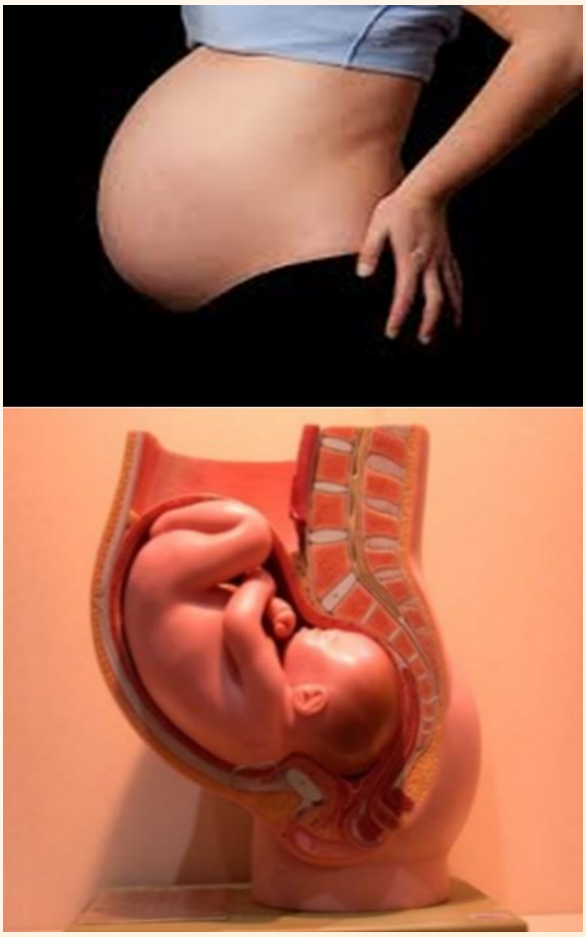
Director's Report

One of the most rewarding parts of working as an immunologist is being free to function as part of a non-organ-based team. This was first highlighted by the opportunities afforded by the pulmonary artery hypertension (PAH) multidisciplinary clinic, where interaction occurs with colleagues in respiratory, cardiology and rheumatology disciplines. Added to this monthly clinic, I also attend a monthly session with colleagues in maternal-foetal medicine, where we share the challenges of patients with immunological aberrations impacting on pregnancy or conception. The set of conditions we are involved in managing is ever-expanding, especially with the growing adoption of assisted fertility approaches: conditions prompting referral to the clinic include management of autoimmune conditions during pregnancy, improving outcomes when there have been recurrent miscarriages or pregnancy complications (clots, eclampsia), and even exploring possible immune contributions to conceptual difficulties.

The clinic began in November 2011, and has been held monthly ever since, with between 4 and 8 patients seen in any given clinic. Prof. Henry Murray provides obstetric expertise based upon his extensive experience in the management of complicated pregnancies, and together we aim to offer a patient-centred assessment where concerns are openly discussed and addressed and an individualised action plan is compiled for each patient. Many of the consults involve planning in individuals who are not yet pregnant, but are being managed for immune conditions such as lupus or rheumatoid arthritis: the goal is to establish an optimal approach to the process of conception and pregnancy monitoring that provides the best chance for happy outcomes for mother and child. Not infrequently, discussion moves on to consider the risks of transmission of autoimmunity to the offspring: in answer to this concern, reassurance is offered, with conditions such as lupus and scleroderma representing a large contribution from "random" factors. Whilst these unpredictable (and poorly understood) factors operate upon a set of (heritable) "susceptibility" genes, the absolute risk for development of autoimmunity in offspring is extremely low (< 1%), especially in the ab



sence of specific antibodies (such as SS-A (Ro) and SS-B (La)).

The famous immunologist Peter Medawar posed a pertinent question that fires our interest in pregnancy immunology: "How does the pregnant mother contrive to nourish within itself, for many weeks or months, a foetus that is an antigenically foreign body?" Or rather – "why didn't your mother reject you?" To explain the selective protection offered to the developing foetus, guarding him/her from immune attack and "rejection", early theories proved somewhat simplistic, proposing that pregnancy conferred a state of relative immunosuppression" much like that experienced in organ transplantation patients undergoing anti-rejection therapies. We have since established that most aspects of immune function during pregnancy are indeed well-preserved: immune cell function and antibody production are generally unimpaired, and infection risk is only elevated for a few specific agents (e.g. influenza, varicella).

It appears that the direction of immune responsiveness changes with each phase of pregnancy, with a predilection for "inflammatory" tendencies to dominate each end of the process (conception/ fertilisation and delivery) in contrast to the middle trimester, where a "less inflammatory" immune response guides the growing foetus through this critical phase. Even this is too simple, however and lessons we've learned about the preservation of the foetus by immune modulation can be applied to other fields, including autoimmunity, cancer and transplantation medicine. The key we wish to unlock in each of these areas is the way the body develops "tolerance", an immunological term for a selective and active immune decision to refrain from targeting certain structures for immune attack or inflammation. It is tolerance that stops most of us from developing autoimmunity, and it is tolerance failure that predisposes to the development of autoimmune conditions such as thyroiditis, MS, lupus, diabetes and over a hundred other conditions in the autoimmune spectrum. Thus, we can expect growing insights into the management of all these conditions as we learn more about the mechanisms operating to induce tolerance during normal pregnancy.

Whilst there is a slightly increased risk of problems during pregnancy in mothers and their offspring for conditions such as lupus (e.g. higher rates of premature delivery and small-for-age babies), this should not be seen as inevitable or immutable. Most will have healthy and uneventful pregnancies, with the best outcomes resulting when conception occurs after prolonged remission or clinical quiescence (at least 6 months). At times women with underlying autoimmune disease require ongoing disease modifying or immunosuppressive therapy during pregnancy to treat persistently active disease or flare-ups: potentially harmful (teratogenic) medications should ideally be discontinued several months before conception, but a range of therapies have demonstrated utility in pregnancy, including hydroxychloroquine (plaquenil), azathioprine (Imuran), and prednisone. For pre-eclampsia and certain clotting tendencies, low-dose aspirin can be useful, and in some circumstances (e.g. recurrent miscarriage, maternal clotting events) this can be augmented by injectable blood-thinners (heparin, etc). Flares of autoimmunity can be safely managed with "bursts" of prednisone at the lowest doses possible (whilst optimising maternal vitamin D and monitoring BP, glucose and weight and also monitoring foetal growth).

The routine perception that autoimmunity was not compatible with motherhood has thankfully been put to rest by such treatment approaches as these; with adequate planning and specialist input, ideally involving multidisciplinary team support, happy outcomes can be expected in the majority of instances. This again highlights the importance of finding ways to live with the autoimmune condition, and pursuing creative and proactive steps to ensure that life is lived as fully and completely as possible.

Best Wishes

Glenn

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