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MANAGEMENT OF ASTHMA IN PRIMARY CARE

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Abstract:

Introduction: *There have been great advances in Asthma focused on asthma across the lifespan and reported on some key findings linked to asthma inception, the microbiome, and the epigenome. Additionally, some new aspects of predicting and preventing asthma exacerbations were reported. It is obvious that research advances are being made in many areas related to asthma, like epidemiology, immunology, microbiology, genetics, biomarkers, and new medications, so much so that it is still difficult for those writing asthma guidelines and strategies to synthesize this work and rapidly apply it to clinical practice. So, reviews of key discoveries are important to keep the clinician abreast of these findings, so that they can be considered in the clinical setting while they await integration into asthma guidelines. Recently a study discussed new findings reported in the Journal of Allergy and Clinical Immunology (JACI) and other publications that relate to respiratory tract infections, air quality, factors that influence long-term outcomes, patient-centered outcomes research, precision medicine, and new observations linked to medications and asthma management.*

Aim of work: *In this review, we will discuss asthma.*

Methodology: *We did a systematic search for asthma using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.*

Conclusions: *There are new advances in the development related to the natural history of asthma and the effect of the environment. No previous era in asthma management that has witnessed the introduction of so many new classes of medications. It is considered a great challenge for doctors and those contributing to asthma guidelines to select relevant pieces of information that should be incorporated into clinical practice. Temporarily, doctors must keep up with these new findings to add benefits to patients by applying strategies that are most likely to be effective.*

Key words: *Air quality, airway hyperreactivity, allergen immunotherapy, allergen sensitization, allergy, asthma, biomarkers, climate, chronic obstructive pulmonary disease.*

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INTRODUCTION:

There have been great advances in Asthma focused on asthma across the lifespan and reported on some key findings linked to asthma inception, the microbiome, and the epigenome. Additionally, some new aspects of predicting and preventing asthma exacerbations were reported. [1] It is obvious that research advances are being made in many areas related to asthma, like epidemiology, immunology, microbiology, genetics, biomarkers, and new medications, so much so that it is still difficult for those writing asthma guidelines and strategies to synthesize this work and rapidly apply it to clinical practice. So, reviews of key discoveries are important to keep the clinician abreast of these findings, so that they can be considered in the clinical setting while they await integration into asthma guidelines. Recently a study discussed new findings reported in the Journal of Allergy and Clinical Immunology (JACI) and other publications that relate to respiratory tract infections, air quality, factors that influence long-term outcomes, patient-centered outcomes research, precision medicine, and new observations linked to medications and asthma management.

In this review, we will discuss the most recent evidence regarding asthma.

METHODOLOGY:

We did a systematic search for asthma using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Air quality, airway hyperreactivity, allergen immunotherapy, allergen sensitization, allergy, asthma, biomarkers, climate,

chronic obstructive pulmonary disease, eosinophils, exacerbation

VIRAL INFECTIONS IN ASTHMATIC PATIENTS AND THE PROMISE OF THERAPEUTIC TARGETS:

Respiratory viruses continue to be a major trigger of asthma exacerbations, adding new insight into the evolution and pathophysiology of asthma. In a study involving 183 asthmatic kids aged 6 to 17 years, Kantor et al [2] concluded that children with rhinovirus infection had more severe exacerbations than those children with virus-negative exacerbations. In this study rhinovirus-triggered asthma exacerbations became more severe as the degree of sensitization to dust mite and mouse increased. Similar to the more severe exacerbations appreciated in the rhinovirus-infected children in the study,

Results from a large study of adults enrolled in an influenza surveillance study revealed that rhinovirus infection is prevalent in adults, with 11% of nasal/throat swabs testing positive for rhinovirus in adults visiting the hospital, emergency department, or outpatient clinic with acute respiratory illness or fever. [3]

In 2016, there was elucidation into the immune response induced by virus-triggered asthma exacerbations, recognizing or further classifying possible therapeutic targets. Han et al [4] explained the role of Toll-like receptor (TLR) 2–expressing macrophages in the airway inflammatory response to rhinovirus, noting that TLR21 macrophages were needed for early stages of airway inflammation in their murine model. In addition, transfer of wild-type macrophages to Tlr2 knockout mice was sufficient to confer airway inflammation after rhinovirus infection. When IL-4–treated macrophages were also transferred, features akin to rhinovirus-infected mice with allergic airways disease were observed. Evaluating the role of resident alveolar macrophages in respiratory syncytial virus (RSV) infection, Naessens et al [5] devised a post–allergic airway inflammation murine model in which treatment with GM-CSF abrogated RSV-induced inflammation and airway hyperreactivity by means of maturing an apparent immature phenotype appreciated in the post–allergic airway inflammation resident alveolar macrophage population. Through constant inoculation of mice with low-dose virus and cockroach allergen, Lynch et al [6] showed that exposure of respiratory virus and cockroach allergen induced a biphasic IL-33 response and impaired antiviral interferon production.

