

The topic of childhood vaccinations is highly controversial with a strong polarization of beliefs among health care professionals and the public. Many conventional medical professionals believe that vaccinations in childhood provide the ultimate form of prevention for infectious diseases (Dennehy, 2001). Strong advocates of this belief system support the funding of research aimed at the development and subsequent delivery of vaccines for every known disease-causing microorganism. Many naturopathic medical professionals believe that there are effective alternatives to preventing infectious disease and that childhood vaccinations are over-prescribed. Strong supporters of this belief system view interventions designed to strengthen the body's own internal defense mechanisms as the best form of prevention for infectious disease.

Regardless of the belief system that health care professionals subscribe to, a number of issues must be considered before an objective, rational, informed decision can be made:

**1) The probability of acquiring the disease**

- This would differ depending on whether the child was staying in a developed country or traveling to a developing nation.

**2) The risks of significant disease caused by the organism**

- It is more difficult to justify vaccinations against microorganisms that only cause relatively benign diseases with very slight risks of complications than to justify vaccinations against common pathogens that cause significant disease with a relatively high risk of complications.

**3) The putative risks of vaccination**

- There are many additives to vaccines that may or may not be associated with significant diseases or reactions. The risks of certain vaccines must be carefully weighed against their reported benefits (Busse, 2004).

**4) The reported efficacy of the vaccine**

- There are a number of vaccines like influenza (Simonsen et al., 2005) and varicella (Galil et al., 2002a&b, Lee et al., 2004, Vazquez et al. 2004) with limited reported effectiveness. The validity of continued support for these vaccines has to be called into question.

**5) Our knowledge of the organism that causes disease.**

- Certain microorganisms like influenza A, rhinovirus and rotavirus undergo significant antigenic variation during their replication (Mims et al., 2004) and therefore, it is highly unlikely that we will be able to accurately predict in what direction they will mutate and design an annual vaccine accordingly.

**6) How vaccines influence the developing immune system.**

- Vaccinations are given to healthy children (and other populations) with the sole purpose of strengthening immune defenses against infectious disease agents. Therefore, vaccines should support and not interfere with immune system functions.

Vaccinations in childhood do not promote the normal development and balance of the immune system. This paper will discuss how vaccines affect the immune system and some of the potential consequences of this. I will also introduce some Naturopathic approaches that might be included to help balance immunity if the choice to vaccinate is made.

### Natural immunity

The immune system must be balanced to provide optimal protection against disease. Disease will occur if the immune system is too weak to mount a sufficient immune response, immunopathology will result from a hyperactive immune response and auto-immunity will result if there is an imbalance between immune responses to self-antigens compared to foreign antigens. Much of the balance for the immune system and therefore, the future protective ability is determined in childhood.

### The Immune system generalized

There are two major types of immune protection, innate immunity and adaptive or acquired immunity. Innate immunity is relatively non-selective and protects against disease from most pathogens, regardless of whether or not there has been previous exposure. Examples of components in the innate immune system include mucosal membrane and skin integrity (the first line of defense are external membranes), optimal acidity in the gastrointestinal tract, reproductive tract and on the skin, other secretions like lysozymes, defensins, mucous and ciliary beating etc. Specific cells like natural killer (NK) cells, phagocytic cells of the mononuclear phagocyte system (Kuppfer cells in the liver, alveolar macrophages in the lungs, microglia in the brain, histiocytes in the skin, dendritic cells in the lymphoid tissue, reticuloendothelial cells in the spleen and osteoclasts in bone), the components of complement, other phagocytic cells like neutrophils, mast cells, monocytes/macrophages and eosinophils. The processes of fever and inflammation also play a major role in our defense against pathogens. Many cellular inflammatory mediators like histamine, kinins, prostaglandins, c-reactive protein and cytokines like IL-1, TNF-alpha and IL-6 are involved in these processes. A relatively recently described inflammatory marker, with unknown function in infection, is calcitonin. Another very important part of innate immunity is to prevent the attachment, colonization and overgrowth of pathogenic microorganisms in the gastrointestinal tract (GIT). An appropriate balance of relatively non-pathogenic, commensal bacteria in the GIT fulfills this role (Roitt et al., 2001).

