
Physiology of the Kidney 201

Nitric Oxide and Endothelin

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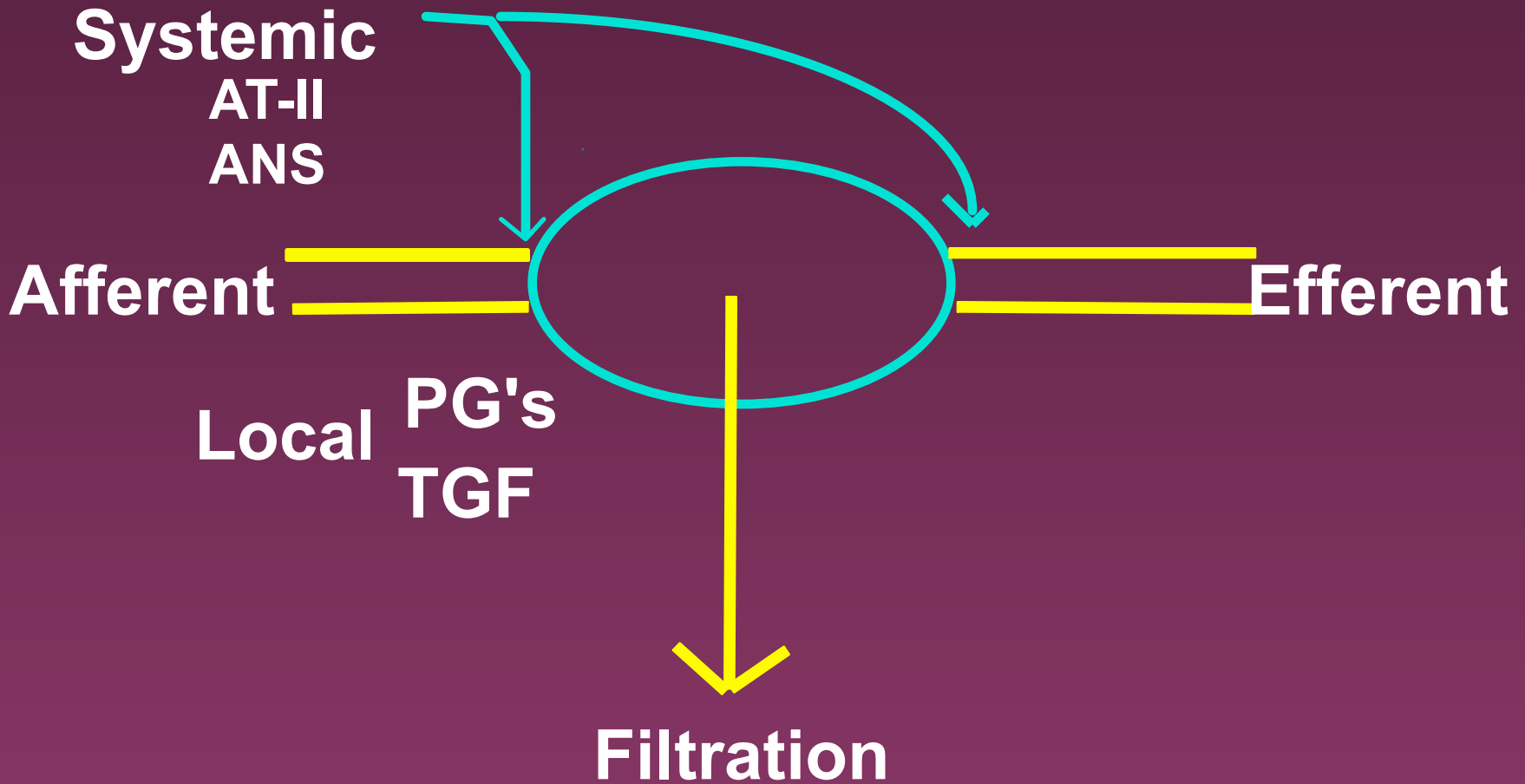
2019

Renal Physiology 201

- Overview of Physiology 101
- Nitric Oxide Physiology
- Endothelin Physiology
- Pathophysiology of the system
- Volume regulation - the big picture.