CHARACTERIZATION OF THE AIRWAY MICROBIOME:

Through comprehensive evaluations of the airway microbiome, main differences between asthmatic patients, nonasthmatic subjects, and those at risk for asthma have been characterized. Regarding at-risk populations, the nasopharyngeal microbiota in more than one thousand infants with bronchiolitis was examined as part of a large multicenter study. In this study, infants with bronchiolitis caused by RSV had a high abundance of Firmicutes and the genus Streptococcus and a low abundance of Proteobacteria and the genera Haemophilus and Moraxella, while infants with bronchiolitis caused by rhinovirus had the opposite trend. It is not obvious if viral infections

increase certain bacterial populations within a community, microbial community populations create environments suitable for viruses, or both. [7]

Studying asthma in old population with established atopic phenotypes, a study performed by AsthmaNet took bronchial brushings from 42 steroid-naive adults with atopic asthmatic, [8] nonasthmatic but atopic adults, and 21 healthy control adults. [9] By profiling samples through 16S rRNAgene sequencing, distinct differences in the bronchial bacterial microbiomes were appreciated in the 3 groups. Among asthmatic adults, the bronchial microbiome at baseline differed according to their responsiveness to inhaled corticosteroid (ICS) treatment.

NOVEL GENETIC ASSOCIATIONS WITH ASTHMA AND THE BIOLOGIC EFFECT OF KNOWN GENE VARIANTS:

By founding of new associations and demonstration of the biologic effects of known gene variations, the association between genetic changes and asthma increased in 2016 . Doublesex and mab-3–related transcription factor 1 (DMRT1) appeared as a new candidate to possibly illustrate sex-specific asthma effects during childhood. [10] A single nucleotide polymorphism (SNP) on chromosome 8 was linked with early lung function decrease in 2 asthma cohorts and was also associated with chronic obstructive pulmonary disease (COPD). [11]

INFLUENCE OF AIR QUALITY AND CLIMATE ON ASTHMA:

Annesi-Maesano [12] added a general view of allergy-specific health issues emerging because of climate change, and future directions linked to climate-related health. Globally, only twelve percent of urban populations breath air that complies with World Health Organization Air Quality Guidelines. Citing NASA data, we learn not only that the earth has experienced a 0.88C/1.48F average worldwide temperature increase since the 1880s but also that 2/3 of this warming has happened since 1975.

Many letters to the editor in the September 2016 edition of the JACI tested traffic-linked air pollution (TRAP)'s affected on asthma. A median regression analysis of patients in a large birth cohort found a marked association between raised exposure to traffic nitric oxides in the first year of life and increased adolescent airways resistance and reactance. Adolescent self-reported psychosocial stress also looks to affect the estimated pulmonary effects of TRAP. TRAP can also influence steroid sensitivity.

In a mouse model of allergen-induced asthma with diesel exhaust particle (DEP) exposure, four days of dexamethasone treatment only partially decreased airway hyperresponsiveness (AHR) in mice exposed to both house dust mite (HDM) and DEPs. These HDM plus DEP–exposed mice were noted to have greater airway neutrophilia in comparison to mice exposed to HDM only. Anti–IL-17A treatment in combination with dexamethasone markedly decreased AHR compared with either treatment alone. [13]

Asthmatic patients suffer clinical symptoms rapidly when exposed to worsening air quality. Explanations of the mechanism of this rapid sensitivity are now being reported. Many research studies, and a recent review in the JACI, [14] have shown how innate lymphoid cells are emerging as key contributors to the pathogenesis of inflammatory disease.

EXPOSURES DURING DIFFERENT STAGES OF DEVELOPMENT AND LONG-TERM SEQUELAE OF CHILDHOOD ASTHMA:

Amongst the well-known risk factors for asthma, new research is aiding to define the level of influence had by these risk factors. The Inner-City Asthma Consortium performed a causal network analysis on a conceptual model of eight possible asthma risk factor domains. They concluded that the model may illustrate about fifty percent of the variance in asthma severity. The two biggest triggers of asthma severity were an allergy pathway starting with allergic sensitization and an environmental tobacco smoke pathway. Amongst the individual domains, pulmonary physiology and rhinitis severity had the biggest effects on asthma severity. Analysis of an Australian longitudinal birth cohort showed that allergic sensitization by twelve months of age was associated with increased risk of wheeze during young adulthood, and lower FEV1, FEV1/forced vital capacity (FVC) ratio, and forced expiratory flow between 25% and 75% of forced vital capacity (FEF25-75) at 24 years of age.