Adaptive or acquired immunity is relatively more specific than innate immunity and requires previous exposure to immunogenic material. There is a certain period of time (often in the thymus gland or bone marrow) where naive cells are “educated” to recognize self versus non-self and react accordingly. This process is necessary for the humoral immune system to amount an appropriate immune response to pathogens. A certain amount of memory is created in the humoral immune system with exposure to pathogens previously encountered initiating a more rapid, more specific response.

The adaptive immune response has two major arms; cell mediated immunity and humoral immunity. Cell mediated immunity protects against intracellular pathogens and therefore, provides a more localized reaction. Humoral immunity protects against extracellular pathogens in the blood, lymph and cell surfaces and therefore, provides a more systemic response. Either arm of the adaptive immune system can be activated during infection; the relative dominance of each arm is largely dependent on which helper T cell set is activated. This depends on the pathogen/ toxin engulfed and presented to the naive T cells and the cytokines subsequently released. If there is a relative abundance of Th2 cell stimulation, the humoral arm is relatively more active. Conversely, if there is a relative

abundance of Th1 cell stimulation, the cell mediated arm is more activated. There are times when it is necessary for one arm of the immune system to be relatively more active than the other. However, it is important that a balance between Th1 and Th2 stimulation is re-attained after these periods of time are over. If one arm remains relatively over-activated for extended periods of time, pathology can result. For example, chronic Th1 polarization is linked to diseases like Hashimoto's thyroiditis, multiple sclerosis, type-1 diabetes mellitus, Crohn's disease, sarcoidosis, uveitis, celiac disease, H. pylori infection, ulcerative colitis etc. The fact that Th1 polarization is linked to H. pylori and H. pylori infections have been associated with Type B gastritis, PUD and arteriosclerosis suggests an indirect link between Th1 polarization and many GIT disorders as well as CVD. Chronic Th2 polarization is linked to asthma, eczema, allergies, endometriosis, cancer and chronic fatigue immune deficiency syndrome and other diseases.

It is important to note that the two main components of the immune system are not mutually exclusive but rely on each other for reinforcement and proper activation. That is, there is never exclusive cell-mediated immunity or humoral immunity but a relative abundance of one or the other.

Our current understanding of the balance between Th1 and Th2 dominated adaptive immunity has recently been expanded to include a gastrointestinal tract derived Th3 cell. Th3 cells differ from other Th cells; they have a different lineage (GIT derived than bone marrow derived), they are not "educated" in the thymus gland and they are stimulated more vigorously by microdoses of antigen rather than macrodoses. Although many of the roles of the Th3 cell are yet to be established, it appears that this cell plays a major role in oral tolerance in the GIT, allowing us to effectively ingest most food substances without reacting to them. They also play a major role in balancing Th1: Th2 levels and therefore, the two major arms of the immune system. The major cytokine involved in initiating Th3 dominant responses is transforming growth factor beta (TGF-beta).

### Mucosal immunity

For the human immune system to develop optimally it must be exposed to infectious microorganisms via the normal pathway of exposure during early years of development. The most common route of acquiring infectious microorganisms is through exposure to mucous membranes of the respiratory and/or gastrointestinal tract. Most pathogens must adhere to mucosal epithelial surfaces in the respiratory and/or gastrointestinal tract to colonize, invade and cause disease. If the pathogens or toxins cannot initially bind to the epithelium, they are washed out of the body by secretions and are therefore, rendered harmless. One of functions of IgA antibodies is to prevent bacteria, viruses and toxins from binding to epithelial surfaces.

