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Catecholamines

- Increased in states of effective circulating volume depletion
- Actions:
  - *Reduction in renal blood flow→preservation of coronary and cerebral perfusion*
  - *Increased Na+ reabsorption*
    - Stimulation of proximal and loop Na^+ transport
    - Alteration in peritubular hemodynamics due to increased arteriolar resistance
    - Activation of RAAS by β_1 receptor activation
  - *Increased Na^+ reabsorption counteracts affects of pressure naturiesis*

Dopamine

- Synthesized in the proximal tububle
- Actions:
  - *Low concentrations: renal vasodilation at afferent/efferent arterioles and interlobular arteries*
    - Increased renal blood flow with no change in GFR
  - *High concentrations: vasoconstriction*
  - *Reduced proximal Na^+ reabsorption*
    - Reduced Na^+ entry via the Na^+-H^+ exchanger by formation of cAMP
    - Reduction in the activity of the Na^+-K^+-ATPase pump

Kinins

- Formed in distal tubule/connecting segment
- Actions:
  - *Minimize renal ischemia by vasodilation*
  - *Decrease inner medullary Na^+ reabsorption*
  - *Impair ADH mediated local water reabsorption*

Erythropoietin

- Produced by fibroblasts in the deep cortex and outer medulla +/- superficial cortex
- Stimulated by reduced oxygen delivery:
  - Sensed by a special sort of heme protein
    - Oxyhemoglobin downregulates EPO gene transcription
    - Deoxyhemoglobin allows EPO gene transcription
  - *Actions: stimulate red blood cell production*

Endothelin

- Found in most kidney cell types
- Formed from Big ET by endothelin converting enzymes
- Bind to two different receptors: ETA and ETB
- Actions:
  - *Regulation of vascular resistance*
    - ETA is a strong vasoconstrictor
    - ETB appears to mediate vasodilation
    - Stimulated by prolonged decrease in renal blood flow
  - *Modulation of fluid and electrolyte transport*
    - Inhibition of tubular sodium and water reabsorption
    - Suppress Na-K-ATPase and Na-H antiporter
      - Via stimulation of prostaglandin E_2 production
    - Antagonize ADH/aldosterone in cortical collecting tubule
      - Via reduction in cAMP accumulation
    - Involved in long-term regulation of fluids/e-lytes
  - *Regulation of cell proliferation and extracellular matrix accumulation*
    - Increases:
      - Release of tissue inhibitor metalloproteinase
      - Release of cytokines stimulating matrix accumulation
      - Production of renal cell fibronectin and collagen

Nitric Oxide

- Basics
  - Nitric oxide synthase adds guanidine nitrogen to molecular oxygen→NO and water
    - Three isoforms of nitric oxide synthase:
      - Neuronal NOS (nNOS)
      - Endothelial NOS (eNOS)
      - Inducible NOS (iNOS)
    - eNOS and nNOS are constitutively active
    - iNOS induced by inflammatory cytokines
- Actions:
  - *Paracrine mediation of many signaling cascades*
    - Activation of guanylate cycline→synthesis of cGMP
    - Formation of S-nitrosothiols from thiol groups
    - Formation of peroxynitrite from superoxide radical
  - *[Physiologic] function as a tonic vasodilator*
    - [Supraphysiologic] result in toxicities
  - *Regulation of renal hemodynamics*
    - Maintains arteriolar dilation at the level of glomerulus and mesangial cell tone
    - Maintenance of systemic blood pressure
  - *Modulation of fluid and electrolyte transport*
    - Increases urinary sodium excretion
      - Inhibition of Na+ entry in cortical collecting duct, Na-H exchange in proximal tubule and Na-K-ATPase in many segments
    - Impairs response to ADH in collecting tubule→increased water excretion
    - nNOS in macula densa blunts tubuloglomerular feedback response
  - *Regulation of damage in response to injury*
    - Mediated by cytokines→iNOS activity in tubular epithelial cells and mesangium
    - Damage by:
      - Suppression of eNOS→vasoconstriction enhances injury
      - Formation of peroxynitrite from NO and superoxide radical

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1. Renal artery vasodilation is achieved by:
    a. Dopamine, low dose
    b. Nitric oxide
    c. Endothelin B
    d. Bradykinin

2. Renal artery vasoconstriction is achieved by:
    a. Catecholamines
    b. High concentration dopamine
    c. Endothelin A

3. Explain why, physiologically, the kidney is a sensible location for erythropoietin production
    a. Kidney is able to dissociate changes in blood flow from changes in oxygenation→Kidney oxygen utilization is predominantly for active transport of sodium, which when blood flow is reduced, there is a decrease in GFR and decrease in sodium reabsorption which means that the oxygen utilization is relatively static. This prevents an inappropriate EPO production

4. Dopamine was at one point considered as a therapeutic for oliguria/anuria due to
    a. Selective efferent arteriolar vasoconstriction→increased GFR
    b. Inhibition of sodium reabsorption at Na-H exchanger leading to a naturiesis
        i. Also inhibits Na-K-ATPase
        ii. Also causes arteriolar vasodilation (afferent, efferent and interlobular)
    c. Peripheral vasoconstriction leading to increased perfusion to the kidneys
    d. Production of prostaglandin E2 causing selective afferent arteriolar dilation and increasing GFR

5. Match each with each other: