Asthma has been defined as the occurrence of dyspneic bronchospasmodic crises that are linked to a bronchial hyperreactivity (BH). Like autoimmune disease, asthma is a chronic disturbance of immunological function that can be controlled to some extent, but not eradicated, by modern drug therapy. In other words, asthma is not just the attacks (crises); asthma is a chronic disturbance of the immune system. The attacks are the “tip of the iceberg.” Hence, any treatment aimed only at relaxing airways and relieving symptoms, be it orthodox or herbal, is superficial and will not change the chronicity of the disease.

Recent research has identified many factors that may contribute to the etiology and morbidity of asthma. Traditional herbal medicine also recognizes the role of inefficient digestion, poor immunity, stress, diet, and unhealthy mucous membranes in the development of the disease. In order to treat asthma more effectively with natural therapies, it is necessary to have an understanding of the causative and sustaining factors that contribute to the disorder. For each individual it is likely that the disease process has been precipitated by a unique and complex interaction of contributive events. A multi-factorial model, which allows the individualization of the patient, yet at the same time incorporates the most likely factors operating in asthma, will be proposed. This in turn requires the synthesis of traditional herbal understanding with the latest research findings, which is fundamental to the practice of modern phytotherapy.

Classification of Asthma

Asthma can be classified as extrinsic (allergic asthma) or intrinsic asthma. Although there has been some confusion with the terms and some medical scientists feel that the classification is meaningless, the differentiation is quite clear. Patients with extrinsic asthma comprise the majority of cases and exhibit a positive skin test to common allergens and foods. Serum IgE levels are usually raised. However, extrinsic asthmatics can still be exacerbated by non-specific stimuli such as cold air and exercise. Intrinsic asthmatics have negative skin tests and chronic infection, and other factors are thought to play a role in the disease process. Intrinsic asthma is usually later in onset and more severe. Aspirin-sensitive asthma (ASA) is one form of intrinsic asthma. Both types of asthma show an increased family occurrence.

The confusion over this classification of asthma probably arises when etiology is considered. It is likely that allergy often plays a role in the development and exacerbation of intrinsic asthma. Similarly, factors such as infection and gastroesophageal reflux (GER) may contribute to extrinsic asthma. Hence, the above classification should serve only as a guide to the different kinds of factors that can operate in asthma; the classification is secondary to the identification of factors in each individual case.

Histological Findings

Asthmatic lungs are characterized by epithelial cell loss, goblet cell hyperplasia, increased collagen deposition, mast cell degranulation, and inflammatory cell infiltration. Asthma is now primarily classified as an inflammatory disorder. The desquamation allows allergens to penetrate more easily and exposes irritant receptors.

Pathophysiology

Bronchoalveolar lavage has revealed the presence of activated helper T-cells in asthmatic lungs. Helper T-cells can be divided into two main types: TH1 and TH2. TH1-cells produce cytokines which are characteristic of the immune response to bacterial infections. The cytokines produced by TH2-cells are characteristic of allergic responses and include interleukin-4, interleukin-5, and granulocyte macrophage colony stimulating factor (GM-CSF). Patients with extrinsic asthma have high levels of these cytokines. In other words, the TH2-cell compartment appears to be overactive (more about this later). Interleukin-5 activates eosinophils, which are the characteristic inflammatory cells in asthma, and interleukin-4 encourages B-cells to produce IgE. So, for extrinsic asthma, the acute symptoms may largely be the work of mast cells, while the chronic inflammation results from the action of TH2-cells on eosinophils. A similar but not identical process may be involved in intrinsic asthma, which is triggered by an unknown antigen, such as a virus or even self tissue. Some scientists feel that a T-cell modulated, eosinophilic bronchitis is the primary abnormality in asthma, while bronchospasm and hyperreactivity are secondary phenomena.

The characteristic inflammatory cells of asthma are mast cells and eosinophils. Other cells also participate in the inflammatory process. Neutrophils have been implicated in sudden onset fatal asthma and bronchial obstruction associated with house dust mite sensitivity. Platelets and monocyte/macrophages also play a role. In particular, platelet activation is a feature of the late inflammatory response to antigen challenge. Endothelial cells also participate in the pathogenic process.

Mediators

A host of inflammatory mediators have been identified in the pathophysiology of asthma. However, some mediators may be more involved in triggering the inflammatory process than others. In this context, important mediators are the cytokines listed above and probably histamine, platelet-activating factor.
(PAF), major basic protein, leukotrienes, and, to a lesser extent, prostaglandins. Patients with ASA have increased PAF responsiveness, reduced prostaglandin levels, and increased leukotrienes compared to normal controls.12,13

The host of inflammatory cells and mediators involved in the pathogenic process means that treatment directed at a single mediator or cell is unlikely to be successful. A multi-faceted approach to treatment is required. This is compatible with herbal therapy, which has traditionally used combinations of plants to treat diseases.