Once the mucosal barrier has been breached, these pathogens are processed by specialized epithelial cells termed M cells and presented to intraepithelial lymphocytes in the Peyer's patches, lamina propria and intraepithelial compartment (Anderson, 2004; Roitt et al., 2001). Specific cytokines released from these activated cells can then stimulate various types of immune responses. One of the most common responses in mucosal membranes results in secretion of the IgA class of antibodies, the most abundant class of antibodies in the body. IgA is manufactured and secreted into gastrointestinal fluid, saliva, tears, urine and other bodily secretions (Roitt et al., 2001). IgA antibodies serve to prevent bacteria, viruses and toxins from binding to epithelial surfaces as well as have some neutralizing effect against certain viral pathogens as they pass through the M cells in the Peyer's patches. Although mucosal immunity is not well understood, we know that viral infections initiate a non-specific increase in NK cell activity, type I interferon production and activation of cytotoxic T

cells (Freihorst and Ogra, 2001). Secretory IgA molecules play an important role in clearing microbial infections and preventing or modifying disease after re-exposure.

There is some evidence that the route of exposure of pathogens triggers an immune system response that is compartmentalized somewhat and will therefore, mount a complete, long lasting immune response only to pathogens reintroduced in the same way. This means that antigens introduced by intramuscular injection, like most vaccines, will stimulate cytokine releases and formation of immunological memory (more specifically IgG and IgM class antibodies) that will work best against re-exposure to pathogens in the blood but not necessarily against disease agents that primarily affect the mucosa. "Parenteral immunization usually fails to stimulate mucosal lymphatic tissues to generate protective IgA antibodies or antigen specific intra-epithelial lymphocytes" (Anderson, 2004). As a result, parenteral vaccines will not provide the best memory and subsequent immune response to pathogens introduced across mucosal barriers; the most common route of subsequent exposure to pathogens. Also B cells and T cells that have the first contact with pathogens or their toxins in the gastrointestinal tract, respiratory tract and genitourinary tract will trigger the formation of immune memory cells that are specialized to provide optimal immunological protection at the site of initial exposure to antigen (Anderson, 2004). This means that developing immunity to pathogens acquired through natural routes provides the best protection against disease from subsequent exposure to the same pathogen.

It is interesting to note that optimal protection against the normal respiratory route of infection by pertussis requires an acute and persistent Th1 response and does not correlate with antibody titer (Rowe et al., 2000). However, the DTPa vaccine tends to induce a more Th2 polarizing reaction, therefore not providing the type of immune response that would provide the best protection against the bacteria causing whooping cough. Some of the more recent vaccine research focuses on developing methods of delivering vaccines that would provide more appropriate "natural" type immune responses (Anderson, 2004).

### **Abnormal Th1: Th2 balance**

The Th1 response is down-regulated during fetal development to prevent the immune system from mounting an inappropriate immune response towards newly developing fetal cells. The majority of immune protection for the fetus comes from the humoral immunity of the mother. This Th2 polarization continues on with the birth of the fetus and the passive immunization that occurs during the passage of IgGs through breast milk (Miyazaka et al., 2003). The cell mediated arm of the immune system of infants begins to develop more strongly as they are exposed to external microorganism, not only during a vaginal birth but also in the environment around them.

In order to mount an appropriate cell mediated immune response a pathogen must become intracellular. The hygiene hypothesis states that children of developed nations live in environments that are becoming too "hygienic" and sterile. These environments do not provide children of developed nations with adequate opportunity to be exposed to pathogens that would trigger the Th1 dominant immune response. As a result, their immune system stays Th2 polarized and they have an increased risk of atopic diseases like asthma, eczema and allergies that are associated with an inappropriate humoral immune response. Although this hypothesis has been hotly debated in the medical literature, it is interesting to note that there is epidemiological evidence that these diseases are much more of a concern in the developed world than in developing nations. Asthma, eczema and allergies are multifactorial diseases and therefore, other factors will play a role in their increased incidence in developed nations. However, the incidence of asthma has continued to increase despite a

reported decrease in the levels of major environmental pollutants in developed nations. Also children of the developed world live with easier access to healthy food and water choices and health care and still have higher incidence of these diseases. However, most studies examining a possible link between DPT vaccination and asthma have failed to show causation (Henderson et al., 1999, Maitra et al., 2003).

