

TropNet-Meeting Torino 2019

Thursday, 28.03.2019

Report of steering committee and coordinator

Overview on the current network status (Christoph Hatz)

75 member sites; 1 new site 2019: St. Gallen

Christoph Hatz reviews the first joint TropNet/Geosentinel Meeting in Porto and is confident that contacts with other networks will be important to avoid redundancies and enhance scientific and policy collaboration in the future.

The six platforms have developed favourably, especially the 'Research', 'Policy Development' and 'Surveillance/reporting' – the latter in collaborative actions with Geosentinel - have made important progress. 'Teaching and Training' and the 'Public' need further attention and visibility, and the 'Network Resources' will be restructured along with the website renewal.

Leishman has been highly successful in establishing published recommendations on diagnostic and treatment issues that are widely recognized and applied worldwide. This group appears to be an ideal model for further working groups of TropNet, such as common interests in malaria and schistosomiasis.

Network coordination & rotation issues of steering & research committee members (Christoph Hatz)

Steering committee: Guido Calleri, Thomas Zoller, Anu Kantele, Jose Munoz, Matthias Schmid, Camilla Rothe, Federico Gobbi, Olivia Veit

According to the replacement rule agreed upon in St. Alban (election for 4 years, then at least 1 year pause, then option to add a 2nd term of another 4 years): To be replaced 2019: Thomas Zoller, Camilla Rothe

Research Committee: Thomas Zoller, Anu Kantele, Philipp Zanger, Andrea Angheben, Mirjam Schunk, Silja Mühler, Matthieu Mechain, Juan Cuadros, Emmanuel Bottieau

According to the replacement rule agreed upon in St. Alban (see above): To be replaced 2019: Anu Kantele, Matthieu Mechain, Silja Bühler

Zeno Bisoffi: It is a suboptimal time to exchange 5 people right now → rules should be adapted to requirements of smooth coordinating TropNet.. The new coordinators will propose new rules for election of committee members within the next 3 months, the constituency should then vote on them before the election of new members of the SC and the RC will take place.

Jan Clerinx: There should be an option for people to be re-elected even if they were in a committee for 4 years.

Ron Behrens: As there is no size restriction, people who want to contribute could join the committees without someone stepping down. There should be no pressure for someone to step down.

Christoph Hatz: There should be an upper limit of how many people can be in a committee.

General consensus: The new coordination team is asked to come up with a options regarding the elections within the next few months. These will then be voted on electronically.

Thomas Zoller: The steering committee has decided on developing a constitution for TropNet.

Annual survey on imported infectious diseases:

P. knowlesi: a few cases are reported every year

Most of the other reported diseases showed stable numbers over the past few years.

Christoph Hatz: the numbers are mainly collected to assess the relevance of the different diseases in the member institutions with regard to their importance for potential studies on diagnostics/treatment

News on the International The Expert Committee for Travel Medicine (Christoph Hatz)

Aims of ECTM: consensus on rational, risk-based recommendations for travel medicine. A platform has been established and expanded over the last years, offering the possibility of discussing travel medicine issues including malaria prevention and vaccination schedules recommendations. The participation of WHO, ECDC, CDC-Atlanta, CATMAT and ISTM have been a landmark in this effort to bring together people of institutions and societies to exchange expertise and practical ideas to enhance evidence based recommendations.

Requirements for the future TropNet website & forum (Thomas Zoller)

The website will have to be transferred to another platform.

Plans and outlook for TropNet from the coordination team (Andrea Angheben)

Points of strength: big number of centres (low representation of Eastern Europe); good internal and external collaboration; annual TropNet Workshop on imported infectious diseases; huge number of imported infectious diseases; great experience

TropNet challenges: increase the number of actively participating centres; funding and legal entity; network historically based on gentlemen's agreement, bylaw?; platforms – excellent idea to further develop

Questionnaire to be discussed within the next two days regarding the future structure of the network etc.

Proposals for the venue of the next TropNet meeting in 2020 (Zeno Bisoffi)

Suggestions: 1. Madrid and 2. Barcelona

The voting will be done electronically.

