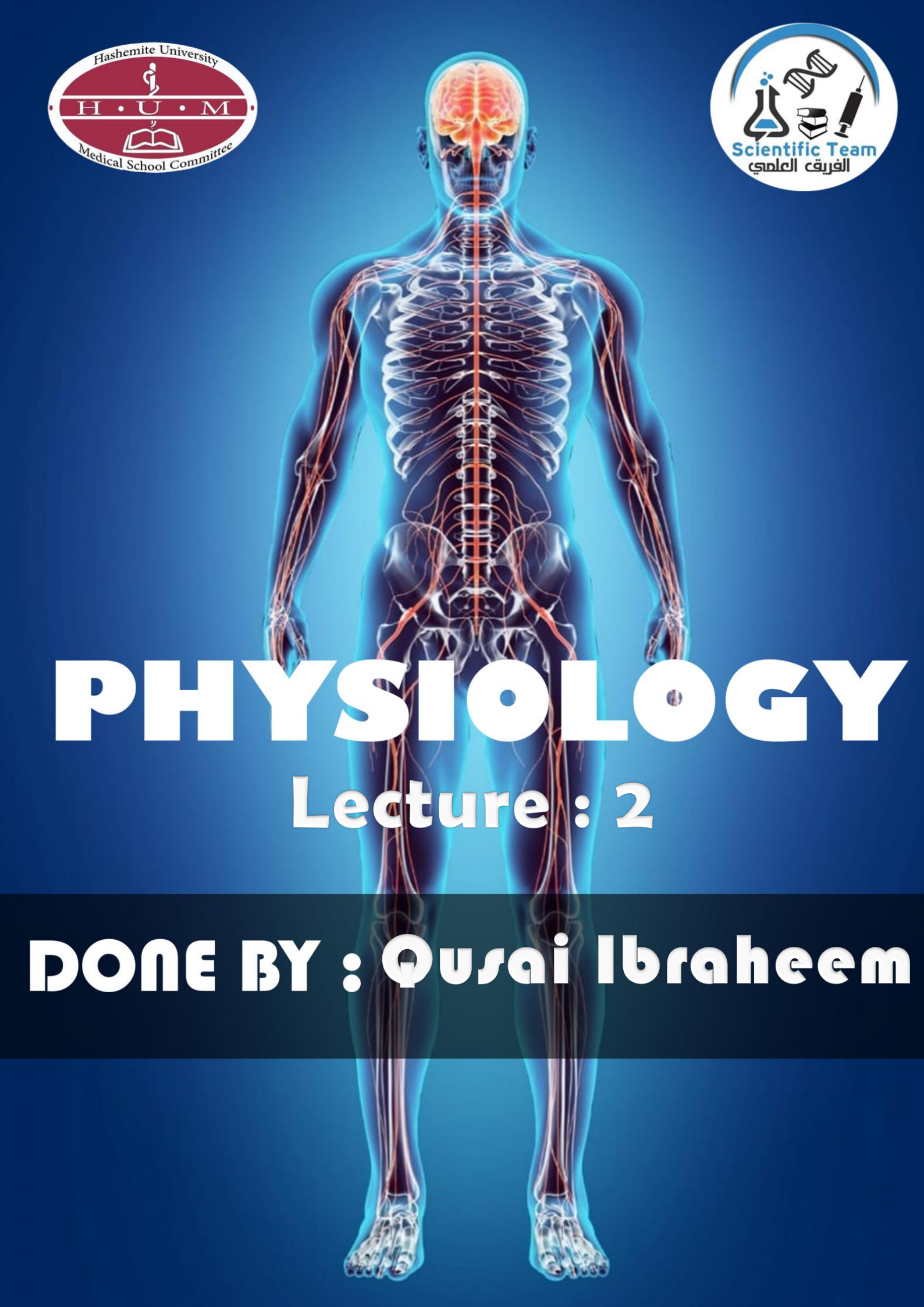


PHYSIOLOGY

Lecture : 2

DONE BY : Qusai Ibraheem

Glomerular Filtration, Renal Blood Flow, and Their Control

urine formation start with filtration of large amount of fluid through capillary to bowman capsule