Another factor that might play a role in the relatively high incidence of Th2 polarized diseases in the developed world are the increased number of childhood vaccinations. Many vaccines, in particular the vaccines derived from acellular or non-viable material, will initiate a poor Th1 response and therefore, will skew the immune system towards Th2 polarization (Rowe et al., 2000, Rowe et al., 2001). It is important to note that there is large amount of individual heterogeneity in the Th1: Th2 responses in infants following vaccinations, with a higher likelihood of Th2 polarization occurring in infants with risks of atopy. This means that children already at risk for allergies will be the most susceptible to further pathology from vaccinations. The presence of aluminum compounds in vaccine adjuvants also stimulates Th2 immunity (Lindblad, 2004); further interfering with immune system balance in vaccinated children.

A large number of Th2 skewing vaccinations in childhood, in addition to the already skewed Th2 polarization of the fetus (Miyazaki et al., 2003) and an abnormally hygienic environment might cause a chronic imbalance of the immune system in susceptible children. This would not only increase their risk of certain immunopathologies but also increase their susceptibility to infectious disease. This link between allergies and autoimmune disease and infant vaccinations has been equivocal in the literature with some studies supporting a link (Hurwitz and Morgenstern, 2000; Kemp et al., 1997, Mari, 2004, McKeever et al., 2004) and other studies denying any significant link (Koppen et al., 2004, Mommers et al., 2004, Nilsson et al., 2003, Roost et al., 2004).

Not all reports have shown that childhood vaccines tend to cause Th2 polarization. For example, one study demonstrated more of a Th1 polarization after vaccination with whole-cell or acellular pertussis vaccines (Ausiello et al., 1997). Also the BCG vaccine, providing somewhat limited protection against infection by *Mycobacterium tuberculosis*, is Th1 skewing (Marchant et al., 1999). It is important to note which vaccinations have recently been given and design your interventions accordingly.

There is some evidence that at least part of the imbalance of Th1: Th2 polarization occurs because Ags from several different pathogenic microbial species are grouped in one single vaccine. For example, antigens to diphtheria, pertussis and tetanus are all grouped together in one vaccine. Similarly antigens to measles, mumps and rubella also are grouped together in one single vaccine. It is possible that an immunization schedule separating the various antigens might initiate a more appropriate immune response (Lavigne et al., 2004). Also vaccines that combine Ags can decrease the immunogenicity of one or more components of the combination vaccine. For example, the immune response to *Haemophilus influenzae* type B (Hib) is decreased when given in combination with DTP (Dennehy, 2001) and an inadequate immune response to varicella also occurs if it is combined with the MMR vaccine (White et al., 1997). Despite this evidence questioning the validity of combining many different Ags in one vaccine, a hexavalent vaccine containing antigens to diphtheria, tetanus, pertussis, poliomyelitis, *Haemophilus influenzae* type B and hepatitis B has been tested and shown to provide sufficient immunogenicity and show at least a preliminary acceptable safety profile (Mallet et al., 2004).

## Re-balancing the Th1 and Th2 cell mediated immune response: repairing the damage done by vaccines

### 1) Drainage of the extracellular matrix: The first intervention after vaccination?

Because of the residual effects of vaccine antigens, adjuvants and preservatives in the body it would be prudent to drain the extracellular matrix after vaccinations. There are numerous products reported to have good drainage effects including products from HEEL, Pascoe and UNDA. Also certain homeopathics like Thuja, Ledum, Silica and Nux Vomica as well as others might be useful to regain the balance of vitality that would be shifted with numerous childhood vaccinations. Timely, controlled removal of vaccine antigens, adjuvants and preservatives through drainage could prevent any initiation of low level inflammatory reactions that might lead to chronic disease.

