



International Journal of Nursing and Medical Investigation

International Peer Reviewed Journal

Review article

Trends in asthma and its management

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Abstract

Bronchial asthma is a long-term condition that affects the airways. It has evolved over time from a symptom-complex to airway inflammation and airway remodeling. Based on this concept it was treated. Early therapies treated most asthma patients with inhalations to remove the foulness or the phlegm in modern terms, then when it was thought to be a disease of smooth airway muscle, bronchodilators were developed but when it was realized airway inflammation to be the cause, controller therapies such as corticosteroids were used. However, with the recognition of airway "remodeling" that occurs in response to allergens, further medications like antihistamines were added. The methods of treatment have been similar to the early period with improved management techniques at present and all these therapies had varying degrees of success. It is interesting to know how asthma was managed diligently from the ancient period. Though there were few changes in treatment, there was always progress in each era and its history has played a significant role in understanding asthma pathogenesis for better treatment and control.

Keywords: Asthma, airway inflammation, concept, historical review, treatment

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1. Introduction

Background of the study

Asthma is primarily a disease of chronic airway inflammation. It has been recognized throughout recorded history. The word asthma comes from the Greek *Aazein* (ασθμα, ασθματος), meaning a "short-drawn breath, hard breathing, or death rattle," and thus, represented multiple breathing maladies rather than a single disease [1]. Bronchial asthma was officially named as a specific respiratory disorder by Hippocrates in 450 BC. There was also an early recognition of the association of asthma with environmental factors, including a relation to certain winds and worsening in certain geographical areas [2]. The term was refined in the latter part of the 19th Century with the publication of a treatise by Henry Hyde Salter entitled "On Asthma and its Treatment". In this scholarly work, Salter defined asthma as "Paroxysmal dyspnoea of a peculiar character with intervals of healthy respiration between attacks", a

description that captures his concept of a disease in which the airways narrow due to contraction of their smooth muscle [3]. He also described black coffee as a treatment for asthmatic spasms, a drink with a high content of the bromine, a derivative of theophylline and theophylline itself. This extraordinary insight into asthma stems from Dr. Salter himself suffering from asthma [3].

Next asthma was attributable to an increase in environmental exposures as in modern era people spend more time indoors with increasing temperatures and humidity where mold and dust mites grow. This gave way to the discovery of reagin by Prausnitz and Küstner in 1921 as a serum substance that could passively transfer allergy to a specific agent (in this case cod allergen) [4] subsequently led to the identification of IgE as the 5th immunoglobulin class IgE by Johansson and Ishizaka [5] And provided the crucial link. Thus we see researches have been conducted in this context

(allergens) and allergic asthma was discovered in this era.

The most extensive studies of allergen levels and sensitization have been conducted using the house dust mite (HDM). Cysteine proteases found in HDM's gut and fecal particles are potent inducers of allergic disease [6]. Studies have demonstrated that there is a dose-response relationship between HDM exposure and allergen sensitization [7]. Woodcock et al. found that using impermeable HDM bedding as a single intervention is ineffective because it does not reduce total HDM exposure [8]. Patients with Allergic asthma are also associated with increased risk of medication use, unscheduled visits, and hospitalization.

By the late nineteenth century, physicians adopted the view that asthma was a distinct disease, which had a specific set of causes, clinical consequences, and requirements for treatment. This led to researchers to be conducted in various specialties on causative factors and new treatment modalities.

The difference to be noted here is that in earlier period, the physicians have tested the medications within themselves, but nowadays the research is done on animals or other human beings and also nurses and paramedical workers are involved in conducting researches, hence the asthma interventions has been widened or broadened, and treatment modalities are expanded focusing not only on medications but also relieving symptoms by home measures and self-management guidelines where education also becomes integral role in asthma treatment and development. Thus, the treatment is based on patient centered approach and evidence based practice in recent years.

