## Asthma

Asthma is certainly not a new disease, with descriptions of its pathogenesis and treatment dating back to Hippocrates and Paracelsus (Floyer, 1698, pA6). Towards the end of the 20th century and into the 21st the prevalence of asthma has increased in the developed world (Holgate and Frew, 2002, p874; Moxham and Costello, 2002, p652).

Once classified as 'extrinsic' asthma for those types with a known cause such as dust mites; and intrinsic asthma for types with no known cause, these terms are now seemingly coming to an end. It is now widely accepted that asthma is a chronic inflammatory disease of the lungs and approximately half of all asthma cases have an allergic component to them (Holgate and Frew, 2002, p874).

Occupational asthma is considered to play an important role in late-onset asthma. However, it appears that many of these cases give a childhood history of respiratory symptoms in keeping with asthma (Holgate and Frew, 2002, p874). Although the strongest predictor of childhood asthma risk is a family history of asthma, particularly from the mother ($p=<0.001$: Darlow et al, 2000, p292; Ball et al, 2000, p540), the increased prevalence of asthma is believed to be more likely due to environmental factors than a genetic shift (Holt, 1995, p44). It has been found that another strong predictor is maternal smoking in pregnancy ($p= < 0.005$; Darlow et al, 2000, p292). Certainly smoking during pregnancy is associated with increased cord blood IgE levels (Landau, 1995, p30-31). A family history of atopy also shows strong associations (Darlow et al, 2000, p292).

## Aetiology - The Terrain of the Patient and the foundations of the terrain: The interrelationship of genetics, immunity and the environment.

Some of the genes controlling the production of the cytokines that play a part in asthma have been identified and are known as the IL-4 cluster. This cluster controls the formation and longevity of mast cells, eosinophils and IgE (Holgate and Frew, 2002, p875). Holt (1995, p44-46) suggests that after inhalation of an antigen - it is transported to the lymph nodes by antigen presenting cells and presented to TH1 (cell mediated immunity) and TH2 (humoral immunity) cells simultaneously. These two T –helper cells are described as 'mutually antagonistic'. TH1 cells secrete IL-12 and IFN –y which inhibit TH2 and TH2 secrete IL-10 which inhibits TH1. He hypothesises that these cells compete for dominance and that the winner establishes a greater population of long-lived memory cells which become the over riding force in subsequent immune responses to that particular allergen. Therefore, if TH2 cells become dominant, IgE response becomes progressively more aggressive and the scene is set for an allergic response. Although this is perhaps a simplified of view of what is probably a much more complex process, the mingling of genes and the environment will play a crucial role in the determination of the immune response. This aspect of the terrain is laid down in early infancy and childhood.

A likely factor for the increased prevalence of asthma is due to improved standards of living causing a reduction in early exposure to microbes, reducing the need of TH1 driven cell mediated immunity to develop (Rook and Standard, 1998, p113). This lack of stimulation of TH1 defences allows sensitisation to common allergens to occur during the early critical phase of development. A study in Poland (Braback et al, 1994, p832) comparing Polish and Swedish children found that polish children experienced a much higher prevalence of the common cold than Swedish children but yet experienced a 5-8 fold lower prevalence of skin test reactivity to common inhalant allergens. Prevalence of asthma is also still low in Australian Aboriginal populations, but the children suffer from almost constant respiratory infections (Christiansen, 2000, p575). Conversely, Holt et al (1990; cited in Landau, 1995, p30) discovered that in the first few weeks after birth, animals were more likely to become sensitised when exposed to inhaled allergens than to develop a tolerance. It is suggested this may be the same for infants. Certainly there is evidence to suggest that time and place of birth can influence the development of asthma (Aberg, 1989, p645).

The leading inhaled allergen responsible for asthma is almost without doubt the house-dust mite (Holgate and Frew, 2002, p875; Landau, 1995, p31). Air pollution is dismissed as a major factor of asthma as the prevalence is often low in developing countries with high air pollution (Landau, 1995, p31). However, this argument does not necessarily stick as it can be reasonably argued that TH1 immunity in children in developing countries may be more dominant. Therefore, they are less likely to succumb to inhaled allergens, including air pollution.