The above considerations also explain the current preference in conventional medicine for steroid use in asthma. These drugs have a broad suppressing effect on many inflammatory mechanisms. In this context, the “magic bullet” is more like an ordinary shotgun.

Factors Associated with Asthma

Differentiation must be made between the causes that initiate or sustain the underlying condition, which are probably factors that result in injury to the lining of the lungs, and the triggers that precipitate the asthmatic attack. While avoidance of the latter group is, of course, important, it is only attention to the former group that will reduce the progression of the disease. There is no better illustration of this issue than the subject of dairy products. Traditional knowledge suggests that consumption of dairy products can lead to a state of unhealthy mucous membranes in sensitive patients. However, these patients may not give a positive skin test to dairy products, and these products may not provoke an acute asthmatic attack. In the classical sense, there is no allergy to dairy products. Yet the avoidance of this food group will, in time, give appropriate patients considerable relief from their asthmatic condition.

a. Allergens

The most significant allergen in the long-term development of asthma is now considered to be the house dust mite.14 However, this does not necessarily mean that the degree of house dust mite exposure will correlate with the day-to-day severity of asthma. This is because sensitivity to the house dust mite feeds the underlying pathological process. It is important that a natural spray for the control of house dust mite be developed. Controlling house dust mite exposure will reduce the chronicity of asthma. Procedures such as covering the mattress, removing carpets where possible, and so on can be quite helpful. For many years, asthmatic patients have been told to avoid using feather filled pillows on their beds. The rationale was that the house dust mite thrives in feathers. However, a study found that the house dust mite allergen content of synthetic pillows was much higher than for feather pillows.15 The age of the pillow is probably more important, and they should be replaced regularly.

Other common factors involved in asthma development may include cats, cockroaches, grass pollens, and mold. Association with severe asthma in children was seen between non-feather bedding, especially foam pillows (in support of the above study), and the current ownership of furry pets or ownership at birth.16 A Finnish study of school children aged seven to 13 found that moisture and mold problems in the school building were linked to respiratory infections and asthma.17

Of course, all the above allergens can trigger an asthma attack, as can many foods, especially dairy products, eggs, and nuts. Dust mite contamination of wheat flour can cause anaphylactic reactions, and cooking had no effect. It was suggested that flour be stored in the refrigerator.18 Royal jelly should be used cautiously as it is now a well-known trigger of asthma attacks.

b. Atopy

Atopic individuals are more likely to develop asthma.19 However, genetic factors are less important than environmental ones. For example, if one identical twin has asthma, the chance of the other twin also having the disease is only about 40%.20 The genetic factors involved in the development of asthma are not well understood.21

c. Air Quality

Maternal or parental smoking has been linked to asthma incidence and severity.22-24 Air pollution parameters such as NO2,25 ozone,26 and particulates27 have also been associated with the incidence of asthma. Exposure to dust, irritants, and allergens at the workplace can also cause asthma. Usually withdrawal from the irritant or allergen results in remission, but in some cases where exposure is prolonged, the asthma becomes self-sustaining despite such withdrawal.

d. Sinusitis

Sinusitis has been associated with asthma in several studies.27,28 This is not considered to be due to aspiration of sinus contents.29 In one study, 79% of asthma cases had chronic rhinitis or rhinosinusitis.30 In 69% of cases, the nasal symptoms coincided with or preceded the onset of asthma. In 59% of associated cases, nasal symptoms coincided with acute asthmatic episodes. Treatment of the nasal condition improved the asthma. The link between sinusitis and asthma is strongest in patients with intrinsic asthma.

The following quotation from an article by Hackman et al. explores this theme more fully:31

"Studies have been performed in both experimental animals and humans which indicate that stimulation of receptors in the upper airway result in bronchoconstriction. As early as 1870, a substantial increase in lower airway resistance was reported by stimulating the nose of cats with either ether or sulphur dioxide.32 Electrical stimulation of the nose was found to result in increased lower airway resistance in cats.33 Even physical intervention, specifically correction of nasal septum deviation, restores normal lower airway function.34"

Histamine challenge studies on patients with perennial rhinitis caused a significant drop in forced expiratory volume in one second.35 The frequent association of paranasal sinus disease and bronchial asthma has been noted for many years. A number of clinical studies as early as the 1920s and 1930s emphasized the importance of sinusitis as a trigger for asthma in many patients.36-38

