Glomerular filtration II

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4.Glomerular capillary oncotic pressure (π_{GC})

- Opposing filtration
- GFR Inversely proportional to π_{gc}.
- Hyperproteinaemia, haemoconcentration

  π_{GC}. is raised - decrease in GFR
- Hypoproteinaemia and haemodilution,dehydration-

  π_{GC} is reduced - increased GFR

Factors That Can Decrease the Glomerular Filtration Rate (GFR)

Physical Determinants*	Physiologic/Pathophysiologic Causes
$\downarrow K_f \rightarrow \downarrow$ GFR	Renal disease, diabetes mellitus, hypertension
$\uparrow P_B \rightarrow \downarrow$ GFR	Urinary tract obstruction (e.g., kidney stones)
$\uparrow \pi_G \rightarrow \downarrow$ GFR	↓ Renal blood flow, increased plasma proteins
$\downarrow P_G \rightarrow \downarrow$ GFR	
$\downarrow A_P \rightarrow \downarrow P_G$	↓ Arterial pressure (has only small effect due to autoregulation)
$\downarrow R_E \rightarrow \downarrow P_G$	↓ Angiotensin II (drugs that block angiotensin II formation)
$\uparrow R_A \rightarrow \downarrow P_G$	↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

* Opposite changes in the determinants usually increase GFR.
K_f, glomerular filtration coefficient; P_B, Bowman's capsule hydrostatic pressure; π_G, glomerular capillary colloid osmotic pressure; P_G, glomerular capillary hydrostatic pressure; A_P, systemic arterial pressure; R_E, efferent arteriolar resistance; R_A, afferent arteriolar resistance.

5.Sympathetic stimulation

- Under normal circulatory conditions-
  Sympathetic tone is minimum.

- Mild-to-moderate stimulation –
  mild effects on RBF because of Autoregulation

- Strong acute stimulation –
  marked fall in RBF due to constriction of both afferent and efferent arterioles. (mainly by a1-adrenergic receptors)

6. State of glomerular membrane

- Size more than 8 nm = impermeable
- Albumin

7. Age

As age increased GFR decreased as CO/RPF decreases.

6.FACTORS AFFECTING GLOMERULAR FILTRATION RATE

1. Filtration coefficient (Kf).
2. Hydrostatic pressure in Bowman's space fluid (P_{BS})
3. Glomerular capillary hydrostatic pressure (P_{GC}).
4. Glomerular capillary oncotic pressure (Π_{GC}).
5. Sympathetic stimulation
6. State of glomerular membrane
7. Age

MEASUREMENT OF GLOMERULAR FILTRATION RATE

- Glomerular filtration rate can be measured by the renal clearance of **inulin, urea and creatinine.**

Renal clearance = volume of plasma i.e. cleared of substance in 1 min by excretion of substance in urine

$$C(mL/min) = UV/P,$$

where

C = Renal clearance of the substance,

U = Urine concentration of substance,

V = Rate of urine flow and

P = Plasma concentration of the substance

1. Inulin clearance test

- Not present naturally in the body.

- Inulin clearance (C in) = volume of plasma completely cleared of inulin per unit time

- Why inulin

1. It is freely filtered by glomeruli and neither reabsorbed nor secreted by tubules,
2. It is biologically inert and non-toxic,
3. It is neither metabolized nor stored in kidney,
4. Its concentration can be easily estimated in laboratory.

Method.

