INTRODUCTION

A. Role of Kidneys: primarily regulation or homeostasis (rather than excretion)

1. Regulation of blood plasma and interstitial fluid composition (homeostasis), especially inorganic ions – electrolyte balance (e.g. Na^+, K^+, Cl^-, Ca^{2+}) and osmolality

2. Regulation of body fluid volume -- fluid balance

3. Regulation of blood plasma and interstitial fluid pH

4. Excretion of (non-volatile) metabolic end products (e.g. urea, uric acid, creatinine, NH_4^+) and "foreign" solutes (e.g. some drugs)

Note: The above are functions are vital; loss of renal function leads to debilitation beginning in about one day and terminating in death in one-two weeks

5. Endocrine organ, secreting

   a. renin, for regulation of Na^+, ECF (extracellular fluid volume), vascular resistance
   b. erythropoietin, for regulation of erythrocyte production
   c. calcitriol, related to calcium regulation

6. Metabolic functions: e.g. peptide degradation, synthesis of NH_3 and H^+

B. General Renal Mechanism of Body Fluid Regulation:

Selective withdrawal of substances from the blood plasma flowing through the kidneys and excretion these substances in the urine (main mechanism)

Note: When renal function is measured, the values generally refer to both kidneys taken together; e.g. renal blood flow refers to the total blood flow rate through both kidneys, renal sodium excretion rate refers to the total excretion of sodium ion by both kidneys

C.. Urine Formation Rate

Normal	1 ml/min	(1.5 L/day)
Normal range	0.4-2 ml/min	(0.5-3 L/day)
Oliguria	< 0.4 ml/min	(< 0.5 L/day)
Anuria	< 0.04 ml/min	(< 50 ml/day)
Polyuria	> 2 ml/min	(> 3 L/day)

INTRODUCTION (continued)

D. Typical Composition of Urine (and Blood Plasma)

	Plasma	Urine
Na^+	145	100 mM/L
Cl^-	105	100
K^+	4.5	90
HCO_3^-	24	1
glucose	90 (5 mM/L)	0 mg/dl (mg%)
plasma proteins	7	0 gm/dl (gm%)
urea	15	900 mg/dl
uric acid	5	45
creatinine	1	120
pH	7.4	6.0
osmolar conc	300	500 mOsm/kg

(Note: mg/dl = mg solute per 100 ml fluid; mg/dl = mg%)

Plasma has a relatively constant composition
Urine composition is variable in order to maintain homeostasis

E. Terms

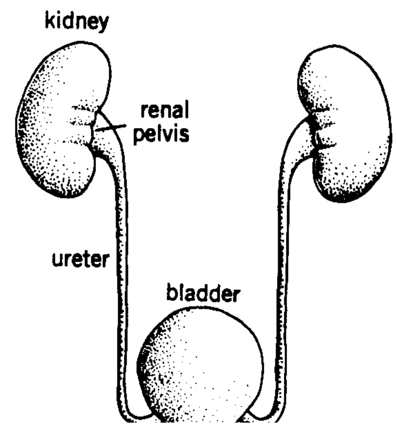
renal	refers to kidney
nephro-	refers to kidney or its functional unit (nephron)
nephritis	inflammation of the kidney
nephrology	medical specialty dealing with the kidney
-uria	refers to urine composition or volume
glucosuria	presence of glucose in the urine
albuminuria	presence of albumin in urine
anuria	no urine formation
urology	surgical specialty dealing with the urinary tract
-emia	refers to blood
uremia	high concentration of urea in blood plasma
diuresis	excretion of a large volume of urine
water diuresis	excretion of a large volume of dilute urine
osmotic diuresis	excretion of a large volume of normal or high osmolarity
diuretic	a substance that causes diuresis
diabetes	certain diseases characterized by diuresis
diabetes mellitus	diuresis characterized by glucose containing urine
diabetes insipidus	diuresis characterized by dilute urine
Clearance	Volume of blood cleared of a substance by the kidneys per unit time (e.g. Na clearance, K clearance, glucose clearance)

FUNCTIONAL ANATOMY OF THE RENAL SYSTEM

A. Kidneys

1. Paired organs, located in the abdominal cavity just below the diaphragm

2. Supplied with blood by renal artery; after passing through the kidney, blood is returned to the heart by the renal vein

