REVIEW ARTICLE

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Treatment of Hypertension in Patients with Asthma

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Asthma and hypertension are common chronic diseases, each with attendant morbidity, mortality, and economic effects. It is estimated that 300 million people worldwide have asthma, and an increase in prevalence to 400 million is anticipated by 2025. Approximately 250,000 asthma-related deaths occur yearly, many of which are believed to be avoidable.[1] In the United States, more than 8% of adults have asthma, with disproportionate representation among women, ethnic minorities, and people who are economically disadvantaged. Asthma-related health expenditures in 2013 were estimated at $80 billion.[2] The presence of hypertension with asthma creates an additional health burden; hypertension is the world's most common modifiable risk factor for cardiovascular disease and death. Worldwide estimates suggest that 874 million adults have a systolic blood pressure higher than 140 mm Hg,[3,4] and the prevalence of hypertension, like that of asthma, is increasing, along with costs, morbidity, and mortality.[5] Elevated systolic blood pressure was the leading global contributor to preventable death in 2015.[6] In the United States, approximately one in three adults has high blood pressure.[7] Since current hypertension guidelines incorporate new evidence that has led to lower thresholds for treatment, the number of persons considered to have hypertension will expand, and the attendant costs will escalate.[3]

Patients with asthma are more likely to have hypertension than those who do not, independent of traditional risk factors.[8] A diagnosis of hypertension is associated with augmented asthma severity,[9] and reduced lung function has been correlated with heightened cardiovascular mortality.[10] Given the bidirectional relationship between compromised lung function and compromised cardiovascular function, the rationale for treating and controlling hypertension in persons with asthma is compelling. Although the effect of blood-pressure control on asthma is largely unexplored, the risk of death from cardiovascular disease is decreased when systolic blood pressure is reduced to levels below 130 mm Hg.[11-14] In this review, we discuss the potential mechanistic links between hypertension and asthma, the influence each condition has on the other, and approaches to the treatment of hypertension in adult patients with asthma.

MECHANISTIC RELATIONSHIP BETWEEN HYPERTENSION AND ASTHMA

Predisposing factors (genetic profile, stress, and age), dietary and lifestyle choices, and inflammatory mechanisms all contribute to the hypertensive asthmatic phenotype. These factors may be important in understanding the development of the condition (Fig. 1).

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Systemic inflammation serves as an underpinning for the burden of disease that accrues from hypertension and asthma.[15] Inflammation is widely accepted as being both fundamental to the pathogenesis of asthma[16] and central to the development of hypertension and its deleterious consequences.[17,18] A large cross-sectional study of middle-aged persons with asthma showed that the prevalence of hypertension was higher among those with lower values for forced expiratory volume in 1 second (FEV_1), with the risk of hypertension increasing as the FEV_1 decreased.[19] Furthermore, C-reactive protein levels, a marker of systemic inflammation related to interleukin-6 and hypertension, were correlated with the rate of loss of FEV_1.[20] Such findings may imply a reciprocal relationship, wherein systemic inflammation influences the disease course for both hypertension and asthma.

Asthma is currently understood as a disorder that is characterized by two main endotypes: type 2 high inflammation and type 2 low inflammation. These subtypes are broadly defined by their predominant underlying mechanism, which is largely determined by the T cells or innate lymphocytes and cytokines that are involved.[21] Each endotype can be further subdivided into multiple phenotypes that are distinguished by clinical features, pathological findings, and biomarkers (chemokines) (Table 1). Owing to the lack of uniform criteria for classifying types of asthma, estimates of the prevalence of type 2 high- and type 2 low-inflammation endotypes vary; however, each endotype appears to represent approximately half the population with asthma.[16]

The Severe Asthma Research Program conducted multiple studies in which patients with asthma were grouped into discreet clusters on the basis of a hierarchical analysis of variables that included clinical characteristics, biomarkers, cellular profiles, lung function, atopic status, responses to treatment, gene expression, and coexisting conditions.[22-24] It is notable that two studies that included hypertension as a variable showed cosegregation of hypertension with asthmatic profiles that are typical for the type 2 low-inflammation endotype.[22,23] Patients with features of the type 2 low-inflammation endotype (older age, later onset of asthma, higher body-mass index [BMI], greater severity of disease, and low atopy) were also more likely to have hypertension (48 of 175 patients [27%]) than patients with the type 2 high-inflammation endotype (50 of 551 patients [9%]).[22] The results of a separate study based on clinical characteristics and assessments of inflammatory cells in blood and sputum showed a significantly higher incidence of hypertension in clusters distinguished by severity of disease, older age, later onset of disease, higher BMI, and greater resistance to treatment with glucocorticoids: 31% (51 of 164 patients) as compared with 11% (28 of 259 patients).[23] These observations suggest that type 2 low inflammatory pathways may provide a pathogenic mechanism that links these two diseases.

