinel surveillance
  - smartphone based sentinel surveillance study in travellers to Latin America

#### 4. Upcoming and proposed TropNet studies

Enteropathogens causing diarrhoea in European travellers to tropical and subtropical countries – a multicentre observational cohort study on geographic distribution, symptoms and antimicrobial resistance (Esther Kuenzli)

- assess pathogens and associated antimicrobial resistances in patients with acute travellers diarrhoea
- participating centers: Basel, Barcelona; more centers needed
- **contact:** esther.kuenzli@swisstph.ch

MAL-RISK pilot study (Thomas Zoller)

- assess the risk factors for transmission from uncomplicated to complicated malaria
- Part I: expert opinion by one senior physician per TropNet site; open to all TropNet sites
  - 29 out of 75 member sites have answered the questionnaire

The European Register of Cystic Echinococcosis: where are we? (Guido Calleri)

- prospective observational multicenter online register
- CE patients
- link with the Echino Biobank (optional)
- objectives: indicate the burden of CE in Europe
- **contact:** [patrizia.rossi@iss.it](mailto:patrizia.rossi@iss.it) (Datenbank) ; [mmar.siles@irnasa.csic.es](mailto:mmar.siles@irnasa.csic.es) (Biobank)

Systematic data collection on drug side effects of some of the more 'unusual' drugs which we use within tropical medicine (Victoria Johnson)

- current proposed studies: benznidazole in Chagas, miltefosine in cutaneous leishmaniasis, thalidomide in Hansen's
- prospective data collection
- looking for working groups to finalise protocols and collect data
- **Contact:** [victoria.johnston7@nhs.net](mailto:victoria.johnston7@nhs.net), [david.moore@lshtm.ac.uk](mailto:david.moore@lshtm.ac.uk), [diana.lockwood@lshtm.ac.uk](mailto:diana.lockwood@lshtm.ac.uk)

A systematic review of treatment of imported schistosomiasis in western countries: it's time for a trial? (Federico Gobbi)

- Background:

- 20% of migrants from Sub-saharan Africa positive for Schistosomiasis
- efficacy of praziquantel lower than expected
- in non-endemic countries no guidelines for treatment and management of schistosomiasis
- systematic review on efficacy of praziquantel:
  - 62.2% received standard treatment
- Idea:
  - multicenter trial in non-endemic countries on the efficacy of praziquantel
  - working group defining 1) diagnostic criteria for schistosomiasis and 2) cure criteria
- **Contact:** federico.gobbi@sacrocuore.it

## 5. Presentations

Latest results of Antwerp Schistosomiasis cluster. Schisto SOS (Jan Clerinx)

- Questions to resolve regarding treatment:
  - single dose of praziquantel sufficient
  - repeat praziquantel after what time
- Real-time PCR in serum in acute schistosomiasis
  - 100% sensitivity, much better than serology (in *S. mansoni*)
  - depending on target sequence (Dra1) 100% sensitivity (in *S. haematobium*)
- SOS schisto study ongoing since 2014
  - aim: to test PCR diagnosis in prepatent and early symptomatic phase
  - results:
    - 171 exposed travelers included
    - 54 with demonstrated infection by PCR
    - PCR Dra1 best diagnostic tool for *S. haematobium*/CAA in urine positive very early, but less sensitive

Christoph Hatz: TropNet has the potential to contribute to this topic and it should be done

**Friday, 18/05/2018**

### 1. Presentations

Filariasis - 2 clinical cases (Isabel Furtado)

Two cases of Loa Loa → one treated with DEC, the other lost to follow up (the first two cases at this hospital)

Chronic melioidosis and/or severe strongyloidiasis with drug measurement and semi-quantitative parasite count (Gilles Eperon)

Case 1: Strongyloides stercoralis hyperinfection syndrome with multiple septic shocks due to *E. coli* in a patient with severe hypogammaglobulinemia; treated with parenteral ivermectin plus albendazole

Zeno Bisoffi: immigrants should be screened for schistosomiasis and strongyloidiasis

A case with multiple infections (Emmanuel Bottieau)

Case of Leishmania infantum in a immigrant from Laos → the patient most probably got infected in Italy (one holiday there), as Laos does not have Leishmaniasis; treatment with local infiltration of pentavalent antimonials  
Additionally: very high eosinophilia

- positive serology for Strongyloides stercoralis
- stool examination positive for Opistorchis viverrini

Gnathostomiasis (Leo Visser)

Patient with recurrent transient solitary swelling; serology for gnathostomiasis positive; retrospectively, the MRI would have shown the track of the parasite in the subcutaneous tissue; successful treatment with ivermectin, followed by albendazole

Eosinophilia does not have to be present!