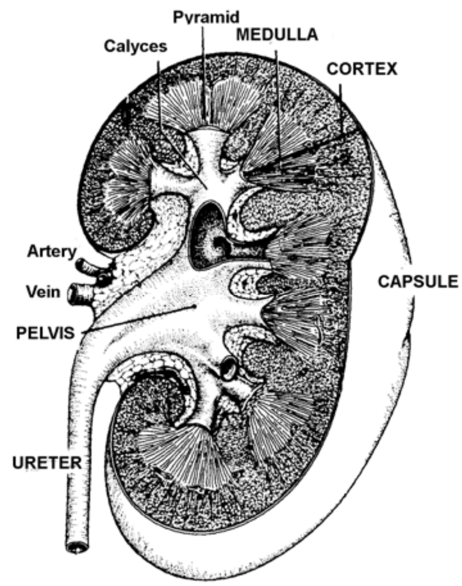


3. Forms urine, which is transported by the ureter to the bladder; excreted from the body at suitable intervals via the urethra (micturition reflex)

   Note: the ureter, bladder, and urethra do not change the composition of urine; when urine leaves the kidney, its composition is fixed

4. Divided into cortex (outer) and medulla (inner) regions

B. Nephron



1. Functional unit: nephron (about one million per kidney); nephron divided into

   a. glomerular region (renal corpuscle)

      1) glomerulus (capillary tuft)
      2) Bowman's capsule (blind end of the nephron)

   b. proximal convoluted and straight tubule

   c. loop of Henle; dips deeply (juxtamedullary nephron) or slightly (cortical nephron) into the medulla; each has thick and thin segments

      1) descending limb
      2) hairpin turn
      3) ascending limb

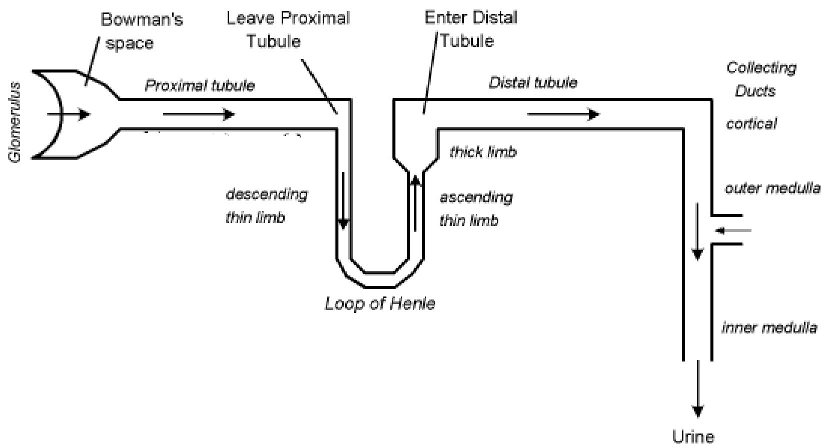
      Note: cortical and juxtamedullary nephrons are distinguished by the cortical location of their glomeruli and the depth to which their loops of Henle penetrate into the medulla

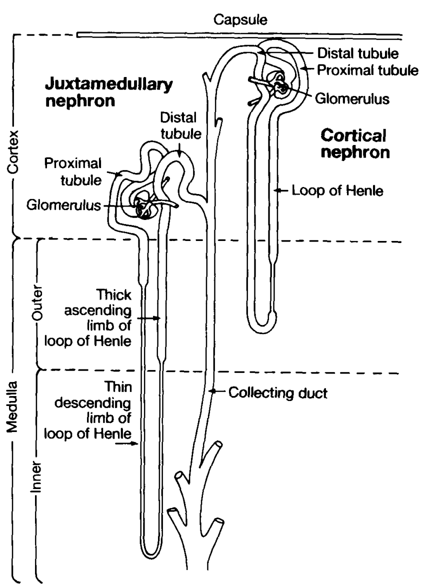
   d. distal convoluted and straight tubule

