ENVIRONMENTAL ENTEROPATHY

Environmental enteropathy: critical implications of a poorly understood condition
Korpe PS. Trends in Molecular Medicine 2012:18:328336

New insights into environmental enteric dysfunction

Child undernutrition, tropical enteropathy, toilets and handwashing
Humphrey J. Lancet 2009;374:1032-1035

- What is environmental enteropathy?
  Environmental enteropathy is a chronic inflammatory state of the duodenum and jejunum, associated with mucosal villus atrophy, crypt hyperplasia and inflammatory cell infiltrate (CD8+ T-cell lymphocytes). The villi are broad and flat with increases in the crypt depth between villi. The surface area available for nutrient absorption is markedly reduced. There is moderate malabsorption, often subclinical, often without diarrhoea. Absorption of essential fats, carbohydrates and vitamins is decreased. Because it is an indolent chronic condition it leads to stunting. Environmental enteropathy is likely to be caused by faecal bacteria ingested in large quantities by young children living in conditions of poor sanitation and hygiene.

- How does it present clinically? What is the earliest age that children show signs of environmental enteropathy? Can a child have environmental enteropathy without diarrhoea?
  In the first 2 years of life the nutrient and energy demands for growth are greatest, in environmental enteropathy there is reduced nutrient absorption by atrophied villi. Pathological changes can be seen as early as 3 months of age. The condition is usually indolent, with growth faltering, stunting, and increased susceptibility to infections.

- What are the likely causes of environmental enteropathy?
  Children living in poor sanitary conditions ingest high concentrations of faecal bacteria, which colonise the small intestine and induce T-cell inflammation (in the lamina propria and epithelial cells), intestinal hyper-permeability, and villus atrophy. The aetiological factors are likely to be unsanitary conditions, high faecal bacteria in the environment (caretaker’s hands, utensils, and toys), poor water quality, lack of toilets, poor quality and poorly prepared complementary feeding of infants, and unsterile washing of infant feeding bottles.

- What is the pathological appearance in the small intestine of children with environmental enteropathy?
  The villi are broad and flat (mucosal atrophy) with increases in the crypt depth between villi. The mucosa is hyper-permeable: the epithelial matrix leaks fluid from the intestinal wall into the lumen and vice versa. Because of this increased permeability there is bacterial and toxin translocation: that is, lipopolysaccharide (the protein found on cell walls of enteric Gram negative bacteria), microbes and other toxins leak into the circulation from the gut lumen. This can lead to a chronic inflammatory state, which results in the use of nutrients away from growth for increased synthesis of acute phase proteins, cytokines, and increased glucose oxidation to fuel the high metabolic rate.

- How are the functions of the small intestine affected by environmental enteropathy? How does this cause disease?
Nutrient absorption reduced because of reduced absorptive surface area
Barrier function that protects from translocation is disrupted
Immune function of the gut is channelled towards T-cell inflammation by the high load of faecal bacteria.

- **What is bacterial translocation and how does this occur? What is LPS?**
  Translocation occurs because of increased mucosal and sub-mucosal permeability. There is bacterial and toxin translocation: lipopolysaccharide (the protein found on cell walls of enteric Gram negative bacteria), microbes and other toxins leak into the circulation from the gut lumen. This leads to chronic inflammation and sepsis-like conditions.

- **What is the lactose: mannitol ratio, and why does this increase in environmental enteropathy?**
  Lactulose is normally absorbed by the small intestine. Mannitol is a large molecule and normally not absorbed. Normally if a person ingests a given amount of a lactulose and mannitol, the amount of lactulose in the stool will be low (because it is absorbed) and the amount of mannitol in the stool will be high (because almost none of it is absorbed). In environmental enteropathy the lactulose: mannitol ratio in the stool is increased. The villous atrophy leads to reduced lactulose absorption (therefore more lost in the stool) and the intestinal hyper-permeability leads to translocation of the large molecule mannitol into the circulation (so less is excreted).

- **How does environmental enteropathy affect vaccine efficacy?**
  Oral vaccines, such as Sabin (OPV) and oral rotavirus vaccines are less immunogenic, because of altered mucosal immunity. There is chronic activation of the mucosal immune system because of ingested faecal bacteria, and this means that oral vaccines might not elicit the same response in the population. It is known that these vaccines are less immunogenic in developing countries, and environmental enteropathy is likely to be the major cause.

- **What are the best ways to treat and prevent environmental enteropathy?**
  WASH: water, sanitation and hygiene. Toilets, handwashing, soap and running water, improved drinking water, exclusive breast feeding, properly prepared complementary feeding, and avoidance of bottle feeding. Growth monitoring of children linked to local household environmental improvements, rather than growth monitoring just being linked to attempts to providing more calories for children who are failing to thrive.