Use of capnographic waveform indices in monitoring non-intubated asthmatic patients within the Emergency Department

by

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This is dedicated to

Yuh Wei, my fiancé

Whom it would be my greatest honour to call my wife

And to my parents

My foundation and my guiding light

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ABSTRAK

Kajian Indeks Gelombang Kapnografi dan penggunaannya untuk pengawasan pesakit asma di Jabatan Kecemasan

Objektif Kajian: Untuk mengkaji sama ada kecuraman Fasa II dan III dan sudut alpha (Q) gelombang kapnografi yang dikaji dapat menunjukkan perubahan dalam keadaan pesakit dengan serangan asma; dan untuk mengkaji sama ada perubahan ini berkaitan dengan perubahan dari segi klinikal dan pengukuran 'peak flow'.

Kaedah: Kami menjalankan kajian prospektif di Jabatan Kecemasan Hospital Universiti Sains Malaysia. 30 pesakit yang mengalami serangan asma akut dikaji dari segi klinikal(kebolehan bertutur, kadar pernafasan, kadar nadi, pulsus paradoxus, bunyi 'wheeze' dan 'pulse oximetry') dan pengukuran 'peak flow' diikuti dengan pengawasan 'sidestream' dengan kapnografi menggunakan 'nasal cannula'. Gelombang kapnografi dicatitkan di dalam kad memori komputer (PC card). Pesakit dirawati dengan 'beta-agonists' dan 'steroids' mengikuti protokol jabatan. Selepas rawatan, bila pesakit dianggap sihat untuk discaj, kajian semula dilakukan dengan kaedah klinikal, pengukuran 'peak flow' dan gelombang kapnografi. Kajian sebelum rawatan dan selepas rawatan dikaji dengan ujian 'paired samples t-test'. Kajian 'correlations' dilakukan untuk mengetahui kaitan antara ketiga-tiga kaedah pengawasan ini. Nilai $p < 0.05$ dianggap ketara (significant).

Keputusan: Terdapat perubahan ketara sebelum dan selepas rawatan dari segi klinikal; kebolehan bertutur ($p = 0.002$), pulsus paradoxus ($p = 0.007$), wheeze ($p < 0.001$) dan pulse oximetry ($p = 0.035$); malah tiada perubahan ketara dalam kadar nadi ($p = 0.052$) dan kadar pernafasan ($p = 0.739$). Pengukuran 'peak flow' juga menunjukkan perubahan yang ketara selepas rawatan ($p < 0.001$). Dalam kajian gelombang kapnografi, terdapat perubahan ketara pada kecuraman Fasa III ($p < 0.001$) dan sudut alpha ($p < 0.001$) tetapi ini tidak jelas pada kecuraman Fasa II. ($p = 0.35$). Kajian kaitan (correlations) tidak menunjukkan kaitan yang kuat antara pengukuran ketiga-tiga kaedah ini.

Kesimpulan: Ketiga-tiga kaedah iaitu klinikal, pengukuran 'peak flow' dan kajian indeks gelombang kapnografi dapat menunjukkan perubahan pada pesakit asma selepas rawatan. Kajian gelombang kapnografi ada beberapa kelebihan; iaitu ia tidak memerlukan kebolehan dan keupayaan pesakit melakukan ujian, dan membolehkan pengawasan berterusan. Kajian gelombang kapnografi dapat dicadangkan untuk pengawasan pesakit asma dalam Jabatan Kecemasan jika analisa gelombang dengan komputer dapat dilakukan.

ABSTRACT

Use of Capnographic Waveform Indices in monitoring non-intubated asthmatic patients within the Emergency Department.

Study Objective: To determine if the slope of Phase II and Phase III, and the alpha angle (Angle Q) of the expiratory capnographic waveform measured via computer-recognizable algorithms, can reflect changes in bronchospasm in acute asthmatic patients presenting to the Emergency Department; and to assess the correlation of these changes with clinical severity scoring and peak flow measurements.

Methods: We carried out a prospective study in a university hospital Emergency Department. 30 patients with acute asthma were monitored with clinical severity scoring (speech pattern, respiratory rate, pulse rate, presence of pulsus paradoxus and wheeze, and pulse oximetry) and peak flow measurements, and then had a nasal cannula attached for sidestream sampling of expired carbon dioxide. The capnographic waveform was recorded onto a PC card for analysis. The patients were treated with inhaled beta-agonists and steroids according to departmental protocols. After treatment, when they were adjudged well for discharge, a second set of results was obtained for clinical severity scoring, peak flow measurements and capnographic waveform recording. The pre-treatment and post-treatment results were then compared with paired samples t-test analysis. Simple and canonical correlations were performed to determine correlations between the 3 assessment methods. A p value of below 0.05 was taken to be significant.

