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# EDITORIAL

# Infections and body weight: an emerging relationship?

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In the April issue 2002 (pages 464–468), Dart *et al*[1] published their study examining relationship between antibodies to *Chlamydia pneumoniae* and various risk factors for coronary heart disease (CHD). Although this is not the first study of its kind, the results are certainly of interest. Several studies have shown an association between *C. pneumoniae* and CHD,[2–4] whereas some studies have failed to observe this link.[5–7] Dart *et al*[1] hypothesized that the association of *C. pneumoniae* with CHD is in fact due to its association with risk factors of CHD. The authors screened 43 newly identified cases of CHD and 127 matched controls without CHD, who were attending health screening clinics in Australia, for the presence of serum IgG and IgM against *C. pneumoniae*, *C. trachomatis* and *C. psittaci*. None of the subjects had IgM against chlamydia and only four were positive for *C. trachomatis* and/or *C. psittaci*.

The prevalence of seropositivity for *C. pneumoniae* was not significantly different for subjects with or without CHD. Similarly, a number of known CHD risk factors such as hypertension, serum lipids and glucose levels lacked a significant difference between the antibody positive and negative groups. The antibody positive group had significantly greater body mass index (BMI) and smaller low-density lipoprotein (LDL) particle size. Antibody prevalence was significantly greater for subjects with insulin levels above the median and for those with LDL particle size below the median. These are the main positive findings of the study. However, after multivariate analysis, only BMI continued to be associated with seropositivity.

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Although a lack of association of *C. pneumoniae* antibodies with CHD negates the basic premise of the author's hypothesis, an association of increased BMI with seropositivity is very intriguing. It is difficult to explain greater prevalence of antibodies in the highest BMI quartile as well as greater BMI of the antibody-positive subjects. As the authors point out, impaired immunity of obese subjects is unlikely to account for the observed effect. Only about 10% of the subjects were obese and it is not known whether immune response of even non-obese subjects is linked to their BMI. Also, unlike *C. pneumoniae*, antibodies to *C. trachomatis* and *C. Psittaci* did not show such a selective or high prevalence among those with higher BMI. The third explanation offered by the authors, which has neither been proved nor disproved in the study, is that *C. pneumoniae* infection may be causally related to increased BMI.

Although the increase in BMI due to *C. pneumoniae* infection appears somewhat implausible, after the well-known demonstration of the causative role of *Helicobacter pylori* in gastric ulcer the involvement of infections in body weight gain may not be far-fetched. Indeed, an emerging body of evidence in the recent literature has shown an association of several infections with obesity. Starting with the report of Canine Distemper Virus causing obesity in mice,[8] five viruses have been shown to cause obesity in animals.[9,10] Of the five viruses, two adenoviruses, avian adenovirus SMAM-1 and human adenovirus Ad-36, are associated with human obesity.[11,12] In addition to the role of infections, the evidence linking inflammation with obesity is steadily accumulating. Elevated levels of interleukin-6[13] and C-reactive proteins[14] are observed in obese individuals. Interestingly, in a 3 y follow-up study, Duncan *et al*[15] showed that markers of inflammation can predict weight gain in middle-aged adults. It is not clear whether the inflammation linked to obesity was due to any particular infection. Considering the well-documented adipose tissue involvement with modulators and mediators of immune response,[10] a close interaction of adipose tissue, immune system, inflammation and certain

infections is conceivable. It appears that, in the presence of certain infectious agents, this interaction leads to expansion of adipose tissue. The mechanism involved in this process is not completely understood.

The etiology of obesity is multifactorial, and includes obesity of neural, endocrine, pharmacological, nutritional, environmental, seasonal, genetic, idiopathic or of viral origin.[16] The identification of various etiological factors is *critical and fundamental* to appropriately targeting obesity treatment, in order to increase the success rate. Therefore, new factors hinting at a causative role in weight gain deserve a very careful consideration. To date, none of the claims has conclusively demonstrated a role of pathogens in human obesity. Perhaps, some (or none) of the claims will survive the scrutiny of future investigations. As for *C. pneumoniae*, the observed association with BMI may prove to be a causation, or may have another explanation, hitherto unknown.

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