Nutrition & the Immune system

By Dr Paul Clayton

There is good reason to believe that levels of individual and herd immunity are generally sub-optimal; and this has inevitable consequences in terms of increased susceptibility to infectious illness, and an increased incidence of cancers.

There are many reasons for sub-optimal immunity, such as the widespread use of immuno-suppressant medications (including glucocorticoids and chemotherapeutic agents), and the increasing prevalence of HIV, which in 2004 had infected a cumulative total of 70 million people worldwide and is projected to reach 100 million by 2010. To these must be added stress, which suppresses immune function via the classical hypothalamic-adrenocortical loop, and depressive illness that acts in exactly the same way. In this hyper-mobile world, you can't forget air travel: a trans-Atlantic flight exposes the traveller to the equivalent of 4 whole-body X-rays, and all the while you are inhaling the respiratory pathogens exhaled by your fellow-passengers. No wonder long-haul flights are so often followed by an URTI! And then last, but by no means least, is malnutrition.

TWO TYPES OF MALNUTRITION

Type A malnutrition, characterised by a deficiency of a single micronutrient (often the water-soluble vitamins C, B1 and B3) and often combined with calorific deficit, is uncommon in the developed nations. Instead, what we see is a pattern of multiple micro- and phtonutrient depletion, generally combined with calorific balance or excess. This is termed Type B malnutrition, or dysnutrition; and it is emerging as a likely common cause of the majority of the degenerative diseases, and much of the process of ageing as we know it.

The reasons for this prevalent pattern of multiple micronutrient depletion are structural and well established. Perhaps the single most important cause of Type B malnutrition is that we don't eat enough. This sounds paradoxical, given that we are getting fatter, but we actually eat far less than we used to. Read, for example, accounts written by the diarists James Boswell or Samuel Pepys of the vast lunches and dinners that were regularly consumed by our relatively recent ancestors. But then remember that those diners and lunchers walked or rode horseback where we drive, climbed stairs where we take elevators, and burned calories to keep warm where we turn up the central heating.

Looked at through a longer lens, humans were designed to live active lives, and to consume between 3 and 4 thousand calories per day. No longer hunter-gatherers, we live sedentary lives, working at a computer screen during the day and basking in the glow of the cathode ray tube at night. The result is that we burn, on average, slightly fewer than 2,000 calories a day. Our appetites have indeed shrunk, but not quite to match; thus leaving most of us in a slight but persistent state of calorie excess, which explains, over time, the weight gain.

But by cutting our food intakes in half, we have at a stroke halved our intakes of many of essential micronutrients. To make matters worse, our dietary habits are out of joint. We no longer eat very much unprocessed foods, but increasingly rely on pre-processed, pre-cooked and ready to eat meals and snacks which in many cases are significantly less nutritious than the original ingredients would have been.

These and other factors have dramatically reduced our intakes of such valuable micro- and phyto-nutrients as flavonoids, sterols, phospholipids, methyl groups, selenium and resistant starch; resulting in the wide-spread problem of Type B malnutrition we see today. But does it matter? Well, yes ….A person who is depleted in anabolic co-factors and the anti-catabolic agents is heading for

trouble. Tissue renewal is down, tissue decay and breakdown are up; he or she is now catabolically dominant, accumulating tissue damage, and heading towards clinical illness.

To make matters worse, Type B malnutrition generally worsens as we age, due to such factors as dental problems, difficulties with swallowing, a deteriorating sense of taste and appetite, and often reduced finances. This neatly explains why we become progressively more catabolically dominant, and ever more likely to become diseased, as the years and decades pass. It also explains why, as we age, our immune functions tend to become ever more compromised.