There is evidence to suggest that childhood vaccination can stimulate a dominant TH2 memory imprint and subsequently inhibit the expression of TH1 immunity (Singh, Hahn and Sercarz, 1996, p1613-1622). As childhood vaccinations are not freely available in the developing world this is certainly another aspect to contemplate. Holt, Sly and Bjorksten (1997, p54) suggest that lipopolysaccharides from the cell walls of friendly microbial flora in the gastrointestinal system interact with dendritic cells (DC) to secrete IL-12 which ultimately inhibits TH2. Certainly animals of many different species kept in germ free environments fail to develop TH1 immunity until they are provided with normal gut flora (Inagaki et al, cited in Holt, Sly and Bjorksten, 1997, p54). Consequently, the importance of healthy gut flora cannot be emphasised enough. As antibiotics destroy commensal gut flora and are still overused in developed countries it is reasonable to assume this is now another factor in asthma today.

## The interrelationship of the gastrointestinal system, parasympathetic nervous activity and the bronchial tree.

In ‘A Treatise of the Asthma’ the first writings of asthma in English, Sir James Floyer (1698) gave a detailed account of his own severe asthmatic attacks. Even at this time it was observed that the breathing difficulties were due to ‘a constriction of the bronchia’ and that this was associated with ‘weakened nerves’. He documented how

an attack began – not with difficulties in breathing - but with eating meat in the afternoon, followed with 'loose stools, flus of urine and a great spitting and drowsiness of the head'. He also describes 'the inflations of the nervous fibres of the skins of the stomach' and 'frequent retching and yawning many times'. In the evening time comes ' a stiffness and rigidity of the lungs'. Many of the symptoms he describes appear to relate to vagotonia due to insufficient digestion. Poor digestion provokes the parasympathetic nervous system into stimulating liver, gallbladder and stomach secretions and peristalsis to aid digestion. T In the early part of the last century, George Bray (1931, p181-197) set out to prove what he deemed to be 'oft quoted and well established facts'- that gastrointestinal insufficiency preceded asthma. He did this fairly conclusively by testing the stomach acid of 200 asthmatic children between the ages of six months and twelve years and comparing them to healthy controls. Approximately 80% of children with asthma had some degree of hypochlorhydria as compared to less than 10% in healthy controls. Another interesting finding in this study was that deficiency in acid secretion was more pronounced before the age of seven years and that towards puberty, gastric secretion improved. Certainly a tenuous correlation with modern day literature can be made here. Moxham and Costello (2000, p651) state that the peak age of onset of asthma is five years of age. Landau, (1995, p30-31) states that 60% of those with mild episodic asthma will cease to wheeze by adult life. Sadly, there appears to have been little continuation of investigation in this area.

## General Syndrome of Adaptation– the stress response.

It appears that psychological stress and emotional factors are a frequently quoted factor in asthma, both by sufferers and healthcare practitioners alike (Busse et al, 1995, p249). However, proving this effectively is difficult as it requires following complex psychoneuroimmune pathways that are still poorly understood by the scientific community. Despite this, it is interesting to note that asthmatic students sitting exams released more IL-5 as compared to normal controls who released more IL-2 (Kang et al, 1996, 179). As IL-5 is a cytokine secreted from TH2 cells and is involved in the inflammatory processes responsible for airways hyper responsiveness, one can only be left to contemplate the theory of TH2 cell dominance once more and its interactions within psychoneuro-immune mechanisms. It has been noted that stressful family functioning may influence the age of onset of asthma in children whose terrain is already genetically susceptible (Mrazek, 1991, cited in Schedlowski and Tewes, 1999, p319). Another factor in the GSA is the parasympathetic rebound after a period of sympathetic activation (Schedlowski and Tewes, 1999, p321). This over activation of the parasympathetic nervous system occurs in order to compensate for a period where the terrain has been subjected to the stress response. Whilst the fight or flight response of the sympathetic nervous system elicits desirable mechanisms to counteract asthma, the parasympathetic rebound will illicit the undesirable ones.

## Phytotherapy – Terrain Medicine

As cases of asthma seen by the phytotherapist will vary greatly, no hard and fast formula can be applied within terrain medicine. The terrain of the patient will vary greatly and a thorough case history paying particular attention to genetic predisposition; others forms of atopy; vaccinations and any side effects encountered; diet and digestive functioning; level of exposure to common infections throughout childhood; use of antibiotics throughout life; and emotional well-being of the patient. Other factors within the terrain such as endocrine function should also be taken into account. The following herbs are proposed individually, but can be used as part of a prescription in the treatment of the terrain in asthma.