PATIENT-CENTERED OUTCOMES RESEARCH REFLECTS PATIENT PRIORITIES AND ENGAGES STAKEHOLDERS:

The National Asthma Education and Prevention Program Expert Panel Report, [15] which was last revised in 2007, adds guidance for the treatment of asthma. For the most part, it is informed by efficacy studies. These described studies include patients most probably to benefit and who are treated under the most promising conditions. but, a limitation of these

well-controlled studies is that the interventions are not always efficient when applied in the real world.

CLINICAL RISK FACTORS:

Wells et al provides support to this patient-centered approach by showing that neither self-reported race-ethnicity nor race defined by genetic ancestry predicted ICS response; rather, baseline lung function and self-reported asthma control do, stressing the need to find methods to make sure optimal lung function, asthma control, and elimination of barriers to accessing care.

NEW INFORMATION ON ASTHMA MEDICATIONS:

In 2016, encouraging new drugs as add-on management for poorly controlled asthma were introduced, and the safety of well-known drugs, known as LABAs, was revisited. The addition of roflumilast, a selective phosphodiesterase 4 inhibitor, in conjunction with montelukast to the controller regimen of adults with poorly controlled asthma despite the use of at least medium-dose ICSs with a LABA led to in a statistically marked increase in prebronchodilator FEV1 from baseline, improved morning peak expiratory flow (PEF), and enhanced daytime symptom scores compared with placebo with montelukast. [16] But, there was no change in prebronchodilator PEF or asthma control questionnaire scores. QGE031 (ligelizumab), an anti-IgE antibody with a higher binding affinity for IgE than omalizumab, elicited a 3- and 16-fold greater increase in provocative allergen concentrations to decrease the FEV1 by 15% compared with omalizumab and placebo, respectively, in adults with mild allergic asthma. [17]

MANAGEMENT:

In 2016, focus was placed on evaluation of drugs adherence and creation of comprehensive school-based asthma support networks. In a population-based study, only thirty three percent of children showed high ICS adherence.91 likewise, by using reimbursement data, only twenty four percent of adults and pediatric patients upheld regular ICS adherence 1 year after a period of regular ICS use. The unique barriers for poor medication adherence are age specific, requiring tailored approaches.92 Additionally, inhaled medications pose a unique difficulty to adherence, requiring proper technique for adequate drug delivery.

Advances are exploring ways to target low adherence. Use of the Propeller Health Asthma Platform (Propeller Health, Madison, Wis), an electronic monitoring device system, declined short-acting b-agonist use and increased short-acting b-agonist–free days in children and adults.

The use of an acoustic recording device attached to an inhaler concluded that only twenty percent of patients used their inhaler in the correct manner at the correct interval, emphasizing the need to address not only number of actuations but also technique errors. The School-based Asthma Management Program was developed to foster multidirectional communication between children, families, clinicians, school-based personnel, and the community to promote better pediatric asthma care.88 The School-based Asthma Management Program identified 4 essential parts to establish this connection: a circle of support between the aforementioned groups, asthma management plans, comprehensive asthma education for school personnel, and assessment and remediation of school-based asthma triggers.

The benefit of such a multidisciplinary school-based program was highlighted through the Step-Up Asthma Program, which used asthma counselors as a bridge between subspecialty asthma care, primary care providers, school nurses, and families. Over a 2-year period, the program higher the number of asthma action plans, increased use of rescue and controller medications in schools, enhanced asthma knowledge scores, improved inhaler technique, and decreased asthma exacerbations.

CONCLUSIONS:

There have been great advances in Asthma focused on asthma across the lifespan and reported on some key findings linked to asthma inception, the microbiome, and the epigenome. Additionally, some new aspects of predicting and preventing asthma exacerbations were reported. There are new advances in the development related to the natural history of asthma and the effect of the environment. No previous era in asthma management that has witnessed the introduction of so many new classes of medications. It is considered a great challenge for doctors and those contributing to asthma guidelines to select relevant pieces of information that should be incorporated into clinical practice. Temporarily, doctors must keep up with these new findings to add benefits to patients by applying strategies that are most likely to be effective.

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