**46. Jahrestagung der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie**

***46th Annual Meeting of the Austrian Society of Tropical Medicine and Parasitology***

# „Triple M – Molecules, Models & Men: Concepts and Reality"

**Programm**
***Programme***

ÖGTP

**Kurzfassungen**
***Abstracts***

Medizinische Universität Innsbruck
Innsbruck
22. – 24. November 2012

**www.oegtp.at**

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(in chronologischer Reihenfolge, fettgedruckt: Plenarvorträge)
(*in chronological order, bold: plenary lectures*)

**22.11.2012**

**23.11.2012**



**24.11.2012**



**KURZFASSUNGEN DER POSTER/*ABSTRACTS OF POSTERS***
(in chronologischer Reihenfolge, *in chronological order*)

# THURSDAY, NOVEMBER 22nd

08.30 – 09.30 Entrance and registration

09.30 – 09.45 **WELCOME ADDRESS**
Helga FRITSCH (Vice Rector of the Medical University Innsbruck)
Werner POEWE (Chairman Department of Neurology)
Erich SCHMUTZHARD (Local Organiser)
Anja JOACHIM (President of the ÖGTP)

09.45 – 11.00 **VETERINARY PARASITOLOGY I**
Chair: Anja JOACHIM & Georg DUSCHER

09.45 – 10.20 **PLENARY LECTURE**
**Cornelia SILAGHI (Munich):**
***Anaplasma phagocytophilum* - a wide-spread tick-borne zoonotic pathogen**

10.20 – 10.40 **Georg DUSCHER,** N. BIRO, R. FARKAS, A. JOACHIM: Can *Anaplasma phagocytophilum* variants from different hosts be assigned to distinct "domestic" or "sylvatic" cycles?

10.40 – 10.55 **Lukas SCHWARZ***, A. JOACHIM, H.L. WORLICZEK: *Isospora suis* - immunisation of sows

11.00 – 11.30 *Coffee break*

11.30 – 12.30 **VETERINARY PARASITOLOGY II**
Chair: Heinrich PROSL & Helmut SATTMANN

11.30 – 11.45 **Barbara RICHTER**, M. BRINKMEIER, C. SCHWERING, M.G. VRHOVEC, N. NEDOROST, N. PANTCHEV: New insights into cryptosporidioses of tortoises

11.45 – 12.00 **Franz ALLERBERGER**: Trichinella meat inspection of domestic pigs: public health requirement or practiced for its own sake?

12.00 – 12.15 **Walter GLAWISCHNIG**, A. SAILER: Findings of *Alaria alata*-mesocercariae in Austrian wild boars (*Sus scrofa*)

12.15 – 12.30 **Helmut SATTMANN**, L. GAUB, C. HÖRWEG, H. PROSL, J. WALOCHNIK: The American Liver Fluke *Fascioloides magna* in Austria – epidemiology of an invasive parasite of cervids

12.30 – 13.30 *Lunch break*

13.30 – 15.30 **EXPERIMENTAL / MOLECULAR PARASITOLOGY**
Chair: Michael DUCHÊNE

13.30 – 13.45 S. SCHLOSSER, J. MATT, V. BAUMANN, M. TAZREITER, D. LEITSCH, **Michael DUCHÊNE**: *Entamoeba histolytica* and metronidazole: 46 years of successful chemotherapy - but how does it work?

13.45 – 14.00 **Martin KASNY**, J. DVORAK, D. OPAVSKY, L. SKORPIKOVA, P. HORAK, B. KOUDELA: Antigenic protein molecules from *Trichinella spiralis*/*T. britovi*/*T. pseudospiralis* L1 larvae excretory-secretory products and their diagnostic potential

14.00 – 14.15 **Irma SCHABUSSOVA**, O. UL-HAQ, E. HOFLEHNER, J. AKGÜN, A. WAGNER, G. LOUPAL, A. JOACHIM, B. *RUTTKOWSKI*, R.M. MAIZELS, U. WIEDERMANN: *Oesophagostomum dentatum* extracts modulate responses to vaccines and prevent the development of allergy in mice

14.15 – 14.30 **Martina ONDROVICS***, A. JOACHIM, R. B. GASSER, M. MITREVA, E. RAZZAZI-FAZELI, K. SILBERMAYR: Effects of hydrolase inhibitors on proteomic profiles of *Oesophagostomum dentatum* larvae

14.30 – 14.45 **Andrea SCHROLL***, P. LACKNER, C. WEICHSELBRAUN, E. SCHMUTZHARD, G. WEISS: Regulation of Tim-3 and Tim-4 during *Plasmodium berghei* ANKA (PbA)-induced experimental cerebral malaria (ECM) in susceptible (C57BL/6) and resistant (BALB/c) mice

14.45 – 15.00 **Karina M. WECHSELBERGER***, B. TAFERNER, R. BEER, G. BROESSNER, R. HELBOK, A. DIETMANN, M. FISCHER, N. SINGEWALD, E. SCHMUTZHARD, P. LACKNER: NMDA-receptor mediated excitotoxicity is involved in the pathogenesis of experimental cerebral malaria

15.00 – 15.15 **Benjamin WACHTER***, M. SYROWATKA, A.OBWALLER, J. WALOCHNIK: Efficacy of curcumin on *Trichomonas vaginalis* strains with varying metronidazole susceptibilities

15.15 – 15.30 **Joachim SCHMUTZHARD**, C. H. KOSITZ, P. LACKNER, R. GLUECKERT, H. RIECHELMANN, E. SCHMUTZHARD, A. SCHROTT-FISCHER: Hearing impairment in murine cerebral malaria: A histomorphologic examination of the inner ear

15.30 – 16.00 *Coffee break*

16.00 – 18.00 **PIMP YOUR PARASITE - TOOLS AND CHALLENGES**
(organized by NYP@ - Network for Young Parasitologists Austria)
Chair: Hanna WORLICZEK & Irma SCHABUSSOVA

16.00 – 16.30 **Aaron MAULE**, P. McVEIGH, L. ATKINSON, J. DALZELL, A. MOUSLEY, N. MARKS (Belfast): Drug and vaccine targets in parasites: making validation relevant using RNAi

16.30 – 16.50 **Dieter LIEBHART**, M. ASIF ZAHOOR, P. GANAS, B. JASKULSKA, M. HESS (Vienna): In vitro attenuated and virulent *Histomonas meleagridis* target different organs in turkeys, independent of co-cultivated bacteria

16.50 – 17.20 **Astrid HOLZER** (České Budějovice): Detection of microparasites, their pathways and proliferation sites using qPCR and in situ hybridisation

17.20 – 17.40 **Jan DVOŘÁK** (Prague): Genetic manipulations of schistosomes: reality or wishful thinking?

17.40 – 18.00 **Sacha HANIG***, R. ENTZEROTH, M. KURTH (Dresden): Reporter gene strategies to illuminate the wall formation in *Eimeria* - news from the inside of a black box

**18.30** **GENERALVERSAMMLUNG für Mitglieder der ÖGTP**
***GENERAL ASSEMBLY (members of the ÖGTP only)***
**MEET THE EXPERTS / GET TOGETHER** at the meeting area

# FRIDAY, NOVEMBER 23rd

08.30 – 09.00 Entrance and registration

09.00 – 10.30 **EPIDEMIOLOGY/IMMUNOLOGY/VACCINOLOGY**
Chair: Ursula WIEDERMANN

09.00 – 09.45 **PLENARY LECTURE**
**Geoffrey TARGETT (London):**
**The mysteries of immunity to malaria**

09.45 – 10.10 **Birgit FRAUSCHER**: Narcolepsy - association with influenza and/or influenza vaccine

10.10 – 10.30 **Maria PAULKE-KORINEK**, M. KUNDI, B. LAABER, N. BRODTRAEGER, C. SEIDL-FRIEDRICH, B. SCHMIDLE-LOSS, I. ZWAZL, H. KOLLARITSCH: Long-term follow up ten years after booster immunization against tick-borne encephalitis

10.30 – 11.00 *Coffee break*

11.00 – 13.00 **CLINICAL TROPICAL MEDICINE incl. MALARIA**
Chair: Harald NOEDL & Martin HADITSCH

11.00 – 11.30 **PLENARY LECTURE**
**Erich SCHMUTZHARD (Innsbruck):**
**Adjunctive therapies in severe malaria and acute bacterial meningitis**

11.30 – 11.45 **Arlette BAXMANN***, A.S. WINKLER, W.P. MATUJA, E. SCHMUTZHARD: The prevalence and phenomenology of febrile seizures in an urban Tanzanian population

11.45 – 12.00 **Klaus BÖCK**, C. PSCHAID, R. TOPAKIAN, K. STIEGLBAUER, S. DOPPLER, J. TIM VON OERTZEN, R. PICHLER: *Mononeuritis multiplex* - association with infectious conditions and familial background in a tropical environment

12.00 – 12.15 **Josua KEGELE***, H. HURTH, P. LACKNER, P. ZOROWKA, A. SCHROTT-FISCHER, E. SCHMUTZHARD, T. AGBENYEGA, A. ENIMIL, J. SYLVERKEN, J. SCHMUTZHARD: Otoacoustic emission testing in West African children with sickle cell disease

12.15 – 12.30 **Fabian AREGGER***, S. BUNK, J. SCHMUTZHARD, P. ZOROWKA, A. OTIENO, E. SCHMUTZHARD: Oto-acoustic emissions (OAE) as an alternative method for ICP measurement, a case report

12.30 – 12.45 **Lukas OBERHAMMER***, V. MUIGG, H. HURTH, J. KEGELE, F. AREGGER, S. BUNK, R. HELBOK, P. LACKNER, E. SCHMUTZHARD, P. ZOROWKA, A. SCHROTT-FISCHER, A. FLAMEN, T. AGBENYEGA, A. OTIENO, P. KREMSNER, J. SCHMUTZHARD: Hearing impairment in children with severe and non severe *Plasmodium falciparum* malaria by means of otoacoustic emission testing

12.45 – 13.00 **Paul SWOBODA**, M. TREIBER, M. MUELLER, H.P. FUEHRER, W.A. KHAN, I.P. CHOWDHURY, J.H. RIEDL, H. NOEDL: Intravenous azithromycin combination therapy for the treatment of severe falciparum malaria - a pilot safety and efficacy trial in uncomplicated falciparum malaria in Bangladesh

13.00 – 14.00 *Lunch break*

14.00 – 15.00 **POSTERSESSION I**
Chair: Christoph HÖRWEG

01 **Elisabeth DIETERSDORFER***, A. KIRSCHNER, A. INDRA, B. SCHRAMMEL, U. SCHEIKL, J. WALOCHNIK: Freeliving amoebae as reservoirs and training grounds for legionellae – the relevance of the viable but non culturable state

02 **Ute SCHEIKL***, A. TSAO, M. HORN, A. INDRA, J. WALOCHNIK: Amoebae as vehicles for bacteria - a pilot study: development of a screening system for free-living amoebae (FLA)

03 **Andreas R. HASSL**: Putative vectors of Central European lacertilian and chelonian unicellular blood parasites

04 B. HINNEY, E. HAAS, M. KAMMERMAIR, **Anja JOACHIM**: *Giardia* in dogs and cats in Austria - zoonotic risk and comparison of tests

05 **Adelheid G. OBWALLER**, M. WEILER, T. J. NAUCKE, G. MOOSEDER, H. ASPÖCK, J. WALOCHNIK: Phylogeographic survey on *Phlebotomus* spp. in Eastern Europe

06 **Katja SILBERMAYR**, A. C. GILL, B. SEIDEL, P. HUFNAGL, A. INDRA, A. JOACHIM, G. DUSCHER: Detecting *Dirofilaria* spp. in Austrian mosquitoes

07 **Hans-Peter FUEHRER**, M. TREIBER, K. SILBERMAYR, T. BAUMANN, P. SWOBODA, A. JOACHIM, H. NOEDL: A case of canine dirofilariosis in rural southeastern Bangladesh

08 **Martin KASNY**, C. CANTASCESSI, J. MULVENNA, N. D. YOUNG, A. AZIZ, R. LEONTOVYC, P. HORAK, R.B. GASSER: *Fascioloides magna*: exploration of secretome and transcriptome

09 **Larissa GAUB***, A.-S. FEIX, C. HÖRWEG, H. SATTMANN, J. WALOCHNIK: A molecular approach to the occurence and distribution of trematodes in eastern Austria

15.00 – 16.00 **POSTERSESSION II**
Chair: XXX

10 **Nora WUTTE***, M. PALFNER, H. AUER, G. RUCKENBAUER, T. VALENTIN, K. SEEBER, R. KRAUSE, M. HÖNIGL: Toxocariasis and DRESS syndrome in an oncological patient: a case report

11 O. GRAF, H.P. FUEHRER, P. STARZENGRUBER, A. SIEDL, V. HOFECKER, W. A. KHAN, **Harald NOEDL**: Mis- and overdiagnosis of severe malaria in the Chittagong Hill tracts in south-eastern Bangladesh

12 **Manfred NAIRZ**, U. SCHLEICHER, A. SCHROLL, T. SONNWEBER, I. THEURL, S. LUDWICZEK, H. TALASZ, G. BRANDACHER, P.L. MOSER, M.U. MUCKENTHALER, F.C. FANG, C. BOGDAN, G. WEISS: Nitric oxide-dependent regulation of ferroportin-1 controls macrophage iron homeostais and immune function in *Salmonella* infection

13 **Johnnie AKGÜN***, I. SCHABUSSOVA, A. WAGNER, A. JOACHIM, B. RUTTKOWSKI, U. WIEDERMANN: Interaction of parasitic infections and vaccines

14 **Erol ERDIK**, W.H. WERNSDORFER: Pharmakodynamische Interaktion zwischen Lumefantrin und Retinol bei *Plasmodium vivax*

15 **Jonas A. HOHLWEG***, A. WAGNER, I. SCHABUSSOVA,

B. RUTTKOWSKI, A. JOACHIM, U. WIEDERMANN: Parasite-derived molecules for prevention and therapy of allergy

16 **Anelia DIETMANN**, B. WALLNER, I. GSTREIN, F. DEISENHAMMER, A. GRIESMACHER, A. WINKLER, W. MATUJA, A. KIDUNDA, L. JILEK-AALL, E. SCHMUTZHARD: Nodding syndrome is not associated with circulating Anti-NMDA-Receptor and Anti-VGKC-Receptor Antibodies or decreased pyridoxine (Vit. B6) serum levels

17 **Alexandra ILLE**: *Borrelia* relapsing fever as a socio-economic burden

16.00 – 16.30 *Coffee break*

16.30 – 18.00 **EMERGING INFECTIONS & CO-INFECTIONS / CASE REPORTS**
Chair: Erich SCHMUTZHARD

16.30 – 17.15 **PLENARY LECTURE**
**Martin GROBUSCH (Amsterdam):**
**MDR & XDR mycobacterioses**

17.15 – 17.40 **Martin HADITSCH**: Emerging Threats (on the doorstep to Europe?): pathogen-transmission-resistance

17.40 – 17.50 **Maria KITCHEN**, M. WILHELM, S. MOSER-OBERTHALER, R. HÖPFL, G. RATZINGER, V. NGUYEN, M. SCHMUTH: Pitfalls in diagnosis and treatment of cutaneous larva migrans: unusual cases from a dermatology clinic

17.50 – 18.00 **Maria KITCHEN**, M. BODENBERGER, R. HÖPFL, I. HELLER, W. JUDMAIER, M. SCHMUTH: Case report: Liver injury, fever, urticaria and eosinophilia during the acute phase of infection with *Fasciola hepatica*

18.00 **Casting of the ballots for Junior Award/Poster Prize**

19.00 **EVENING** at the Glasmalerei

19.30 **HANDING OVER OF THE TRAVEL GRANTS** *(courtesy of ÖGTP)*
**HANDING OVER OF THE JUNIOR-AWARD** *(sponsored by Pfizer)*
Lecturer with an asterisk * are registered for the „Junior-Award“
**HANDING OVER OF THE POSTER-PREIS** *(sponsored by Pfizer)*
Poster with an asterisk * are registered for the „Poster-Preis“

# SATURDAY, NOVEMBER 24th

**FORTBILDUNG ÄRZTE / APOTHEKER** (in German language)

| | |
|---|---|
| 08.30 – 09.00 | Entrance and registration |
| 09.00 – 11.00 | **NEUES AUS DEM IMPFWESEN UND AUS DER REISEMEDIZIN**<br>Chair: Ursula WIEDERMANN |
| 09.00 – 09.30 | **Herwig KOLLARITSCH**: Reisemedizinisch relevante Impfstoffe in der Pipeline |
| 09.30 – 10.00 | **Maria PAULKE-KORINEK**, M. KUNDI, B. LAABER, N. BRODTRAEGER, C. SEIDL-FRIEDRICH, B. SCHMIDLE-LOOS, I. ZWAZL, U. WIEDERMANN, H. KOLLARITSCH: Boosterintervalle nach FSME-Impfung |
| 10.00 – 10.30 | **Ursula WIEDERMANN**: Impfungen für das Gesundheitspersonal |
| 10.30 – 11.00 | **Harald NOEDL**: Neues zur Malariaprophylaxe und Etablierung eines Kurses in Reise- und Tropenmedizin (CGMM & OEGTP) |
| 11.00 – 11.30 | Coffee break |
| 11.30 - 13.30 | **KLINISCHE RELEVANZ DER (IMMUN-)DIAGNOSTIK**<br>Chair: Horst ASPÖCK & Klaus JANITSCHKE |
| 11.30 – 11.55 | **Stefan WÖHRL**: Ist ein Blutstropfen wirklich genug? - Stellenwert der *in vitro* Diagnostik bei Allergien |
| 11.55 – 12.20 | **Cornelia LASS-FLÖRL**: Pilzinfektionen und labordiagnostische Verfahren: Sinn und Unsinn |
| 12.20 – 12.40 | **Ingrid REITER-OWONA**, A. HOERAUF: Toxoplasmose-Diagnostik - ärztliche Fürsorge oder Abzocke? |
| 12.40 – 13.00 | **Ralf IGNATIUS**: Neue Methoden der Diagnostik von Darmprotozoen |
| 13.00 – 13.20 | **Herbert AUER**, R. SCHNEIDER: Der Hundebandwurm und seine Geschwister |
| 13.30 - 14.00 | *Coffee break* |
| 14.00 - 15.00 | **TELEVOTING: KNIFFLIGE FRAGEN IN DER REISE- UND TROPENMEDIZIN** *(sponsored by MSD)*<br>Moderation: Herwig KOLLARITSCH |
| 15.00 | END |

