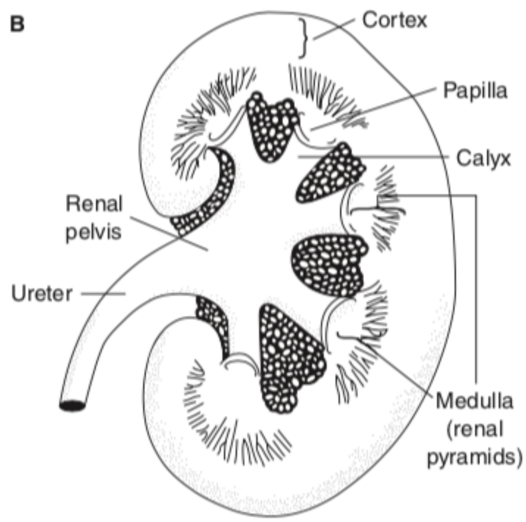
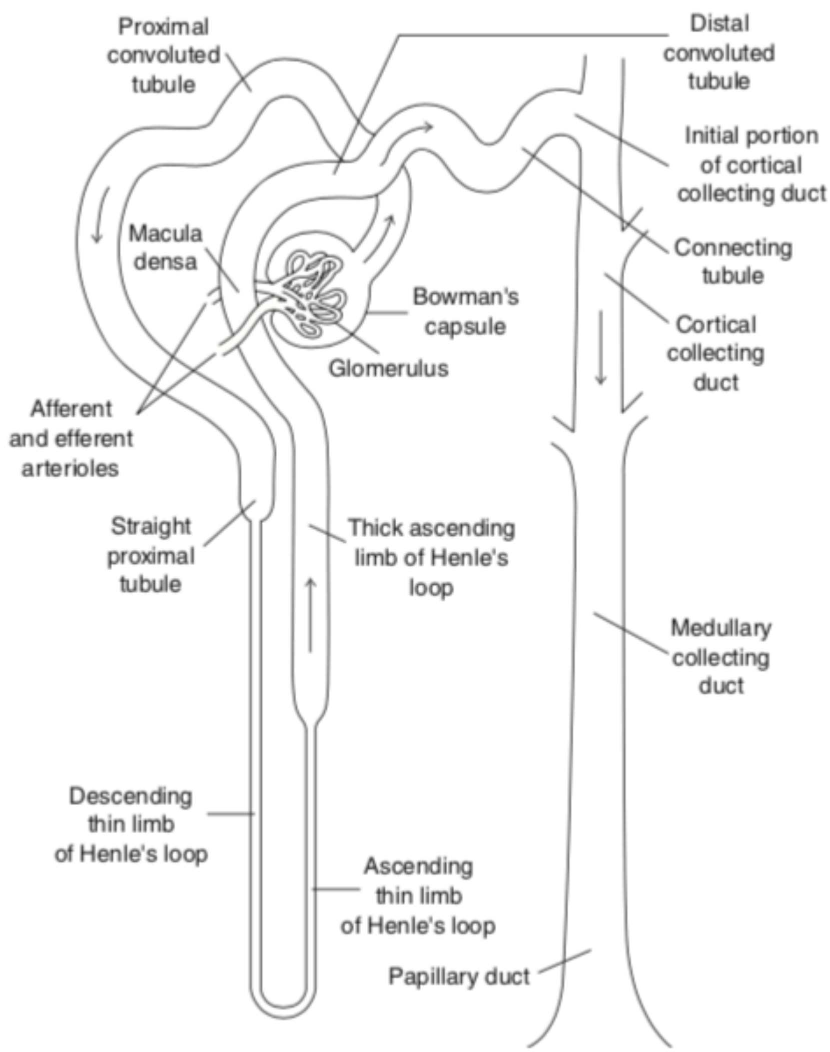
VANDER'S RENAL PHYSIOLOGY CHAPTER 1-3 REVIEW QUESTIONS

