NEWS IN BRIEF

THE ROAD AHEAD FOR DENGUE

Two recent articles in *Science Translational Medicine* have opened new avenues in the prevention and treatment of lethal dengue disease. Researchers from the Australia have unraveled much of the mystery of lethal dengue disease. In 2000, their group had developed a way to test for dengue by measuring concentrations of the NS1 protein in the bloodstream. They then chanced across a study from Thailand which found that patients with higher NS1 levels went on to have more severe disease. So they started wondering whether NS1 actually had a direct effect besides being just an infection marker. They found that the NS1 protein activated mouse macrophages and human peripheral blood lymphocytes via toll-like receptor 4 (TLR4) resulting in a massive release of inflammatory cytokines. What they then demonstrated is breathtakingly important. They demonstrated that this uncontrolled inflammatory response could be blocked by using TLR4 antagonists and antibodies against TLR.

The second set of researchers from University of California found that when mice were injected with NS1, they threw up an inflammatory response with endothelial leakage; and when they were injected with both NS1 and a sublethal dose of dengue virus 2 it resulted in a lethal inflammatory storm. But if the mice were immunized previously with NS1 or if they were given monoclonal antibodies against NS1, they were protected against lethal dengue disease.

These landmark studies have shown that NS1 protein will be an important constituent for any vaccine against dengue and drugs that target NS1 or TLR4 might be potentially effective against lethal dengue disease. (*Science Translational Medicine 9 September 2015*)

BEDAQUILONE FOR TUBERCULOSIS

Bedaquilone belongs to a new class of drugs called the dairiquinolones, and acts by inhibiting the mycobacterial ATP synthetase. It received fast track approval by the Food and Drug Administration (FDA) at the end of 2012 for the treatment of adults with multidrug-resistant pulmonary tuberculosis. It is being touted as the second major advance in the field of tuberculosis after Expert MTB/Rif test was developed in 2010.

The Director General of Health (India) announced that it will become available in India within the next three months. It recently underwent clinical trials at national level for safety and efficacy. Four nodal cities – Mumbai, Chennai, Bangalore and Kolkata – will control its distribution to required districts. Its distribution will be strictly regulated. The dose in adults is 400 mg daily for two weeks followed by 200 mg thrice a week for a maximum of 22 weeks. Adverse effects are mainly cardiac and hepatic. (*The Indian Express 11 September 2015*)

NEONATES WITH DIABETES WHO REQUIRE NO INSULIN

In the 1970's, the entity of maturity onset diabetes of the young (MODY) was first described. This was a peculiar kind of diabetes distinct from both Type I and Type II. These were young people who developed diabetes but did not require insulin, did not go into ketosis, and often responded to oral suphonylureas. Some never developed the complications of hyperglycemia and never required any drugs. In the 1990's, it was confirmed that mutations encoding for the glucokinase gene HNF1A and HNF4 A were responsible for these manifestations in some of the people. Though MODY accounts for just 1-2% of diabetes, we need to know when to suspect it. Neonatal diabetes (onset <6 mo of age), strong family history of diabetes, type 1 diabetes who need less than 0.5 units/kg/day of insulin, persistently detectable C-peptide and negative antibody status are good clues. In type 2 diabetes those who are non obese or lacking markers for metabolic syndrome also need to be worked up for MODY.

A recent multicentric study evaluated all the genes associated with neonatal diabetes (diabetes with onset <6 mo) using comprehensive next-generation sequencing. Causal mutations have been identified in 82% of patients. Patients with mutations in the glucokinase gene did not need any treatment and identification of a potassium channel mutation indicated that patient will respond to oral sulphonylureas. (*The Lancet 2015;386:934-5*)

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