Glomerular Physiology

Blood flow determinants



Renal Physiology 201

- Explosion of Research in NO and ET
- In the last 4 years, over 3000 publications each.

Nitric Oxide

- Functions:
 - Regulate BP
 - Neurotransmitter
 - Suppress Pathogens
- Studies describe Pathophys. in:
 - Pregnancy/Pre-eclampsia
 - HTN
 - Hepatic Failure

Endothelin

- Function:
 - » Most potent vasoconstrictor
- Studies describe broad range of Pathophysiologic conditions.
 - » Hypertension
 - » Pulmonary Hypertension

Why is this Important?

- Inhibitors and Antagonists being developed which you will use soon
- You already use some:
 - » Nitroprusside
 - » Isordil/NTG
 - » Viagra
- Endothelin receptor antagonist
 - » Ambrisentan, Bosentan for Pulm Htn

Nitric Oxide - NO

- Uncharged molecule - can go anywhere
- Unpaired electron - highly reactive
- Chemical generation:
 - » Arginine + O₂-----> NO + Citrulline
NOS

Enzyme Production

- Nitric Oxide Synthase (NOS)

- » Two Types

- Constitutive

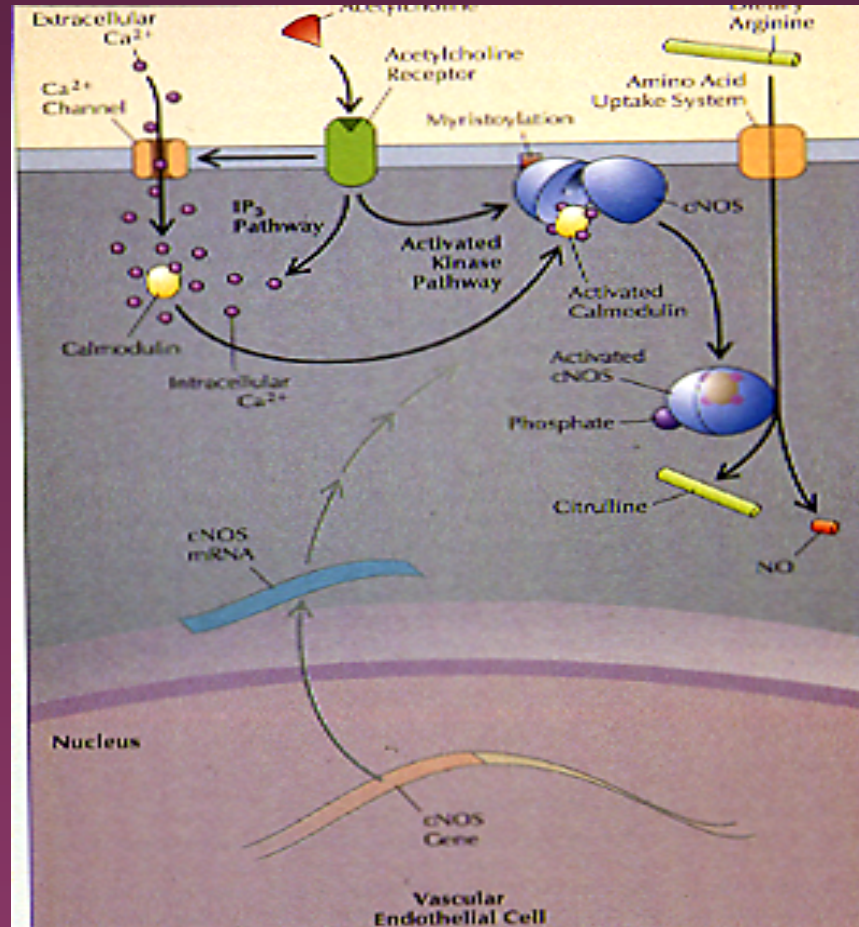
- vasodilator
- neurotransmitter

- Inducible

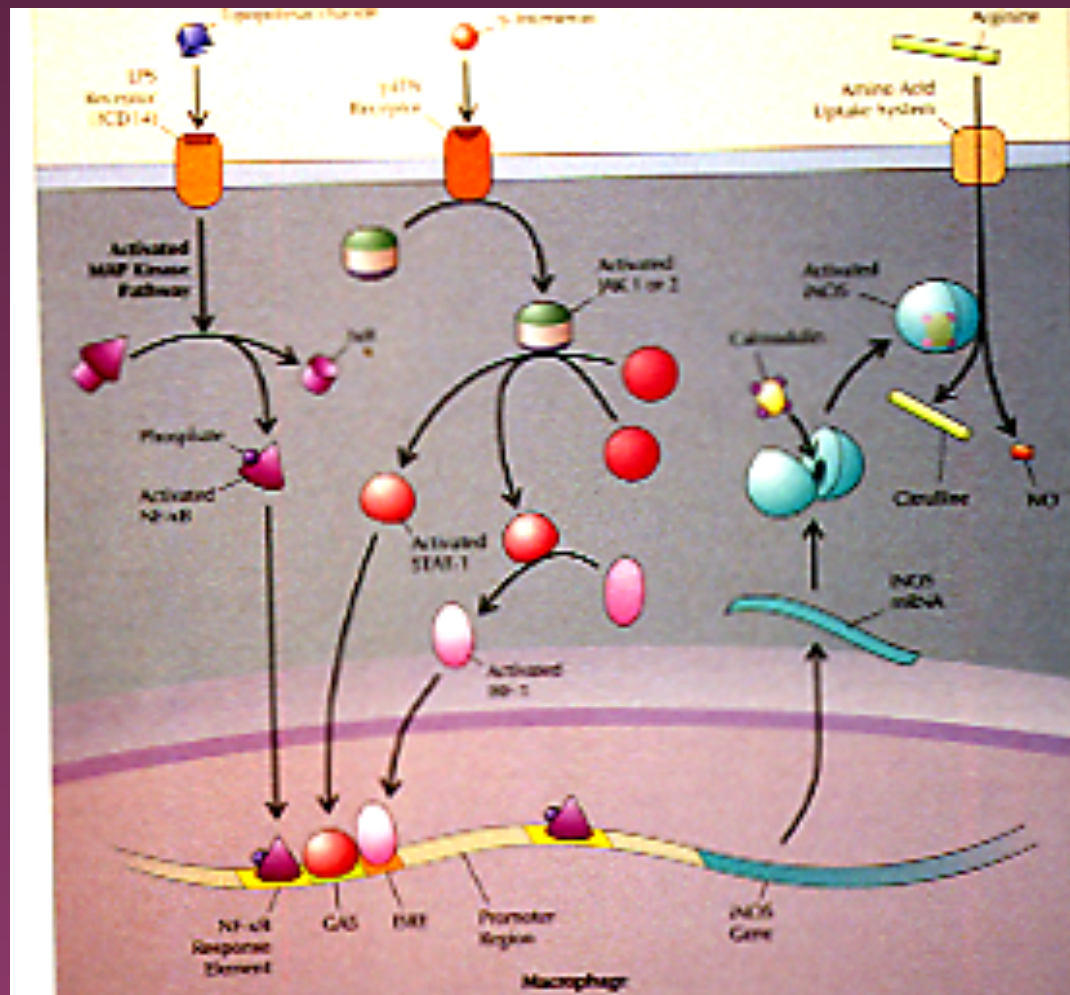
- Free radical scavenger
- Pathogen killer

NITRIC OXIDE

Constitutive



NITRIC OXIDE Inducible



Nitric Oxide

- Targets:

- » Vascular Smooth Muscle
- » Neurons
- » Pathogenic bacteria

- Effects:

- » Vasodilator
- » Feedback for ET-1
- » Neurotransmitter
- » Free Radical/Killer

NonVascular Functions of NO

- Modulates immune response
- reduces toxicity of oxygen radicals
- reduces adhesion of neutrophils, etc
- inhibits mast cell degranulation

Clinical Aspects of N.O.