Label the diagrams below

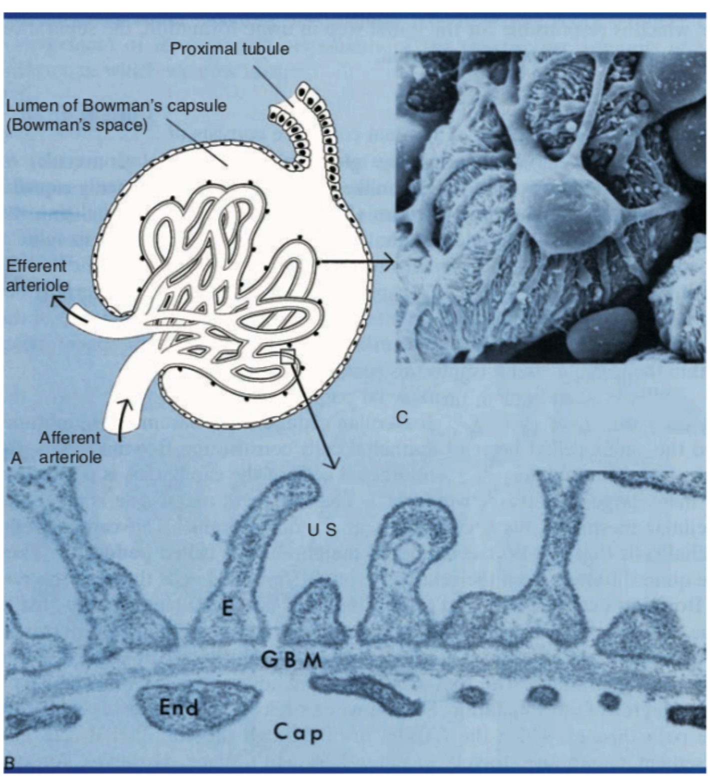




- Basic unit of the kidney = nephron (each kidney contains approximately 1 million nephrons
- Nephron = glomerulus (tuft of capillaries between the afferent and efferent arterioles) + series of tubules lined with continuous epithelial cells
- Glomeruli are located within the cortex
- Tubules are located in the cortex and medulla
- Fluid filters across the glomerulus -> Bowman's space -> proximal tubule (initial convoluted segment then pars recta) -> loop of Henle (thin descending limb + think ascending limb + thick ascending limb/ macula densa) -> distal convoluted tubule -> connecting segment -> collecting tubule -> calyces -> renal pelvis -> ureters -> bladder
- Glomerulus is a tuft of capillaries interposed between the afferent and efferent arterioles. Each glomerulus is enclosed within an epithelial cell capsule, i.e. Bowman's capsule, which is continuous with the epithelial cells that surround the glomerular capillaries and the cells of the proximal convoluted tubule.

What 3 layers form the filtration barrier through with all filtered substances must pass?

1. **Fenestrated endothelium** of the glomerular capillaries
   - freely permeable to everything in the blood except red blood cells and platelets
2. **Glomerular basement membrane**
   - Gel-like meshwork of glycoproteins and proteoglycans
3. Single layer of **epithelial cells**
   - Attached to GBM by discrete foot processes/ podocytes
   - Spaces between adjacent pedicels constitute the path through which filtrate travels to enter Bowman's space
   - Slit diaphragms bridge the slits between the pedicles, which act as a adherent junctions
   - Ultimately permits the filtration of large volumes of fluid from the capillaries into Bowman's space, but restricts the filtration of large plasma proteins, such as albumin



Name that structure!
This cell acts as a phagocyte to remove any trapped material from the glomerular basement membrane: Mesangial cell. Mesangial cells also contain a large numbers of myofilaments that can contract in response to a variety of stimuli in a manner similar to vascular smoth muscle.

