

# Parasites in Pregnancy

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## Preface

Pregnancy presents unique challenges to mammalian physiology and in particular to the immune system. In response, these systems accommodate the pregnancy by undergoing extensive adaptations; it is therefore of little surprise that the relationship between a parasite and host can be fundamentally altered when infection occurs during pregnancy. Understanding the nature of this interaction is important to improve both the treatment and management of parasitic infection during pregnancy. It was with this in mind that the concept of a special Symposium on the subject of *Parasites in Pregnancy* was developed for the XIth International Congress on Parasitology held in Glasgow in 2006. This Special Issue of *Parasitology* is drawn from the excellent papers presented at this Symposium. Special thanks are due to the British Society for Parasitology, the ICOPA XI organising committee and Cambridge University Press, without which the Symposium and production of this volume would not have been possible.

This volume begins with a broad overview of the subject of *Parasites in Pregnancy*. The paper of Petersen highlights how both protozoan and helminth infections share the common feature of complex and varied interactions with the mammalian immune system by discussing briefly malaria, *Toxoplasma gondii* and *Trypanosoma cruzi* and the helminth infections *Onchocerca volvulus*, *Wuchereria bancrofti* and schistosomiasis.

Malaria in children, particularly in sub-Saharan Africa, has dominated the literature but pregnant women also have an increased risk of malaria infection, which can cause complications for both the mother and the child. Malaria infection is thought to cause 400 000 cases of severe maternal anaemia per year and contributes significantly to maternal deaths (thought to be 10 000 per year), in addition to the impact on low birth weight of the infant and its associated mortality. In this volume, several groups describe how molecular approaches have identified

mechanisms underpinning the pathology seen in pregnancy associated malaria (PAM) and thus highlighted potential therapeutic leads. In the papers from the Scherf and Hviid groups we are introduced to the concept of specific variant surface antigens (VAR2CSA) expressed on the surface of the *P. falciparum*-infected erythrocyte in isolates taken from pregnant women. Nunes and Scherf examine possible modes of switching to explain the presence of these variants, predominantly in pregnant women, suggesting that the environment generated during pregnancy (such as hormone levels) might directly induce the expression of this category of *var* gene through its action on promoter sequences. Hviid and Salanti review our knowledge of the gender-specific immune response seen for PAM isolates, showing that this response correlates with clinical protection, and describe how knowledge of the acquired immune response could contribute towards the development of a vaccine.

As well as providing a specific immune target in PAM, VAR2CSA also acts as a ligand for chondroitin sulphate A (CSA) which was shown by Duffy and colleagues to be responsible for adhesion in the placenta during malaria infection and its role in PAM is described in his review along with how clinicopathological presentations might modify the disease outcome in both the mother and the child. Finally in their review, Rogerson and Boeuf dissect the evidence that has contributed to our knowledge of PAM biology and suggest a range of parameters that should be recorded as part of clinicopathology studies as well as suggesting mechanisms that could contribute to inflammation in the placenta during PAM and the tools required to understand the host response during infection.

There is currently considerable excitement within the malaria research community that a VAR2CSA-based vaccine could provide protection against the PAM component of disease and much of the research cited in these reviews supports this optimism. As

more research has been carried out the complexity of the biology surrounding PAM has increased and a number of critical questions have remained unanswered as well as new ones arising, but the overall tenet that VAR2CSA could provide broadly reactive immunity has largely been retained and efforts to design effective vaccine candidates are well-advanced.

The final two papers in this volume focus on two further apicomplexan parasites, which although they share some of the same biology of *Plasmodium*, appear to be unique in their contrasting interactions in pregnancy. *Toxoplasma gondii* has long been recognised as an important cause of abortion and foetal abnormality in women if it is contracted for the first time during pregnancy. In the paper by Pfaff *et al.*, the paramount role of the cellular immune response during *Toxoplasma* infection is outlined and its implications discussed for the outcome of pregnancy. Specifically, the cytokine IFN- $\gamma$  appears to have a dual role in this process; while its beneficial effects in the control of toxoplasmosis are well known, it also seems to have transmission-enhancing effects that may directly harm the developing foetus.

Parasites are not just important during human pregnancy, but also have the potential to interfere with the course of pregnancy in other mammals. Toxoplasmosis, for example, is an important cause of abortion in domestic animals such as sheep, where it has a significant economic impact on the farming industry. Similarly, the closely related parasite *Neospora caninum* causes abortion in cattle, although

there are subtle but important differences between the two parasites both in terms of transmission and their specific interactions during pregnancy. In the final paper of this volume, Innes discusses how pregnancy poses a problem for the immune system of cattle infected with *Neospora*. As the dam is essentially carrying a semi-allogeneic tissue graft (the foetus) without immunological rejection taking place, the pregnancy is facilitated by the cytokine environment in the placenta favouring regulatory Th-2-type cytokines, whose role is to counteract the pro-inflammatory Th1-type immune responses. Protective immunity to *N. caninum*, similar to many other intracellular parasites, involves Th1-type immune responses, which appears to pose a problem for the dam trying to control a *Neospora* infection during pregnancy.

This special issue brings together some of the varied research in the field and serves to highlight the fact that above all, the interaction of parasites during pregnancy cannot be summarised in a generalised model. On the contrary, each parasite-host system displays complex interactions resulting from their unique evolutionary journeys with their respective hosts. It is hoped that this volume will serve not just to review the area, but to stimulate research into what is a fascinating, but perhaps somewhat overlooked area of host-parasite biology.

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