- Cirrhosis

- » decreased BP, low SVR, angiogenesis
- » NOS inhibitors work, sort of.

- Pregnancy

- » reduced response to angiotensin
- » natural inhibitor found in pre-eclampsia

ENDOTHELIN

- Three Types
- Produced by endothelial cells, most renal cell types.
- Two receptor types, A and B

ENDOTHELIN

- Stimulators:
 - » Vasoconstrictors
 - » Thrombin
 - » Hypoxia
 - » Low shear stress
 - » Cytokines

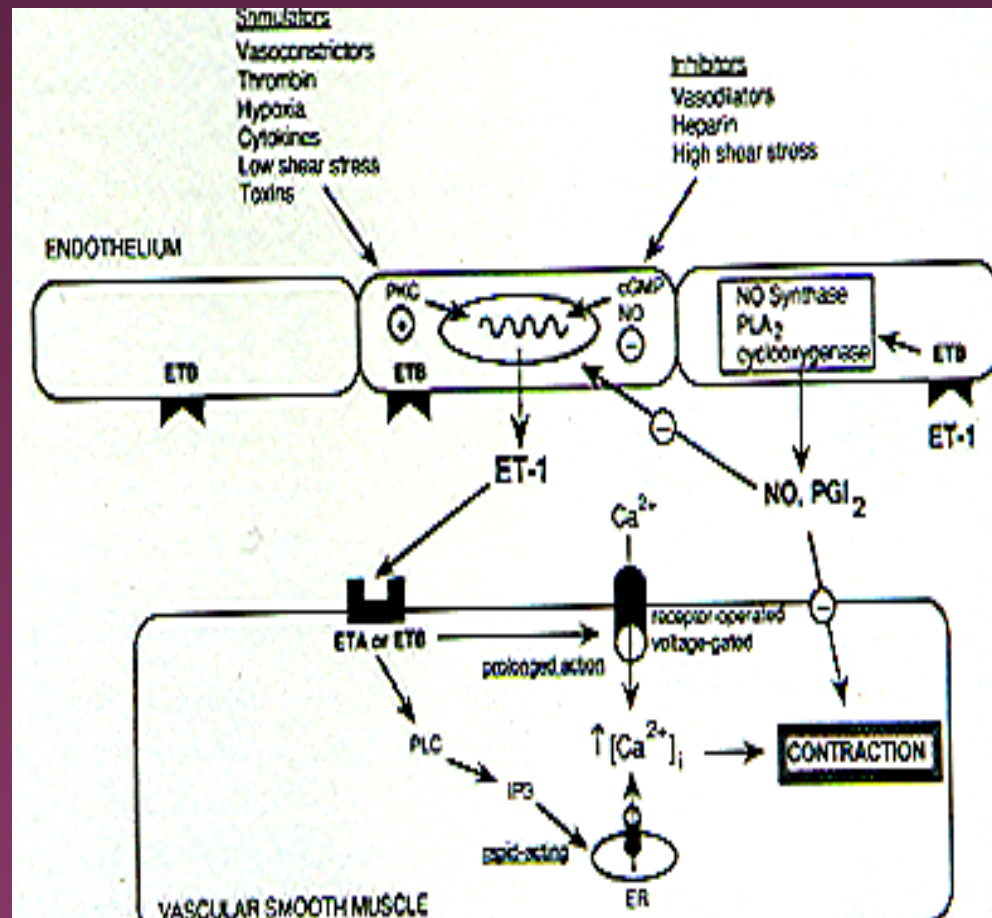
ENDOTHELIN

- Inhibitors of production
 - » Vasodilators
 - » Heparin
 - » High shear stress

ENDOTHELIN

- Feedback inhibition by Nitric Oxide, PGI₂
- Also inhibited by activation of ET-B receptor on the endothelial cell