Area of specialized cells in the thick ascending limb, closest to Bowman's capsule: Macula densa

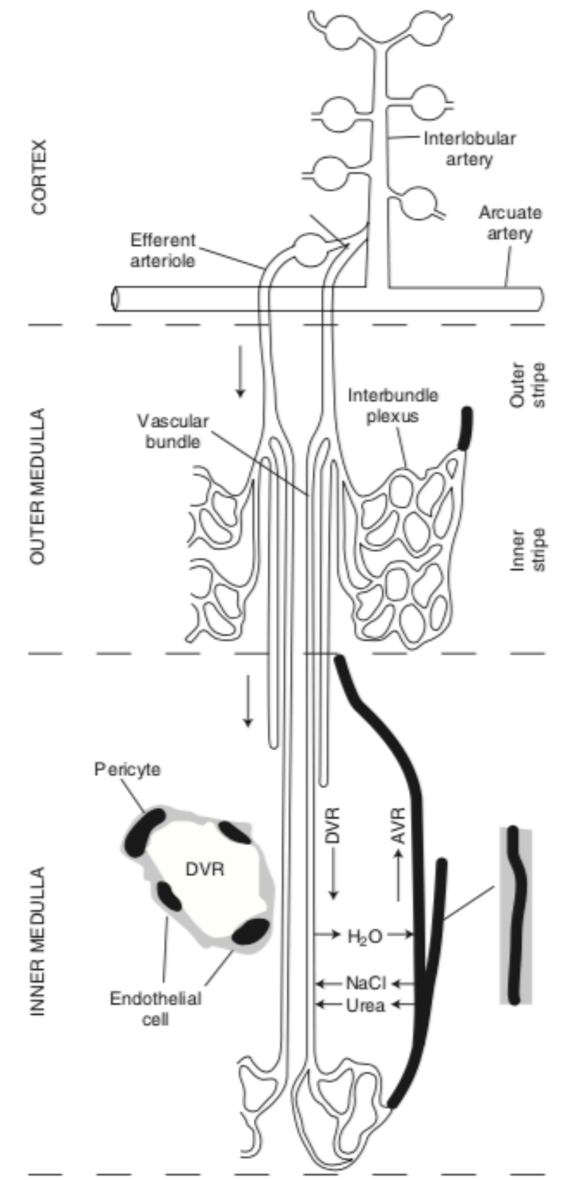
Area where renin is released: juxtaglomerular apparatus

What cells make up the juxtaglomerular apparatus? What is the relevance of the JGA?
Made up of granular cells, extraglomerular mesangial cells,
3 cell types of the juxtaglomerular apparatus:
1. Granular cells or juxtaglomerular cells: differential smooth muscle cells in the walls of the afferent arterioles -> secrete renin
2. Extraglomerular mesangial cells
3. Macula densa cells: specialized thick ascending limb epithelial cells (detectors of the luminal content of the nephron at the very end of the thick ascending limb and contribute to the control of GFR and renin secretion)

Describe the passage of blood flow through the kidneys.
Renal arteries -> interlobar -> arcuate -> interlobular branches -> afferent arterioles -> glomerular capillaries -> efferent arterioles -> peri-tubular capillaries -> renal veins

Blood enters each kidney via the renal artery, which then divides into progressively small branches: interlobar, arcuate and interlobular arteries (usually called cortical radial arteries). From the interlobular arteries, a series of arterioles branches off, each leading to a glomerulus, i.e. afferent arterioles. Glomerular capillaries recombine to form another set of arterioles, called efferent arterioles. The efferent arterioles then subdivide into a second set of capillaries (peritubular capillaries), which are profusely distributed throughout the cortex. The peritubular capillaries rejoins to form the veins by which blood ultimately leaves the kidneys.

How is blood flow to the renal medulla different than blood flow to the renal cortex?
The medulla receives much less blood than the cortex. There are no glomeruli in the medulla. Efferent arterioles in from the juxtamedullary glomeruli (rather than branching into peritubular capillaries), instead descend downward into the out medulla where they divide many times to form bundles of parallel vessels, i.e. the **vasa recta**. The descending vasa recta are like arterioles, with pericytes containing smooth muscle but become more capillary like as they descend. The ascending vasa recta have fenestrated endothelium, like that found in the glomerular capillaries, playing a role in water and solute exchange between plasma and the interstitium, which is essential for the formation of concentrated urine.



