Hypertension substantially increases the risk for coronary heart disease, stroke, retinopathy, and nephropathy. In patients, hypertension usually clusters with the other components of the metabolic syndrome, such as microalbuminuria, central obesity, insulin resistance, dyslipidemia, hypercoagulation, increased inflammation, and left ventricular hypertrophy. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.

Therefore, numerous studies have been conducted to identify the relationship between hypertension and inflammation. Clinical data demonstrated that hypertension is clearly linked to inflammation, because C-reactive protein levels are reported to be associated with future development of hypertension. In addition, basic and clinical research have also demonstrated that upregulation of genes related to inflammation, such as tumor necrosis factor-α, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, to name a few, was observed in target organs and/or circulation of hypertensive animals and patients. Increase in tissue and/or circulating levels of inflammatory cytokines suggest that the production of these cytokines increases the risk of plaque rupture.

However, how hypertension causes inflammation is not clear. Does high blood pressure directly cause inflammation, or do other humoral factors related to hypertension promote inflammation? Many researchers suspect that angiotensin II (Ang II) may be responsible for the inflammatory changes. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.

Therefore, numerous studies have been conducted to identify the relationship between hypertension and inflammation. Clinical data demonstrated that hypertension is clearly linked to inflammation, because C-reactive protein levels are reported to be associated with future development of hypertension. In addition, basic and clinical research have also demonstrated that upregulation of genes related to inflammation, such as tumor necrosis factor-α, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, to name a few, was observed in target organs and/or circulation of hypertensive animals and patients. Increase in tissue and/or circulating levels of inflammatory cytokines suggest that the production of these cytokines increases the risk of plaque rupture.

However, how hypertension causes inflammation is not clear. Does high blood pressure directly cause inflammation, or do other humoral factors related to hypertension promote inflammation? Many researchers suspect that angiotensin II (Ang II) may be responsible for the inflammatory changes. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.

Therefore, numerous studies have been conducted to identify the relationship between hypertension and inflammation. Clinical data demonstrated that hypertension is clearly linked to inflammation, because C-reactive protein levels are reported to be associated with future development of hypertension. In addition, basic and clinical research have also demonstrated that upregulation of genes related to inflammation, such as tumor necrosis factor-α, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, to name a few, was observed in target organs and/or circulation of hypertensive animals and patients. Increase in tissue and/or circulating levels of inflammatory cytokines suggest that the production of these cytokines increases the risk of plaque rupture.

However, how hypertension causes inflammation is not clear. Does high blood pressure directly cause inflammation, or do other humoral factors related to hypertension promote inflammation? Many researchers suspect that angiotensin II (Ang II) may be responsible for the inflammatory changes. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.

Therefore, numerous studies have been conducted to identify the relationship between hypertension and inflammation. Clinical data demonstrated that hypertension is clearly linked to inflammation, because C-reactive protein levels are reported to be associated with future development of hypertension. In addition, basic and clinical research have also demonstrated that upregulation of genes related to inflammation, such as tumor necrosis factor-α, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, to name a few, was observed in target organs and/or circulation of hypertensive animals and patients. Increase in tissue and/or circulating levels of inflammatory cytokines suggest that the production of these cytokines increases the risk of plaque rupture.

However, how hypertension causes inflammation is not clear. Does high blood pressure directly cause inflammation, or do other humoral factors related to hypertension promote inflammation? Many researchers suspect that angiotensin II (Ang II) may be responsible for the inflammatory changes. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.

Therefore, numerous studies have been conducted to identify the relationship between hypertension and inflammation. Clinical data demonstrated that hypertension is clearly linked to inflammation, because C-reactive protein levels are reported to be associated with future development of hypertension. In addition, basic and clinical research have also demonstrated that upregulation of genes related to inflammation, such as tumor necrosis factor-α, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, to name a few, was observed in target organs and/or circulation of hypertensive animals and patients. Increase in tissue and/or circulating levels of inflammatory cytokines suggest that the production of these cytokines increases the risk of plaque rupture.

However, how hypertension causes inflammation is not clear. Does high blood pressure directly cause inflammation, or do other humoral factors related to hypertension promote inflammation? Many researchers suspect that angiotensin II (Ang II) may be responsible for the inflammatory changes. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.

Therefore, numerous studies have been conducted to identify the relationship between hypertension and inflammation. Clinical data demonstrated that hypertension is clearly linked to inflammation, because C-reactive protein levels are reported to be associated with future development of hypertension. In addition, basic and clinical research have also demonstrated that upregulation of genes related to inflammation, such as tumor necrosis factor-α, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1, to name a few, was observed in target organs and/or circulation of hypertensive animals and patients. Increase in tissue and/or circulating levels of inflammatory cytokines suggest that the production of these cytokines increases the risk of plaque rupture.

However, how hypertension causes inflammation is not clear. Does high blood pressure directly cause inflammation, or do other humoral factors related to hypertension promote inflammation? Many researchers suspect that angiotensin II (Ang II) may be responsible for the inflammatory changes. Of importance, obesity, atherosclerosis, insulin resistance, hyperinsulinemia, hyperlipidemia, essential hypertension, type 2 diabetes mellitus, and for coronary heart disease are components of the metabolic syndrome and are associated with elevated plasma levels of C-reactive protein, interleukin-6, and tumor necrosis factor-α, which are markers of inflammation. This suggests that the metabolic syndrome is a low-grade, systemic, inflammatory condition. Hence, instituting antinflammatory measures might be beneficial in preventing or halting the progression of the metabolic syndrome in high-risk populations.
affected the gene of the soluble form of the VEGF receptor, Flt, into muscle of mice studied after Ang II infusion. Secretion of the soluble form of Flt into the circulation removed VEGF binding to the target receptor. Using this technique, they clearly demonstrated that VEGF is responsible for Ang II–induced vascular inflammation and structural changes such as wall thickening. However, unresolved questions still lie ahead. One of the missing links is how Ang II activated VEGF signaling. It is controversial whether Ang II directly activates VEGF. The relationship between VEGF and another transcription factor related to inflammation, NFkB, is also still unclear. In addition, the article by Zhao et al demonstrated the important finding that hypertension and cardiac hypertrophy were not affected by the blockade of VEGF signaling. Thus, there is still a missing link between inflammation and hypertension and cardiac hypertrophy. Further efforts to find the links between hypertension and other common diseases such as the acute coronary syndrome are necessary. Application of in vivo gene transfer will help provide further information to find these missing links.

References
Is Vascular Endothelial Growth Factor a Missing Link Between Hypertension and Inflammation?
Ryuichi Morishita

Hypertension. 2004;44:253-254; originally published online July 19, 2004;
doi: 10.1161/01.HYP.0000138689.29876.b3
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/44/3/253

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/