# Interaction of parasitic infections and vaccines

**Johnnie Akgün [1], Irma Schabussova [1], Angelika Wagner [1], Anja Joachim [2], Bärbel Ruttkowski [2], Ursula Wiedermann [1]**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Medical University Vienna, Austria
[2]Institute of Parasitology, University of Veterinary Medicine Vienna, Austria
E-mail: johnnie.akguen@meduniwien.ac.at

Parasites have developed strategies to suppress the immune response of their hosts in order to promote their persistence and to limit pathology. This immunosuppression may also have an impact on unrelated antigens. Pre-existing parasite infection may interfere with responses to vaccines.
Here, we employ the experimental system of murine *Toxoplasma gondii* infection to investigate the impact of parasitic infection on experimental vaccinations.
Mice were infected orally with *T. gondii* oocysts and immunised either with an oral vaccine (cholera toxin) or a systemic vaccine (diphtheria toxoid) during the acute or chronic phase of infection.
The preliminary data show an increase of all antibody subclasses in sera and gut lavages of infected and vaccinated mice compared to non-infected vaccinated mice. Furthermore, splenocytes, mesenteric lymphocytes and lung cells from infected and vaccinated mice restimulated *in vitro* with cholera toxin or diphtheria toxoid show altered cytokine levels in comparison to cell cultures derived from animals which were only vaccinated.
Additionally, after systemic immunisation with DT the number of *T. gondii* DNA copies in the brain of *T. gondii* infected mice was reduced by 50 % compared to unvaccinated *T. gondii* infected mice. The underlying mechanism of the reduced brain cysts are currently under investigation.
Our preliminary data demonstrate that *T. gondii* not only has a strong impact on vaccine responses but that vaccination with DT reduces severeness of infection in terms of reduced brain cysts of the parasite.
Similarly, vaccine responsiveness during infection with helminth parasite *Trichuris muris* will be evaluated. Our final goal is to identify the influence and underlying immunological pathways of parasitic (co)infections on vaccine responsiveness as well as of the course of infection.

# Trichinella meat inspection of domestic pigs: public health requirement or practiced for its own sake?

**Franz Allerberger**

Österreichische Agentur für Gesundheit und Ernährungssicherheit (AGES), Bereich Öffentliche Gesundheit, Spargelfeldstr. 191, 1220 Vienna, Austria
E-mail: franz.allerberger@ages.at

Trichinellosis is a human infection caused by the nematode *Trichinella* spp. The infection is acquired by ingesting larvae in raw or inadequately cooked, contaminated meat, especially pork; wild boar-, bear -, walrus-, dog- and horse-meat have also been documented as sources of infection. Veterinary control over the slaughter of food animals to ensure food safety, particularly meat inspection, was introduced in Austria in 1924 to prevent trichinellosis from pork infected with the muscle larvae of *Trichinella spiralis*. Today, testing is performed by artificial digestion of pooled samples as requested by VO (EG) 2075/2005. The prevalence of *Trichinella* in industrially kept fattened pigs (*Sus scrofa domestica*) was declining over the years. This downward tendency has been observed worldwide and is presumed to be related to the indoor housing system of pigs, where feeding with *Trichinella*-containing meat is precluded and vermin in the stables is under control. Recent trends in consumer habits indicate a shift towards consumption of "animal-friendly" or "organic" pigs, which include increased exposure of the pig to the environment. Pigs reared in organic farms and free-ranging pigs could have increased opportunities of contact with *Trichinella* compared to animals reared in close confinement, but up to now, it has not been shown that "animal-friendly" or "organic" husbandry increases zoonoses. Wild boars (*Sus scrofa*) are well known – but in our region often also overestimated - reservoirs for *Trichinella* spp.: in Switzerland none of 10.000 wild boars (approximately 6000 shot per year) tested positive during the last years (as of 29. March 2012); in Germany only 1 to 14 per 100.000 wild boars tested positive (250.000 to 400.000 shot per year). In Austria the prevalence for *Trichinella* spp. in wild boar is very low. In the last years there was only one positive animal confirmed by the National Reference Laboratory. Nevertheless, as a public health requirement the exigency of mandatory meat inspection of wild boars sold to the public in Austria should be beyond question. However, the official meat inspection of 5.5 million domestic pigs per year did not identify one positive carcass during the last two decades. In view of lack of any evidence for public health benefit, the need for routine testing of every single pig reared in today's industrial indoor housing systems for *Trichinella* must be severely scrutinized.

# Oto-acoustic Emissions (OAE) as an alternative method for ICP measurement, a case report

**Florian Aregger[1,4], Sebastian Bunk[1,4], Joachim Schmutzhard[1], Patrick Zorowka[2], A. Otieno[3,5], Erich Schmutzhard**

Departments of Neurology[1], Otorhinolaryngology[2], Hearing, Voice and Speech Disorders[3], Medical University Innsbruck, Austria[4]
[5]Kemri Kondele Children´s Hospital of the New Nyanza Provincial General Hospital, Kisumu, Kenya
E-mail: erich.schmutzhard@i-med.ac.at

In 2000 Frank et al published a small study in which they introduced the idea to use OAE as a non-invasive method of ICP measurement. We present the case of a 12 year old Kenyan boy who developed a severe hydrocephalus malresorptivus as a consequence of tuberculous-meningitis. Despite appropriate antibacterial treatment he did not improve. The comatose (Glasgow Coma Scale (GCS) 5) patient did not react, neither to acoustic nor to painful stimuli.
The results of our 1st OAE measurement showed a poor correlation ratio (best measurement left ear: 56%, right ear: 32%, normal: >60%). After spinal tapping and withdrawal of CSF (twice 30ml each time) the OAE results improved significantly (left 83%, right 80%), the patient showed slight improvement, now being mildly responsive (GCS 7-8).
This definitely helped to make the decision to implant a ventriculo-peritoneal shunt even though the cCT had not shown any obvious improvement of the hydrocephalus.
We would like to pick up Frank´s idea and present OAE as a potential easy-to- method to objectivise relative changes in ICP in particular in low-income countries in which the neurosurgical intervention, i.e. implantation of a ventriculo-peritoneal shunt is neither routine not without risks

Ref.: Frank AM, Alexiou C, Hulin P, et al (2000).Non-invasive measurement of intracranial pressure by oto-acoustic emissions(OAEs) - a report of preliminary data. Zentralbl Neurochir 61; 177-180.

# Der Hundebandwurm und seine Geschwister

**Herbert Auer, Renate Schneider**

Abteilung f. Medizinische Parasitologie, Institut f. Spezifische Prophylaxe u. Tropenmedizin. Zentrum f. Pathophysiologie, Infektiologie u. Immunologie, Medizinische Universität Wien, Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: herbert.auer@meduniwien.ac.at

Seit mehr als zweihundert Jahren wissen wir, dass *Echinococcus granulosus*, der dreigliedrige Hundebandwurm, der Erreger der zystischen, benignen Echinokokkose des Menschen ist. Morphometrische, epidemiologische und vor allem molekulargenetische Untersuchungen haben jedoch gezeigt, dass Hundebandwurm nicht gleich Hundebandwurm ist, sondern dass es innerhalb der Spezies *E. granulosus* mehrere Stämme gibt, die sich in der phänotypischen Ausprägung (Adultstadium), in ihren Lebenszyklen (z. B. Spektrum der Zwischenwirtsspezies) und auch in ihren geographischen Verbreitungsgebieten unterscheiden.
Wir kennen heute innerhalb der Spezies *E. granulosus* zehn verschiedene Genotypen (G1 – G10), von denen manche bereits als eigene Spezies angesehen werden (G1 - 3: *E. granulosus* s.str.; G4: *E. equinus*, G5: *E. ortleppi*, G6 -10: *E. canadensis*).
In den letzten Jahren wurden in unserem Institut frisches und in Alkohol konserviertes Operationsmaterial sowie Paraffinblöckchen von über 100 Patienten (österreichischer und ausländischer Provenienz) mit zystischer Echinokokkose auf spezifische DNS untersucht. Wir konnten in unserem Patientengut sowohl den weltweit verbreiteten G1-Stamm (Schafstamm, *E. granulosus* s. str.), als *auch E. canadensis* (G6: Kamelstamm, G7: Schweinestamm) und *E. ortleppi* (G5: Rinderstamm) diagnostizieren. Wir konnten überdies zeigen, dass sich der Schafstamm und der Schweinestamm im Menschen unterschiedlich klinisch manifestieren.

# The prevalence and phenomenology of febrile seizures in an urban Tanzanian population

**Arlette Baxmann[1], Andrea Sylvia Winkler[2], William P Matuja[3], Erich Schmutzhard[1]**

[1]Department of Neurology, Medical University Innsbruck, Austria
[2]Department of Neurology, Technical University, Munich, Germany
[3]Department of Neurology, Muhimbili Centre of Health and Allied Sciences, Dar es Salaam, Tanzania
E-mail: arlette.baxmann@student.i-med.ac.at

**Objective:** A large scale screening was conducted to ascertain the prevalence and phenomenology of febrile seizures among an urban Tanzanian population.
**Methods:** A random cluster sampled population of close to 50.000 individuals was screened on febrile seizures by trained field workers in a two-stage door-to-door survey in 2010. The affected subjects were reviewed by final-year medical students in a personal interview under supervision of a neurologist. The diagnosis of febrile seizures was made by taking the patient's medical history.
**Results:** A history of febrile seizures was found in 20 out of 33.346 screened individuals. In the study population younger than twenty, the adjusted rate was 185 per 100.000 respectively 295 per 100.000 in an even younger population. The average age at onset was 20 months, the highest incidence with 3 years of age. More than half of the seizures (65%) met the classification criteria of complex seizures. In the majority fever was caused by malaria, followed by respiratory and gastrointestinal infections. 70% of the convulsing children were brought to the hospital, 45% were treated with traditional medicine. Recurrence was found in 80% of the children and two had developed epilepsy after a seizure-free interval.
**Conclusion:** In our research, we observed a lower prevalence of febrile seizures in urban Tanzania than it is reported from rural territories and western countries. Underreporting of seizures due to insufficient ability of retrospection and stigmatization might have contributed to a low rate. Compared to previous studies we found an increased rate of complex and recurrent seizures.

# Mononeuritis multiplex – association with infectious conditions and familial background in a tropical environment

**Klaus Böck, Carmen Pschaid, Raffi Topakian, Karl Stieglbauer, Stefan Doppler, Joachim Tim von Oertzen, Robert Pichler**

Wagner-Jauregg Hospital, Linz, Austria
E-mail: klaus.boeck@gespag.at

Mononeuritis multiplex is simultaneous or sequential involvement of individual noncontiguous nerve trunks, either partially or completely, evolving over days to years and typically presents with acute or subacute loss of sensory and motor function of individual nerves. Electrodiagnostic studies will show multifocal sensory motor axonal neuropathy. It is caused by, or associated with, several medical conditions, as diabetes mellitus, vasculitis, sarcoidosis and infectious diseases.
We present two recent (2012) case reports of patients from our Department of Neurology:

**Case #1**
A 51yr old Caucasian woman from Upper Austria presented with lumbago and progressive weakness of the left lower limb since three weeks. Electrophysiology revealed sensory motor neuropathy. MRI of the lumbosacral plexus was normal, CT and bone scan indicated sacroileitis. Laboratory parameters searching for vasculitis were mostly normal, but revealed diabetes mellitus with a HbA1c of 9.4%. Cancer or active sarcoidosis were excluded by FDG-PET/CT. Lumbar punction presented normal laboratory values. But additional serologic examination showed positivity for IgG antibodies of treponema pallidum. As mononeuritis multiplex was assumed in our patient – which underlying conditions might be related to this symptom? Which therapeutic approaches might lead to amelioration of her clinical afflictions?

**Case #2**
A 36yr old male hispanic, born in tropical Tolima, Colombia, and living since his academic education in Linz, Austria, was sent by his treating neurologist to our hospital for further evaluation of progressive pain and muscular weakness of both upper extremities since three weeks. This was his second hospitalisation, but now, as symptoms had progressed, electrophysiology confirmed the clinical suspicion of mononeuritis multiplex. MRI presented inflammation in the left cervicobrachial plexus. A biopsy of the left biceps muscle was without abnormalities. ACE was mildly elevated, but FDG-PET/CT did not show active sarcoidosis or a suspicous tumor. Focal hypermetabolism was detected in a cutaneous nodule of the right axilla due to an inflammatory process associated with his familial pemphigus Hailey-Hailey. Might there be a relation of these conditions, e.g. the dermatological disease figuring as a trigger of neurolgogical symptoms?
Born in the tropics as well as in central Europe does qualify for any associated process – probably causative – to mononeurits multiplex.

# Freeliving amoebae as reservoirs and training grounds for Legionellae – the relevance of the viable but not culturable state

**Elisabeth Dietersdorfer[1], Alexander Kirschner[2], Alexander Indra[3], Barbara Schrammel[1], Ute Scheikl[1], Julia Walochnik[1]**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Kinderspitalgasse 15, 1090 Vienna, Austria
[2]Institute for Hygiene and Applied Immunology, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Kinderspitalgasse 15, 1090 Vienna, Austria
[3]Austrian Agency for Health and Food Safety (AGES), Vienna, Austria
E-mail: elisabeth.dietersdorfer@meduniwien.ac.at

Freeliving amoebae are known to be reservoirs and vehicles for a wide range of bacteria, amongst others, important human pathogens like *Legionella pneumophila*.
Under poor nutrient conditions, *L. pneumophila* is not able to grow in the absence of amoebae. In some cases, like after disinfection, they can even enter the viable but non culturable (VBNC) state. If a formerly nonculturable legionella strain enters a host cell, which is normally an amoebae, it may become resuscitated and culturable again. Furthermore it has been shown, that pathogenic legionellae become more invasive for human macrophages after intracellular replication in amoebae. Our aim is to provide a comprehensive overview over the VBNC-legionellae, investigating their infectious potential.

Supported by the Austrian Science Fund (FWF)

# Nodding syndrome is not associated with circulating Anti-NMDA-Receptor and Anti-VGKC-Receptor Antibodies or decreased pyridoxine (Vit. B6) serum levels

**Anelia Dietmann[1], Bernd Wallner[1], Ingrid Gstrein[1], Florian Deisenhammer[1], Andrea Griesmacher[1], Andrea Winkler[2], William Matuja[3], Aslam Kidunda[4], Louise Jilek-Aall[5], Erich Schmutzhard[1]**

[1] Department of Neurology, Medical University, Innsbruck, Austria
[2] Department of Neurology, Technical University Munich, Germany
[3] Division of Neurology, Muhimbili Medical Centre, Dar es Salaam, Tanzania
[4] Mahenge District Hospital, Tanzania
[5] Department of Psychiatry, University of British Columbia, Vancouver, Canada
E-mail: anelia.dietmann@i-med.ac.at

**Background:** Head nodding syndrome (NS) is an epidemic epileptic encephalopathy, characterized by rhythmic dorsoventral movements of the head. EEG changes such as spike- and slow wave activity or 2.5 Hz per second spike-wave pattern have been described suggesting an absence type epileptic nature of disease. The underlying cause of the NS remains so far unknown. In the present study we investigated potentially causative agents in serum of patients with NS, other epilepsy type and community controls. First, since nutrition and vitamin status has been proposed as contributing factors to disease development and recently pyridoxine dependent epilepsies have been described, pyridoxine serum levels were measured. Second, since anti-neuronal receptor antibodies have been shown to cause epilepsy syndromes, sera were evaluated for the presence of anti-NMDA (N-methy-D-aspartate) and anti-VGKC (voltage gated potassium channel complex) receptor-antibodies.
**Methods:** Anti-NMDA- and Anti-VGKC (LG1 and Caspr2)-receptor antibodies were examined in serum samples of patients and healthy controls by a commercially available cell-based indirect immunofluorescence antibody detection test. Pyridoxine (Vitamine B6) levels were measured in patients and healthy controls serum according to routinely performed procedures in the central laboratory of the Innsbruck Medical University.
**Results:** Auto-antibodies against NMDA or VGKC (LG1 or Caspr2) Receptors could not be detected in serum of patients suffering from NS (n=22) or primary generalized epilepsy without NS (n=1). Also sera of community controls without epilepsy but positive skin snip for onchocerosis were tested (n=7), whereof 1 sample was positive for anti-VGKC Caspr2 receptor antibodies. Mean pyridoxine levels in patients with NS (n=10, 2,45+-1,6 µg/L) compared to patients with primary generalized epilepsy (n=10, 1,94 +- 1,79 µg/L) and community controls (n=8, 3,68 +- 1,54 µg/L) without any type of epilepsy but onchocercosis were not significantly different. However, mean pyridoxine levels are significantly lower compared to the normal range in Europeans (6-18µg/L).
**Discussion:** Nodding syndrome is not associated with serum anti-NMDA or anti-VGKC receptor antibodies. Furthermore, NS is not associated with decreased pyridoxine serum levels. Further studies are required to clarify the cause of this disease entity of an epidemic epileptic encephalopathy.