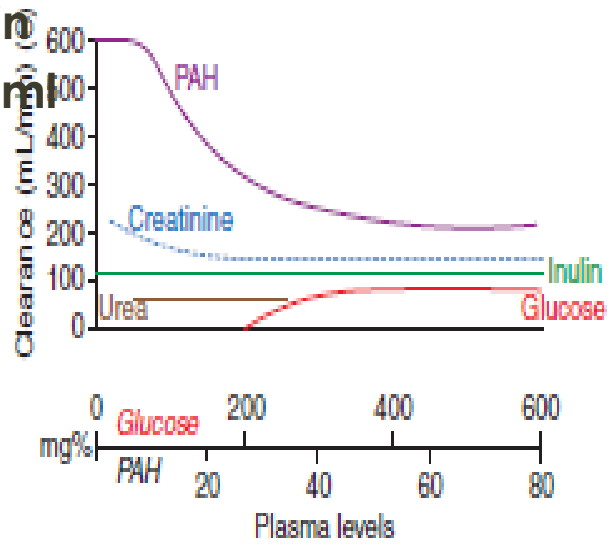
- Single bolus dose of inulin injected intravenously
- Then continuous intravenous infusion at rate which compensates for its loss in urine.
- This is important to achieve a constant level of plasma conc. of inulin.

$$C_{inulin}(\text{or GFR}) = \frac{U_{in}V}{P_{in}} = 35 \times \frac{0.9}{0.25} = 126\,\text{mL/min}$$

- Urine concentration of inulin (uin) = 35 mg/ml,
- Urine flow rate (V) = 0.9 ml/min
- Plasma concentration of inulin (pin) = 0.25 mg/ml

- Clinical applications :

comparison



1. C x = C in

- Substance characteristics equal to inulin
- Substance only filtered, not reabsorbed not secreted
- E.g. mannitol

2. C x < C in

- Clearance below than inulin
- Substance filtered and reabsorbed
- e.g. glucose

3.Cx > C in

- Clearance above than inulin
- Substance filtered and reabsorbed & secreted.
- e.g. PAH

2. Creatinine clearance test

- less accurate than inulin clearance
- In clinical practice preferred because in inulin method, it does not requires a continuous intravenous infusion.

Creatinine-

- Endogenous substance
- plasma value = 0.6–1.5 mg/dL.
- It is filtered by glomeruli and only marginally secreted by tubules.
- The value of creatinine clearance is close to GFR

Method

- Creatinine content of 24 h urine collection
- Midpoint of the urinary collection period are estimated.
- Plasma concentration in sample collected

$$C = \frac{UV}{P}$$

- Normal value = 80 -110 ml/min
- Declines with age in healthy individuals.(Because of decreased muscle mass)

- Creatinine clearance as kidney function test in disease.
- Fall in GFR may be the earliest clinical sign of renal disease

3. Urea clearance test

- Urea is end product of protein metabolism.
- Filtered by glomeruli, THEN it is partly reabsorbed by renal tubules.
- Urea clearance is less than GFR & it is influenced by protein content of diet = not as sensitive as creatinine clearance

METHOD

- Empty bladder by voiding- record time
- After 1 hr- void again
- Quantity of urine measured
- Urea measured

- Max urea clearance= UV/P
  - U=urea conc in urine
  - V=volume of urine excreated
  - P=urea conc. In plasma

  - Below 75% should take seriously
  - Below 50 % will be dangerous signal for kidney

MEASURMENT OF RBF

- Electromagnetic flowmeter
- PAH- Fick principle
- Filtration fraction

$$FF = GFR/RPF$$

RENIN ANGIOTENSIN SYSTEM

Angiotensinogen

↓ renin

Angiotensin I

↓ (lung/kidney/plasma)ACE

Angiotensin II – Efferent arteriole constrict, GFR/RBF increase

↓ lung

Angiotensin III

ANGIOTENSIN II

- Vasopressor effect , arteriolar constrictor, 4-5 times potent than NE, Increase systolic and diastolic BP
- Adrenal cortex- Aldosterone-increase reabsorption of Na
- Facilitate release of NE by direct action on post ganglionic sympathetic neuron
- Contraction of mesangial cell- Decrease GFR
- Increase Na- H exchange in PCT – Na reabsorption increase
- Increase water intake- increase BP, Increase ADH/ACTH Action

REGULATION OF GFR

1. Autoregulation
2. Nervous regulation
3. Hormonal regulation

1. AUTOREGULATION

a) CHANGING RENAL VASCULAR RESISTSTANCE

- The RBF & GFR remain constant over a wide range of renal arterial pressures (80–200 mm Hg)

Mechanisms Of Myogenic mechanism

- When renal arterial pressure is raised,

- Afferent arterioles are stretched,

- It contract and increase the vascular resistance.