In this regard, McGrath, et.al (2009) along with the University of California San Francisco has conducted a 24-week randomized, controlled trial to determine if individualized instruction in asthma self-management adds significantly to the effects of self-monitoring alone on patients' adherence to inhaled corticosteroids (ICSs), medications that can help reduce inflammation in the airway and prevent asthma attacks. In the study, 84 adults with asthma self-monitored their symptoms and kept a daily log of their peak expiratory air flow. Of that group, 45 patients were randomly selected to receive a personal 30-minute session that included asthma information, personally relevant allergen exposure reduction, a personal action plan, and instruction in the correct use of their inhalers. During the study period, adherence to ICSs was consistently higher in the intervention group compared with the control group. In addition, participants in the intervention group experienced fewer nighttime awakenings, a marker of asthma control. Intervention participants also used rescue inhalers less frequently, experienced an increased sense of control over their asthma, and had a significant decrease in their levels of tryptase, which is released from cells in the presence of allergens [9].

Hence the management techniques of recent era proves to be more successful in asthma control, adherence to

treatment, having less nighttime awakenings that can reduce the work/school days of absenteeism, fewer asthma exacerbations, less emergency visits and fewer medications use which avoids side effects of the drugs thus facilitate improved the quality of life.

Significance and need for the study

Asthma is a disease of the small airways of the lung. It is a chronic inflammatory condition that makes it hard to get air in and out of lungs during asthma attacks. Asthma can be a life-threatening disease if not properly managed. In an asthma attack, 3 things happen a. the wall of the airway gets swollen and inflamed b. the muscles surrounding the airway spasm (squeeze down) c. mucus fills the air passages. These 3 things make the airway narrower, so it's harder to get air through, and less oxygen reaches the blood. When people have an asthma attack – they can feel chest tightness, throat tightness, they can wheeze (a musical whistling sound), and can cough a lot.

In the recent years, the morbidity and mortality of population due to asthma is increasing despite the advances being made in the understanding of this disease and availability of improved medications and information on treatment. In India, according to WHO an estimated 57,000 deaths were attributed to Asthma in 2004 and it was seen as one of the leading cause of morbidity and mortality in rural India. In 2005, 300 million people suffer from Asthma globally, 255, 000 people died of asthma and over 80% of asthma deaths are reported from low and lower-middle income countries [10]. According to the global burden of asthma report (GINA), over 50 million suffer from asthma in Central and Southern Asia and an absolute 2% increase in the prevalence of asthma in India would result in an additional 20 million people with this disease. According to the Asthma and Allergy Foundation of America, asthma control is difficult for 20 million asthma sufferers in the US alone. The National Institute of Allergy and Infectious Diseases reports (2007) spending related to asthma at \$19.7 billion.

Asthma is under-diagnosed and under-treated, creating a substantial burden on individuals and families and possibly restricting individuals' activities for a lifetime [10]. Today Asthma is a familiar and growing disease and has increasing prevalence, but its story goes back to the ancient world, as we know from accounts in ancient texts from China, India, Greece, and Rome. It was treated with acupuncture and Ayurveda. It is established that the prevalence rate of bronchial asthma and allergic rhinitis is about 10 to 15% irrespective of the area in which people live whether it is industrial, urban, or rural. Asthma is not just a public health problem for high-income countries: it occurs in all countries regardless of the level of development. Over 80% of asthma deaths occur in low and lower-middle income countries. [10]. This gave way to conduct researches on drugs as well as on asthma interventions. Thus asthma demands the efforts to be continued in identifying causative and risk

factors, pathogenesis and progress in the development of asthma management. Asthma may be at present considered as an incurable disease, but actually, asthma is a curable disease if appropriately managed. Moreover, with good treatment and management, a person with asthma can live a normal and active life.

Historical perspectives of asthma

Earliest History

The history of asthma traces back to ancient times. Ancient Chinese (c. 3000 – 250 B.C.) used 'remedies' for asthma and their most prominent treatment involved breathing fumes of herbs that contained what's today known as a crude form of ephedrine from which they could inhale beta-agonists as these herbs were heated on a brick. Shen Nong, the father of Herbal Chinese Medicine, first tasted ephedra (a plant) to treat asthma-like symptoms. Ephedra treated bronchospasms, congestion, and mucus secretion. The Chinese introduced it to the Greeks and gradually the method of treatment spread to other civilizations [11].