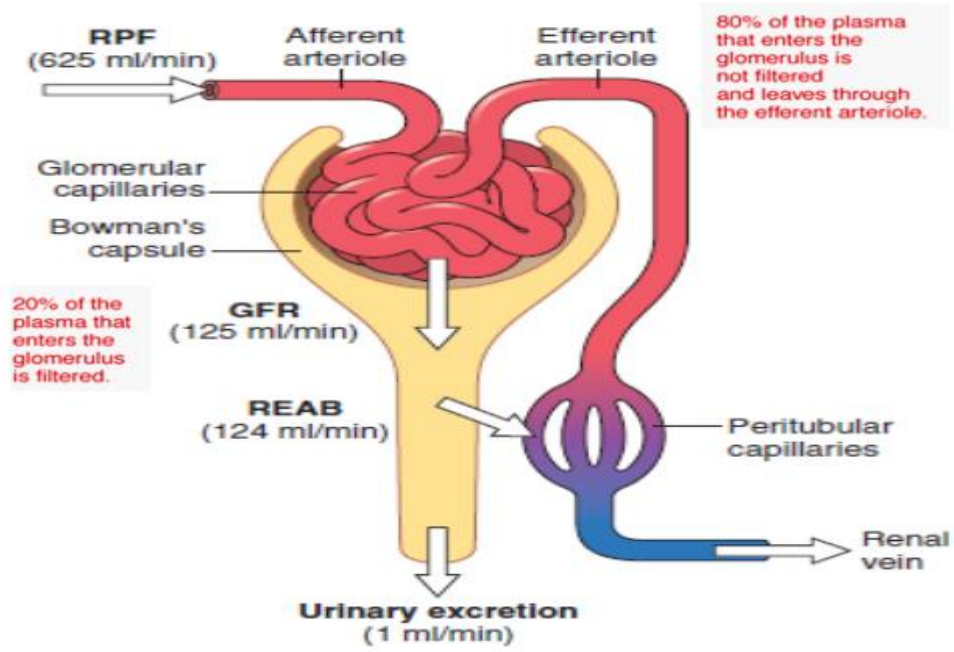
Importance of Glomerular Filtration: Remove waste products and the Waste products are poorly reabsorbed by the tubules so get rid in the urine

plasma volume= 3 L, GFR is about 180 L/day → entire plasma can be filtered and processed about 60 times/day. This high GFR allows the kidneys to precisely and rapidly control the volume and composition of the body fluids.

هسا احنا حكينا المحاضرة الماضية انو الcardiac output تقريبا5000ml\min منها الplasma تقريبا
3000ml(3L) والباقي هوcell زيRBC,WBC, platelet تقريبا2000 ml\min وحكينا انو النسبة الي بتروح للkidney تقريبا22% يعنب تقريبا الplasma تساوي 625ml\min والcell تقريبا475ml\min هسا الي بصيرلو filtration هو الplasma تقريبا الي بصيرلوfiltration هو 20% يعني تقريبا 125ml\min ول حولناها لday بطلع 8000L\day ومعلومة ثانية بما انو20% من الplasma بس filter ف80% ما بصيرلها filter

هسا ال kidney عندها القدرة على الfiltration 60 مرة باليوم وهاض بخلي الkidney------ rapidly control the volume and composition of the body fluid

• Glomerular filtrate composition is about the same concentration in plasma, except for large proteins , blood cells, Ca & FA because bound to protein so decrease in filtrate



معلومة من الرسمة هسا احنا حكينا انو 125ml\minبصيرلهاfiltration بس كم الي بنزل للurine بس1ml\min و124ml\min بصيرلوreabsorption

Glomerular capillary filtration barrier

The glomeruli capillary filtration barrier contain tree layer: the endothelium of capillary, the basement membrane and the epithelial layer called podocyte

Fenestrated endothelium

-endothelium are richly negative charge that prevent the filtration of protein

- pores exclude blood cells and large plasma proteins (-ve charges)

Basement membrane

contain collagen and Proteoglycan gel

large amount of water and small solute can filter and prevent filtration of plasma protein because of negative charge association with proteoglycan

Podocytes not continuous foot like processes (-ve charges) the foot process separate by Slit diaphragm pores through which glomeruli filtration pass and have also negative charge give more restriction to filtration of plasma protein

Filterability of Solutes Across Glomerular Barrier depend on:

• Molecular size (inverse relationship): if the increase size, the rate of filtration to these solute is less

• Electrical charge (-ve charged large molecules are filtered less easily than +ve charged molecules of equal molecular size due to electrostatic repulsion, any defect→ proteinuria/albuminuria

Albumin have the ability to pass the glomerular membrane because there size less than pore but because the negative charge and the electrostatic repulsion not filter

In the certain kidney disease ,the negative charges in basement membrane are lost so some low protein molecule like albumin is filter → proteinuria/albuminuria

• Shape (rigid or deformable)

Filterability of Solutes Across Glomerular Barrier

Filterability of 1.0 means= substance is filtered as freely as water; [plasma] =[Bowman's capsule]

Filterability of 0.75 =substance is filtered only 75% as rapidly as water

Table 27-1 Filterability of Substances by Glomerular Capillaries Based on Molecular Weight

Substance	Molecular Weight	Filterability
Water	18	1.0
Sodium	23	1.0
Glucose	180	1.0
Inulin	5500	1.0
Myoglobin	17,000	0.75
Albumin	69,000	0.005

