Three decades of gastroenterology in Soweto South Africa: from descriptive to scientific observations
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Chapter 9

Persistent Low Prevalence of Western Digestive Diseases in Africa: Confounding Aetiological Factors

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Hypothesis
In the context of poverty in infancy, an adverse environmental situation conditions the gut and paradoxically, acts as a protective factor against subsequent digestive diseases in adulthood.

Introduction
One of the major differences in disease patterns between adult African and Western populations is the relative paucity of digestive diseases such as cancers (except for oesophageal cancer), adenomatous polyps, diverticular disease, inflammatory bowel disease, and appendicitis. This situation prevails despite the presence of environmental factors which favour increases in their occurrences. In contrast, their incidence is high in Western populations, although they were very much lower at the turn of the last century. Urbanisation of Africans is accompanied by changes in environmental factors and lifestyles. The significance of these changes is the subject of this paper.

Diet
In African countries, considerable changes in diet have occurred and are continuing, with falls in the intake of plant foods but rises in those of animal origin. In South Africa, among rural Africans a generation ago, of the total energy intake, protein supplied 10-11%, fat 15-20%, and carbohydrate 70-75%. Dietary fibre intake averaged 30-35 g daily. Later, in an urban area in the Cape Peninsula, the corresponding proportions were 13%, 25%, and 60%. Mean fibre intake was much lower (17 g daily). In Johannesburg, a recent study showed that the proportions of nutrients supplying energy were protein 14%, fat 30%, and carbohydrates 35%. Mean total daily energy intake was 2150 kcal, with 82 g of protein, 74 g of fat, 250 g of carbohydrate, and 14 g of fibre. Maize meal (previously and still the case in many families) is the staple food but is being replaced by bread, mainly white bread. Consumption of fruit, vegetables, and meat is low because of their cost. Of major significance, the marked reduction in fibre intake and rise in fat consumption has been associated with a reduced intake of antioxidants. Simultaneously, however, approximately one tenth of urban
Africans are now sufficiently better off to have a dietary intake and pattern approaching that of the white population.\textsuperscript{15}

In consonance with the hypothesis which focuses on the nature of environmental factors in childhood is the belief that relatively low energy intake during early childhood inhibits rumorigenesis in later life.\textsuperscript{16} Most African children live in poor conditions and under nutrition is usual, as manifested by the high proportions (15-35\%) who are less than the fifth centile of reference standards for growth.\textsuperscript{17} As mentioned, the staple diet of children is maize meal which, although relatively low in fibre, is high in resistant starch\textsuperscript{18}

**Non-dietary changes**

In recent generations of Western populations there has been a continuing reduction in physical activity, at work, and in relation to transport and leisure. In children, fewer participate in games, and the attractions of television and "movies" are obvious.\textsuperscript{19,21} In Africans, physical activity is falling considerably in urban dwellers. Additionally, smoking and alcohol consumption, particularly in men, are rising.\textsuperscript{22,23} The adverse effect of low physical activity is well known.\textsuperscript{24}

**Lack of basic facilities and its impact on a population in transition**

Most urban Africans are very poor although there is a steady but small increase in the proportion who are more prosperous. Electricity supply, sanitation, access to clean water, and housing have improved considerably in some regions, more so in city dwellers, but these changes have occurred relatively recently. A large proportion of urban dwellers, particularly "squatters", do not have access to these facilities.\textsuperscript{25} The influence of environmental conditions on future health issues is embodied in the "hygiene" hypothesis of Barker and coworkers.\textsuperscript{26,27} Thus regarding the rise in appendicitis, they attributed it to improvement in water, supplies and sewage disposal in Britain in the late 19th century. These changes greatly reduced exposure of infants and children to enteric organisms which in turn altered children's responses to later virus infections so that they now triggered appendicitis.

**Relationship between bacterial flora and immunology of the gut**

The intestinal interface comprises bacteria and the immunological defence system. Initial colonisation of the gut by indigenous microflora begins early in infancy and
matures slowly during weaning. Once the bacterial ecosystem is established, the relative frequencies of the various bacteria remain stable in the healthy host.\textsuperscript{28}

The gut microflora contribute to the health of the host in many ways, including fermentation, vitamin synthesis and antagonism to transient and pathogenic microbes. They are a powerful protective barrier between the internal and external environment, thus presenting a constant challenge to antigens such as food and potentially pathogenic microorganisms.\textsuperscript{28} Establishment of an indigenous microflora has a particularly strong impact on immunophysiological regulation of the gut. A wide range of Western diseases are associated with intestinal inflammation, aberrant antigen absorption, and immune responses. These include food allergy in infants and inflammatory bowel disease.\textsuperscript{26} Yet these disorders/diseases are uncommon in African populations. Hence we suggest that bacterial flora and immune responses rises differ in African compared with Western populations. There is evidence that in African infants the bacterial flora are qualitatively different and produce significantly more short chain fatty acids, specifically butyrate, than white children.