### Boswellia serrata

Boswellia serrata is a traditional anti-inflammatory Ayurvedic remedy and is sold as a treatment for arthritis under the name of SallakiTM. It is a branching tree found in India, the Middle East and North Africa. Underneath the bark lies the medicinal oleo-gum resin which contains terpenoids, oils and gum. Approximately 16% is essential oils (Ammon, 1996, p67).. The most important constituent of Boswellia is thought to be the boswellic acids, with particular attention being paid to acetyl-11-keto-B-boswellic acid (AKBA). This has been shown to specifically block the inflammatory pathways of 5-lipoxygenase including the LTB4 pathway (Safayhi et al, 1996, p71). This is responsible for lymphocyte regulation and is involved with the production and actions of cytokines. Other leukotriene pathways involved are the cysteinyl leukotrienes. These cause bronchoconstriction and mucous secretion (Ammon, 1996, p69). An in-vivo study has shown that an alcoholic extract of Boswellia can inhibit both cell mediated and humoral immunity. However, the inhibition of humoral immunity was greater - being almost total (Sharma et al, 1988, p162). These results suggest that Boswellia can allow TH1 cells greater dominance by dampening down TH2 driven immunity further than the TH1. A full clinical trial has taken place to verify the effect of the whole resin and the results were extremely encouraging. In this six week, double-blind, placebo controlled study it was found that 70% of subjects taking 300mg of resin three times a day for six weeks showed an improvement of their symptoms. This was compared to 27% of subjects on a dummy pill reporting an improvement in symptoms (Gupta et al, 1998, p511). Whilst there appears to be a placebo effect taking place in the control group, a result of 70% in the Boswellia group cannot be ignored. Dosage and contraindications • 300mg of resin 3 times a day (Gupta et al, 1998, p511) No contraindications known (Singh, Bani and Singh, 1996, p87-90)

### Coleus forskohlii

Coleus forskohlii has a long history of use in Ayurvedic, Siddha and Unani medicine. It grows on the Indian plains and in the foothills of the Himalayas and is a member of the Lamiaceae family. The root is the part used medicinally and is also the part that contains the diterpene forskolin – the constituent responsible for many of the beneficial effects seen from the root. No other species of Coleus contains forskolin (Bone, 2001, p103; Murray and Pizzorno, 1999, p673, Pengelly, 1997, p48). The therapeutic actions of Coleus forskohlii in asthma are several fold and therefore Coleus can be considered a herb to strike at several different factors at once. The basic mechanism of action of forskolin is the direct activation of cAMP (Seamon and Daly, 1981, p201). This has been found to inhibit IgE mediated mast cell degranulation and histamine release, levels of histamine release being directly correlated to the concentration of forskolin administered (Marone et al, 1987, p18). Platelet activating factor is also inhibited (Murray and Pizzorno, 1999, p675). Increased levels of cAMP also causes the relaxation of bronchial muscles (Lichey et al, 1984, p167). Other sites of smooth muscle are also relaxed - of particular interest in this case is the arteries and its hypotensive effects (Murray and Pizzorno, 1999, p675). These additional spasmolytic actions are particularly poignant when considering the long term effects of asthma on the heart. Forskolin has been shown to be positively inotropic, reducing preload, therefore improving the function of the left ventricle (Lidner et al, 1978, cited in Murray and Pizzorno, 1999, p675). Coleus forskohlii's third mechanism of action is in the treatment of digestive insufficiency. Forskolin has been shown to increase gastric secretions of hydrochloric acid, pepsin, amylase and pancreatic enzymes (Bone, 2001, p104; Murray and Pizzorno, 1999, p676). As previously discussed, stimulation of these secretions causes a decrease in parasympathetic activity and a subsequent relaxation of the bronchial tree. This three pronged mechanism of Coleus may be particularly suitable for longer-term sufferers of asthma because of its beneficial effects on the heart. Dosage and Contraindications It is suggested by Pizzorno and Murray (1999, p676) that the dosage should be based upon the level of forskolin and that therefore a standardised extract should be used. Certainly Bone (2001, p106) believes that the properties of forskolin alone does not necessarily advocate the efficacy of the whole herb. • A standardised extract containing 18% forskolin is recommended 2-3 times daily. • Anywhere between 2 - 15g of the dried root a day is recommended. • ¬6-12ml of a 1:1 fluid extract is recommended Coleus is contraindicated in Hypotension and peptic ulcer. It should be used with caution in conjunction with other medication as it can cause precipitation.