Results: There was significant improvements pre-treatment and post-treatment in 4 parameters in the clinical severity scoring, namely speech pattern ($p = 0.002$), pulsus paradoxus ($p = 0.007$), wheeze ($p < 0.001$) and pulse oximetry ($p = 0.035$); but there was no significant difference in pulse rates ($p = 0.052$) or respiratory rates ($p = 0.739$). Similarly, peak flow measurements also showed significant improvements post-treatment ($p < 0.001$). On the capnographic waveform, there was a significant difference in the slope of Phase III ($p < 0.001$) and alpha angle ($p < 0.001$); but not in Phase II slope ($p = 0.35$). Correlation studies done between all three assessment methods did not show strong correlations neither between the measurements itself nor the magnitude of change pre-treatment and post-treatment.

Conclusion: Clinical severity scoring, peak flow measurements and capnographic waveform indices can indicate improvements airway diameter in acute asthmatics within the Emergency Department. Capnographic waveform analysis presents several advantages in that it is effort-independent, and provides continuous monitoring of normal tidal respiration. They can be proposed for the monitoring of asthmatics within the Emergency Department when specific computerised indices can instantly analyse the capnographic waveform and report the indices in a recognizable and reproducible form.

Introduction 1

Capnography comprises the continuous analysis and recording of carbon dioxide concentrations in respiratory gases. 'Time capnography' (commonly just referred as capnography) is the continuous plot of levels of expired carbon dioxide over time producing a capnogram. This allows for visual inspection of changes in CO_2 concentrations by means of a waveform display, paper recording or even digitised measurements. It is the analysis of such waveforms that forms the basis of this study.

Capnometry, discrete measurements of carbon dioxide concentrations, was first developed during the Second World War as a means of monitoring the internal environment of submarines [O'Flaherty, 1994]. In the 1950s, capnometers were used experimentally during anaesthesia to measure expired CO_2. But it was only in the early 1980s that capnometry became widely used mainly in the anaesthetic practice [Smalhout & Kalenda, 1981]. Today, capnography is considered to be essential in monitoring metabolic and respiratory functions during anaesthesia. Its role has spread beyond the realms of anaesthesia and capnography is now used in Emergency Medicine to confirm and verify endotracheal tube placement, monitor

ventilatory status of respiratory impaired patients, monitor ventilation of patients during sedation/analgesia, evaluate ventilator settings and circuit integrity, assess effectiveness of cardio-pulmonary resuscitation, and for early detection of changes in airway resistance and circulatory collapse.

Recently technological advances in capnography especially in the ability to accurately measure and display real-time recordings of expired carbon dioxide induced significant interest in *time capnography* and *volumetric capnography* (the plot of capnogram tracing against total expired volume). Furthermore, newer detection methods e.g. Microstream® technology has allowed for more accurate recordings in smaller samples; thereby extending the use of capnographic monitoring not only to non-intubated patients but even in paediatric patients. Much in line with these advances, scientists and clinicians are looking into other uses of capnography; among them, the analysis of the capnographic waveform to provide information on airway obstruction in non-intubated asthmatic patients.

The normal capnogram has an almost square-wave pattern, [Figure 1.1] marked by alternating inspiratory ($P_{insp}CO_2$ equals zero) and expiratory phases [Berrengo & Cutilloa, 1961; Smalhout & Kalenda, 1981; You et al, 1994]. Expiration itself consists of 3 successive phases: **1)** a latency phase (Phase I), corresponding to the expiration of the anatomical dead space ($P_{exp}CO_2$ equals zero), which is indistinguishable from the preceding inspiration; **2)** slope phase

(Phase II) marked by a very rapid rise in $P_{exp}CO_2$, corresponding to expiration of mixed air; and **3)** plateau phase (Phase III), reflecting the elimination of alveolar air (slightly increasing $P_{exp}CO_2$) resulting in a peak at the end of tidal expiration. ($P_{et}CO_2$ close to alveolar carbon dioxide tensions P_ACO_2) [You et al, 1994; Bhavani-Shankar, 2000]. The end-tidal peak is occasionally referred to as the end-tidal point. In certain normal individuals especially in the obese and pregnant women, the terminal segment of the plateau phase often shows a terminal upswing. This is frequently referred to as Phase IV as it closely reflects a similar Phase IV in single breath testing of expired Nitrogen (SBT-N2) [Bhavani-Shankar 2000]. The capnographic waveform then terminates with inspiration with a sudden and sharp drop in measured CO_2 to atmospheric levels (Phase 0).