ENDOTHELIN



ENDOTHELIN

Target

- Vascular Smooth M.
- Renal Tubules
- Mesangial cells

Effect

- Vasoconstriction
- Sodium excretion
- Proliferation, accumulation of Matrix, and contraction.

ENDOTHELIN

Clinical Aspects

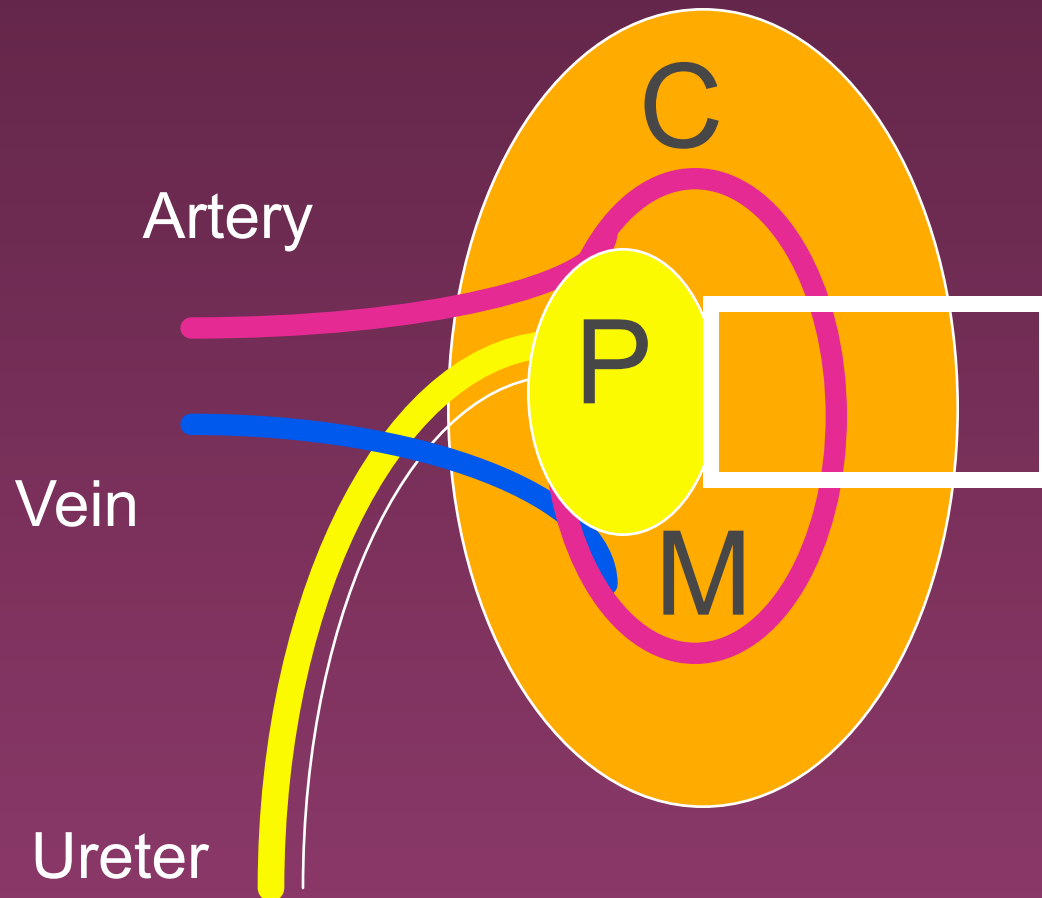
- ATN
- Contrast nephrotoxicity
- Cyclosporine nephrotoxicity
- Endotoxic shock
- Hypertension and Pulmonary Htn
- Chronic renal failure

WHY IS THE KIDNEY THE SMARTEST CORTEX IN THE BODY?