The degree of inflammation in patients with hypertension and asthma reflects the conjoint effect of both conditions. Hypertension skews T cells toward a proinflammatory (type 1 helper T-cell [Th1 cell]) phenotype, characterized by increased interferon-γ responses and decreased type 2 helper T-cell (Th2 cell) responses.[25] In asthma, enhanced airway hyperresponsiveness and severe disease are associated with elevated levels of interferon-γ.[26] Correspondingly, in hypertension, interferon-γ and Th1-cell polarization contribute to blood-pressure elevation and its sequelae.[17]

Interleukin-17 has also been shown to play a major role in the development of hypertension and its related end-organ damage in both studies in animals and in vitro models. Interleukin-17 induces a proinflammatory phenotype in vascular smooth-muscle cells by enhancing the release of mediators, including interleukin-6, CXCL8 and CXCL10, and C-reactive protein.[27] Both anti–interleukin-17 treatment and genetic deletion have been shown to reduce hypertension in studies in animals.[17,27] A role for interleukin-17 is also evident in some patients with severe asthma in whom an elevated level of interleukin-17 is correlated with neutrophil infiltration, airway hyperresponsiveness, and a lack of sensitivity to glucocorticoids. In these patients, interleukin-17 is capable of inducing secretion of proinflammatory cytokines from lung structural cells and airway smooth muscle, including tumor necrosis factor α, interleukin-1β, granulocyte colony-stimulating factor, and interleukin-6 as well as the chemokines CCL11 (eotaxin) and CXCL8 (interleukin-8), which are important in airway inflammation and remodeling.[28,29] Surprisingly, in one trial, the targeting of interleukin-17 failed

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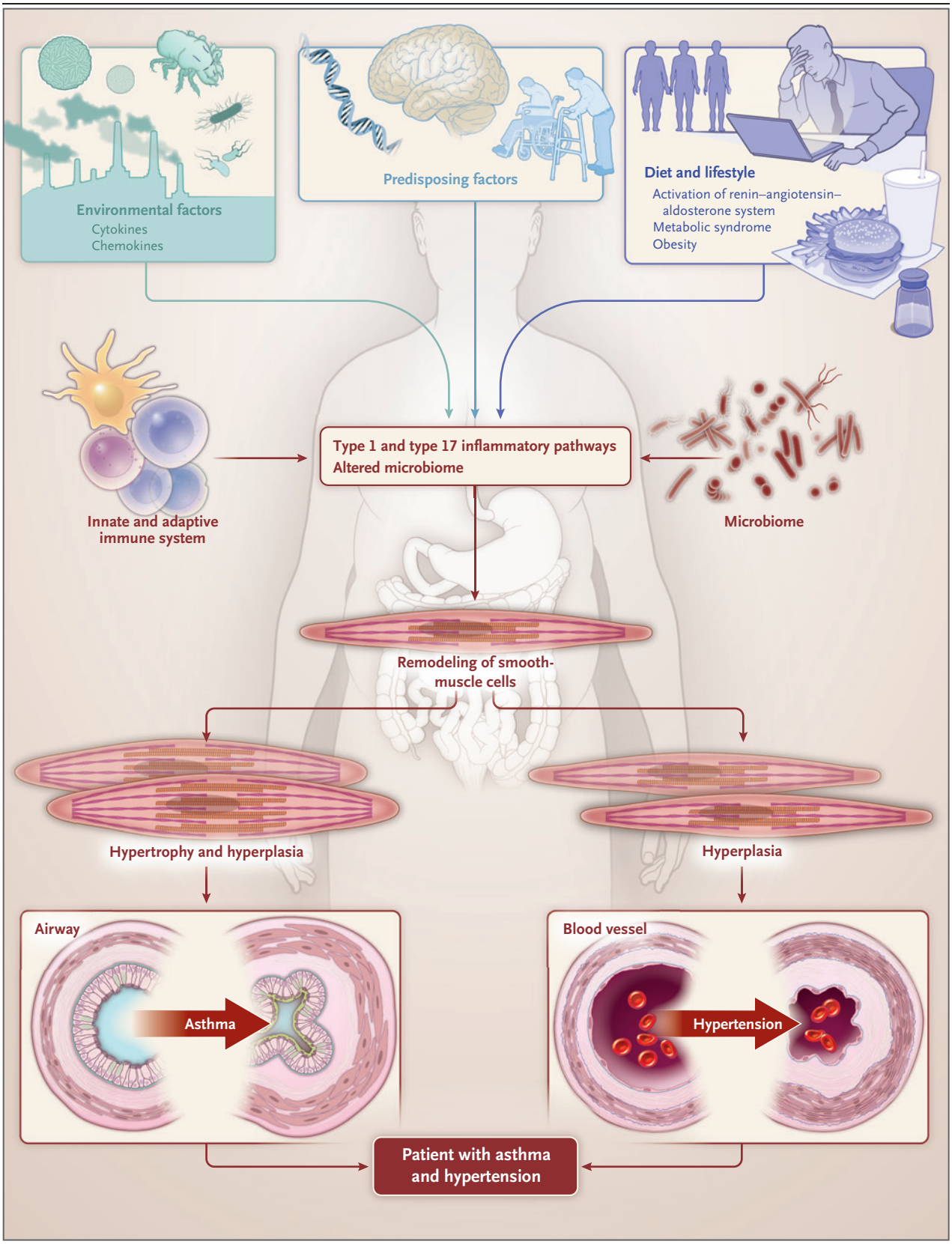

