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## EDITORIAL

### HOW THIS HAPPENED ?

Cholera is, without parallel, a fascinating disease. It is a disease which may cause death in a few hours, has terrified mankind from recorded times, and decimated vast areas. Yet, in apparent behaviour, the organism is relatively innocent. It remains confined to the intestine and does not even invade or cause damage to any of the body tissues. Study of cholera toxin has been most rewarding, shedding light not only on the pathogenesis of this disease but on the mechanism of action of many other bacterial toxin(s) and of electrolyte secretion by the intestinal epithelium. Much has been learned about the behaviour of this and, through this, of many other organisms, but many fundamental questions remain unanswered.

Perhaps the most amazing part of the story of cholera is in its epidemiology. In the early Sixties the El Tor biotype of this organism, long accepted as non or mildly pathogenic since its first isolation by Gottslich in 1905, suddenly appeared to develop full pathogenic potentialities, enabling it to cause extensive scattered epidemics over nearly half of the globe and virtually replace the pathogenic classical strain, which till then ruled the scene. So much so that the World Health Organization had to revise its definition of cholera and include the El Tor biotype also as the causative organism for this disease (1). Bacterial variation is a well known fact and acquisition or loss by bacteria of virulent characteristics need cause no surprise. What was fascinating, however, is the fact that this newly-emergent El Tor biotype refused to co-exist with the classical biotype and, wherever it went, replaced it. The invisible magic wand of El Tor did what man had failed to do with all his resources and ingenuity. Though man is known to be the only proven host and survival of the organism outside the human body generally is believed to be short, recent studies (2) have raised a strong probability that the organisms sometimes persist in suitable acquatic environments outside the human body for long periods and may initiate fresh infection from the environment after lapse of many years. Whether this really happens and, if so, how, remains to be clarified.

To add to the confusion the original pathogenic biotype, the classical one, which apparently was completely replaced from the scene by its competitor, has, without any explanation, reappeared, apparently from nowhere, and is taking its vengeance over the El Tor strains by nearly eliminating them from Bangladesh in three months time (3). It is possible that this change may have started in some other countries too but has not yet been noticed, because in many of the developing countries biotyping is not normally carried out as a routine. This take-over by classical is really amazing when one remembers that about a decade back these El Tors started replacing the classical and succeeded in eliminating them from the scene over nearly half the globe, so much so, that in spite of intensive search, classical vibrios were rarely detected for many years.

After a decade of disappointing results with cholera vaccines, interest has again been focused on such research. Attempts are now being made to design a *Vibrio cholerae* strain from which the gene coding for the damaging portion of the toxin has been removed. It is proposed that this castrated vibrio be administered orally in a live form--a form which hopefully, will establish infection and stimulate immune mechanisms as the natural vibrio does, but without being able to produce the disease. Considerable progress in this attempt has already been made and further success seems likely.

In the replacement of the classical strain by El Tor in Sixties and the present replacement of El Tor by classical in Bangladesh we have a situation in which a dreaded pathogen, A, has been replaced by another, B. Unfortunately in this instance B is almost equally pathogenic. If B could be replaced by another which will not produce the disease, like the strain we wish to have for the proposed oral cholera vaccine from which the gene coding for the harmful portion of toxin has been removed, then we may be able to achieve what one could never have dreamt before. But before that we must know how an organism A has learned how to displace its next of kin B, from the ecological niches in which B could be present. It is well-known that the El Tor biotype suppresses the classical biotype when the two are grown together in broth. However, in preliminary studies, the classical biotype isolated in 1982 appears to grow almost equally well along with the El Tor when the two are grown

together (4). The present classical biotype may, therefore, be better equipped to compete with the El Tor, than the classical biotypes isolated in the Sixties. Tests normally carried out for differentiating classical and El Tor strains have not so far detected any significant differences between the classical and El Tor biotypes isolated in 1982/83 and those isolated a decade ago (4). This suggests that, in addition to accepted taxonomic traits for identifying biotypes from each other, there may be other crucial biological characteristics that can give a new strain an advantage which confers on it the power to displace another biologically related strain from its places in nature.

Variation in the determinants of adhesion to gut epithelial cells, special modes of survival in ecological niches outside the human body, and competitive advantage over other bacteria under conditions of limited nutrient supply are only a few of the unlimited guesses for study which one could make with equal justification. The task is difficult and the answers may lie beyond the present range of our vision. But a situation like this may not occur again in the near future. Therefore, the importance of applying at an early stage the best current technology and expertise to identify the characteristics that have allowed the rapid and sudden dominance of one biotype over another is obvious. Understanding these key characteristics may be of fundamental importance not only for the control of cholera, but for other bacterial diseases as well. The big question, therefore, is, how this has happened. HOW?

## References

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