TropNetEurop

5th Workshop on

Imported Infectious Diseases

2004

September, 18th-19th

Antwerp

European Network on Imported Infectious Disease Surveillance
www.tropnet.net

PROGRAMME

5th TropNetEurop Workshop 17-18/09/2004

Date & Time		Speakers
Friday, 17/09/2004		
15^{00}-15^{15}	Introduction	Jan Clerinx, Antwerp
15^{15}-17^{00}	Report of steering committee and co-ordinator • Membership issue • Reporting • Financing opportunities for the network	Ron Behrens, London Anders Björkmann, Stockholm Joaquim Gascon, Barcelona Tomas Jelinek, Berlin Alberto Matteelli, Brescia Nick Mühlberger, Berlin
17^{00}-17^{30}	**Afternoon break**	
17^{30}-19^{00}	Report of steering committee and co-ordinator (continued) • Contacts to other networks and organisations • Consequences from the inauguration of ECDC Election of coordinator Election of steering committee	
19^{45}	**Dinner**	
Saturday, 18/09/2004		
8^{45}-9^{00}	Introduction	Tomas Jelinek, Berlin
Scientific presentations I: Malaria		
9^{00}-9^{30}	10 year trends of imported malaria, typhoid and hepatitis	Ron Behrens, London
9^{30}-10^{00}	Vivax malaria	Nick Mühlberger, Berlin
10^{00}-10^{30}	Grey-zones in malaria prophylaxis: proposal of a Delphi method study	Guido Calleri, Torino
10^{30}-11^{00}	**Break**	
Scientific presentations II: Other parasites		
11^{00}-11^{30}	Determining the infection status in schistosomiasis	Bruno Gryseels, Antwerp
11^{30}-12^{00}	Imported schistosomiasis: morbidity and diagnostic features	Jan Clerinx, Antwerp
12^{00}-12^{30}	Imported leishmaniasis: SIMPID data	Nick Mühlberger, Berlin
12^{30}-13^{00}	The Antwerp Fever Study	Emmanuel Bottieau, Antwerp
13^{00}-14^{00}	**Lunch break**	
Scientific presentations III: Networking		
14^{00}-14^{30}	Serology EQA Scheme	Peter Chiodini, London
14^{30}-15^{00}	Database structures for pre and post exposure patients	Graham Fry, Dublin
15^{00}-15^{30}	The National Travel Health Network and Centre (NaTHNaC)	David Hill, London
15^{30}-16^{00}	Are our techniques of pre-travel counselling effective?	Ron Behrens, London
16^{00}-16^{30}	**Afternoon break**	
Scientific presentations IV: TropNetEurop Studies		
16^{30}-17^{00}	Dengue Study I	Ole Wichmann, Berlin
17^{00}-17^{30}	Dengue Study II	Joaquim Gascon, Barcelona
17^{30}-18^{00}	Treatment study in uncomplicated malaria	Martin Grobusch, Tübingen
20^{00}	**Dinner**	

WORKSHOP ORGANIZER AND LOCAL CONTACT ADDRESS

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MEETING VENUE

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Nationalstraat 155
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Belgium

WELCOME

Dear Colleagues and Collaborators,

This meeting will mark the fifth year of TropNetEurop operations and this is a suitable time to examine the past and to formulate new ideas for the future.

All by all, being a voluntary joint effort of the collaborating centres without any external financial backing, the TropNetEurop enterprise can be rightfully regarded as successful, both as a forum to establish collaborative ties between centers of clinical expertise in tropical medicine, as well as a platform to pool data. The latter effort has resulted in regular reports and publications that are noteworthy.

This year, the Institute of Tropical Medicine, Antwerp (ITMA) has the privilege to invite the members contributing to TropNetEurop for the first lustrum workshop, on the 17th and 18th of September , 2004

On behalf of Prof.Bruno Gryseels, Director of the ITMA, and his collaborators, we would extend a warm welcome to all participants to our city on the banks of the river Scheldt, and it is our wish that the meeting will be fruitful and entertaining as well.

Enjoy your stay in Antwerp!

Dr. Jan Clerinx
Site manager TropNetEurop Antwerp

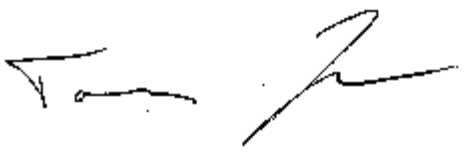
Dear colleagues!

TropNetEurop has now passed its 5th successful year. Though the network and its members have changed in parts, it still unites 46 specialized centres all over Europe. Within the network, we see an average of 63.000 patients post travel per year. This remains the largest effort of imported infectious disease surveillance world-wide.

It took only a very short time span to develop TropNetEurop to a renown reference in the field of imported infectious diseases. The large output of widely distributed material shows the value of our work. This success was achieved through considerable effort from all members who continue to put in extra time and work to make the network possible. My heartfelt thanks for all this enthusiasm!

I am looking forward to an exciting meting in Antwerp. On behalf of all members of the network, I wish to express our special thanks to the local organising team of this workshop, especially to Jan Clerinx, who made the meeting possible.

Berlin, Sept, 10th, 2004



Tomas Jelinek

ACKNOWLEDGEMENTS

Financial support for the workshop from following sources is gratefully acknowledged:

- GlaxoSmithKline
- Abbott
- Hofmann LaRoche

CONTENTS

MINUTES OF THE 4TH TROPNETEUROP WORKSHOP, 2003

Participants

The workshop was joined by 31 participants from 22 countries.

Jorge Atouguia	Lisbon		Claudia Jelinek	Berlin
Anders Björkmann	Stockholm		Tomas Jelinek	Berlin
Peter Chiodini	London		Nikolai Mühlberger	Berlin
David Lalloo	Liverpool		Marie-L Holthoff-Stich	Würzburg
Finn T Black	Aarhus		Frank Pettersen	Bergen
Bjørn Myrvang	Oslo		Ida Gjørup	Copenhagen
Martin Grobusch	Tübingen		Matthias Schmid	Newcastle-upon-Tyne
Ole Wichmann	Berlin		Olivier Bouchaud	Bobingny
Jan B Christensen	Tromso		Georges Soula	Marseille
Svein Gunnar Gundersen	Kristiansand		Jan Clerinx	Antwerp
Annette Kapaun	Heidelberg		Alberto Matteelli	Brescia
Gerd Boecken	Kronshagen		Joaquim Gascon	Barcelona
Ulf Bronner	Stockholm		Ron Behrens	London
David Hill	London		Andreas Skulberg	Oslo
Mogens Jensenius	Kristianssand		Gunnar Hasle	Oslo
Østein A. Strand	Bergen			

Friday

Bjorn Myrvang: Welcome

Tomas Jelinek: Presentation of the network situation (see workshop proceedings)

- Presentation of mission and goals of the network
- Research activities are increasing
- Increasing size of the network, >6000 reports at the moment, 47 member sites
- Relapses in malaria patients: it is agreed that case definitions and a special form are needed, work is relegated to coordinator and steering committee
- Presentation of 11 new members
- Summary of TropNetEurop presence at conferences and of recent publications
    - The network has published 6 additional papers since June 2002
    - A workshop on "Post Travel Screening Surveillance" by TropNetEurop at the 8th CISTM as well attended
- It was agreed that members of the network should check with their local ethics committees for clearance of data reporting
- The assembly agreed that there should be no merger between TropNetEurop workshops and meetings of other groups, like TropEd

- The 5th TropNetEurop Workshop will be hosted by Jan Clerinx in Antwerp at September, 17./18., 2004.

Alberto Matteelli : Nothern Italy study on Dengue in Travellers

See also abstract in the workshop proceedings!

- 23 cases included in analysis
- 62.5% diagnostic sensitivity at first clinical observation
- The study design may be interesting for TropNetEurop

Ole Wichmann. Dengue virus infection travelers

See also abstract in the workshop proceedings!

- Ole proposed a new study on the immunological response, liver involvement and laboratory parameters in dengue patients
    - The study proposal and the affiliated questionnaire will be submitted to the steering committee and circulated later to the members of the network

Joaquim Gascon: Spanish study of Imported Dengue Fever

No abstract available!

- Objectives: evaluation of new methods for differential diagnostics with nested PCR and multiplex molecular diagnostics for identification of genotypes
- Amount of TropNet participation: 3-4 Centres with high numbers of dengue-patients
- Costs for lab methodology will be covered, current TropNet Form and special form will be needed to fill in, blood aliquots must be collected

Nikolai Mühlberger: Questionnaire changes necessary for dengue fever reporting

- Moving so closer to the WHO definitionen
- Introduction of a new field in Dx for "Antibody increase in serum pair"
- The new fax form is already in the proceedings and will be send by email.

Discussion of all dengue presentations of the afternoon

- The ideas of Ole and Joachim compatible, the questionnaire Ole designed covers the aims of Joachim
- Ethical clearance has to be done
- Calculate sufficient numbers / power of study
- Seroprevalence data of interest, bit beware of selecetion bias
- Focus on certain areas (Africa?)
- Two samples are difficult to get, because often people do not turn up again
- Steering committee will talk about the proposals and will mail it around

Saturday

Ida Gjorup: Interaction between HIV and Malaria

See also abstract in the proceedings!

- This study has already started
- Nick Mühlberger presents the Network datas to this study
  - Until now, there is no single case reported with the separate study form
- Only limited data on the effect of falciparum malaria on HIV
- Effect of HIV infection on course of malaria: HIV infected infants were more anaemic
- Pregnant woman are also more on risk of getting malaria, and having increased anaemia

- Study protocol: want to collect 20 or more non-immun patients with falciparum-malaria and HIV co-infection. Separate form has been created for completion together with the TropNetform

- Presently data of reported cases of falciparum malaria with HIV co-infection:
- There are 16 cases in database since 1999, this are 0.3% of all reported malaria-cases
- A link to the MALHIV study is located on the TropNet website, it is possible to download the questionnaire and the study protocol

- Lively discussion focussing on disease prevalence

Alberto Matteelli: Malaria in Chinese immigrants

See also abstract in the proceedings!

Between November 2002 and march 2003,17 cases of malaria in Chinese immigrants were observed in Italy. A further cluster of 12 cases has occurred in August, 2002.Previously two other clustershave been described, during summer of the year 2000, when a significant number presented with severe disease. All of the patients gave a history of transit through an African country, majority in Ivory Coast.

- How can TropNet improve serveillance?
- Is there a potential for the sispersion of the SARS Virus can reach Africa
- Nick Mühlberger: presenting the data bases
  - 23 Chinese migrants were reported in the network
  - the region of infection shifted between 2000 and 2003 from east to west Africa

- Short discussion how medical care is available for illegal people in the different countries. In few it is possible to get acute-care without personal identification (Italy, UK)

Tomas Jelinek: SARS

See also abstract in the proceedings

- Clinical case definition has a low sensitivity (25.4%)
- Children do not get severe symptoms
- Age is a major predictor: the older the patient are, the complicated SARS will be
- How effect was the SARS travel-warning?
- www.sarsreference.com very helpful to get information

- Do we need a new case definition for Europe?