### 2) Healing the GIT

The gastrointestinal tract, including the buccal cavity, pharynx and esophagus, is actually part of the external environment and therefore, is one of the first areas (other than skin) that are exposed to pathogens. As a result, the GIT plays a vital role in immunity. For example, at some point in their lifecycle, 65-90% of immune cells circulate through the gastrointestinal tract. Also, much of the initiation of an appropriate immune response like Th1 and Th2 balance occurs with the help of GIT derived Th3 cells and intraepithelial lymphocytes. Other cells of the gut associated lymphoid tissue (GALT) and mucosa associated lymphoid tissue (MALT) like M cells, intraepithelial lymphocytes and Paneth cells also play roles in optimizing immunity. Other immune components of the GIT include acid and mucosal barriers, selective epithelial junctions and an extensive population of diverse natural flora that help regulate the GALT as well as prevent over-colonization of potentially more pathogenic organisms. An important part of the GIT's role in immunity is to provide a selective barrier to the entry of pathogens, and inadequately digested food particles (especially proteins) that might initiate an over active immune response.

There are many naturopathic interventions that are useful in healing the GIT. These include prevention of irritation of the GIT mucosa and therefore, over stimulation of immune system through optimal dietary and lifestyle choices. Supplementation with L-glutamine, gamma-oryzanol, short chain fatty acids, n-acetyl glucosamine or with herbs like *Glycyrrhiza glabra*, *Althea officinalis*, *Ulmus fulva* also can help heal the GIT mucosa. This paper only will describe the role of probiotics in rebalancing Th1:Th2 levels in the GIT.

#### **Probiotics:**

There is some evidence that certain strains of probiotics are useful in balancing the Th1: Th2 response to pathogens. For example, one recent study demonstrated that a preparation containing *Bifidobacterium infantis*, but not *Lactobacillus salivarius* was effective in normalizing IL-10 to IL-12 levels in peripheral blood mononuclear cells of persons with IBS and therefore, relieving their symptoms (O'Mahony et al., 2005). Another recent study demonstrated that *Lactobacillus GG* by itself, but not in combination with other probiotics, is beneficial in treating the atopic dermatitis in IgE sensitized infants (Viljanen et al., 2005). The probiotic strains used in these studies could have decreased symptoms of IBS and atopic dermatitis by shifting the immune system away from a polarized Th2 response. This effect of probiotics on Th1 modulation has been demonstrated in a number of other studies (Braat et al., 2004, Cross et al., 2004, Maassen et al., 2000, Mohamadzadeh et al., 2005, Perdigon et al., 2002, Sudo et al., 2002). Other studies have shown that

*Bifidobacterium lactus*, *Bifidobacteria lactus* and several *Lactobacillus acidophilus* strains all tend to have varying abilities to promote a more Th1 response whereas, *Lactobacillus salivarius* is more Th2 skewing (Nigel Plummer, 2004; personal communication).

Several probiotic products, like HMF Neogen (Genestra), Th-1 probiotics (AOR) and ProbioKids™ (Metagenics) have been designed specifically for infants to assist with their immune system balancing. The ultimate form of health prevention might be to breast feed after applying strain specific probiotics to the nipple of the nursing mother (Nigel Plummer, Ph.D., personal communications).

There is some evidence that the non-pathogenic yeast, *Sacchromyces boullardii* , (Buts et al., 1990, Rodrigues et al., 2000), specific strains of probiotics like *Escherichia coli* O83 (Lodinova-Zadnikova et al., 2004, Vancikova et al., 2003) and *Lactobacillus* species (Perdigon et al., 1999) increase the production of IgA. IgA is found in body secretions such as saliva, intestinal juice, tears and milk and helps prevent pathogenic attachment to epithelial cells like mucosal cells and epidermal cells. An increased level of IgA in the first two years infancy is correlated with a decreased incidence of allergy (Bottcher et al., 2002).