هسا من الجدول بنشوف انو الelectrolyte زي الNa وكمان الglucose الfilterability تساوي الwater لذلك هو filter freely

هسا في كمان الinulin الfilterability مثل الwater وهاي المادة مابصيرلها فبتستعمل لحساب ال glomeruli filtration rateوراح تنشرح بالمحاضرات الجاي

هسا الmyoglobin الfilterability هي0.75 يعني نسبة 75% من الwater filtration

اما الalbumin الfilter value is very low so not

Determinants of Glomerular Filtration Rate

هسا الglomerular filtration rate(GFR) معنا بعتمد على عاملين هم:

1-net filtration pressure(NFP) 2-the glomerular capillary coefficient(Kf)

وهذول العاملين بتناسبو طرديا مع الGFR فلو حطيناهم بمعادلة

GFR=NFP*Kf

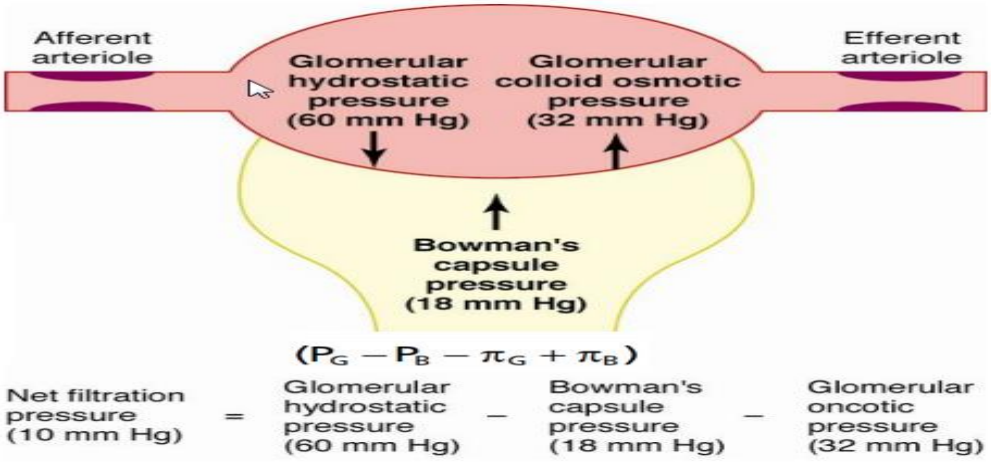
هسا نبلش نحكي عن اول عامل وهو الNFT هسا هاض بعتمد على عاملين وهم:

1-force favor filtration :which promote filtration 2-force oppose filtration

هسا الforce favor filtration بتصمن الcapillary hydrostatic pressure(PG) وهي تقريبا بتساوي 60mmHgوال colloid oncotic pressure of the protein in bowman capsule ولانو مافي protein فمقداره يساوي صفر filtration

اما الforce oppose filtration وهي القوة الي بتمنع الfiltration الي هم ال colloid osmotic pressure in of the glomeruliالي هي تقريبا بتساوي 32mmHg والhydrostatic in bowman capsule الي هي تقريبا18mmHg

هسا لو حمعنا هاي القوى بتطلع معنا الnet filtration rate =10mmHg



هسا نيجي على العامل الثاني الي هو(Kf)the glomerular capillary coefficient هسا الKf بعتمد على عاملين هم الpermeability of glomerular membrane another name called hydraulic conductivity والعامل الثاني هو الsurface area of glomeruli capillary

هسا نيجي نحسب الKf هسا احنا حكينا قبل انو الGFR هو 22% من الplasma والي هي تقريبا 125ml\min وكمان حسبنا الNFR والي هو 10mmHg

هسا احنا طلعنا معادلة قبل هي: GFR=NFR*Kf لو عدلنا على المعادلة بتصير:Kf=GFR\NFR

Kf=125\10=12.5ml\min\\mmHg

These value Very high compared to other body capillaries Kf (0.01) so rapid rate of fluid filtration

هسا احنا حكسن قبل انوKf يتناسب طرديا مع GFR وبالتالي

↑ Kf→↑GFR

↓Kf →↓GFR

Changes in Kf probably do not provide a primary mechanism for normal day to-day regulation of GFR so the regulation of GFR depend on mainly on hydrostatic pressure in glomeruli capillary
but some disease cause lower Kf by reducing number of glomeruli capillary so reduce surface area or increase thickness of the glomeruli capillary membrane so reduce premeability

Like: -chronic hypertension, obesity/diabetes mellitus which increase the thickness of the glomeruli capillary membrane so reduce premeability

-glomerulonephritis which decease surface area

معلومة:الfiltration fraction هي النسبة منrenal plasma flow الي بصيرلهاfiltration وحكينا انها 20%=0.2
هسا هاي حسيناها من المعادلة الاتية :FF=GFR\Renal plasma Flow=125\625=0.2

هسا خلينا نحكي عن العوامل الي بتاثثر على الhydrostatic pressure in bowman capsule

Increase the hydrostatic pressure in bowman capsule reduce GFR but decrease the hydrostatic pressure in bowman capsule increase GFR

Normally hydrostatic pressure in bowman capsule changes as a function of GFR, not a physiological regulator of GFR

But it is change in pathological state such as Tubular Obstruction like in kidney stones, tubular necrosis or Urinary tract obstruction like in Prostate hypertrophy/cancer

Which lead to increase the hydrostatic pressure in bowman capsule so lead to decrease HFR

In some state reduce the pressure of the hydrostatic pressure in bowman capsule like hydronephrosis (dilation of the renal pelvic)

هسا العوامل الي بتاثر على الcapillary colloid osmotic pressure

As blood passes from the efferent arteriole through the glomeruli capillary to efferent arterioles ,the plasma protein concentration increase about 20% because the net filtration of fluid into bowman capsule and plasma protein not filter so the concentration of plasma protein increase

So the normal colloid osmotic pressure enter capillary is 28 mmHg then increase to 36mmHg when reach efferent arteriole

So there two factor influence on glomeruli capillary colloid osmotic pressure :

1-artrial plasma colloid osmotic pressure

2- the filter fraction of plasma that filter by glomeruli capillary

Increasing the arterial plasma colloid osmotic pressure lead to rise in glomeruli capillary colloid osmotic pressure lead to decrease GFR

Also increase the filtration fraction lead to increase protein concentration and rise colloid osmotic pressure

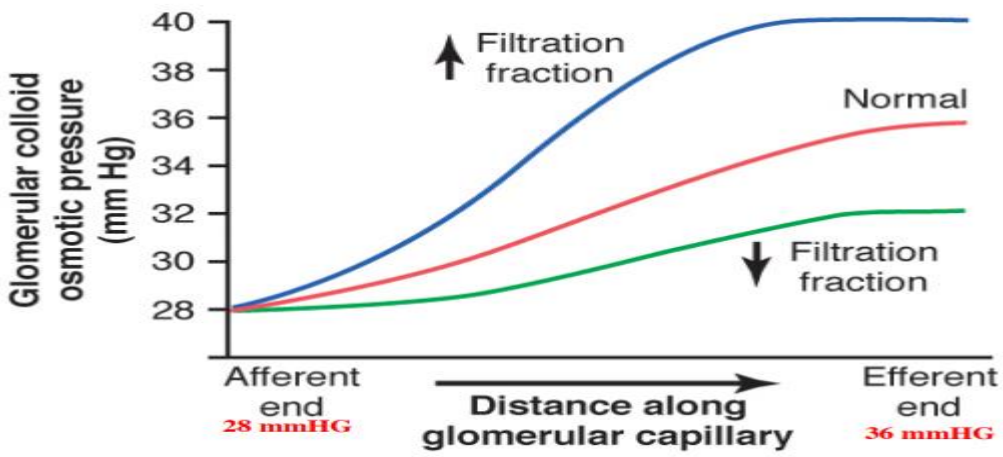
Filtration fraction depend on GFR if increase GFR increase filtration fraction

And depend on renal plasma blood flow if decrease renal plasma blood flow but the GFR is constant the filtration fraction increase so high increase in colloid osmotic pressure

لو اجينا شرحناها بالارقام هسا الrenal plasma flow حكينا انو 625ml\min هسا لو فرضنا انها قلت ل500 وحافظنا على الGFR الي هو125 النسبة بينهم راح تزيد

With increase renal blood flow, lower fraction of the plasma fraction of plasma filter so slower rise of colloid osmotic pressure

هسا اكيد ال renal blood flow بتاثر على الGFR في حال كان ال hydrostatic pressure ثابت بس في حال قل الrenal blood flow بصير regulation للGFR انو يضل ثابت بانو يزيد الhydrostatic pressure وراح نيجي للmechanism لقدام



The factor influence on glomeruli hydrostatic capillary pressure

↑ PG → ↑ GFR

Changes in PG serve as the means **for physiological regulation of GFR**

Factors affecting Glomerular Capillary

hydrostatic Pressure (PG) :

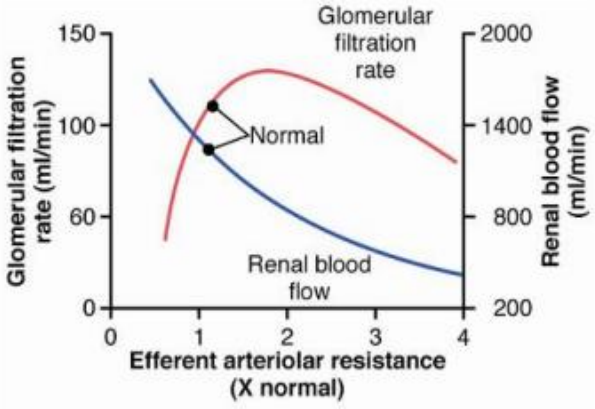
1-increase in Arterial pressure lead to increase GRF but this buffered by autoregulation (constant PG)