With regard to the immunological reaction to previous Infections\textsuperscript{30}, in a study in 60 healthy subjects living in a poor squatter area near Johannesburg it was found that mean immunoglobulin (Ig) G levels in men and women were 18.33 (4.59) g/l and 18.44 (4.53) g/l, respectively.\textsuperscript{31} For developed populations for both sexes combined, corresponding mean values of 10.2 g/l and 7.2 g/l have been reported in Australia\textsuperscript{32} and Finland,\textsuperscript{33} respectively. For the subclasses, mean values for IgG, (10.96 g/l for men, 10.67 g/l for women, and 4.9-11.4 g/l for a reference African control group) were close to the upper limit of normal. Values for IgG: in squatters were 3.34 g/l for men 3.15 g/l for women, and 1.5-6.4 g/l for the reference African control group. The IgG\textsubscript{1}/IgG\textsubscript{2} ratio was 3.3. For measure merits of IgE (a surrogate marker for previous parasitic infection), IgG\textsubscript{1} and IgG\textsubscript{2} levels in Helicobacter pylori positive Africans in Soweto it was found that a high percentage of subjects had IgE and IgG\textsubscript{1}/IgG\textsubscript{2} levels above the normal range and hence was consistent with a high prevalence of previous gastrointestinal infections.\textsuperscript{34}

The delicate balance between bacteria and immune mechanisms is illustrated by the interplay between H pylori and the human host. H pylori is ubiquitous in Africa, with acquisition in childhood being the rule.\textsuperscript{35, 36} However, its association with gastrointestinal pathology (duodenal ulcer, gastric ulcer, and gastric cancer), although
high in Western populations, has a variable but often low distribution in Africans. Presumably, *H. pylori* evades host immune responses by various mechanisms.\(^{17}\)

Natural *H. pylori* infection leads to a systemic and mucosal antibody response with induction of IgG, IgA, and secretory IgA. However, this response fails to eradicate the infection which usually persists throughout life. The infection induces a predominantly Th1 response that fails to clear the organism and may therefore contribute to tissue damage.\(^{37}\) This behaviour may be due to production of proinflammatory cytokines such as interleukin IL-1, IL-2, and IL-8.\(^{39}\) Mucosal protection against non-invasive bacterial infection is best mediated by a Th2 response (SIgA and IgG), which is induced by IL-4, IL-5, and IL-6.\(^{36}\)

Recently, it has been reported that in mice, progression of *Helicobacter* induced gastritis and gastric atrophy mediated by type 1 helper cells was modulated by concurrent parasitic infection.\(^{40}\) There was a shift in the pattern of cytokine expression consistent with a Th2 immune response and corresponded to a significant reduction in mucosal hyperplasia, mucosal metaplasia, and glandular atrophy. In recent studies, measurements were made of the IgG subclass antibody response, considered to be a biomarker of the T helper cell response in *H. pylori* positive children and adults from Soweto, Germany, and Australia.\(^{41}\) It was found that in Sowetans, the IgG subclass response was predominately I-G, (suggestive of a Th2 response) whereas in Australian and German groups it was a predominately IgG2 subclass response 'suggestive of a Th1 response). It was concluded that the immune response to *H. pylori* in Africans in Soweto may relate to childhood exposure to a myriad of gastrointestinal pathogens.

**Conclusion**

Developing countries almost invariably are characterised by poor sanitation and housing, with overcrowding and lack of access to clean water. Rapid urbanisation is occurring in many regions of Africa, leading to marked changes in lifestyle-diet, decrease in physical activity but increases in smoking and alcohol consumption, all features of populations in transition. However, despite some environmental factors which favour an increase in the incidence of Western degenerative diseases, the incidence remains low. It is our belief that the critical events which occur in early infancy lay the foundations for a healthy gastrointestinal tract which can withstand insults that may occur in later life. Central to this hypothesis is the quality of the intestinal bacteria, the integrity of the immune
system, and dietary factors in early childhood. It is believed that this combination of factors may explain the paucity of Western digestive diseases in African adults, despite the rising prevalence of factors propitious for their increase.

References
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