   e. collecting tubule/duct

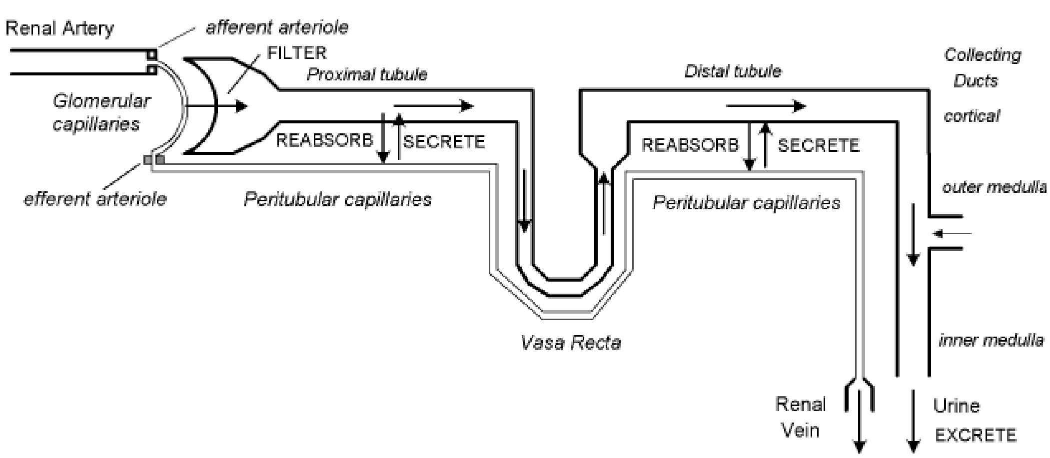
FUNCTIONAL ANATOMY (continued)

B. Nephron (continued)





C. Vascular Bed



RENAL BLOOD FLOW

A. Functional Anatomy of Microcirculation

1. Portal system (capillary beds in series), paralleling the nephron

renal arteries ==> afferent arterioles ==> glomerular capillaries ==> efferent arterioles ==> proximal peritubular capillaries ==>

vasa recta ==> distal peritubular capillaries ==> collecting duct capillaries ==> renal venules and veins

B. Values

1. Normal (resting) blood flow: 1.2 L/min (20-25% of cardiac output)
   Normal (resting) plasma flow: 650 ml/min

   Note: the high blood flow is required to furnish the kidney with sufficient plasma for filtration, reabsorption, etc.

2. Range: the highest renal blood flow occurs at rest; progressively increasing activity or stress progressively reduces renal blood flow; under extreme conditions (e.g. shock), renal blood flow can be reduced to almost zero

C. Control

1. Autonomic: major normal influence on renal blood flow

   a. sympathetic vasoconstrictors: very effective
   b. adrenal medulla: reinforces direct sympathetic constriction

   Note 1: The above contribute to the reduction of renal blood flow in stress

   Note 2: Although the nerves innervating the kidney aid in regulation of renal blood flow and renal transport, they are not essential for normal renal function

   Note 3: At sufficiently low systemic arterial pressure, renal blood flow can be reduced to levels compromising renal function and even kidney survival

GLOMERULAR FILTRATION

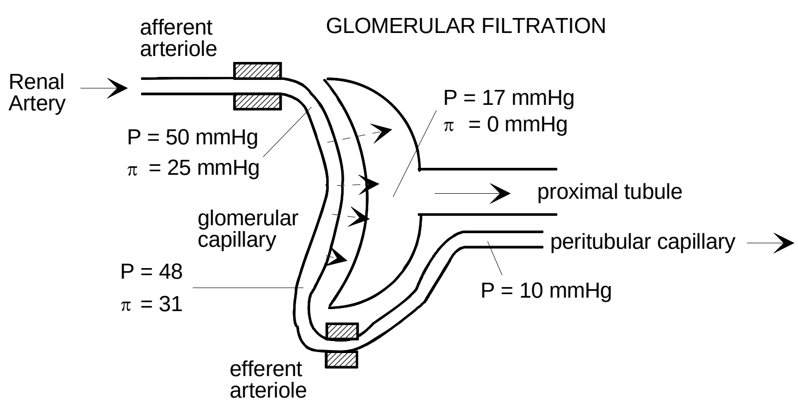
A. Role: formation of the initial fluid entering the nephron

B. Composition of the glomerular filtrate: ultrafiltrate of plasma, due to size-selective filtration: nonselectively permeable to small particles but not very permeable to larger particles, such as blood cells and plasma proteins

C. Mechanism: passive filtration

1. Forces: hydrostatic pressure determined by renal arterial and venous pressures, and by vasomotor state of afferent and efferent arterioles; osmotic pressure determined by plasma protein concentration

   Because of the resistance of the efferent arterioles, the hydrostatic pressure in glomerular capillaries is higher than in most other capillaries and the hydrostatic pressure difference forcing fluid out of the capillaries is greater than the osmotic pressure difference attracting fluid back into the capillaries, or **$\Delta P > \Delta\pi$**