A recent study indicated that 75% of patients admitted with status asthmaticus had abnormal sinus X-rays.39 Although more objective evidence that sinusitis triggers or exacerbates asthma would be helpful in further clarifying this issue, the data suggest that patients who present with difficult-to-control asthma will improve when coexistent sinusitis is cleared by medical and/or surgical treatment. This can be considered as strong suggestive evidence for an etiologic role of sinusitis in lower airway disease.40

The eosinophil appears to play an important role in mediating injury to bronchial epithelium in chronic asthma. Recently, the role of the eosinophil in chronic inflammatory disease of paranasal sinuses was investigated with tissue from patients who underwent surgery for chronic sinusitis. Sinus tissue from patients with sinusitis who also had chronic asthma and/or allergic rhinitis was extensively infiltrated with

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> eosinophils. In contrast, sinus tissue from patients with chronic sinusitis alone had no eosinophils.

Another proposed mechanism for sinusitis as an aggravator of asthma is local stimulation of irritant receptors by inflammatory mediators with resultant reflex bronchospasm. Leukotrienes, prostaglandin (PG) D2, and histamine levels were measured in maxillary sinus lavage fluid obtained during surgery for chronic sinusitis. The levels of leukotrienes, histamine, and PGD2 in sinus fluid were significantly elevated and in the range associated with local inflammation and irritant receptor stimulation.\(^{41}\)

e. Poor Digestion

A number of researchers in the 1930s found a high incidence of hypochlorhydria in asthmatic patients.\(^{42}\) In these studies, the test meal method was used. This method is now considered inappropriate for the assessment of histological hypochlorhydria. However, it does assess for functional hypochlorhydria, that is, a deficiency of vagal stimulation of acid production. Hydrochloric acid therapy improved the asthma.\(^{42}\) Since this kind of gastric deficiency is due to deficient vagal output, the use of bitter herbs that act through a vagal reflex to increase gastric digestion is indicated.\(^{43}\)

Gastroesophageal reflux (GER) has been linked to asthma in several studies. In fact, strong evidence exists that GER is an important etiological factor for some asthmatics. Monitoring of esophageal pH revealed GER in seven out of nine patients with persistent asthma.\(^{44}\) In another study, 61% of patients with intrinsic asthma exhibited GER.\(^{44}\) Studies on children concluded that asthma symptoms were more often elicited by exposure of the distal esophagus to gastric acid, possibly by a vagal reflex, than by aspiration of gastric juice.\(^{46}\) However, other studies have implicated the importance of aspiration.\(^{47,48}\) In support of the reflex hypothesis, subjects with GER but not asthma showed a significantly greater bronchial reactivity to histamine than normal matched controls.\(^{49}\)

Treatment of GER by surgery or drugs can result in improvement or cure of asthma.\(^{45,50,51}\) Prognosis for cure was most favourable in cases of intrinsic asthma with a predominance of nocturnal crises.\(^{52}\) Acid suppressive therapy with the proton pump inhibitor omeprazole improved asthma symptoms in 73% of asthmatics with GER.\(^{53}\)

g. Infection and Infestation

Viral infections are known to exacerbate asthma. Viral infection in the upper airways frequently triggers a deterioration in bronchial hyperreactivity in asthmatics.\(^{59}\) Most hospital admissions for asthma occur over the winter months and soon after the start of school terms.\(^{59}\) Viral infections also worsen asthma in adults.\(^{60}\)

Some evidence suggests that viral infections may also contribute to the development of asthma, especially in children. About 92% of children hospitalized with respiratory syncytial virus (RSV) bronchiolitis in the first year of life subsequently developed symptoms suggestive of asthma within five years.\(^{61}\) Of this group, 71% had clinical evidence of asthma.\(^{61}\) Recurrent upper respiratory tract infections are associated with asthma risk in children,\(^{53}\) and 37% of children with viral lower respiratory tract infections in infancy subsequently developed asthma.\(^{62}\) The incidence of asthma is higher in respiratory therapists than in the general population. The difference develops after entry into the profession.\(^{63}\) It has also been suggested that aspirin-sensitive asthma results from a chronic viral infection.\(^{64}\)

Despite this, the evidence on the role of respiratory infections in the development of asthma is currently seen to be conflicting, with some studies suggesting a protective role of viral infection in early childhood and others indicating a link with asthma worsening.\(^{65}\) The issue here could be the type of viral infection. Some infections may help the immune response shift more to a TH1-type response (more about this later), whereas others may precipitate a chronic inflammation that leads to asthma. As noted above, the connection between RSV and asthma seems marked and this has been supported by more recent studies.\(^{66,67}\) In particular, one study found that early infection with RSV appears to increase the tendency to develop an allergic response (as indicated by levels of IgE antibodies and skin prick tests).\(^{66}\)