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Figure 1 (facing page). Pathophysiology and Disease Expression in Patients with Asthma Who Have Hypertension.
A combination of genetic factors, nervous system dysfunction, and age may predispose some persons with asthma to hypertension. Diet and lifestyle influence the likelihood of the development of obesity and metabolic syndrome and the consequent enhancement of systemic inflammation. Production of interleukin-6 from adipose tissue contributes to both airway and vascular disease. Stress is another common cofactor that increases the severity of disease. In patients with a high-salt diet, both inappropriate activation of the renin–angiotensin–aldosterone system (RAAS) and alterations in the microbiome are linked to hypertension development and more severe disease. Environmental factors, including pollutants, microbes, and viruses, can serve as stimuli for innate immune responses, activating proinflammatory type 1 or type 17 responses. Exposure to allergens such as dust mites may play a role in inflammation that is independent of adaptive type 2 high-inflammation responses, activating cytokine cascades by means of protease-activating receptors. Innate and adaptive immune profiles in persons with asthma who have hypertension appear predominantly as a type 2 low-inflammation endotype. In asthma, this endotype contributes to airway hyperresponsiveness, smooth-muscle hypertrophy and hyperplasia, structural remodeling, and mucous secretion. In patients with asthma who have hypertension, the inflammatory environment leads to increases in vascular tone and blood pressure.

Table 1. Predominant Features and Characteristics of Endotypes and Phenotypes in Asthma.*

Characteristic	Type 2 High Endotype	Type 2 Low Endotype
Phenotype and clinical profile		
Atopic	Early onset, glucocorticoid sensitive	—
Late onset	Often accompanied by chronic sinus disease	—
AERD	Polypoid rhinosinusitis with respiratory reaction after exposure to aspirin or other NSAID	—
Nonatopic	—	Adult onset
Obesity	—	Female preponderance
Older age	—	Late onset; often steroid insensitive
Cytokines	Interleukin-4, -5, and -13; GM-CSF	TGF-β, interferon-γ, interleukin-6, -17, -1β, and -8, TNF-α
Cellular	Eosinophilic	Neutrophilic or paucigranulocytic
Onset	Frequently younger age but severe asthma may develop in older age	Usually present in older age
Atopy	High	Low
Glucocorticoid responsiveness	Usually responsive, particularly in mild and moderate asthma	Often relatively refractory
Severity	Variable, can be severe	Often severe

* AERD denotes aspirin-exacerbated respiratory disease, GM-CSF granulocyte–macrophage colony-stimulating–factor, NSAID nonsteroidal antiinflammatory drug, TGF-β transforming growth factor β, and TNF-α tumor necrosis factor α.

to ameliorate symptoms in patients with severe asthma[30]; however, a subgroup analysis identified patients with highly reversible depression in FEV_1 who had some improvement, as reflected by the Asthma Control Questionnaire. The functional role of interleukin-17 in the contraction of smooth-muscle cells may offer a partial explanation for the more favorable response in this subgroup.[31]

Experimental evidence supports the concept that elevated interleukin-6 levels can drive the differentiation of CD4+ T cells through interaction with transforming growth factor β to promote skewing toward type 17 helper cells (Th17) cells, leading to a reduction of regulatory T cells (Tregs). Tregs play a protective role in the development of hypertension that is related in part to production of interleukin-10[27] and play a critical role in the regulation of asthma development.[32]

Interactions among interferon-γ, interleukin-17, and interleukin-6 have the potential to affect disease expression for both hypertension and asthma