- The increased vascular resistance which offsets the effect of increased arterial pressure

- Thereby maintains a constant RBF and GFR

- Low perfusion pressure
- Angiotensin II involved
- Constriction of efferent arteriole
- So GFR will increase

So ACE inhibitor use long term lead to Renal failure

High protein diet –

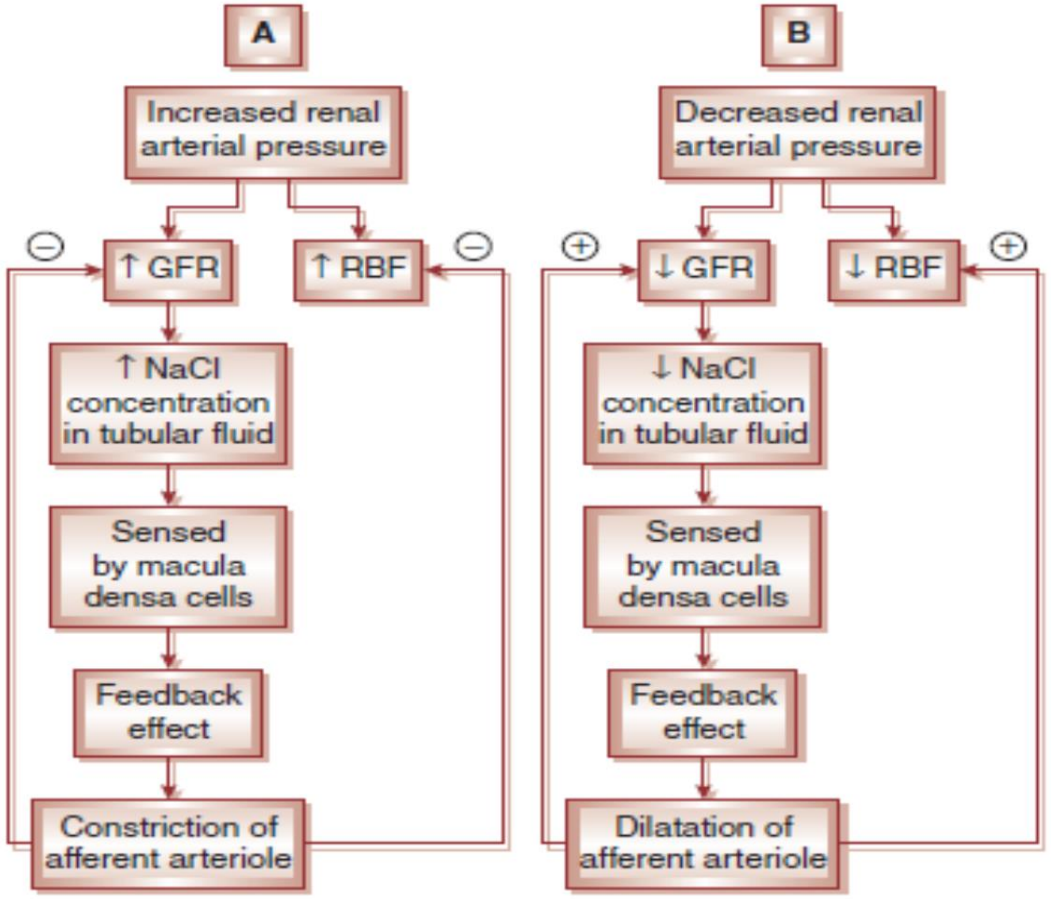
- Increase A.A
- Increase A.A. reabsorption
- Increase Na reabsorption
- Macula densa sensitize it
- Tubuloglomerular feedback mechanism
- Decrease afferent arteriole resistance
- Increase GFR

