

IMMUNITY IN CHOLERA AND VACCINE DEVELOPMENT: PROBLEMS AND PROSPECTS

ASOKE C. GHOSE*

*The acute diarrheal illness cholera is considered to be one of the ancient diseases in the recorded history of human civilization. Despite advances made in the health care delivery and research, the disease continues to affect a large population worldwide, particularly those living under low socio-economic conditions. A major effort to control cholera has been to develop a safe and effective vaccine. Unfortunately, the initial efforts, which started as early as in 1884, were unsuccessful due to various reasons. With the advancement of our knowledge on cholera, its causative bacterium *Vibrio cholerae* and the toxin produced by multiplying vibrios in the intestine, a resurgence of activities in the area of cholera vaccine research was noted. This was also prompted by data obtained from epidemiological and human volunteer studies which demonstrated that clinical cholera does provide some form of immunity to the disease. These and other studies also emphasized on (a) the protective role of local antibodies that are secreted in the intestine and, (b) the relative importance of antibacterial over antitoxic immunity in cholera. An understanding of mucosal immunology made it clear that oral, rather than parenteral, vaccines are better suited to stimulate intestinal immunity. These considerations initiated concerted efforts to develop oral vaccines that can be delivered as live (attenuated) or killed (inactivated) organisms. Availability of recombinant DNA technology made it possible to develop genetically engineered live oral vaccine strains with deletion(s) of the gene(s) encoding one or both the subunits of cholera toxin. Although many of these strains induced satisfactory level of protection in human volunteer and/or field studies, adverse side effects and other safety concerns were the important constraints for their further development. The killed vaccines, that are usually free from any adverse reactions and cost-effective, have also generated promising data in some of the recently conducted human trials. One such bivalent cholera vaccine is currently undergoing controlled field trials under a joint public-private partnership venture.*