Several studies have investigated other possible mechanisms for viral involvement in asthma pathophysiology. Viruses probably increase bronchial hyperreactivity through epithelial and parasymptathetic nerve receptor damage, polymorphonuclear-dependent inflammation, and increased mediator release.\(^{68}\) This may lead to abnormalities in nervous control of respiratory smooth muscle.\(^{69}\)

In contrast, bacterial infection has been linked to adult onset asthma. A study found that repeated or prolonged exposure to Chlamydia pneumoniae could have a causal association with wheezing, asthmatic bronchitis, and asthma.\(^{70}\) Patients with evidence of C. pneumoniae exposure comprised 81% of 26 patients with asthmatic bronchitis, 100% of asthmatic bronchitics 40 years and older, and eight out of ten patients with asthma. Although measured antibody titres to C. pneumoniae were lower than those used to diagnose acute infection with this organism, the study results suggested that an ongoing mild or secondary infection with this organism contributes to the pathogenesis of wheeze.

A hypersensitive response to mycobacteria following antituberculosis therapy and subsequent release of tuberculosis antigens caused an asthma-like syndrome in several patients.\(^{71}\) Hence, it is possible that excessive antibiotic use may contribute to asthma via a similar mechanism. Preincubation of mononuclear cells with autogenic bacterial antigens enhanced histamine releasing factor in 12 of 25 asthma patients and only one of 15 control subjects.\(^{72}\) No specific bacterial strain was identified as having the sole stimulatory property. In a multicenter study, 27% of 193 asthma patients experiencing acute exacerbation had significant levels of bacteria in their sputum.\(^{73}\)

A group of 12 adult patients with asthma and chronic fungal skin infection were found to have hypersensitivity to Trichophyton spp.\(^{74}\) Several patients had many of the features...
of late onset intrinsic asthma. A Russian study in children with bronchial asthma living near a microbiological factory found that most were hypersensitive to Candida. Asthma has also been associated with parasitic infestation with Strongyloides stercoralis.

b. Salt Intake and Dehydration
Regional sales of table salt in England and Wales are strongly correlated with deaths from asthma in men and children. A study of 138 men found a close relation between BH and 24-hour urinary sodium excretion. Other studies gave conflicting results. A large randomized controlled trial of slow sodium supplementation showed an increase in BH in men, but not women, and a low salt intake was correlated with improved asthma in men. Several mechanisms for this association have been postulated, such as an increase in circulating NaK-ATPase inhibitors or a decrease in catecholamine concentration. Exercise-induced asthma may be related to dehydration of the intrathoracic airways during hyperpnea. A high salt intake may interfere with rehydration of the airways. Mouth breathing as a result of sinusitis may also cause airways dehydration.

i. Hormonal Factors
Glucocorticoid insufficiency related to various adrenal and extra-adrenal mechanisms has been associated with asthma in a Russian study. Reduced nocturnal catecholamine and cortisol levels, which are a natural part of circadian rhythm, may be linked to the nocturnal exacerbation commonly associated with asthma. It has been postulated too that an increase in brain norepinephrine can reflect depression of the hypothalamic-pituitary adrenal axis. A similar increase was found in asthmatic children compared to controls.

Premenstrual asthma has been observed and has been improved by progesterone injection. Dynamic changes in hormone concentrations during the perimenstrual period are thought to be responsible for the rise in emergency admissions of asthmatic women at this time. Hormonal variation may prove to be a significant and independent risk factor for acute exacerbations of asthma. Although the observed four-fold increase in emergency admissions suggested that hormonal variation may influence the timing of an asthma attack, the severity of symptoms was no worse than that among women who presented at any other time in their menstrual cycle.

j. Poor or Imbalanced Immune Response
IgG-subclass deficiency, which is an important factor in the susceptibility to recurrent infections, was a common finding in patients with asthma and obstructive bronchitis, and asthmatic children. Children with elevated serum IgE levels and absent secretory IgA have a high risk of contracting asthma. One of the most notable recent developments in theories about the cause of asthma is the so-called "hygiene hypothesis." This hypothesis holds that children growing up in cities, and particularly in a sanitized environment, experience a relative absence of exposure to pathological micro-organisms that results in poor and imbalanced development of the immune system. The additional role of the excessive use of antibiotics also needs to be considered in this context.

This hypothesis is supported by the observations that the asthma incidence is higher in industrialized countries and is increasing, and is relatively lower in rural areas compared to urban environments. The results of many epidemiological studies suggest that asthma prevalence has increased because of something lacking in the modern environment, which is suggested to be exposure to common childhood infections. Measles has been suggested as one such protective infection.

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At the level of the immune system, this lack of exposure is thought to result in a persistent TH2 immune response that leads to allergen sensitisation and production of IgE antibodies. In contrast, exposure to certain bacterial and viral infections in early childhood is thought to shift the balance more towards a TH1 immune response. Naturally, this is also influenced by the genetic predisposition of the individual. This hypothesis suggests a possible role for the Ayurvedic herb Tylophora indica, a traditional treatment for asthma that may be able to modify T-cell immune response and shift the balance back towards a TH1-type of response.
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m. Aspirin-Sensitive Asthma

Patients with Aspirin-Sensitive Asthma (ASA) show negative skin tests with atopic allergens and are intolerant to aspirin and other chemical agents such as non-steroidal, anti-inflammatory drugs (NSAIDs), sulfites, and tartrazine. A particular syndrome, Samter’s Syndrome (SS), is characterized by asthma, nasal polyposis and/or sinusitis, vasomotor rhinitis, and aspirin-sensitivity. Patients with this syndrome are sensitive to some NSAIDs, but are generally not sensitive to tartrazine.

ASA and SS are probably acquired, and it has been postulated that a virus is involved. It is suggested that some time after viral exposure, specific cytotoxic T-lymphocytes are produced. The resulting mediator release precipitates the asthma attack. However, one study suggested increased leukotriene C4 and histamine are more likely to contribute to ASA rather than decreased PGA2.

Traditional Factors Associated with Asthma

a. Poor Digestion

Flower in his Treatise of the Asthma published in 1698 wrote the following: Some writers...have observed the hypochondriac symptoms in the stomach and conclude the asthma...wants digests.... It is commonly observed that fullness of diet, and all debauches render the fits most severe, and a temperate diet makes the fits more easy.... The defect of digestion and mucilaginous slime in the stomach are very obvious and observed by writers.

Salter in 1868 stated the following: ...the precursory symptoms are connected with the stomach and consist of loss of appetite, flatulence, costiveness, and certain peculiar uneasy sensations in the epigastrium; but here I think we have something more than mere premonitory signs; I think the relation of these symptoms to the spasm which follows is often something more than mere premonitory signs; I think the relation of these symptoms to the spasm which follows is often that of cause and effect.

b. Unhealthy Mucous Membranes and Diet

Mucus secreted by mucous membranes (MM) is normal and has many important physiological functions. When MM become unhealthy, the nature and the quantity of the mucus changes. This can be referred to as a catarrhal condition. The degree of catarrhal congestion of the lungs can vary in asthma and is best assessed by auscultation and case history. The association of chronic sinusitis with asthma is indicative of unhealthy MM. Despite the excessive mucus, catarrhal MM are thought to provide less protection than healthy MM and, in the case of asthma, render the lungs more prone to damaging environmental factors such as allergens and pathogens.

Diet is a significant factor in causing a catarrhal state of the respiratory MM. Excessive protein, refined carbohydrate, or salt consumption can lead to excessive and unhealthy mucus production. In some individuals, particular food groups, especially dairy and/or wheat, can also contribute to this process.

Catarrhal MM can also be regarded as a vicarious elimination due to inefficient detoxication and elimination in the body. Hence, in traditional terms, the detoxifying and eliminative processes need to be stimulated.

c. Stress

Traditionally, asthma has been regarded as imbalance in the autonomic nervous system. Stress and nervous anxiety contribute to this imbalance, which may also cause muscular tension in the diaphragm and disturb the rhythmic nature of the breathing apparatus.

It has been postulated that asthma results from a disturbance of the rhythmic activity of the respiratory center in the brain. This disorder is then reflected in the airways and the respiratory muscles through their respective innervations, causing a subclinical template of asthma. This rhythmic disturbance is reflected in the EEG of asthmatic patients which generally contain certain abnormalities.

References

17. Carpi J. Mite-contaminated foods linked to anaphylaxis. Family Practice News. 2006; May 1, 19.
Phytotherapy and Asthma


83. Early respiratory viral infections and the development of asthma. In Watanabe, H, Shibuya T. Eds.) 1990; 44(7); 552-554.


88. van Alderen WM, Meijer CG, Oosterhof Y, Bron AO. Epidemiology and the concept of underlying mechanisms of nocturnal asthma. Respiratory Medicine. 1993; 87 suppl: B-39.


