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National Impact of Allergies

The most common allergic disorder, allergic rhinitis (AR), is a lifelong debilitating condition which, if untreated, results in significant health and economic consequences (1-5). In this article, I detail how a lack of access and non-adherence to effective AR treatment incurs these consequences and reinforces the need for patient education and evidence-based treatment and prevention guidelines.

Approximately 60 million Americans are affected by allergic diseases, ranking AR as the third-leading chronic disease in the U.S. among individuals younger than 45, and the fifth leading cause of chronic disease among all Americans (2, 4). Up to 30 percent of all adults and 40 percent of all children suffer from AR (1, 3, 4). Internationally, the prevalence of AR is increasing, particularly in developed countries (3-5). This upsurge in prevalence is demonstrated by noting that since 1995, the number of Americans suffering with AR has doubled to 37 million (6). This increased prevalence of AR has led to a concomitant enhancement of direct and indirect health-related costs that should encourage aggressive intervention to ensure clinically favorable and cost-effective outcomes (1-5).

The Economic Impact of Allergies

When considering the impact of lost productivity and days off from work on the 60 million Americans with AR, the health related-expenditures attributable to AR are significant. In 2010, Americans with AR spent approximately \$17.5 billion on health related costs, lost more than six million work and school days and made 16 million visits to the doctor (7). Outpatient visits account for approximately one-third (36 percent) of AR-related direct costs and prescription medications account for nearly the entire remainder (7). It is not uncommon for over-the-counter (OTC) and prescription medications to be used in combination to treat the bothersome symptoms of nasal allergies (4, 7, 8). In fact, a recent survey reported that many adults with AR use two to four medications simultaneously to control their AR symptoms (8). When parents were surveyed about which medications their children used for allergy symptom relief, more than half (54 percent) reported the use of an OTC medicine, whereas slightly fewer (48 percent) reported use of prescription medications. Because costs for OTC medications are not usually included in the estimated expenditures and are reportedly equivalent to costs for prescription medications, health care expenditures attributable to AR may be underestimated (4, 8, 9, 12).

AR usually precedes and is associated with other chronic related allergic and non-allergic diatheses, including asthma, chronic sinusitis, otitis media with effusion, upper respiratory tract infections and sleep disorders (4, 9, 10). The presence of AR with such comorbidities, particularly in association with asthma, significantly increases health service utilization and health-related expenditures (9-11).

U.S. patients are in dire need of a proven and long lasting treatment for seasonal and perennial AR. Since 1995 the number of Americans suffering from AR alone has doubled to 37 million (6). This collective upsurge in the prevalence of all seasonal and perennial AR in the U.S. has further led to increased direct and indirect medical-related costs.

In contrast to symptomatic drug treatment (e.g. antihistamines and nasal steroids), which only temporarily relieves allergy symptoms (4, 5, 9, 12-14) allergen-specific subcutaneous immunotherapy (SCIT) is a disease-modifying therapeutic modality, thereby reducing the need for long-term treatment, the progression of allergic rhinitis to asthma (15- 17) and the development of new allergies (18-20). The clinical benefits of SCIT have been shown to persist for an additional three to 12 years after discontinuation of a 2.5- to 5.0-year treatment course (21, 22). It therefore stands to reason that the clinical benefits of SCIT also encompass economic benefits (12).

Allergic Rhinitis and Comorbidities

AR is characterized as a substantial clinical burden and manifested by congestion, rhinorrhea, sneezing, and nasal and ocular pruritis (4, 9, 23). Also characteristic, although less common, are dry cough, sleep disturbance, headache, facial pain, and ear pain (4, 9). Symptoms of the illness can significantly reduce quality of life. Adults and children demonstrate physical discomfort, psychomotor dysfunction; disrupted sleep results in daytime somnolence and reduced alertness; impaired cognitive functioning, job performance, and learning often are diminished; and lost time from work, school, and leisure activities occurs (8, 24, 25). Historically, investigators have documented an association between allergic rhinitis and asthma, sinusitis, otitis media with effusion, recurrent respiratory tract infections and sleep disorders (9).