- TropNet is ideally situated to perform SARS surveillance
  - This can be done by a syndromic approach, looking for fever patients
  - Confirmation by virus detection necessary

Joaquim Gascon: Histoplasmosis in Spanish travellers

See also abstract in the proceedings

- A large number of Spanish travellers go to Latin America. Several cases of acute pulmonary Histoplasmosis have been diagnosed in Barcelona. Only 10% of the immune competent people effected by H capsulatum develop a clinical illness. The main objectives of the presented study is to learn the risk of infection by H. capsulatum in travellers to Latin America. Latex and Double diffusion serologies were performed in 179 and 192 travellers respectively. Altogether, 342 travellers were recruited. 20% of travellers to Latin America were HST positive. Conclusion: Travellers who go to Latin America have a considerable of H. capsulatum infection. HST is a good method for screening histoplasmosis in Europe.
- The test is an in house kit of the Barcelona institute - the antigene can got from Barcelona , if somebody is interested

Mogens Jensenius: Africa tick bite fever in travellers

See also abstract in the proceedings

- African tick bite fever is an emerging infectious disease .Recent epidemiological studies indicate that upon 5 % of short term safari travellers may acquire African tick bite fever. Symptoms are flu-like illness .Lymphopenia is common. Treatment with doxycycline or fluoroquinolones is associated with rapid improvement and defervescence in most cases.
- Doxy as prohylaxis might work, but we do not know 100 %
- Does malaria-prohylaxise influence the risk?
- No acquired immunity

Nikolai Mühlberger: Malarone resistance and cytochrome b mutations: preliminary data from the TropNetEurop filter paper study

See also abstract in the proceedings

- 388 respectively 291 of the 464 samples were successfully tested for the presence of AAT- and TCT- mutations.
- Detection of one case of AAT- mutation, and no case of TCT mutation. The prevalence of AAT- mutation in patients treated in Europe for falciparum malaria can therefore be calculated with 95% confidence to be in-between 0.01%-1,43%.
- Analysis of a sub sample of 30 patients treated only with Malarone revealed that AAT-mutation is highly associated with treatment failure. The mutation was present in one of 4 patients with treatment failure, but in none of 26 successfully treated patients.
- AAT- mutation seems sufficient, but not necessary for Malarone treatment failure.
- No new information was gained about the mutations influence on Malarone effectiveness.

Andreas Skulberg: Is there an infectious disease threat to Scandinavia from Russia and the Baltic states?

See also abstract in the proceedings

- The epidemiological situation on infectious diseases in Russia and three Baltic states give reasons for grave concern.
- The amount of multi drug resistant tuberculosis is among the highest in the world. Different political and social factors influence disease epidemiology.
- The HIV epidemic is spreading rapidly since 1999.
- Economic crises and collapse of the vaccination program were the cause for the diphtheria outbreak in 1995/96
- Health sector reform is needed
- Close collaboration within the countries and with European countries are needed
- More information at www.baltichealth.org
- There are already started collaboration between the Baltic states and skandinavia

Jorge Atouguia: Update on human African Trypanosomiasis

No abstract available!

- Discussion:
  - Prognoses is complete recovery after successful treatment
  - Cardiac involvement is imported
  - Results with new drusg are quite good, but only when started treating in an early stage

Peter Chiordini: Gnathostomiais as an emerging infection

See also abstract in the proceedings!

- Discussion:
  - Who many cases have we seen in TropNet?
  - Issue of cross reactivity of ELISA testing

Gunnar Hasle: Venomous animals

See also abstract in the proceedings!

- About 60 000 people die every year because of snakebites.

Jan Clerinx: Clinical and paraclinical aspects of severe malaria

No abstract available!

- Study of complicated vs uncomplicated malaria
  - Minor complications vs major complications
  - complication score vs outcome
  - mean laboratory values vs complication status
  - mean laboratory values vs severity
  - general signs and symptoms vs severity
- 296 patients with malaria included, 19% with complicated malaria
- complications of severe malaria were shown
- description of early and late complications
- Five cases of fatal malaria presented, 4 of them due to doctors delay
- Conclusions from the study
- Diarrhea is marker of severe disease
  - Vomiting is not associated with severe malaria
  - Mortality is associated with high initial complication score

- Uncomplicated malaria does not evolve in serious complications when adequately and promptly treated
- Evaluating additional paraclinical routine markers of severe disease may be useful

Ron Behrens: Risk factors for Malaria in UK, travellers to the Gambia

No abstract available!

- Increase of patients with falciparum malaria returning from Gambia since 1999, 2000 and 2001
- Case control study
- Visiting Gambia between September1, and December 31 2002
- 1680 questionnair sended, 41 % retouned
- main reasons for travel: 87% holiday, 70% had visit Gambia previously
- protective measures: 87% using chemoprophylaxis, 36% mefloquine, 47 % used chloroquine&proguanil

- Summary:
  - mefloquine highly protective (89%)
  - chloroquine&proguanil have only 43% protective efficacy!
  - Adherence to all preventative measure was poor
  - Widespread failure in implementation of national malaria prevention policy

Ron Behrens: Ten year trend (1990-2000) of Malaria imported into the UK

No abstract available!

- Most of the data come from surveillance reports of malaria
- Dominator data for number of visits (face to face interviews at the airport; 250000 interviews /year) were given
- 128%increase in visits, 87% increase in malaria, so in fact a decrease of incidence
- non-tourist destinations are most risky parts (Sierra Leone vs Kenya)
- risk malaria is now lower than ever
- a large proportion of malaria in the UK occurs in London in Africans
- Paediatric malaria in east London: 211 children from 1996-2001 were diagnosed with malaria
  - Only e few took adequate prophylaxis
  - Delays of diagnosis
  - 10% of this children had severe malaria
- Vivax malaria:
  - Shown time to onset after arrival of P. vivax
- Conclusions:
  - Variable malaria risk
  - Decreasing overtime
  - More risk for business travellers!

Martin Grobusch: Treatment study in uncomplicated malaria: Malarone vs Riamet

This malaria therapy study within the network will yield information of use for therapy guidelines and determination of a therapeutic standard. A brief update on the evolution of the study concept is given. Information on the current state of protocol development and other relevant details will provide by email.

MISSION AND GOALS OF TROPNETEUROP

- to maintain a collaborative network of European professionals dealing with imported infectious diseases;

- to create European consensus for clinical guidelines for diagnostic and therapeutic procedures in imported infectious diseases;

- to identify emerging pathogens by sampling returning international travellers, immigrants, and foreign visitors;

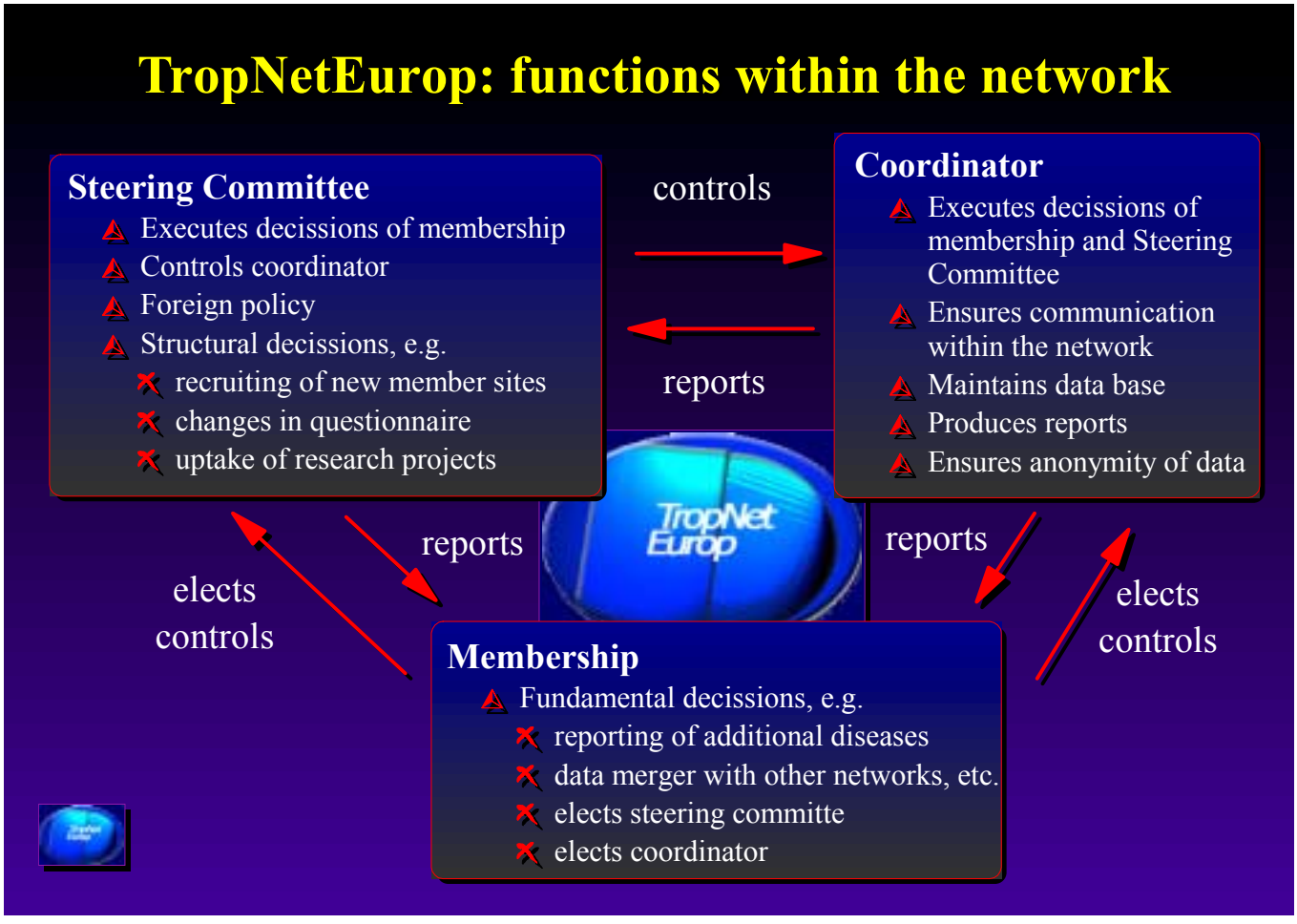
- to add information and accuracy to the current, divergent European systems of disease notification;

- to provide grounds for cluster investigation and intervention strategies by Public Health authorities;

- to provide the basis for permanent research collaboration of infectious disease centres in Europe

TROPNETEUROP: RULES & REGULATIONS

1. Membership only by clinical sites, no minimal number of patients
2. Exclusion criteria for members need to be defined, steering committee also decides on inclusion
3. Management structure: every site has one site manager and one vote (only when submitting data!)
4. Steering committee: five members including one network coordinator(elected for two years)
5. Regular meeting of membership every year necessary
6. All members decide on fundamental issues regarding the network
7. Members should decide on steering committee work at annual meetings:
   steering committee submits questions, proposals to all members, reviews research proposals
8. Network coordinator manages day-to-day work
9. Data are owned by all reporting members
10. Publication of results: all site managers of reporting sites are named as co-authors (in order of number of reported patients). TropNetEurop should always be mentioned. All publications go through review by steering committee.
11. Ownership of funds: though network infrastructure should be financed, funds will be managed by members that applied for them



CURRENT SITUATION OF TROPNETEUROP

TropNetEurop has started in April, 1999 with few selected members of TropMedEurop, the European Association for Tropical Medicine. From the beginning, support has been surprisingly strong and it has been very easy to recruit new member sites. TropNetEurop covers now 12% of all malaria patients in Europe and probably a similar percentage of patients diagnosed with dengue fever and schistosomiasis .