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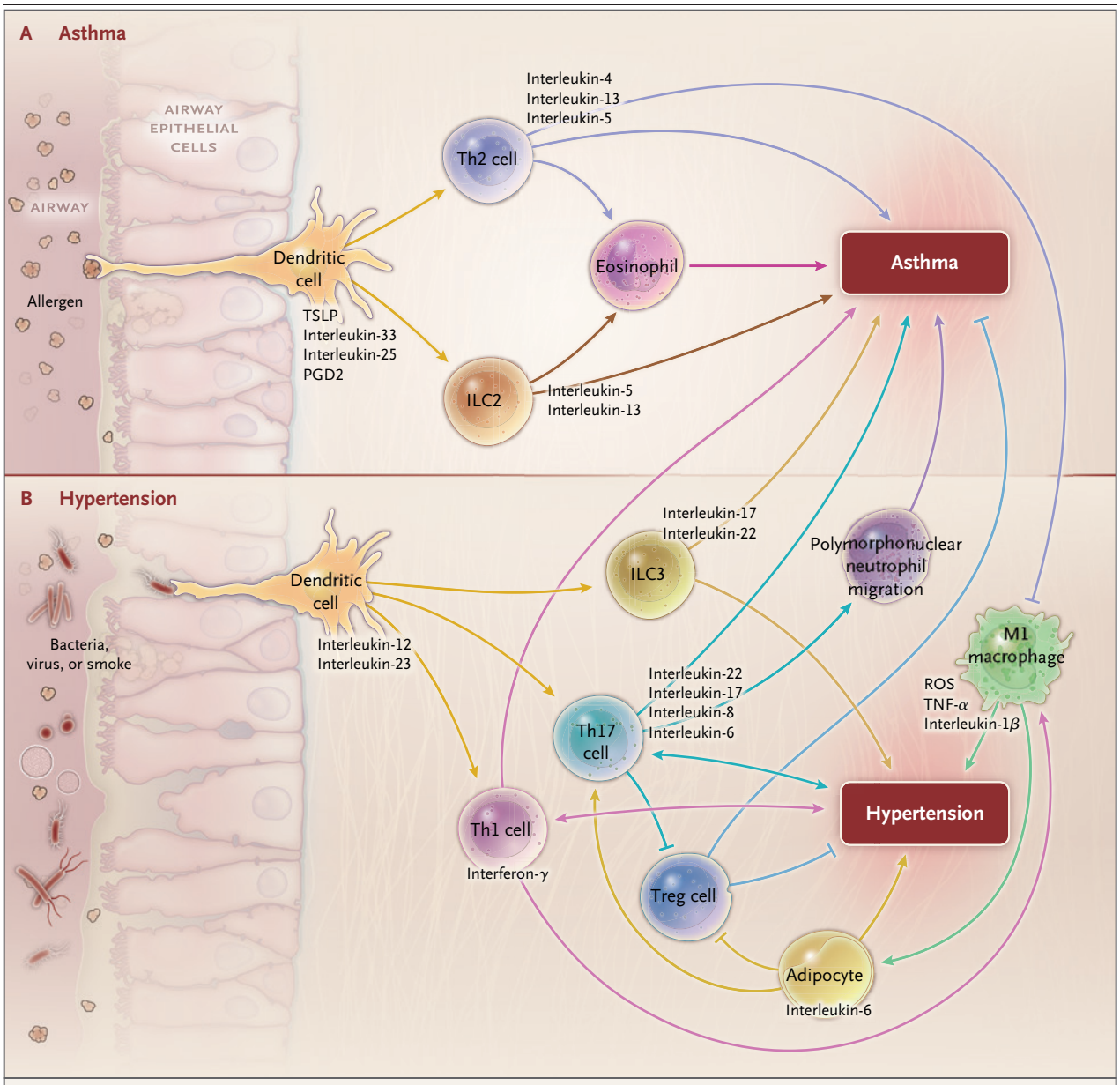

Figure 2. Inflammatory Pathways in Patients with Asthma Who Have Hypertension.

Type 2 high asthma (Panel A) has not been mechanistically linked to hypertension. In addition, type 2 cytokines such as interleukin-4 and interleukin-13 promote the M2 phenotype in macrophages rather than the M1 phenotype implicated in hypertension. Type 2 low asthma has multiple mechanistic links with the inflammation involved in hypertension (Panel B). Type 1– and type 17–biased immune responses may dually influence both the expression and the severity of asthma and hypertensive disease. Interferon-γ also promotes M1 macrophages that both activate adipocytes and directly contribute to hypertension, whereas interleukin-6 participates in down-regulating regulatory T cells (Tregs) that inhibit both hypertensive and asthmatic inflammation. ILC2 and ILC3 denote group 2 and group 3 innate lymphoid cells; PGD_2 prostaglandin D_2; ROS reactive oxygen species; Th1, Th2, and Th17 type 2, type 3, and type 17 helper cells; and TSLP thymic stromal lymphopoietin.