Define the following terms in reference to renal function.
Filtration: process by which water and solutes in the blood leave the vascular system through the filtration barrier and enter Bowman's space
eg. freely filtered substances: Na+, K+, Cl-, bicarb, glucose, urea, amino acids, peptides like insulin and ADH
eg. freely filtered, 'almost' completely reabsorbed - glucose
Secretion: process of moving substance into the tubular lumen from the cytosol of epithelial cells that form the walls of the nephron
Reabsorption: process of moving substances from the lumen across the epithelial layer into the surrounding interstium, and then typically into surrounding blood vessels
Excretion: exit of the substance from the body, i.e. via urine

Match the following anatomic locations with the correct description
Site of filtration - Glomerulus
Reabsorbs about 2/3 of filtered water, sodium and chloride - Proximal tubule
Reabsorbs organic molecules like glucose and amino acids - Proximal convoluted tubule
Site of secretion of the a number of organic waste products like urate and creatinine - Proximal convoluted tubule
Reabsorbs significant portions of potassium, phosphate, calcium, bicarbonate - Proximal convoluted tubule
Absorbs about 20% of filtered sodium and chloride and 10% of filtered water - LOH
Senses sodium and chloride content of the lumen and generates signals that affects RAAS - macula dense
Absorb about 5% of water and salt - distal tubule or connecting tubule
Cells are strongly responsive to ADH and aldosterone - collecting tubule
Plays a major role in regulation of urea absorption and acid-base balance - medullary collecting tubule

Innervation to the kidney is primarily from which part of the autonomic nervous system?
Sympathetic. There is negligible parasympathetic input. Neural signals originate in sympathetic celiac plexus. Sympathetic signals exert major control over renal blood flow, GFR and release of vasoactive substances.

Name that hormone!
Main regulator of sodium and potassium - Aldosterone
Main regulatory of water excretion - Antidiuretic hormone

The kidneys received about 20 percent of cardiac output.

State the formula for how flow, pressure and resistance are related.

Q = ΔP/R

Q = flow

ΔP = mean pressure in the artery - mean pressure in vein

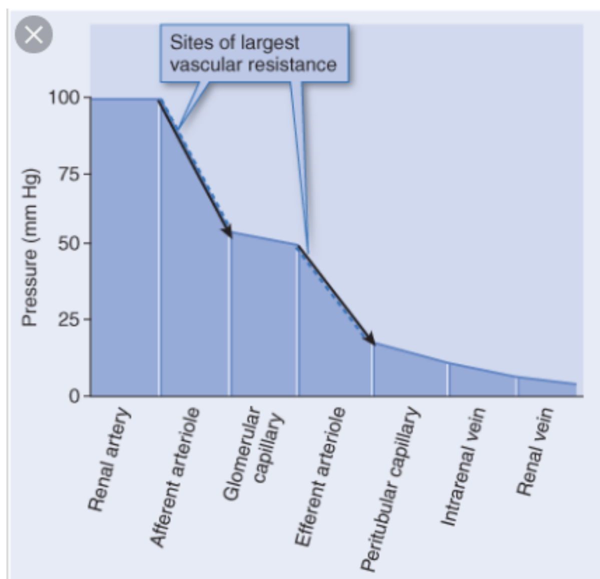
R = total vascular resistance

Total renal blood flow is determined many by the mean pressure in the renal artery, and the contractile state of the smooth muscle of the rental arterioles. A change in arteriolar resistance produces the same effect on RBF regardless of whether it occurs in the afferent arteriole or efferent arteriole as these vessels are in series. This is not the same for GFR.

As described by Poiseiulle's law, resistance to blood flow is determined by which 3 factors?

1. Blood viscosity
2. Length of the blood vessels
3. Arteriolar radius

$$R = \frac{8\eta l}{\pi r^4}$$



Hydrostatic pressures in the two capillary beds of the renal vascular are very different. Where are capillary hydrostatic pressure higher — in the glomerulus or in the peritubular capillaries?