A balance in the numbers and types of bacteria in the GIT also prevent the attachment, colonization and overgrowth of more pathogenic microorganisms. Healthy bacteria can out-compete more pathogenic bacteria for finite space and resources and therefore, help balance the immune system.

The optimal growth of these “friendly” bacteria can be aided with providing them with fuel for their survival like inulin, fructooligosaccharides, arabinogalactans, and short chain fatty acids (eg. butyrate, caprylic acid etc.). An optimal balance of healthy bacteria can be maintained through the ingestion of plain yogurt, with live bacterial cultures, or Bio-K products or Kefir.

### 3) Healing the Liver

The liver is a critical organ in the immune response (Seki et al., 2000). For example, it is the site of synthesis of the proteins of complement, immunoglobulins and many of the inflammatory mediators, including the acute phase proteins. It also is the site of detoxification and modification of many potentially damaging immunogenic substances (Kmic, 2000, Knolle and Gerken, 2000). Immune cells based in the liver (termed liver sinusoidal endothelial cells) also play a role in immune tolerance, down-regulating inappropriate Th1 responses (Seki et al., 2000, Knolle et al., 1999).

Finally the liver is an important site for the storage and metabolism of vitamin A. Vitamin A has many important roles in immunity including macrophage activation and maintenance of mucosal integrity (Weiringa et al., 2004). Optimal vitamin A status in infants is largely dependent on breast feeding and optimal liver function. It is interesting that there is direct connection between the liver and GIT, via the enterohepatic circulatory system, and that both organs are so vital in an appropriate immune response. Furthermore, there is some evidence that the homing of certain T cells to the GIT is dependent on retinoic acid synthesized by gut derived dendritic cells (Iwata et al., 2004), suggesting a close link between optimal immunity and Vitamin A metabolism.

### 4) Supplements to directly balance Th1:Th2 levels

There are several products, in addition to probiotics, that have been developed that will help balance the Th1 and Th2 immune system. For example, oral Traumeel (Heel) has been shown to modulate

inflammatory cytokines in immunocytes (Porozov et al., 2004), possibly by stimulate TGF-beta expression, Th3 secretion and therefore, Th1: Th2 levels (Alta Smit, MD and Bruno van Brandt, MD, personal communications). Products based on plant sterols and sterolins like Moducare (Purity Life Products; Thorne), Sterolin 117 (Ecotrend), Phytophenols (Cyto-Matrix), Chol SAP-15 (NFH) also have been shown to modulate Th1:Th2 balance (Bouic and Lamprecht, 1999).

Supplementation with bovine colostrum also has been shown to stimulate a Th-1 type response in mice (Yoshioka et al., 2005) and therefore, might be an additional strategy to help balance the immune system after vaccination. It is interesting to note that breast milk and colostrum contains a significant amount of transforming growth factor-beta. Transforming growth factor beta secretion is necessary for IgA production (Ogawa et al., 2004, Sonoda et al., 1989) and also is the cytokine used in the initiation of oral tolerance (Kalliomaki et al., 1999), through the signaling of a Th3 response. Ideally the immune modulating effects from TGF-beta on infant immunity should come from an extended period of at least 8 months to a year of breast-feeding. I believe that it would be prudent to wait until an infant's GIT integrity and immune system were better developed before introducing a foreign source of milk. However, supplementation by bovine colostrum like ColostOfferin (Douglas Labs), All-life colostrum (AOR) etc. might be a necessary intervention in some situations.

**Nutrient deficiencies** also might cause an inappropriate polarization of the immune response. For example, a zinc deficiency will result in an inadequate Th1 response, whereas a vitamin A deficiency produces a Th2 dominant response (Beck et al., 1997, Weirenga et al., 2004). Providing optimal nutrition to breast feeding mothers and their infants can be another intervention aimed at balancing the immune system.