Report on ongoing TropNet studies & studies with TropNet participation

TropNet Research Committee Report (Thomas Zoller)

- oversees, coordinates and guides all research activities in TropNet
- creates and maintains a register of ongoing and future studies
- definition: two or more TropNet member sites; approved by research committee; uses the name "TropNet" in publications
- review process: cover letter and protocol to research committee; reviewed by RC within 4 weeks; coordinator makes final decision for implementation of project
- support by RC: active information of network members, calls for participation, assistance with selection of sites
- effective for all new studies starting after May 2017

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

TropNet Severe Malaria Study: closed -> 2 publications

HaemoART and TOX-Art: closed -> under analysis

- prospective observational study on patients with uncomplicated malaria
- 130 patients included; final publication expected mid-2019

Severe Malaria Pharmacovigilance System SMPS: closed -> under analysis

- Retrospective observational study
- focus on pharmacovigilance after intravenous artesunate
- 331 cases from 16 TropNet centres included

MAL-RISK I pilot study: under analysis

- expert survey on outpatient treatment in tropical medicine referral centres
- first study with participation of GeoSentinel member sites
- 44 sites took part
- results are basis of planning for part II (retrospective study) and III (prospective study)

MAL-RISK II and III: planned

LeishMan: update on status and ongoing activities (Andreas Neumayr)

- Aim: standardizing diagnosing/treating Leishmaniasis
- 8 European countries. Current coordination: Gert Van der Auwera, Antwerp
- Database: currently > 350 clinical cases
- Collaboration with WHO in the pipeline for 2019 onwards

Approaches in making malaria prevention recommendations (Christoph Hatz)

- ECTM: Switzerland, Germany, Austria, England, Denmark, Netherlands, Belgium, Italy, France, Spain
- Associated members: WHO, CDC, ECDC, CATMAT
- Not aimed at developing common regulations but a platform to discuss evidence and practical, feasible recommendations
- Suggested role of TropNet: (i) selected country members required to increase coverage within Europe, and (ii) expand survey to all member countries and provide coordination internationally on "policy" platform

Ongoing, Upcoming and proposed TropNet studies

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

- still ongoing
- 2nd line treatment with quinacrine shows better cure rates than albendazole & chloroquine (clinical and parasitological cure). Albendazole & chloroquine show better cure rates than re-treatment with a nitroimidazole.
- 1 case treated with quinacrine had to stop treatment due to adverse effects – unclear, if symptoms really were caused by quinacrine

Decision: data on treatment will be published; surveillance on quinacrine side effects will be continued

Ron Behrens: the safety issue should be clearly addressed in the publication

TropNet-ZikaPLAN WP (EU-funded project): Zika virus infection in European travellers (Andreas Neumayr/Jose Munoz)

- Last year: 25 cases were diagnosed
- Basel: change of strategy: collecting well characterized Zika-negative samples (persons for whom we have past-travel and flavivirus vaccination history)
- Other work packages:
 - o Persistence & infectivity of zika virus in semen (Ralph Huits, Antwerp): published
 - o Proof-of-concept study with baited-filter-paper-mosquito traps (Pie Müller/Laura Vavassori, Basel): ongoing
 - o Smartphone based sentinel surveillance study in travellers to Latin America and other Zika affected countries in order to assess the incidence of zika-/arboviral-typical symptoms in travellers (Jose Munoz, Barcelona): ongoing

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

- enrolment still ongoing
- additional centres needed

EuropeSchistoTropNet Platform: update and future perspectives (Federico Gobbi)

- Systematic review on treatment of Schistosomiasis
- Dosage between 45-80mg/kg
- Different timing of dosages
- 34 answers which show high heterogeneity

Plan: multicenter RCT in non-endemic countries to assess the efficacy of praziquantel: one dose vs. multiple doses

Problem: diagnostic criteria; case definition; assessment of cure (serology suitable?)

Challenge: to agree on a prospective, robust diagnostic study (common case definition, inclusion and follow up criteria etc.)

TropNet Schistosomiasis Platform Meeting 9-10th May 2019

Add in: Consider Strongyloides treatment trial (treatment of Strongyloides with Ivermectin): single dose as effective as 4 doses.

News on urine / serum CAA and whole antigen ELISA IgM in schistosomiasis (Jan Clerinx)

Available tests: Schisto ELISA and IFAT, Schisto PCR, Schisto antigen capture tests (CAA & CCA)

- antibody tests show a maximum sensitivity of 40% after the acute phase (D28-35)
- cumulative PCR shows a sensitivity of around 91%
- cumulative CAA (urine and serum) shows a sensitivity of 90-97%

Initial results of the collab. study: "Evaluating feasible tools for etiological diagnosis of fever to guide empirical treatment in returning travellers (EFFORT study)" (Daniel Camprubi)

Systemic febrile illness account for 23.8% of hospitalization in returning travellers

Unknown aetiology is the most common cause (apart from *P. falciparum* in travelers returning from Africa)

