Malaria and helminth coinfection: new insights for malaria control

Malaria and helminth infections often coincide geographically in tropical regions. The implications of concomitant malaria and helminth infections have been mainly explored in animal models indicating that their interaction can alter the course of malaria infection and disease. In recent years it has become clear that chronic helminth infections alter the immune system both at the innate and the adaptive level affecting responses to third party antigens. Few studies in human populations have so far shown contradictory results; helminth coinfections seem to either exacerbate or curtail severity of malarial disease. It is important to gain in-depth knowledge of the interaction between these parasites in humans in the context of controlling malarial parasites and clinical disease.

Read more ......

Project expired September 2009
About the project

Malaria and helminth infections often coincide geographically in tropical regions. The implications of concomitant malaria and helminth infections have been mainly explored in animal models indicating that their interaction can alter the course of malaria infection and disease. In recent years it has become clear that chronic helminth infections alter the immune system both at the innate and the adaptive level affecting responses to third party antigens. Few studies in human populations have so far shown contradictory results; helminth coinfections seem to either exacerbate or curtail severity of malarial disease. It is important to gain in-depth knowledge of the interaction between these parasites in humans in the context of controlling malarial parasites and clinical disease. Much effort is going into developing vaccines; these have to be delivered to populations living in areas endemic for helminths. If there are strong interactions, then vaccine efficacy will be affected. It is important to plan ahead and aim to build up strong teams in endemic regions that are able to do research in the area of coinfection both diagnostically and immunologically. Although there are experts in endemic areas, they are often segregated into "malaria team" or "helminth team" with often little interaction. The present proposal aims to bring together a group of Dutch, German, Indonesian and Malaysian experts in the area of malaria and helminth parasitology/diagnosis, epidemiology and immunology, to train a number of medical doctors, nurses and scientists by organising workshops and laboratory based courses. With the view to the future this will stimulate Regional as well as International Cooperation, will disseminate knowledge and will allow new grant applications to be prepared that will answer the question of whether and how helminths affect the course of malaria infection and disease with important implications for future malaria control programs.

Objectives

Overall Objectives
The overall aim of the project is to deliver the information and tools necessary for researchers in Asian countries to produce robust data on malaria and helminth coinfection and their immunological interaction. This will set the stage for future international cooperation to understand the influence of helminth infections on the course of malarial infection and disease.

Specific Objectives
The Specific Support Actions program will be used to transfer knowledge and technology between European, Malaysian and Indonesian experts in the area of malarial and helminth coinfection, in order to prepare a team with the ability to carry out high quality research in this important area. This will be achieved by:

- **Distance based learning and workshops in European and Asian centers:**
  1. To train medical staff in clinical assessment and scoring of malarial disease including good clinical practice and ethical issues.
  2. To train in setting up of specific epidemiological studies (data base organisation, power calculations, logistics)
  3. To develop questionnaires in a locally specific and culturally sensitive manner which will estimate malarial disease

- **Laboratory based teaching in European and Asian centers:**
  4. Training in malarial diagnosis quality control and the advanced diagnosis of Plasmodium spp by means of quantitative PCR
  5. Training in helminth diagnosis quality control and the advanced diagnosis of filarial, hookworm, Ascaris and Trichiuris infections by quantitative PCR and when appropriate by immunological methods
  6. Standardized procedure for collection of blood by finger prick, whole blood stimulation assays and preservation of blood for RNA extraction
7. Demonstration of immunological methods that measure antibodies and cytokines
8. Demonstration of molecular biological methods that measure gene expression by quantitative PCR and determine genetic polymorphisms

Pilot Study:
9. The trained personnel will carry out pilot studies to determine the prevalence of malarial and helminth coinfections and the immunological interaction between these two infections