There are several studies demonstrating that **essential fatty acid balance** in mothers will influence neonatal immunity. One study in rats, showed that the ratio of omega 3 to omega 6 oils in maternal rats influenced the oral tolerance of their offspring (Korotkova et al., 2004). Another randomized, placebo controlled trial in humans showed that fish oil supplementation to nursing mothers modified neonatal cytokine profiles and subsequent allergic responses (Dunstan et al., 2003). Fish oil supplementation also positively influenced IgA levels in breast milk (Dunstan et al., 2004) suggesting that supplementation might play a role in mucosal immunity. Fish oils also modulate the production of prostaglandin E2, and therefore indirectly affect the production of TNF-alpha (Trebbles et al., 2003; Sundrarjun et al., 2004), a cytokine associated with Th1 mediated immunity.

Because of the significant ability of the long chain polyunsaturated fatty acid (LCPUFAs) in fish oils to modulate Th1:Th2 levels it has been suggested "that supplementation of appropriate amounts of LCPUFAs during perinatal period protects against atopy, asthma, auto-immune diseases, type 1 and type 2 diabetes mellitus, hypertension, coronary heart disease, metabolic syndrome X, lymphomas, leukemias and other cancers, schizophrenia, depression and other adult diseases in which low-grade systemic inflammation plays a significant role (Das, 2004)". Dietary n-3 polyunsaturated fatty acids (PUFA) to either breast feeding mothers or to their children may represent a mode of balancing a Th1 polarized immune system and therefore, prevent allergies, asthma or eczema.

##### 5) Breast feeding to balance Th1:Th2 levels

Without a doubt, the best preventative advice that a naturopathic doctor can recommend is that mothers breast feed for an extended period of time. The current Canadian Pediatric Society recommendations are that infants should receive breast milk exclusively for the first 6 months of life.



This is a very conservative recommendation and should be used as a bare minimum. Breast milk contains many immune modulating substances (Hanson et al., 2003, Kunz et al., 1999, Rodriguez-Palmero et al., 1999) and therefore, should be continued as long as possible for optimal immune balancing effects. It is important to recognize that the quality of breast milk passed from mother to infant has a profound impact on developing immune system. Many naturopathic interventions based on optimizing health in the breast feeding mother, and therefore the quality of their breast milk, will directly benefit their infants.

### **The effects of chronic stress on the immune system**

An optimally functioning immune system also depends on a balance between the hormones DHEA and cortisol. DHEA tends to push the immune system towards a Th1 response, whereas cortisol tends to initiate more of a Th2 response. There is evidence that breast milk does contain a significant amount of cortisol (Rodriguez-Palmero et al., 1999) and that these levels are directly related to maternal plasma cortisol levels (Patacchioli et al., 1992). Therefore a sub-optimal stress response in the mother could raise cortisol levels in breast milk to levels that might have a deleterious effect on the developing immune system of the infant. There also is evidence that cortisol, and other steroid hormone levels change in amniotic fluid during gestation (Sippell et al., 1981) and therefore, the initiation of optimal immune balance in children might begin with balancing a mother's stress response during pregnancy.

There are many interventions that a naturopathic doctor can recommend to help maintain an optimal DHEA: cortisol balance and therefore, modulate the immune system. These interventions would be difficult to initiate in an infant but can be implemented in the mother, with the benefits passed to the infant via the breast milk. For example, cortisol and DHEA are cholesterol derived and therefore, dietary intake, liver health, bile synthesis and secretion and enterohepatic circulation are involved in their optimal metabolism. Each one of these hormones also is synthesized in the adrenal cortex and therefore, a balanced adrenal gland function also might play a significant role in their optimal metabolism.

