DATE: September 16, 1975

TO : Dr. Joshua Lederberg

FROM : Gary M. Gray, M.D. G D+-L 50091

SUBJECT: Potential Use of Cholera Toxin for Treatment of Serious Constipation in Diverticulitis.

Dear Professor Lederberg:

I sincerely regret the long delay in responding to your memo regarding this subject. But I wanted to give it some thought before answering. Cholera toxin appears to act by stimulating adenylate cyclase to synthesize cyclic AMP which in turn stimulates the active secretion of chloride ion. As far as we know at this time, sodium ion and water follow so that isotonicity is maintained. The major action of the toxin appears to be in the small intestine, although it may also have some action in the colon. Interestingly enough, it has been recently shown that a new gastrointestinal hormone vasoactive intestinal peptide (VIP) which has a structure similar to secretin and glucagon appears to act in exactly the same way as cholera toxin to stimulate adenyl cyclase, cyclic AMP and active secretion of isotonic fluid. It has not yet been demonstrated that cholera toxin releases VIP, however,

I think the problem with attempting to use cholera toxin for constipation arises in the great difficulty that might arise in trying to properly control the amount of active secretion that might be provoked. Constipation is usually an idiopathic problem that can be readily handled by manipulating the diet and giving osmotically active substances that will retain water within the intestinal lumen. For many people, it is normal to have only one or perhaps two bowel movements per week; we do from time to time run into young adults who seem to have bowel movements even less frequently. On the other hand, other people normally have as many as three per day. I do have some opinions about constipation in childhood, but have to admit that they are not firmly based on scientific fact. I would be happy to chat with you about this sometime if you wish.

Best regards.

Sincerely,

Gary

Gary M. Gray, M.D.
Associate Professor and Head
Division of Gastroenterology

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GRAY, G.