Egypt (c. 3000 – 1200 B.C.) Ebers Papyrus, written around 1550 B.C., tells how ailments such as asthma, hepatitis, bubonic plague, dandruff, and more were cured in ancient Egypt. Asthma back then was considered a disorder or foulness of the *metu* (canals or vessels) or duct, and so thought to distribute air and water to the organs, as well as lungs. Physicians tried to heal the ducts by removing the foulness. Seven stones were heated, and on one stone the herb mixture was placed on it and covered with a perforated jar. A stalk of reed was placed in the hole, and the patient would then put his mouth on this stalk and inhaled the smoke or fumes. The process was repeated with the remaining stones [12].

Greek- Rome (c. 1000 B.C. – A.D. 200)

The Greek and the Romans believed that asthma was caused due to demonic possession or magic. Hippocrates (460-360 BC) was considered to be the father of modern medicine. He first discovered that patients suffering from asthma developed a hunch back. He also understood the relation between respiratory problems and environment. The *Corpus Hippocraticum*, by Hippocrates, is the earliest text where the word asthma is found as a medical term. We are not sure whether Hippocrates meant asthma as a clinical entity or as merely a symptom. Hippocrates said spasm linked to asthma were more likely to occur among anglers, tailors, and metalworkers [2]. Aretaeus of Cappadocia (100 AD), an ancient Greek master clinician, wrote a clinical description of asthma. Galen (130-200 AD), an ancient Greek physician, wrote several mentions of *asthma*, which generally agreed with the Hippocratic texts and to some extent those of Aretaeus of Cappadocia. The first etiological link with bronchospasm was made by Galen [13,14]. He described asthma as bronchial obstructions and treated it with owl's blood in wine. While in Rome, treatments included bleeding, hot wet compresses, diuretics, purgatives. Around A.D. 23-79, Pliny the

Elder found pollen to be another source for respiratory problems. He recommended ephedra to be mixed in red wine to cure asthma. In addition, he came up with a folklore remedy of drinking the blood of wild horses, fox liver in red wine or millipedes soaked in honey. There was also evidence discovered that the ancient Greeks had at least briefly studied asthma under Hippocrates in the 4th Century B.C [12].

Ancient Hebrew (c. 3rd Century B.C. – A.D. 700)

Asafoetida was used for digestion and elimination of oil from the lungs. This treatment prevented asthma, whooping cough, and bronchitis. The Jews believed that the only time a person sneezed was at the time of his death and in case he did not die; he would thank God. They believed that the sneeze released the soul through the nose (12). This concept of treatment links with the present GERD as one of the risk factor for causing asthma.

India (c.800 – A.D. 500) Proud to say the Indian medicine system was quite developed and became the backbone of European pharmacy in the 17th century. Stramonium obtained from thorn apple helped in treating asthma. The British army practiced this method of treatment [12].

America (A.D. 1600) In ancient America, a mixture of plants and religious customs treated respiratory problems. Mexicans and South Americans used rubber to make an enema syringe and treated chest disorders and rheumatism. After Colombus discovered the New World, the dried root of the Brazilian shrub called ipecacuanha and balsam were used. Cocaine was another Incan remedy that was later used to treat rhinitis and asthma. Physicians also believed that tobacco could open blocked airways. Among many medical texts, Maimonides (1135-1204 AD), physician of Sultan Saladin who lived in Andalusia (Spain) wrote *Treatise of Asthma* for Prince Al-Afdal, a patient of his. Maimonides revealed that his patient's symptoms often started as a common cold during the wet months. Eventually, the patient gasped for air and coughed until phlegm was expelled. He suggested to treat asthma with rest, avoidance of opium, good personal and environmental hygiene and emphasized the importance of dietary factors that include chicken soup [13,14].