After a major consolidation phase during the second half of 2000, when several inactive members opted to join the mailing list "friends & observers" rather then participating in the reporting system, recruitment of new member sites has continued. TropNetEurop wishes to interest all major European "centres of excellence" on Imported Infectious Diseases. Currently, the network has 46 members sites.

	N	%
Member Sites	46	100.0
Sites reporting electronically	23	50.0
Reported Patients	7628	100.0
Patients reported electronically	1544	20.2
Reported Diagnoses	7640	100.0
Malaria	5979	78.3
Schistosomiasis	890	11.6
Dengue	771	10.1

Member sites of TropNetEurop:

No	Institution	Site Director
1	Department of Infectious Diseasesand Tropical Medicine, University Hospital of Aarhus, Skejby Hospital, Aarhus, Denmark	Prof. F.T. Black
2	Prins Leopold Instituut voor Tropische Geneskunde, Clinical Services, Antwerp, Belgium	Dr. J. Clerinx
3	Sección de Medicina Tropical, Hospital Clinic, Barcelona, Spain	Dr. J. Gascon
4	Unitat de Malalties Tropicals, Importades i Vacunacions Internationales, Institut Català de la Salut, Barcelona, Spain	Dr. J. Gómez i Prat
5	Swiss Tropical Institute, Basel, Switzerland	Dr. C. Hatz
6	Centre for tropical medicine and imported infectious diseases (CTID), Division of infectious diseases, Medical Dept., Haukeland University Hospital, Bergen, Norway	Dr. Øystein Strand
7	Berlin Institute of Tropical Medicine, Berlin, Germany	Dr. T. Jelinek
8	Medizinische Klinik mit Schwerpunkt Infektiologie, Charite/Campus Virchow-Klinikum, Berlin, Germany	Dr. T. Zoller
9	Consultation de médecine tropicale, Hôpital Avicenne, Bobigny, France	Dr. O. Bouchaud

10	Médecine interne et Maladies tropicales, Hôpital St André-CHU, Bordeaux, France	Prof. DJM Malvy
11	Bradford Royal Infirmary, Infection and Tropical Medicine, Bradford, UK	Dr. P. McWhinney
12	Clinica di Malattie Infettive e Tropicali, Universitá di Brescia, Italy	Dr. A. Matteelli
13	Surgeon General's Department, Army Medical Directorate, FASC Camberley, UK	Dr. A. Green
14	Consulta de Medicina do Viajante, Departamento de Doenças Infecciosas, Hospital Universitário, Coimbra, Portugal	Prof. S. da Cunha
15	Department of Infectious Diseases M 5132, University of Copenhagen, Denmark	Dr. I. Gjørup
16	Hvidovre Hospital, Dept. of Infectious Diseases, Hvidovre, Denmark	Dr. J. Iversen
17	Tropical Medical Bureau, Dublin	Dr. Graham Fry
18	Institute of Maritime and Tropical Medicine, Gdynia, Poland	Prof. A. Kotlowski
19	Tropenmedizin, Abteilung Tropenhygiene und Offentliches Gesundheitswesen, Universitatsklinikum Heidelberg, Germany	Dr. A. Kapaun
20	Aurora Hospital, Helsinki, Finland	Prof. H. Siikamaki
21	Epidemiological Services, Military Medical Academy, Hradec Kralove, Czech Republic	Dr. J. Beran
22	Schiffahrtmedizinisches Institut der Marine, Infektion-, Tropen- und Präventivmedizin, Kronshagen, Germany	Dr. G. Boecken
23	Travel Clinic, Policlinique Médicale Universitaire, University of Lausanne, Lausanne, Switzerland	Dr. B. Genton
24	Städtische Kliniken "St. Georg", Leipzig, Germany	Dr. M. Schulze
25	Universidade Nova de Lisboa, Instituto de Higiene e Medicina Tropical, Lisbon, Portugal	Dr. J. Atougia
26	Hospital for Tropical Diseases Travel Clinic, London, UK	Dr. R. Behrens
27	Microbiologia Clinica, Ctra. de Meco, Alcala de Henares, Madrid, Spain	Dr. J. Cuadros
28	Tropical Medicine & Clinical Parasitology Unit, Infectious Diseases - Microbiology Department, Hospital Ramon y Cajal, Madrid, Spain	Prof. R. Lopez-Velez
29	Hospital Carlos III, Instituto de Salud Carlos III, Madrid, Spain	Dr. S. Puente
30	Division of Infectious Disease, Fundación Jiménez Díaz, Madrid, Spain	Dr. M. de Górgolas
31	Centre de Formation et de Recherche en Médecine et Santé Tropicale, Faculté de Médicine, Marseille, France	Prof. J. Delmont
32	Department of Infectious Diseases & Tropical Medicine, University of Munich, Germany	Dr. M. Schunk
33	Centro per le Malattie Tropicali, Ospedale S. Cuore, Negrar (Verona), Italy	Dr. Z. Bisoffi
34	Department of Infection & Tropical Medicine, Newcastle General Hospital, Newcastle-upon-Tyne, UK	Dr. M.L. Schmid
35	Department of Infectious Diseases, Ullevaal University Hospital, Oslo, Norway	Prof. B. Myrvang
36	Institut de Medicine et Epidemiologie Africaine, IMEA, Hôpital Bichat - Claude Bernard, Paris, France	Prof. J.P. Coulaud

Institutions and partners of TropNetEurop (continued)		
No	**Institution**	**Site Director**
37	Department and Clinic of Tropical and Parasitic Diseases, Karol Marcinkowski University of Medical Sciences, Poznan, Poland	Dr. M. Paul
38	Central Hospital of Rogaland, Stavanger, Norway	Dr. Åse Berg
39	Karolinska Hospital, Department of Medicine, Unit of Infectious Diseases, Stockholm, Sweden	Prof. A. Björkmann
40	Karolinska Institute, Division of Infectious Diseases, Huddinge University Hospital, Stockholm, Sweden	Prof. U. Hellgren
41	Osp. Amedeo di Savoia, Div. "A" Malattie Infettive, Torino, Italy	Dr. Guido Caleri
42	University Hospital of Tromsø, Norway	Dr. JB Christensen
43	Institut für Tropenmedizin, Eberhard-Karls-Universität Tübingen, Germany	Prof. J. Knobloch
44	Sektion Infektionskrankheiten, Universität Ulm, Germany	Prof. P. Kern
45	Kaiser-Franz-Josef-Spital der Stadt Wien, 4. Medizinische Abteilung mit Infektions- und Tropenmedizin, Vienna, Austria	Dr. H. Laferl
46	Missionsärztliche Klinik, Würzburg, Germany	Prof. K. Fleischer

TropNetEurop: Members and Patient Encounters

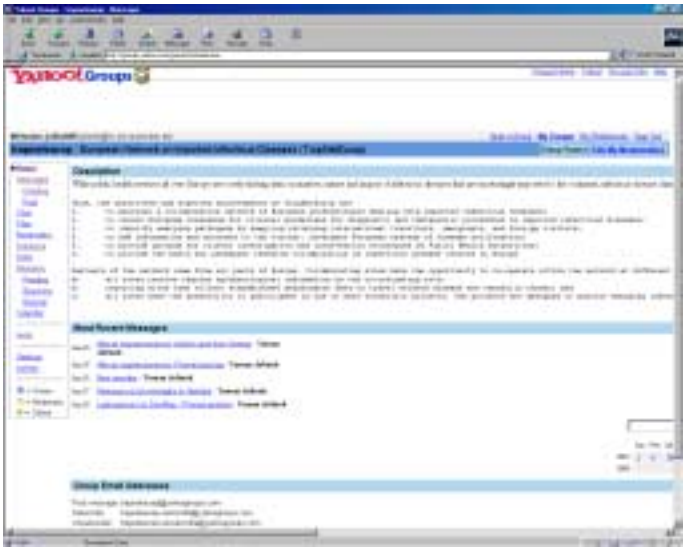
Nº	Town	Site Manager	In- and outpatients [per year]	Pre-travel advises [per year]
1.	**Aarhus**	F. T. Black	350	800
2.	**Antwerp**	J. Clerinx	7700	12000
3.	**Barcelona – Hospital Clinic**	J. Gascon	1400	6000
4.	**Barcelona - Drassanes**	J. Gòmez i Prat	6000	12000
5.	**Basel**	C. Hatz	2500	10000
6.	**Bergen**	O. Strand	50	600
7.	**Berlin - IFT**	T. Jelinek	4000	27000
8.	**Berlin - Charite**	T. Weitzel	400	0
9.	**Bobigny**	O. Bouchaud	500	0
10.	**Bordeaux**	JMD. Malvy	500	12000
11.	**Bradford**	P. McWhinney	150	0
12.	**Brescia**	A. Matterelli	400	30
13.	**Camberley (UK Armed Forces)**	A. Green	0	0
14.	**Coimbra**	S. da Cunha	50	800
15.	**Copenhagen - CMP**	I. Bygbjerg	300	2000
16.	**Dublin**	G. Fry	1200	12000
17.	**Gdynia**	A. Kotlowski	7000	6000
18.	**Hamburg**	G. Burchard	5000	5000
19.	**Heidelberg**	A. Kapaun	1400	6000
20.	**Helsinki**	H. Siikamaki	300	0
21.	**Hradec Králové**	J. Beran	300	2000
22.	**Kronshagen (Bundeswehr)**	G. Boecken	500	1000
23.	**Lausanne**	B. Genton	300	12000
24.	**Leipzig**	M. Schulze	200	4000
25.	**Lisbon**	J.V. Costa	400	3100
26.	**London**	R. Behrens	5000	8000
27.	**Madrid - Principe de Asturias**	J. Cuadros	100	75
28.	**Madrid - Ramon y Cajal**	R. Lopez-Velez	550	0
29.	**Madrid - Carlos III**	A. Benito	450	0
30.	**Madrid - Jiménez Díaz**	M. de Górgolas	100	200
31.	**Marseille**	J. Delmont	2500	3000
32.	**Munich**	M. Schunk	1700	13000
33.	**Negrar (Verona)**	Z. Bisoffi	2000	1500
34.	**Newcastle**	M. Schmid	1500	300
35.	**Oslo**	B. Myrvang	1500	5000
36.	**Paris**	J.P. Coulaud	1500	6500
37.	**Poznan**	M. Paul	100	350
38.	**Stavanger**	A. Berg	100	0
39.	**Stockholm - Karolinska**	S. Britton	1500	15000

TropNetEurop: Members and Patient Encounters (continued)