Typical glomerular pressures are near 60 mm Hg in a normal unstressed individual, whereas peritubular pressures are closer to 20 mm Hg. The high glomerular pressure is crucial for glomerular filtration, whereas the low peritubular capillary pressure is equally crucial for the tubular reabsorption of fluid.

What 2 characteristics determine if a molecule is able to be filtered at the glomerulus?

1. Size selectivity
   - allows filtration of small particles and water, while restricting passage of large molecules (>7000 Da)
   - Albumin is nearly completely excluded from filtration (molecular weight 66,000 Da)
   - Both GBM and slit diaphragms contribute to size selectivity. Endothelial cells do not contribute to size selectivity as the fenestrae are relatively wide open
2. Charge selectivity
   - 2nd major determinant in filtration across the glomerulus
   - negatively charged molecules are filtered to a lesser extent than positively charged molecules
   - Electrostatic repulsion by cell coats of endothelium, podocytes and GBM

What are the two major determinants of glomerular filtration rate?

1. Rate of renal blood flow (i.e. arterial blood pressure)
2. Changes in Starling's forces, mostly dictated by changes in resistance of the afferent and efferent arterioles

Write out Starling's Law in reference to GFR

Rate of filtration = hydraulic permeability x surface area x net filtration pressure

$GFR = LpS (P_{GC} - \pi_{GC}) - (P_{BC} - \pi_{BC})$

$GFR = LpS (P_{GC} – P_{BC} – \pi_{GC})$

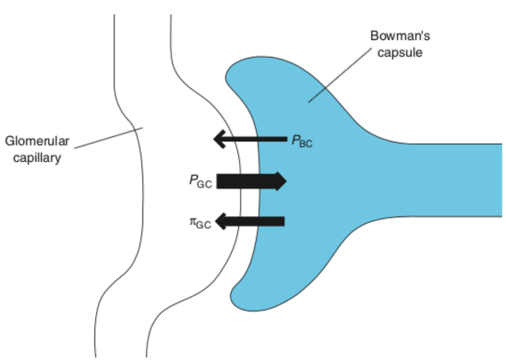
LpS = permeability of the capillary wall + surface area available for filtration (filtration coefficient)

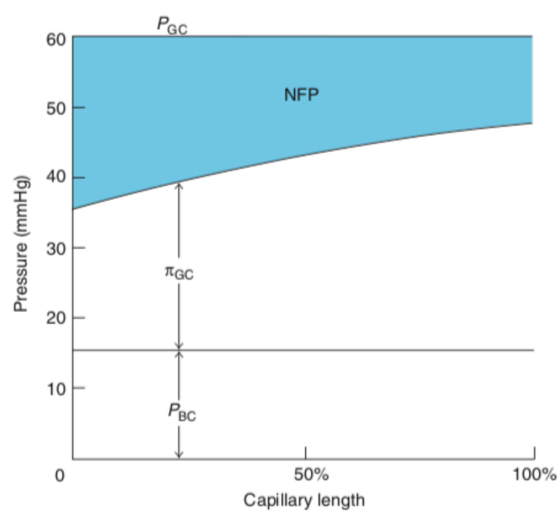
P_{GC} = hydraulic pressure in the glomerular capillary

