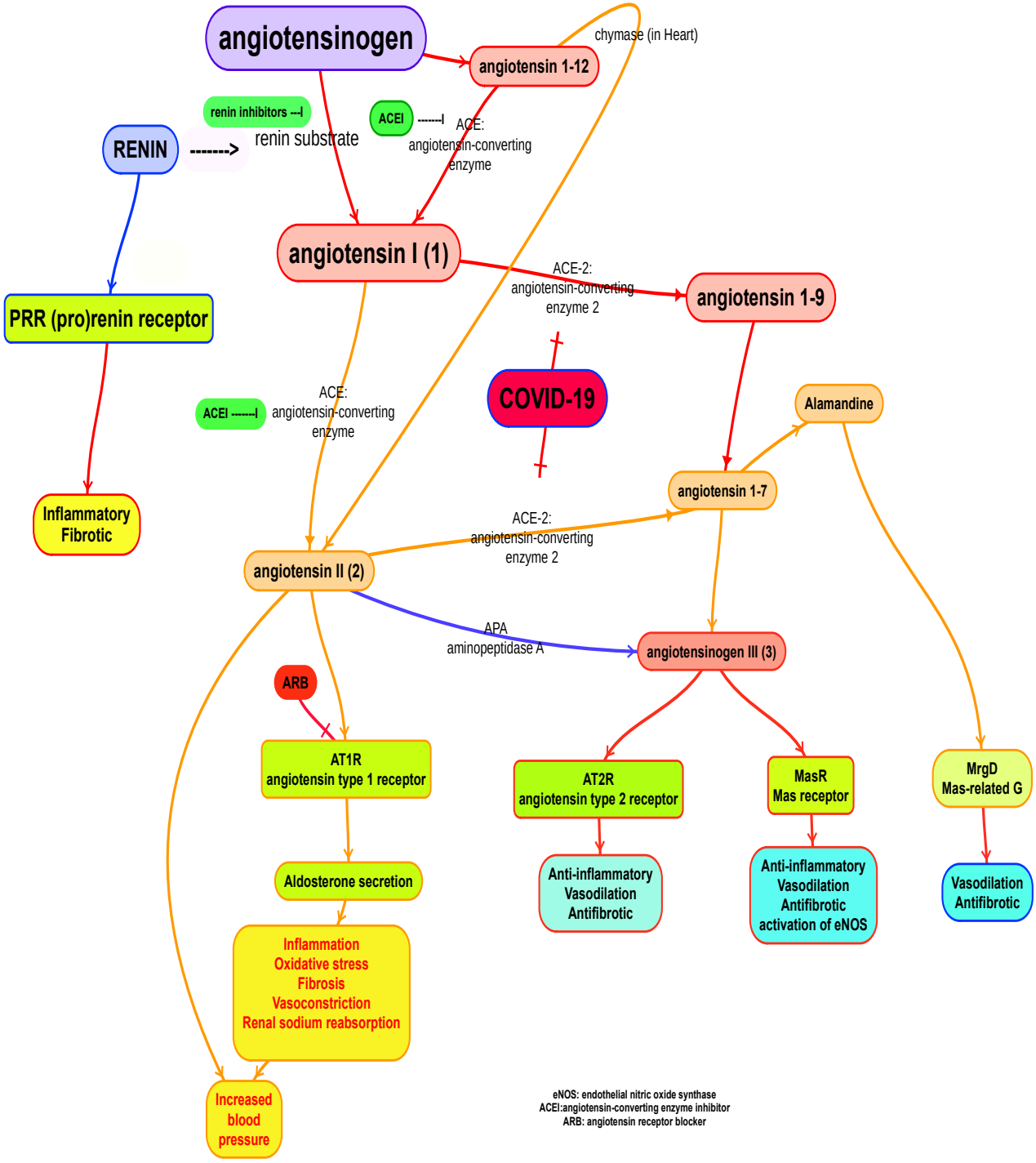
RAAS: The Renin - Angiotensin - Aldosterone System



Renin–Angiotensin–Aldosterone System: A Primer

THE BASICS

The Renin–Angiotensin–Aldosterone System has numerous physiologic functions throughout the body. Its effect on blood pressure is the most widely publicized as it is the target of pharmaceuticals to treat hypertension.

The Problem Enzyme: ACE

Angiotensinogen is the initial substrate which is converted by renin to angiotensin I and then to angiotensin II, by endothelial angiotensin-converting enzyme (ACE). Angiotensin II is most abundantly produced in the lungs and binds to the angiotensin type 1 receptor (ATR1). This leads to aldosterone secretion, vasoconstriction, sodium retention, inflammation, scarring, and increased blood pressure.

Relevant Pharmaceuticals

ACE inhibitors (ACEIs) block the conversion of angiotensin I to angiotensin II.

Angiotensin receptor blockers (ARBs) interfere with the binding of angiotensin II with angiotensin type 1 receptor (AT1R).

The Good Enzyme: ACE2

Angiotensin-converting enzyme 2 (ACE2) is responsible for initiating a series of steps eventuating in the conversion of Angiotensin II to Angiotensin III. Angiotensin III lowers blood pressure, decreases inflammation and scarring, and prevents inappropriate cellular proliferation.

The pharmaceuticals for treating hypertension do not bind to ACE2. They target ACE and AT1R.

Covid-19 and RAAS

ACE2 is present on lung alveolar epithelial cells. The Covid-19 virus binds to ACE2, and the resulting complex enters the lung alveolar cell. This reduces the amount of ACE2 available to decrease angiotensin II and its detrimental effects. Also, the loss of ACE2 lessens the number of beneficial products produced via ACE2. Therefore, the villain, ACE, has less opposition to its inflammatory and detrimental downstream effects.

What is the difference between ACE2 and ACE2 receptor?

ACE2 is an enzyme on the surface of type II pneumocytes, as well as many other cell types in the body. Under normal physiological circumstances, it is not a receptor. ACE2 is an enzyme that converts Angiotensin II to anti-inflammatory and anti-hypertensive products. However, when infected with SARS-CoV-1 or SARS-CoV-2, ACE2 acts as a “functional” receptor for viral entry into the cell.

RAAS inhibitors, ACE2 and Prognosis

Select preclinical studies have suggested that RAAS inhibitors may increase ACE2 expression. It has been hypothesized that this may increase the risk of infection, but decrease the severity of the illness as well as mortality. As of now, proof of RAAS inhibitors role in disease outcome remains to be determined.

Patients taking ACE-i and ARBs who contract COVID-19 should continue treatment, unless otherwise advised by their physician (Statement from the American Heart Association, the Heart Failure Society of America and the American College of Cardiology, March 17, 2020)

References

1. Naomi DL Fisher, M., *Overview of the renin-angiotensin system.* UpToDate, 2020.
2. Vaduganathan, M., et al., *Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19.* New England Journal of Medicine, 2020.
3. Guo, J., et al., *Coronavirus Disease 2019 (COVID-19) and Cardiovascular Disease: A Viewpoint on the Potential Influence of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers on Onset and Severity of Severe Acute Respiratory Syndrome Coronavirus 2 Infection.* J Am Heart Assoc, 2020. **9**(7): p. e016219.