

---

# How Does Metabolic Acidosis Cause Chronic Kidney Disease Progression?

# Disclaimer

---

The content contained within this slide deck is for educational purposes only. Not for promotional purposes or re-distribution.

---

# Donald Wesson, MD, MBA

Professor of Medicine  
Texas A&M University College of Medicine

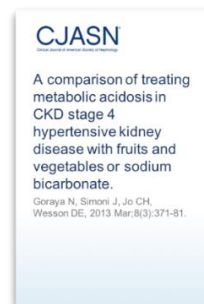
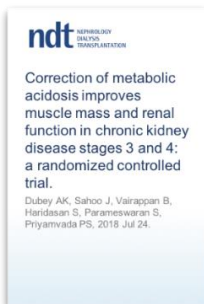
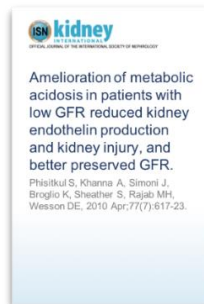
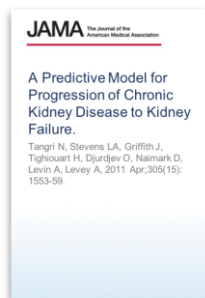
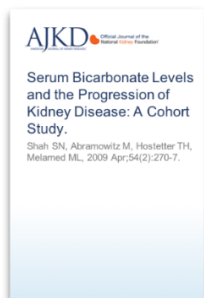
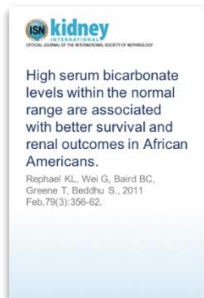
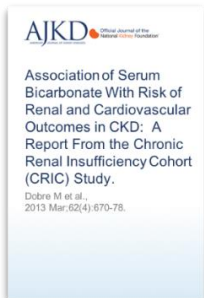
President  
Baylor Scott and White Health and Wellness Center