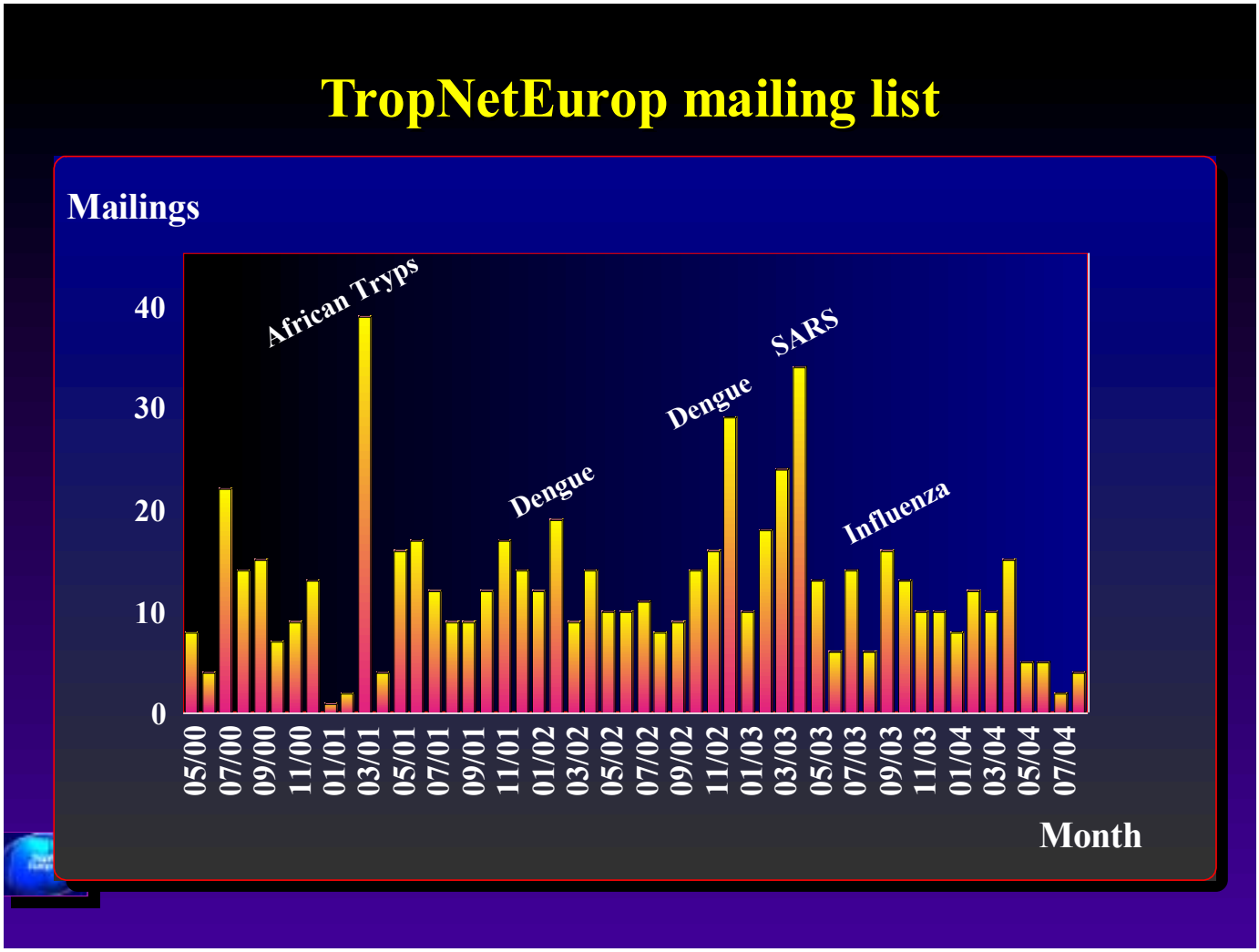
N°	Town	Site Manager	In- and outpatients [per year]	Pre-travel advises [per year]
40.	**Stockholm - Huddinge**	U. Hellgren	400	15000
41.	**Torino**	G. Caleri	800	2000
42.	**Tromsø**	J. B. Christensen	50	300
43.	**Tübingen**	J. Knobloch	1000	6000
44.	**Ulm**	P. Kern	1000	2500
45.	**Vienna – KFJS**	H. Laferl	450	0
46.	**Würzburg**	K. Fleischer	300	450
	TOTAL		**63,500**	**213,505**

COMMUNICATION

a) The Mailing List



The TropNetEurop mailing list is managed by the coordinator. Primarily for reasons of convenience, a group list at Yahoo!.com has been chosen for this purpose. All mailings to TropNetEurop go through this group servers and have been approved by the coordinator. The list server cannot be accessed by non-members. Only selected messages are forwarded to the outside by the coordinator. The list is one of the most valuable features of TropNetEurop, enabling all members to communicate rapidly in an exclusive setting.



b) Monthly Reports

Monthly reports on accumulated and analysed data have been mailed on (almost) monthly basis since April, 1999. Outfit and content of the reports have changed, feedback was overwhelmingly positive. TropNetEurop members receive the reports as WinWord-files which is supposed to make use of the graphics in lectures and presentations easy. Every figure can be copied to any presentation programme (such as PowerPoint) and modified for further use. In the same way as data in the data base are owned by all TropNetEurop members, so are reports and their content. Members can use the material without further permission, yet acknowledgement of the network is encouraged.

Recently published material:

- Mühlberger N, Jelinek T, Behrens R, Gjørup I, Coulaud JP, Clerinx J, Puente S, Burchard G, Corachán M, Grobusch MP, Weitzel T, Zoller T, Kollaritsch H, Beran J, Iversen J, Hatz C, Schmid M, Björkmann A, Fleischer K, Bisoffi Z, Guggemos W, Knobloch J, Matteelli A, Schulze MH, Laferl H, Kapaun A, McWhinney P, Lopez-Velez R, Fätkenheuer G, Kern P, Zieger BW, Kotlowski A, Fry G, Cuadros J, Myrvang B, for the TropNetEurop and SIMPID Surveillance Networks. Age as a Risk Factor for Severe Manifestations of Falciparum Malaria in Non-immune Patients – Observations from TropNetEurop- and SIMPID-Surveillance Data. *Clin Infect Dis* 36 (2003) 990-995.
- Grobusch MP, Mühlberger N, Jelinek T, Bisoffi Z, Corachán M, Harms G, Matteelli A, Fry G, Hatz C, Gjørup I, Schmid M, Knobloch J, Puente S, Bronner U, Kapaun A, Clerinx J, Nielsen LN, Fleischer K, Beran J, da Cunha S, Schulze M, Myrvang B, Hellgren U, for the European Network on Surveillance of Imported Infectious Diseases (TropNetEurop). Imported Schistosomiasis in Europe: Sentinel Surveillance Data from TropNetEurop. *J Travel Med* 10 (2003) 164-169
- Wichmann O, Jelinek T, Peyerl-Hoffmann G, Mühlberger N, Grobusch MP, Gascon J, Matteelli A, Hatz C, Laferl H, Schulze M, Burchard G, da Cunha S, Beřan J, McWhinney P, Kollaritsch H, Kern P, Cuadros J, Alifrangis M, Gjørup I, for the European Network on Surveillance of Imported Infectious Diseases (TropNetEurop). Molecular surveillance of the antifolate-resistant mutation I164L in imported African isolates of *Plasmodium falciparum* in Europe: sentinel data from TropNetEurop. *Malaria J* 2 (2003) 17
- Mühlberger N, Jelinek T, Gascon J, Probst M, Zoller T, Schunk M, Beran J, Gjørup I, Behrens RH, Clerinx C, Björkman A, McWhinney P, Matteelli A, Lopez-Velez R, Bisoffi Z, Hellgren U, Puente S, Schmid ML, Myrvang B, Holthoff-Stich ML, Laferl H, Hatz C, Kollaritsch H, Kapaun A, Knobloch J, Iversen J, Kotlowski A, Malvy DJM, Kern P, Fry G, Siikamaki H, Schulze MH, Delmont J, Paul M, Gómez i Prat J, Lehmann V, Bouchaud O, da Cunha S, Atouguia J, Boecken G. Epidemiology and Clinical Features of Vivax Malaria Imported to Europe: Sentinel Surveillance Data from TropNetEurop. *Malaria J* 3 (2004) 5
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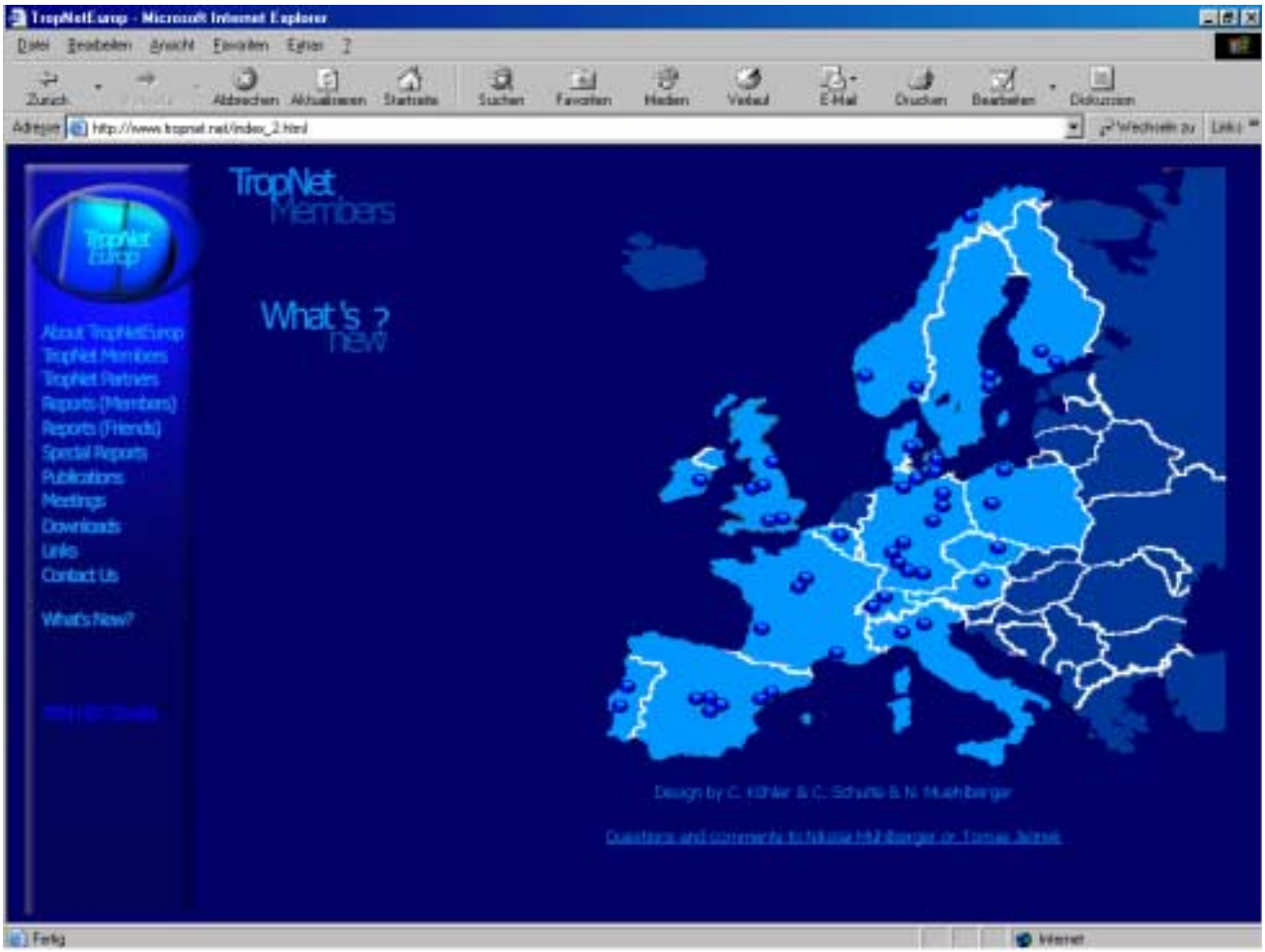
Material in print:

- Wichmann O, Mühlberger N, Jelinek T, Alifrangis M, Peyerl-Hoffmann G, Mühlen M, Grobusch MP, Gascon J, Matteelli A, Laferl H, Bisoffi Z, Burchard G, Cuadros J, Hatz C, Gjørup I, McWhinney P, Beran J, da Cunha S, Schulze M, Kollaritsch H, Kern P, Fry G, Richter J. Screening for mutations related to Malarone® resistance in treatment failures and other imported isolates of Plasmodium falciparum in Europe. *J Infect Dis* (in print)

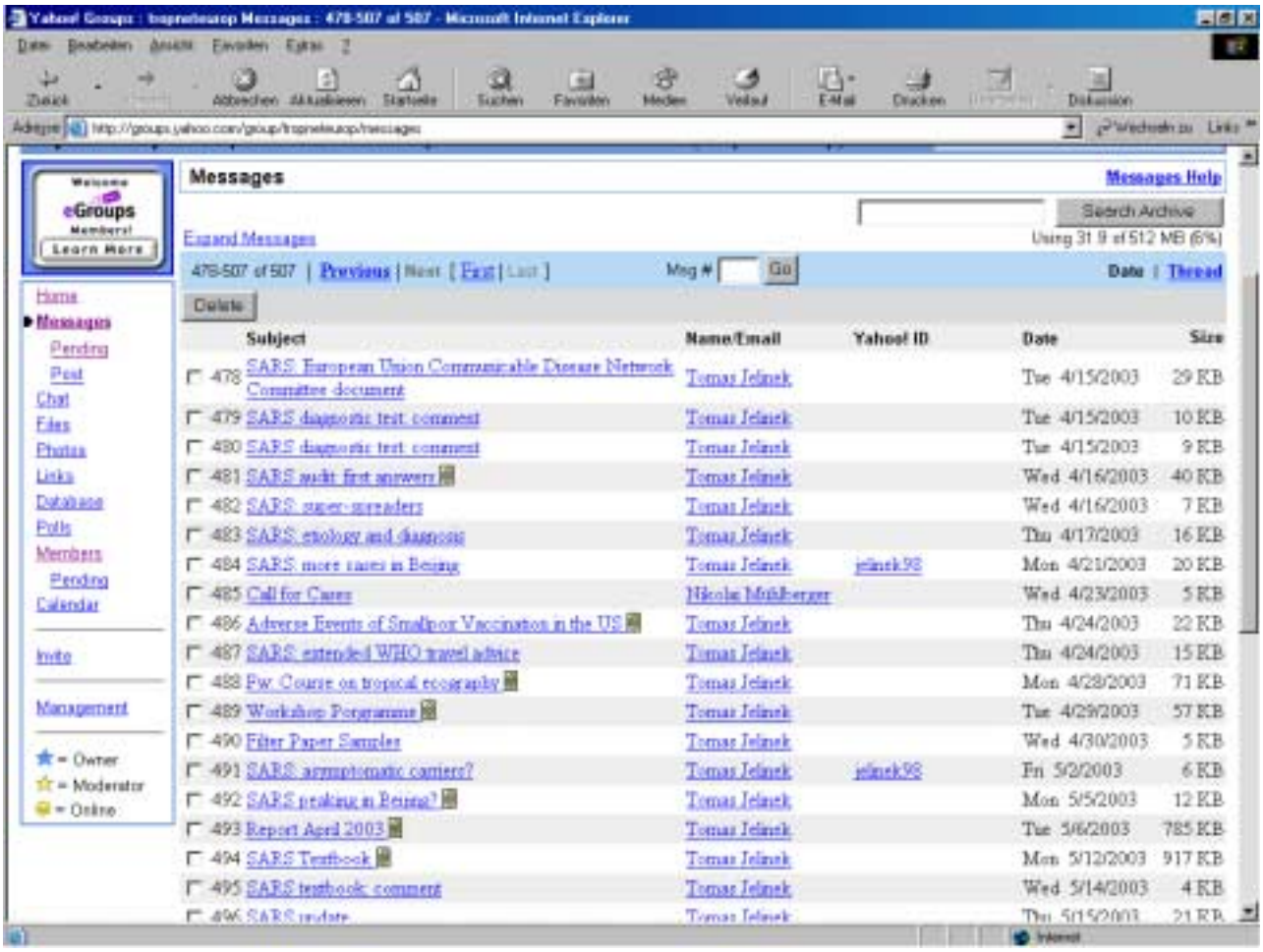
c) The Web Site

The TropNetEurop web site can be accessed by everybody at www.tropnet.net. The site provides basic information on the network and its members, offers contacts to the coordinator and the members and informs about recent reports and "sentinel events". A password protected area for members only gives access to all reports of TropNetEurop. We do not monitor access numbers to the web site, but feedback has been predominantly positive. The award-winning site has been created by Clemens Schulte and is now managed by Nikolai Mühlberger.



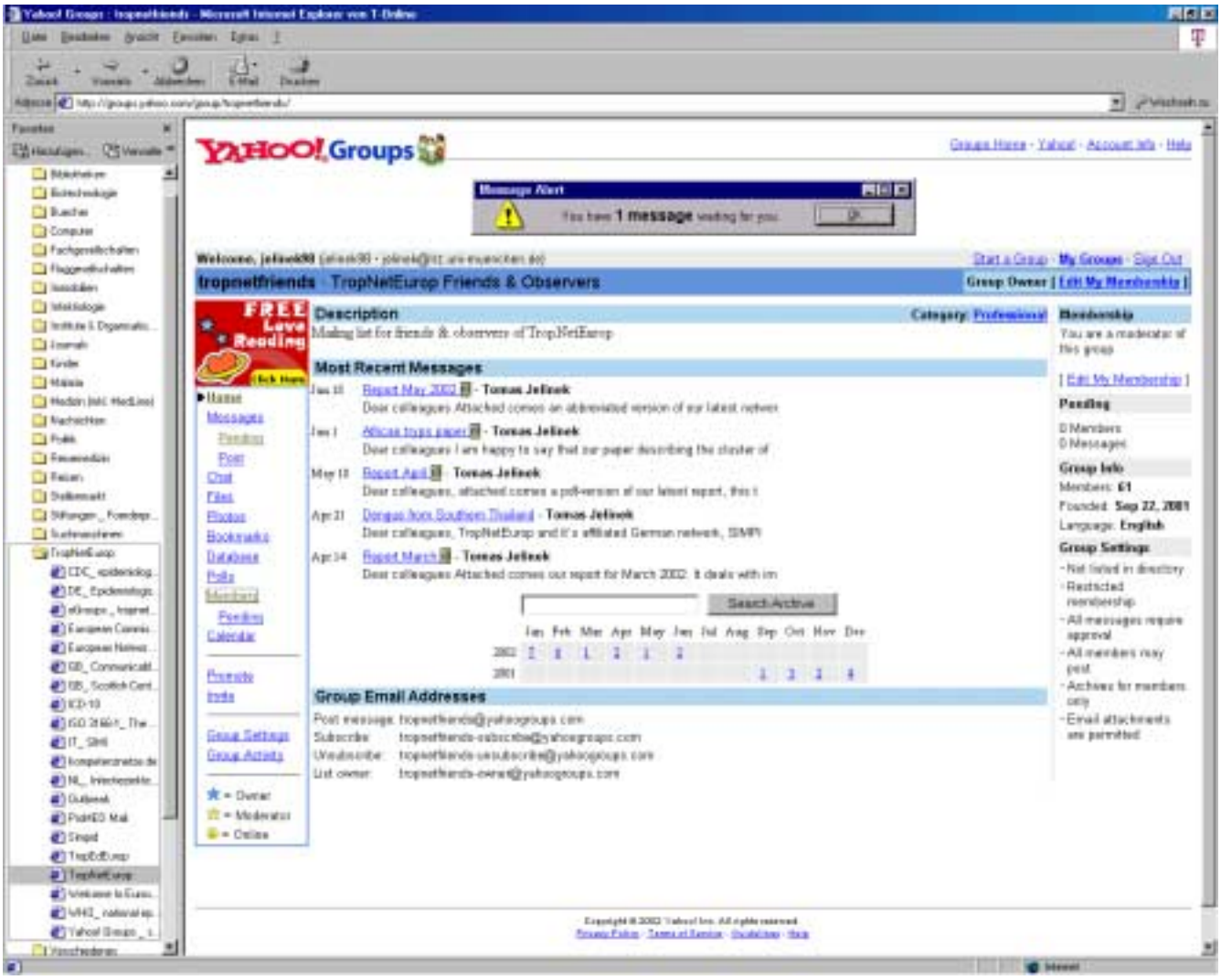
d) Special Reports and "Sentinel Events"

The extremely high level of awareness for "sentinel events" of all network members has ensured several impressive successes of TropNetEurop. The latest example is the description of a cluster of dengue fever in Thailand. TropNetEurop is contacted by several national public health agencies for information on disease activity and has formed a permanent collaboration with the German Robert Koch Institute.



e) Friends & Observers

Following increasing demand, a second TropNetEurop mailing list had to be created. This list is targeting all interested medical staff, that are not able or willing to participate actively at TropNetEurop. It also aims to include public health staff in Europe, at WHO and in countries that are visited by European travellers. This list is managed by the network coordinator and is not open for discussion. Currently it has 71 members. Feedback has been overwhelmingly positive and close contacts to several recipients have developed. This has led repeatedly to the notification of "sentinel events" through members of this mailing list to TropNetEurop.



IMPORTANT REMARKS ON DATA QUALITY

Quality of TropNetEurop surveillance data has clearly increased as more and more sites switched to electronic reporting. Presently, 23 (50%) of the 46 TropNet-sites report electronically. Electronic reports make up 21% of our data.

However, data quality is still unsatisfactory in some respects. Some flaws should be pointed and ruled out.

1. **Duplicate or multiple-reporting**
   270 (3.5%) of 7829 TropNet cases could be identified as duplicate notifications. The actual number of duplicates might be even higher.

   Counter measure:
   Please report patients' exact data of birth, which helps to detect and eliminate potential duplicates. Avoiding multiple-reporting would of course be preferred.

2. **Final diagnosis Tertian malaria**
   The final diagnosis Tertian malaria is too unspecifc for analyses that focus on Plasmodium species.

   Counter measure:
   Please specify the P. species (P. vivax or P. ovale), if possible.

3. **Diagnosis of Dengue-fever**
   The TropNet definition for confirmed dengue-cases has been modified in 2003. According to the new definition, a serological diagnosis needs to be confirmed by antibody increase in serum pair. Single antibody measurements can only yield probable diagnoses. To account for the change, the diagnostic category "Antibody increase in serum pair" was added to our paper- and electronic-questionnaires in 2003. However, since older versions of our questionnaire are still in use, dengue cases might be miss-classified.

   Counter measure:
   Please do not report on outdated questionnaires.

4. **Final diagnosis DHF, cerebral malaria, complicated malaria**
   Final diagnoses like DHF (A91) and cerebral (B50.0) or complicated malaria (B50.8) are rarely used, even if information given in the complication section suggest their justification. Miss-classified final diagnoses could be recoded, however, the information given on complications is often insufficient in respect of the strict case definition. As a consequence, complicated cases, which are a major outcome of TropNet-surveillance, might be missed.

   Counter measure:
   Please use DHF, cerebral malaria and complicated malaria as final diagnoses, if applicable.