Asthma in middle history or middle ages

As Europe began to emerge as a society in the middle Ages, several countries began to look at asthma in hopes of finding a cure. According to the Asthma & Allergy Foundation of America, Jean Baptiste Van Helmont, a Belgium physician during the 16th century, wrote that asthma originated in the pipes of the lungs. In the 17th century, Bernardino Ramazzini, an Italian physician, knew to some as the father of sports medicine noted a connection between asthma and organic dust. He also recognized exercise-induced asthma.

As Western medicine developed, the nature of asthma became clearer, and its basis in the lungs recognized. But cultural perceptions of the disease shifted too. By the 18th century, with the recognition that the disease was centered on the lungs, the idea of environmental triggers such as dust and smoke first became recognized. And with that, asthma also became identified as a disease of artisans. In 1860, Henry Hyde Salter (1823–71) proposed a classification into extrinsic and intrinsic asthma, based on the nature and putative mechanism of various stimuli (e.g. animal dander or emotional stress) inducing episodes of bronchospasm. Things changed again in the 19th century, as medical understanding grew with the advent of the stethoscope and new techniques such as percussion of the chest. New treatments included the promotion of mountain spas, for asthma now rose in social status, and became associated with the upper classes and the literati. For Marcel Proust and Charles Dickens, asthma shaped their lives and their creativity [12].

Perceptions of asthma in modern period

Clearly, society as a whole has come a long way in just the past few decades. Throughout most of history from Ancient Egypt and Greece, asthma was treated as a physical condition. Even in the 16th and 17th centuries, asthma was identified as being a pulmonary condition and that dust and exercise could be triggered. However, At the beginning of the 20th-century asthma was seen as a psychosomatic disease - an approach that probably undermined any medical breakthroughs at the time. This concept was somewhat similar to 18th century relating to emotional stress that induced bronchospasm. During the 1930s to 1950s, asthma was known as one of the *holy seven* psychosomatic illnesses [12].

Asthma was described as psychological, with treatment often involving, as its primary component, psychoanalysis, and other 'talking cures'. Psychoanalysts thought that patients with asthma should be treated for depression. Thus in the past, it was thought asthma was mainly an emotional disorder. This psychiatric theory was eventually refuted and asthma became known as a physical condition. So today it is known that the basis of bronchial asthma is the hyper-irritability of and biochemical abnormality in the cells lining airways. However, a subgroup of individuals who are under or have undergone stressful situations may find themselves suddenly wheezing. Therefore while emotional stress can be a significant triggering factor in asthma, it is not the sole cause. This form of asthma appears to be primarily a psychosomatic disease³. In addition, research shows that negative emotions such as panic and depression can affect the respiratory system, in effect bringing on an asthma attack in people with the disease [12, 15]. Thus asthma appears to be a psychological disorder affecting physical well being of the person. So the individual needs to be sound in both physical and psychogenic energies of life.

Trends in management of asthma (then and now)

Bronchial asthma was treated by drinking an incense mixture known as Kyphi in ancient Egypt. Seneca (c.4 BC-AD 65) Ancient Rome's philosopher-fixer recommended relaxing to control asthma. He was not a supporter of potions (Mixture or drink), magic and herbs. He simply recommended relaxing and thinking of something that makes the person happy.

Epinephrine was first referred to the treatment of asthma in 1905 [20]. Oral corticosteroids began to be used for this condition in the 1950s while inhaled corticosteroids (17,18,19) and selective Short-Acting Beta Agonist came into wide use in the 1960s [20]. Asthma, as an inflammatory disease, was not really recognized until the 1960s when anti-inflammatory medications started being used. During the late 20th Century, medicine advanced to the point where hundreds of studies have been done, potential genetic causes have been identified, a long list of asthma attack triggers has been obtained and innumerable management strategies have been devised to help people avoid a high number of attacks [4]. During the first half of the 20th century, bronchospasm was treated with bronchodilators. But due to over-reliance on these drugs, an epidemic of asthma death was reported in Australia, the US and the UK that peaked in the mid-1960s (isoprenaline-related) and a second peak in New Zealand in the mid-1980s (high dose fenoterol-related) [20]. Although since the early 1920s asthma death was known to be associated with extensive inflammation and structural changes in the airways, [20] it paved a way for anti-inflammatory drugs.