# Can *Anaplasma phagocytophilum* variants from different hosts be assigned to distinct "domestic" or "sylvatic" cycles?

**Georg G. Duscher[1], Nora Biro[2], Robert Farkas[2], Anja Joachim[1]**

[1]Institut für Parasitologie, Department für Pathobiologie, Veterinärmedizinische Universität Wien, Veterinärplatz 1, 1210 Vienna, Austria
[2]Department of Parasitology and Zoology, Faculty of Veterinary Science, Szent Istvan University Budapest, Hungaria
E-mail: georg.duscher@vetmeduni.ac.at

The intracellular tick-transmitted bacteria *A. phagocytophilum* affects many mammalian hosts including humans. Nevertheless their reservoirs and transmission paths still await to be elucidated. In this study a single nucleotide polymorphism at position 500 nt in the groESL sequence was used to separate various isolates from Hungary and Austria into two groups. The differentiation into the A- and the G-variant has been described for human isolates and is now compared with samples from dogs, cats, horses, cattle, red deer and questing/engorged ticks alongside sequences available in Genbank. Positive samples from four dogs, four horses, one cat, one cattle, one red deer, four questing and 30 engorged ticks (from red deer) were analyzed. A segregation of the A-variant among wild and domestic ruminants and an accumulation of G-variants in humans, dogs, possibly cats and horses, were observed. This led to the assumption that there are distinct "sylvatic" and "domestic" ecological cycles. However, this segregation is not displayed exclusively and overlapping variants exist. Nevertheless, further studies based on this rapid analysis could help tracing infection ways and exposing reservoirs.

# Genetic manipulations of schistosomes: reality or wishful thinking?

**Jan Dvořák**

Institute of Molecular Genetics Prague, Vídeňská 1083, 142 20 Prague 4, Czech Republic
E-mail: jan.dvorak@img.cas.cz

Schistosomes are notoriously known parasitic flatworms causing schistosomiasis. This tropical disease represents significant public health problem in 76 countries with more than 210 million people infected. There is no vaccine and chemotherapy relies on a single drug, praziquantel. Chronic infections can persist for decades, severe morbidity results from host immune responses to eggs in tissues and death is common. Moreover, schistosomes are actively interacting with the host physiological processes. These evasive and immuno-modulatory strategies represent "state of art" among host-parasite interactions. Studies of these and many other aspects of schistosomiasis have been often hammered by the absence of methods allowing genetic intervention and/or stable cell lines. Unlike other eukaryote systems, the means to manipulate schistosomes genetically are undeveloped. Therefore, genetic manipulations involving RNAi knockdown, various methods of transgenesis and also schistosome cell line isolations have received much attention of late. Numerous reports about RNAi and transgenic manipulations have been published recently. Despite this herculean effort there are still many obstacles and limitations which make these methods not suitable for routine laboratory work. Concrete examples and issues will be presented and discussed.

# Pharmakodynamische Interaktion zwischen Lumefantrin und Retinol bei *Plasmodium vivax*

**Erol Erdik, Walther Wernsdorfer**

Institut für Spezifische Prophylaxe und Tropenmedizin, Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: erol.erdik@gmx.net

*Plasmodium vivax* accounts for 25-40 % of all malaria infections resulting in 132-391 million clinical cases per year. Although generally regarded as benign infection, this paradigm has been challenged in the last years. Retinol showed a protective effect against malaria infection in clinical studies and slight growth inhibition of plasmodium cultures was observed in a number of in vitro studies. In combination with different antimalarials retinol improved their activity in a low to high magnitude, depending on the substance used.
This study was conducted with the objective of testing the synergism between lumefantrine and retinol following the method of Tasanor et al. with isolates dating back to 2007 from Mae Sot, northwestern Thailand.
Five parallel series were tested: lumefantrine and retinol alone, lumefantrine in combination with retinol low (900 nM), medium (1100 nM) and high (1300 nM) corresponding to the 50th, 65th and 80th levels of the physiological mean concentrations of healthy adults.
The mean IC50, IC90 und IC99 values which were obtained are as follows.
For lumefantrine: 26.67 nM, 537.07 nM and 6209.50 nM, respectively for the combination with retinol low: 7.39 nM, 99.70 nM and 822.08 nM, for the combination with retinol medium: 4.50 nM, 23.99 nM and 93.89 nM, for the combination with retinol high: 4.07 nM, 21.70 nM and 85.01 nM. These significant results suggest a strong synergism between lumefantrine and retinol.
Compared to the sensivity data collected for lumefantrine in Mae Sot in 2003 and 2001 there was no significant change in lumefantrine sensivity.

# Narcolepsy– association with influenza and/or influenza vaccine

**Birgit Frauscher**

Department of Neurology, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria
E-mail: birgit.frauscher@i-med.ac.at

Narcolepsy is a chronic neurological disorder with a reported incidence of 0.80 per 100.000 in the general adult population, and 0.30 per 100.000 in children < 17 years of age. Cardinal features of narcolepsy are excessive daytime sleepiness, cataplexy, sleep paralysis, hypnagogic hallucinations, and disturbed nocturnal sleep. For a diagnosis of narcolepsy with cataplexy polysomnographic registration demonstrating a sleep latency < 8 minutes plus ≥ 2 sleep onset REM episodes in the multiple sleep latency test, or alternatively assessment of hypocretin-1 levels in the cerebrospinal fluid ≤ 110 pg/mL is necessary. Narcolepsy is an autoimmune disease which was only recently demonstrated by two large multi-center genome-wide association studies finding a special variant in the t-cell receptor locus alpha and the purinergic receptor subtype P2RY11. As of August 2012, > 600 narcolepsy cases (including more than 100 in adults) have been reported spontaneously to the EudraVigilance database following the influenza A(H1N1)pdm09 vaccination. Several systematic studies from Norway and Sweden were published revealing an association between an increase of childhood narcolepsy and H1N1 vaccination with influenza A(H1N1)pdm09 vaccination. In Finland, Partinen et al. found a 17-fold increase of narcolepsy in children < 17 years of age in 2010 compared to the years 2002-2009. Association with influenza A(H1N1)pdm09 vaccination in other European and non-Kaukasian countries as well as non-AS03 H1N1 vaccines are either not present or unclear. Apart from the association between childhood narcolepsy and influenza A(H1N1)pdm09 vaccination, a study from China found a 3-fold increase of narcolepsy in 2010 which they attributed to the H1N1 influenza itself but not with the vaccine since only 5.6 % of affected children were vaccinated. In summary, evidence exists that there are both an association with H1N1 influenza itself as well as with influenza A(H1N1)pdm09 vaccination in the Scandinavian countries in which vaccination rates with influenza A(H1N1)pdm09 were highest. Whether both result in narcolepsy precipitation or in an increased ratio of lifelong narcolepsy remains speculative.

# A case of canine dirofilariasis in rural southeastern Bangladesh

**Hans-Peter Fuehrer[1,2,3], Moritz Treiber[2,3], Katja Silbermayr[1], Timo Baumann[1,3], Paul Swoboda[2,3], Anja Joachim[1], Harald Noedl[2,3]**

[1]Department of Pathobiology, Institute of Parasitology, University of Veterinary Medicine Vienna, Austria.
[2]MARIB, Malaria Research Initiative Bandarban, Bandarban, Bangladesh
[3]Department of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Vienna, Austria
E-mail: harald.noedl@meduniwien.ac.at

*Dirofilaria immitis* is a parasite of domestic and wild canids and felids in tropical, subtropical and temperate regions throughout the world, while its relative *D. repens* is documented in the Old World only. The canine heartworm (*D. immitis*) is the causative agent of canine and feline cardiopulmonary dirofilariasis, whereas *D. repens* causes canine and feline subcutaneous dirofilariasis. Both species are known to cause zoonotic diseases, namely human pulmonary (*D. immitis*), subcutaneous (*D. repens*) and ocular (*D. repens*) dirofilariasis.

Both, *D. immitis* and *D. repens* are known to be endemic in several South and Southeast Asian countries (e.g. India and Malaysia), but there has previously been no information about the presence of these pathogens in Bangladesh.

We present a case of suspected canine dirofilariasis identified in a dog in rural southeastern Bangladesh.

# A molecular approach to the occurrence and distribution of trematodes in eastern Austria

**Larissa Gaub [1,2,3], Anna-Sophia Feix [1,3], Christoph Hörweg [1], Helmut Sattmann [1], Julia Walochnik [2]**

[1] Museum of Natural History Vienna, Burgring 7, 1070 Vienna, Austria
[2] Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Kinderspitalgasse 15, 1090 Vienna, Austria
[3] University of Vienna, Dr.Bohr-gasse 3-9, 1030 Vienna, Austria
E-mail: larissa.gaub@gmail.com

Digenetic trematodes are widespread endoparasites. In a previous study the infection rates with *F.magna* in the intermediate host snail *Galba truncatula* from the floodplains of the Danube were investigated. The aim of the current study is to test the distribution of *F. magna* in the floodplains of the Leitha. Within this screening programme for trematodes it is also aimed to test the distribution and abundance of avian schistosomes in pulmonate freshwater snails as intermediate hosts. Until now, a total of 929 snails have been collected, measured and examined under a microscope for the presence of digenetic trematodes. The samples of affected snails were tested by PCR with modified primers and by sequencing. In 4 out of 687 collected *G. truncatula* trematodes were found microscopically as well as by molecular methods. Altogether it was shown that potentially pathogenic trematodes do occur in this region.

# Findings of *Alaria alata* – mesozercariae in free-living Austrian wild boars (*Sus scrofa*)

**Walter Glawischnig[1], Andreas Sailer[2]**

[1] Institute for Veterinary Disease Control Innsbruck, Austrian Agency for Health and Food Safety (AGES), Technikerstrasse 70, 6020 Innsbruck, Austria
[2] Institute of Zoology, University of Innsbruck, Technikerstasse 25, 6020 Innsbruck, Austria
E-mail: walter.glawischnig@ages.at

*Alaria alata* is an intestinal trematode which infests wild carnivores e.g. foxes. Eggs are being shed into the environment and develop in two different intermediate hosts (snail host; amphibian host). In addition to the amphibian intermediate host, there are also paratenic hosts (e.g. wild boar) in the development cycle of *Alaria* spp. In this potential intermediate hosts, the mesocercariae can survive and stay infective in the musculature or in different organs but do not undergo any further development.
Detection of *Alaria alata*–mesocercariae in wild boars, which are called in German „Duncker`scher Muskelegel" are reported from several European countries but until resently not from Austria. For this reason we conducted a study were we examined muscle samples from 490 free-living Austrian wild boars of different age and sex by *Alaria alata* mesoceraiae migration technique for the presence of this parasite. The game originated from four different provinces in Austria (Lower Austria n= 372, Upper Austria n=2, Burgenland n=106, Styria n=10). Animals were hunted during the hunting season 2011/2012.
Totally we found in 10 wild boars the presence of this parasite. These findings indicate a prevalence of about 2% of the examined animals. In each positive wild boar one to fife mesocercariae per 30 gram muscle tissue could be detected. All 10 positive animals originated from Lower Austria. This province counts for about 70% of the Austrian annual hunting bag of wild boars.
The results of our study show the presence of *Alaria alata*-mesocercariae in Austrian wild boars. As a former study proved the occurrence of *Alaria alata* in foxes our findings confirm the assumption that this parasite is present also in wild boars. In meat inspection of wild boars for *Trichinella* spp. by digestion methods the detection of *Alaria alata*-mesocercariae can cause confusion when assessing the meat. Several reports about cases of human larval alariosis have been published in North America. About the zoonotic potential of *Alaria alata* there is still a lack of knowledge. It is unclear if affected wild boars present a risk factor as a potential source of infection for humans.

# Mis- and Overdiagnosis of Severe Malaria in the Chittagong Hill Tracts in South-Eastern Bangladesh

**Oliver Graf, Hans-Peter Fuehrer, Peter Starzengruber, Anja Siedl, Verena Hofecker, Wasif Ali Khan, Harald Noedl**

Institut für Spezifische Prophylaxe und Tropenmedizin, Abteilung Experimentelle Tropenmedizin und Feldforschung
Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: oliver.j.graf@gmail.com

Malaria remains a major health problem in Bangladesh. The highest prevalence of malaria is typically found in the Chittagong Hill Tracts in south-eastern Bangladesh in close proximity to the Indian and Myanmar borders. Reports published by the Bangladeshi Ministry of Health suggest extremely low case fatality rates for malaria in general (0.06% in 2007) and for severe malaria (SM) in particular (0.44% in 2007) in Bandarban District, one of three Hill Tract districts. At the same time the reports suggest a high proportion of SM among all malaria cases and a low proportion of parasitologically confirmed malaria cases, thereby raising the suspicion that malaria in general and especially SM might be overreported due to inadequate diagnostic facilities. Frequent cases of mis- and overdiagnosis of SM have been reported from trials conducted in Africa. However, so far hardly any data have been available from South Asia.

The presented study was conducted at the Bandarban Sadar Hospital (BSH), the district hospital of Bandarban. Data were obtained from all patients admitted to the BSH with a diagnosis of SM. Blood slides were taken and examined by expert microscopists for parasitological diagnosis of malaria and the presence of any of the defining criteria for SM based on the WHO 1990 and 2000 definitions was verified for each of these patients.

Almost half of the patients (n = 45; 49.4%; 95% CI 39.4 - 59.5) out of 91 patients admitted with a diagnosis of SM had a negative blood smear for malaria, ten (11.0%; 95% CI 6.1 - 19.1) had a positive blood smear for *P. vivax* only while only the remaining 36 (39.6%; 95% CI 30.1 - 49.8) had a positive blood smear for *P. falciparum*. Just six patients (6.6%; 95% CI 3.1 - 13.6) met at least one of the criteria for SM. Based on the exclusive use of either the WHO 1990 or the WHO 2000 definition two (2.2%; 95% CI 0.6 - 7.7) and four (4.4%; 95% CI 1.7 - 10.8) patients were classified as SM cases, respectively. There was one fatality among the 91 patients which occurred in a patient with a malaria-negative blood smear.

These findings suggest an obvious tendency to misdiagnose non-malarial febrile illnesses and uncomplicated malaria cases as SM in the BSH resulting in inadequate treatment of the patients. Therefore there is an urgent need for training programs in SM diagnosis as well as for further trials to detect and characterize the diseases falsely diagnosed as SM.

# MDR & XDR mycobacterioses

**Martin Peter Grobusch**

Center of Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Department of Internal Medicine, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1100 DE Amsterdam, The Netherlands
E-mail: m.p.grobusch@amc.uva.nl

This talk will be focusing on tuberculosis, and reasons for, dimension of, clinical and therapeutic aspects of, and ways out of the problem of mounting multi- and extensively drug-resistent tuberculosis (M/XDR-TB), exemplified by the South African experience, one of the hotbeds of DR-TB.
The current tuberculosis pandemic evolves alongside, and benefits from, the HIV co-pandemic, and whilst recent progress has been made in improving global surveillance, and in decreasing incidence and prevalence rates globally, prevalence and mortality reduction as laid down in the Millenium Development Goals will most likely not be achieved by 2015. One of the major problems arising over the past couple of years is drug resistance.
The first part of the talk will highlight the global dimension and possible causes of the problem.
The second part of the talk will explain how strategies to diagnose and to treat drug-resistant tuberculosis only emerged over the past couple of years, and this will be demonstrated with the example of Sizwe Hospital in Johannesburg, South Africa, which evolved from a Hospital for Tropical Diseases to an exclusive MDR-and XDR-TB health care facility with 268 beds exclusively dedicated to this purpose.
The third part of the talk will highlight ongoing and further research into improving diagnostics and drugs to curb drug-resistant tuberculosis, not without stressing that the by-and-large underlying problem is the failure of health systems, and that without addressing this, novel interventions will be bound to fail.

# Emerging threats: pathogen – transmission – resistance

**Martin Haditsch**

TravelMedCenter Leonding, Austria
Labor Hannover MVZ GmbH, Germany
E-mail: leonding@travelmed.at or m_haditsch@syscomp.de

Traditionally – at least in the Western hemisphere – „tropical diseases“ are perceived to be infectious diseases acquired in the tropics, mostly. Thus for becoming a specialist in tropical medicine in the past it needed training to acquire knowledge and skills in diagnosing and treating these (partially rare and exotic) diseases (which by the way mainly was and still is focused on virology and parasitology).
Due to various reasons this situation seems to be changing nowadays: these comprise the growth of international / transcontinental travel (including migration, refugees and asylum seekers), social and economic factors in most of the areas of the (sub-)tropics, climate change, the dynamics of global trade (kind, speed and volume), changing behavioural patterns (raising awareness of preventive medicine measurs as compared to the traditional treatment of diseases; impact of hygiene) as well as (over-)use of anti-infective drugs (incl. growth promoting substances in veterinary medicine).
Visible proof of change are (re-)emerging vectors and/or pathogens outside traditional endemic areas, diversified modes of transmission (e.g. via blood products or organ transplants) and the detection (and if possible the treatment) of highly resistant organisms emerging in these areas. Few years ago the WHO published a new list of so-called neglected tropical diseases, amongst them non-infectious diseases like snake-bites.In addition we should not forget the enormous efforts (workload and costs) linked to surveillance, detection, registration and notification (as well as treatment, respectively).
This lecture hast he aim to give an update on specific events and epidemiological trends and their (possible) impact on medicine in tropical and non-tropical areas. By showing (and discussing) some examples this might render helpful in raising awareness for this increasingly important topic.