D. Glomerular Filtration Rate

1. Normal value: 120-125 ml/min (for 70 kg human)

PROXIMAL TUBULE TRANSPORT

A. Role: Initial adjustment of tubular fluid by reabsorption (main mechanism) and by secretion

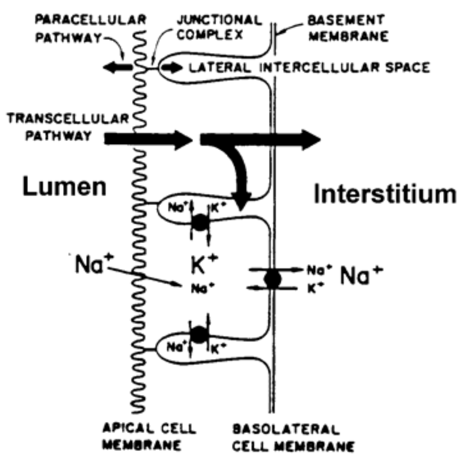
Reabsorption:	Transport from tubular lumen to peritubular capillary blood
Secretion:	Transport from peritubular capillary blood into the tubular lumen

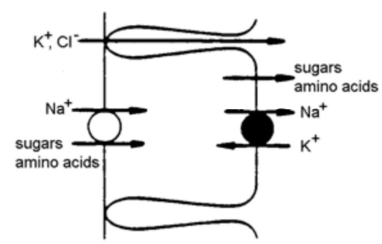
B. Active Reabsorption (direct active transport and cotransport – secondary active transport, symport)

1. Based on Na^+ active transport (actually Na-K-ATPase) pump at the interstitial (baso-lateral) cell membrane (leading to low intracellular Na^+), and carrier-mediated cotransport at the luminal (apical) membrane powered by the Na^+ luminal-intracellular concentration gradient

2. Substances actively reabsorbed compared with the amount filtered; reabsorbed mainly by the transcellular pathway (through cells)

Sodium ion	about 70% (60-80%, including passive component)
Glucose	complete; cotransported with sodium
Amino acids	complete; cotransported with sodium
Plasma proteins	complete (only small amount filtered)





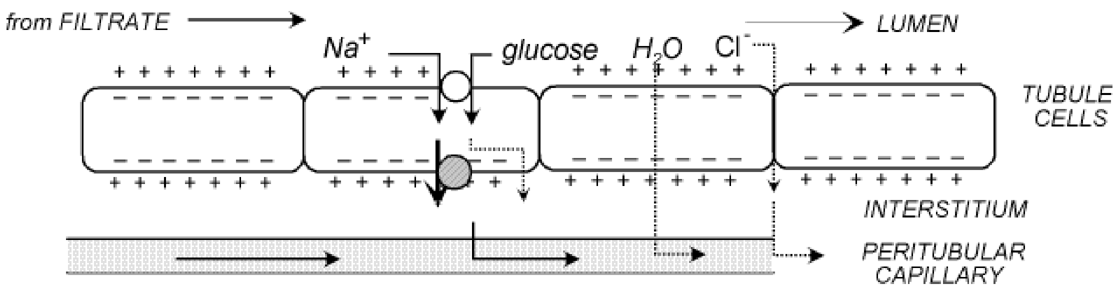
C. Passive Reabsorption: due to concentrating effect of active reabsorption followed by water reabsorption

Chloride ion	paracellular
Bicarbonate ion	variable (depends in part on H^+ secretion)
Potassium ion	most or all
Urea	about 40% (because of limited permeability)
Water	about 70% (60-80%) (due to osmotic effect of particle reabsorption plus tubule-peritubular capillary pressure difference)

PROXIMAL TUBULE TRANSPORT (continued)

C. Passive Reabsorption (continued)

Mechanism: Active particle reabsorption (particularly Na^+) creates a small osmotic gradient between the luminal fluid and the spaces between tubule cells on the interstitial surface. The osmotic gradient causes water to be reabsorbed because the proximal tubule is very permeable to water. The water reabsorption concentrates the remaining dissolved substances (including Na^+), and, if they are readily permeable, the resulting concentration gradient leads to their reabsorption at about the same rate as water.



Note: The above mechanism maintains proximal tubule fluid approximately iso-osmotic with plasma

D. Active Secretion

1. Mechanism: cotransport with Na^+ ion reabsorption (antiport)

2. Substances secreted, e.g.

<u>Exogenous</u> (introduced from outside the body)
Para-aminohippurate (PAH)
Certain pharmacological agents (e.g. penicillin)

<u>Endogenous</u> (produced within the body)
Hydrogen ion (Na^+ antiport)

