Unit II – Problem 3 – Handout (2): Asthma

Asthma

Asthma is an obstructive airway disorder characterized by reversible airway narrowing, mucus hypersecretion, chronic inflammation, and episodic shortness of breath. Severe recurrent bouts of asthma lead to airway scarring, termed *remodeling*, which is not reversible and can lead to an increased frequency and severity in asthma exacerbations and lung infections. Asthma can be allergen provoked, which is termed *atopic*, or asthma may be due to unknown factors and termed *intrinsic*. There is a broad consensus that the prevalence of asthma has increased dramatically in most industrialized countries over the past several decades, prompting the development of several asthma study cohorts that have attempted to address asthma incidence, etiology, prevention, and control. What has come to be appreciated in the past decade due to the use of conditional gene expression systems, and transgenic animals, is the true complexity of the multiple molecular pathways that are involved in the development and progression of asthma and the understanding that asthma is more accurately characterized as a collection of diseases comprising a syndrome rather than a distinct homogenous entity. Therefore, in terms of a cure, there is no single "magic bullet" with regard to the treatment or the prevention of asthma.

Incidence, Prevalence, and Cost Burden

In 2004, the incidence of asthma worldwide was estimated at 300 million people, and it was predicted that by the year 2025, this number would increase to 400 million. In the United States, it has been estimated that as many as 11% of the population may be afflicted. Asthma often develops in childhood, although incident adult cases are not uncommon. Estimates indicate that 28% to 78% of young children with asthma ultimately have symptom resolution once adulthood is reached, while 6% to 19% continue with severe forms of the disease. Asthma is the third leading cause of hospitalization among persons less than 18 years of age in the United States, and according to the Centers for Disease Control and Prevention, the prevalence of asthma among U.S. children increased from 3.6% in 1980 to 5.8% in 2003. Not surprisingly, there is a significant cost burden associated with health care for asthma. In 2002, the total direct medical costs relating to asthma were estimated to be $9.4 billion, with indirect costs comprising an additional $4.6 billion. Of these direct costs, 33.0% were due to hospitalization, and 39.4% were related to prescription drug costs.

Diagnosis

Asthma is a complex disease to diagnose with a single parameter. The definitive diagnosis of asthma is a clinical one made on the basis of a patient's medical history, physical examination, and assessment of the reversibility of airway obstruction. In most studies, questionnaires are used to assess whether subjects have had symptoms of asthma or have ever received a diagnosis of asthma from a physician. This type of assessment is highly subjective to a patient's and a physician's understanding and awareness of asthma and has brought speculation as to whether the number of asthma cases has really increased so dramatically or whether there is simply a higher public awareness of the disease coupled with a greater willingness on the part of physicians to diagnose patients as having asthma. One study that illustrates this conundrum well is a study in Scotland that showed that the proportion of children reporting asthma symptoms who also received a diagnosis of asthma increased from 28% in 1964 to 64% in 1999.

Risk Factors for Incidence and Exacerbations

The risk factors associated with asthma appear to involve both genetic and environmental components. Clinical population studies have shown that the risk of allergic disease such as asthma is inherited. In families in which one parent has allergic disease, including asthma, at least 30% of the children will

also be allergic; if both parents have the disease, the risk rises to 50%. In children, risk factors for asthma have been identified as wheezing, familial history of asthma, atopy, obesity, being male, an increase in eosinophils in the peripheral blood, severe infections of the lower respiratory tract, and increased IgE. In adults, the risk factors for asthma include cigarette smoking, rhinitis, atopy, familial history of asthma, and being female. The susceptibility to asthma that may be attributable to genetic predisposition has been estimated to be as high as half of all cases. Chromosome linkage studies have shown that regions on chromosome 6p and 12q are involved in susceptibility to allergy and asthma. However, studies involving monozygotic twins raised in different environments and having differing degrees of asthmatic disease have illustrated the complex interaction of the environment and genetics.

Several environmental factors have been studied for their impact on allergy and asthma sensitization. In urban areas, air pollution, especially diesel exhaust, nitrogen dioxide, and sulfur dioxide have been shown to be major contributors to the development and severity of asthma through the augmentation of previous allergen-specific IgE responses and the capacity to promote the primary sensitization to a new allergen. Exposure to tobacco smoke is highly associated with susceptibility to asthma, and a meta-analysis concluded that parental smoking is very likely to be causally related to both acute respiratory tract illnesses in infancy and the incidence of childhood asthma. There are also studies that have shown that active smoking is associated with the onset of asthma in adolescents and adults.

The environmental impact of living in rural areas has long been known to confer a protective influence against the development of asthma. This is thought to be due to the concurrent exposure of children to bacterial proteins called endotoxins, and potential allergens, while the immune system is still developing. This serves to confer an immunologic tolerance to classic allergens rather than promote an asthmatic response. The "hygiene hypothesis" relates to this phenomenon. According to this theory, our largely indoor and hygienic Western lifestyle has decreased our exposure to outdoor environmental allergens and bacterial proteins and, therefore, has increased our likelihood of developing asthma.

Psychological stress has also been shown to play a role in both the incidence and exacerbation of asthma, and there is an association between depressive disorders as well as anxiety disorders and asthma. The mechanism by which stress influences asthma is by altering hormonal components of the endocrine system, such as cortisol and catecholamines, which in turn alters the polarization of the immune response toward an allergic phenotype.

Epidemiologic studies continue to identify and evaluate risk factors for the development or exacerbation of asthma. Episodic exposures to toxicants will continue to be evaluated by documented studies of adverse health effects with comparisons to measured exposures, hospital admissions, or lost school days. Prospective cohort studies or population-based surveys will also continue to evaluate chronic exposures to toxicants and the incidence or prevalence of asthma. Future trends in asthma epidemiology are likely to focus on the combination of specific genetic and environmental factors in the etiology or contribution of the disease and will continue to be challenged by the difficulties of characterizing chronic exposures, multiple contaminant exposures, and study design limitations. It is clear that there are multiple contributing factors to asthma for which epidemiologic studies have been invaluable as far as their contribution to better understanding the syndrome as a whole.