*Disclosure: Dr. Wesson is a consultant to Tricida, Inc.*

---

# Metabolic Acidosis is Both a Complication of CKD and an Underlying Cause of CKD Progression

# Studies Show Low Serum Bicarbonate Levels are Independent and Modifiable Risk Factor for CKD Progression



# Adaptive Response to an Accumulating Acid Load

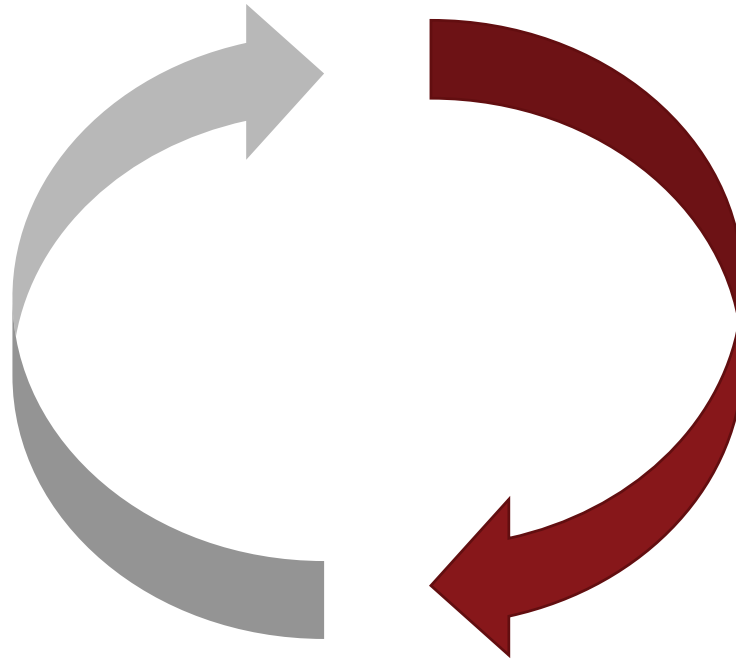
---

Acutely Increases  
Acid Excretion



# Adaptive Response to an Accumulating Acid Load

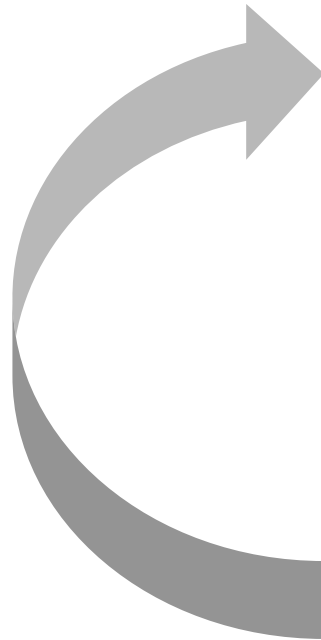
Acutely Increases  
Acid Excretion



Chronically Leads  
to Kidney Damage  
and Furthers CKD  
Progression

# Adaptive Response to an Accumulating Acid Load

Acutely Increases  
Acid Excretion



**Early Diagnosis and  
Treatment May  
Mitigate Chronic  
Deleterious Effects of  
Metabolic Acidosis**



# Sensors Monitor the Tubule Lumen and Coordinate Responses to Maintain Acid-Base Homeostasis

## Cellular and Membrane Sensors

sAC

Pyk2

GPR4

V-ATPase

ET<sub>B</sub> Receptor

ET-1 Receptor

ATA1 Receptor

ERK 1/2 Kinase

Erb 1/2 Receptor

**ACID**

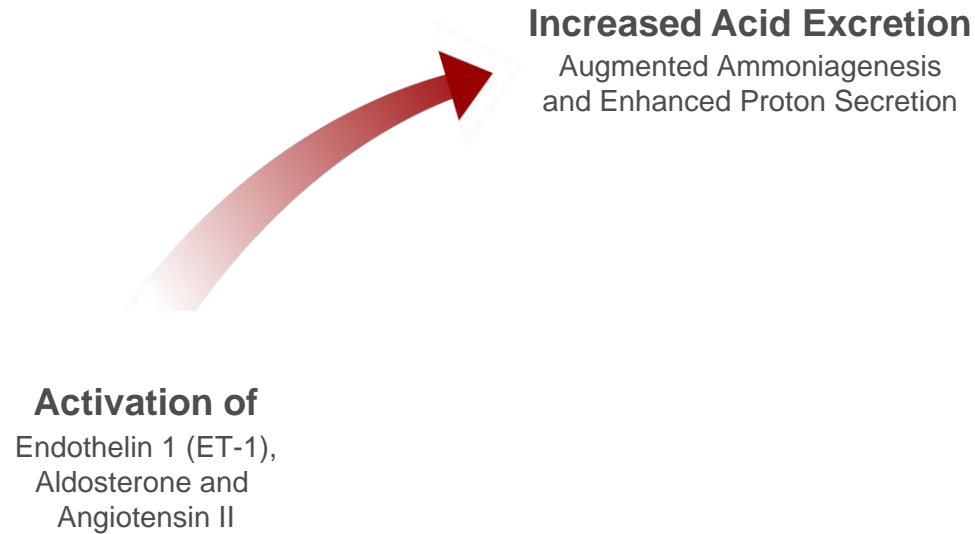
**BASE**

# Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria

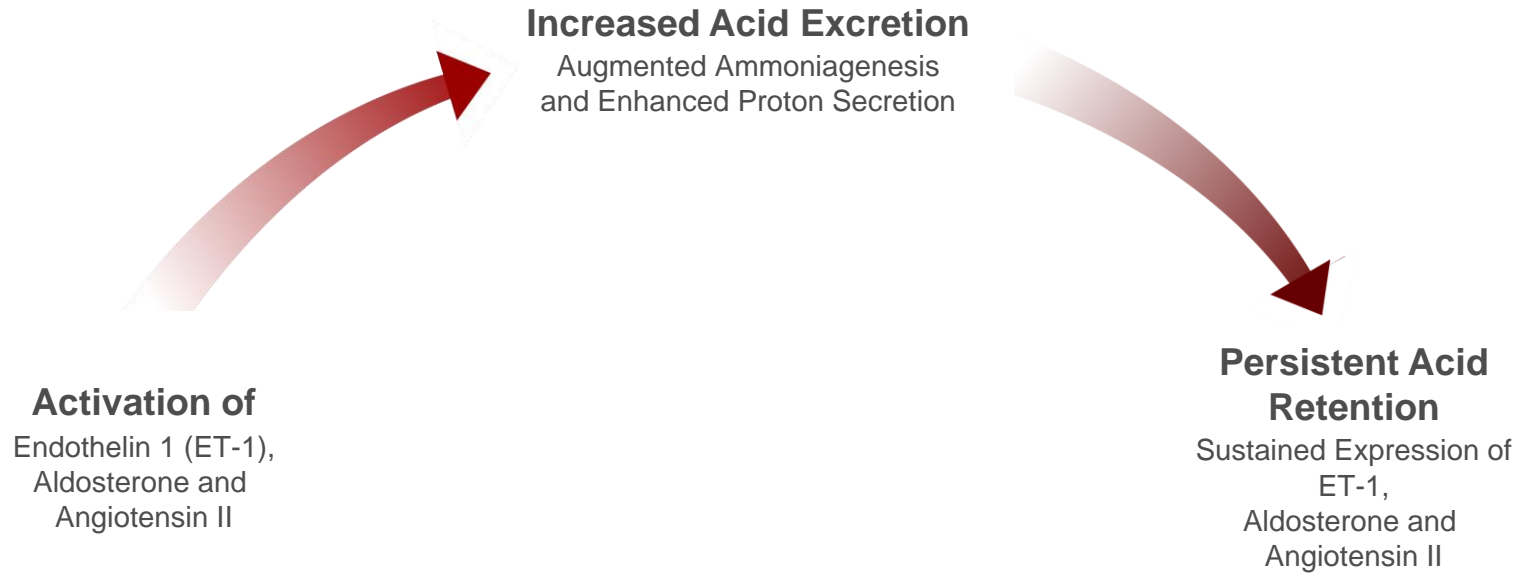
---

**Activation of**  
Endothelin 1 (ET-1),  
Aldosterone and  
Angiotensin II

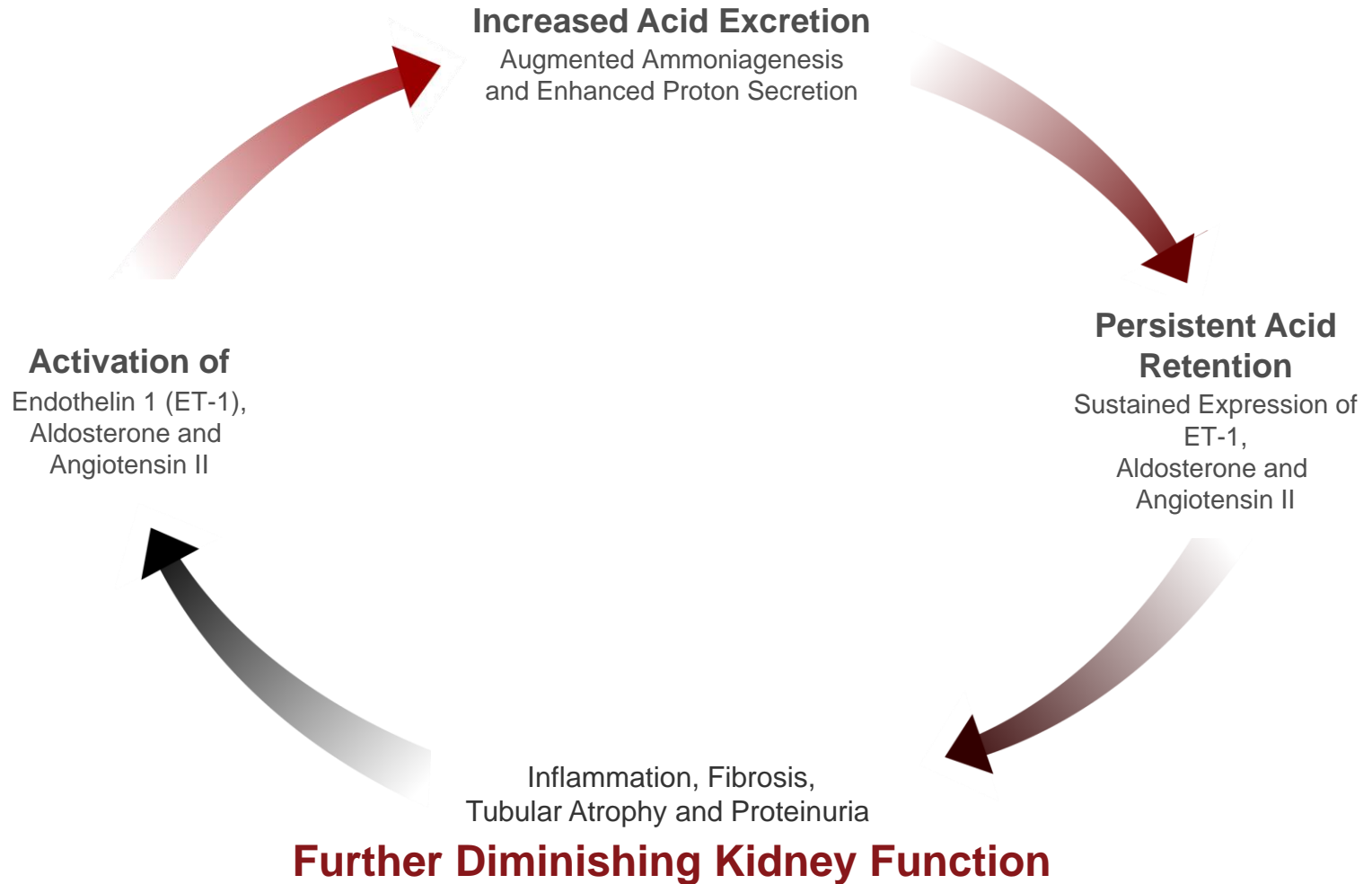
# Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria



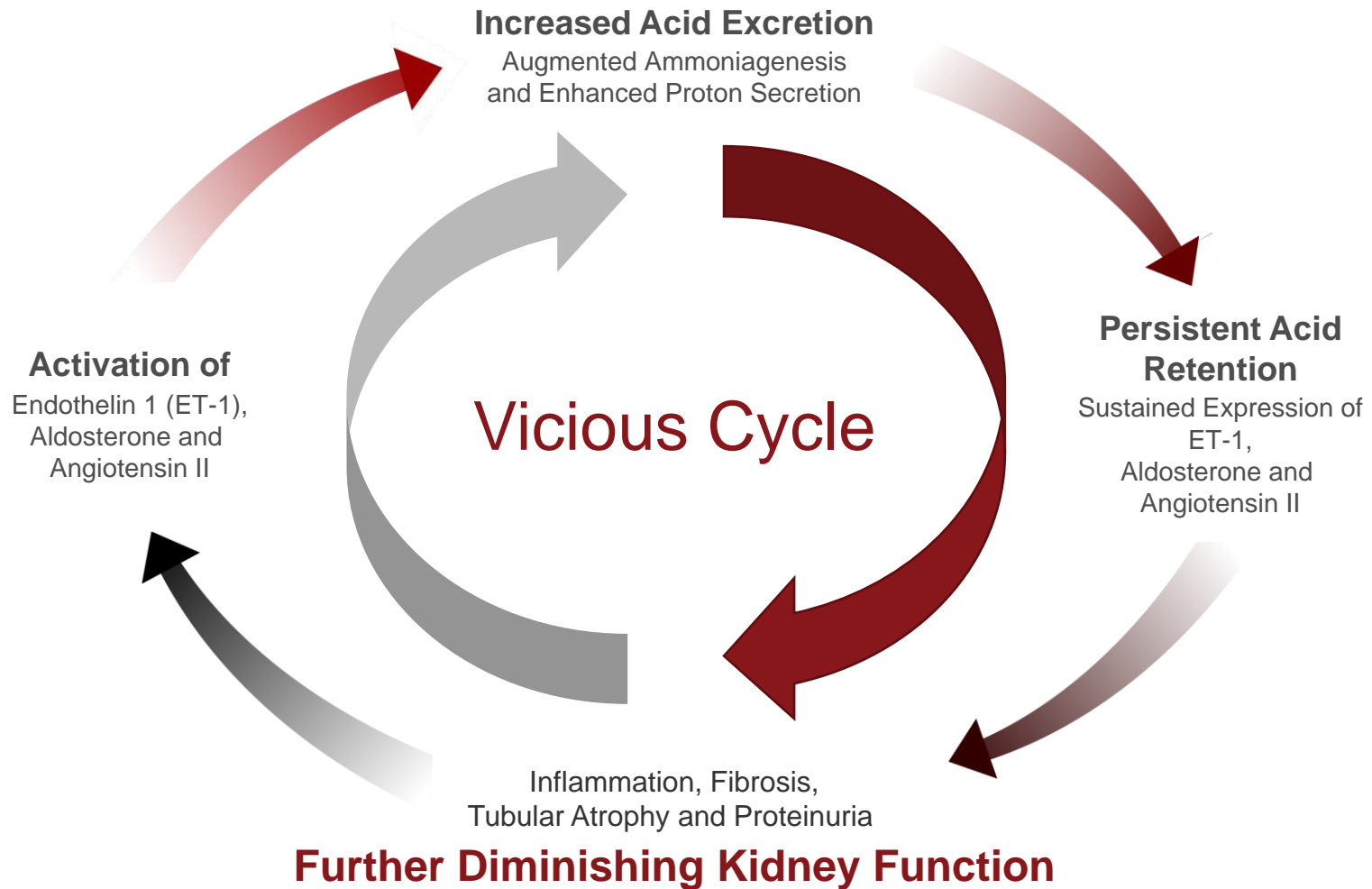
# Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria



# Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria



# Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria



---

A Positive Adaptive Response to Metabolic  
Acidosis can become Maladaptive and  
Promote CKD Progression,  
Underscoring the Need to Treat Metabolic  
Acidosis

---

# The End