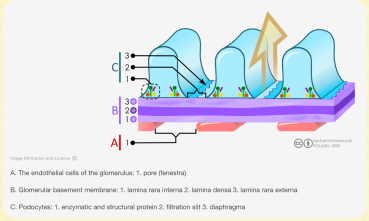
Agents causing Relaxation and Contraction of the Mesangial Cells

Pearl #1358 • Physiology

Relaxation	Contraction
• ANP • Dopamine • PGE2 • cAMP	• Endothelins • Angiotensin II • Vasopressin • Platelet-derived growth factor • Thromboxane A2 • PGF2 • Leukotrienes C4 and D4 • Histamine



A. The endothelial cells of the glomerulus; 1. pore (fenestra)

B. Glomerular basement membrane: 1. lamina rara interna 2. lamina densa 3. lamina rara externa

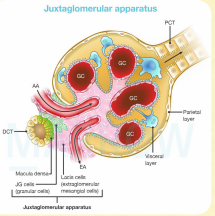
C. Podocytes: 1. enzymatic and structural protein 2. filtration slit 3. diaphragma

Differences between Cortical and Juxtamedullary Nephron

Pearl #1366 • Physiology

Features	Cortical nephron	Juxtamedullary nephron
Location of glomerulus	Upper region of cortex	Near junction of cortex and medulla
% of total nephrons	85%	15%
Size of glomeruli	small	larger
Loop of Henle	Short extend up to outer layer of medulla	Long extend deep into the medulla
Efferent arterioles	Large diameter break into peritubular capillaries	Small diameter continue as vasa recta
Rate of filtration	Slow	High
Major function	Excretion of waste products in the urine	Concentration of urine by countercurrent mechanism

Juxtaglomerular apparatus



Term	Equation
Clearance rate	Us ×V / Ps
Glomerular filtration rate	Uinulin × V / Pinulin
Clearance ratio	Cs/Cinulin
Effective renal plasma flow	ERPF=CPAH=UPAH ×V / PPAH
Renal blood flow	RPF / (1– Hematocrit)
Excretion rate	Us ×V
Reabsorption rate	=Filtered load –Excretion rate =(GFR×Ps)–(Us ×V)
Secretion rate	Excretion rate–Filtered load

Cs - clearance rate of substance "s"

EPAH - PAH extraction ratio

ERPF - effective renal plasma flow

GFR - glomerular filtration rate

P - plasma concentration

PAH - para-aminohippuric acid

PPAH - renal arterial PAH concentration

RBF - renal blood flow

RPF - renal plasma flow

S - a substance

U - urine concentration

V - urine flow rate

VPAH - renal venous PAH concentration

% of filtered Na reabsorbed	Part of nephron	Main transporter involved
60	PCT	Na^+ –H^+ exchanger
30	Thick ascending limb of the loop of Henle	Na^+ –$2Cl^-$–K cotransporter
7	DCT	Na–Cl cotransporter
3	Collecting ducts	ENaC channels (regulated by aldosterone to permit homeostatic adjustments)

Water Transport along Nephron

Pearl #1333 • Physiology

Segment	Mechanism of Water Reabsorption
Proximal tubule(67%)	Osmosis, AQ 1
Loop of Henle (15%)	Descending thin limb only; aquaporin 1 channels
Distal convoluted tubule(0%)	No water reabsorption (Reabsorption + with ADH)
Collecting duct (8-17%)	Passive

Effect	GFR	RPF	FF(GFR/RPF)
Constriction of afferent arteriole (eg. Sympathetic stimulation)	↓ (caused by ↓ P_{GC})	↓	No change
Constriction of efferent arteriole (eg angiotensin II)	↑ (caused by ↑ P_{GC})	↓	↑ (↑GFR/↓RPF)
Increased plasma protein	↓ (caused by ↑ π_{GC})	No change	↓ (↓GFR/unchanged RPF)
Decreased plasma protein	↑	-	↑
Ureteral stone / constriction of the ureter	↓ (caused by ↑ P_{BS})	No change	↓ (↓GFR/unchanged RPF)

PCT	DCT
Brush border present in the apical membrane	No brush border
Cytoplasmic carbonic anhydrase (type 2 & type 4) present	Cytoplasmic carbonic anhydrase (type 2 only)
Has 'leaky' tight junctions	Has 'tight' tight junctions
Paracellular transport is possible via leaky tight junctions	No paracellular transport