Relationship between Allergic Rhinitis and Comorbidities

A. Asthma

The incidence of allergic rhinitis in asthmatic adults can be as high as 58 percent (9). Investigators have documented the frequent association of AR with asthma. Allergen exposure and AR development often precedes the development and onset of asthma suggesting an etiologic association (26-33). In particular, AR and positive allergy skin tests have been thoroughly studied and defined by investigators as risk factors for the development of asthma (30-33). Of note, the treatment of AR reduces the incidence and severity of asthma (34-37). There is a significant increased global prevalence of AR and Asthma which has lead to a concomitant enhancement of direct and indirect health-related costs (4). Remarkably, the initiation of SCIT treatment effectively addresses the core pathophysiology of AR and investigators demonstrated that SCIT prevents the onset of asthma in patients with AR (15-17) and in others; it diminishes the asthmatic severity and morbidity (32-37). Thus, SCIT treatment diminishes health care expenditures for this large patient population (5, 12-14).

B. Sinusitis

Acute and chronic sinusitis are identified in 31 million Americans each year (38). AR has been documented to be a predisposing factor in 30 percent of patients with acute maxillary sinusitis (39), in 78 percent of individuals suffering with extensive sinusitis (40), and in up to 67 percent of patients who had symptoms of chronic sinusitis with unilateral involvement (9, 41). In contrast, 80 percent of patients with bilateral sinusitis suffered with AR (9, 42-45). Furthermore, an association between extensive sinus disease and asthma was documented in 71 percent of patients. Because of the significant association of AR with sinusitis (9, 38-45), the effective treatment of individuals with AR should diminish the development of sinusitis and thereby diminish health care-related costs.

C. Otitis Media with Effusion & Dental disorders

Acute otitis media with effusion (OME) is an inflammatory disorder of the middle ear frequently associated with eustachian tube dysfunction and the loss of hearing in children (9). OME is commonly linked with AR (46-49). This AR-linkage is corroborated by observing that the prevalence AR in children with OME ranges up to 50 percent (9, 48, 49).

Allergic rhinitis is a risk factor for the development of orthodontic malocclusions. The incidence of malocclusions is almost three times greater in obligate mouth breathers (a common finding in moderate and severe AR) than in unaffected individuals (9, 50).

D. Respiratory infections

There is a reciprocal relationship between AR and respiratory viral infections (9). Childhood viral infections have been reported as risk factors for the development of allergic rhinitis and asthma (9, 51-56). In contrast, the expression of intercellular adhesion molecule 1, which is the receptor for 90 percent of human rhinoviruses, is up

regulated upon allergen exposure. This may in turn enhance the susceptibility of atopic individuals to rhinovirus infections (4, 9).

Nasal mucociliary clearance is the first line of defense of the respiratory tract ciliated epithelium against inhaled pathogens (57). AR, as a rhinopathic disorder is in part, characterized by alterations in nasal mucociliary clearance. In AR, the rhinopathic consequence is impaired mucociliary clearance which investigators have associated with a predisposition to respiratory infections (57, 58).

E. Sleep disorders

AR has a profound effect on normal nocturnal breathing. This in turn contributes to aberrant patterns of sleep (4, 59, 60). Approximately 57 percent of adult patients and 88 percent of pediatric patients with AR experience sleep disruptions (4, 60, 61). These sleep disruptions contribute to daytime fatigue, learning performance disorders, work inefficiency, behavioral disorders, and attention-deficit disorders (4, 9, 59-62).

AR is a risk factor for obstructive sleep apnea syndrome (OSAS) due to the associated nasal obstruction, enlarged tonsils and adenoids, and an elongated face characteristic of chronic AR, all of which constitute a smaller upper airway size. The size of the upper airway determines the severity of the OSAS. Thus, adequate treatment of AR would diminish the severity of OSAS. Effective treatment of AR may prevent the occurrence of OSAS and reduce the severity of existing OSAS (63, 64).

Treatment with Allergen-Immunotherapy

Most allergy sufferers spend their entire lives battling their symptoms without knowing the exact cause of their reactions. Often, they treat their undiagnosed allergies with over-the-counter and prescription drugs that only mask the symptoms (4, 5, 9, 12-14). Over 100 years of scientific research and medical practice (4, 5, 9) have proven that the only lasting relief from allergies is immunotherapy, which induces immunologic tolerance by introducing a patient to the administration of safely increased doses of an allergen(s).