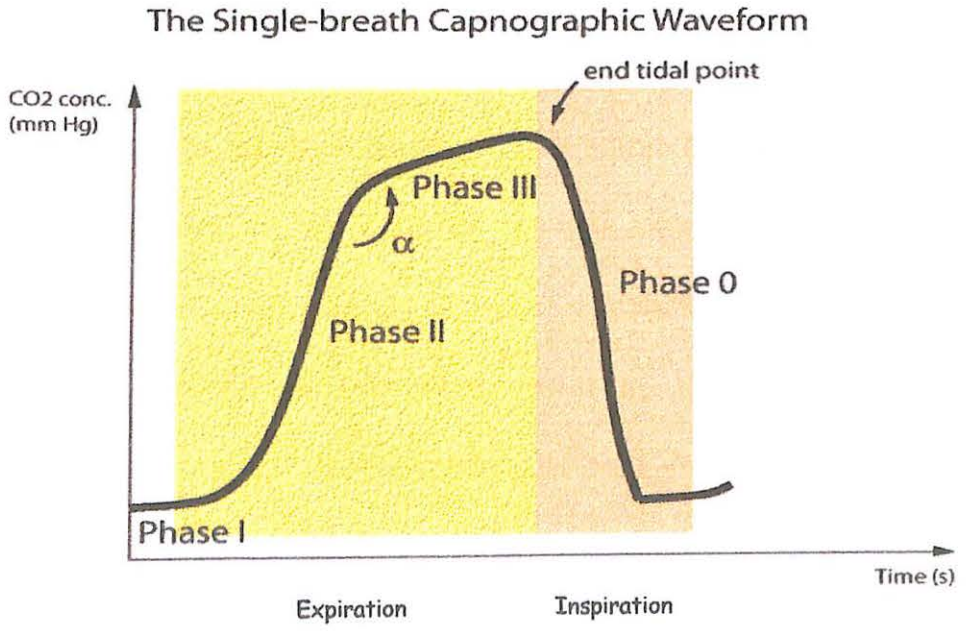

Figure 1.1: The Single Breath Capnographic Waveform

This well-defined shape of the normal capnograph depends on a variety of factors. Normal aerobic metabolism will consume oxygen and result in the production of carbon dioxide. This will be carried by an adequately functioning circulatory system to the lungs where, in the normal lung, matched gas distribution and alveolar ventilation with pulmonary perfusion will ensure normal gas exchange. In the absence of bronchial obstruction, the verticality of Phase II indicates a regular separation front between the anatomical dead space air and alveolar air. The elimination of alveolar air is synchronous and this is reflected by the sudden rise of Phase II and the subsequent elimination of alveolar air, which is indicated by the almost horizontal plateau of Phase III.

Asthma is a disease characterized by bronchial hyper-reactivity, inflammatory exudates and mucous plugging. The hallmark of asthma is the narrowing of the smaller airways causing obstruction to flow within the airways especially during expiration. In asthma, airway obstruction causes regional decreases in airflow and consequently, alveolar ventilation. This is responsible for the "parallel heterogeneity" of ventilation-perfusion ratios (V/Q ratios). Each bronchopulmonary territory is characterized by its own V/Q and determining its own P_ACO_2. Alveolar air is then evacuated at different times during expiration resulting in desynchronisation. This results in increased mixing of alveolar air from certain bronchopulmonary territories with dead space air from other territories. On the capnogram, this causes deformation of the normal curve, marked by the loss of verticality of Phase II, opening of the angle between Phase II and Phase III (Alpha

angle also known as Angle Q) and the increased inclination of Phase III [You et al, 1994]. In severe cases, the capnogram takes on a "shark's fin" appearance. These changes in the capnogram are of particular interest as they indicate changes in airflow. This may provide the means for closer, continuous and objective monitoring of airway diameter and airflow in patients with acute asthma. [Figure 1.2]