Indeed, sub-optimal immunity is prevalent in elderly in the community (Eddington et al ’99, Bogden et al ’94, Jain ’02, Meydani et al ’97, Ravaglia et al 2000); and responds well to basic nutritional support. Perhaps more worryingly, the same problem is found in hospitals. In recent studies of hospital admissions, it was found that up to 69% were malnourished (Gallagher-Alredd et al ‘96), which was sufficiently severe in 30-40% of cases to cause leucopenia (Bistrian et al ’76, Naber et al ’97). Introducing immuno-suppressed patients into an environment where antibiotic resistant bacteria are selectively bred is like introducing petrol to a match, and explains why the struggle to reduce the incidence of hospital-acquired infection via improved hygiene has been so unproductive. A more sensible approach would be to ensure adequate nutrition, a strategy shown to be effective in a number of studies (ie Daly et al ’84, Andrassy et al ’85, Fietkau ’98).

The evidence strongly suggests that if you want to maximise your chances of remaining free of bacterial and viral infection, and given the prevalence of Type B malnutrutrition, a comprehensive micro-nutritional support programme is a good starting point. But you can do more. Many micronutrients play an essential role in immune function (at least 20, according to the scientific literature), but some may be more important than others; and they affect many different aspects of immune function.

TWO IMMUNE SYSTEMS

The immune system can be divided into two distinct but over-lapping sub-systems; the innate and the adaptive immune systems. The adaptive immune system is the one with the memory function, and is involved in immunisation, allergy and auto-immunity. Once the adaptive immune system has learned to recognise an enemy (after an initial infection or after vaccination), it remembers the enemy's characteristics. On second exposure to the threat the memory cells recognise it, and generate an immune response involving highly specific weapons such as antibodies. This is a powerful, sophisticated and highly specific system, but it is complex, slow to mount and often insufficient to protect the host against the first onslaught of a virulent bacterium or virus.

The very complexity of the adaptive immune system can cause problems. In autoimmune disease the adaptive immune system confuses an element in the body with a pathogen that it partly resembles, and attacks the host's own tissues (as in rheumatoid arthritis, Multiple Sclerosis, Systemic Lupus, Hashimoto's thyroiditis etc). In allergy, the adaptive immune system over-reacts to a stimulus such as animal dander or a species of pollen, and causes the well-known symptoms of allergic conjunctivitis, rhinitis or asthma.

The innate immune system is rather more basic. In evolutionary terms it is much older than the more sophisticated acquired immune system. It is less specific; and its key components are macrophages and Natural Killer (NK) cells. Broadly, these patrol the body and look out for anything that doesn't belong there. If macrophages spot a bacterium they swallow it whole and try to digest it. If NKcells recognise a virally infected cell or a cancer cell in the body they will kill it so that it cannot produce more viruses, or replicate.

Perhaps because the innate immune system is an older system, and also because it was long believed that it could not be manipulated in any therapeutically useful way, the innate immune system has been overlooked as a therapeutic target. That, however, is all changing. It is now widely understood that it is the innate immune system that keeps us healthy most of the time. After all, we are crawling with pathogens every second, but overt infection, when the adaptive immune system is activated, is relatively infrequent. Babies with genetic errors that damage the adaptive immune system can live into their 20's or even 30's, given adequate medical care; foetuses carrying genetic errors that knock out innate immune function are invariably still-borne. And finally, 75% of all life forms possess only an innate immune system, and manage very well indeed without an adaptive immune system; these are the arthropoda.

Unlike the adaptive immune system, the innate immune system springs into action the moment it recognises the presence of a pathogen. It is our first line of defence; the adaptive immune system is the second line.

NUTRITION FOR THE IMMUNE SYSTEMS

As the numbers of antibiotic resistant bacteria in our environment continue to increase, it makes good sense to ensure that your immune systems are working as effectively as possible. But as with the acquired immune system, there is persuasive evidence that the innate immune system is too often in disrepair, due again to malnutrition.

As with the immune system overall, therefore, a comprehensive micronutrient support programme is a good foundation. Onto that foundation you can add a second layer of very specific innate immune support agents. They include vitamin D, the trace element selenium, and the 1-3, 1-6 beta glucans derived from yeast. The beta glucans in particular have a very critical role to play, as they actively prime innate immune cells via the CR3 receptor (Czop & Austen '85); one of a small group of so-called Toll-like receptors which must be occupied if the overall innate immune system is to respond appropriately to the presence in the body of a pathogen (ie Mukhopadhyay et al '04).

