Post-Infectious IBS

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Definition

We have defined Post infectious IBS (1) as acute onset Rome II criteria positive IBS developing after an infectious illness characterised by two or more of the following; fever, vomiting, acute diarrhoea, positive stool culture. Post infective IBS is of particular interest because it is "nature's experiment". Unlike most other IBS there is a clearly defined start date, and the condition is more homogenous, being mostly D-IBS.

Epidemiology

There have been at least 5 prospective studies of patients with culture positive infective gastroenteritis showing that 7 -31% progress to develop post infective IBS (PI-IBS) when assessed 3-6 months after infection (Table 1). When compared with uninfected controls two studies have shown an increased risk of developing IBS OR = 10.1, 95% CI = 3.32-30.69 (2;3).

Risk factors for developing PI-IBS

The strongest risk factor for developing PI-IBS is the duration of initial illness. Those with an initial illness lasting >21 days were 11.4(2.2-56) [mean (95% CI)] times more likely to get PI-IBS than someone whose illness was < 7 days. Females were also more at risk than males (RR 3.4(1.1-9.5) while those over 65 years were at reduced risk (RR 0.36(0.1-0.9) (4). Gwee also found females at greater risk (RR 2.5) but when Hypochondriasis was controlled for the gender effect was no longer significant (5). Later studies also found that when depression and anxiety were controlled for female sex was no longer a significant factor (6) suggesting it is merely a confounder acting via the known greater incidence of such adverse psychological factors in females. Adverse life events also increase

the risk of PI-IBS (RR 2.0(1.7-2.4) (5). When just a single organism is considered then bacterial toxicity appears important with a RR of 10.5(1.4-76) of developing persistent bowel dysfunction after *C. jejuni* infection if the bacteria produced elongation of HEp2 cells in culture (7).

Clinical Features

The clinical features fit the D-IBS subtype of IBS with pain, loose stools, urgency, bloating and mucus per rectum all significantly increased(5). A 5 year follow up study showed recovery to normal bowel habit in only 40% overall and none of those with chronic psychiatric disease (8).

Pathophysiological Changes Following Infection

These include an immediate acceleration of transit (5) and development of rectal hypersensitivity. Small intestinal permeability is also increased in virtually all individuals, however in those who develop PI-IBS, this abnormality persists for years(9). Following *Campylobacter jejuni* enteritis there is a universal rise in mucosal inflammatory cells including T lymphocytes (CD4+ and CD8+), calprotectin positive macrophages (CD68+ve) and enteroendocrine cells. These changes, which were seen in nearly all individuals at two weeks, started to subsided but remained abnormal even at 12 weeks (9). The increased risk of PI-IBS with evidence of greater inflammatory changes has been shown by two authors Gwee (5) and Dunlop (6). A recent study from China also confirms these findings (10), which were however found both in PI-IBS and D- IBS without an obvious infective precipitant. Lymphocytosis was noted in this study, not only in the rectum, but also throughout the colon and the terminal ileum, where mast cells were also increased. Mucosal lymphocytosis is likely to be associated with increased mucosal inflammatory cytokines and increased levels of interleukin-1β mRNA as have been demonstrated in PI-IBS, both during infection and 3 months afterwards (10;11).

Enteroendocrine cell (EC) hyperplasia is also a feature noted after Campylobacter enteritis with an approximately 25% increase in EC cell numbers in those who develop PI-IBS compared with infected controls who did not develop IBS (6).

Evidence of altered serotonin bioavailability

Several studies have indicated increased release in D-IBS (12) (13) (14). An enhanced release of 5HT was seen in 15 PI-IBS patients compared with 15 constipated IBS and 15 healthy controls (13).

Role of Mast Cells

Although mast cells are not increased in rectal biopsies of PI-IBS they are increased in terminal ileal biopsies (10). Furthermore, biopsies of the descending colon in IBS have been shown to release more histamine and mast cell tryptase(15), agents which are known to excite afferent nerves.

Effect of inflammation on serotonin transporter

Increased plasma levels of 5HT might be due not to increased release but to impaired clearance. One recent study (16) has shown reduced mucosal immunostaining for SERT and reduced mRNA in colonic biopsies from both D-IBS and constipated IBS, similar to that seen in ulcerative colitis. Animal studies suggest than inflammation can impair expression of SERT which might underlie some cases of PI-IBS.

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Table 1

Incidence of Post infectious IBS after culture positive gastroenteritis

Author (Reference)	Year	N	Percent developing IBS	Comment
Gwee et al (17)	1996	75	31%	Hospitalised patients with infective gastroenteritis
Neal et al (4)	1997	390	7%	Community cases
Thornley et al (7)	2001	180	9%	Community cases Campylobacter infection
Dunlop et al (6)	2003	747	13%	Community cases Campylobacter enteritis
Parry et al (18)	2002	500 cases 705 controls	16% v 1.9%	Community cases Case control design
Ji et al (19)	2005	101 cases 102 controls	7% v 0%	Salmonella outbreak Case control design