# Reporter gene strategies to illuminate the wall formation in *Eimeria* – News from the inside of the black box

**Sacha Hanig[1], Rolf Entzeroth[1], Michael Kurth[2]**

[1] Technische Universität Dresden, Biologie, Institut für Zoologie, Spezielle Zoologie & Parasitologie, Dresden, Deutschland
[2] Technische Universität Dresden, Biologie, molekulare Biotechnologie, Dresden, Deutschland
E-mail: Sacha.Hanig@tu-dresden.de

One of the keys to understand the biology of coccidia is their ability to survive adverse environments and conditions. Surrounded by two oocyst walls and protected by sporocysts, eimerian parasites are masters in overcoming mechanical and chemical stress. The challenge of investigating oocyst wall formation by molecular methods is the stage specificity of this process.
The *Toxoplasma gondii* DHFR-TSm2m3 pyrimethamine resistance gene was fused with the yellow fluorescent protein (YFP) encoding sequence to provide continuous pyrimethamine resistance and fluorescence in the *Eimeria* parasite from a single transcript. The permanent YFP signal of transgenic parasites allows differentiating transgenic parasites from wild type parasites throughout the entire life cycle. Within three passages under pyrimethamine treatment, a strain with 100% transformed sporulated oocysts of the parasite was isolated. This new method provides the potential to produce and monitor transgenic *Eimeria* strains without additional fluorescence activated cell sorting (FACS). The chimeric fluorescent reporter is utilized as a continuous internal control for plasmids containing stage specific promoter and genes. An *Eimeria tenella* gamogony gene specific regulatory sequence was utilized to confer macrogamont specific tandem dimer tomato (tdtomato) reporter gene expression in *Eimeria nieschulzi*.
This chimeric reporter system was applied to investigate wall formation and its involved proteins in more detail.

# Putative vectors of Central European lacertilian and chelonian unicellular blood parasites

**Andreas R. Hassl**

Institut für Spezifische Prophylaxe und Tropenmedizin, Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: andreas.hassl@meduniwien.ac.at

Within the last years some intraerythrocytic apicomplexian protozoa were detected in red blood cells of native lizards and allochthonous sliders hitherto unknown to occur in Central Europe. The hemogregarines *Karyolysus latus* parasitized Croatian *Algyroides nigropunctatus*, *Podarcis muralis*, and *P. melisellensis*; and *K. lacertae* was first found in red blood cells of Lower Austrian *Zootoca vivipara*; and free-living, allochthonous sliders (*Trachemys scripta*) are infected with the nearctic Plasmodiid blood-parasite *Haemoproteus degiustii* (syn. *H. metchnikovi*) in Carinthia. All of these apicomplexian parasites need a vector for transmission and/or a second host besides the reptilian host to complete the life-cycle.

In the absence of the European pond turtle leech, which is the specific, monophagous vector of palearctic turtle hemogregarines, *H. degiustii* either causes parasitemiae for decades in the hitherto non-reproducing slider populations, or it uses *Chrysops relictus* or another Crysops horse fly as native vector, in an analogous way to its transmission by *Chrysops callidus* in North America.

Although most Palearctic Karyolysus species complete their life-cycles in Ophionyssus mites in the laboratory, the effectiveness of the postulated life-cycle in the wild is dubious. Transmission of a blood parasite by the bite of an infectious tick appears to be much more efficient than the postulated ingestion of engorged mite nymphs; and ticks stuck to lizards are much more abundant in nature than molesting mite nymphs. Thus, one can hypothesize an association of *Karyolysus latus* with the Mediterranean rodent tick, *Haemaphysalis concinna*, as more than 90 % of the lizards infected with Karyolysus were found to be infested with Ixodid ticks.

# Giardia in dogs and cats in Austria- zoonotic risk and comparison of tests

**Barbara Hinney, Eva Haas, Manuel Kammermair, Anja Joachim**

Institut für Parasitologie, Department für Pathobiologie, Veterinärmedizinische Universität Wien,
Veterinärplatz 1, 1210 Vienna, Austria
E-mail: barbara.hinney@vetmeduni.ac.at

*Giardia duodenalis* is a protozoan parasite of which some genotypes are zoonotic. To get an insight into the abundance of zoonotic genotypes in Austria 74 dogs and 60 cats that were diagnosed positive for *Giardia* by flotation were tested by PCR and sequencing of the SSUrRNA. Only 12 samples (11 dog and one cat sample) were suitable for sequencing. All dogs were infected with the dog-specific assemblages C and D. The cat's isolate remained unclear. We concluded that the conserved SSUrRNA-Sequence is not suitable to differentiate at the sub-assemblage level. Further studies will be performed using multilocus PCR. In addition we also compared flotation, *Giardia* AG-testing and the PCR method. There was no correlation between these methods. The most sensitive method was the *Giardia* AG-test (85%) while only 47.8% of samples showed to be positive by PCR. Of all positive samples only 30% of dogs showed diarrhoea as a clinical sign. As a large number of the tested animals were clinically healthy despite the presence of *Giardia* we recommend that testing and treatment is limited to those patients showing clinical signs or a potential zoonotic risk.

# Parasite-derived molecules for prevention and therapy of allergy

**Jonas A. Hohlweg[1], Angelika Wagner[1], Irma Schabussova[1], Bärbel Ruttkowski[2], Anja Joachim[2], Ursula Wiedermann[1]**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria
[2] University of Veterinary Medicine, Vienna, Austria
E-mail: jonas.hohlweg@meduniwien.ac.at

Epidemiological and experimental data clearly indicate that infections with certain parasites, such as *T. gondii*, an ubiquitous intracellular parasite affecting most mammals including humans, are associated with reduced development of allergic diseases. We have previously shown that *T. gondii* infection before and after sensitization (preventive/therapeutic model) reduced allergic immune responses in a mouse model of birch pollen allergy. In preliminary studies we detected that immunosuppressive effects are not only linked to infection with the parasite but can also be induced with inactivated *T. gondii*.
It is therefore of interest to identify the immunomodulatory molecules derived from *T. gondii*. To establish whether suppression of allergy could be mediated by soluble products of this parasite, we will test lysates from different infectious stages of *T. gondii*, i.e. oocysts and tachyzoites, for its potential to dampen allergic inflammation in a mouse model of birch pollen allergy. Furthermore, we will use fractionation, proteomic and genomic techniques to identify the immunomodulatory fraction. The obtained fractions/compounds will be further characterized in *in vitro* studies with HEK293 cell lines, transfected with TLR-2, 4, 9, and 11, as well as murine splenocytes and dendritic cells derived from wild type and also from TLR knock-out mice.
The most active immunomodulators will be analyzed in order to use them as adjuvants in conjunction with recently produced allergen chimers for prophylaxis and therapy in well-established mouse models of poly-sensitization. Furthermore, exposure to these *T. gondii* fractions/compounds during the pre- and perinatal period shall clarify whether antigen-independent programming with such parasite derived molecules of the immune system can prevent the development of allergy.

Supported by FWF (SFB F46)

# Detection of microparasites, their pathways and proliferation sites using qPCR and *in situ* hybridisation

**Astrid S. Holzer**

Institute of Parasitology, Biology Centre of the Academy of Sciences of the Czech Republic,
Branisovska 31, 370 05 Ceske Budejovice, Czech Republic
E-mail: astrid.holzer@paru.cas.cz

Due to their small size and cryptic nature the detection and identification of pre-sporogonic developmental stages of myxozoan microparasites in the tissues of their teleost hosts has been difficult. Over the last years we have developed different techniques which are based on the principal of hybridisation of specific labelled RNA probes to parasite DNA in tissue sections (*in situ* hybridisation, ISH) which allows us to localise a certain parasite species, determine its entry locus into the host and its pathways to the target organ. The combination of different detection systems and labels furthermore provides invaluable information on the location of more than one species at the same time and has shined a light on within-host interaction of different myxozoan taxa. The detection of the parasite's proliferation sites by ISH further enables us to study the multiplication of the parasites in specific organs under different conditions (temperature, stage of host development, genetic differences) using quantitative PCR (qPCR). The synopsis of quantitative data obtained from the fish with those obtained from water samples (quantification of infective stages) in combination with experimental laboratory experiments enables to determine the effects of changing environmental parameters on the proliferation rate of the parasites and thus predict emerging diseases in aquaculture. This is of particular importance as climate change impacts worldwide on myxozoan proliferation rates, and there is currently no treatment for myxozoan parasites in fish destined for human consumption.

# Diagnostik von Darmprotozoen: Molekularbiologie und Mikroskopie oder Molekularbiologie statt Mikroskopie?

**Ralf Ignatius**

Institut für Tropenmedizin und Internationale Gesundheit, Charité – Universitätsmedizin Berlin, Spandauer Damm 130 15, 14050 Berlin, Germany
E-mail: ralf.ignatius@charite.de

Die mikroskopische Analyse von Untersuchungsmaterialien, obwohl oftmals durch eine unzureichenden Sensitivität gekennzeichnet, ist nach wie vor Standardmethode in der parasitologischen Diagnostik in den meisten Teilen der Welt. In den vergangenen Jahren wurden molekulare Methoden, wie der Nachweis spezifischer Antigene mittels ELISA oder Nukleinsäuren durch PCR, mit dem Anspruch hoher Sensitivität und Spezifität entwickelt. Die Präsentation gibt einen kurzen Überblick über die Bedeutung neuartiger diagnostischer Ansätze in der medizinischen Parasitologie und diskutiert in diesem Zusammenhang sinnvolle aber auch unsinnige (zumindest aus Sicht des Vortragenden) Beispiele neuer Assays.

# Borrelia relapsing fever as a socio-economic burden

**Alexandra Ille**

Unit Ethnomedicine and International Health, Department of General Practice and Family Medicine, Center for Public Health, Währingerstraße 25, 1090 Vienna, Austria
E-mail: alexandra.ille@chello.at

Tick-borne relapsing fever occurs worldwide and is caused by several *Borrelia* subspecies. In sub-Saharan African countries it is transmitted by *Ornithodoros moubata*, a soft tick that lives in traditional African huts and feeds during the night. Chickens and other fowl are discussed as possible hosts. In the Democratic Republic of Congo the knowledge about epidemiologic data, such as distribution and transmission is poor. During a 10-weeks stay in Isiro, North-Eastern Congo, interviews were conducted with fifteen patients who were hospitalised for relapsing fever. Current infection was assured by higher IgM-levels against *Borrelia*. The aim of the study was to investigate the knowledge about *Borrelia* among the patients and the socio-cultural and socio-economic aspects of its transmission. None of the interviewees was aware of the existence of the disease and their infection due to the fact that doctors on-site declared *Malaria tropica,* that represents itself similar to *Borrelia,* as a cause for the fever and flu-like symptoms. Thus relapsing fever is not seen as a possible differential diagnosis and therefore not treated properly. More sickness absences and less income are the consequences.

# *Fascioloides magna*: Exploration of Secretome and Transcriptome

**Martin Kasny[1], Cinzia Cantascessi[2,3], Jason Mulvenna[3], Neil D. Young[2], Ammar Aziz[3], Roman Leontovyc[1], Petr Horak[1], Robin B. Gasser[2]**

[1]Department of Parasitology, Faculty of Science, Charles University in Prague, Vinicna 7, Prague 14700, Czech Republic
[2]Faculty of Veterinary Science, The University of Melbourne, Parkville, Victoria 3010, Australia
[3]Queensland Tropical Health Alliance, James Cook University, Cairns, Queensland 4878, Australia
E-mail: kasa@post.cz

The giant liver fluke, *F. magna* (close relative to *Fasciola hepatica*) is the most pathogenic fluke of temperate zone. It was introduced to Europe from North America in the second half of the 19th century and spread into several European countries, including Czech Republic. *Fascioloides magna* is primarily infecting cervids, but domestic bovids can be infected too. Although it was proved that the number of areas with fascioloidosis is still growing, the risk of pathogenic impact of *F. magna* on populations of free-living and farm animals is generally underestimated and *F. magna* is still not systematically monitored. Unfortunately the detail knowledge of biology and elementary findings of molecular biology of this parasite are also insufficient. Therefore we performed deep analyses of *F. magna* adults secretome and transcriptome.

*Acknowledgement: This study was also supported by the Czech Science Foundation (Grant No. 206/09/H026), the Czech Ministry of Education (Grant No. MSM LC06009 and MSM 0021620828) and partially supported by Competition of Charles University Research Centers (Grant UNCE No. 204017) and the Program for Development of Scientific Areas at Charles University (Grant PRVOUK No. P41).*

# Antigenic protein molecules from *Trichinella spiralis*/*T. britovi*/*T. pseudospiralis* L1 larvae excretory-secretory products and their diagnostic potential

**Martin Kasny[1], Jan Dvorak[2,3], David Opavsky[2], Lucie Skorpikova[4], Petr Horak[1], Bretislav Koudela[5,6]**

[1]Department of Parasitology, Faculty of Science, Charles University in Prague, Vinicna 7, 12844 Prague, Czech Republic.
[2]Institute of Parasitology, Biology Centre, ASCR, v.v.i., Branisovska 31, 37005 Ceske Budejovice, Czech Republic
[3]Institute of Molecular Genetics, Prague, Czech Republic Institute of Molecular Genetics of the ASCR, v.v.i., Videnska 1083,142 20 Prague 4, Czech Republic
[4]Parasitology Research Group, Department of Botany and Zoology, Faculty of Science, Masaryk University, Kotlarska 267/2, 611 37 Brno, Czech Republic
[5]Department of Virology, Veterinary Research Institute, Hudcova 70, 62132 *Brno,* Czech Republic
[6]Department of Pathological Morphology and Parasitology, Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Science Brno, Palackeho 1/3, 612 42 Brno, Czech Republic
E-mail: kasa@post.cz

Trichinellosis is a worldwide important zoonosis affecting wild/domestic animals and people. In the European Union (EU) over ca 200 million of domestic animals are examined every year for trichinellosis, although the percentage of positive cases is extremely low; in the Czech Republic the case of trichinellosis among domestic pigs has not been recorded for sixty years and human case has not been published for at least 50 years. The preventive and requisite official screening for trichinellosis in meat samples is in EU regulated by rigorous legislation adopting the "digestive method" for verification of meat safety (Regulation of European Commission No. 2075/2005). Due to the very low animal and public health risk of trichinellosis in EU and substantial economic costs of periodic testing there is increasing requirement for modification of EU legislative approach to trichinellosis control and also for development of alternative effective and cheap diagnostic tools enabling reliable surveillance of trichinellosis. Therefore we have focused on identification of potential Trichinella L1 larvae antigenic protein molecules from excretory-secretory products and their preparation in recombinant form for further serodiagnostic applications.

*Acknowledgement: Ministry of Agriculture of the Czech Republic (Grant No. QH81069) and The Ministry of Education, Youth and Sports of the Czech Republic (KONTAKT II, Grant No. LH12096).*

# Otoacoustic emission testing in West African children with sickle cell disease

**Josua Kegele, Helene Hurth, Peter Lackner, Patrick Zorowka[1], Annelies Schrott-Fischer[2], Erich Schmutzhard, Tsiri Agbenyega[2], Anthony Enimil[3], Justice Sylverken[3], Joachim Schmutzhard[2]**

Departments of Neurology, [1]Hearing, Speech and Voice Disorders and [2]Otorhinolaryngology, Medical University Innsbruck, Austria
[3]Department of Pediatrics, Komfo Ankokye Teaching Hospital, Kumasi, Ghana

Sickle cell anemia is the most common haemoglobinopathy in the world. It is mainly found among the Afro-American and sub-Saharan African population but also in Mediterranean countries. Due to a point mutation in exon 1 of the beta hemoglobin gene the viscosity and flexibility of the erythrocytes is reduced, thus, their lifetime being shortened. Chronic anemia, end-organ damage and episodes of vascular occlusion are the consequences. Whereas in adults both, neurological disorders and hearing loss, are well-described complications of sickle cell disease, little is known about these manifestations in children.
Transitory evoked otoacoustic emission testing (OAE), an easily applicable and reliable way of measuring the inner ear´s function, more precisely, the function of the outer hair cells, was used to investigate sickle cell children's hearing capacity.
In our study centre in Kumasi, Ghana, 35 children, either homocygote or compound heterocygote for the haemoglobin beta mutation causing sickle cell disease, have undergone OAE tests. They were compared to a 118 age-matched healthy controls.
The results of the otoacoustic emission measurements did not show any difference between the two study arms' outer hair cell function. Although patients younger than ten years frequently have already experienced infarctions in various organs the inner ear seems to be protected against early function loss in some way.
Further investigation are needed to exactly understand the pathophysiology of hearing loss in later age and find an appropriate way of delaying or even preventing the development of hearing loss with its social and psychological consequences in sickle cell patients.

# Pitfalls in diagnosis and treatment of cutaneous larva migrans: unusual cases from a dermatology clinic.

**Maria Kitchen[1], Manuel Wilhelm[2], Sabine Moser-Oberthaler[1], Reinhard Höpfl[1], Gudrun Ratzinger, VanAhn Nguyen[1], Matthias Schmuth[1]**

[1]Univ.Klinik für Dermatologie und Venerologie, Anichstraße. 35, 6020 Innsbruck, Austria
[2]Facharzt für Dermatologie, Urichstraße 43, 6500 Landeck, Austria
E-mail: maria.kitchen@uibk.ac.at

Cutaneous larva migrans (CLM) is a skin disease commonly seen in travelers returning from the tropics. The lesions are caused by intradermal migration of non-human filariform hookworm larvae which cannot mature in humans. While the typical serpiginous skin lesions are easily diagnosed and treated, unusual presentations can be misdiagnosed and cause prolonged morbidity. We present 3 cases of CLM which were difficult to diagnosed and/or treat.
Case 1 is a 34-year old Caucasian male who presented with itchy papular lesions on the soles of both feet and was initially treated for plantar psoriasis.
Case 2 is a 54-year old Caucasian male who suffered from extensive follicular larva migrans on the buttocks for several months and was only cured after repeated courses of albendazole and ivermectin.
Case 3 is a 29-year old Caucasian male with pruritic inflammatory papules on the trunk. Despite extensive diagnostic procedures including skin biopsies and tissue cultures the correct diagnosis was only made later in the course of illness. He then rapidly responded to anthelminthic treatment and after resolution of perifocal oedema and inflammation serpiginous tracks became obvious.
These cases highlight the importance of careful history taking in individuals presenting with atypical skin lesions. In case of exposure to CLM empiric anthelminthic treatment can be considered.