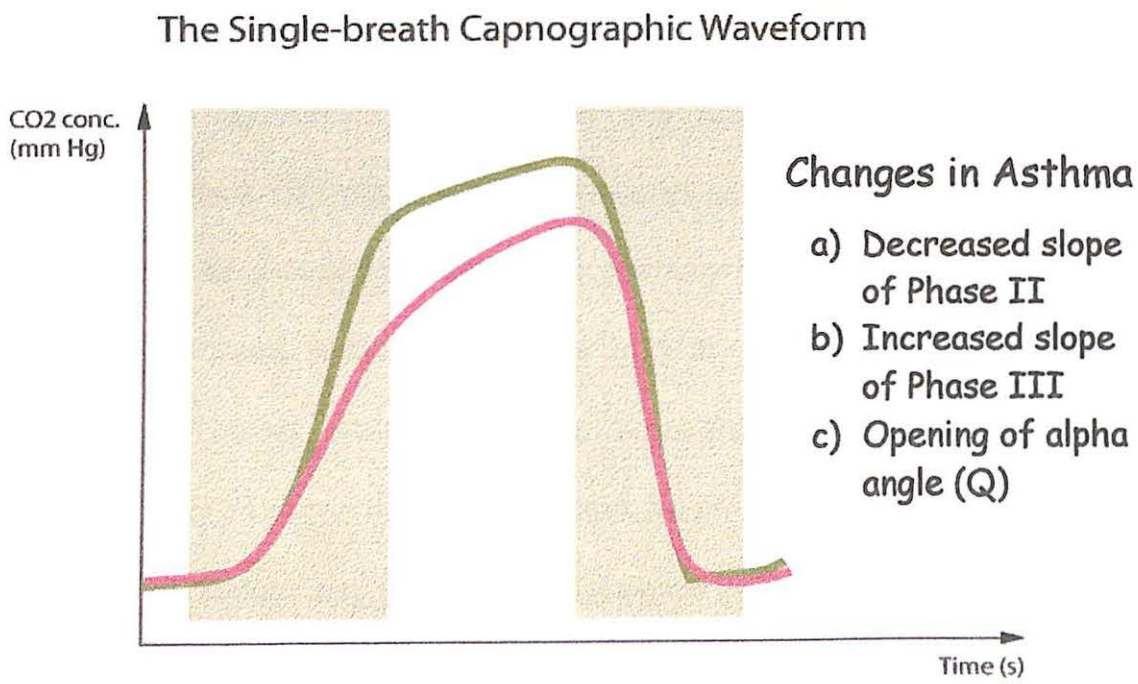

Figure 1.2: The Capnographic Waveform – Changes in Asthma

Bertrand You et al in a landmark study on adult asthmatics described various waveform indices such as slopes of different parts of the capnogram as well as areas subtended by different parts of the curve, and correlated these indices with different degrees of airway obstructions quantified with spirometric findings [You et al, 1994]. They reported strong correlations of the capnographic indices with the spirometric parameters and suggested that capnographic waveform analysis may be used in the monitoring of asthma.

Asthmatics who present to the Emergency Department with acute attacks of asthma are often required to perform forced expiration manoeuvres to assess the degree of airway obstruction and thereby, the severity of the attack. These manoeuvres are then repeated post-treatment to confirm the return to baseline status. These forced expiration manoeuvres (namely PEFR – peak expiratory flow rate or FEV_1 – forced expiratory volume in first second) allow for objective monitoring of asthmatic patients besides standard clinical assessment. The readings are based on percentage of expected values, which would depend on the patients' age, sex, height and weight; or as a percentage of best baseline reading. These manoeuvres have been well studied and documented to accurately assess severity of bronchospasm and they form the basis of almost all monitoring of asthmatics within Emergency Departments throughout the world. However, there are several limitations to forced expiration manoeuvres. Most significantly, they require an active and technically correct effort to perform such manoeuvres. Often, spirometric measurements depend on whether medical staffs are able to explain,

motivate and guide patients to perform the manoeuvres properly and whether patients are willing and able to do them. Very often, this difficulty precludes the use of these measurements in children, the elderly, and the very dyspnoeic patient. Not knowing the pre-treatment peak flows and not knowing baseline peak flow levels now render any post treatment peak flow less useful. Apart from that, spirometric measurements may delay starting nebuliser therapy. Also, they are point-of-time measurements and therefore, not useful for early detection of deterioration of the patient while in the Emergency Department. Many doctors then rely purely on clinical judgement in monitoring asthmatics within the Emergency Department and deciding if these patients are adequately treated and safe for discharge. Many clinical parameters have been identified in attempting to objectively assess severity of the attack; few however are able to define specific clinical grounds for the safe discharge of asthmatics from the Emergency Department. It is this lack of objectivity, when forced expiration manoeuvres cannot be used, that occurs today.

Capnography offers several advantages in this aspect; it is non-invasive, non-effort related and cooperation-independent of the patient. It does not interfere with the administration of oxygen nor does it delay onset of nebuliser therapy. In fact, continuous monitoring of patients can be done during their nebuliser therapy, and throughout their stay in the Emergency Department. It is this aspect of capnographic monitoring that greatly interests many clinicians and researchers alike.

Unfortunately, the analysis of the capnographic waveform is still a concept in its infancy. Waveform indices that show satisfactory sensitivity (high correlations with spirometric parameters) are still being studied. Computerized measurements of these indices, their memorization and visualization in the form of trend curves could then constitute a useful tool for asthma monitoring. The computerized analysis and display of capnographic waveform indices as numerical data would greatly simplify and thereby promote use of capnography for the purpose of monitoring asthmatic patients during an asthmatic attack.

This study was undertaken to identify capnographic waveform indices that correlate with spirometric parameters, and to use entirely computerized algorithms to obtain and analyse these indices.

Objectives 2

The objectives of this study are as follows:

I. To record and analyse the expiratory capnographic waveform via sidestream monitoring using a nasal cannula in patients presenting to the Emergency Department with an acute attack of asthma.

II. To analyse the changes in the capnographic waveform after treatment with symptomatic improvement and on discharge from the Emergency Department

III. To assess these patients with clinical severity scoring and peak flow measurements pre-treatment and post-treatment.

IV. To correlate the changes in the capnographic waveform to changes in clinical severity scoring and peak flow measurements.