Unilateral elephantiasis (Jan Clerinx)

Chagas, disease Network in Madrid: results of prenatal screening in the last 6 years (Elena Trigo)

- 70 doctors from more than 17 hospitals reporting to the network
- study of prevalence of chagas disease in pregnant women
- multicentre prospective cross-sectional study (01/2011-12/2016)
- 9'600 women screened -> prevalence 2.9%

Strongyloidiasis in Spain (Redivi cohort, about 1200 cases) (Fernando Salvador)

- Collaborative network (22 centres), started 2009
- Results:
  - 1'279 patients with strongyloidiasis, 6.4% with immunosuppression
  - mostly asymptomatic
  - most common countries of origin: Sub-saharan Africa and South America
  - 80% had eosinophilia, stool microscopy was positive in 17.4%, 22.5% culture positive, 98.8% serology positive
  - ivermectin significantly better regarding cure than albendazole

ETVAX ETEC vaccine clinical trial in Benin (Anu Kantele)

- oral vaccine given at 2 visits
- regular stool samples at certain time points or in case of diarrhea
- 327 diarrhea cases, 77% in Benin, 23% in Finland

Long-term memory after fractional dose yellow fever vaccine (Leo Visser)

- high sero-conversion rates in all age groups (lowest in 2-5 years with 95% (87-98%))
- published Feb 2018 in NEJM
- 10-year protection rate (PRNT<sub>80</sub>): intradermal 54%, subcutaneous 55% → around 80% of people are still protected after 10 years
- Conclusion: fractional dose very effective, preliminary results suggest long-lasting immunity; minimum vaccine potency 1000 IU/dose

Imported Malaria in Adults: a retrospective study of admissions to an Infectious Diseases Department in Coimbra (Flavia Cunha)

- men more commonly than women
- most patients infected in Sub-Saharan Africa
- less than 1 in 10 patients had taken chemoprophylaxis
- mostly *P. falciparum*
- most common i.v. treatment was quinine, for oral regimen, ALT was the most commonly prescribed treatment

The study is a 5-year retrospective analysis about mixed-species malaria (Ruben Carvalho)

- 10% mixed malaria
- less symptoms but more severe
- mixed malaria had more severe lab abnormalities
- lower parasitemia in mixed infections

E-Health: Results of the Barcelona remote monitoring platform (Jose Munoz)

- 4000 travellers, 11% used the app, 33% contacted a medic during their trip
- 29% received chemoprophylaxis
- risk of travel associated diseases increases with duration of travel
  - 23.8% of travellers have at least one symptom
- antimalarials adverse events recorded every 5 days
- telemedicine: 50% of patients can be helped on the phone (most common problems: cutaneous lesions (30%), diarrhoea (24%), fever (15%))
- BG: could the project be expanded to other centres?

- JM: aim is to scale it up to other centres

#### Zika dynamics in fluids (Adrian Sanchez)

- to assess dynamic of ZIKV in several fluids
- study design: samples at baseline and every 4 weeks
- vaginal fluid: positive result at day 37; clearance between 37 and 69 days after symptom onset
- semen: clearance between day 23 and 107 after symptom onset
- serology: all patients with positive PCR had a positive IgG but two had a negative IgM

#### Delusional parasitosis (Leo Visser)

Case reports

#### Entamoeba dispar as cause of chronic amoebic colitis? (Flavia Cunha)

#### Malaria in Brescia, a tragic unusual case and vivax malaria experience (Francesco Castelli)

Child with malaria in northern Italy (without travel history)

#### Fever in a traveller from Nepal (Isreal Molina)

Diagnosis: Hanta-Virus infection

#### Do we need to do 3 malaria films in returning travellers? (Matthias Schmid)

- one RDT and one blood film might be enough
- could this study be repeated prospectively and influence guidance?

**Consensus:** specialised centres do not need such guidelines and peripheral hospitals with less expertise in diagnosing malaria should repeat slides until you have an alternative diagnosis

## **2. Clinical cases**

Christine Morch, Khawaya Tamim, Quizzing: Andreas Neumayr, Camilla Rothe, Anu Kantele, Jose Munoz