P_{BC} = hydraulic pressure in Bowman's capsule

π_{GC} = oncotic pressure in the glomerular capillary

π_{BC} = oncotic pressure in Bowman's capsule = 0



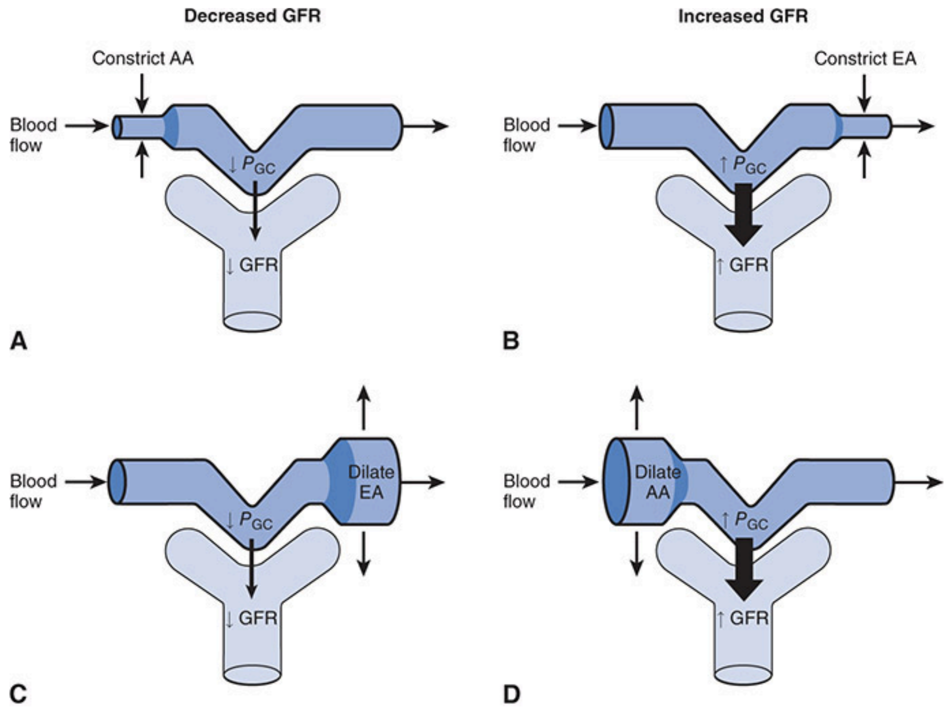


Give an example of how each of the above factors can be altered.

1. **Filtration coefficient:** Can be altered by contraction of glomerular mesangial cells, which reduces the surface area available for filtration. This is controlled by various chemical messengers and can be affected by glomerular disease and drugs as well.
2. **P_{GC} (hydraulic pressure in the glomerular capillaries):** Altered by changes in afferent and efferent arteriolar resistance
3. **P_{BC} (hydraulic pressure in Bowman's capsule):** Changes in this are of very minor physiologic importance. Hydraulic pressure in Bowman's capsule can increase in cases of urinary obstruction, resulting in decreased GFR.
4. **π_{GC} (oncotic pressure in the glomerular capillaries):** At beginning of capillary is identical to plasma oncotic pressure, so any disease that reduced plasma protein will reduce oncotic pressure and may result in increased GFR. Along the length of the glomerular capillary, more fluid is filtered and the glomerular capillary oncotic pressure rises.

Fill in the following chart with the correct change (increase/ decrease/ no change) to the glomerular hydrostatic pressure, glomerular filtration rate, and renal blood flow.

	P_{GC}	**GFR**	**RBF**
Constriction of afferent arteriole	Reduced	Reduced	Reduced
Constriction of efferent arteriole	Increased	Increased	Reduced
Dilation of afferent arteriole	Increased	Increased	Increased
Dilation of efferent arteriole	Reduced	Reduced	Increased
Constriction of both the afferent and efferent arterioles	No effect?	No change?	Reduced
Dilation of both the afferent and efferent arterioles	No effect?	No change?	Increased