Surveillance Questionnaire for Imported Infectious Diseases (TropNetEurop)

(Fax to 0049-30-30116-888, att. Dr. T. Jelinek)

Clinic ID	Patient ID	Date Initial Visit (DD/MM/YY)	Inpatient / Outpatient	Inpatient days	Sex	Date of birth (DD/MM/YY)
		/ /			M F	/ /

Country of birth	Country of residence	Citizenship	If born outside Europe, give date of first arrival	(DD/MM/YY)
				/ /

HISTORY OF RECENT TRAVEL List, in order, journeys to all countries relevant for this visit, and indicate most likely country of infection by checking	Trip Duration (number of days)	Trip Ended (DD/MM/YY)
		/ /

1.	4.
2.	5.
3.	6.

Detailed information on likely place of infection (town, area):

Pre-Travel counselling by health care provider? Yes No Don't know

Malaria Chemoprophylaxis: None Chloroquine Proguanil Mefloquine Doxycycline Atovaquone/Proguanil

Other:

Compliant Yes ….No

Patient Classification	Reason for most recent travel	Chief complaint (CHECK ALL THAT APPLY)	
Immigrant / Refugee	Tourism	Asymptomatic Screening	Lymphadenopathy
Foreign visitor	Visiting Relatives/Friends (VRFs)	**Or:**	Musculoskeletal
European, lives/works in Europe	Business	Fever	Diarrhoea
European, lives/works outside Europe (urban)	Immigration	Fatigue	Vomiting
European, lives/works outside Europe (rural)	Research / Education	Skin	ENT
	Missionary/Volunteer/ Humanitarian	Respiratory	Genitourinary
	Military	Headache	Neurologic
	Other		Psychologic
			Other:

Date of symptoms onset: (DD/MM/YY) / /

DIAGNOSIS AND TREATMENT	1. Notification Dx	2. Notification Dx	3. Notification Dx
Working Dx			
Final Dx			
How was Dx achieved? [1]	P D A SP M G C O	P D A SP M G C O	P D A SP M G C O
Treatment (1. drug)			
Treatment (2. drug)			
Treatment (3. drug)			
Treatment (4. drug)			

[1] ***Diagnostic Procedures:*** *P=Pathogen detection D=DNA detection A=Antigen detection SP=Antibody increase in serum pair (IgM or IgG) M=IgM detection G= IgG detection C=Clinical reasoning O=Other*

Accompanying Diagnoses: **1.** _____ **2.** _____ **3.** _____

COMPLICATIONS? Yes No If Yes, which? _____

DEATH? Yes No If Yes, why? _____

TropNetEurop Questionnaire for Additonal Data on Malaria Patients with HIV (TropNet MALHIV-Study)

Fax together with surveillance report of same patient to 0049-30-30116-888, att. Dr. T. Jelinek. In case of electronic reporting, please fill in TropNet/SIMPID ID assigned by your Sentry Software.

CLINIC ID	TropNet/SIMPID ID: (Fill in, if malaria case has been reported electronically)	Patient ID: (Fill in, if malaria case has been reported on paper)
	/ . . / : :	

Parasitemia measured on consecutive treatment days of malaria treatment (%):					
Day 0:	Day 2:	Day 3:	Day 7:	Day 14:	Day 28:
Thrombocyte count measured on consecutive days of malaria treatment (billion/l):					
Day 0:	Day 2:	Day 3:	Day 7:	Day 14:	Day 28:
Treatment failure: Yes No					

HIV-Parameters measured before, during and after malaria episode: (please fill in measurements and dates)			
CD4 count (n/µl)		**HIV Viral load (copies/ml)**	
Last before malaria:	**DATE:** / /	**LAST BEFORE MALARIA:**	**DATE:** / /
Lowest during malaria:	**DATE:** / /	**LOWEST DURING MALARIA:**	**DATE:** / /
First after malaria:	**DATE:** / /	**FIRST AFTER MALARIA:**	**DATE:** / /
Lowest count ever:	**DATE:** / /	**HIGHEST LOAD EVER:**	**DATE:** / /

Year of initial HIV-Diagnosis:		
AIDS-defining events: Yes No	**If yes, please check applying ICD10 categories:**	
B20	Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases	
B21	Human immunodeficiency virus [HIV] disease resulting in malignant neoplasms	
B22; B23, B24	Human immunodeficiency virus [HIV] disease resulting in other diseases or conditions	

Current antiretroviral therapy (HAART): Yes No	If yes, please list current drugs (generic name):
1.	**2.**
3.	**4.**
5.	**6.**
Duration of current HAART (Months):	**Total duration of antiretroviral treatment (Months):**
Current prophylaxis against PCP and Toxoplasmosis (Cotrimoxazol, Sulfadiazin, Daraprim): Yes No	

TropNetEurop Questionnaire for Additonal Data on Dengue Patients (TropNet Dengue-Study)

Fax together with surveillance report of same patient to 0049-30-30116-888, att. Dr. T. Jelinek. In case of electronic reporting, please fill in TropNet/SIMPID ID assigned by your Sentry Software.

CLINIC ID	TropNet/SIMPID ID: (Fill in, if dengue case has been reported electronically)	Patient ID: (Fill in, if dengue case has been reported on paper)
	/ . . / : :	

ELISA
(IgM1 and IgG1 = first serum sample; IgM2 and IgG2 = convalescent sample if collected; Day#= days after onset of fever)

PanBio-ELISA **other:** **not performed**

IgM1: U	IgG1: U	Day#(1):	IgM2: U	IgG2: U	Day#(2):

Haemagglutination Inhibition assay (HAI) (in paired serum samples) **not performed**

1st :	Day#(1):	2nd :	Day#(2):	Serotype:

Laboratory measurements:			
GOT/ASAT (max): U/l	DAY#:	MAXIMUM HEMATOCRIT: %	DAY#:
GPT/ALAT (max): U/l	DAY#:	PLATELET COUNT (MIN): X10^3/µL	DAY#:
Bilirubin (max): U/l	DAY#:	WBC (MIN): X10^3/µL	DAY#:
Duration of increased liver enzymes in days:		PROLONGED PTT? No Yes (_____-TIMES)	
Evidence of capillary leakage (hematocrit rises ≥ 20% from baseline or average hematocrit for age, sex and population, or drops ≥ 20% after sufficient fluid therapy, or hypo-albuminaemia, pleural effusion, or ascitis) No Yes, when?		LDH: U/l Day#:	

Relevant additional history	
Duration of fever: days	
History of previous dengue infection:	No Yes, when?
History of previous travel to dengue endemic country?	No 1-3 times > 3 times Last trip: years ago
Previous vaccination against	None Yellow fever Japanese Encephalitis TBE
Time between last vaccine and febrile crisis:	<2 months 2months-2 years 2-10 years >10 years

Relevant additional clinical signs and symptoms
Bleeding disorder: No Yes: petechiae other skin bleeding positive tourniquet test
epistaxis gum bleeding GI-bleeding negative tourniquet test
others: onset of bleeding disorder:

SCIENTIFIC PRESENTATIONS I: MALARIA

Epidemiological trends in visits made by UK residents in hepatitis A, enteric fever (EF) and malaria imported to the UK

Ron Behrens (1,2) , Bernie Carroll (1)
(1)Hospital for Tropical Diseases, (2) London School of Hygiene and Tropical Medicine. London

Data on travel by UK residents was obtained from the International Passenger Survey. The Public Health Laboratory Service provides surveillance reports of travel-associated hepatitis A, enteric fever and malaria, based on laboratory confirmed infection. Infection rates were calculated per 10,000 annual visits by UK residents to WHO defined endemic regions.

Results: The number of visits between 1990 and 2000, to tropical regions increased by 146% (from 3.1 to 7.7 million) while visits to malaria endemic regions increased by 163% (from 0.8 to 2.1 million). Over this period reported cases of all species malaria remained static (2096 and 2069) which adjusted for travel, is a 60% reduction in incidence.

World wide enteric fever (S.typhi & paratyphi A & B) rates over the same period, fell by 67% (0.8 to 0.3 cases/10,000 visits) with a similar decline noted from the Indian Sub-continent (ISC) from where 85% of imported cases are reported. The travel adjusted decline was three fold over the 10 years. Hepatitis A reports fell by 94%. Rates declined from 1.9 in 1990 to 0.1 cases/10,000 visits by 2000. Cases from the Indian Sub continent (30% of total) declined by 89% by 2000(199 to 21 cases); a 23 fold travel adjusted fall. Between 1990 and 2000 prescriptions for typhoid (1.3m doses) and hepatitis A (1.6m doses) vaccine use increased well above increase in travel..

Conclusions: A steep and sustained fall in rates of travel-associated hepatitis A infections occurred alongside a steady decline in enteric fever rates. Vaccine prescribing increased above the increase in number of visits over the decade. Malaria incidence fell by 60% with a 1.6 fold increase in visits to endemic countries. Ethnic travellers were at significantly higher risk of these diseases. Prophylactic measures contribution to the substantial decline of imported hepatitis A and typhoid is unclear, but malaria risk appears to be less, although there are groups, where the risk has not changed.

Vivax malaria

Nick Mühlberger, Berlin Institute of Tropical Medicine, Germany

Background: *Plasmodium vivax* is the second most common species among malaria patients diagnosed in Europe, but epidemiological and clinical data on imported *P. vivax* malaria are limited. The TropNetEurop surveillance network has monitored the importation of vivax malaria into Europe since 1999.

Objectives: To present epidemiological and clinical data on imported *P. vivax* malaria collected at European level.

Material and Methods: Data of primary cases of *P. vivax* malaria reported between January 1999 and September 2003 were analysed, focusing on disease frequency, patient characteristics, place of infection, course of disease, treatment and differences between network-member countries.

Results: Within the surveillance period 4,801 cases of imported malaria were reported. 618 (12.9%) were attributed to *P. vivax*. European travellers and immigrants were the largest patient groups, but their proportion varied among the reporting countries. The main regions of infection in descending order were the Indian subcontinent, Indonesia, South America and Western and Eastern Africa, as a group accounting for more than 60% of the cases. Regular use of malaria chemoprophylaxis was reported by 118 patients. With 86 (inter-quartile range 41–158) versus 31 days (inter-quartile range 4–133) the median symptom onset was significantly delayed in patients with chemoprophylaxis ($p<0.0001$). Common complaints were fever, headache, fatigue, and musculo-skeletal symptoms. All patients survived and severe clinical complications were rare. Hospitalisation was provided for 60% and primaquine treatment administered to 83.8% of the patients, but frequencies varied strongly among reporting countries.

Conclusions: TropNetEurop data can contribute to the harmonisation of European treatment policies.

Grey-zones in malaria prophylaxis: proposal of a Delphi method study

Guido Calleri, Osp. Amedeo di Savoia, Div. "A" Malattie Infettive, Torino, Italy

As in most decision in medical practice, recommending or not malaria chemoprophylaxis to travellers is based on a risk/benefit balance. Factors to be taken into account are many (e.g. destination, length of stay, season, precise itinerary, type of accommodation, individual factors, individual adherence to chemoprophylaxis, etc.)
International guidelines recommend chemoprophylaxis whenever a risk is described, but the degree of risk is variable between 3% (Papua NG), and 0,05% (Latin America) per month; moreover the risk may be very inhomogeneous inside the same area or state. As far as length of stay is concerned, of course the risk of drug related adverse events is roughly constant, while malaria risk is time related.
Also other factors are often ill-defined.
This means that every single factor to be evaluated has a sort of grey zone, in which the balance is difficult and highly subjective. Thus everyone of us may be setting his personal strategic threshold in a different site, and guidelines cannot help us in particular situations.
Trials are difficult to perform because of the low homogeneity of the casistic, and the need of large numbers.
A different approach to the problem might be to evaluate the opinion of experts in this field: this could show us the degree of consensus which is present, stimulate internal debate, suggest behaviours and allow us to transmit such ideas to peripheral travel clinics

The Delphi method.