(Fig. 2). Together, these cytokines stimulate the inflammation, smooth-muscle activation, and fibrinogenesis that are fundamental to airway and cardiovascular disease. Thus, persons who have both hypertension and asthma appear to compose a patient subgroup with difficult-to-treat disease who are at increased risk for end-organ damage.

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OBESITY AND METABOLIC DYSFUNCTION

Elevated interleukin-6 levels and systemic inflammation result in metabolic dysfunction that increases the morbidity associated with both hypertension and asthma. Secretion of proinflammatory cytokines, notably interleukin-6, by adipocytes and inflammatory macrophages in white adipose tissue is of pathogenic importance in asthma,[33] a condition in which interleukin-6 appears to be a biomarker for metabolic dysfunction and severe disease.[34] Elevation of interleukin-6 levels has been identified in association with hypertension in studies in humans and animals, in which it has been shown to be related to disease development.[35,36]

SMOOTH-MUSCLE REMODELING AND VASCULAR BIOLOGY

Smooth-muscle remodeling, driven in substantial part by inflammatory cytokines, is a critical component of both asthma and hypertension.[37-39] Hyperplasia and abnormal contracture of the smooth-muscle cells surrounding the airway play an important role in airway obstruction in asthma. Similarly, the abnormal contraction and proliferation of smooth-muscle cells are well recognized as features of the vascular remodeling and endothelial abnormalities associated with hypertension.

Genetic factors clearly affect the expression of asthma and hypertension; however, the relevant interrelations are complex and difficult to dissect. Polymorphisms in β-adrenergic receptors on smooth-muscle cells have been reported in patients with both hypertension and asthma, but their importance in disease manifestation may lie in their modulation of the response to antagonists and agonists, which could have more influence on treatment outcomes than on disease causation.[40] In contrast, modification of the vascular smooth-muscle cell phenotype in response to local environmental influences is thought to play a critical role in the pathogenesis of hypertension and asthma as well as atherosclerosis.[41]

DIETARY SALT

Dietary salt intake has long been considered to be relevant to the development of cardiovascular conditions. Early observations associating higher salt intake with blood-pressure elevation have been refined to identify subpopulations of salt-sensitive and salt-insensitive persons.[42] The responsiveness of the kidneys, sympathetic nervous system, and vasculature to salt has been observed.[43] The immune system may be important in responsiveness to salt. For example, Th17 cells appear to play a role in mediating the relationship between salt exposure and hypertension.[17,18,27] In a mouse model, high-salt diets promoted the generation of Th17 cells through alterations in the gut microbiome, with depletion of *Lactobacillus murinus.* Salt-sensitive hypertension is prevented by treatment with *L. murinus,* which has a modulating effect on Th17 cells. Evidence suggests that the effect is related to the tryptophan metabolites produced by this organism.[44] Healthy persons on a high-salt diet are also reported to have reduced levels of lactobacillus, elevated levels of Th17 cells, and elevated blood pressure, all of which support the proposition that higher salt intake plays a role in inflammation in humans.[44-46] At present, similar information related to dietary salt content in patients with asthma is lacking.

MANAGEMENT OF DISEASE IN PATIENTS WITH ASTHMA AND HYPERTENSION

The mechanisms linking asthma and hypertension not only are of theoretical interest but also have implications for therapy and disease management. The treatment of hypertension in a patient with asthma should involve a multifactorial approach that involves control of both conditions, treatment of coexisting conditions, and the institution of lifestyle modifications (Fig. 3).

PHARMACOLOGIC TREATMENT OF HYPERTENSION IN PATIENTS WITH ASTHMA

In the 2017 report of the American College of Cardiology–American Heart Association Task Force on clinical practice guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults, hypertension was categorized as either stage 1 (130–139/80–89 mm Hg) or stage 2 (>140/>90 mm Hg).[3] Pharmacotherapy was recommended for patients who have or who are at high risk for cardiovascular disease at stage 1 and for all patients at stage 2. It is noteworthy that the threshold for a diagnosis of hypertension was lowered in the 2017 guidelines, a development that has led to substantial controversy, since it has expanded the percentage of adults in the United States with a diagnosis of hypertension from 32% to 46%.