V. To analyse the capnographic waveform with indices that may be included in any future computerised algorithm for waveform analysis.

Literature review 3

In this chapter, we will look into the available literature not just on asthma and the monitoring of asthmatic patients, but also into capnography and its current uses. We will look into the basis of capnographic monitoring and steps in attempting to analyse the capnographic waveform. And we will attempt to demonstrate the basis for the waveform analysis undertaken in this study.

3.1 Asthma

These are exciting times for anyone interested in asthma. Never in history has progress in the understanding and management of asthma been so rapid or the outlook for the future so promising. With the improved understanding in the nature and pathogenesis of asthma, coupled with new laboratory methods of cellular and molecular biology, a deeper understanding of the problem and its solution has emerged. New clinical techniques of biopsy and bronchoscopic lavage has brought with it the advantages of earlier definitive diagnosis and thereby treatment of patients. New techniques of monitoring asthma suggest the possibility of improved care of patients not only within the Emergency Department, but also within the home itself. The management of asthma is getting rid of its "emergency room" stigma, and taken on a much more comprehensive and systematic

approach. Recent changes in the philosophy of treatment, which comes partly from a better understanding of the biology of the disease and partly from improvements in drug research and drug therapy, have spearheaded a paradigm shift in the medical community's approach toward the management of asthma.

As we appear to be headed toward greater understanding of the disease, asthma is getting to be a greater problem. The expanding population with a greater urban component, and a worsening environmental problem, has resulted in burgeoning numbers of patients with asthma, and with it, higher mortality each year. The increased cost of inpatient healthcare and the decreased population-bed ratio has seen higher pressures on the medical community to justify admissions on one hand, and adequately treat and safely discharge patients on the other. Asthma is a problem that personifies this very problem. The status of the patient with an acute attack may change dramatically within hours. It is no surprise that one of the main issues in the management of patients with an acute attack of asthma within the Emergency Department is whether to admit or to discharge these patients [Brenner & Kohn, 1998]. Careful assessment of these patients seem to be the key with a multitude of clinical indicators, spirometric parameters and other monitoring devices and techniques being used. We will review in further detail the assessment and management of asthmatic patients in an acute attack within the Emergency Department.

3.1.1 Historical Aspects

Recognizable clinical descriptions of asthma date from antiquity. In the past, the word asthma had been used to refer to almost any sort of difficulty in breathing especially if it was paroxysmal or episodic. By the end of the nineteenth century, asthma had been known to be an inflammatory disease with recognized airway obstruction and increased mucous production [Flint, 1879; Curschmann, 1883]. For most of the twentieth century however, attention was placed mainly on "bronchospasm" with the physiologists defining the adrenergic, cholinergic and non-adrenergic innervation of the bronchial smooth muscle, and the pharmacologists developing effective bronchodilatation. The consequence of this emphasis was that the most widely accepted definition of asthma, that of the American Thoracic Society in 1962, considers asthma as reversible airway narrowing with hyper-responsiveness and did not mention inflammation [American Thoracic Society Committee on Diagnostic Standards, 1962]. It has only been in the last decade of the twentieth century that the idea of asthma as an inflammatory disease has been fully accepted. This idea though, is definitely not new. In 1908, Ellis, studying the pathology of fatal asthma, described eosinophils in the bronchial wall as well as in the sputum and blood [Ellis, 1908]. Dunnill called attention to the fact that the characteristic mucous plugs that occlude the airway were not simply a secretion of mucous glands; but a complex exudate that included fibrin and other serum proteins, inflammatory cells and degenerating ciliated epithelium [Dunnill, 1960]. Naylor described "creola bodies", clumps of desquamated epithelial cells, in sputum expectorated during an acute attack [Naylor, 1962]. This characteristic pathology of asthma has sometimes led to it being referred to as "chronic

desquamating eosinophilic bronchitis". While we now acknowledge the inflammatory basis in the pathogenesis of asthma, coming up with an acceptable definition of asthma itself is still a subject for much debate.

Early attempts at defining asthma were hampered by the lack of agreement about the definitions of this disorder. Part of the problem relates to the lack of specificity of respiratory symptoms. Initial nomenclature of asthma included any patient who had difficulty in breathing, especially if it was episodic and if there was wheezing. Later, when it was shown that some patients with left ventricular failure had similar paroxysms, asthma became divided into *cardiac asthma* and *bronchial asthma*. It was much later when the nature of circulatory changes in left ventricular failure became better understood and better terms became available that the inappropriate term of 'cardiac asthma' was finally discarded and bronchial asthma tended to be known as asthma again. The problem still existed then in the over-reliance of wheezing to diagnose asthma. Now we know that asthma has varied presentations, many of them subtle. It was only relatively recent that nocturnal dyspnoea was recognized as a common feature of asthma. Exercise-induced asthma was not clearly documented until 1966 [McNeil, 1966]. Even cough has now been identified as the main presenting complaint of an asthmatic attack in some patients [McFadden, 1975; Carrao et al, 1979]. This lack of specificity and varied presentations is part of our difficulty in defining asthma. Osler recognized this with his famous aphorism "All that wheezes is not asthma".