E. No Transport (neither reabsorption nor secretion)

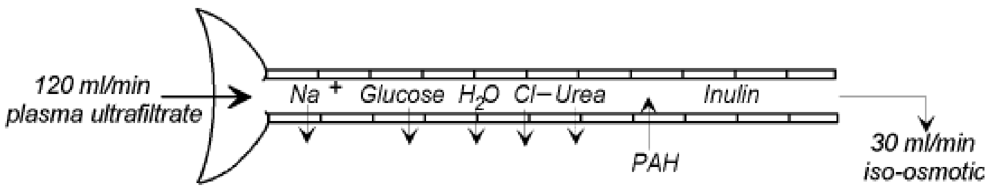
1. Not actively transported and tubule impermeable to diffusion

Creatinine (endogenous protein metabolism product)

Note: Creatinine clearance can be used as an index of glomerular function

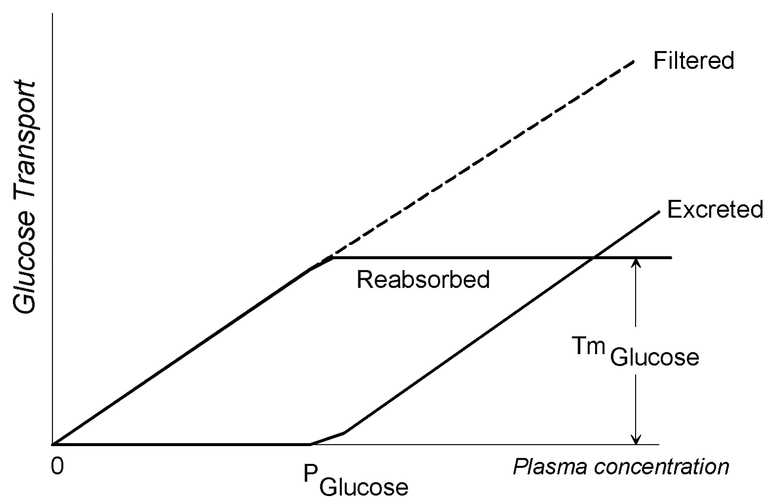
PROXIMAL TUBULE TRANSPORT (continued)

Summary: Entering the proximal tubule at a rate of about 120 ml/min is an ultrafiltrate of blood plasma. As a direct or indirect consequence of active transport, about 70% of the amount filtered is reabsorbed and returned to the body by way of the peritubular capillaries and renal veins. Since the proximal tubule is quite permeable to water, the tubular fluid remains iso-osmotic to plasma, but its composition is changed (e.g. no glucose, higher urea and creatinine concentrations, about the same sodium and chloride concentrations). The remaining fluid leaves the proximal tubule and enters the loop of Henle at a rate of about 30-35 ml/min.



F. Tubular Transport Maximum [T_m]: For many substances transported by carriers (active transport or facilitated diffusion), there exists some maximum rate for their transport; this is termed their tubular transport maximum or T_m

Examples: Glucosuria in diabetes mellitus
Albuminurea in nephritis



LOOP OF HENLE (& INITIAL DISTAL TUBULE) TRANSPORT

A. Role: establishes an appropriate osmotic environment for the adjustment of fluid balance

B. Active Reabsorption

Sodium ion	about 75% of amount entering loop
Chloride ion	about 70% of amount entering

C. Passive Reabsorption

Water	about 25% of amount entering

D. No Transport

Creatinine

LOOP OF HENLE TRANSPORT (continued)

Summary: Because the reabsorption of sodium and chloride (the major dissolved substances) is much more rapid than the reabsorption of water, the tubular fluid becomes quite hypo-osmotic (to about one-third the osmolality of plasma). Thus, a hypo-osmotic fluid leaves the loop of Henle (and enters the distal tubule) at the rate of about 20 ml/min.

COLLECTING TUBULES/DUCT TRANSPORT

A. Role: Final adjustment of the fluid to be excreted in order to maintain homeostasis

B. Reabsorption (variable)

  1. Active transport

     Na^+ osmotic and electrolyte balance
     Cl^- osmotic and electrolyte balance

  2. Passive electrochemical diffusion or osmosis

     urea body fluid balance
     H_2O osmotic and body fluid balance

  3. Associated with renal metabolism

     HCO_3^- acid-base balance

C. Secretion (variable)

  1. Active transport

     K^+ electrolyte balance
     H^+ acid-base balance

  2. Associated with renal metabolism

     NH_4^+ acid-base balance

D. No Transport

  1. Tubule impermeable

     creatinine

Summary: leaving the collecting duct (to be excreted as urine) is a fluid of varying composition, varying osmolality (hyper-, hypo-, or iso-osmotic), varying pH, and varying volume (0.2 to 20 ml/min), as required to satisfy homeostasis.