Occasional viewpoint

'Tropical sprue': some early investigators favoured an infective cause, but was a coccidian protozoan involved?

Overwhelming evidence now exists that 'tropical sprue' ('post-infective tropical malabsorption') has an infective basis; progression to the overt clinical syndrome—from an initial acute gastrointestinal infection—is probably under genetic control. The nature of the initiating infection might well differ in disparate geographical locations. Historically, many physicians had considerable reservations about such an aetiological background. Two early twentieth century clinical investigators (both clearly ahead of their time) seem however, to have been convinced that microorganisms (including protozoa and fungi) played a significant role.

In 1912, Charles Begg (1852–1931) considered 'tropical sprue' to be associated with the proliferation of luminal micro-organisms; in fact, he wrote: 'That the disease is caused by an invasion of micro-organisms (in the small-intestine) was first suggested by me in 1890, and is now the generally accepted theory'. On an epidemiological tack, Begg cited an 'outbreak of sprue in a Chinese port' in which 'evidence pointed strongly to a certain water-supply being the cause of all the cases that occurred there'. He seems to have been significantly influenced in his conclusion(s) by a necropsy report compiled by a Dr Wethered in January 1890 and quoted by George Thin:

'In the jejunum (wrote Begg) slight inflammatory reaction was noticed, as shown by the presence of exudation cells, and some destruction of Lieberkühn's follicles; but the most severe changes were found in the ileum where 'the morbid process began ..., and extended from there' and 'The mucosa was almost entirely destroyed, being replaced by a structureless material containing leucocytes, and here and there the remains of a follicle ... The mucoid material ... was studded with rod-shaped bodies that had taken on some stain, but this proved fugitive ...'. He also recorded observations on faecal flora: 'Out of a number of organisms contained in a single drop of fluid motion, thirteen distinct varieties were isolated, each of which was developed in gelatin and was perfectly distinctive'. Begg was of the opinion that the disease was '... frequently complicated by the presence of parasitic enteroza (hemithmus), and especially anchylostomum (sic)'.

In 1915, P H Bahr (later Sir Philip Manson-Bahr) (1881–1966) divided the possible causes of tropical sprue (which 'Contrary to the opinion hitherto held ... occurs amongst the natives irrespective of race or mode of life') under: climatic, dietetic, and specific. Beneath the last heading (in a search for a 'specific' pathogen) he considered: verminous (hemithmic), bacillary, and fungoid theories. Bahr cited evidence (which he considered most compelling) for the latter and referred to a paper (on fungi) by A Castellani and G C Low; he concluded: 'They consider that sprue is really a communicable protozoal disease'. He also devoted an entire (albeit short) chapter on 'Evidence in favour of and against regarding sprue as a blastomycotic infection'. Bahr seems to have been convinced that 'yeasts' were aetiologically important, and wrote of '... cells (in faecal samples which) resemble yeasts in shape and in their affinity for iodine (a property peculiar to the group)'; 'From a microscopical examination alone (he concluded) it is almost impossible to decide whether these structures (are) pure yeasts or organisms identical with Blastocystis enterocola ...'.

Despite incontrovertible evidence that 'tropical sprue' has an infective basis, doubt about the identity of the initiating pathogen(s) remains. Although ileal (and jejunal) colonisation with mixed faecal flora (largely bacterial) seems likely, the possible role of one or more protozoan parasites as being initially relevant aetiologically has again come to the fore; Cryptosporidium parvum, Isospora belli, (possibly Blastocystis hominis), and most recently Cyclospora cayetanensis have been identified in faecal samples (and small intestinal biopsy specimens) of people suffering from various forms of prolonged infective diarrhoea. 7 8 Jejunal histology (the small intestine has a limited variety of responses to injury) and absorption defects in early cases of 'tropical sprue' and C cayetanensis infection are similar; also, the natural history of these diseases can be impossible to differentiate on clinical grounds. Limited evidence exists that a C cayetanensis infection rapidly responds to co-trimoxazole, 10 but efficacy of this and other antimicrobials (apart from tetracycline) has not been adequately evaluated in 'tropical sprue'. Castellani and Low's 1913 prediction that 'tropical sprue' will 'ultimately turn out to be an infectious disease, probably of protozoal origin' has been given a new impetus. Some of the early twentieth century observers might in fact have been several decades ahead of their time!

Differentiation of coccidia from yeast (and other fungal) spores can even today, prove difficult. Numerous small intestinal biopsy specimens (most preserved in paraffin wax blocks) from former times remain extant in pathology laboratories worldwide; careful examination—using appropriate staining techniques (especially those recently developed for identification of small intestinal coccidia)—might assist in elucidation of the aetiology of 'tropical sprue' encountered in past ages.

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