# Case report: Liver injury, fever, urticaria and eosinophilia during the acute phase of infection with *Fasciola hepatica.*

**Maria Kitchen[1], Maresa Bodenberger[1], Reinhard Höpfl[1], Ingrid Heller[2], Werner Judmaier[3], Matthias Schmuth[1].**

[1]Univ.Klinik für Dermatologie und Venerologie, Anichstraße 35, 6020 Innsbruck, Austria
[2]Sektion für Hygiene und Mikrobiologie, Medizinische Universität Innsbruck, Fritz-Pregl-Straße 3, 6020 Innsbruck, Austria
[3]Univ. Klinik für Radiologie, Anichstraße 35, 6020 Innsbruck, Austria
E-mail: maria.kitchen@uibk.ac.at

In October 2010 a 35-year old man presented with fever, malaise and generalized urticaria. There was no relevant medical history and the clinical examination revealed no other abnormalities. Laboratory results showed raised liver transaminases and a marked eosinophilia (3880cells/µl). Abdominal ultrasound and stool microscopy were normal. The patient was treated with antihistamines.
In January 2011 fever and rash had subsided, but he still felt somewhat unwell and his laboratory results were unchanged. He was admitted to our hospital and we found a positive serology for *Fasciola hepatica* (IgG ELISA). Abdominal ultrasound was still normal, but the MRI of the liver showed hypodense lesions with surrounding oedema compatible with the hepatic stage of the parasites. Parasite eggs were finally detected in the stool.
The patient was treated with 1000mg of triclabendazole and experienced several bouts of colicky abdominal pains. Thereafter he fully recovered and has felt perfectly fine ever since.
The follow-up in October 2011 still showed some eosinophilia (977/µl) and residual necrotic lesions with oedema in the liver MRI, so we repeated the anthelminthic treatment with triclabendazole in double dose (2x1000mg). By July 2012 the eosinophil count had dropped to 480/µl and the remaining MRI abnormities were considered to be scars.
Fasciola hepatica infections can occur in the cattle raising rural areas of Austria through ingestion of cercariae in contaminated water or on vegetables. Our patient has probably acquired the infection during numerous out-door activities around his Tyrolean home town in the summer of 2010.

# Reisemedizinisch relevante Impfstoffe in der Pipeline

**Herwig Kollaritsch**

Institut für Spezifische Prophylaxe und Tropenmedizin, Medizinische Universität Wien, Vienna, Austria
E-mail: herwig.kollaritsch@meduniwien.ac.at

Die forschende pharmazeutische Industrie hat in den letzten Jahren wenige Neuentwicklungen von Impfstoffen vorgelegt, die reisemedizinisch relevant sein könnten. Nunmehr sind zahlreiche Neuentwicklungen nahe der klinischen Reife.
Eine der ganz besonders dringend erwarteten Neuerungen betreffen Impfstoffe gegen Dengueviren. Nunmehr liegen die ersten Ergebnisse einer Phase IIb Feldstudie aus Thailand vor, die leider enttäuschend sind. Die Ursachen hiefür sind vermutlich vielschichtig.
Ebenfalls mehr und mehr im Blickpunkt sind Neuentwicklungen gegen WNV, das zunehmend auch in Europa Fuss fassen dürfte. Auch hier sind erste Phase II Studien veröffentlicht, die sehr vielversprechend wirken.
Ein Dauerbrenner sind Neuentwicklungen gegen Typhus. Konjugierte Vi-Antigenimpfstoffe sind schon länger entwickelt, allerdings sind erst jetzt erste klinische Daten vorliegend, die diesen Impfstoffen eine sehr gute Immunogenität bescheinigen. Ihr Einsatz hat reisemedizinisch sicher Potential.
Von nur regionaler Bedeutung für Australien ist die Entwicklung eienr Ross river Vakzine. Der hier verwendete Totimpfstoff hat in erster klinischer Anwendung hervorragende Resultate erzielt.
Impfstoffe gegen Chikungunya sind bisher sehr stiefmütterlich behandelt worden. Nunmehr gibt es einen interessanten Ansatz, der zwar erst präklinisch getestet wird, jedoch Potential besitzt: Ein auf einem Masern-Lebendvektor beruhender Impfstoff, der eine österreichisch-französische Entwicklung ist wird Anfang 2013 in einer ersten Phase I Studie evaluiert.
GSK hat schon 2011 erste Daten einer Phase III Untersuchung mit einere RST,S Vakzine gegen Malaria vorgelegt, allerdings dürfte dieser Impfstoff trotz akzeptabler Wirksamkeit im Endemiegebiet niemals Einzug in die Reisemedizin finden.
Zwei Impfstoffe, die nicht unmittelbare Reiseimpfstoffe sind, jedoch indikationsentsprechend für die Gruppe der Reisenden ebenfalls ineressant sein werden, sind neue Impfstoffe gegen Herpes zoster (nun als inaktivierte Vakzine vorgestellt) und gegen Borreliose, letzterer wird im Gegensatz zum seinerzeit eingeführten monovalenten *B. burgdorferi* s.s. Impfstoff nunmehr polyvalent sein und damit alle epidemiologisch relevanten *B. burgdorferi* species in Europa USA und Asien abdecken. Erste Phase II Daten sind in der Auswertung und vielversprechend.

# Pilzinfektionen und labordiagnostische Verfahren: Sinn und Unsinn

**Cornelia Lass-Flörl**

Sektion für Hygiene und Medizinische Mikrobiologie, Medizinische Universität Innsbruck,
Fritz-Pregl-Straße 3, 6020 Innsbruck, Austria
E-mail: cornelia.lass-floerl@i-med.ac.at

Aufgrund des vielfältigen Erscheinungsbildes und der wechselnden unspezifischen klinischen Symptome, gestaltet sich die Diagnose der invasiven Pilzinfektionen sehr schwierig. Gerade bei immunsupprimierten Patienten kann eine starke Diskrepanz zwischen einer eher milden Symptomatik bei bereits fortgeschrittener Infektion beobachtet werden. Unter den Pilzen stellen *Candida* species und *Aspergillus* species die häufigsten Erreger dar, in den letzten Jahren wurden jedoch auch zunehmend Infektionen mit Hyalohyphomykosen festgestellt. Schon Ende der 70er Jahre wird die Wichtigkeit einer frühzeitigen Diagnose und die schnelle Einleitung einer antimykotischen Therapie hingewiesen.
Zur mikrobiologischen Diagnostik von Pilzinfektionen stehen verschiedene Werkzeuge zur Verfügung. Angewandt werden kulturelle, mikroskopische, serologische und molekularbiologische Methoden. Welches Nachweisverfahren zum Einsatz kommt hängt vom Patientengut, der Immunitätslage und vom zur Verfügung stehenden Untersuchungsmaterial ab. Meist ist eine Kombination mehrerer Testverfahren nötig, um zu einer gesicherten Diagnose zu kommen.
Die Serodiagnostik von Pilzinfektionen umfasst den Nachweis von Antikörpern gegen Pilzantigene und den Nachweis von Antigenen aus dem Serum, Liquor oder ggfs. Urin. Die Zurzeit verfügbaren Antikörpersuchtests für *Candida*- als auch *Aspergillus*-Spezies können bei immunsupprimierten Patienten verzögert oder abgeschwächt reagieren, wodurch die Interpretation der Titerkinetik erschwert wird. Die Ergebnisse von Antigentests werden durch den Immunstatus weniger beeinflusst, die in der Literatur angegebenen Zahlen zur Sensitivität und Spezifität der gebräuchlichen Tests schwanken und werden vom Patientengut beeinflusst. Der Nachweis von Kapsel-Polysaccharid-Antigen bei *Cryptococcus neoformans* ist ein zuverlässiger Marker für die serologische Diagnostik der Kryptokokkose. Ebenso weisen Antikörpersuchtests für den Nachweis von außereuropäischen Mykosen zufriedenstellende Ergebnisse auf. Die Interpretation serologischer Assays sollte nur synoptisch mit der Klinik erfolgen. Molekularbiologische Methoden haben sich bislang in der Routinediagnostik für Pilz-Infektionen nicht durchsetzen können. Der genaue Stellenwert der PCR muss noch abgeklärt werden, der Einsatz ist bislang Speziallaboratorien vorbehalten.

# *In vitro* attenuated and virulent *Histomonas meleagridis* target different organs in turkeys, independent of co-cultivated bacteria

**Dieter Liebhart, Muhammad Asif Zahoor, Petra Ganas, Barbara Jaskulska, Michael Hess**

Clinic for Avian, Reptile and Fish Medicine, Department for Farm Animals and Veterinary Public Health, University of Veterinary Medicine, Veterinärplatz 1, 1210 Vienna, Austria
E-mail: dieter.liebhart@vetmeduni.ac.at

Histomonosis (syn. blackhead disease) is a severe disease of chickens and turkeys caused by the protozoan parasite *Histomonas meleagridis*. To date, no prophylactic or therapeutic treatment is available in most industrial countries; however, experimental vaccination of turkeys with a life vaccine was shown to be highly effective.
The aim of the present work was to investigate i) the degree of attenuation of continuously *in vitro* cultivated histomonads and ii) the influence on the virulence of co-cultivated bacteria that are essential for the existence of the parasite. For that, the clonal culture *H. meleagridis*/Turkey/Austria/2922-C6/04, grown with different strains of bacteria obtained from the caecum of a diseased turkey, was propagated *in vitro* for more than two years or 295 passages. In a preliminary study, turkeys of different groups were infected with short-term *in vitro* cultivated parasites (21 passages) or 95, respectively 295 passages. Histomonads passaged 21 times caused severe morbidity and mortality. In contrast to that, no clinical signs were found in turkeys that were infected with the same clonal culture passaged 95 or 295 times. Necropsy revealed severe lesions in caeca and livers of birds infected with short-term cultivated parasites. Organs of turkeys that received histomonads after 95 *in vitro* passages displayed moderate lesions and birds infected with parasites following 295 passages did not contract any lesions. Additionally, the presence of histomonads passaged 21 or 95 times could be demonstrated in caeca, livers and lungs of host birds by PCR and immunohistochemistry, contrary to avirulent parasites of passage 295 which were restricted to the caeca of the birds.
In a continuative experiment the effect of co-cultivated bacteria on the virulence of histomonads was investigated: the original bacteria of the clonal culture were replaced by the laboratory strain *E. coli* DH5α before turkeys were infected with P21 or P295. Again short-term cultivated parasites caused total fatality whereas *in vitro* attenuated histomonads did not cause clinical signs or lesions.
In the present study it could be shown that the level of attenuation of a clonal culture of *H. meleagridis* is linked to the number of *in vitro* passages and the accompanying bacterial flora has no influence on the parasite's virulence. *In vitro* cultivation of the parasite for 295 passages yielded in complete avirulence fulfilling a crucial prerequisite of a safe vaccine candidate.

# Drug and vaccine targets in parasites: making validation relevant using RNAi

**Aaron Maule, Paul McVeigh, Louise Atkinson, Johnathan Dalzell, Angela Mousley, Nikki Marks**

Queen's University Belfast, School of Biological Sciences, Medical Biology Centre, Belfast
E-mail: a.maule@qub.ac.uk

Helminth parasite control remains heavily reliant on a small portfolio of front-line anthelmintics and the utility of many of these has been undermined by drug resistance. Even with some recent additions to the anthelmintic armoury (derquantel, emodepside, monepantel), the relatively limited range of control options mean that drug resistance is inevitable. Further, the pervasive on-farm approaches to anthelmintic administration in which all animals are treated regardless of infection status has accelerated the development of drug resistance in animal parasites; the mass-drug administration programmes could expose similar problems for human medicine. In the absence of vaccine-based control there is a constant need for new chemotherapeutics to treat drug-resistant parasites and to increase therapeutic options to slow their development. The empirical approaches that discovered all of the current anthelmintics have been replaced by mechanism-based drug discovery that relies on a pipeline of validated drug targets that are amenable to drug screens. Accumulating genomic and transcriptomic datasets are providing the fodder for *in silico* target discovery efforts. However, meaningful validation of these targets is a critical need if these resources are to be exploited effectively for worm control. Flatworms have lacked a platform to facilitate robust target validation. Whilst *C. elegans* has provided a surrogate validation platform for nematode parasite drug targets, even this relies on assumed functional homology and excludes genes associated with 'parasitism'. The ability to trigger RNA interference (RNAi)-based post-transcriptional gene silencing in a variety of nematode and platyhelminth parasites has provided much hope for its exploitation for 'in-parasite' control target validation. We have developed RNAi methods for trematode (*Fasciola hepatica*), cestode (*Moniezia expansa*) and plant parasitic nematodes (*Meloidogyne incognita* and *Globodera pallida*) that facilitate gene silencing in these species. Whilst flatworms and plant parasitic nematodes appear broadly susceptible to RNAi, its application to animal parasitic nematodes has been hindered by inconsistent responses and variable susceptibilities. Further, the absence of suitable bioassays undermines phenotype detection and the utility of even the most robust RNAi platform. In spite of these issues, RNAi continues to inform gene function in some parasites and there is much hope that it can be developed as a robust target validation screening tool that will serve anthelmintic discovery needs.

# Nitric oxide-dependent regulation of ferroportin-1 controls macrophage iron homeostasis and immune function in Salmonella infection

**Manfred Nairz[1], Ulrike Schleicher[2], Andrea Schroll[1], Thomas Sonnweber[1], Igor Theurl[1], Susanne Ludwiczek[1], Heribert Talasz[3], Gerald Brandacher[4], Patrizia L. Moser[5], Martina U. Muckenthaler[6], Ferric C. Fang[7], Christian Bogdan[2], Günter Weiss[1]**

[1]Department of Internal Medicine I, Clinical Immunology and Infectious Diseases, Medical University of Innsbruck, Austria
[2]Mikrobiologisches Institut – Klinische Mikrobiologie, Immunologie und Hygiene, Universitätsklinikum Erlangen und Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany
[3]Biocenter, Division of Clinical Biochemistry, Medical University of Innsbruck, Austria
[4]Department of Plastic and Reconstructive Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA
[5]Department of Pathology, Medical University of Innsbruck, Austria
[6]Department of Pediatric Oncology, Hematology and Immunology, University of Heidelberg, Germany
[7]Departments of Laboratory Medicine and Microbiology, University of Washington, Seattle, WA, USA
E-mail: guenter.weiss@i-med.ac.at

The transcriptional expression of nitric oxide (NO) synthase-2 (NOS2) is controlled by iron, while NO affects the binding activity of iron regulatory proteins and cellular iron homeostasis. We therefore postulated that iron homeostasis and the formation of NO are closely linked during host immune responses to microbial pathogens. By examining the reciprocal interactions between NO production and iron homeostasis, we found that NO upregulated the expression of ferroportin-1 (Fpn1), the major cellular iron exporter. *Nos2*$^{-/-}$ macrophages displayed an increased iron content due to reduced Fpn1 expression and allowed for an enhanced iron acquisition by intracellular *Salmonella enterica* serovar Typhimurium. *In vivo*, *Nos2* gene disruption or inhibition of NOS2 activity led to a significant accumulation of iron in the spleen and its macrophages. Mechanistically, lack of NO formation resulted in impaired nuclear factor erythroid 2-related factor-2 (Nrf2) expression, whereas pharmacological NO donors enhanced the binding activity of Nrf2 in peritoneal macrophages, subsequently leading to increased Fpn1 transcription and cellular iron egress. Following infection of *Nos2*$^{-/-}$ macrophages or mice with *S.* Typhimurium, the iron accumulation was paralleled by a reduced cytokine (TNF-α, IL-12 and IFN-□) expression and an impaired pathogen control, all of which were restored upon administration of the iron chelator deferasirox or hyperexpression of Fpn1 or Nrf2. These data illustrate that the accumulation of iron in *Nos2*$^{-/-}$ macrophages and mice counteracts a proinflammatory and antibacterial host immune response and suggest that part of the protective effect of NO results from its ability to prevent an iron overload in macrophages.

# Neues zur Malariaprophylaxe und Etablierung eines Kurses in Reise- und Tropenmedizin (CGMM & OEGTP)

**Harald Noedl**

Institut für Spezifische Prophylaxe und Tropenmedizin, Arbeitsgruppe Experimentelle Tropenmedizin und Feldforschung, Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: harald.noedl@meduniwien.ac.at

Die sich zunehmend verändernde Epidemiologie der Malaria stellt immer wieder neue Anforderungen an die Prophylaxe und Therapie insbesondere der Malaria tropica. Nach WHO Schätzung sterben auch heute noch etwa 655.000 Menschen jedes Jahr an Malaria. Neben der fehlenden Verfügbarkeit neuer Therapien stellt die zunehmende Ausbreitung von Resistenzen selbst gegenüber der neuesten Generation von Malariatherapeutika eine große Herausforderung dar. Dieser Vortrag konzentriert sich daher auf die Grundlagen der Malariaprophylaxe in Zeiten veränderter Epidemiologie und zunehmender Ausbreitung von Resistenzen.