Source: Douglas C. Eaton, John P. Pooler: *Vander's Renal Physiology*, 9e
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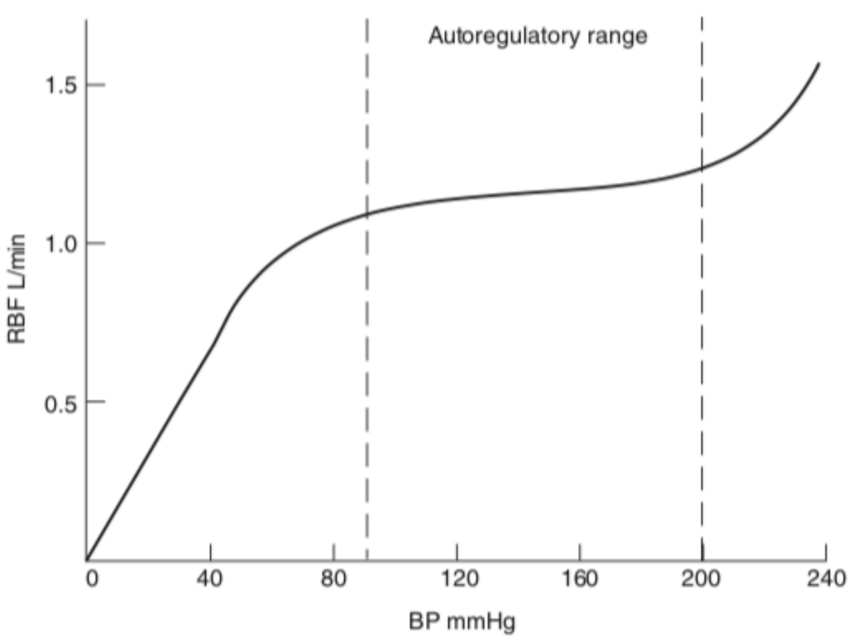
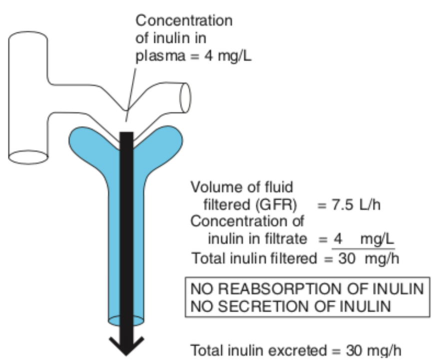
Autoregulation allows the kidneys to regulate GFR independent of renal blood flow, preventing excessive pressure natriuresis and hypertensive damage to glomerular capillaries (as the pressure in these capillaries is much higher than elsewhere in the body). Draw a graph representing the relationship between renal blood flow and blood pressure.



Explain the two main mechanisms by which autoregulation occurs.

1. Myogenic response:
   1. myogenic stretch receptors in the walls of the afferent arteriole sense increase pressure and promote constriction and vice versa
   2. fast acting and protects the glomeruli from short-term fluctuations in blood pressure
2. Tubuloglomerular feedback:
   1. Macula densa senses amounts of sodium and chloride delivery
   2. More filtered chloride results in more chloride delivery to macula dense, resulting in secretion of transmitter agents into the interstitial space that reduce the filtration in the nearby glomerulus via constriction of the afferent arteriole and contraction of the glomerular mesangial cells
   3. Low levels of sodium allow higher filtration rate
   4. Mediators of TGF: adenosine (induces constriction of afferent arteriole), thromboxane (vasoconstrictor), nitric oxide (vasodilator)

Insulin is freely filtered by the glomerulus but it is largely reabsorbed, thus its renal clearance is very low.
Inulin is freely filtered by the glomerulus but is not reabsorbed or secreted by the nephron, thus its renal clearance is very high. Inulin's clearance (volume of plasma cleared per unit time) is equivalent to GFR.



The gold standard for measure GFR is inulin clearance.
Inulin is infused at a constant rate, and urine is collected. If GFR is normal, between 2.5-3.5% of plasma inulin is removed every minute and must be replaced by infusion.
A more routine method of measuring GFR is creatinine clearance.
Creatinine is an end-product of skeletal muscle metabolism. It is freely filtered but no reabsorbed. A small amount is excreted by the proximal tubule, so creatinine clearance is slightly higher than GFR (by about 10-20%). A patient's urine is collected for 24 hourrs. Blood and urine creatinine concentrations are compared. Typically we just use plasma creatinine as a surrogate for GFR.

Calculate creatinine clearance (mL/min) using the following information.
Volume of urine produced over 24 hours = 4000 mL
Urine creatinine = 60 mg/dL
Plasma creatinine = 1.5 mg/dL

$$C_X = \frac{U_X}{P_X} \bullet V$$

Cx = clearance of X
Px = plasma concentration of X
V = urine flow rate
Ux = urine concentration of x

Cx = (4000 mL/ 24 hours) x (60 mg/dL over 24 hours) / 1.5 mg/dL
Cx = 111 mL/min