2- increase Afferent arteriolar resistance lead to reduce capillary hydrostatic pressure and decrease GFR and decrease renal plasma flow so filtration fraction is constant but if dilatation increase both hydrostatic and GFR and increase plasma flow but also filtration fraction is constant

3- increase Efferent arteriolar resistance lead to rise glomeruli hydrostatic pressure and GFR increase slightly and decrease plasma blood flow so filtration fraction is increase so glomeruli colloid osmotic pressure increase

But if the constriction of efferent arteriole is more sever ,the rise in the colloid osmotic pressure is increase more than hydrostatic pressure because plasma protein concentration increase rapidly so the net filtration rate decrease so the GFR decrease

↑ RE →↑ FF & πG → πG >PG → net ↓GFR



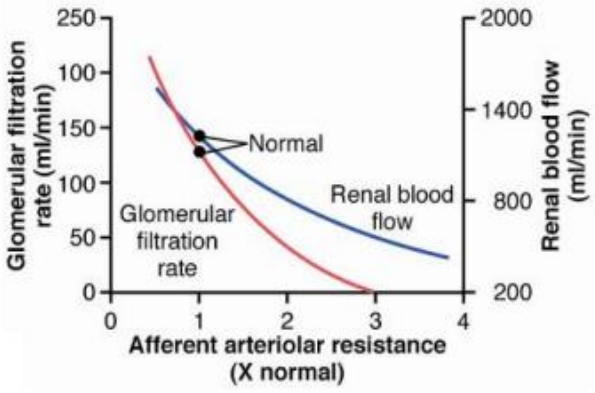


Table 27-2 Factors That Can Decrease the Glomerular Filtration Rate

Physical Determinants*	Physiological/Pathophysiological 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 a small effect because of 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)

Renal blood flow

• High blood flow (1100 ml/min ~22% of cardiac output)

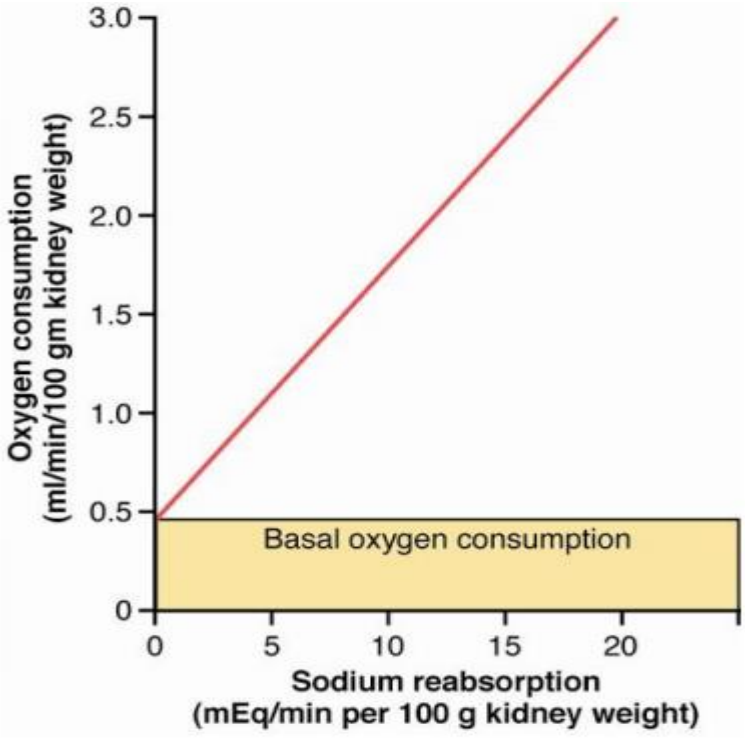
• High blood flow to the kidney exceed needed for high rates of GFR that necessary for regulation of body fluid volume and solute concentration

• Oxygen and nutrients delivered to kidneys normally greatly exceeds their metabolic needs

• A large fraction of renal oxygen consumption is related to higher rate active Na reabsorption

so if renal blood flow reduce and less GFR are reduce Na filter so less Na reabsorb and less O2 consumption

↓renal blood flow& GFR →less Na is filtered →less Na is reabsorbed →less O2 consumed



Determinants of Renal Blood Flow (RBF)

1-difference between renal artery pressure and renal vein pressure

renal artery P=systemic arterial pressure -----main arterial pressure=100mmHg

renal vein P=3-4 mmHg

2-total renal vascular resistance(R) =sum of all resistances in kidney vasculature (arteries, arterioles, capillaries &veins)

RBF = DP/R

Most of renal vascular resistance resides in:

1-interlobular arteries

2-afferent arterioles

3-efferent arterioles

Control resistance of these vessel by sympathetic , various hormonal and local renal control mechanism

↑ resistance of any of vascular segments of kidneys →↓RBF and vice versa if renal artery & renal vein pressures remain constant.