Erstmals seit den 1990er Jahren wird das Center for Geographic and Migration Medicine in Zusammenarbeit mit der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie im kommenden Jahr wieder einen Tropenkurs anbieten (Certificate in Tropical and Travel Medicine). Dieser Kurs richtet sich an alle Kollegen, die an einer Vertiefung oder Auffrischung ihres Wissens im Bereich Tropen- und Reisemedizin, Parasitologie und Public Health interessiert sind. Der Lehrgang wird in englischer Sprache abgehalten und besteht aus einem vierwöchigen theoretischen und praktischen Kurs, der an der Medizinischen Universität Wien abgehalten wird, sowie zwei Wochen praktischer Felderfahrung im Nordosten Äthiopiens in Zusammenarbeit mit der Universität Gondar.

# Hearing impairment in children with severe and non-severe *Plasmodium falciparum* malaria by means of otoacoustic emission testing

**Lukas Oberhammer, Veronika Muigg, Helene Hurth, Josua Kegele, Fabian Aregger, Sebastian Bunk, Raimund Helbok, Peter Lackner, Erich Schmutzhard, Patrick Zorowka[1], Annelies Schrott-Fischer[2], Arnaud Flamen[3], Tsiri Agbenyega[4], Allan Otieno[5], Peter Kremsner[6], Joachim Schmutzhard[2]**

Departments of Neurology, [1]Hearing, Speech and Voice Disorders and [2]Otorhinolaryngology, Medical University Innsbruck, Austria
[3]Medical Research Unit Albert Schweitzer Hospital, Lambaréné, Gabon
[4]Department of Pediatrics, Komfo Ankokye Teaching Hospital, Kumasi, Ghana
[5]Department of Pediatrics, District General Hospital, Kisumu, Kenya
[6]Institute for Tropical Medicine, University Tübingen, Germany
E-mail: lukas.oberhammer@student.i-med.ac.at

More than 225 million malaria cases occurred worldwide in 2009 (WHO Malaria Report). Whereas mortality rate is rather well known, little is known about morbidity so far. In murine experimental malaria impairment of hearing is caused early in the course of disease by severely impaired function of the inner ear. Hearing impairment is an essential long-term sequel as it affects a child's life in many ways, leading to disturbance in language development, disadvantages in school, possibly resulting in lack of education and social shortcomings.

Otoacoustic emission testing allows – in an objective way - to measure the inner ear function, more precisely, the outer hair cell function. It is easily applicable without any specific cooperation of the patient, therefore it can be used even in infants; thus, a possible hearing impairment can be detected at a very early stage of the disease.

In a three-centre clinical study in Lambaréné (Gabon), Kumasi (Ghana) and Kisumu (Kenya) more than 500 children aged between six months and ten years were tested. We recruited patients with severe and non-severe malaria, divided into different therapy groups with either artesunate or quinine as antimalarial drugs.

As hearing loss has been suspected to be caused by malaria treatment or even *Plasmodium falciparum* itself, multiple otoacoustic measurements before and after treatment were performed in children with severe malaria, in order to evaluate the potential influence of anti-plasmodial therapy.

Distinct results of each patient group, severe malaria and non-severe malaria, divided into quinine and artesunate recipients, including follow-up testing, are compared with a matched control group of healthy African children.

# Phylogeographic survey on *Phlebotomus* spp. in Eastern Austria

**Adelheid G. Obwaller[1], Martin Weiler[2], Torsten J. Naucke[3], Gerhard Mooseder[4], Horst Aspöck[5], Julia Walochnik[6]**

[1] Federal Ministry of Defence and Sports, Division of Science, Research and Development, Austria
[2] Austrian NBC Defence School, Austria
[3] Department of Zoology, Division of Parasitology, University of Hohenheim, Stuttgart, Germany
[4] Department of Dermatology and Tropical Medicine, Military Hospital Vienna, Austria
[5] Institute of Specific Prophylaxis and Tropical Medicine, Medical Parasitology, Medical University Vienna, Vienna, Austria,
[6] Institute of Specific Prophylaxis and Tropical Medicine, Centre for Pathophysiology, Infectiology and Immunology Medical University Vienna, Kinderspitalgasse 15, 1090 Vienna, Austria,
E-mail: julia.walochnik@meduniwien.ac.at

Sandflies (Psychodidae: Phlebotominae) are known as vectors of viral, bacterial, and parasitic pathogens such as phleboviruses, *Bartonella* spp. or *Leishmania* spp. In Europe, sandflies, are known to be endemic in the Mediterranean region however, there is growing evidence of endemic populations of sandflies also in Central Europe and these populations might further expand with a potential climate change. In Austria, the occurrence of *Phlebotomus (Transphlebotomus) mascittii* was first proven in 2010, in Carinthia.
In the present study (2012 – 2015) we will investigate the occurrence of sandflies in Eastern Austria. Moreover, we will, perform a phylogenetic analysis of all Austrian sandfly strains available and including also strains from Hungary, Germany, and the Balkans. Furthermore, all sandflies will be investigated for potential infections with *Leishmania* spp. and phleboviruses and the seroprevalence of *Leishmania* spp. within the Austrian Army will be evaluated.

# Effects of hydrolase inhibitors on proteomic profiles of *Oesophagostomum dentatum* larvae

**Martina Ondrovics[1a], Anja Joachim[1b], Robin B. Gasser[2], Makedonka Mitreva[3], Ebrahim Razzazi-Fazeli[4], Katja Silbermayr[1b]**

[1a] Recipient of a DOC-fFORTE-fellowship of the Austrian Academy of Sciences at the Institute of Parasitology, Vetmeduni Vienna, Austria
[1b] Institute of Parasitology, Vetmeduni Vienna, Austria
[2] Faculty of Veterinary Science, The University of Melbourne, Victoria, Australia
[3] Genome Institute and Department of Genetics, Washington University School of Medicine, USA
[4] VetCore Facility, Vetmeduni Vienna, Austria
E-mail: martina.ondrovics@vetmeduni.ac.at

Parasitic roundworms (nematodes) of animals and humans are of major socioeconomic importance worldwide. Widespread anthelmintic resistance has stimulated research towards designing alternative intervention and control strategies against these parasites. Central to this effort could be the discovery of new drug targets through an improved understanding of the fundamental biology of development processes including the parasite's moulting. Various enzyme inhibitors are known to perturbe the development of nematodes. Here, we investigate the effects of four different hydrolase inhibitors on the *in vitro* development of third-stage (L3s) to fourth-stage (L4s) larvae in *Oesophagostomum dentatum*. When cultivating this parasite in medium containing 12.5 μM 1,10-phenanthrolin-monohydrate, 125 μM iodoacetamide, 1.4 mM 1,2-epoxy-3-(4-nitrophenoxy)propane, or 5 mM sodium fluoride for 14 days, a dose-dependent developmental inhibition of 100%, 93.9%, 93.0%, and 90.8%, respectively, was observed. The proteomic profiles of larvae incubated in individual inhibitors were compared with untreated controls using high-resolution, two-dimensional gel electrophoresis, followed by mass spectrometric and bioinformatic analysis. In total, 22 significantly differentially expressed proteins were identified and annotated using an expressed sequence tag (EST) data for *O. dentatum*. KEGG and GO analyses revealed that most (59.1%) of the proteins identified were inferred to be associated with moulting, cuticle formation, growth and larval development. All of these 13 proteins were shown to be down regulated in the development-inhibited cultures compared with controls; in addition, 18.2% of the proteins identified were predicted to be involved in stress responses, 36.4% in locomotion and 45.5% in metabolic processes. In conclusion, our results indicate a specific inhibition of the expression of at least 13 proteins of *O. dentatum* that might be relevant for its transition from L3 to L4 *in vitro*. These findings assist in understanding the molecular biology of moulting and development in nematodes, and suggest that some of these proteins might represent new drug target candidates.

# Long-term follow-up ten years after booster immunization against tick-borne encephalitis

**Maria Paulke-Korinek[1], Michael Kundi[2], Brigitte Laaber[1], Natascha Brodtraeger[1], Claudia Seidl-Friedrich[1], Birgit Schmidle-Loss[1], Ines Zwazl[1], Herwig Kollaritsch[1]**

[1] Department of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Kinderspitalgasse 15, 1090 Vienna, Austria
[2] Institute of Environmental Health, Center for Public Health, Medical University of Vienna Kinderspitalgasse 15, 1090, Vienna, Austria
E-mail: maria.paulke-korinek@meduniwien.ac.at

**Background:** There is little information on the long-term immunogenicity of vaccines against tick-borne encephalitis (TBE). The current project was designed to evaluate long term seroimmunity in subjects up to ten years after TBE booster immunization.
**Methods:** 430 subjects with documented basic immunization against TBE (vaccinations at the intervals 0-1-12 months), a minimum of one booster dose and an interval of at least three years to the last booster dose were re-vaccinated irrespective of the antibody levels in 2002. Antibody titers were assessed starting 21 days after the booster dose, annually between two and six years post-booster as well as eight and ten years later. In year eight and ten, immunity was assessed with neutralization test and in subjects without previous exposure to flaviviral antigen also with Enzygnost®, a commercially available ELISA method. Titers of 10 according to the neutralization test were used as a surrogate parameter for protection.
**Results:** Eight and ten years after the booster dose, 178 and 183 subjects returned for antibody testing. The cumulative seroprotection rates in the population eight and ten years after the booster dose were 86.8% and 77.3%, respectively. The proportion of subjects who lost protective antibodies between year eight and ten was higher than in the preceding eight years. Furthermore, antibody titers were significantly lower in subjects aged above 50. In subjects whose antibody levels declined below protective levels of 10 according to the neutralization test, a single booster dose against TBE was highly effective and re-established protection.
**Conclusion:** In this population**, s**eroprotection against TBE waned in a disproportionately high percentage of subjects between year eight and ten. However, a booster dose is highly effective in this population even if antibody titers declined below protective levels.

# Boosterintervalle nach FSME-Impfung

**Maria Paulke-Korinek[1], Michael Kundi[2], Brigitte Laaber[1], Natascha Brodtraeger[1], Claudia Seidl-Friedrich[1], Birgit Schmidle-Loss[1], Ines Zwazl[1], Ursula Wiedermann[1], Herwig Kollaritsch[1]**

[1] Institut für Spezifische Prophylaxe und Tropenmedizin, Medizinische Universität Wien, Kinderspitalgasse 15, 1090 Vienna, Austria
[2] Institut für Umwelthygiene, Zentrum für Public Health, Medizinische Universität Wien, Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: maria.paulke-korinek@meduniwien.ac.at

**Hintergrund:** Bis heute gibt es keine publizierten Daten zum Thema Langzeitimmunogenität zehn Jahre nach Impfung gegen Frühsommermeningoencephalitis (FSME), weshalb die vorliegende Studie im Jahr 2002 gestartet wurde.
**Methoden:** Bei 430 gesunden, freiwilligen Personen mit dokumentierter Grundimmunisierung gegen FSME (Schema 0-1-12 Monate) wurde nach einer Blutabnahme unabhängig vom Ausgangs-Antikörperspiegel eine einmalige FSME-Auffrischungsimpfung appliziert. Danach wurden mittels Neutralisationstest Titerbestimmungen durchgeführt, und zwar nach drei Wochen, zwischen Jahr zwei und Jahr sechs jährlich sowie acht und zehn Jahre später. Werte größer als 10 im Neutralisationstest wurden als Surrogatparameter für einen sicheren Schutz gegen FSME angenommen.
**Ergebnisse:** Acht und zehn Jahre nach der FSME-Auffrischungsimpfung wurden 178 und 183 Personen untersucht. Die kumulativen Seroprotektionsraten im Jahr acht und zehn lagen bei 86.8% und 77.3%. Zwischen den letzten beiden Untersuchungsjahren (Jahr acht und Jahr zehn) stieg der Anteil jener Probanden deutlich an, bei denen kein sicherer Schutz gegen FSME laut NT-Ergebnissen detektiert wurde. Die Antikörperspiegel lagen bei Personen ab dem 50. Lebensjahr signifikant niedriger als bei jenen untersuchten Studienteilnehmern, die jünger als 50 Jahre alt waren. Bei jenen Personen, bei welchen zehn Jahre nach FSME-Impfung keine sicher schützenden Antikörper mehr nachweisbar waren, war eine einmalige FSME-Booster-Impfung höchst effektiv und konnte einen sicheren Schutz wiederherstellen.
**Zusammenfassung:** In der vorliegenden Untersuchung wurde gezeigt, dass zwischen Jahr acht und Jahr zehn nach FSME-Impfung bei einem überproportional hohen Anteil an Personen sicher schützende Antikörper gegen FSME laut Neutralisationstest verloren gehen. Auch bei jenen untersuchten Personen, bei welchen zehn Jahre nach FSME-Impfung keine sicher schützende Antikörperspiegel mehr nachweisbar waren, war eine einzelne Auffrischungsimpfung gegen FSME höchst effektiv.

# Toxoplasmose-Diagnostik – ärztliche Fürsorge oder Abzocke?

**Ingrid Reiter-Owona, Achim Hörauf**

Institut für Medizinische Mikrobiologie, Immunologie und Parasitologie, Universitätsklinikum Bonn,
Sigmund-Freud-Str. 25, 53105 Bonn, Germany
E-mail: reiter-owona@microbiology-bonn.de

Die Wertigkeit der Toxoplasmose-Diagnostik, insbesondere beim Schwangerschafts-Screening, wird derzeit kontrovers diskutiert. Im Sinne einer Nutzen-Schaden-Bilanz bewerteten „unabhängige“ Experten vom Medizinischen Dienst des Spitzenverbandes Bund der Krankenkassen (MDS) ein Screnning sogar als negativ (IGeL-Monitor). Dieser Einschätzung widersprechen Experten der PEG-Arbeitsgruppe „Toxoplasmose“. In Deutschland ist die Qualität der Diagnostik hoch und unterliegt einer regelmäßigen Qualitätskontrolle. Weiterhin sind die gültigen Therapie-Richtlinien offensichtlich so effizient, dass eine schwere Schädigung des Kindes nur bei nicht oder zu spät therapierten Schwangeren beobachtet wird. Ein erfolgreiches Screening setzt also voraus, dass auffällige Befundkonstellationen so schnell wie möglich auf ihre Schwangerschaftsrelevanz überprüft werden um die Therapie frühzeitig einzuleiten.
Bei Immunsupprimierten kann eine schnelle und zielgerichtete Diagnostik sogar lebensrettend sein.
Anhand von Fallbeispielen werden mögliche Fehler bei der Präanalytik, der Analytik und der Interpretation von Laborergebnissen dargestellt und diskutiert.

# New insights into cryptosporidiosis of tortoises

**Barbara Richter[1], Melissa Brinkmeier[1], Christian Schwering[2], Majda Globokar Vrhovec[3], Nora Nedorost[1], Nikola Pantchev[3]**

[1]Institut für Pathologie und Gerichtliche Veterinärmedizin, Department für Pathobiologie, Veterinärmedizinische Universität, Veterinärplatz 1, 1210 Vienna, Austria
[2]Kleintierpraxis in Fritzlar, Wehrenpfad 3, 34560 Fritzlar, Germany
[3]Idexx Vet Med Labor, Mörikestr. 28/3, 71636 Ludwigsburg, Germany
E-mail: Barbara.Richter@vetmeduni.ac.at

Although cryptosporidiosis has been well known for some time in snakes and lizards very little information is available on this parasitosis in tortoises. One recently named *Cryptosporidium* species (*Cryptosporidium ducismarci*) and one *Cryptosporidium* genotype vaguely called “tortoise genotype” seem to be the most common ones to infect this reptilian group (Testudines). Both have been associated with clinically diseased tortoises in single cases. In some of these cases the symptoms vanished after treatment with paromomycin, which is the preferred therapy of cryptosporidiosis in reptiles. However, clinical data still is scarce and there have been no pathologic studies on animals infected with the *C.* tortoise genotype. Thus, it has not been confirmed that the *C.* tortoise genotype actually can infect the chelonian gastrointestinal tract instead of just being passed in the feces as a pseudoparasite.
Recent investigations show that cryptosporidial infections in tortoises are quite common with a prevalence of 9% in tortoises submitted routinely for pathological examination. However, only in some cases an association of cryptosporidia with gastrointestinal disease seemed feasible. With in-situ hybridization and DNA sequencing it could be confirmed that the *C.* tortoise genotype can be found lining the surface of the gastric epithelium in naturally infected tortoises.

# The American Liver Fluke *Fascioloides magna* in Austria – epidemiology of an invasive parasite of cervids

**Helmut Sattmann[1], Larissa Gaub[1,2,3], Christoph Hörweg[1], Heinrich Prosl[1,4], Julia Walochnik[2]**

[1] Museum of Natural History Vienna, Burgring 7, 1010 Vienna, Austria
[2] Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Kinderspitalgasse 15, 1090 Vienna, Austria
[3] University of Vienna, Dr. Bohrgasse 3-9, 1030 Vienna, Austria
[4] Institute of Parasitology, Department for Pathobiology, University of Veterinary Medicine Vienna, Veterinärplatz 1, 1210 Vienna, Austria (retired)
E-mail: helmut.sattmann@nhm-wien.ac.at

*Fascioloides magna* is a digenean trematode parasitizing the liver of cervids and using lymnaeid snails as intermediate hosts. The species was first introduced to Europe and recorded for the first time in the 1870s in Italy and spread over the decades into several European countries. In 2000 it was first recorded in Austria in the wild, namely in the Danube flood plains east of Vienna. *Galba truncatula* was proofed to serve as intermediate host. Approximately 15,000 specimens of *G. truncatula* in total have been investigated for the occurrence of the parasite at several years and localities. In 2004/2005 the parasite´s occurrence in snails was still restricted to one place at the southern Danube banks at Fischamend, whereas in 2008 records of infected snails came also from the northern backwaters at Orth. The prevalence in the first period was less than 0.03 %, while in the second period 0.23 % of *G. truncatula* were found to be infected. Infection rates of red deer (*Cervus elaphus*), which were revealed by parallel studies, showed similar deviations but infection rates in deer were 100 to 200 fold higher than in snails. Deviations of prevalence may be explained by environmental factors like differing floods and variable annual course of temperature, but also by the fact that at one location the deer populations had been medicated.