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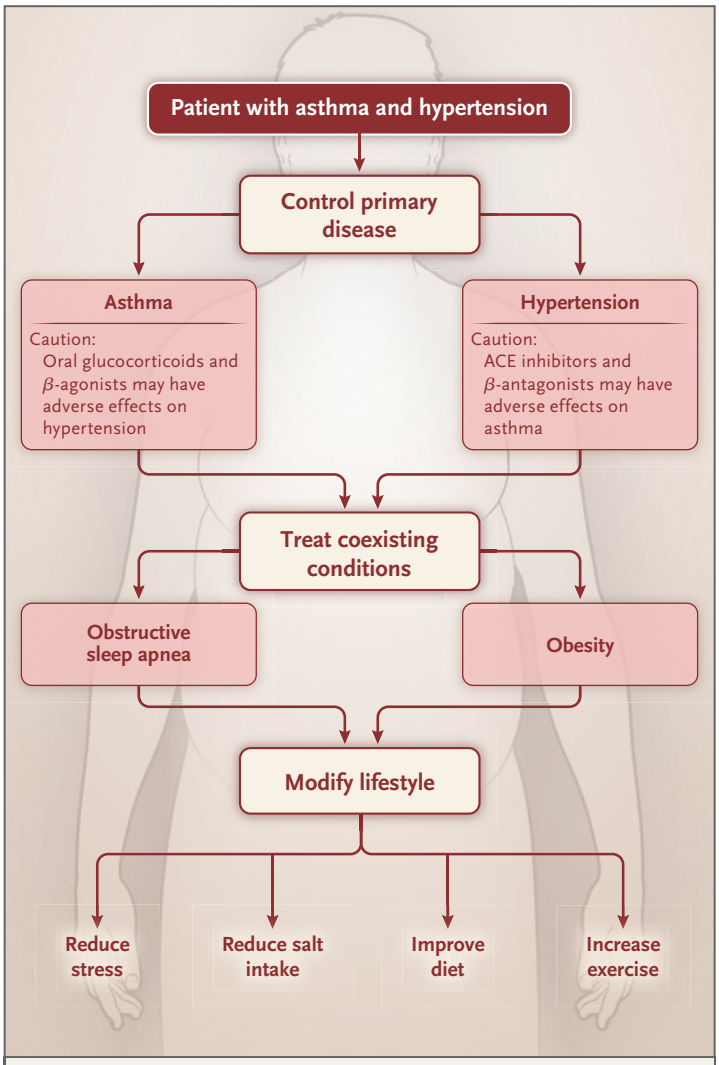

Figure 3. Approaches to Treatment.

Gaining control of hypertension and asthma is the initial step in treatment, with specific cautions regarding pharmacologic treatment. Patients should be monitored for deleterious effects. It is essential to identify and treat coexisting conditions, which have the potential to increase the severity of disease. Lifestyle modifications are of fundamental importance, with an emphasis on dietary modifications (including reduced salt intake, moderate intake of ethyl alcohol [found in beer, wine, and distilled spirits], and increased potassium intake), stress reduction, exercise, and weight loss (as needed).

What does the treatment of hypertension generally accomplish, and how might that treatment affect patients with asthma? To date, all-cause mortality has not differed significantly among patients with hypertension treated with any of the four major classes of first-line antihypertensive agents (Table 2). The degree of blood-pressure reduction rather than the choice of antihypertensive medication appears to be the major determinant of outcome.[47] In patients with asthma, however, additional issues related to various pharmacologic agents should be considered.

Beta-Blockers

Some caution should be used when introducing beta-blockers to patients with asthma owing to concerns regarding both unopposed bronchoconstrictive signals and therapeutic response to β_2-agonists. Furthermore, beta-blockers are not generally recommended as monotherapy for the treatment of hypertension in patients with most conditions, although there may be specific indications for patients with congestive heart failure who have arrhythmias or who have had myocardial infarction.[3,4]

Beta-blockers may be either nonselective, targeting both the β_1 and β_2 adrenergic receptors, or relatively cardioselective, predominantly targeting the β_1 receptor. Selective beta-blockers differ in their relative potency against β_1 and β_2 receptors, and their selectivity may be decreased at higher doses. Asthma exacerbations and even fatal outcomes have been reported after treatment of glaucoma with eyedrops that contain nonselective beta-adrenergic blockers.[48,49] A meta-analysis of randomized, blinded, placebo-controlled trials reported relatively small but significant declines in FEV_1 in patients who had received short-term treatment with a selective or nonselective beta-blocker, but a significant increase in symptoms was reported only in patients who received nonselective blockers.[50] A subgroup of patients did have a decline in FEV_1 of 20% or more after short-term exposure to selective beta-blockers. A decrease in the response to short-acting β_2 agonists (SABAs) was noted, with selective beta-blockers blunting the response and nonselective blockers abrogating the response.[50] Long-term exposure to beta-blockers is associated with a lower risk of bronchospasm than short-term exposure. In clinical practice, beta-blockers have been used in patients who had disease that was stable, who did not have evidence of reduced FEV_1, did not increase use of SABAs, and did not have an increase in symptoms with continued treatment.[9,51] Nevertheless, the use of beta-blockers in patients with unstable disease or those with severe airway obstruction requires vigilance.