Inherited Causes of Nephrotic Syndrome

Pearl #2270 • Pathology

Gene involved	Protein	Disease Phenotype	Inheritance Pattern
NPHS1 (Ch.19q)	Nephrin	Congenital Nephrotic syndrome (Finnish Type)	Autosomal recessive
NPHS2 (Ch.1q)	Podocin	Steroid resistant nephrotic syndrome	Autosomal recessive
TRPC6	Transient receptor potential cation channel 6	Adult onset FSGS	Autosomal dominant
ACTN4	Alpha-actinin 4	FSGS	Autosomal dominant

Summary of Transport Across Proximal and Distal Portions of the Nephron

Pearl #1334 • Physiology

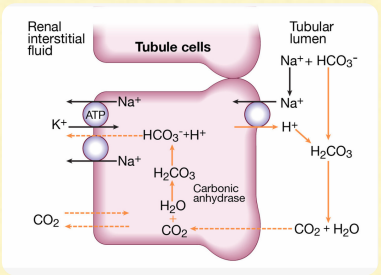
Proximal Tubule	
Reabsorption	**Secretion**
67% of filtered Na^+ actively reabsorbed, not subject to control; Cl^- follows passively	Variable H^+ secretion, depending on acid-base status of body
All filtered glucose and amino acids reabsorbed by secondary active transport; not subject to control	Organic ion secretion; not subject to control
Variable amounts of filtered $PO4^{3-}$ and other electrolytes reabsorbed; subject to control	
65% of filtered H_2O osmotically reabsorbed; not subject to control	
50% of filtered urea passively reabsorbed; not subject to control	
Almost all filtered K^+ reabsorbed; not subject to control	
Distal Tubule and Collecting Duct	
Reabsorption	**Secretion**
Variable Na^+ reabsorption, controlled by aldosterone; Cl^- follows passively	Variable H^+ secretion, depending on acid-base status of body
Variable H_2O reabsorption, controlled by vasopressin	Variable K^+ secretion, controlled by aldosterone

Tubule Characteristics

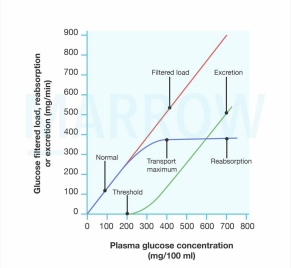
Pearl #1335 • Physiology

Segments	Active NaCl Transport	Permeability		
		H_2O	NaCl	Urea
Proximal tubule	++	++	+	+
Thin descending limb	0	++	+	+
Thin ascending limb	0	0	+	+
Thick ascending limb	++	0	0	0
Distal tubule	+	+ADH	0	0
Cortical collecting duct	+	+ADH	0	0
Inner medullary collecting duct	+	+ADH	0	+ADH

KEY: ADH, antidiuretic hormone; NaCl, sodium chloride; 0, minimal level of active transport or permeability; +, moderate level of active transport or permeability; ++, high level of active transport or permeability; -ADH, permeability to water or urea is increased by ADH.



Splay is due to separation between filtered load and excretion. It occurs due to **different transport maximums of different nephrons**.



