New hope for preventing death from septicaemia

Septicaemia, or sepsis, is the clinical name for blood poisoning by bacteria. It is the body's extreme response to an infection. Sepsis happens when an infection you already have gets into the blood stream and triggers a chain reaction throughout your body. Without timely treatment, sepsis can rapidly lead to tissue damage, organ failure, immune paralysis and ultimately death. It is estimated to affect nearly 49 million people worldwide every year leading to 11 million deaths which account for 19.7% of the total global death toll. Being a deadly condition that takes just 24 hours to manifest; sepsis is a bigger killer than all cancers combined. Currently, no effective treatment of sepsis exists. Although better supportive care has improved death rate, the cost of treatment is high with all patients having to be treated in ICU. The US, for example, spends $ 24 billion annually for treatment of sepsis. The mechanism underlying development of sepsis remains elusive and, despite its high prevalence, no new therapies have been developed in the last three decades. Failure rates of clinical trials of sepsis treatments continue to be high and a global clarion call has been sounded for new approaches to treatment of sepsis. Scientists at Tata Memorial Centre, Mumbai have discovered one such new approach which has been recently published in the journal PLOS ONE (https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0229017).

Since cancer patients with immune-compromised systems often fall prey to this deadly condition, scientists at ACTREC, the R&D arm of TMC, have been seeking

efficacious and cost effective solutions to the treatment of sepsis. The research group had earlier on, made the fundamental discovery that shattered chromosome particles called cell-free chromatin that are released from the billions of cells that die in the body every day, as a part of the body's normal physiological process, can enter into healthy cells leading to cell death and inflammation. Although, initially, this phenomenon was thought to be the underlying cause of ageing, and related disorders such as cardiovascular disease, diabetes, Alzheimer's disease and cancer, the researchers have identified the same phenomenon to be the root cause of sepsis.

Having established the trajectory, they tested different remedies for inactivating the deadly chromatin particles thereby preventing sepsis. A mouse-model was used in which animals were first injected with a bacterial toxin called lipopolysaccharide (LPS); this was followed by three chromatin deactivating substances. The results demonstrated that virtually all parameters of sepsis showed a marked downward trend. This included prevention of inflammation, tissue cell death, reversal of immune paralysis, coagulopathy and fatality from sepsis. Of the three agents that inactivated cell-free chromatin, of particular interest was an Ayurveda- like combination of a plant polyphenol and minute quantities of metallic Copper. The plant polyphenol used in the study is called Resveratrol which is mainly derived from skin of red grapes. Resveratrol has been widely tested in the West for its health benefits in multiple conditions but had shown minimal effects. Researchers at TMC/ ACTREC had discovered that Resveratrol in much smaller quantities when combined with minuscule amounts of Copper becomes remarkably active and able to combat sepsis. Although Resveratrol is not mentioned in the Ayurvedic pharmacopeia, it is

very similar to substances widely used in Ayurveda which are derived from fruits, berries and plants and often used in conjunction with metallic elements, particularly Copper. Research at TMC is now in its next level in the form of a clinical trial on patients with sepsis. If this trial is successful, it may help to save millions of lives globally at a fraction of the current treatment cost.