Now in contemporary era knowledge, and research has crept into the medical science. The treatment is currently based on evidence-based practice and patient-centered management and no more an intuitive (unthinking) as in ancient period. Health care professionals focus on the comfort of patients and relieving symptoms, only after learning the patients' history and environmental factors, and performing a physical examination, treatment is given depending on the cause and number of diagnostics tests being done and the progress of treatment also evaluated.

The government also takes much effort in identifying high-risk patients and treating them providing free of cost medications in health centers. Health workers like nurses make a home visit and provide health education regarding home care management. One of such type of management is peak flow self-management plan.

Peak flow rate monitoring and a written asthma action plan help the patient to recognize symptoms early. The patients are instructed to perform the peak flow monitoring and to note down the readings of peak flow in peak flow diary. The asthma action plan shows daily treatment, such as what kind of medicines to take and when to take them. In addition, it describes how to control asthma long term and how to handle worsening asthma, or prevent exacerbations/attacks [21]. The plan also explains when to call the doctor or go to the emergency room.

Literature related to symptoms and peak flow self-management of asthma patients

A study was conducted to determine whether there is a correlation between changes in asthma symptoms during treatment and changes in lung function, as measured by peak expiratory flow by Dorinsky et.al, 2001 that has shown that there is a strong correlation between lung function as expressed as peak respiratory flow and symptom management. The effect of patient education in asthma has been studied by a randomized controlled trial (Galipos et.al, 2002) and has recorded a 6 percent improvement in lung function (FEV1) in the study population in twelve months. Another study was conducted by Malarvizhi et al (2015) on "Effectiveness of Peak Flow Guided Self Management Plan on Asthma Health Outcomes among Patients with Bronchial Asthma. The randomized controlled trial design was used. Interventions given to the group was Self Management plan guided by peak flow measurements that resulted in less number of visits to Outpatient department, days off work. The study concluded that Peak flow guided self-management plan reduces the episode of asthma and improves quality of life [22]. Kaya, et.al (2009) also conducted a study on Self-management plans for asthma control and predictors of patient compliance to evaluate the impact of peak flow or symptom-based self-management plans on asthma control and patients' quality of life and to determine the main psychosocial factors that affect compliance with these plans. Of the 63 patients, 85% of them had moderately or severely persistent asthma. Personal asthma plans increased optimal asthma control

significantly. Emergency visits, antibiotic treatments, systemic corticosteroid treatments, and unscheduled visits were fewer than the previous year. Control parameters were better in the PFM group. After the self-management education, the quality of life dimensions, i.e., vitality, total mental and general scores of both groups increased. Compliance with the action plans was better in the PFM group. No statistically significant association was found between demographic parameters and the compliance. The study concluded Introduction of self-management plans improved illness control and quality of life in asthma patients [23]

Literature related to written action plan for asthma patients

According to the National Asthma Council of Australia, the use of written action plan has been found to reduce hospital visits and absenteeism from work. Douglas et al. Interviewed 62 adult patients who visited ED for an asthma exacerbation and found that the most common reason for them not to have a written action plan was that their doctors did offer or discuss it with them [24]. In a randomized controlled trial, Ducharme et al. studied the effect of providing a written action plan for 219 children. The experimental group had higher adherence to the treatment regimen and medical follow-up as compared to the group that did not receive asthma action plan [25]. Abramson *et al.* Conducted an interesting research to study the contribution of using the written action plan to death from asthma. They found that the use of the written action plan was associated with 70% reduction in risk of death [26].

My Asthma Action Plan
Age ≥ 5 years

Patient Name: _____
Medical Record #: _____
Physician's Name: _____
Physician's Phone #: _____
DOB: _____
Completed by: _____ Date: _____

Long-Term-Control Medicines	How Much To Take	How Often	Other Instructions
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
Quick-Relief Medicines	How Much To Take	How Often	Other Instructions
		Take ONLY as needed	NOTE: If this medicine is needed frequently, call physician to consider increasing long-term-control medications.

Special instructions when I feel ● **good**, ● **not good**, and ● **awful**.