Autoregulation

Intrinsic ability of kidneys to regulate its own blood flow to maintain GFR

Autoregulation → constant RBF & GFR over P changes 80-170 mmHg

Two mechanisms involved in renal autoregulation:

1. Myogenic response

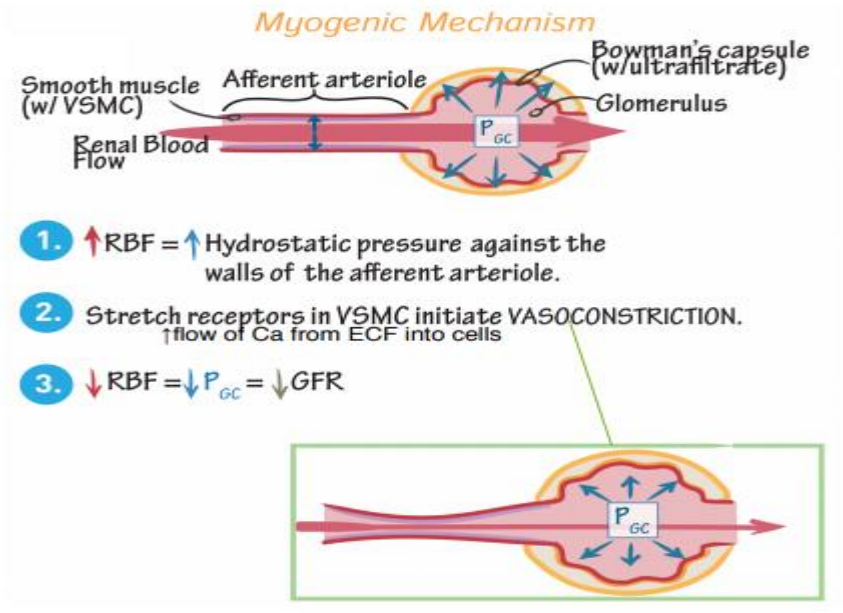
2. Tubuloglomerular feedback

-myogenic response:

Is the ability of blood vessel to resist stretching during increase arterial pressure to elp to maintain constant RBF and GFR

On when increase pressure smooth muscle of blood of afferent arteriole stretch and these smooth muscle have stretch sensitive Ca channel

So when stretch these channel open and allow Ca enter from extracellular to to muscle cause them to contract this help prevent excessive increase RBF and GFR



-Tubuloglomerular feedback

The kidney has feedback mechanism that link in change in NaCl concentration at the macula densa with control of renal arteriolar

The macula densa sense change in volume deliver to distal tubule so if decrease GFR ,the flow rate in tubule is slow so increase reabsorption of NaCl so reduce NaCl at the macula densa and these decrease concentration decrease initiate signal from macula densa which cause :

-decrease resistance of afferent arterioles by produce prostaglandin E2 and bradykinin so increase hydrostatic pressure in glomeruli capillary and help return GFR

-and by increase release renin from the juxtaglomerular cell and the renin release and act on angiotensinogen and convert it to angiotensin I and then from the ACE in the lung convert to angiotensin II

And angiotensin II constrict the efferent arteriole so increase hydrostatic pressure in glomeruli capillary so help to return normal GFR

And when increase GFR , the NaCl that reach macula densa is increase

So macula desa release adenosine which constrict the afferent arteriole and so decrease hydrostatic pressure and return GFR to normal

Factors increasing the sensitivity of tubuloglomerular feedback:

i. Adenosine

ii. Thromboxane

iii. Prostaglandin E2

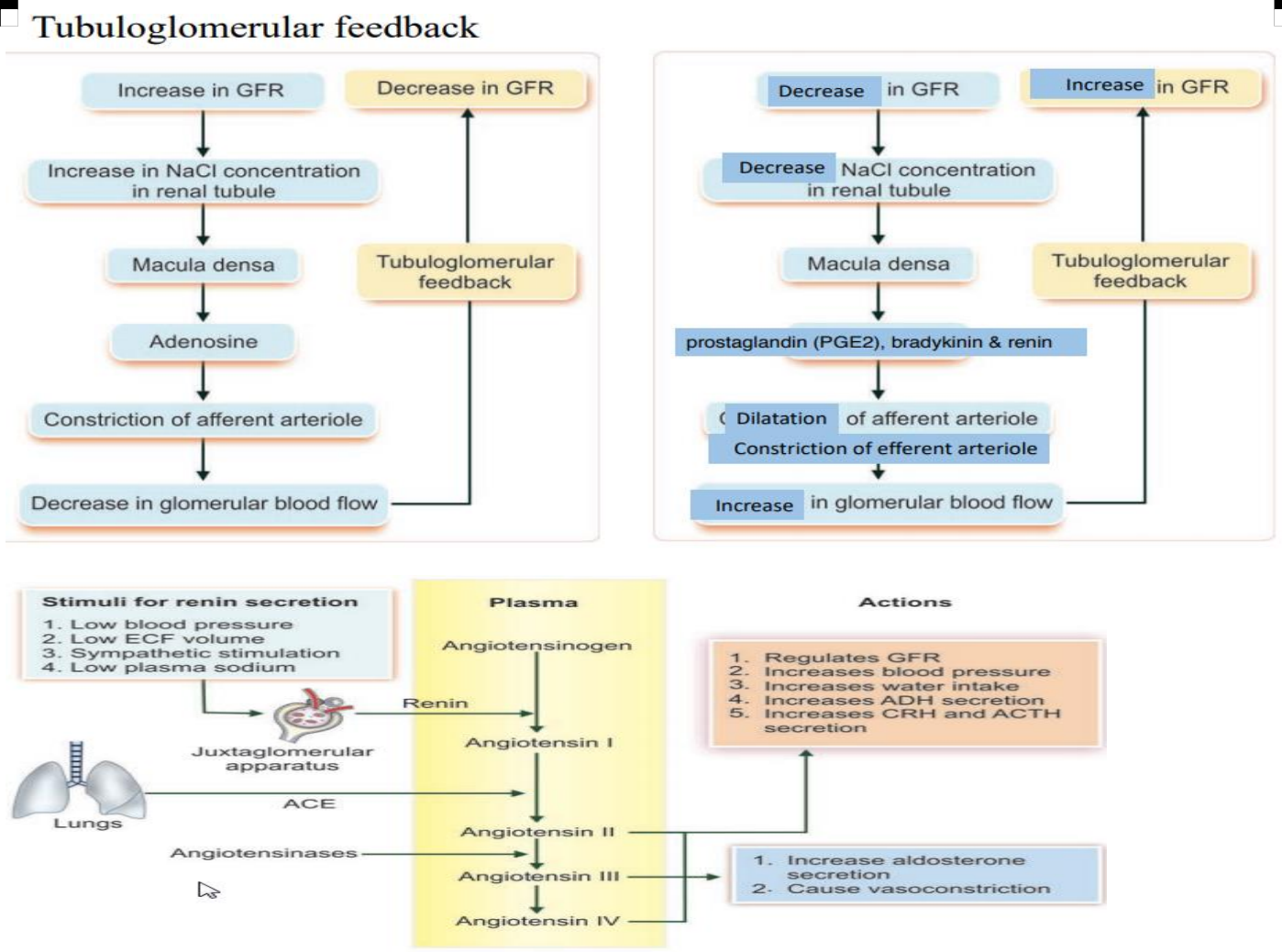
Factors decreasing the sensitivity of tubuloglomerular feedback:

i. Atrial natriuretic peptide

ii. Prostaglandin I2

iii. Cyclic AMP (cAMP)

iv. Nitrous oxide



Other Factors That Influence GFR

• Fever, pyrogens: increase GFR

• Glucorticoids: increase GFR

• Aging: decreases GFR 10%/decade after 40 yrs

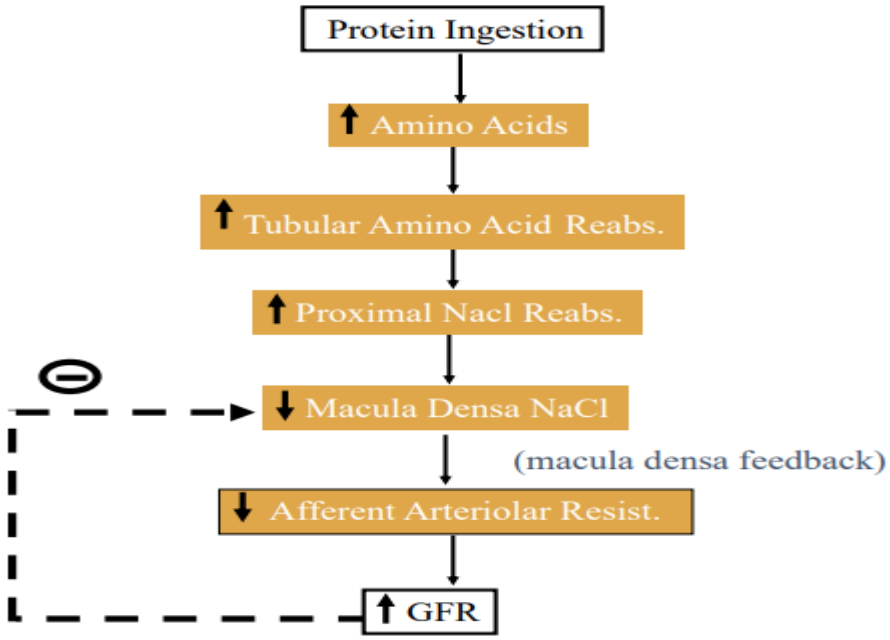
• Hyperglycemia: increases GFR (diabetes mellitus)