Volume regulation

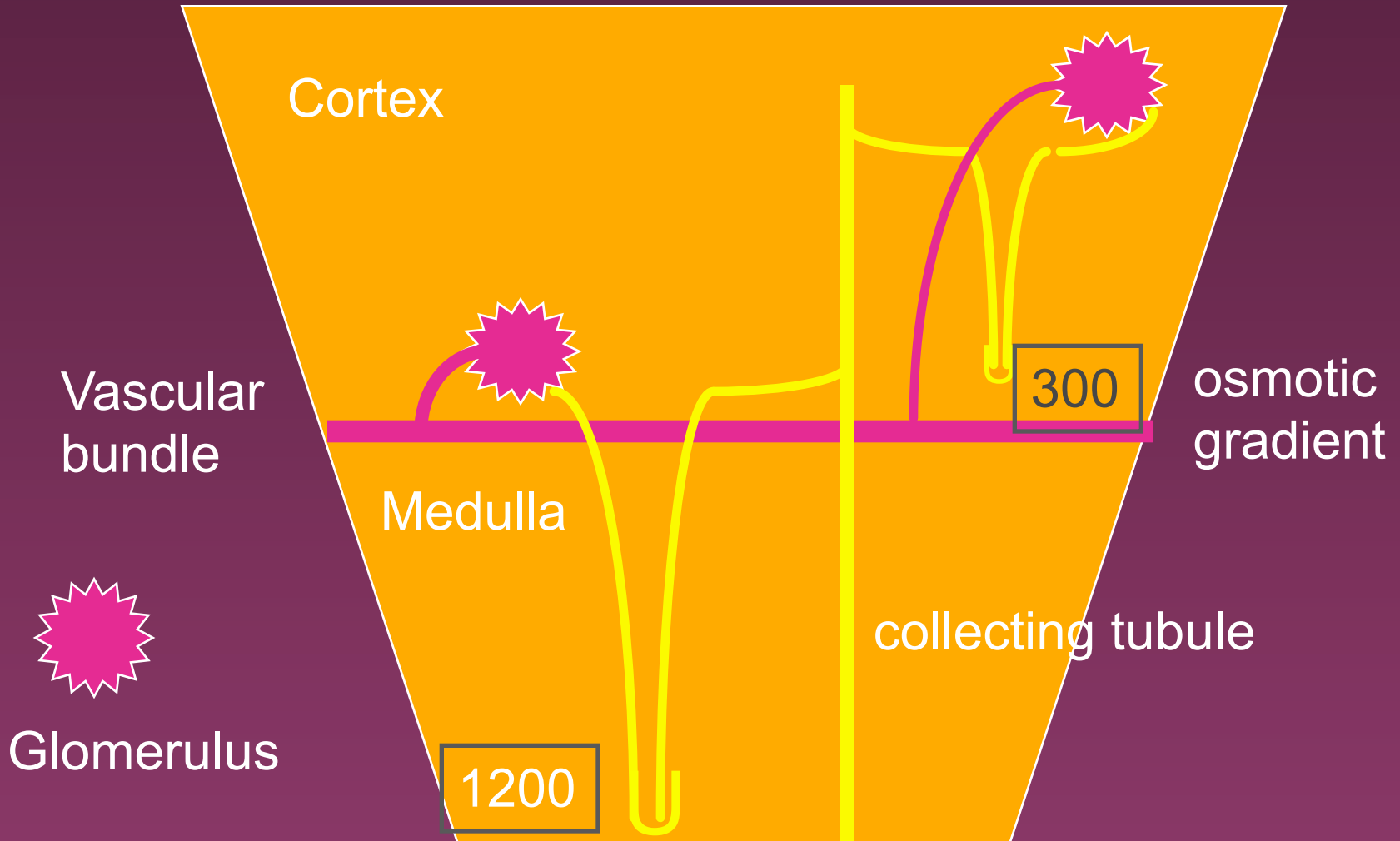
- Active Sensors
 - » Renal Autonomic nerves
- Passive system
 - » Like a system of lakes and spillways

