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

Chronically Leads to Kidney Damage and Furthers CKD Progression
Adaptive Response to an Accumulating Acid Load

Acute: Increases Acid Excretion

Chronic: 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_B Receptor
- ET-1 Receptor
- ATA1 Receptor
- ERK 1/2 Kinase
- Erb 1/2 Receptor

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

Increased Acid Excretion
Augmented Ammoniagenesis and Enhanced Proton Secretion

Activation of
Endothelin 1 (ET-1), Aldosterone and Angiotensin II
Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria

**Increased Acid Excretion**
Augmented Ammoniagenesis and Enhanced Proton Secretion

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

**Persistent Acid Retention**
Sustained Expression of ET-1, Aldosterone and Angiotensin II
Chronic Response to Acidosis Promotes Inflammation, Fibrosis, Tubular Atrophy and Proteinuria

Increased Acid Excretion
Augmented Ammoniagenesis and Enhanced Proton Secretion

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

Inflammation, Fibrosis, Tubular Atrophy and Proteinuria

Further Diminishing Kidney Function

Persistent Acid Retention
Sustained Expression of ET-1, Aldosterone and Angiotensin II
Increased Acid Excretion
Augmented Ammoniagenesis and Enhanced Proton Secretion
Persistent Acid Retention
Sustained Expression of ET-1, Aldosterone and Angiotensin II

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

Inflammation, Fibrosis, Tubular Atrophy and Proteinuria
Further Diminishing Kidney Function

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