

RELATIONSHIP BETWEEN ANTIBIOTIC THERAPY, CFS, SLEEP, AND MURAMYL PEPTIDES

Chronic Fatigue Syndrome (CFS) is a medical condition which is currently diagnosed on the basis of clinical assessment (15,21,26,35), and exclusion of other known causes of fatigue (15,16,35). There is no well accepted evidence of a single specific pathological process in CFS to date (11,13,15,18,21,26,36), and no specific therapy which is generally accepted to be curative (11,18,16,35,36). The syndrome may represent a final symptom complex representing a number of different medical conditions (3,10,11,14,25,35). Putative causative agents include: chronic viral infection (10,13,15,16,30,33,39,40,41); alterations in limbic system neurochemistry (4,10,12,32,37); allergy (10,13,16); chronic immune activation (17,22,26,29,30,38); exposure to environmental toxins (9,3,7,3); and psychological stress (1,13,32,36). We summarise here long-term observations of a group of patients who fulfil the CDC criteria for CFS, and who demonstrate a remarkable similarity in their medical history and onset of symptoms.

Of 98 consecutive patients referred to a medical practice in Sydney in whom the final diagnosis of CFS was made, 62 (63%) presented with the a history of long-term use of broad spectrum antibiotics (more than 6 months continuous use, or 12 months intermittent use over a 3 year period). In this group, the most commonly reported antibiotics were the tetracyclines.

After the cessation of antibiotics in these 62 patients, the following pattern of symptom complexes were observed;

1. Irritable Bowel Syndrome (IBS) within 3 years (55/62 patients, 89%)
2. development of specific sleep complaints (long sleep latency, frequent nocturnal awakenings, sleep 'inertia', and daytime sleepiness) (40/62 patients, 65%)
3. development of both IBS and these specific sleep complaints (40/62 patients, 65%)
4. between 3 and 8 years following the cessation of antibiotics, the development of CFS (62/62 patients, 100%).

We hypothesise that disturbances in intestinal microflora caused by broad spectrum antibiotic use (9), may lead to the development of altered sleep patterns and ultimately CFS. Muramyl peptides from the cell wall component of bacteria in the gut have been shown to modulate mammalian sleep (7,8,9). While not synthesised by mammalian cells, muramyl peptides are now accepted as a part of normal mammalian physiology . They are known to induce the immune response, slow-wave sleep, fever and malaise, anorexia and adipsia, and to activate the acute phase response. In addition, certain infections of the gastrointestinal tract have been linked with CFS (25).

Much of the complex symptomatology of CFS, as well as the high incidence of IBS and sleep disorders in the group, may be explained by these and other known effects of muramyl peptides. IBS has also been found to be associated with specific sleep disorders (18,31).

Sterilisation of the gut and subsequent recolonisation with non-pathogenic enteric bacteria resembling normal human bowel flora has been shown to significantly improve IBS in certain patients (3), and our experience suggests that patients so treated frequently experience improvements in both quality of sleep and severity of CFS symptoms.

We note the unexpectedly high proportion of referred patients with CFS who fitted this particular pattern of onset of CFS, and suggest that this may represent either a bias in the pattern of referral of patients to this particular medical practice, or a common history for many sufferers of CFS which had not previously been noted because of the long latency between initial antibiotic use and subsequent development of CFS.

We conclude that long-term broad-spectrum antibiotic use may be a significant factor in the onset of CFS.

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