The Delphi method allows us to search for subjective opinions and validate them by means of a discussion within the same group of persons (defined experts).
It has been used in the last 50 years to do forecasts, to evaluate phenomena in the absence of measurable data, and to establish criteria for decision making. It has been applied in the medical field only in the last few years, but now Medline records 50-80 articles per year using this method, mostly in the field of cost-benefit analysis, evidence based medicine, appropriate dosage of drugs.

Procedures.

The classic method has 3 phases: one to explore the topic, the second to analyse, the third to evaluate. During the three phases questionnaires are administered to a panel of experts. From the first phase onward questionnaires tend to be more structured and questions tend to be more closed.
During every phase the questionnaire can be administered more than once: during every round the global results are revealed to the experts, so that everyone can modify his opinion in consequence of this indirect communication with the group.
The communication of results is anonymous, so that everyone may be influenced by the group's opinion but not by singles, and may feel free to modify his position.
The method tends to produce consensus, and rounds may be repeated until the maximum possible consensus is reached. Then the next phase is started.
The whole process may be made more simple by defining in advance the most obvious ideas, or by using practical cases or graphs.

TropNet study.

In our setting the panel of expert is composed of all TropNet members. The group is big enough provided all or most members are interested in participating to the study. Questionnaires will be sent and replied by e-mail.
A working group, made out of 5-6 members is needed to discuss the basic ideas of the topic, to prepare the questionnaires, ant to draw the conclusions.
An expert in the method is needed to coordinate the working group, to build the questionnaires and evaluate the results.

References (Delphi method).

- Adler M, Ziglio E. Gazing into the oracle: the Delphi method, Jessica Kingsley. Harmondsworth (1995)
- Dalkey NC. Delphi. Rand Corporation, New York.(1967)
- Dalkey NC, Helmer O. The use of experts for the estimation of bombing requirements: a project Delphi experiment. Rand Corporation, New York. (1951)
- Linstone H, Turoff M. The Delphi method: techniques and applications. Addison Wesley, Reading (Mass.) (1975)
- Sackman H.Delphi assessment: expert opinion: Forecasting and group procedure. Rand Corporation R-1283-PR, Santa Monica (Cal.)

SCIENTIFIC PRESENTATIONS II: OTHER PARASITES

Determining the infection status in schistosomiasis

Bruno Gryseels, Prins Leopold Instituut voor Tropische Geneeskunde, Antwerp, Belgium

DIAGNOSIS OF SCHISTOSOMIASIS IN TRAVELERS: A RETROSPECTIVE STUDY

J.Clerinx, W.Schrooten, E.Bottieau, A.Van Gompel, J.Van Den Ende, T.Vervoort.
Dept.of Clinical Sciences, Institute for Tropical Medicine Antwerp (ITMA), Belgium

Introduction: Though schistosomiasis is frequently observed in persons returning from endemic areas, determining the intensity of infection in an individual patient has been a major problem upto now.
In this retrospecive study, we first look at associated demographic, geographic, clinical and paraclinical parameters associated in egg-positive persons attending the outpatient clinic of the ITMA. In the second part we assess the diagnostic value of potential surrogate parameters of active schistosomial disease in persons presenting with a positive serology for Schistosoma sp., in order to define the most suitable strategy for screening.
Methods: In the first part, all travellers and immigrants attending the outpatient dept.of the ITMA from 1-1-1997 till 1-6-2004, presenting with schistosoma eggs in concentrated stool or urine were included. Associated variables studied included age, sex, etnic origin, country of infection, clinical symptoms, serology (ELISA and IHA), abs.eosinophil count, ALAT/ASAT, IgE, urine and stool microscopy before and after concentration for parasites. In the second part, all patients attending the IMTA clinic from 1-1-2000 till 1-6-2004 presenting a positive serological test (ELISA and/or IHA positive) were included. Associated parameters included age, sex, serology, abs.eosinophil count, IgE, and urine and stool microscopy before and after concentration for parasites.
Results: From 1-1-1997 till 1-6-2004 schistosoma eggs were detected in 170 persons: S.mansoni (Sm) in 141 (83%), S.hematobium (Sh) in 27 (16%) and mixed infection in 2 (1%). 66% were of caucasian origin, 68% were male, and all were infected in subsaharan Africa. Sh was predominantly contracted in west and southern Africa, Sm in central Africa. A positive result for at least one serological method was observed in 92%. ELISA was positive in 79%, and IHA in only 70%, indicating a high level of discordance between tests, and a mediocre sensitivity for the individual tests for detecting active disease. There was no useful correlation between EPG, eosinophilia and IHA titer.
Sh was most frequently associated with hematuria (41%) and Katayama fever (22%), whereas Sm cases were asymptomatic in 64%, had abdominal symptoms in 19% and Katayama fever in only 2%. Urine sediment was abnormal in 81% of patients with Sh, and in 23% with Sm. Diagnosis of Sh was established by urine concentration in 80%, and by stool concentration in 66%.
In 877 patients with positive ELISA and /or IHA and a faeces concentration test performed, eggs of Schistosoma sp. were detected in 95 (11%). Eosinophilia was significantly higher in egg + patients (median 650/mm3) than in egg – patients (median 240/mm3), but sensitivity and specificity was too low to be clinically useful as a surrogate marker of egg excretion at any level.
Conclusion:
Apart from hematuria and Katayama syndrome, symptoms are of little value for the diagnosis of active schistosomiasis. Eosinophilia is an essential marker for Katayama syndrome, and may be useful as an indicator of probable active infection in patients without stool or urine sample results. Katayama syndrome is predominantly seen in patients with S.hematobium infection. A urine concentration test fails to detect ova in a substantial part of patients with active S.hematobium infection.
To detect active schistosomiasis in travelers, workup should include at least 2 different qualitative serological tests, an eosinophil count, a urine concentration test and a feces concentration test for ova of Schistosoma sp.

Imported leishmaniasis in Germany: sentinel surveillance data 2001-2004

Weitzel T (1), Mühlberger N (1), Jelinek T (1), Schunk M (2), Bogdan C (3), Ehrhardt S (4), Arasteh K (5), Schneider T (6), Peyerl-Hoffmann G (7), Fätkenheuer G (8), Boecken G (9), Probst M (10), Zoller T (10), Peters M (11), Weinke T (12), Gfrörer S (13), Klinker H (14), Holthoff-Stich M-L (15); for SIMPID (Surveillance importierter Infektionen in Deutschland)
(1) Institut für Tropenmedizin, Berlin; (2) Universitätsklinikum München; (3) Medizinische Mikrobiologie und Hygiene, Freiburg; (4) Bernhard Nocht Institut für Tropenmedizin, Hamburg; (5) Auguste-Viktoria-Krankenhaus, Berlin; (6) Universitätsklinikum Benjamin Franklin, Berlin; (7) Universitätsklinikum Freiburg; (8) Universitätsklinikum Köln; (9) Schifffahrtsmedizinisches Institut, Kronshagen; (10) Universitätsklinikum Charité, Berlin; (11) Praxis für Innerer Medizin und Tropenmedizin, Hamburg; (12) Klinikum Ernst von Bergmann, Potsdam; (13) Marienhospital, Stuttgart (14); Universitätsklinikum Würzburg; (15) Missionsärztliche Klinik, Würzburg

Leishmania infections are endemic in more than 80 tropical and subtropical countries. In Germany leishmaniasis is not a notifiable disease. Therefore, SIMPID, the German surveillance network for imported infections, included leishmaniasis into its spectrum of surveillance. From 2001 to 2004, the 56 participating SIMPID centers reported 42 cases of Leishmania infections (16 visceral [VL], 23 cutaneous [CL], and 3 mucocutaneous [MCL]). In total, 69% of the patients were male. The median age was 37 years. 31% of VL patients and 4 % of CL/MCL patients were HIV-coinfected ($p<0.05$). Most of the patients were European travelers, mainly tourists. The median travel duration was 30 days. Most frequently, leishmaniasis was acquired in European countries (48%), where VL was predominant; followed by Latin America (28%), where only CL or MCL occurred. Less frequently, cases were imported from Africa and Asia. The relative geographical risk calculated by the number of yearly travelers to different regions was significantly higher in Latin America than in all other regions and Asia compared to Europe. The median time from onset of symptoms to diagnosis was 85 day in VL and 61 days in CL/MCL. In patients with VL the main symptoms were fatigue and fever, complications occurred in 5 patients, and 1 patient died. The most frequently used drugs were amphotericin B in VL and sodium stibocluconate in CL/MCL. Parenteral treatment was used in 82% of patients with CL/MCL. Miltefosine was given in 1 patient with VL and 3 patients with CL/MCL.

The presented data provides epidemiological and clinical details of imported leishmaniasis in Germany. Although most leishmaniasis cases were acquired in Mediterranean countries, the risk of leishmaniasis was probably highest in Latin America. Patients with VL were significantly more often HIV-coinfected highlighting the known risk of this patient group for VL. Long term travel and male gender were other probable risk factors. The delayed diagnosis is probably due to the unfamiliarity of physicians with leishmanial infections. Treating VL amphotericin B was mostly used, whereas in CL/MCL a variety of local and systemic therapies were applied.

FEVER AFTER A STAY IN THE TROPICS: A 4-YEAR PROSPECTIVE STUDY

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Introduction: Most studies which investigated the causes of imported febrile illnesses were retrospective and/or hospital-based, giving limited information on the entire spectrum of febrile diseases after a tropical stay.
Methods: Our study included prospectively all travellers and immigrants attending the out- and in-patient departments of the ITMA after a stay in a tropical area during the previous year, and presenting with fever in the last 3 days prior to consultation. Diagnoses were established according to WHO and CDC guide-lines. The outcome of each febrile episode (cure, death, chronic course) was assessed during a follow-up visit or a phone contact.
Results: Between 2000 and 2004, 1480 febrile episodes were included, occurring in 1404 patients. 70 % of travelers had visited subsaharan Africa. Hospitalization was required for 419 (28.3%) episodes, 34 of which required intensive care. Complete follow-up data were available for 97.2% of all episodes; 1320 (91.8%) were cured within 3 months; 108 developed a chronic course, mostly due to tuberculosis (n=27) and/or HIV infection (n=89); 8 patients died, of whom 5 with complicated *Plasmodium falciparum* malaria.
No specific diagnosis was found in 343 (23.2%) patients. All these patients recovered completely, except one who was diagnosed later with peritoneal tuberculosis. Tropical diseases were diagnosed in 611 (41.3%) episodes, and cosmopolitan infectious diseases were identified in 495 (33.5%) episodes. A non-infectious diagnosis was established in 31 (2.1%) patients. Among the tropical diseases (n = 611), malaria was diagnosed in 435 (29.4%) episodes (of which 80% were due to *P.falciparum*), rickettsial infections in 49 (3.3%), dengue in 47 (3.1%), acute schistosomiasis (Katayama) in 28 (1.9%), typhoid and paratyphoid fever in 15 (1%), and invasive amoebiasis in 9 (0.6%). Hospitalization rate of tropical diseases varied from 10.2% for the rickettsial infections to 66.7% for invasive amoebiasis.
Conclusion: Tropical diseases were the leading cause of fever in travelers, and almost one third of episodes were due to malaria. Cosmopolitan infectious diseases were also frequently identified, and a substantial number of diagnoses remained unspecified. Most of the tropical diseases were serious conditions, often requiring hospitalization, but mortality was exclusively related to *P.falciparum* malaria. Expertise in diagnosis and management of leading tropical diseases should be a priority in all health care structures taking care of travellers and migrants.