Objectives:

- identify causes of undiff. fever
- identify clinical, lab and diagnostic predictors for doxycycline responsive illnesses
- identify pathogens causing undiff. fever in returning travellers

Aim: 1000 febrile patients

Prelim results: 58% undiff. fever

- almost 50% returning from Africa
- 20% arboviral infection
- 14.2% other viral
- 3.9% bacterial
- 3.9% non-infectious
- 26.8% doxycycline responsive illness (rickettsiae, leptospirae, anaplasma, coxiceila, T. pallidum)
 - o RF for DRI : rural area, travelling to America, tache noire; retroorbital pain made DRI less likely
- 29.1% no known aetiology

Conclusion :

- 1 in 4 patients with non-malarial undifferentiated fever have DRI
- 50% of patients with non-malarial undifferentiated fever received the wrong empirical antibiotic treatment
- Source of infection: TD, resp. infection, skin/soft tissue infection, urinary tract infection

Friday, 29.03.2019

Presentations

Management of cystic echinococcosis in Spanish centres based on a survey of specialized clinicians (Fernando Salvador)

Survey in Spain assessing diagnosis, treatment and follow up of cases with echinococcosis:

- 15% extrahepatic cases, 26.5% of cases in immigrant population
- PAIR available in 46.2% in centres
- Access to drugs: 97% albendazole, 87% mebendazole, 84% praziquantel
- 35.9% follow WHO protocol

- Conclusion: high variability in duration of treatment, PAIR availability, availability of drugs, serological tests etc

Retrospective comparative multicenter study of imported *P. falciparum* malaria in patients with and without diabetes mellitus. Final results (Gerardo Rojo Marcos)

Matched case-control study (1:3) in African immigrants with semi-immunity

Results:

- 46 patients, 138 controls
- higher percentage of thick smear negative malaria in patients with DM
- higher parasitaemia in patients with DM
- no difference in the number of hospitalisations, and the length of hospital stay; no mortality in both groups

Descriptive study of cutaneous leishmaniasis diagnosed in Vall d'Hebron University Hospital, emphasizing the treatment outcome (Fernando Salvador)

- 50 cases of leishmaniasis, 42 cases with cutaneous leishmaniasis (2012-2018)
- Country of origin of the patients: 59% Spain, 33% Morocco
- 22% of patients under immunosuppression
- 56% single lesion, 37% multiple lesions, 5% mucosal involvement, 1 case with generalized leishmaniasis
- Identification of species in 22 cases: 16 cases with *L. infantum*, 6 cases with *L. major*
- 50% local treatment, 40% systemic treatment (mostly Ampho B)
- Cure rate: 97.6%, no relapse

Results from MyHealth, an international project funded by the European Commission and coordinated by PROSICS Barcelona: immigrant health needs (infectious diseases, chronic diseases and mental health) from a professional and immigrant view using focus groups, individual interviews and online surveys (Nuria Serre)

- Aim: to improve the health care access of vulnerable immigrants and refugees
- www.myhealthonthemove.net

Presentations

Results of expert survey on outpatient treatment of *P. f.* malaria - MAL-RISK I (Tilman Lingscheid)

- 44 centres, 61% outpatient treatment yes, 39% outpatient treatment no
- majority of referral centres practice outpatient therapy
- no standardized management and criteria
- based on questionnaire no fatalities

Andreas Neumayr: probably one of the most important "soft criteria" against outpatient treatment is the duration of illness at presentation: more than 3 days of illness pose an increased risk for complications

Severe malaria pharmacovigilance system SMPS - first analysis of data (Florian Kurth)

- 331 cases, 16 centres
- 38% Caucasian, 56% African, 2% Asian, 2% other
- top 5 countries of infection: Mali, Nigeria, Equatorial Guinea, Cameroon, Senegal
- 95% *P. falciparum*, 5 cases *P. vivax*, 3 cases *P. ovale*, 2 cases mixed infection
- 306 cases severe malaria, 25 cases uncomplicated malaria
- median duration of Artesunate: 2 days
- Outcome data
 - 4 patients (1.2%) died
 - 40 adverse drug reactions with possible relation to artesunate
 - 3 elevation of liver enzymes

- 1 severe neutropenia
- 36 haemolytic anaemia

Congenital malaria in Europe (Saba Gebremeskel Tekle)

- Literature review: 28 cases of CM reported in Europe (1978-2018)
- In babies born to mothers from malaria endemic areas, congenital malaria has to be considered in case of unexplained fever after birth