Selenium is important too, as it is critical to NK cell function (Kiremidjian-Schumacher & Roy '98); selenium depletion is particularly prevalent in the UK (Rayman '97), and has been shown to impair immune responses to viral infection (ie Beck et al '03). Like selenium, vitamin D is also essential to innate immune cell functions (ie Wang et al '04, Malbriss et al '05); and also like selenium, depletion is very common (Norman et al '07, Vieth et al '07). Supplementation with D at doses of up to 10,000 IU's / day is therefore also recommended (Norman et al '07, Vieth et al '07),

THE LACTOPEROXIDASE SYSTEM

Finally, let us consider the lactoperoxidase (LPO) system, a major innate immune effector mechanism, which plays a critical role in the defence of the respiratory and gastrointestinal tracts (ie Wijkstrom-Frei et al '03).

The salivary, mammary and other glands secrete LPO well as the thiocyanate ion (SCN-, derived from diet). The enzyme catalyzes the oxidation of SCN- by hydrogen peroxide (H2O2). The H2O2 is excreted by oral bacteria and by host cells in amounts which vary with the state of cellular metabolism, diet and other factors. Oxidized forms of SCN- inhibit the growth, respiration and metabolism of many species of bacteria, including staphylococci (Johansen et al '97), streptococci, E. coli, pseudomonads (Bjork et al '75, Reiter et al '76), Haemophilus influenzae (Wijkstrom-Frei et al '03) and many others. As a result of the rapid consumption of H2O2 by LPO, host cells are

protected from a toxic build up of this potent oxidizing agent. (The major product of the reaction, OSCN-, does not harm human cells.)

LPO is iron-dependent (ie Sharonov '95), and as iron depletion and indeed deficiency is among the most common nutritional problems likely to be encountered – and certainly among women of child-bearing age – iron supplementation should also be considered as an essential element in any pharmaco-nutritional programme designed to support immune function.

ALLERGY

We cannot leave the subject of immune function and malfunction without commenting on the dramatic rise in asthma and allergy that has occurred over the last 30 years. As the genetic makeup of our populations have not altered in this very short period of time, it is clear that environmental factors must be responsible for the changes; and the prevailing theory which purports to explain this change is the 'hygiene hypothesis.' According to this theory, advances in sanitation and medicine have reduced the burden of infection and/or pathogenic challenge to an abnormally low level, leading to immune imbalance. More specifically, the level of macrophage activation determines their pattern of secretions of the interleukins IL 6, 10 and 12; which in turn, act on naïve T-helper (TH0) cells, to affect TH1 / TH2 ratios. Low levels of macrophage activation (as in an over-sanitised environment) lead to a reduced TH1 / TH2 ratio, and this abnormally low TH1 / TH2 ratio is considered to be central to the generation and maintenance of allergy.

1-3, 1-6 beta glucans, by mimicking a mould infection, and via activation of the CR3 receptor, trigger intense macrophage activity. These innate immune cells then change their pattern of interleukin secretion back to a more 'normal' one, and restore a more 'normal' TH1 / TH2 ratio (ie Kirmaz et al '05, Dillon et al '06) NB.'Normal' here means an immunological configuration better suited to dealing with an environment containing multiple and chronic pathogenic challenges, such as the environment we evolved in.

SUMMARY

Sub-optimal immune function is common-place, and undoubtedly contributes to unnecessarily high rates of infection in hospitals and in the community. Type B malnutrition is a common cause of this reduction in immuno-competence, together with the lack of 1-3, 1-6 beta glucans in our diet, due to over-sanitation of the food chain. A wide-spectrum pharmaco-nutritional support programme, which includes the key micro- and phyto-nutrients together with 1-3, 1-6 beta glucans, will improve overall immune performance in most cases and must be one of the most cost-effective ways of reducing the burden of infection – and allergy - in all areas of clinical practice.

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