SCIENTIFIC PRESENTATIONS III: NETWORKING

External Quality Assessment Scheme for Parasite Serology

Peter Chiodini, Department of Clinical Parasitology, Hospital for Tropical Diseases, London

At the TropNet Europ meeting in Barcelona in 2002, results from the NEQAS Parasitology EQA Schemes for blood and faecal parasite microscopy were presented. Results were encouraging, but the need for parasite serology EQA in addition to the existing Scheme for serodiagnosis of *Toxoplasma* infection was highlighted.

A pre-pilot Scheme which contained sera to be tested for antibodies to *Schistosoma*, *Entamoeba histolytica*, *Echinococcus granulosus* and *Toxocara* was therefore commenced in January 2003. *Strongyloides stercoralis* was added from October 2003 onwards. 24 laboratories are now enrolled.

Performance by participating laboratories was generally good and will be presented in detail in Antwerp. However, a range of different assays was in use, many of them in-house. This has implications for the care of patients who may have tests in one country, then present for further management in another. In addition to EQA, work towards closer harmonization of test methods between European centres should be considered.

Software and Database Designs for Tropical Medicine

Richard Boyd, Tropical Medical Bureau, Dublin

The use of software based applications in medicine has been around for many years, but the last 10 years has seen the most rapid growth. Today all types of information relating to a patient can be stored digitally. This is not limited to textual and empirical information but can include images such as x-rays, photographs and ECG results. Each medical discipline and the various support services like the laboratory will have its own needs and requirements from any software based application. Even within the same discipline these needs may be interpreted differently and developed using different software platforms and environments. Obviously there is a need for different systems to communicate with each other and understand the data exchanged.

Software systems for Tropical Medicine are no different in that they must meet the needs of the user and have the ability to exchange and interpret information from other applications whether related to Tropical Medicine or not. For example a Tropical Medicine application should be able to request, receive and interpret results for a laboratory application.

The requirement for inter-system communication has led over the years to the development of different standards in system design. The aim is to define the interfaces between systems. An analogy would be defining which side of the road a car should drive on or what defines a traffic light and what its properties of red, amber and green mean. The principle standards which have emerged are HL7 from the US and the European CEN/TC251.

After a system model has been agreed the next task is to interpret the information each system exchanges. For example what defines a laboratory result, what information should it contain, and what are the agreed codes to identify a certain type of test. Probably the two standards of interest to practitioners of Tropical Medicine are ICD 10 for disease diagnosis and LOINC for defining laboratory results.

By combining an agreed system design and coding system the ultimate aim is create a universal Electronic Health Record (EHR). Based principally around XML the EHR is made up of tags, codes and values in an XML format which disconnected and diverse software systems are able to interpret, analysis and present meaningful information to the end user.

The first challenge for Tropical Medicine and its close relative Travel Medicine is to understand what its requirements are? What is involved in a consultation and what information should be recorded, in other words what is a Tropical Medicine Health Record? The second is to ensure that a Tropical Medicine Health Record is able to exchange and understand information received or requested from a laboratory, infectious disease, primary care or other software system used in hospitals, clinics and ancillary organisations. This presentation will provide an overview of the various standards available and provide a possible framework for a Tropical Medicine application.

Setting National Standards: The Role of the National Travel Health Network and Centre (NaTHNaC)

David R. Hill, MD, Director, NaTHNaC, Hospital for Tropical Diseases, London, and Honorary Professor, London School of Hygiene and Tropical Medicine, London.

Providers of travel medicine services in the United Kingdom vary from General Practice surgeries to specialized travel clinics. The far majority of care is rendered in the GP surgery by a practice nurse. Complex decision-making is required to advise on use of specific vaccines, to decide on the destination-specific choice of malaria chemoprophylaxis, and to counsel travelers with special needs. It is important that practices have access to expert advice and to standardized protocols for their decision making. NaTHNaC has been funded by England's Department of Health to contribute to this expertise with the goal of protecting British travellers. The objectives of NaTHNaC are to:

- Develop and disseminate consistent and authoritative national guidance for health professionals who advise the public traveling abroad
- Provide a telephone advice line for health care professionals on complex situations relating to the health of travellers
- Carry out surveillance of infectious and non-infectious hazards abroad
- Administer Yellow Fever Vaccination Centres
- Collaborate with health professionals in travel medicine
- Engage the travel industry, insurance industry, and relevant government bodies in constructive dialogue towards a unified preventive approach
- Facilitate the training of health care and other personnel in the provision of best quality travel health advice
- Define short-term and long-term research priorities in travel medicine

It will be important to review travel medicine practice over time to see if implementing expert advice and standards leads to more consistent advice between practices, cost-effective use of vaccines for travel, and improved health of travellers.

Health beliefs and communication in the travel clinic consultation as predictors of adherence to malaria chemoprophylaxis

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Background

Health beliefs have been found to influence behaviour and used to successfully predict health behaviour. Health beliefs are generally considered amenable to change during a consultation. Addressing health beliefs during the consultation may improve adherence to advice and reduce risk taking by travellers. This study examines whether behaviour be effectively changed during a routine travel clinic consultation.

Purpose

To determine whether adherence to malaria prophylactic medication could be predicted by: (i) health beliefs specified by the Health Belief Model and the Theory of Planned Behaviour, (ii) communication during the consultation in a travel clinic.

Methods

Consecutive travellers (N = 130) attending a London travel clinic and due to travel to a malarious region participated. Consultations were conducted by one consultant physician and four nurses. Health beliefs were measured pre- and post-consultation. The consultations were coded from audiotape using the Roter Interaction Analysis System and a malaria content analysis system. Adherence was assessed by a follow-up telephone interview.

Results

Perceived susceptibility to malaria, perceived benefits of medication and intentions to adhere increased as a result of the consultation, and the perceived permanent nature of side effects decreased. At follow-up (N = 107), 62% reported full adherence, 26% partial adherence and 12% poor/no adherence. Multiple regression analysis indicated that travellers' adherence to medication recommendations was independently predicted by the number of travellers' questions and statements during the consultation, the number of health professional questions and statements about adherence, travellers' perceptions about the benefits of medication, and the duration of the travellers' trip.

Conclusions

Health beliefs and communication during the travel clinic consultation predicted adherence to preventative medication. The findings also suggested qualitative differences between travellers who adhered fully, partially, or poorly/not at all. Although the clinic consultation had a positive impact, emphasising the benefits of medication and resolving potential barriers to adherence could improve travellers' adherence.

Scientific presentations IV: TropNetEurop Studies

Dengue-study I

Ole Wichmann, Berlin Institute of Tropical Medicine, Germany

In July 2003, the TropNet-Dengue-Study has been launched within the infrastructure of TropNetEurop. Up to now, 62 cases of probable and confirmed cases of dengue fever, including one case of dengue hemorrhagic fever, have been reported with the help of an additional study questionnaire that is accompanying the TropNetEurop case-notification. All TropNetEurop-centres are welcome to participate in this study. The questionnaire can by downloaded under http://www.tropnet.net.

Currently eight centres are participating: four in Germany, three in Spain, and one in Finland. The goal of this study is to collect further epidemiological and clinical data of our dengue-patients. Besides relevant laboratory parameters (liver enzymes, WBC, platelet count, LDH) we are interested in the immunological response of the patients by having a look at the IgM/IgG-ratios or, if performed, the rise in HAI-titres. Therefore, the exact values of the ELISA- or HAI-titres are required!

Mild elevation of liver enzymes has been observed in more than half of the patients, in three more than 5-times above normal (Maximum GOT 588 U/L), and LHD was elevated in more than 66% of the cases. In more than 70% of the patients a leucopenia or thrombocytopenia has been noted on the day of first presentation or during follow-ups, in 42% both. The tourniquet test, if performed at all, was positive in 37% (n=10 out of total of 27). According to the manufacturer's instructions, the serological results can be interpreted in 36 cases to be a primary and in 10 cases to be a secondary dengue infection. The case of dengue hemorrhagic fever has been caused by a secondary infection.

Dengue study II

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Objectives:

To contribute to the Epidemiological Surveillance through:

1- Description of circulating serotypes and introduction of new senotypes in some geographic areas.
2- Early detection of displacement of genotypes by those with higher epidemiological impact (genotypes involved in severity of diseases)

Methodology: 1- Detection of viral RNA through RT-Nested-PCR in the union between the gen of the E-protein and NS1 by using of degenerated oligonucleotides to detect the 4 dengue serotypes but no other flavivirus. By this technique all serotypes have give the same amplification product (328 pb fragment).
2- For genotyping we use the 220pb fragment belonging to the carboxyl terminus of the gE (glycloproteine E) gene . We use this fragment because it is easily available in the gene bank database.

The serotype and genotype characterization of the isolates will be useful to stablish the phylogenetic relationship between them.

Results:

From September 2002 to July 2004, 22 isolates of dengue virus type 1 were found; 9 isolates of dengue virus type 2; 14 isolates of dengue virus type 3 and 5 isolates of dengue virus type 4. Geographical distribution is shown in the slides. The four dengue serotypes have been isolated from Caribbean and India.

From TropNet: 23 cases of Acute Dengue have been studied and 9 genetic sequences obtained.
From Spanish Network: 44 cases of Acute Dengue studied and 14 genetic sequences obtained
From ENIVD: 24 cases studied, from which we obtained the genetic sequence.

TropNet Participants: Hospital Clinic (Barcelona); Humboldt University (Berlin); Hospital Carlos III (Madrid); Hospital Ramón y Cajal (Madrid); Fundación Jímenez Díaz (Madrid); Klinikum der Universität (Munich).

European Observational Multicentre Study: Therapy of Uncomplicated Falciparum Malaria

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Therapy of imported uncomplicated falciparum malaria is by no means conducted uniformly throughout Europe. In fact, treatment strategies vary widely, as demonstrated by data obtained from TropNetEurop centres over the last years, and there is currently no standard therapy contributing centres would agree upon.

Centre-specific, and national, standards of care are based on data predominantly derived from therapeutic studies which have been performed in malaria-endemic areas. For epidemiological and biological reasons, these results are not always easily applicable to imported infections (large ethnically homogenous study cohorts, differences in the immune status of the hosts and vast variations of parasite strains from different geographic areas etc.).

The European multicentre study as described here serves the need to observe and document current therapeutic strategies for uncomplicated falciparum malaria in order to make them comparable. Recently introduced regimens for which a broad database is lacking so far (atovaquone-proguanil, artemether/benflumetol) are in the focus of interest.

This initial malaria therapy study within the framework of TropNetEurop will yield information of use for the harmonization of therapy guidelines and the determination of a therapeutic standard, and provide the platform for further, more challenging studies involving pre-registration substances.

Since almost ten months, the study is now open for recruitment, and a first presentation on the data accumulated so far will be given. However, many centers willing to contribute have not started yet to contribute. Common problems during the start phase of each contributing center, predominantly with getting acquainted with the electronic reporting systems or with the installation of the software will be addressed during presentation and discussion.