3.1.2 Definitions

Ciba Foundation Guest Symposium in 1958 suggested:

> *Asthma refers to the condition of subjects with widespread narrowing of the bronchial airways, which changes in severity over short periods of time either spontaneously or under treatment, and is not due to cardiovascular disease. The clinical characteristics are abnormal breathing, which may be paroxysmal or persistent, wheezing and in most cases relief by bronchodilator drugs.*

The Committee of Diagnostic Standards of the American Thoracic Society suggested in 1962:

> *Asthma is a disease characterized by increased responsiveness of the trachea and the bronchi to a variety of stimuli and manifested by widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy. The term "asthma" is not appropriate for the bronchial narrowing which results solely from widespread bronchial infection, destructive diseases of the lungs or from cardiovascular disorder.*

These definitions are principally in terms of disorders of function; they do not include current understanding of the disease or diagnostic categories. Scadding JG suggested, in his article "Definitions and Clinical Categorization of Asthma", the primary definition of asthma as a disorder of airway function.

"Asthma is a disease characterised by wide variation over short periods of time in resistance to flow in the airways in the lungs."

"Hyper-reactivity of the airways to bronchoconstrictor stimuli, including pharmacological agents and a variety of non-specific chemical and physical agents, can usually be demonstrated. In some cases, specific antigen-antibody reactions, usually with inhaled antigens, can be shown to increase airflow resistance. Diminution of increased resistance in response to bronchodilator drugs or to corticosteroids is also usually demonstrable. Although asthma is characteristically episodic, it may become persistent with only minor variations; in such instances, diagnosis may be justified by indirect evidence that wide variability has been present in the past, and confirmed by later observation of the clinical course, including response to therapy or histologic changes known to be associated with this functional abnormality."

While this definition appears to be more inclusive of current understanding of asthma, the ongoing debate, of whether asthma is a 'disease' or 'condition with a constellation of symptoms', rages on.

3.1.3 Clinical Evaluation

The diagnosis of asthma is based on the presence of variable airway obstruction. Assessment of the severity of illness and hence the need for treatment requires an estimate of the degree of airway obstruction. Such an estimate is often achieved by measurement of expiratory flow rates; but can also be based on the patient's symptoms and physical findings. Characteristically, patients with asthma

have some combination of dyspnoea, wheeze, chest tightness and cough; the salient feature being the episodic nature and high variability of these symptoms. The diagnosis can often be made quickly and accurately from the patient's description of complaints, although spirometric measurements are often required to confirm the diagnosis. Further clues to the diagnosis of asthma include the presence of eosinophils in the sputum and blood, and substantial improvement following bronchodilator therapy.

Shortness of breath is an extremely common complaint in patients with acute asthma. It is related as much to the degree of airway obstruction as to the sense of effort required to achieve adequate ventilation. Nevertheless, there is poor correlation between the sense of dyspnoea and the degree of measurable airway obstruction; partly due to the variable hyperventilation that occurs. Interestingly, many patients complain of greater distress during inspiration than expiration, although all types of intra-thoracic obstruction should be more severe during expiration. Muller et al attributed this to the fact that one of the characteristic features of asthma is the sustained and tonic activity of inspiratory muscles. This allows the chest to be maintained in a relatively inflated position so as to make it possible to expire from the increased elastic recoil of the distended lungs. This excessive muscle activity albeit much of it wasted, is undoubtedly a major cause of the sense of shortness of breath [Muller et al, 1981].

The high velocity of flow through narrowed large airways produces wheeze, which was audible to the patient and the doctor alike. Many patients notice

wheezing during their acute attacks, but it is by no means present all the time, and its absence should not preclude a diagnosis of asthma. Shim and Williams reported that, when present, wheezing was associated with lower PEFR than when it was absent [Shim & Williams, 1983].

The sense of chest tightness is also one of the characteristic symptoms of asthma, probably the most common one. It is likely that this sensation reflects the excessive activity of vagal irritant receptors, known to be a fundamental feature of asthma, rather than as a result of airway obstruction. Cough too is a common feature of asthma. It has been described as one of the common presenting symptoms especially in young children. During the acute attack, it often develops as patients start to improve and the inspissated mucous plugs that have occluded the airways are dislodged into the tracheo-brochial tree so that they can be expectorated [McFadden, 1975]. Carrao et al in 1979 stressed the important clinical point that cough, like dyspnoea, may be the sole manifestation of asthma [Carrao et al, 1979]. The recent recognition of cough as an important symptom of asthma has brought about some changes in the way we manage patients with cough. Hannaway and Hopper, in an article in JAMA 1982, suggested that patients, especially children, with unexplained cough should be given a trial of bronchodilators even if expiratory flow rates are normal [Hannaway & Hopper, 1982].