Until now, no intrusion into other deer populations in Austria has been recorded. Since a game bridge is under construction, which should facilitate migration/genetic exchange and connect red deer from Danube floodplains with adjacent populations, a risk assessment concerning the parasite exchange, should be conducted. As a first step, a survey of aquatic snails of the river Leitha and neighbouring waters were carried out. A number of species – including *G. truncatula* – were recorded and investigated parasitologically. No fasciolids were found, but some interesting other digeneans appeared, like *Trichobilharzia* sp. in *Lymnaea stagnalis*, *Bilharziella polonica* in *Planorbarius corneus*, echinostomids in *Planorbis planorbis* and some others. Nevertheless, the occurrence of stable populations of *G. truncatula* in several locations of the Leitha surroundings enables *F. magna* also to establish its life cycle in this and neighbouring areas.

# *Oesophagostomum dentatum* extracts modulate responses to vaccines and prevent the development of allergy in mice

**Irma Schabussova[1], Onisa Ul-Haq[1], Elisabeth Hoflehner[1], Johnnie Akgün[1], Angelika Wagner[1], Gerhard Loupal[2], Anja Joachim[3], Bärbel Ruttkowski[3], Rick M. Maizels[4], Ursula Wiedermann[1]**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University, Vienna, Austria
[2]Department of Pathobiology, Institute of Pathology and Forensic Veterinary Medicine, University of Veterinary Medicine Vienna, Austria
[3]Institute of Parasitology, University of Veterinary Medicine, Vienna, Austria
[4]Institute of Immunology and Infection Research, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, UK
E-mail: irma.schabussova@meduniwien.ac.at

One third of the human population is currently infected by one or more species of parasitic helminths. While remaining a global health problem, the fact that specific helminth infections have beneficial effects on inflammatory diseases, allergy or autoimmunity, opens the door to novel exciting therapeutic applications of certain live worms or their products for the control of immunopathological conditions. However, the overall down regulation of the immune system might cause impaired responsiveness to vaccines.
In this study, we show that extracts, derived from adult male *Oesophagostomum denatatum* (eMOD) induced Th2 and regulatory responses in BALB/c mice and suppressed responses to the thymus-dependent but not to thymus-independent model antigen. In a mouse model of birch pollen allergy, co-administration of eMOD with sensitizing allergen reduced markedly the production of allergen-specific antibodies in serum as well as IgE-dependent basophil degranulation. Furthermore, eMOD prevented the development of airway inflammation, as demonstrated by attenuation of bronchoalveolar lavages (BAL) eosinophil influx, peribronchial inflammatory infiltrate, and mucus secretion in lungs and IL-4 and IL-5 levels in lung cell cultures. Reduced secretion of Th2-related cytokines by birch pollen-re-stimulated splenocytes and mesenteric lymph node cells was observed in eMOD-treated mice in comparison to sensitized controls. The suppressive effects of eMOD were heat-stable.
Altogether, understanding of the mechanisms of immunomodulation by helminth parasites could be useful on one hand to antagonize immune suppression and thus improve vaccine efficacy, and on the other hand to utilize/modulate immune suppression induced by parasites/products/synthetic analogues to control immunopathology in humans.

# Amoebae as vehicles for bacteria – a pilot study: development of a screening system for free-living amoebae (FLA)

**Ute Scheikl[1*], Allen Tsao[2], Matthias Horn[2], Alexander Indra[3], Julia Walochnik[1]**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Kinderspitalgasse 15, A-1090 Vienna
[2]Department of Microbial Ecology, Faculty Center of Ecology, University of Vienna, Althanstraße 14, A-1090 Vienna
[3]Department of Mycobacteriology and Clinical Molecular Biology, AGES, Währinger Straße 25a, A-1096 Vienna
E-mail: ute.scheikl@meduniwien.ac.at

Free-living amoebae (FLA) are well known as potential human pathogens, but they may also serve as vehicles of dispersal and replicative niches for bacterial pathogens in natural and man-made habitats. In particular, *Legionella pneumophila*, the causative agent of Legionnaires´ disease, replicates in FLA. In addition, the amoebal cysts protect intracellular pathogens against disinfection measures. This can lead to colonization of air conditioning systems, cooling water devices and warm water preparation units, from where the bacteria spread via aerosols. This is why, as part of an interdisciplinary project on the role of FLA as vehicles for bacteria in water systems, we aim to develop real-time PCR assays suitable for routine screening of water facilities and air-conditioning units in Austria. First step is the evaluation of the suitability of own and literature-based established probes and primers, specific for all amoebae relevant as hosts, like *Acanthamoeba*, *Balamuthia*, *Hartmannella*, *Sappinia* and Vahlkampfiidae, respectively *Naegleria.*

# *Entamoeba histolytica* and metronidazole: 46 years of successful chemotherapy – but how does it work?

**Sarah Schlosser, Julia Matt, Volker Baumann, Margit Tazreiter, David Leitsch, Michael Duchêne**

Institut für Spezifische Prophylaxe und Tropenmedizin, Arbeitsgruppe Molekulare Mikrobiologie,
Kinderspitalgasse 15, 1090 Vienna, Austria
E-mail: michael.duchene@meduniwien.ac.at

Metronidazole (Mtz) has been used against *E. histolytica* for 46 years, but many questions remain about its interaction with the parasite. We studied the response of *E. histolytica* to Mtz by two-dimensional gel electrophoresis, microarray hybridization and biochemical methods. No large changes in mRNA or protein expression were observed, but activated Mtz formed covalent adducts with thioredoxin, thioredoxin reductase, superoxide dismutase, and purine nucleoside phosphorylase. Our results challenge the view that Mtz indiscriminately damages proteins. *E. histolytica* thioredoxin reductase itself reduced Mtz, and mainly proteins known to interact with the thioredoxin system were covalently modified. We therefore searched for more thioredoxin interaction partners. As a bait, we used thioredoxin mutated at its active site (C34S), which can bind to its target but no longer release it. We were able to isolate and identify 16 candidates such as serine acetyltransferase-1, purine nucleoside phosphorylase, or aminoacyl-histidine dipeptidase. Oxidatively inactivated recombinant serine acetyltransferase-1 was indeed reduced and its activity restored by wild-type thioredoxin.
Mtz-treated amoebae show several signs of apoptosis, such as DNA degradation. We searched *E. histolytica* extracts for DNase activities and the genome for DNase genes to find out what could cause the observed DNA degradation. The classical apoptotic DNases, caspase-dependent DNase or endonuclease G were absent from the genome, but we identified four mRNAs encoding a member of the endonuclease/exonuclease/phosphatase family, a protein with a 5´-3´ exonuclease domain, a DNA repair endonuclease, and a LINE (long interspersed element) endonuclease as upregulated. Another putative nuclease, TatD1, was not upregulated on the mRNA level, but had recently been shown to be involved in apoptosis in *Trypanosoma brucei*. The recombinant TatD1 showed DNase activity and like the upregulated gene products could be suspected of carrying out the DNA destruction in Mtz-treated amoebae.

Supported by Grant P22037 from the Austrian Science Fund.

# Adjunctive therapy since severe malaria and acute bacterial meningitis

**Erich Schmutzhard**

Department of Neurology, Medical University Innsbruck, Austria
E-mail: erich.schmutzhard@i-med.ac.at

Earliest possible initiation of antiplasmodial or antibacterial chemotherapy is essential both in multiorgan malaria/cerebral malaria and acute bacterial meningitis. In spite of that, mortality and longterm morbidity rates for these two diseases are still high, mortality rates ranging from 5 to 20%, long term sequelae been even higher, in particular, if detailed follow up examination for neurological, neuropsychological, cognitive, developmental or hearing impairment are performed.

This plenary lecture will address the issue of adjunctive therapies in these two infectious diseases of the brain, accepting the fact that invasive, intensive care management is frequently limited in resource poor countries. These adjunctive measures are highly different in settings where intensive care management is possible compared to those areas in which ventilation, volume support, volume resuscitation, catecholamines, ICP monitoring and management, renal replacement therapies etc. are not available. In most tropical settings (i. e., frequently in resource poor countries) such invasive measures are not available.

In spite of that, recently a number of publications have addressed exactly such adjunctive therapeutic measures in cerebral malaria/multiorgan malaria as well as in acute bacterial meningitis. These range from the application of corticosteroids, osmotherapeutics (mannitol or glycerol, respectively), immunomodulation/fever management to management of epileptic seizures, status epilepticus, etc.

In a nutshell, both widely recommended strategies to alleviate increased intracranial pressure, potentially available even in resource poor countries, have been proven to be of limited efficacy, namely, administration of i. v. Dexamethasone and early administration of osmotherapeutics (Glycerol or Mannitol, respectively). In particular, the latter needs in depth discussion, since the form of application and not the application per se might be the decisive issue. What has been shown, both in cerebral malaria and acute bacterial meningitis, is that in resource poor settings continuous application (over 4 days) of osmotherapy is deleterious in these two diseases. What has never been shown is whether bolus administration of an osmotherapeutic, in case of clinical or otherwise proven ICP increase, might alleviate this potentially deleterious ICP increase.

It has been shown that continuous administration of antimicrobial agents together with Paracetamol alleviates both increased body temperature and reduces mortality. Therefore a simple measure as control of increased body temperature (socalled controlled normothermia) might be feasible and helpful in cerebral malaria and acute bacterial meningitis in resource poor countries. In contrast, more “aggressive” therapeutic hypothermia (33-34°C body temperature) has not improved short term mortality in a small prospective pilot trial in patients with acute bacterial meningitis.

# Hearing impairment in murine cerebral malaria: A histomorphologic examination of the inner ear.

**Joachim Schmutzhard[1], Christian Hermann Kositz[2], Peter Lackner[2], Rudolf Glueckert[1], Herbert Riechelmann[1], Erich Schmutzhard[2], Annelies Schrott-Fischer[1]**

[1]Department of Otorhinolaryngology, Innsbruck Medical University, Anichstraße 35, 6020 Innsbruck, Austria
[2]Department of Neurology, Innsbruck Medical University, Anichstraße 35, 6020 Innsbruck, Austria

Several clinical studies have shown a wide variety of neurocognitive impairment in children after surviving severe malaria. Hearing impairment may crucially be related to the reported impairment of language development, thus, possibly being a fundamental cause of this neurocognitive sequela.
This prospective animal study aims to evaluate - in a functional and histopathological approach - the alterations of the vestibulocochlear system throughout the course of severe murine malaria.
The established murine malaria animal model with C57BL/6J mice was used. The hearing threshold has been measured before infection and at the peak of the disease with auditory evoked brainstem responses (ABR).
Immediately after sacrification the cochleae were harvested for further histological processing. The temporal bones were evaluated with light-microscopy and immunohistochemical staining for ICAM 1, cleaved caspase 3 – apoptotic marker - and Connexin 26 – a gap junction protein responsible for the electrolyte circulation in the inner ear.
The ABR measurement showed a significant hearing impairment in the malaria group, whereas the control group didn't show an affection of hearing.
The light microscopic evaluation showed a regular temporal bone structure. In contrast to the brain neither adherence of parasitized red blood cells and inflammatory cells to the micro vascular endothelial cells, nor parenchymal microhaemorrhages and oedema could be found in the inner ear.
The ICAM 1 labeling showed a very strong reaction in the stria vascularis. The staining for cleaved caspase 3, however, did show a positive apoptotic reaction in the fibrocytes of the spiral ligament and the limbus. The Connexin 26 staining did mark positive in the expected structures of the fibrocytes.
Severe malaria leads to hearing impairment in a murine malaria model. The expected affection of the vascular system, which is typical for severe malaria could not be found in the inner ear. The induction of the apoptosis in the spiral ligament and the limbus suggests an impairment of the electrolyte homeostasis in the inner ear as possible pathomechanism. This hypothesis is strongly supported by the Connexin 26 labeling, which labeled positive in the majority of the apoptotic fibrocytes.

# Regulation of Tim-3 and Tim-4 during Plasmodium berghei ANKA (PbA)-induced experimental cerebral malaria (ECM) in susceptible (C57BL/6) and resistant (BALB/c) mice

**Andrea Schroll*[1], Peter Lackner*[2], Carina Weichselbraun[1], Erich Schmutzhard[1], Günter Weiss[2]**

[1]Department of Internal Medicine I, Clinical Immunology and Infectious Disease, Medical University Innsbruck, Austria
[2]Department of Neurology, Medical University Innsbruck, Austria
*these authors contributed equally to this work
E-mail: andrea.schroll@i-med.ac.at

**Background**: The balance between pro-inflammatory and regulatory cytokines in determining optimal T cell and macrophage activation is vital for the successful resolution of microbial infections. In this study, we determined the contribution of T-cell immunoglobulin domain (Tim)-3 and Tim-4 to the regulation of T cell and macrophage responses during Plasmodium berghei ANKA (PbA)-induced experimental cerebral malaria (ECM) in susceptible (C57BL/6) and resistant (BALB/c) mice. Tims are expressed on activated T-lymphocytes and macrophages and can promote cellular phagocytosis and apotosis thereby regulating immune function.
**Methods**: Eight week old BALB/c mice and C57BL/ 6J mice were intraperitoneally infected with $1 \times 10^6$ PbA-parasitised red blood cells (pRBC) from a homologous donor. Infected mice were monitored for neurological symptoms by the Innsbruck cerebral malaria score (ICMS). Parasitaemia was determined by examination of Wright-stained thin blood smears. Spleens, livers and brains were removed for mRNA expression of Tim-3, Tim-4 and different T cell and macrophage cytokines.
**Results**: While basal expression of Tim-3 in the spleen was significantly lower in Balb/c mice compared to C57BL/6 mice the basal Tim-4 mRNA expression of Tim-4 was comparable in uninfected mice. Infection with PbA leads to a more than 16 fold increase of Tim-3 expression in Balb/c whereas Tim-3 was only 2-fold higher in C57BL/6 mice as compared to baseline. Interestingly, while Tim-3 regulation in the liver was comparable in Balb/c and C57BL/6 mice, Tim-4 is significantly down-regulated in infected livers of Balb/c mice and only slightly reduced in C57BL/6 strain. The basal expression of pro-inflammatory cytokines such as IFNg, TNF and IL-6 are significantly higher in C57/BL6 strain, however, their respective induction in PbA infections is exorbitantly higher in Balb/c mice than in C57BL/6 mice. Regulation of the anti-inflammatory cytokine IL10 is comparable in both strains.
**Conclusion**: In summary, our results underscore the differential and complex regulation that governs immune responses to malaria parasites. Further investigation will be necessary to clarify the different regulation of Tim proteins during Plasmodium PbA-induced experimental cerebral malaria (ECM) in susceptible (C57BL/6) and resistant (BALB/c) mice and their role in immune control and course of malarial infection.

# *Isospora suis* – immunisation of sows

**Lukas Schwarz, Anja Joachim, Hanna Lucia Worliczek**

Institute of Parasitology, Department of Pathobiology, University of Veterinary Medicine Vienna,
Veterinärplatz 1, 1210 Vienna, Austria
E-mail: lukas.schwarz@vetmeduni.ac.at

Colostral transfer of maternal antibodies is essential for survival of newborn piglets. These antibodies play an important role for the first defense against pathogens. *Isospora suis* as the pathogenic agent of neonatal porcine coccidiosis causes economic losses in pig production worldwide. Sows have significant amounts of *I. suis*-specific antibodies in their milk which are transmitted to their piglets, especially in the first days of life. In this study a possible role of colostral antibodies in the passive immunisation of neonatal piglets against *I. suis* was evaluated, since in a pilot study a correlation of higher serum IgA titres in piglets and a more solid faecal consistency could be observed.

To obtain information about the protective potential of oral immunisation of sows with infectious *I. suis* oocysts, two sows were infected 14d ante partum (a.p.) with 5 x 20,000 oocysts; two sows remained non-infected. For evaluation of antibody titres (IgG, IgA, IgM) blood and milk samples from the sows were taken 14 and 1 days a.p. and subsequently in weekly intervals till 21 days postpartum.

All piglets were infected on the $4^{th}$ day of life with 1000 oocysts. Faecal samples from piglets were collected daily from the $8^{th}$ till the $22^{nd}$ day of life to investigate faecal consistency and OpG. On the $2^{nd}$ day of life the half of a litter was cross-fostered to the according other litter to compensate litter effects.

Piglets nursed by infected sows showed a longer prepatency and a significantly better faecal consistency. Various significant correlations between higher antibody titres and a milder course of disease were found, especially for IgA titres in the milk. Furthermore, infected sows had significant higher titres than non-infected ones.

In summary, a positive effect of maternal immunisation on the performance of piglets during neonatal porcine isosporosis could be shown. This benefit for the offspring highlights the potential of oral immunisation of sow against *I. suis* as a possible vaccination strategy for new born piglets against this important pathogen.