Proposal: screen pregnant women from endemic regions at first contact with the health system

Descriptive study of paediatric malaria cases diagnosed in Vall d'Hebron University Hospital from 2014 to 2018, and associated risk factors for severe malaria (Toni Soriano)

- 28 patients
- 43% born in Spain (only 25% received pre-travel health advice)
- Median days of fever before diagnosis: 7 days
- 64.3% *P. falciparum*
- 39.3% severe malaria (associated with travel to/from West Africa and CRP > 10mg/dl)

A retrospective study on paediatric malaria cases in Brescia: risk stratification (Lina Tomasoni)

Children < 4 years of age and/or with a Hb < 9g/l show an increased risk for the need of iv treatment with artesunate, the need for blood transfusion or for prolonged hospital stay

Survey on orphan drugs (Guido Calleri)

Plan to do a survey on the availability of orphan drugs in the different countries

Strongyloides among MSM, sexual transmission (Michel Develoux)

- Strongyloidiasis can be transmitted sexually – only one case described in Pubmed
- Several cases in MSM with multiple sexual diseases and sexual contact with men from endemic areas
- Oral transmission is probably underestimated

Autochthonous human and canine strongyloidiasis in Europe (Lorenzo Zammarchi/Letizia Ottino)

- systematic review, 110 publications included
- autochthonous transmission of strongyloides in Europe is not only an issue of the past
- different areas where human and canine strongyloides overlap

Zeno Bisoffi: systematic reviews on topics considered relevant by TropNet members could be something smaller TropNet centres could contribute to the network

Presentations

West Nile Fever in Northern Italy (Guido Calleri)

- first described in Italy in 1998 in horses
- national surveillance since 2012

- 80% asymptomatic, 20% symptoms, < 0.1% fatal
- 2012-2017: around 20 cases/year; 2018 577 cases (230 WNND, 279 WNF, 68 blood donors, 1 imported)
- EU member states reported 1503 human cases in 2018 (times 7.5 compared to 2017)
- Increase in number of cases most probably caused by climate factors (hot spring, humid period)

Clinical and molecular characterization of the 2017 Chikungunya outbreak in a large urban area in Central Italy (Emanuele Nicastrì)

- high additional work load
- coordination is key
- real time surveillance data from the frontline workers
- between week 35-40 an outbreak is always possible in the region of Rome

Rickettsial infections in febrile outpatients from Tanzania (Peter Sothmann)

Talk not given

Monkey malaria: an historical overview (Spinello Antinori)

see slides

A UK outbreak of monkeypox (Matthias Schmid)

- 3 cases
- case 3 was a HCW taking care of case 2
- two treatments available in the UK: Tecovirimat, Brincidofovir
- vaccination (Imvanex) not licensed in the UK; all staff in contact with patients were offered vaccine but a lot of vaccine was used in post-exposure for patients 2 and 3; overall well tolerated vaccine without causing vaccinia syndrome as non-replicating

Clinical cases

A lump in the eye (Frank Olav Pettersen)

Onchocerca lupi contracted in Turkey

A cluster of congenital Chagas disease in Milan: the relevance of family study (Spinello Antinori)

Children of women diagnosed with Chagas disease should be offered testing

Clinical case (Natalia Rodriguez)

Mixed infection with *P. falciparum* and *P. malariae* leading to splenomegaly and proliferative glomerulonephritis and acute kidney injury, following a Fournier gangrene.

Controversial cases of Lyme diagnosis (Elena Trigo Esteban)

Case treated for "chronic lyme disease" even though serology was negative

A skin disorder from the Swiss Alps (Andreas Neumayr)

Pyemotes ventricosus dermatitis (presenting with a "comet sign")

Two cases of atypical salmonella infection localizations (Giulia Gardini)

- abscess of the right testis following an episode of typhoid fever

- *Salmonella enteritidis* in blood culture: infectious aortitis (*Salmonella* spp. most common cause for infectious aortitis (40%))

Fatal babesiosis (Eve Hamilton/Uli Schwab)

- under treatment with Rituximab for Waldenstroem Macroglobulinaemia
- thick smear positive -> trophozoites (?)
- postmortem: diagnosis of babesiosis (*Babesia microti* ELISA and IFAT positive)
- important: febrile thrombocytopenia requires a bloodfilm!

Person to person transmission of amoebiasis (Maria Joao Goncalves)

- wife of the patient was diagnosed with amoebic colitis in May 2018 after a stay in India; symptoms in the patient started in August 2018

Protocol: Esther Kuenzli

April 2019