THE RESPONSE TO GLUTARALDEHYDE TOXOID IN HUMAN VOLUNTEERS - A PROGRESS REPORT

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The immunogenicity of glutaraldehyde-prepared cholera toxoid(Wyeth 11201) is being examined in human volunteers, and available data have been compared with those of volunteers receiving formaldehyde toxoid(Wyeth 00101) and the field trial lot of glutaraldehyde toxoid(Wyeth 20101). The effects of interval between doses of plain toxoid, aluminum phosphate adsorbed toxoid, and protaine aluminum phosphate adsorbed toxoid on serum antitoxin levels have been studied. Antitoxin titers were determined by passive hemagglutination titration (PHA) with highly purified choleragen-sensitized erythrocytes. Although not comletely available at this time, anti-ermeability factor and anti-ileal loop titers will be correlated with the PHA titers. Vibriocidal antibody titrations have been performed to monitor the somatic antigen content of the toxoid vaccines.

The data indicate that glutaraldehyde toxoids elicit significantly lower geometric mean antitoxin responses than a formaldehyde toxoid(Wyeth 00101) previously examined and shown to be unsatisfactory because of reversion of a small amount of the toxoid to active toxin. PHA titers and limited anti-PF titers suggest that the field trial lot of glutaraldehyde toxoid is at least as immunogenic as a previous experimental lot of glutaraldehyde toxoid(Wyeth 11201). Vibriocidal titrations of sera from volunteers and hyperimmunized rabbits reveal that the somatic antigen content of the field trial lot(20101) is considerably lower than that of toxoid(11201). Preliminary vibriocidal data suggest that an alhydrogel formalin toxoid(Wellcome PX 389) also under study contains little somatic antigen.

Our previous observations with American volunteers showing that aluminum phosphate adjuvanted toxoids do not enhance immunogenicity beyond that obtainable with plain toxoid have been confirmed. The superior immunizing properties of aluminum phosphate adjuvanted toxoid in rabbits, previously reported by the Wyeth laboratories, have also been confirmed in that species despite the lack of adjuvant effect in man. Furthermore, the maximum height of the PHA

antitoxin response in man to secondary immunization, regardless of interval between the doses(4, 8, or 12 weeks), is equal to or only slightly higher than the maximal response after primary immunization. The effect of interval between doses upon the ultimate duration of elevated titers must await analysis of later samples. To the extent that they are available, antitoxin and vibriocidal responses will be presented to support these observations.

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