Formulae in renal physiology

Pearl #2330 • Physiology

Term	Equation
Clearance rate	Us ×V / Ps
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Clearance ratio	Cs/Cinulin
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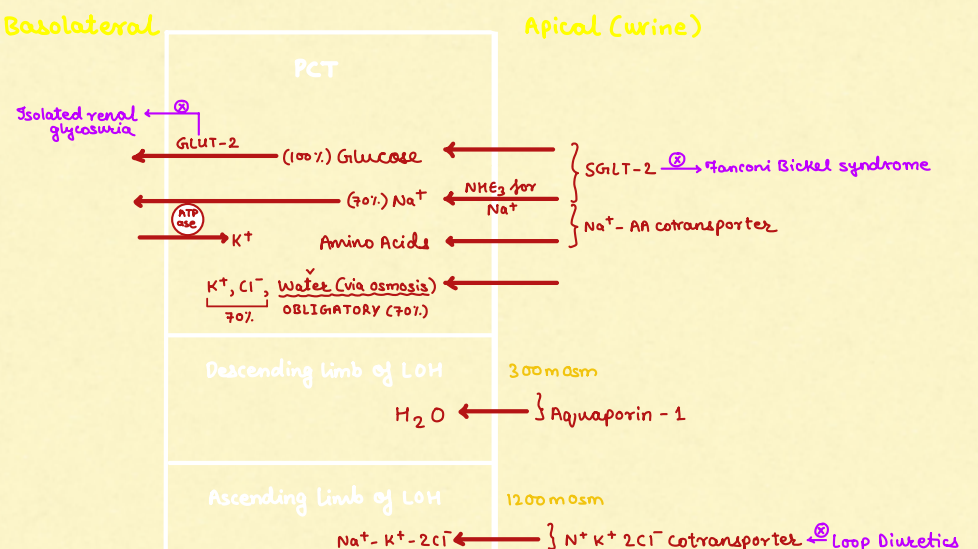
Excretion rate	Us ×V
Reabsorption rate	=Filtered load –Excretion rate =(GFR×Ps)–(Us ×V)
Secretion rate	Excretion rate–Filtered load

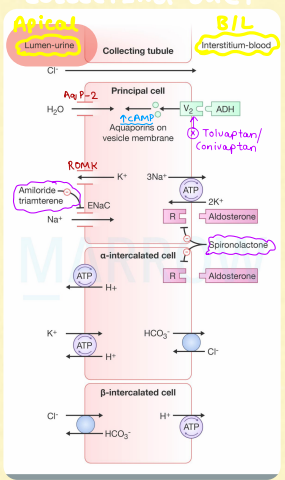
Cs - clearance rate of substance "s"

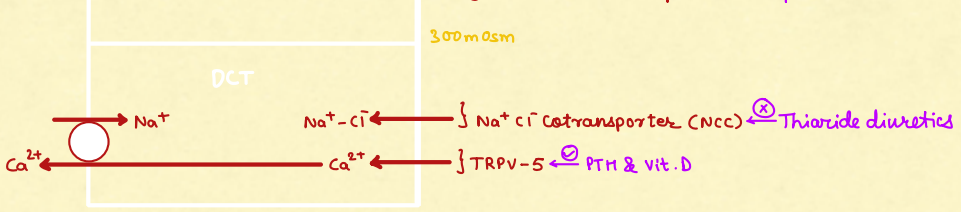
Transport Proteins involved in the Movement of Na+ and CL- across the Apical Membranes of Renal Tubular Cells

Pearl #1332 • Physiology

Site	Apical transport	Function
Proximal tubule(60%)	Na^+/glucose co transport	Na^+ uptake , glucose uptake
	Na^+/inorganic phosphate Cotransporter	Na^+ uptake, phosphate uptake
	Na^+ amino acid Cotransporter	Na^+ uptake, amino acid uptake
	Na^+/lactate Cotransporter	Na^+ uptake, lactate uptake
	Na^+/H^+ exchanger	Na^+ uptake , H^+ extrusion
	Cl^- / base exchanger	Cl^- uptake
Thick ascending limb(30%)	Na^+–K^+–$2Cl^-$ Cotransporter	Na^+ uptake, Cl^- uptake, K^+ uptake
	Na^+/H^+ exchanger	Na^+ uptake, H^+ extrusion
Distal convoluted tubule(7%)	NaCl Cotransporter	Na^+ uptake, Cl^- uptake
Collecting duct(3%)	Na^+ channel (ENaC)	Na^+ uptake







*) SGLT-2 defect :- Fanconi-Bikel syndrome

GLUT-2 defect :- Isolated Renal Glycosuria

*) Cl^- exists in Basolateral ClCNKB (Chloride channel KB) & Barttin a protein in the cell membrane is essential for Normal functioning of ClCNKB

Barter's syn :- Loss of function mutation of any of the following :-

i) ClCNKB , ii) ROMK , iii) Na-K-$2Cl^-$ & iv) Barttin

Characterised by → Hypovolemia (Chronic Na^+ loss), Hypokalemia & Alkalosis

*) Overacting ENa$^+$channels → Liddle's Syndrome

*) Defect in NCC (Na^+Cl^- symporter) → Gitelman Syndrome