

peri-conceptional folic acid, have yet not shown significant associated reductions in stillbirth rates [2].

In this issue of *Indian Pediatrics*, a study from a teaching hospital in North India evaluated the clinical, behavioral and health-care associated risk factors of intrapartum perinatal mortality (IPPM) [3]. They reported that a large proportion of women deliver at home or reach health facilities late during labor. In addition, limited round-the-clock coverage, lack of trained health care personnel and non-adherence to standard management protocols contributed to increased IPPM. Low socioeconomic status, absence of hemoglobin and urine examination during pregnancy, obstructed labor, and a delay in seeking health care were significant risk factors for intrapartum-related perinatal mortality among emergency obstetric referrals [3]. The mode of delivery did not affect the IPPM; previously, timely delivery, often by caesarean section or instrumental vaginal delivery, has been shown to reduce associated intrapartum stillbirth, and has been credited for the relatively low intrapartum stillbirth rates in high-income countries. A recent meta-analysis, outlined the clear advantage of strategies like comprehensive emergency obstetric care packages, including caesarean section in breech delivery, and induction of labor (vs expectant treatment) in post-term pregnancy. Other advanced interventions such as amnioinfusion and hyperoxygenation need further evidence before their use can be advocated as a policy [5]. A number of studies have shown that suboptimal care, particularly inadequate, inappropriate, or delayed care of complications such as obvious fetal distress, placental abruption, breech presentation, twin pregnancy, or eclampsia, is associated

with increased perinatal mortality [6].

While most of the success stories on reduction in perinatal mortality are in relation to developed countries and mostly in term babies, a lot needs to be desired in resource-poor countries where further research is still needed to decrease the alarmingly high rates of perinatal mortality and to define more appropriate interventions.

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## T-cells and Cardiac Complications in Infectious Mononucleosis

DEBBIE VAN BAARLE

*Department of Internal Medicine and Infectious Diseases, and Department of Immunology, University Medical Center Utrecht, Lundlaan 6, 3584EA Utrecht, Netherlands. d.vanbaarle@umcutrecht.nl*

**I**nfectious mononucleosis (IM) is characterized by symptoms which are thought to be caused by -either directly or indirectly-the expansion of CD3+CD8+ T-cells after acute Epstein-Barr virus-infection resulting in a decreased CD4/CD8 ratio. Over 50% of the T-lymphocytes response may be EBV-specific [1,2]. Several viral infections (coxsackie B3, influenza, parvovirus B19, varicella-zoster, cytomegalovirus) have been described to be associated with cardiac complications, including pericarditis, myocarditis and

pericardial effusion [3-5]. However, there is not much known about the involvement of cardiac complications in EBV-induced IM, except for a few case studies. The study by Papadopoulou, *et al.*, [6] in this issue of *Indian Pediatrics* for the first time sets out to analyze the occurrence of cardiac complications in infectious mononucleosis in a systematic manner. They evaluated 25 children suffering from IM during the acute phase of infection and after 3-6 months for cardiac complications and relate these cardiac complications to CD3+CD8+ T

cell counts and CD4/CD8 ratio's. As anticipated, the study showed that CD3+CD8+ T-lymphocytes were increased and CD4/CD8 ratios were decreased in all IM patients. Interestingly, echocardiography revealed mild pericardial effusion in 13/25 patients, of which 12 had very low CD4/CD8 ratios. In most patients all abnormal lymphocyte populations returned to normal within 6 months as did any cardiac complication. Interestingly, persistence of mild pericardial effusion was seen in five patients. In these children CD3+CD8+ T cells were elevated and CD4/CD8 ratios were decreased.

Although one of the difficulties in performing these kind of studies lies in identifying symptomatic EBV-infections, as the symptoms are mostly non-specific, the authors analyzed EBV seroconversion data and performed T-cell phenotyping, making the diagnosis of infectious mononucleosis more straightforward and therefore patient selection was done properly. Although the authors did a great job in performing this study and linking the cardiac complications to T-cell counts, they could have discussed the mechanism behind the occurrence of these cardiac complications better and include discussion on other viruses which have previously been implicated in the context of cardiac symptoms. The authors try to link the high T-cell numbers to the cardiac complications, but state that this could be the result of high load. Unfortunately, no attempt was made to actually measure the viral load to elucidate this.

So the question remains whether cardiac complications are caused by direct cytopathic actions of the virus or by virus-initiated autoimmunity of the expanded T cells [7]. Seko, *et al.*, [8] showed restricted usage of T-cell receptor *Valpha-V beta genes* in infiltrating cells in the hearts of patients with acute myocarditis and dilated cardio-myopathy, suggesting that an antigen-specific T-cell subset plays a role. In addition, autoimmune effects are suggested as the underlying mechanism for myocardial cellular destruction and ventricular dysfunction in children following infection with varicella zoster virus [8]. The involvement of T-cells was also implicated in an experimental myocarditis model in mice after infection with influenza A virus. It was shown that not the virus directly, but some function of the host against viral evasion mediated myocarditis as it was abolished by X-irradiation. As myocarditis did not develop in congenitally athymic nude mice suggests that T-cells play a critical role in the development of myocarditis [9]. As the EBV-specific T-cells at the acute phase are characterized by lack of expression of CD27 indicative of high effector function [10], it may well be that these T-cells are involved in cardiac complications.

Additional studies are required to prove this.

Although the context of the study by Papadopoulou, *et al* was less clear and the link to autoimmunity effects could have been discussed, at least their paper suggests that very low CD4/CD8 ratio may be taken as a surrogate marker for pericardial effusion and increased CD3+CD8+ T-cells after 3 months are associated with persistence of pericardial effusion and may thereby identify patients at continuous risk. Additional analyses are required to establish cutoff values of T-cell phenotypes for cardiac complications.

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