

## **Discussion**

Spontaneous abortion (resorption) in mice is thought to represent a rejection of the semi-allogeneic fetoplacental unit by activated NK cells and activated macrophages<sup>(13, 16)</sup>. These cells infiltrate maternal mesometrial decidua at the site of implantation and the frequency of implantation sites with such an infiltrate is proportional to the percentage of embryos that resorb.<sup>13</sup> Murine resorptions are characterized by focal necrosis at the junction of the fetal trophoblasts and the decidua, an infiltrate with polymorphonuclear leukocytes at sites of necrosis and along the walls of large vessels in the decidua, and by thrombosis and hemorrhage<sup>(17, 18)</sup>.

There are two main sources of this polymorphonuclear cell (PMN) infiltration; firstly, when thrombin is generated, it will activate IL-8 secretion by endothelial cells, and as a consequence IL-8 recruits PMNs<sup>(19,20)</sup>. Secondly, pro-inflammatory cytokines like IFN- $\gamma$  and TNF- $\alpha$  induce endothelial adhesion molecules and increase the transendothelial migration of the recruited leukocytes<sup>(2,7,21)</sup>.

All these studies support the present, which showed increase in the expression of endothelial ICAM-1 and ICAM-3 on tissue infiltrating leukocytes, making these CAMs good indicators and participating in the pathology of pregnancy loss. Furthermore, recent studies showed that enhanced decidual IL-8 expression interacts with constitutively expressed ICAM-1 in decidual endothelium to modulate neutrophil trafficking into hemorrhagic and inflammatory first trimester deciduas<sup>(20)</sup>. In addition, other studies showed increase in ICAM-1 surface expression on endothelial cells of preeclamptic women in comparison with pregnant normotensive and non-pregnant women<sup>(22)</sup>. Therefore, midgestation measurements of circulating ICAM-1 and VCAM-1 (above the cutoff) have a high

predictive value and may identify up to 55% of pregnant women who will later develop a severe pregnancy-related complication<sup>(23)</sup>.

Mast cell- and macrophage-derived cytokines engage with their receptors on endothelial cells. This will ultimately lead to activation of nuclear transcription factors that modulate the biosynthesis of endothelial CAMs that mediate leukocyte rolling (E-selectin) and adherence (ICAM-1, VCAM-1)<sup>(2)</sup>. Which is in line with our previous study on the same groups of women showing significant increase in the transcriptional factor (NF- $\kappa$ B) and the pro-inflammatory cytokine (IFN- $\gamma$ ) in the recurrent loss group as compared with other two groups<sup>(24)</sup>, and significantly higher surface expression of endothelial VCAM-1 in the same group also (unpublished data).

This study also showed that ICAM-1 and ICAM-3 expressed on the trophoblasts in some cases indicating that these CAMs might really have a role in the adherence, implantation and vascular invasion as mentioned in other studies<sup>(14, 25)</sup>.

## **References**

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