Allergen Immunotherapy (IT) is a therapeutic modality directed towards diminishing a patient's sensitivity to allergens. It involves introducing the patient to increasing amounts of an allergen (e.g. pollen, mold) through a series of customized single-injections, over the course of several years. Immunotherapy desensitizes the patient to the allergen that triggers their symptoms, ultimately allowing patients to be exposed to these allergens without any subsequent allergic reaction.

IT is the only known disease-modifying treatment for allergies. The results of IT can be life-changing and significantly increase the quality of life while simultaneously diminishing morbidity (4, 5, 9, 65). IT has been shown to diminish symptoms of allergic rhino conjunctivitis (4, 5, 9), and decrease the severity of allergic-asthma (32, 33, 35-37). Remarkably, IT also prevents the onset of new allergies and allergic asthma (15-20).

The Economic Impact of Immunotherapy

In the majority of cases, immunotherapy, results in: significant clinical improvement, the diminished utilization of antihistamines and nasal steroids, diminishing the severity of allergic asthma and reducing the utilization of asthma medications, and diminishing the severity of the other comorbidities of sinusitis, OME, respiratory infections and sleep disorders (4,5,9). As a consequence, there are fewer physician visits, and fewer hospitalizations. These outcomes diminish the economic-burden associated with AR and comorbidity treatment.

Numerous studies have examined the potential economic benefit of AR treatment with SCIT. The vast majority of study outcomes demonstrated significant savings to patients, government agencies, and insurance companies when SCIT was utilized. Hankin et al. completed 3 economic studies (12-14), the longest a retrospective 11-year (1997–2008), matched cohort, claims analysis of Florida Medicaid adult enrollees with AR (14). After 18 months, total mean health care costs for inpatient (\$10,352 vs. \$14,796, $P = .003$), outpatient (\$2466 vs. \$4181, $P < .0001$), pharmacy (\$5636 vs. \$6321, $P < .0001$) and total health care services (\$10,626 vs. \$17,912, $P < .0001$) were significantly lower for patients who were administered SCIT. Significant total health care savings were realized within 3 months of SCIT initiation (\$1932 vs. \$3189, $P < .0001$). Remarkably, 18-month total cost savings per patient with SCIT were 41 percent (14). Similar results were promulgated by several European investigators (66-69). In conclusion, the unambiguous principle is that SCIT provides significant cost benefits. In the US, total health care cost savings of 33 percent and 41 percent have been reported for US children and adults with AR (with or without asthma), respectively, within 18 months of SCIT initiation (12-14). Considering the suboptimal duration of SCIT treatment reported for US patients (12, 13) estimated US cost savings conferred by SCIT are likely to be greater among patients who adhere to the suggested 3-year minimum course of treatment.

The initial course of immunotherapy is one year, but maximal benefits are achieved after three to five years of SCIT administration (4, 13). Immunotherapy is very effective in greatly decreasing or eliminating the symptoms of allergies. Up to 85 percent of patients receive a complete elimination or significant reduction in allergy symptoms using immunotherapy (71). Most insurance plans cover allergy testing and immunotherapy.

Shortage of Allergists to Administer Immunotherapy

There is a growing shortage of allergists in the United States. Without intervention, it is estimated that the number of full-time equivalent (FTE) allergist/immunologists will decline about 7 percent from 3,660 in 2006 to 3,400 in 2020. Meanwhile, demand for these physicians is projected to increase by 35 percent over the same period (to more than 5,550 in 2020). While seasonal and perennial AR generates considerable health-related costs, reduces the patient's quality of life, and workforce and school productivity, not nearly enough specialists exist to treat the number of patients in need.

Until now, the only disease-modifying and long term relief for allergies, in the form of IT, has remained primarily in the hands of allergists. However, the majority of patients with AR are treated by primary care providers and not Board Certified Allergists (4, 5). In addition, recent studies (70) demonstrated the ability of primary care physicians to diagnose and assess individuals with AR.

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