

Nick Brown , *Editor in Chief***NORTHERN PAKISTAN: 240727**

The view today from Islamabad airport is muddy, hardly a vindication of the decision to fly to the Karakoram heartland but given the seasonal lashing the highway tarmac en route for the K2 hinterland has endured and the inevitable subsequent landslides, might, after all still prove to be the right one. We'll be joined by several young children, some en route for a few days' Himalayan air experience with their parents, some travelling back to their bucolic hillside homes. All, quite rightly, curious about everything in their surrounds and innocent to the outside world has to offer. In some way, they, or their as yet unborn siblings, could all be affected at some point in their lives by the themes my selections this month describe so articulately.

**TOXIC SHOCK**

However good the existing observational data, however meticulously the confounding is addressed, there are some situations where only a randomised controlled trial has the (let's say) gravitas to change practice. Toxic shock syndrome is a rare, but high mortality-associated super antigen mediated consequence of Group A, C and G streptococcal and

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staphylococcal-triggered toxin release. Until recently, use of immunoglobulin has been largely anecdotal and personal, the potential to counter activated T cell released cytokines the argument on a 'won't do any harm' basis. Aurelie Portefaix colleagues from multiple centres in France address the uncertainty with a feasibility, efficacy study to gauge the logistics of a trial on IGG vs albumin to formally test superiority. Simon Nadel puts these barriers into perspective, suggesting that the rarity of the condition would require such a huge recruitment network that, though the question as valid as ever, we might never get trial corroboration. Sometimes, that's how it goes, but (reflecting on the adage), good observational data is worth more than an underdone RCT. *See pages 717 and 695*

**SMOULDERING**

It's worth reiterating that congenital malformations even now rank as the fourth highest cause of neonatal mortality in LMICs. Given the related disability and organ decompensation, though, maybe it isn't so surprising when many are undetected antenatally. Trevor Duke and colleagues in Papua New Guinea investigate incidence of WHO and ICD defined malformations in East New Britain using geospatial mapping and find hard-to-ignore clustering around the (still semi-active) volcano in Rabaul. Impossible to infer causality with certainty but, given the potential for preventability, a thought

provoking finding that demands further interrogation. *See page 702*

**NIRSEVIMAB**

The excitement generated by last year's hot-on-the-heels of each other RSV whole infant prevention trials (one maternal one infant) is still, rightly, palpable. They did not just test, but proved beyond any reasonable doubt that both methods were effective, feasible, acceptable and economically sound. The results demanded policy change and (and here appropriate credit must be afforded) without hesitation the headlines were seized on. In the UK the maternal option has been adopted and will be launched very soon. In Spain, the infant approach was preferred, the similar effectiveness of each allowing a choice best suited to existing infrastructure. Initial results from Ermengol Congol, Spanish Ministry of Health, Barcelona and colleagues don't just 'not disappoint', they exceed expectations. Comparing two groups born in 2023, one nirsevimab vaccinated the other not, they estimated an on-the-ground effectiveness of ca 88% (HR 0.12) for medical-intervention-requiring infection and >90% for PICU admission (HR 0.099) in the exposure group. The only comparable unhindered, evidence to implementation journey of recent times has been Covid vaccination. Even so, gratifying proof, that it can be done, all actors in this drama deserving praise. *See page 736*

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