# *Anaplasma phagocytophilum* - a wide-spread tick-borne zoonotic pathogen

**Cornelia Silaghi**

Vergleichende Tropenmedizin und Parasitologie, Veterinärmedizinische Fakultät, Leopoldstr. 5, 80802 Munich, Germany
E-mail: cornelia.silaghi@tropa.vetmed.uni-muenchen.de

*Anaplasma phagocytophilum* is an obligate intracellular bacterium transmitted by ticks. It is wide-spread across the Northern hemisphere and the main vector in Europe is *I. ricinus*, but *A. phagocytophilum* has also been detected in other tick species. *A. phagocytophilum* has been reported in questing ticks from at least 28 European countries with average prevalence ranging from 0.5% to 25%. A vertebrate reservoir host is necessary for completion of the endemic cycle in nature. Roe deer is suggested to be one of the main reservoir hosts, but *A. phagocytophilum* has also been detected in several other mammalian species, such as other cervid species, or hedgehogs.

*A. phagocytophilum* causes granulocytic anaplasmosis in humans (HGA), but also in dogs, horses, occasionally cats and it also causes tick-borne fever in ruminants. In the USA, HGA is the second most important tick-borne disease after Lyme borreliosis with about 5,000 cases reported by 2008. In Europe, on the contrary, only about 70 clinical cases have been documented so far. The hypothesis was raised that this may be due to *A. phagocytophilum* strains of differing levels of pathogenicity.

In recent years, we collected >18.000 ticks (mainly *I. ricinus* and also *D. reticulatus*) in parks, renatured and natural forest areas in Germany, and more than 8,000 ticks were screened for *A. phagocytophilum*. The results obtained are on the one hand confirming that public parks are focal points for *A. phagocytophilum* in Germany, but on the other hand we observed a decrease in prevalence from 2009 to 2010 in Bavarian city parks which was statistically significant. Investigations in ticks collected during the following years showed a further decrease in prevalence in 2011 and a rise again in 2012. Reasons for this are thus far unknown, but raise the hypothesis that year-to-year variation may play a more significant role than habitat structure, because similar variation were also observed in forest areas. Several scenarios are thinkable for causing this, such as changes in numbers of competent or incompetent host, or a change in e.g. climate which may influence the abundance of hosts, the questing activity of ticks or the host-tick contact rates.

A comparative analysis of the partial *16S rRNA* gene of *A. phagocytophilum* from the host-seeking *I. ricinus* revealed a variety of variants, but in nearly three quarters of *A. phagocytophilum*-positive ticks, the variant "A" was found. This variant may potentially be less pathogenic than variant "B" which was present in only ~3% of *A. phagocytophilum*-positive questing ticks. Considering an average infection rate with *A. phagocytophilum* of ~4% in questing *I. ricinus* ticks in Germany, just a little more than 1 in 1000 *I. ricinus* harbour the human pathogenic prototype variant "B". Investigations on the genetic variability of *A. phagocytophilum* derived from different host species and involving other partial genes also revealed different variants and phylogenetic analysis of the derived sequences showed a tendency of clustering of sequences of certain host species groups together. However, whether this genetic variability reflects actual variants of varying pathogenicity remains to be investigated in an experimental setting.

# Detecting *Dirofilaria* spp. in Austrian mosquitoes

**Katja Silbermayr[1], Alessandra Christina Gill[2], Bernhard Seidel[3], Peter Hufnagl[4], Alexander Indra[4], Anja Joachim[1], Georg Duscher[1]**

[1]Institute of Parasitology, University of Veterinary Medicine, Veterinärplatz 1, 1210 Vienna, Austria
[2]University of Liverpool, Leahurst, Neston CH64 7TE, UK
[3]Technical Consultancy for Ecological Research, 3680 Persenbeug, Austria
[4]Agency for Health and Food Safety, Institute for Medical Microbiology and Hygiene, Währingerstrasse 25a, 1090 Vienna, Austria

Recently there has been an increase in infections with the filarial parasite *Dirofilaria repens* in Austrian dogs. With increasing cases of canine dirofilariosis we started a nationwide mosquito surveillance program in 2011, with the aim of detecting microfilariae directly in its vector, the female mosquito.
From July to October a total of 36 locations across all nine Austrian provinces were sampled using BG-Sentinel mosquito traps equipped with $CO_2$ and a chemical BG-lure attractant. A total of 4177 mosquitoes were collected and assigned to 149 separate pools according to the mosquito species, the trapping location and date. The samples were subjected to automated DNA extraction and stored at -80°C for further analysis.
The most abundant species in the tested sample set was *Culex pipiens* (87.7 %) followed by *Aedes vexans* (5.2 %) and *Culex modestus* (3.7 %). The presence of filarial DNA was examined by quantitative real time PCR (qPCR) using fluorescence labeled probes. A 93 bp long fragment of the 12S mitochondrial gene was amplified for the detection of filarial infections using a universal filarial qPCR TaqMan assay. The limit of detection (LOD) was estimated to be 11 fg of parasite DNA using serial dilutions. Accordingly dilutions ≤ 3 fg did not result in an amplification of the target gene. Out of the 149 analyzed pools, five resulted in a positive amplification curve. Four of the positive pools were classified as belonging to the *Culex pipiens* group and one as *Aedes flavescens.* Four of the positive pools were located in eastern and southeastern parts of the country, the other was from Tyrol. Positive samples will be subjected to conventional PCR of the COI gene to obtain sequence data for subsequent identification of filarial species.
Based on our present findings we are continuing the national mosquito monitoring and surveillance program. This study provides the first set of comprehensive data of mosquito-borne filariae in vectors across Austria.

# Intravenous azithromycin combination therapy for the treatment of severe falciparum malaria - a pilot safety and efficacy trial in uncomplicated falciparum malaria in Bangladesh

**Paul Swoboda[1], Moritz Treiber[1], Milena Mueller[1], Hans Peter Fuehrer[1], Wasif Ali Khan[2], Imong Prue Chowdhury[2], Julia Hedwig Riedl[1], Harald Noedl[1]**

[1]Institut für Spezifische Prophylaxe und Tropenmedizin, Zentrum für Pathophysiologie, Infektiologie und Immunologie, Arbeitsgruppe Experimentelle Tropenmedizin und Feldforschung, Kinderspitalgasse 15, 1090 Vienna, Austria
[2]ICDDR,B (International Centre for Diarrhoeal Disease Research, Bangladesh), Dhaka, Bangladesh
E-mail: harald.noedl@meduniwien.ac.at

In our recent studies, the combination of oral azithromycin and artesunate has proven to be a promising and safe alternative for the treatment of uncomplicated falciparum malaria, particularly for sensitive populations such as pregnant women and small children. However, this combination can only be expected to exert its full effect when used intravenously for the treatment of severe malaria. As long as bacterial coinfections and misdiagnosis remain common causes of death in severemalaria-like illnesses, an antibiotic with broad antimicrobial spectrum and antimalarial activity could offer numerous advantages over traditional antimalarials by covering a wide range of pathogens commonly associated with bacterial coinfections in severe malaria as well as many of the pathogens causing illnesses frequently misdiagnosed as severe malaria. We are currentlyconducting a randomized, controlled open label pilot trial in uncomplicated falciparum malaria patients to assess the safety and efficacy of intravenous azithromycin-artesunate combination therapy as a potential alternative treatment for severe malaria. Sixty-four subjects were randomized to 1 of 2 cohorts at a ratio of 2:1, receiving either 5 doses of intravenous azithromycin-artesunate (10 mg/kg azithromycin plus 2.4 mg/kg artesunate) within 4 days or intravenous artesunate (5 doses at 2.4 mg/kg over 4 days) followed by oral artesunate until completing a full 7-day course. Primary clinical outcomes are safety and tolerability. Secondary outcome is cure (ACPR) on days 28 and 42. The follow-up of patients is still ongoing, but a preliminary analysis suggests that the intravenous combination is well-tolerated and efficacious, combining the rapid parasite reduction of artesunate with the advantages of a broad spectrum antibiotic with antimalarial activity. Enrollment has been completed and among these 64 included subjects all patients had cleared parasitemia by day 3 and so far only one reemergence of parasitemia during the follow-up has been observed. Follow-up is expected to be completed in October 2012.

# The mysteries of immunity to malaria

**Geoffrey Targett**

Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
E-mail: geoff.targett@lshtm.ac.uk

Progress has been made in control of malaria but the burden of disease remains huge and substantial further progress aimed at elimination and eventual eradication will almost certainly require one or more vaccines of high efficacy. A better understanding of how immunity is acquired naturally will help in development of candidate vaccines but there are many aspects of the immunity that are poorly understood, even a mystery as to how and why they develop. Thus there is now evidence of immune responses in the skin following inoculation of parasites by mosquitoes that may affect immunity to later infection. It is unclear whether a good immunity to the pre-erythrocytic stages will be best achieved with sub-unit or whole organism vaccines. The very limited success in developing vaccines to the clinically important blood stages is due to the parasites ability to subvert or evade host immunity. The key to eliminating malaria is now recognised as stopping transmission but naturally acquired immunity to the sexual (transmission) stages seems to promote transmission as much as stop it.
Immunity is not sterile and there are many asymptomatic carriers who can still transmit infection to mosquitoes. What is the nature of a natural immunity that allows these low grade infections to persist and keep the malaria life cycle going. Developing vaccines may be as much about avoiding some immune responses that occur naturally as inducing protective immune responses.

# Efficacy of curcumin on *Trichomonas vaginalis* strains with varying metronidazole susceptibilities

**Benjamin Wachter[1], Michael Syrowatka[1], Andreas Obwaller[2], Julia Walochnik[1]**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Austria
[2]Orphanidis Pharma Research GmbH, Wilhelminenstrasse 91/IIf, 1150 Vienna, Austria
E-mail: n0709876@students.meduniwien.ac.at

Trichomonosis, the disease caused by *Trichomonas vaginalis*, is the most common curable STD with 174 million cases per year worldwide. The emerging resistance against the current standard therapy with metronidazole is pushing the search for alternative drugs. The purpose of this work was to determine the efficacy of curcumin, a derivate of *Curcuma longa*, on *T. vaginalis* strains (ATCC 30001, ATCC 30236 and ATCC 50138) with different metronidazole susceptibilities. In microtiter assays the effective concentrations (ECs) were evaluated with dilution series of curcumin and standard doses of metronidazole, miltefosine and pentamycin. All cells were killed at concentrations of 800 µg/ml curcumin within 6h or 400 µg/ml within 24h. The $EC_{50}$s ranged from 181.68 µg/ml in the metronidazole sensitive strain (ATCC 30001) to 307.08 µg/ml in the normal metronidazole susceptible strain (ATCC 30236).

# NMDA-receptor mediated excitotoxicity is involved in the pathogenesis of experimental cerebral malaria

**Karina Maria Wechselberger[1], Taferner B[1], Ronny Beer[1], Gregor Broessner[1], Raimund Helbok[1], Anelia Dietmann[1], Marlene Fischer[1], Nicolas Singewald[2], Erich Schmutzhard[1], Peter Lackner[1]**

[1]Department of Neurology, Innsbruck Medical University, Innsbruck, Austria
[2]Department of Pharmacology and Toxicology, Center for Molecular Biosciences Innsbruck and Institute of Pharmacy, University of Innsbruck, Innsbruck, Austria
E-mail: karina-maria.wechselberger@student.i-med.ac.at

A major cause of morbidity and mortality of *Plasmodium falciparum* malaria is cerebral malaria (CM). Mortality is high and neurological sequelae are observed in approximately 20 % of the survivors. A deeper understanding of the underlying neuropathological substrates is missing yet. In addition to ischemia and inflammation, excitotoxicity might be an important factor. The current study investigates the role of NMDA receptor mediated excitotoxic cell death during CM and its potential for the development of adjunctive treatment strategies.
C57BL/6J mice were infected intraperitoneally with 1 million *Plasmodium berghei* ANKA parasitized red blood cells of a homologous donor. Cerebral Microdialysis was performed and glutamate levels were measured. Animals showing clinical signs of cerebral malaria were randomized for treatment with artesunate, MK801 (a non-competitive antagonist on the NMDA receptor), artesunate and MK801 or vehicle over 5 days. Survival and clinical outcome was scored. Brains were further processed for histochemistry.
Glutamate levels were significantly elevated in mice with CM compared to control animals. Glutamate peaks were noted before and after clinical signs of CM developed. Subsequently NMDA antagonisation was investigated. Twenty eight animals were randomized. No animals survived in the MK801 or vehicle treated group. In contrast, 33.3% the animals in the artesunate group and 74.1% in the MK801 / artesunate combination treatment group survived. Kaplan Meier survival curves yielded a significantly longer survival of the animals in the combination treatment group compared to the vehicle or MK801 treatment group. In addition MK801 treated animals showed significantly prolonged survival compared to vehicle treated animals, although cumulative survival was 0% in these two groups. Histological analyses yielded a lower number of microhemorrhages and Fluoro-Jade B positive cells in the artesunate/MK801 treated animals compared to artesunate treated mice.
In conclusion, glutamate levels in the brain are increased early in the course of CM. Treatment with MK801, a non-competitive antagonist of the NMDA receptor, rescues mice from CM. NMDA-receptor mediated excitotoxicity plays a role in the pathogenesis of CM and could represent a target for adjunctive treatment strategies.

# Impfungen für das Gesundheitspersonal

**Ursula Wiedermann**

[1]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University, Vienna, Austria
E-mail: ursula.wiedermann@meduniwien.ac.at

# Ist ein Blutstropfen wirklich genug? – Stellenwert der in vitro Diagnostik bei Allergien

**Stefan Wöhrl**

Floridsdorfer Allergiezentrum, Franz-Jonas-Platz 8/6, 1210 Vienna, Austria, http://www.faz.at
E-mail: woehrl@faz.at

Seit Ende der 60-er Jahre des 20. Jhdts. zwei Forschergruppen, das japanische Forscherehepaar Ishizaka zeitgleich mit dem Schweden Gunnar Johannson IgE als das pathophysiologische Prinzip hinter der Soforttypallergie (Typ 1 Allergie nach Coombs & Gell) erkannten, hat sich die *in vitro* Diagnostik mittels Bestimmung von Allergen-spezifischem IgE zur Diagnose allergischer Erkrankungen etabliert. Immer wieder gab es von Seiten der Anbieter der IgE Tests sowie von einigen Forschungsgruppen Versuche, die Diagnose allergischer Erkrankungen auf die *in vitro* Diagnostik zu reduzieren. In letzter Zeit wurde die in vitro Diagnostik mit gentechnisch hergestellten, standardisierbaren Proteinen sehr stark favorisiert. Hat aber jeder positive IgE Wert aber wirklich eine Bedeutung? Warum vertrauen klinische tätige Allergologen weltweit immer noch auf ihre Hauttests mit Pricktestsubstanzen, bei deren Herstellung Naturprodukte als Ausgangsstoff dienen, bei denen moderne Anforderungen an Reproduzierbarkeit nicht anwendbar sein können. Ist das nur Tradition? Diese Zustände können für Nicht-Spezialisten verwirrend erscheinen. Wie immer gibt es keine einfachen Antworten. Die Dilemmas werden aufgrund eines Fallberichts, der auf moderner Allergenchip Diagnostik basiert, aufgearbeitet werden.

# Toxocariasis and DRESS Syndrome in an Oncological Patient: A Case Report

**Nora Wutte[1], Michael Palfner[2], Herbert Auer[3], Gerald Ruckenbauer[4], Thomas Valentin[2], Katharina Seeber[5], Robert Krause[2], Martin Hönigl[2]**

[1] Univ. Klinik für Dermatologie und [2] Univ. Klinik für Innere Medizin, Klin. Abteilung für Pulmonologie und [4] Institut für Hygiene, Mikrobiologie und Umweltmedizin der Medizinischen Universität Graz, Austria
[3] Medizinische Parasitologie der Medizinischen Universität Wien, Vienna, Austria
[5] AGES Medizinmarktaufsicht, Zulassung & Lifecycle Management, Austria
E-mail: michael.palfner@medunigraz.at

A 45 year old male was admitted to the dermatology department with fever and a generalised, multiforme-like exanthema with pustulation on the upper arms. He had received antibiotic treatment (Amoxicillin / Clavulanic Acid) from his treating family physician one week ago due to fever, lymphadenopathy and exanthema. Laboratory tests showed a white blood cell count of 11.02 $10^3/\mu l$, with 62% eosinophils and elevated liver enzymes. The level of C-reactive protein was at 32.6 mg/l (normal limit <8). No focus of infection was found in urinalysis, chest X-ray, blood cultures, CT scan and normal LDH-levels ruled out progression of the known malignant disease. Due to rising liver enzymes, eosinophilia, fever and systemic symptoms, the patient was diagnosed with DRESS syndrome to aminopenicilline, and responded well to systemic steroid therapy.
Serology for Toxocara and Ascaris came back positive a few days later. Stool was again sent for microscopy and found positive for Giardia lamblia which was treated with a 5-day course of metronidazole. Control of serology showed a markedly increase of Toxocara TES ELISA Ig G (70U, normal limit <20U) confirming toxocariasis, while Ascaris IgG decreased indicating cross-reaction. The patient had developed pruritus and eosinophils were found to be 7.9 $10^3/\mu l$ (normal limit <0.7). Anamnesis revealed contact to wild living cats, travel history was unremarkable. Total IgE was 1689 U/l (normal limit <100). Antiparasitic therapy with albendazole 400mg bid for 5 days was initiated, eosinophilia resolved and the patient had no further complaints.
Although makulopapulous or multiforme-like exanthema has not yet been described in literature, Toxocariasis is known to cause a wide spectrum of cutaneous manifestations. Whether our patient had toxocariasis mimicking a drug reaction, or whether both DRESS Syndrome and toxocariasis occured in the same patient remains open for discussion.

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**von**

**21. – 23. November 2013**
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