• Dietary protein: high protein increases GFR ,low protein decreases GFR

High protein diet lead to increase amino acid in the blood which is filter by kidney and reabsorb in the proximal tubule and because the amino acid and Na is absorb together by co-transport so increase amino acid reabsorb also stimulate Na reabsorb so decrease deliver Na to macula densa

So the macula densa decrease afferent arteriole resistance so increase RPF and GFR an dthis increase GFR maintain allow more Na excretion to maintain at normal level and also protein metabolism produce urea so increase GFR to rid waste product

At the similar mechanism to glucose which need Na to reabsorb



Control of GFR and RBF by:

• Neurohormonal

• Local (autacoids, Intrinsic)

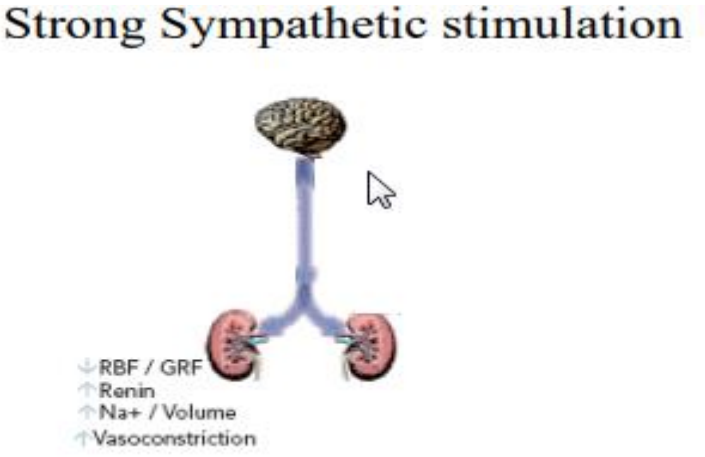
-Neurohormonal regulation of GFR and RBF

the afferent and efferent arteriole are richly innervated by sympathetic nerve fiber so strong activation of sympathetic lead to constrict the renal arterioles and decrease RBF and GFR

also stimulate renin release and increase Na+ reabsorb

In healthy person, sympathetic have little influence on RBF.

• Sympathetic is important in acute disturbances (e.g. defense reaction, brain ischemia, or severe haemorrhage)



Hormonal regulation of GFR and RBF

Norepinephrine, epinephrine constrict afferent and efferent arterioles that cause decrease RBF and GFR but have little effect except in sever condition such as hemorrhage

Endthelin is release from damage vascular endothelial cell is cause vasoconstriction in renal blood vessel ,it is increase in some vascular injury such as toxemia of pregnancy, chronic uremia, renal failure which lead to renal vasoconstrictor and decrease GFR

Angiotensin II:

• Powerful Constrict Efferent arterioles so rise hydrostatic pressure and GFR but reduce RBF so prevents ↓ PG & GFR

• Physiological conditions

•and because decrease flow through peritubular capillary lead to↑ Na and water reabsorption

• angiotensin II increase in low Na diet, volume depletion & ↓ arterial P

• NO & PG Counteract the angiotensin II mediated vasoconstriction in afferent A

So afferent arteriole is protected from angiotensin II mediated vasoconstriction by release NO and prostaglandin

Endothelial derivative nitric oxide :

Vasodilator so increase RBF and GFR

• Help in Na & H2O excretion

So if administration drug inhibit NO lead to increase vascular resistance and lead decrease GFR so lead to hypertension

Prostaglandin:

Vasodilator so increase RBF and GFR include PGE2 and PGI2 and bradikinin

• important only when there are other disturbances that are already tending to lower GFR

• Inhibited by NSAIDs so decrease GFR

Table 27-4 Hormones and Autacoids That Influence GFR

Hormone or Autacoid	Effect on GFR
Norepinephrine	↓
Epinephrine	↓
Endothelin	↓
Angiotensin II	↔ (prevents ↓)
Endothelial-derived nitric oxide	↑
Prostaglandins	↑

نهاية التلخيص سامحونا على اي اخطاء