Cortisol levels are elevated during periods of hypoglycemia. This suggests that optimal blood sugar balance, through diet and supplementation also might play an important role in immune system balance. Optimal blood sugar balance becomes even more crucial in maintaining a balanced immune system in infants where the hepatic enzymes for glycogenolysis and gluconeogenesis (major enzymes for glucose metabolism) are not yet fully developed (Hume et al., 2002, Hume et al., 2005). Therefore, another naturopathic intervention to balance cortisol levels and therefore, immune system Th1:Th2 response might be to balance blood sugar levels in the breastfeeding mother and/or ensure that the food the infant receives will not result in chronically elevated blood glucose levels.

High levels of cortisol might indicate an inappropriate stress response. Balancing cortisol levels and therefore, the Th2 arm of the immune system in the mother and her breast milk could include lifestyle interventions like mild to moderate exercise, deep breathing techniques, meditation, yoga etc. designed to positively express and relieve stress. It is interesting to note that there also is a link between maternal stress and the level of IgAs in breast milk (Groer et al., 1994, Groer et al., 2004). This suggests that another important regulatory of childhood immunity, IgA, could also be optimized by balancing the stress response of the mother.

### **Maternal allergies and breast milk**

There is a different cytokine profile in the breast milk of allergic mothers compared to non-allergic mothers. Atopic mothers have higher IL-4, IL-5 and IL-13 levels than mothers without allergies (Bottcher et al., 2000). All breast milk has varying levels of IL-6, IL-10 and TGF-beta, cytokines associated with IgA synthesis and down-regulation of inflammation (Bottcher et al., 2000, Sonoda et al., 1989, Muller et al, 1995). These studies emphasize the importance of breast feeding in the prevention of atopic illness in infants. It also suggests that the cytokine profile of breast milk can be modulated. There are many different naturopathic interventions that can help reduce allergies in the mother, change the cytokine profile of her milk and therefore, indirectly benefit the development of the immune system of her breast feeding infant.

One other product shown to have benefit in modulating an overactive Th2 response is an extract from the seed of *perillic frutescens* (Ishihara et al., 1999). Although the exact mechanism is unknown, one of the active ingredients of this seed extract, rosmarinic acid, inhibits the expression of IL-4 and IL-5 (Sanbongi et al., 2004), two cytokines involved in the initiation of an allergic response.

### **Conclusion**

There are significant pressures placed on parents to vaccinate their children. As naturopathic doctors we must be able educate parents objectively about the risks and benefits of vaccination. We also must be able to inform them of the effects of vaccinations on the developing immune system and the naturopathic interventions that are available to protect their children from some of the consequences of these side-effects. As NDs we can assist patients in making an informed decision about childhood vaccinations and immunity.

It is important to understand that the current conventional medical model of infectious diseases is based primarily on Louis Pasteur's germ theory and therefore, assumes that there is a direct link between a single organism and a single disease. We are discovering that in most cases of infectious diseases such a direct link cannot be made. Many, if not all diseases, are multifactorial, with numerous different causes and therefore, a preventative approach based solely on the hopes of eliminating one of the potential known causes is far too limiting. A naturopathic doctor's understanding of the critical role of biological terrain in the establishment and development of infectious disease should provide patients with much more effective tools in preventative health care.

Interventions that provide the best protection from the development of infectious disease must be multifactorial. There is considerable benefit in developing and maintaining a robust immune system capable of mounting an appropriate response to a wide variety of pathogenic challenges. Relying solely on childhood vaccinations to provide protection against significant harm from infectious disease is like putting the seat belt on in your car and still driving recklessly. The seat belt, aka the vaccine, really provides a minimal amount of protection. A more significant amount of protection comes from obeying the rules of the road (read terrain) and driving (living life) in a safe, conscious manner. Similarly, we can gain more significant protection from infectious disease in our life's journeys if we obey the laws of nature and have balance amongst the physical, mental and spiritual aspects of our lives.

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