GREEN ZONE

I feel **good**.
(My peak flow is in the **GREEN** zone.)

YELLOW ZONE

I do **not** feel good.
(My peak flow is in the **YELLOW** zone.)
My symptoms may include one or more of the following:

- Wheeze
- Tight chest
- Cough
- Shortness of breath
- Waking up at night with asthma symptoms
- Decreased ability to do usual activities

RED ZONE

I feel **awful**.
(My peak flow is in the **RED** zone.)
Warning signs may include one or more of the following:

- It's getting harder and harder to breathe
- Unable to sleep or do usual activities because of trouble breathing

Danger! Get help immediately!

PREVENT asthma symptoms everyday:
☐ Take my long-term-control medicines (above) every day.
☐ Before exercise, take _____ puffs of _____
☐ Avoid things that make my asthma worse like: _____

CAUTION. I should continue taking my long-term-control asthma medicines every day **AND**:
☐ Take _____
 If I still do not feel good, or my peak flow is not back in the Green Zone within 1 hour, then I should:
☐ Increase _____
☐ Add _____
☐ Call _____

MEDICAL ALERT! Get help!
☐ Take _____ until I get help immediately.
☐ Take _____
☐ Call _____

Call 9-1-1 if you have trouble walking or talking due to shortness of breath or lips or fingernails are gray or blue.



Advanced technology in asthma treatment Bronchial thermoplasty.

It is an invasive new treatment option approved by the US Food and Drug Administration in April 2010. Ever since it is used in US, Canada, and the UK. Here thermal energy is delivered to the airways via a bronchoscope to reduce excess airway smooth muscle and replaced with connective tissue. It has shown to increase the level of asthma control and improve quality of life and opted for steroid-resistant asthmatics. The treatment has been shown to be safe and effective over at least five years [29].

Internet and asthma

Internet facility provides patients asthma information in online at home or anywhere and at any time. They can talk with their doctors taking an appointment to manage asthma with just a click. It also guides asthma patients providing asthma planned courses that provide direction in taking the medications as well avoiding asthma triggers, responding to symptoms, overseeing the level of asthma and emergency care only when needed. In regard to this Basyouniet al (2014) conducted a study on Online Health Information Needs for Patients with Asthma in Saudi Arabia. A self-administered questionnaire was administered to 83 asthma patients attending the outpatient pulmonary clinic. Approximately two-thirds of participants who use the Internet have searched for asthma information online. Thirteen percent of the participants reported that the Internet was their main source of information about asthma, and 33.7% reported that the Internet was their favorite additional source of information about asthma. Seventy-eight percent of the participants were interested in an asthma information Web site in the Arabic language. Employment and higher income were associated with participants who chose the Internet as the favorite source of additional information about asthma (OR 4.5, 95%CI 1.6–12.7) and (OR 4.2, 95%CI 1.4–12.5), respectively, and an education level higher than high school was associated with participants who previously had looked for online information about asthma (OR 11.2, 95%CI 3.8–33.5) [30].

In the era of computer and mobile technology, some health-care providers and researchers have utilized available technology as means of delivering asthma

education. Burns *et al.* pilot-tested web-based asthma self-management programme in 51 adult asthmatic patients and found that this form of delivery increased patients' asthma knowledge, improved asthma control and enhanced quality of life.

Conclusion

As you see, the work and fight against asthma have been happening for as long as we've recorded history. However, only a few of those thousands of years can show significant progress, and these are the most recent years. During the modern era, enormous efforts are taken to improve the asthma management techniques that are simpler, cost-effective and still advanced having the goal of asthma control thereby improving the quality of life. The life expectancy for mild asthmatics is the same as for those who do not have asthma, which is about 80 years. Numerous researchers are conducted in present era regarding improvement in treatment in order to reduce the morbidity and disability and increase life span of asthma patients. At this rate, perhaps we'll all see the day where a cure is found and asthma is eradicated.

Conflict of interest: Nil

Source of funding: Self

Ethical clearance: Not required as it involved only collecting of information about asthma.

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