BSL increase

- Na glucose symport
- Increase glucose reabsorption in tubule
- Increase Na reabsorption
- macula densa sensitize it
- glomerular feedback mechanism
- Decrease afferent arteriole resistance
- Increase GFR

b) Tubuloglomerular feedback mechanisam

- Arterial pressure increase
- Increase P GC
- Increase GFR
- Increase reabsorption of NaCl



- Sensed by macula densa cells

1. **Feedback effect constriction of afferent arteriole-** decrease GFR & RBF

2. **increase renin secretion** – increase angiotensin II- increase efferent arteriolar resistance- Decrease GFR

3. **Increase Na K ATPase activity-** increase ATP hydrolysis- increase adenosine formation- increase Ca via adenosine A1 receptor- constriction of afferent arteriole- decrease GFR & RBF

c) Intrarenal reflex

- Intrarenal neurogenic components and smooth muscle
- Inhibited by KCN/papaverin/procain

d) Cell sepration theory/ viscocity theory

2.NERVOUS REGULATION

- T4 –L2

* Under normal circulatory conditions, sympathetic tone is minimum.

* Mild-to-moderate stimulation of sympathetic nerves usually has mild effects on RBF because of autoregulation mechanism.

* Strong acute stimulation of sympathetic nerves may produce marked fall in RBF (even to 10–30% of normal) temporarily due to constriction of both afferent and efferent arterioles.

* Mainly by α1-adrenergic receptors and to a lesser extent by post-synaptic α2-adrenergic receptors.

3.HORMONAL REGULATION

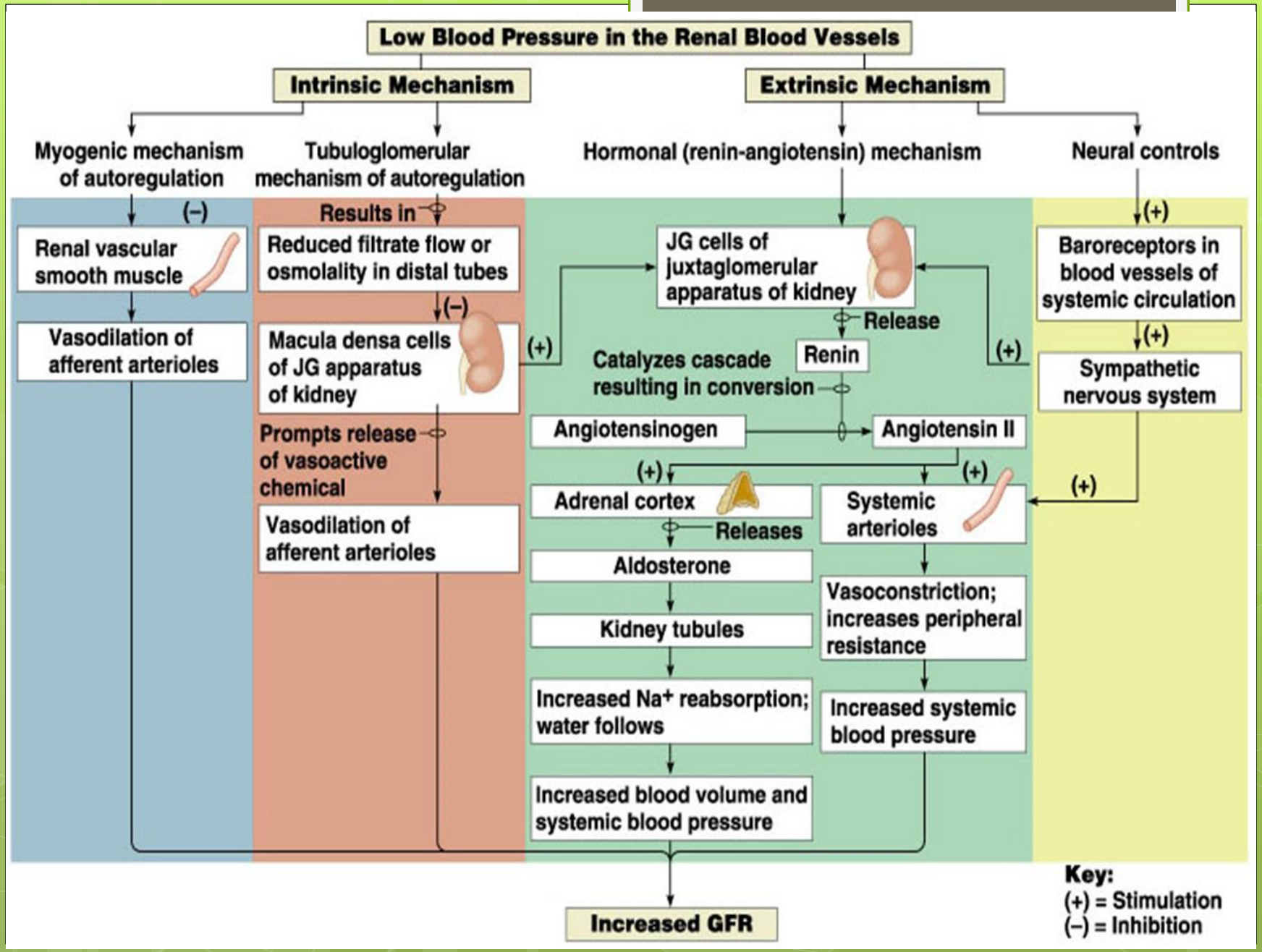
1. Hormones that cause vasoconstriction of afferent and efferent arteriole, and thereby decrease RBF and GFR include:

* Norepinephrine, Angiotensin II, Endothelin- Hemostasis

2. Hormones that cause vasodilatation and thereby increase RBF & GFR include:

* Prostaglandins, Nitric oxide (NO),Bradykinin, Atrial natriuretic peptide (ANP),Glucocorticoids, Dopamine ,Histamine, Ach

* High protein diet – Increase P_{GC} - Increase RBF


Low Blood Pressure in the Renal Blood Vessels
Intrinsic Mechanism
Extrinsic Mechanism
Myogenic mechanism of autoregulation
Tubuloglomerular mechanism of autoregulation
Hormonal (renin-angiotensin) mechanism
Neural controls
(–)
Renal vascular smooth muscle
Vasodilation of afferent arterioles
Results in
Reduced filtrate flow or osmolality in distal tubes
(–)
Macula densa cells of JG apparatus of kidney
Prompts release of vasoactive chemical
Vasodilation of afferent arterioles
(+)
JG cells of juxtaglomerular apparatus of kidney
Release
Renin
Catalyzes cascade resulting in conversion
Angiotensinogen
Angiotensin II
(+)
(+)
Adrenal cortex
Releases
Aldosterone
Kidney tubules
Increased Na+ reabsorption; water follows
Increased blood volume and systemic blood pressure
(+)
(+)
Systemic arterioles
Vasoconstriction; increases peripheral resistance
Increased systemic blood pressure
(+)
Baroreceptors in blood vessels of systemic circulation
(+)
Sympathetic nervous system
Increased GFR
Key:
(+) = Stimulation
(–) = Inhibition

GFR

1. Definition
2. Normal value
3. Variation
4. Calculation (different pressures acting on glomerular membrane)
5. Factors affecting GFR
6. Regulation of GFR
7. Measurement of GFR
8. Renin angiotensin system

QUESTIONS

LONG QUESTION

1. GFR
2. RENIN ANGIOTENSIN SYSTEM

SHORT NOTE

1. DYNAMICS OF GFR
2. FILTRATION FRACTION
3. ANGIOTENSIN II
4. FACTORS AFFECTING GLOMERULAR FILTRATION RATE
5. REGULATION OF GFR
6. RENAL CLEARANCE TEST
7. MEASUREMENT OF GFR