Medical History

2021 : The First Centenary of BCG Vaccination in Human

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Forewords :

Lady Mary Wortley Montagu observed variolation in Constantinople and brought it to Britain in 1721. In Shetland Isles, Johnnie Notions had the reputation of not having lost a single patient with his self-devised inoculation. On May 14, 1796, Edward Jenner, the father of immunology, inoculated James Phipps with cow's small pox blister-fluid (as his 17th recorded case) , and to prove his hypothesis of induced immunity, he later challenged Phipps by injecting with variolous material successfully with no subsequent disease manifestations.

125 years after, on July 18, 1921, the first ever inoculation in human with a novel vaccine against tuberculosis was done through oral route on an orphan neonate in Charité Hospital, Paris by Benjamin Weill-Halle and Raymond Turpin in the philanthropic view to save the posthumous baby from potential risk of developing neonatal tuberculosis, as its mother died of pthisis soon after giving birth to a healthy baby.This vaccine was developed and already tested on animals by Calmette and Guérin. Initially it was named as include "Vaccin Bilié de Calmette et Guérin vaccine" and later on, as "Bacille de Calmette et Guérin vaccine" or BCG, in short.

Thus, this 2021 is the first centenary of BCG vaccination in human.

Brief History :

Being challenged in 1895 by Theobald Smith regarding differences in phenotypes between human and bovine tuberculosis, Robert Koch revisited his previous thinking (1882) of identical natures of human and bovine tuberculosis bacilli. By 1901 Koch distinguished *Mycobacterium bovis* from *Mycobacterium tuberculosis*.

This very finding and the success of vaccination in preventing smallpox inspired the immunologists to draw a parallel relationship between bovine tuberculosis and to frame a corollary that infection with bovine tuberculosis might also be protective against infection with human tuberculosis. But, their overzealous inoculation of unmodified M.bovis—as virulent as M. tuberculosis— in Italy in the late 19th century ended with disastrous results.

During such doldrums , Albert Calmette, a French physician and bacteriologist, and Camille Guérin, a veterinarian, were working at the Institut Pasteur de Lille (Lille, France) in 1908, ushered with a new idea in an effort to attenuate the bacilli. They tried subculturing virulent strains of the tuberculosis bacillus using different arbitrary culture media. They noted a glycerin- potato mixture grew bacilli well , but it was difficult to get homogenous suspension of bacilli. Upon intuitively adding ox bile into the medium, they astonishingly noted less clumping tendency and lesser virulence of the bacilli. And this pre-empted them to undertake 239 subculturing over 13 years, even through the period of WW I .In 1919, they succeded to isolate avirulent bacilli, which were found to be unable to cause tuberculosis disease in research animals. Calmette and Guerin transferred to the Paris Pasteur Institute in 1919. The BCG vaccine was first used in humans in 1921 in Charité Hospital, Paris. It was a successful endeavour; but public acceptance of the vaccine was not apt, might be due to a disaster. In the summer of 1930 in Lübeck, 240 infants were vaccinated in the first 10 days of life; almost all developed tuberculosis and 72 infants died— due to improper storage of the BCG with virulent strains in the same incubator.

Dr R G Ferguson, working at the Fort Qu'Appelle Sanatorium in Saskatchewan, and few other forerunners developed the practice of vaccination against tuberculosis. In 1928, BCG was adopted by the Health Committee of the League of Nations (predecessor to the WHO)). But because of controversy and opposition, it took nearly two more decades to be widely used. In post WW II period (from 1945 to 1948) relief organizations (International Tuberculosis Campaign or Joint Enterprises) vaccinated over eight million babies in eastern Europe and prevented the predicted post-war surge in TB.

Further Scopes :

BCG vaccine helps in preventing tubercular meningitis in infancy and childhood.

BCG also has some effectiveness against Buruli ulcer infection and other nontuberculous mycobacteria infections.

Additionally it is sometimes used as part of the treatment of non–muscle-invasive bladder cancer (NMIBC). BCG has been one of the most successful immunotherapies.

BCG has also been tried in colon cancer and colorectal cancer.

Early inoculation with BCG vaccine, particularly in low income countries, tentatively exert a beneficial non-specific effect of on overall mortality, through reduction of sepsis and respiratory infections.

As of 2017, BCG vaccine is in the early stages of being studied in type 1 diabetes.

Use of the BCG vaccineis claimed to provide protection against COVID 19. However, epidemiologic observations in this respect are ambiguous. Spanish, French, German and Dutch research entities are preparing trials using genetically-modified BCG vaccine in this regard. BCG vaccine is in phase III trials in health care workers in Australia and Netherlands. BCG vaccine is being evaluated in Greece and Poland. Polish scientists are investigating on the immune training effect of BCG vaccine. The WHO has not yet recommended its use for prevention.

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Reference

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