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Table 2. Pharmacologic Agents and Indications.

Drug Class	Indications	Side Effects and Cautions	Asthma-Specific Considerations
Thiazide-type diuretic	First-line or add-on drug	Monitor sodium and potassium levels and, in older patients, hyponatremia.	Reduced potassium levels with increased use of short-acting beta-agonists, theophylline, and glucocorticoids
Angiotensin-converting–enzyme inhibitor	First-line or add-on drug for chronic kidney disease, congestive heart failure, and myocardial infarction	Monitor potassium and creatinine levels. Risk of angioedema is 2 to 4 times as high in black patients. Avoid in pregnant patients.	Cough; possible increase in asthma morbidity
Angiotensin-receptor blocker	First-line or add-on drug for chronic kidney disease, congestive heart failure, and myocardial infarction	Monitor potassium and creatinine levels. Avoid in pregnant patients.	Reduced bronchial hyperresponsiveness
Calcium-channel blockers			
Dihydropyridine	First-line or add-on drug	Edema; may worsen proteinuria and left ventricular outflow-tract obstruction.	Possible favorable effects on smooth-muscle contraction and on triggering factors
Nondihydropyridine	First-line or add-on drug	Constipation and heart block may occur when used with beta-blockers.	Possible favorable effects on smooth-muscle contraction and on triggering factors
Beta-blockers	Not recommended as monotherapy; particular concerns for patients 60 yr of age and older (i.e., increased fatigue, decreased exercise tolerance, inferior therapeutic outcomes); indications include congestive heart failure, myocardial infarction, and arrhythmias	Bradycardia, fatigue, heart failure, and insomnia may occur. Peripheral circulation may be impaired. Glucose and lipid metabolism and ability to exercise may be affected.	Bronchospasm; caution in patients whose asthma is unstable and in patients with severe obstruction

Angiotensin-Converting–Enzyme Inhibitors

As is the case in the general population of patients with hypertension, angiotensin-converting–enzyme (ACE) inhibitors are useful in patients with asthma and hypertension — they are not contraindicated. However, clinical confusion regarding asthma control can arise during treatment, because an ACE inhibitor–related cough may develop in exposed patients.[52] The incidence of this side effect is unclear, ranging from 2.8 to 40% depending on ethnicity, genotype, presence of underlying cardiovascular disease, methodology of assessment, and the specific ACE inhibitor used.[52-56] ACE inhibitors have also been associated with escalating severity of asthma in some patients with hypertension.[57] In a case–control trial involving patients with hypertension and asthma, ACE inhibitors were associated with increased asthma morbidity, including increased use of SABAs, increased emergency-department visits or hospitalizations, and increased use of systemic glucocorticoids.[9] Given that ACE inhibitors are considered to be a major drug class for the treatment of hypertension, clinicians should be alert to the fact that the use of these drugs can be deleterious in a minority of patients with asthma.

Angiotensin-Receptor Blockers

Angiotensin-receptor blockers (ARBs) may be the preferred drugs that act on the renin–angiotensin system for use in patients with asthma who have hypertension. Levels of circulating angiotensin II and renin were found to be increased in patients with severe asthma during exacerbations as compared with those without exacerbation.[58] Experimental infusion of angiotensin II also led to a decrease in FEV_1 and an increase in symptoms of chest tightness or cough in patients with mild asthma.[58] Inhibition of angiotensin II type 1 receptors has resulted in slight abatement in bronchial hyperresponsiveness.[59] ARBs appear to target pathways that would address both hypertension and asthma. ARBs do

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not appear to result in either cough or increased airway responsiveness, even in patients who are unable to take an ACE inhibitor.[60,61]

Calcium-Channel Blockers

There are theoretical benefits associated with the use of calcium-channel blockers in patients with asthma who have hypertension. This class of medication decreases smooth-muscle contraction; alleviates the bronchoconstriction that may occur in response to a variety of stimuli, including certain antigens, exercise, histamine, and cold air; and induces mild bronchodilation.[62] In clinical practice, however, calcium-channel blockers have not been shown to have a salutary effect on asthma outcomes.[63,64] Nonetheless, given their physiological profile and efficacy, calcium-channel blockers are a favored treatment for persons with asthma who have hypertension.[3,4,65,66]

