

Repeated miscarriages may be explained by deficient T cells

Abi Berger, *science correspondent, BMJ*

Women who experience unexplained recurrent abortions may have a different immune profile from women who have full term pregnancies.

Sergio Romagnani and his colleagues at the University of Florence have discovered that there is a significant difference in cytokine production between women who seem to miscarry recurrently without reason and women who do not (*Nature Medicine* 1998;4:1020-4). If these observations are confirmed, it may be possible to find a way to intervene therapeutically in future pregnancies.

In general, when an immune response is mounted against an infectious organism or foreign tissue the response is rapid removal or rejection by T helper 1 (Th1) cells. In mouse models it has been shown that during pregnancy the immune response at the placental level usually switches to the less aggressive T helper 2 (Th2) response. This switch is designed to prevent the "foreign" fetus from being rejected, but at the same time may allow infections to take hold.

In order to see what happens in humans, the Italian researchers grew clones of T cells taken from the placental decidua of women

who had had recurrent miscarriages and compared them with T cell clones taken from women who had chosen to undergo termination of pregnancy. They found that the T cell clones from the two groups produced different amounts of some cytokines.

For example, the clones from the women who had miscarried produced much smaller quantities of leukaemia inhibitory factor (LIF), interleukin 4 (Il 4), and interleukin 10 (Il 10) compared with the T cell clones taken from the women who chose to abort their pregnancies. These three cytokines are all associated with a Th2 immune response, and the difference suggests that miscarriage may become more likely in some women because for some reason they fail to switch to a Th2 immune response during pregnancy.

The hormone progesterone is critical for healthy implantation of the fetus, and progesterone has been shown to favour production of the Th2 type cytokines, resulting in the production of higher amounts of Il 4 and LIF in peripheral blood (*Journal of Immunology* 1995;155:128-33). In the second part of its research Romagnani's team also showed that LIF



Cardiac rehabilitation programmes in the United Kingdom concentrate on low risk, white, male patients who have had a heart attack, according to a report from the NHS Centre for Reviews and Dissemination at the University of York (*Effective Health Care Bulletin* 1998;4(4)). The report says that services should meet the needs of all groups, including women, elderly people, members of ethnic minorities, and patients with all types of heart disease. The full text can be found on the internet (www.york.ac.uk/inst/crd).

production by T cells is increased in the presence of progesterone. Professor Romagnani therefore suggests that there is an interaction between progesterone and these Th2 cytokines at the placenta which must be responsible for successful fetal implantation.

So far these observations have been in vitro only, and the researchers have sampled a very small number of women (four in the miscarriage group and six in the control group). However,

these 10 women produced a total of 668 T cell clones. If these differences are confirmed in vivo and a specific time can be identified when the switch from Th1 to Th2 is critical then, according to Professor Romagnani, "it might be possible to identify those women who could benefit from the administration of drugs that stimulate the local production of LIF and other Th2 cytokines to prevent further miscarriages." □

New, more virulent strain of HIV found

Scott Gottlieb, *New York*

French scientists have identified a new strain of HIV that is highly replicative and may escape the detection of current screening tests. The new strain could potentially trigger a new pandemic of HIV infection.

The new strain was isolated by Dr François Simon of the Bichat Hospital in Paris from a 40 year old woman living in Cameroon, Africa, who had been diagnosed as having AIDS. The new isolate does not belong to either of the two existing

HIV-1 subgroups – M (major) and O (outlier). Instead, Dr Simon and colleagues have classified the virus as an N strain (*Nature Medicine* 1998;9:1032-6).

Dr Simon and colleagues had originally set out to do an epidemiological survey in Cameroon, a country in west central Africa whose citizens are known to be afflicted by a remarkable diversity of retroviruses. All the subtypes of HIV-1 group M (A to H) circulate in Cameroonian patients, and the HIV-1 group O has been reported almost exclusively in native Cameroonians.

For their study, the scientists differentiated the isolates they found serologically by using site specific peptides corresponding to known regions on strains of HIV-1 subgroups M and O and a

strain of simian immunodeficiency virus (SIV). But they found, to their surprise, that one strain of the virus was negative with group M and group O peptides, reacting solely with the SIV peptide.

The team isolated and characterised the aberrant strain, which they designated YBF30. They found that, phylogenetically, the new strain was most closely related to SIV, but, on detailed genetic analysis, the new strain was as distinct from both of the two SIV strains known to date as it was from HIV-1 groups M and O and could be considered as the prototype strain of a new HIV group.

To determine if other viruses related to YBF30 were circulating in Cameroon, the scientists then generated peptides corresponding to the YBF30 virus and used them to screen serum samples

taken over the past decade from 700 Cameroonians infected with HIV. Of these samples, three (0.4%) reacted strongly with peptides specific for the new strain. Two of these samples were poorly documented and could not be traced to their source. The third was collected from a Cameroonian patient with AIDS, who was subsequently found to be infected with the YBF30 strain.

In an accompanying editorial, Dr Simon Wain-Hobson of the Pasteur Institute in Paris, suggested that the new strain could cross international boundaries, with potential to cause a new pandemic: "Will N-group HIV-1 turn up outside of Africa? Undoubtedly. Once again, the tremendous genetic flexibility of retroviruses and RNA viruses in general is brought to the fore." □