II THE PATHOGENESIS OF CHOLERA DIARRHOEA

by

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This lecture is not merely an intellectual exercise but attempts to show that the goal of all research is rational and specific treatment and control of cholera should be based on a complete knowledge of the processes of the disease.

1. Normal secretion of water and electrolytes into the gut - estimates vary from 7 to 50 litres daily.
2. Normal re-absorption of these electrolytes and water by the gut requiring various metabolic, osmotic processes.
3. Cholera, with massive amounts of watery, electrolyte-rich stool, is therefore a disease of increased secretion which exceeds the gut capacity to absorb, decreased absorption of normal secretions or a combination of both.
4. Electrolyte composition of cholera stool and upper intestinal fluid in cholera (Na, K, Cl, CO_2).
5. Relationship of Na and K concentrations to stool rate, suggesting that cholera stool originates in the small intestine.
6. Cholera stool essentially a protein-free plasma filtrate, slightly modified in its passage through the gut.
7. Of the electrolytes noted only Na cannot be absorbed by a cholera patient. K, bicarbonate and distilled water can be somewhat absorbed.
8. Consequence: cholera may be thought of as a defect in absorption of Na (and therefore accompanied by water and other ions) or hypersecretion of plasma water and electrolytes which exceed gut capacity to re-absorb Na.
9. Evidence for primary defect in absorption of Na:
   a. frog skin sodium transport inhibition
   b. radio-isotopic studies in man with cholera
   c. decrease in jejunal enzyme associated with movement of sodium
   d. by analogy: malabsorption of other materials (d-xylose, vitamin B_{12}, fat, folate)

10. Evidence for hypersecretion

a. Old theory of muconal denudation - disproved by in vivo jejunal biopsies, failure to recover in stool intravenously injected isotopically labelled protein sized molecule.

b. Studies with Miller-Abbot tube in cholera patients: suggested source of diarrhoea above the ligament of Treitz (i.e. duodenal hypersecretion.

c. Cholera toxin:

i. found in supernate of cholera stools and culture filtrates;

ii. cause delayed vascular permeability in rabbit skin with induration, swelling and leakage of intravenously injected dye into site;

iii. causes passage of fluids into rabbit ileal loops;

iv. antibodies to toxin in convalescent cholera patients;

v. action in vivo on dogs and man in producing cholera like diarrhoea when given orally.

The toxin is not purified and may have several components.

11. Source of diarrhoea

a. ileum in dogs

b. intubation studies in man: their design to study parts of the intestine

12. Action of oral glucose on Na absorption in gut of normal and cholera patients. Speculation on possible use in oral fluid replacement.

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