Thiazides

Low-dose thiazides, used alone or in combination with other agents, such as calcium-channel blockers, are often prescribed for the treatment of hypertension.[67] In asthma, high doses of a β_2 agonist can be associated with hypokalemia, which appears to be more severe in patients who take diuretics and are thus subject to the resultant arrhythmogenic potential.[68] For a patient with asthma and hypertension who is receiving diuretics as well as a β_2 agonist, the addition of a glucocorticoid or theophylline may further enhance the risk of hypokalemia.

PHARMACOLOGIC TREATMENT OF ASTHMA IN PATIENTS WITH HYPERTENSION

Hypertension is a leading cardiovascular complication of the use of systemic glucocorticoids.[69] Since persons with asthma who have hypertension often have a severe asthma phenotype and receive long-term or high-dose treatment with systemic glucocorticoids, blood-pressure control may become an issue. Similarly, frequent use of SABAs as a rescue medication is also of concern with respect to cardiovascular risk.[70] Adjusting pharmacologic management in this patient population to minimize the required dosages of systemic glucocorticoids and SABAs is therefore of particular importance. Approaches to the treatment of severe, difficult-to-treat asthma have recently been reviewed.[21] Current biologic therapies predominantly target the type 2 high-inflammation endotype, but agents for the treatment of the type 2 low-inflammation endotype are also under investigation.[21,71]

Obstructive Sleep Apnea

Obstructive sleep apnea is associated with hypertension and is thought to promote the inflammatory cascades involved in both cardiovascular disease and asthma.[72] The intermittent hypoxia that typifies obstructive sleep apnea activates pathways mediated by nuclear factor kappa light-chain enhancer of activated B cells (NF-κB), releasing mediators integral to systemic inflammation and vascular pathology.[19,72] Although the effect of treatment for obstructive sleep apnea on blood-pressure control has yet to be clearly delineated,[3,4] treatment appears to effect a reduction in inflammatory markers that may contribute to the development of hypertension.[72]

Obesity

The global obesity epidemic has coincided with the growing prevalence of hypertension and asthma.[6,73] In the United States, two thirds of the population are considered to be overweight or obese.[74] For every 5% increase in weight, the risk of hypertension rises by 20 to 30%.[75] Obesity has also been directly associated with asthma severity.[76,77] Conversely, weight loss improves multiple outcomes in obese persons with asthma.[78] Thus, weight loss is important for obese persons who have both asthma and hypertension. However, the treatment of obesity is extremely difficult, requiring a multidisciplinary approach.[79]

Lifestyle

Trends in the general population, including increases in dietary salt intake, ingestion of calories from sources other than vegetables and fruits, obesity, and reductions in physical activity have likely contributed to the increased prevalence of hypertension and, possibly, of asthma.[6,73] Patients with both conditions may benefit from lifestyle modifications, including changes in diet, restriction of salt intake, and increased physical activity.[80-82] Weight loss can effect decreases of approximately 1 mm Hg in blood pressure for each kilogram lost as well as reductions in car-

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diovascular mortality. Each of these nonpharmacologic interventions has the potential to reduce systolic blood pressure by 3 to 8 mm Hg and diastolic blood pressure by 1 to 4 mm Hg.[4,83-85] A healthful diet and exercise can also have a favorable influence on asthma outcomes, even in nonobese patients.[86]

Stress has been linked to increased susceptibility to a variety of diseases, including hypertension and asthma.[87-89] Although controlled outcome studies of the effect of stress reduction on patients with hypertension and asthma are lacking, it would be of interest to investigate nonpharmacologic approaches, such as transcendental meditation and mindfulness-based stress reduction.

CONCLUSIONS

Persons with both hypertension and asthma represent an important subset of the globally escalating number of persons with cardiovascular and airway disease. Experimental evidence from studies in animals and observations in human disease highlight smooth-muscle activation, vascular dysfunction, and systemic inflammation as unifying characteristics within this cohort. The influence of type 1 and type 17 inflammatory pathways is noteworthy for increasing the severity of disease in patients who have hypertension and severe asthma who are also obese and have metabolic dysfunction. The treatment of patients with both hypertension and asthma should involve an integrated approach that includes pharmacotherapy and changes in lifestyle. A combination of interventions — including diet modification, salt restriction, stress reduction, and weight loss — that target shared pathophysiological mechanisms may be of value for these patients.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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