Renal Structure



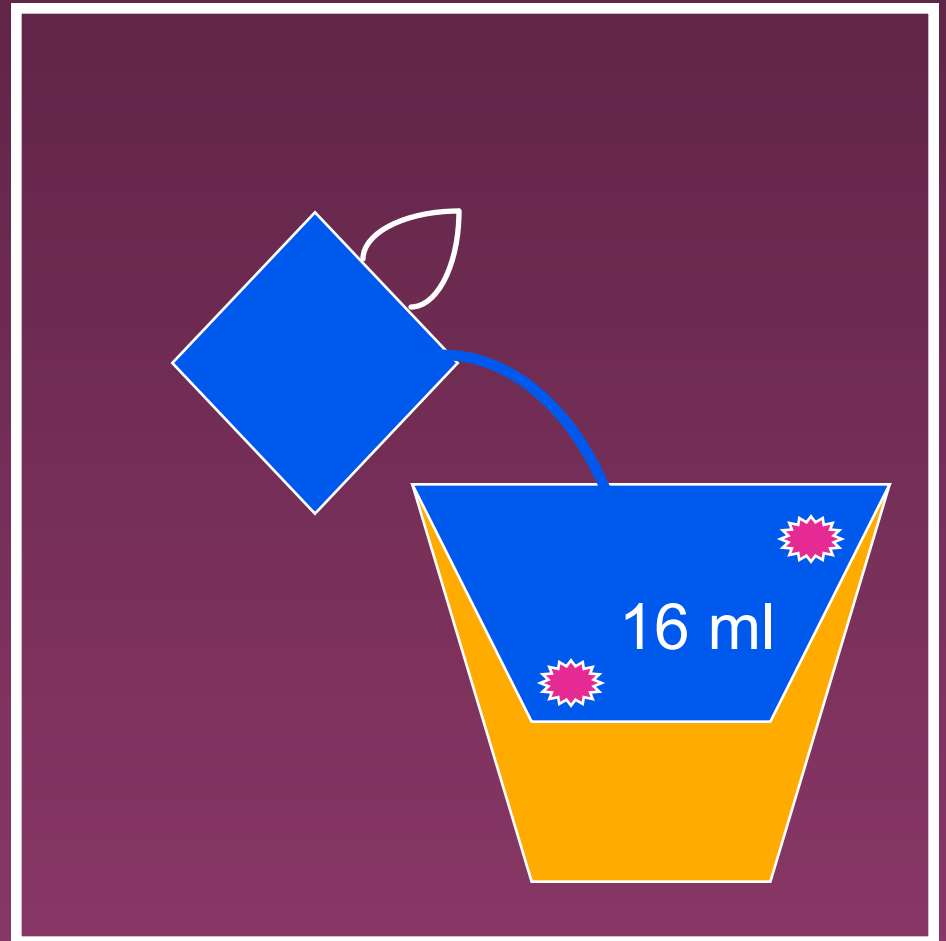
Renal Structure

Renal Structure



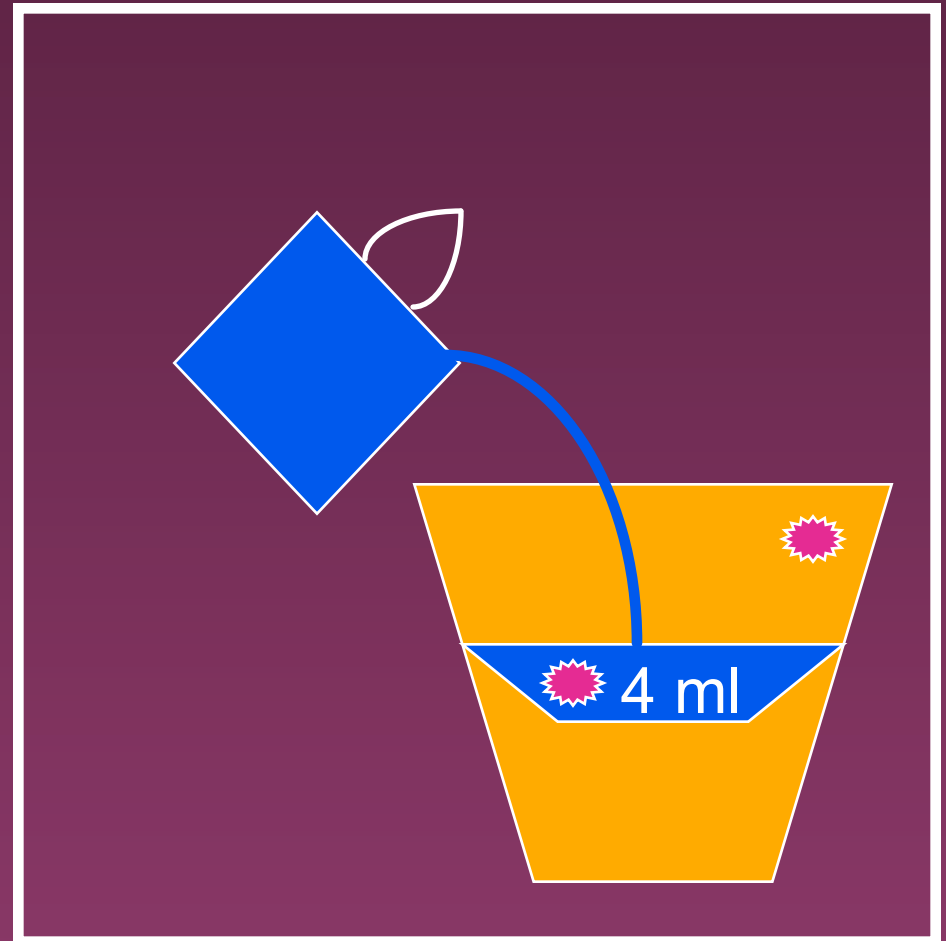
Pathologic States

- Hypertension



Pathologic States

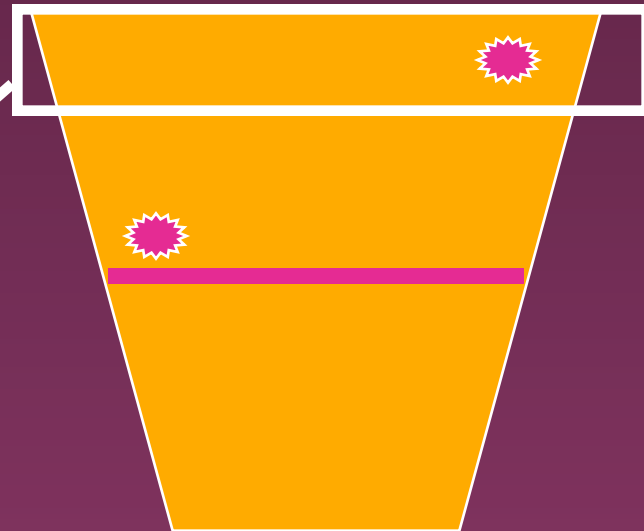
- CHF
- Renal Artery Stenosis



Pathologic States

- Glomerular senescence

Lower perfusion pressure
= low shear stress
--> stimulates ET



Glomerular Sclerosis

Summary

- Physiology and Pathophysiology of
 - » Nitric Oxide
 - » Endothelin
- Physiology and structural aspects of volume regulation

Summary

- Keep learning
- Be the patients advocate
- Be active in managing the system.