**Lavandula officinalis/angustifolia**

Lavandula officinalis/angustifolia are members of the Lamiaceae family and have been cultivated all over Europe, although Lavandula is native to the sunny mountain slopes of the Mediterranean. The flowers are the parts used (Weiss, 2000, p269). Lavandula's principal active constituent is in its volatile oils, particularly linalool (Lis-Balchin and Hart, 1999, p540). The reaction of the terpene alcohols with acetic acids forms esters whose main action is antispasmodic and sedative (Pengelly, 1997, p66). The antispasmodic effects of Lavandula are thought to post synaptic and most likely mediated thorough cAMP (Lis-Balchin and Hart, 1999, p541). It is also considered a

chologogue (Weiss, 2000, p269). Various studies of have been carried out on Lavandula investigating its mood enhancing effects. The most coherent of these is an investigation into right and left brain activity of adults and infants after inhalation of Lavandula as measured by an EEG (Sanders et al, 2002, p1305). Here it was found that regardless of the subjects normal temporal lobe dominance, after inhalation of lavender there was a greater activity measured in the left frontal lobe in all subjects. Greater left frontal activation is associated with greater approach behaviour and a less depressed effect. Lavandula is considered to have an sympatholytic and parasympatholytic action on the autonomic nervous system (Nicholls, 2003) A study on the effects of a lavender foot bath was carried out in Japan (Saeki , 2000, p6). Although parasympathetic activity was deemed to be significantly increased in both the lavender group and the control, it was found that the lavender group showed a delayed reaction in the balance of parasympathetic activity. It has also been discovered that Lavandula slightly inhibits cortisol responses, suggesting a gentle sympatholytic action (Kawakami et al, 2002, p73) These actions will be useful in dealing with the sympathetic stress response and any subsequent parasympathetic rebound that may cause spasm in the bronchial tree. It has been found (Kim and Cho, 1999, p221) that Lavandula inhibits immediate type allergic reactions by inhibition of mast cell degranulation in-vivo. However, it is also documented that Lavandula can cause rare allergic reactions (Brandao, 1986, p249). Lavandula will be a useful adjunct in any asthmatic prescription where there are emotional stressors. Its gentle nature makes it a herb particularly suitable for children and could help to avert an early onset of asthma where there is stressful family functioning. Its perceived chologogue action will naturally be a useful adjunct for the digestive system. It is not inconceivable that Coleus forskohlii may help potentiate the spasmolytic and anti-allergic effects of Lavandula due to its more potent cAMP activating properties. Dosage and contraindications • 2-4ml per dose/day of a 1:5 tincture- adjust for children. • 2-3 drops of essential oil can be put neat on the skin – in small amount of base oil for small children No contraindications known (Bartram, 1996, p264)

## Conclusion

The aetiology of asthma has significant relativity. The terrain and its adaptation and adaptability within the environment is multifactorial and all factors can be thought to interrelate. As the trajectory of the terrain is laid down in infancy and early childhood - it is left to speculate the effects of vaccinations that begin at eight weeks and continue into childhood. Is the control of infection in a cleaner and more sanitised society allowing TH1 lymphocytes to become latent - leading to TH2 dominance? Is asthma and other forms of atopy such as eczema a fair price to pay for the benefits of immunisation? The health of the gut plays a crucial role in asthma and cannot be ignored, especially in infants. There appears to be two mechanisms of gastrointestinal dysbiosis that precipitate asthma. Lack of hydrochloric acid causes vagal stimulation and corresponding bronchoconstriction and mediator release. Lack of commensal gut flora causes a decrease in TH1 lymphocytes and a corresponding rise in allergen specific TH2 cells. There can be no doubt these two mechanisms will profoundly interrelate. As antibiotics kill off commensal gut flora and pave the way

for gut dysbiosis it can only be assumed that antibiotics are another factor in the increased prevalence of asthma. Putting genes aside, gut dysbiosis could be viewed as a leading cause of allergic and non-allergic asthma both past and present. Gnotobiotic societies could be viewed as a leading cause of the increased prevalence of asthma today. The developed world is unlikely to banish vaccinations and antibiotics and regress back to high levels of infectious exposure, this is not instantaneously desirable anyway. Certainly the all powerful pharmaceutical companies can and will do everything in their power to prevent it, although obviously their motives are not always for the good of public health. But new and innovative ways of manipulating the immune system into cell-mediated dominance maybe possible. Early intervention with administration of fructooligosaccharides or even green clay in infancy and childhood will promote commensal gut flora. This could have a positive, deep-seated and lasting effect on the terrain. It will help promote the desirable immune responses needed to successfully fight the infections that some of the new perpetrators in asthma - antibiotics and vaccinations - are trying to eradicate. This will lessen the need for them. Prevention is always better than cure –catching susceptible individuals at a young age may prove beneficial.