

CHOOSING WISELY

Many of the tests and interventions, which doctors routinely carry out, may be unnecessary. The ‘Choosing Wisely’ campaign is an attempt to reduce this. Each medical society is asked to suggest a list of top five tests or treatments that doctors of their specialty commonly overuses. This serves as a red flag to alert physicians to stop and reconsider the test or intervention.

For example, in the ‘choosing wisely’ list of the American Academy of Pediatrics Section on Surgery, the first is to avoid the routine use of whole body computed tomography (CT) scanning in pediatric trauma patients. This will reduce both radiation and costs. The second is to avoid CT scanning as the first line modality to diagnose appendicitis. They recommend use of ultrasound as the first modality, and suggest use of CT scan only in equivocal cases. The third is to avoid referring children with umbilical hernia to a pediatric surgeon until the age of 4-5 years. The fourth is to avoid the use of post-operative opioids in pediatric patients and use acetaminophen or non-steroidal anti-inflammatory agents instead. The fifth is to avoid routine fundoplication during gastrostomy insertion for children in the absence of reflux.
(*Choosing wisely.org 4 November 2019*)

IMMUNOLOGICAL AMNESIA AFTER MEASLES

It has long been recognized that after measles epidemics, there would be a spurt of overall childhood mortality. The reason has long been considered to be a measles-induced immunosuppression. Now, immunologists from Boston (USA) have documented how measles produces this immunological amnesia.

In 2013, there was an epidemic of measles in the Netherlands. Blood samples of 77 of these children before and after the measles episode had been preserved. Samples of children who had received the MMR vaccine were also collected, before and after vaccination. Using a new tool called VirScan, antibodies to various viruses and bacteria before and after the measles attack were analyzed. It was found that 11-73% of antibodies had been erased after the measles infection. This drop in antibody levels was not seen after MMR vaccine. This loss of antibodies was due to measles-induced permanent damage to the memory cells in the bone marrow. The authors suggest that revaccinating these patients might help to rebuild the immunological memory and reduce long-term mortality. The study is important in light of the fact that measles infections worldwide trebled in the first half of 2019.
(*Science 1 November 2019*)

A VACCINE TO PREVENT TUBERCULOSIS

One-fourth of the world’s populace has latent infection with *Mycobacterium tuberculosis*. These adults are a reservoir, of whom 5-10% will go on to develop active tuberculosis. Computer modeling has suggested that eliminating the infection in this pool will play a major role in the global fight against tuberculosis.

A new vaccine M72/AS01 has now demonstrated robust immune response in adults with latent tuberculosis. In a recent randomized controlled trial, the vaccine or placebo was administered to 3575 adults with a positive interferon gamma release assay but no active tuberculosis. On follow-up at 3 years, the incidence of bacteriologically proven tuberculosis was 0.3/100 person years in the vaccinated group *versus* 0.6/100 person years in the placebo group. The overall vaccine efficacy was 49.7%.

This vaccine has also been studied in Gambian infants who had received BCG vaccination. They received the M72/AS01 vaccine as a booster 4-7 months after the BCG vaccine. Immune response in the form of CD4 T cell activation and antibody production against *M. tuberculosis* was found to be far superior in the group that received the new vaccine. This vaccine marks a new strategy in the fight against tuberculosis.
(*NEJM 29 October 2019*)

TRIKAFTA FOR CYSTIC FIBROSIS

Trikafta is a combination of elexacaftor-tezacaftor and ivacaftor. The FDA has now approved the use of this in patients with cystic fibrosis above 12 years of age, and with atleast one delta 508 mutation. This follows two phase-3 trials published recently. In one trial, there was a 13.8 point increase in FEV1 after 4 weeks, a reduction of pulmonary exacerbations by 63%, and a reduction in sweat chloride by 41.8 mmol/L after use of the medication. In the other study, Trikafta was used in patients homozygous for the delta 50 mutation. There was a 10 percentage point improvement in FEV1 and 45.1 mmol/L reduction in sweat chloride.

Elexacaftor and tezacaftor are called CFTR correctors. They correct the processing and trafficking of the F508del-CFTR protein, and enables it to reach the cell surface. In contrast ivacaftor is called a potentiator. It increases chloride transport by potentiating the channel-open probability. The combination of these three drugs is being described as a major breakthrough in the therapy of cystic fibrosis.
(*Lancet October 31 2019; NEJM November 7 2019*)

GOURI RAO PASSI
gouripassi@gmail.com