3.1.4 Predisposing factors

Bronchial hyper-reactivity is commonly seen in asthmatics. The relationship between increased bronchial responsiveness and asthma is still unclear. While many studies have demonstrated increased bronchial responsiveness in asthmatics, the link to airway inflammation is unproven. The relationship between increased bronchial responsiveness and airway inflammation is thought to be the key in understanding why some bronchial responsiveness is associated with clinical disease and some is not. This hyper-reactivity is the cause of the varied responses of asthmatics to external stimuli, which may be physical, chemical or even biological agents. Symptoms may follow exposure to specific agents but more often than not, symptoms develop without any identifiable cause.

Genetic factors are involved in the development of asthma and a large percentage of patients have a family history of asthma or allergic disease. However, what is not clear is the degree to which familial factors are due to inheritance rather than a common environment. In many asthmatic children, attacks are clearly related to seasons in the year or to exposure to certain pets (notoriously to cats) or to ingestion of certain foods. Sensitivity to mites is increasingly recognized in asthmatics. This certainly prompts suspicion of an allergic basis for the condition [Platts-Mills, 1989].

Environmental factors play an important part in asthma. Exposure to environmental agents may produce airway inflammation in the susceptible segment of the population. A wide variety of common environmental events such

as respiratory infections [Gurwitz et al, 1980], atopy or allergy [Cockcroft, 1979], air temperature and humidity [Deal, 1979], and exercise [McFadden, 1979] are known to influence airway responsiveness. In adults however, specific antigens are rarely of major importance in causing an acute exacerbation. Often, attacks are precipitated by viral infections. There has been a great deal of epidemiological and clinical evidence that viral, but not bacterial infections are a major cause of worsening of asthma [Sherter & Polintsky, 1981; Busse, 1990]. This is important clinically as it defends the wisdom of intensifying therapy at the first sign of upper respiratory illnesses to prevent severe airway obstruction.

There is a long list of substances in the working environment and in the natural environment that are associated with worsening asthma and a careful occupational history is of utmost importance in adult asthmatics [Bernstein, 1981]. A change in the surrounding environment is an important cause of new-onset asthma or worsening of existing asthma. Another common cause for worsening of asthma is exercise or breathing of cold air. These events are coupled, as McFadden showed that bronchoconstriction that follows exercise is related to heat loss in the respiratory tract [McFadden, 1981]. Another common feature seen in many asthmatics is the development or worsening of symptoms at night. Hetzel and Clark described the circadian rhythm of peak expiratory flow rates in both normal people and asthmatics. PEFR is lowest between 3 am and 6 am [Hetzel & Clark 1980]. As a result, it is common for patients to wake up early in the morning with symptoms of asthma [Todisco, 1980].

Among other causes that have been associated with worsening of asthma are associated sinusitis, gastro-oesophageal reflux, onset of menstruation, emotional factors and drugs. 2 groups of drugs are especially important in asthmatics. Aspirin and to a lesser extent, all non-steroidal anti-inflammatory agents (NSAIDs) may induce asthmatic attacks in sensitive subjects [Weber, 1979]. The mechanism of this is not clear; it is not immunologic but rather apparently relates to effects on arachidonic metabolism. The other group of provocative agents are the beta-adrenergic blocking drugs. There have been reports of asthmatic attacks first developing after taking these drugs or even after their application as eye-drops in the treatment of glaucoma. Although bronchoconstriction does not occur in normal subjects who are given beta-blockers, they do occur in asthmatics [Zaid & Beall, 1966]. The fact that beta-blockers have no effect in normal patients but do have such an explosive effect in asthmatics, suggests that in patients with asthma, endogenous catecholamines are essential in maintaining bronchodilatation. Beta-blockers should therefore, be avoided by all patients with asthma.

History of severe asthma requiring intubation is essential information. Although such life-threatening asthma is relatively rare, probably occurring no more commonly than in 0.2 percent of patients with asthma per year, and although it generally does not occur until a patient has had asthma for many years, once it occurs it is apt to occur again [Williams, 1980].

3.1.5 Physical Examination

Physical examination of patients during the acute asthmatic attack should reveal not just the diagnosis, but also some idea of the severity of the attack. Many clinical parameters have been proposed toward this end and almost all of them consider changes in wheeze, presence of pulsus paradoxus, initial pulse rates and respiratory rates, and accessory muscle function as parameters to indicate severity of the attack.