Why these objectives?
In many parts of the tropical world both malaria and helminth infections are prevalent and therefore coinfections can be common. Chronic helminth infections have strong modulatory activities and carry specific molecules that are immunologically active in terms of stimulating Th2 responses as well as driving strong regulatory networks characterized by production of high levels of suppressory cytokine IL-10 by monocytes. These responses have been shown to affect the development of inflammatory diseases such as inflammatory bowel disease, allergies or autoimmunities. Moreover, immune responses to regular vaccines have been shown to be affected. However, these effects are not uniform; in a small subset of infected individuals, helminths seem to fail to induce strong hyporesponsiveness and this group shows high levels of circulating TNF and often develops immunopathology. It is there not surprising that there are conflicting data in human studies on how helminth infections interact with malarial parasites. In some studies, intestinal helminths have been shown to be associated with increased risk of developing severe malaria, while in others, a protective effect has been reported. As currently, a large number of anti-malarial vaccines are getting ready for clinical trials, it is going to be essential to determine the effect of coinfections. It is important to have robust data not only on whether helminths affect the course of malarial infections and disease but also to discriminate the type of helminth infection. Intestinal helminths have a restricted anatomical niche, whereas infections such as schistosomes or filarial worms are systemically localised and might exert profound effects on the immune system. Thus the diagnostic methods that detect malarial and helminth infections with high sensitivity would be an essential part of the project. Another aspect that needs attention is the standardised protocols for clinical scoring of malarial disease. Part of the conflicting results obtained on interaction between helminths and malaria may result from different scoring systems used. A good coordination between clinicians, health workers and diagnostic laboratory staff is needed to allow high quality data to be generated. Finally, many of the centers in endemic regions work as isolated entities. For example, at the Department of Parasitology in Jakarta, experts on malaria are based within a unit that run studies on malaria epidemiology/immunology in isolation while another set of experts working on helminth infections study the epidemiology, diagnosis and immunology of intestinal and filarial helminth infections. The collaboration between the two groups will allow the teams in Jakarta to carry out studies of coinfection rather than each infection in total isolation.

The data on interaction between helminths and malaria can be used for:

1. policymaking regarding national helminth treatment programs: for example if helminth infections mask immunological mechanisms that confer resistance to malarial parasites, then anti helminth treatment would have to be implemented with particular attention to the vulnerable group. On the other hand if the regulatory network induced by presence of helminths protects against severe malaria, then, national control programs will have to adjust their drug delivery policy taking into account those at most risk
2. for the same reasons outlined above, when testing vaccines, it might be important to treat all patients involved in trials with anti helminths to determine vaccine efficacy more accurately
3. the studies can shed light on the specific mechanisms involved that curtails immunity or prevents severe malaria with the view to future novel therapeutics
Agenda

Meetings

The first COINFECT meeting has been held in Leiden, The Netherlands at October 11th 2006.

Workshops

From 8-11 January 2008 a workshop has been held in Jakarta, with the title "new insight malaria control"
Programme of the workshop
Tools and protocols

Supali T, Djuardi Y, Wibowo H, van Ree R, Yazdanbakhsh M, Sartono E.

Regulatory T cells in human geohelminth infection suppress immune responses to BCG and Plasmodium falciparum.

Does treatment of intestinal helminth infections influence malaria? Background and methodology of a longitudinal study of clinical, parasitological and immunological parameters in Nangapanda, Flores, Indonesia (ImmunoSPIN Study).
Other funded programs

- Global view of food allergy (funded by the EU)
- T cell regulation and the control of helminth infections (funded by the EU)
- Parasitic infections and inflammatory diseases: the web of immune responses, host, genetics and environmental exposure (funded by the Royal Netherlands Academy of Arts and Sciences)

Relevant publications

Publications: helminths protect against malaria


Publications: helminths have negative effect on malaria


Publications: mechanisms underlying malaria and helminth coinfection


Websites project partners

Leiden University Medical Center

Eberhard Karls University of Tuebingen

University of Indonesia

University of Sans Malaysia