The most well known hallmark of asthma is the presence of wheezing. Passage of air through narrowed airways results in turbulent flow, producing wheeze. This wheeze is typically polyphonic, of differing intensity and tone from time to time, and from place to place over the chest. It is usually more notable during expiration when airways are narrower, but it may occur throughout inspiration and expiration especially in severe disease. On the other hand, some patients have such severe airway obstruction as to be unable to generate sufficiently rapid airflow to produce any wheeze at all resulting in a 'silent chest', Shim and Williams reported that wheezing in both inspiratory and expiratory phases were associated with a lower PEFR than expiratory wheezing alone. They also reported significant correlations between the intensity of wheezing and the reduction of PEFR; and wheezing throughout expiration was associated with lower PEFR than end-expiratory wheezing alone [Shim & Williams, 1983]. Unfortunately, these findings are relatively subjective and do not allow for accurate assessment of severity by itself.

As discussed previously, excessive activity of inspiratory muscles serves to maintain maximal inflation. Some have suggested that the detection of the activity of the inspiratory muscles, notably the scalenes and sternocleidomastoids, may indicate severity of disease. Muller et al reported on the relationship between severity of airway obstruction and the palpable activity of scalene muscles, notable only during inspiration in mild cases but present throughout the respiratory cycle in patients with severe asthma [Muller et al, 1981]. This activity of the inspiratory muscles are clearly seen in the severe asthmatic who makes rapid forceful inspiratory efforts and then more slowly expires; up to the point of development of muscular fatigue and respiratory arrest.

Pulsus paradoxus relates to the fall of blood pressure during inspiration as a result of the very negative pleural pressures generated during an acute attack of asthma. It had been suggested that the amount of this fall bears a rough relationship to the severity of airway obstruction. Rebuck and Reed reported in their article that pulsus paradoxus was absent in patients with $FEV_1 > 40\%$ but present in all patients with a $FEV_1 < 20\%$ [Rebuck & Reed, 1971]. However, this relationship is imperfect; patients with severe airway obstruction may not have pulsus paradoxus and patients with pulsus paradoxus need not have marked reduction of flow rates. The development and the magnitude of pulsus paradoxus is more a function of the respiratory effort of the patient. An anxious patient with moderate airway obstruction may generate very high negative pleural pressures and pulsus paradoxus; on the other hand, a patient with severe obstruction and respiratory fatigue may not be able to produce much negative pleural pressure at

all. Also the difficulty in measuring the fall in blood pressures during inspiration negates the use of this parameter accurately in the clinical setting.

Many patients in an acute asthmatic attack are often tachycardic and tachypnoeic. Cooke et al pointed out that an initial rapid pulse rate for more than 130 beats/min has been associated with severe dyspnoea, severe airway obstruction and in-hospital complications [Cooke et al, 1979]. Though many clinical scoring systems for assessment of severity of asthma do quote pulse rate as a clinical parameter, this is not useful in deciding if the patient is fit for discharge as most patients are persistently tachycardic post-treatment mainly due to the effects of the inhaled beta-agonists. Tachypnoea is much less useful a clinical scoring parameter reflecting more of the degree of effort and anxiety of the patients than the severity of airway obstruction. Furthermore, one of the signs of respiratory muscle fatigue and impending apnoea is a decrease in respiratory rates.

Physical examination alone often is unable to objectively and reliably identify the severity of the patient's condition. Studies have proven that physicians vary greatly in their assessment of the severity of airway obstruction, and their assessment correlates poorly with lung function [Shim & Williams, 1980]. Furthermore, physicians perform poorly at attempting to predict the PEFR of patients presenting to the Emergency Department. Clinical parameters are often associated with some degree of subjectivity and uncertainty. No single parameter is sufficiently sensitive to be used on its own. On the whole, most scoring scales for assessment of severity of asthma use a combination of clinical parameters to more

accurately reflect the condition of the patient. While these clinical parameters have found favour in assessing severity during initial presentation, their use becomes much less relevant after treatment has been initiated; that is, these scores cannot reliably identify patients who are well enough for discharge. The persistent lack of objectivity and the inability to quantify the changes before, during and after treatment limits the use of clinical parameters to assess severity of an acute attack of asthma.

3.1.6 Arterial Blood Gases

It is not necessary to measure the arterial blood gases to diagnose asthma. Nevertheless, they do reflect the severity of the attack and the ventilatory status of the patient. Irritant receptor activity and anxiety causes hyperventilation commonly seen during the acute attack of asthma [McFadden & Lyons, 1968]. Due to this hyperventilation, most patients have respiratory alkalosis initially. When the airway obstruction becomes severe, patients may not be able to maintain the required alveolar ventilation, or when development of respiratory muscle fatigue ensues, the arterial carbon dioxide tension rises. The arterial blood gases now reflect this rise in P_aCO_2 to normal and above normal levels with a concomitant acidic pH. In addition, development of lactic acidosis resulting from increased respiratory muscle activity and, possibly, diminished hepatic function either from elevated venous pressures or from decreased hepatic artery blood flow, will worsen the acidosis. It has been shown that the development of lactic acidosis, characterized by a pH lower than predicted from the P_aCO_2 and an anion gap of more than 15 mEq/L, indicates severe asthma that is apt to lead to ventilatory failure [Kelsen et al, 1978].