Lord Nephros, we pray that you will shower your wisdom upon us all.
HOMER W. SMITH, 1895-1962

SCIENTIST, TEACHER, EXPLORER, PHILOSOPHER, NOVELIST AND PERENNIAL STUDENT
Superficially, it might be said that the function of the kidneys is to make urine; but in a more considered view one can say that the kidneys make the stuff of philosophy itself.

Homer Smith
MAJOR FUNCTIONS OF THE KIDNEY

♦ REGULATION OF BODY FLUID VOLUME
♦ REGULATION OF OSMOTIC BALANCE
♦ REGULATION OF ELECTROLYTE COMPOSITION
♦ REGULATION OF ACID-BASE BALANCE
♦ REGULATION OF BLOOD PRESSURE
♦ ERYTHROPOIESIS
♦ EXCRETION OF WASTE PRODUCTS AND FOREIGN SUBSTANCES
SYSTEM REQUIREMENTS

♦ PROCESS LARGE VOLUME OF FLUID

♦ LARGE SURFACE TO VOLUME RATIO

♦ CLOSE CONTROL

♦ MINIMAL ENERGY COST

♦ RETAIN NUTRIENTS
PROCESS LARGE VOLUME OF FLUID:

- Renal Blood Flow (RBF) = 1.2 L/min, >1700 L/day, 20-25% of cardiac output.

- Renal Plasma Flow (RPF) = 660 mL/min, 950 L/day

- Glomerular Filtration Rate (GFR) = 125 mL/min, 180 L/day
SYSTEM REQUIREMENTS

LARGE SURFACE TO VOLUME RATIO:

2,000,000 nephrons in the two kidneys

<table>
<thead>
<tr>
<th>Blood Flow:</th>
<th>Glomerular Filtration:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1200 mL/min</td>
<td>125 mL/min</td>
</tr>
<tr>
<td>0.006 mL/min/nephron</td>
<td>0.000063 mL/min/nephron</td>
</tr>
</tbody>
</table>

Excretion Rate:

~1 mL/min
~0.0000005 mL/min/nephron
<table>
<thead>
<tr>
<th></th>
<th>Plasma Conc. mM</th>
<th>Filtered/day mmoles</th>
<th>Excreted/day mmoles</th>
<th>Percent Reabsorbed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>140</td>
<td>25,200</td>
<td>103</td>
<td>99+</td>
</tr>
<tr>
<td>Cl</td>
<td>105</td>
<td>18,900</td>
<td>103</td>
<td>99+</td>
</tr>
<tr>
<td>HCO$_3^-$</td>
<td>25</td>
<td>4,500</td>
<td>2</td>
<td>99+</td>
</tr>
<tr>
<td>K</td>
<td>4</td>
<td>720</td>
<td>100</td>
<td>86+</td>
</tr>
<tr>
<td>Glucose</td>
<td>5</td>
<td>900</td>
<td>trace</td>
<td>100</td>
</tr>
<tr>
<td>Urea</td>
<td>5</td>
<td>900</td>
<td>360</td>
<td>60</td>
</tr>
</tbody>
</table>
ANATOMY OF THE NEPHRONS

Cortical nephron
- distal tubule
- proximal tubule
- glomerulus

Juxtamedullary nephron
- juxtaglomerular apparatus

Henle’s loop
- thick segment
- thin segment

Collecting tubule

Cortex

Medulla
- Outer
- Inner
BASIC NEPHRON FUNCTIONS

1. Filtration
2. Reabsorption
3. Secretion
4. Excretion
SOLUTE-NEPHRON INTERACTIONS

FILTRATION ONLY

- Inulin
- Iothalamate

FILTRATION + SECRETION

- Hippurates, Penicillin
- Furosemide

FILTRATION + REABSORPTION

- Na. Cl, Urea
- Glucose
First to apply a magnifying lens to the kidney.

Discovered that the kidney is not parenchyme but a mass of tubules.

“...the substance of the kidneys is nothing else than an aggregate of an infinite number of vessels of a kind peculiar to itself. Having cut through any part of the kidney, certain fibres or filaments extending from the outer surface to the hollow or pelvis are quite plainly visible ...If therefore you compress these filaments from their further end...you will find water welling up everywhere. If you are not afraid to present this to your tongue, you will discover a certain saltiness and in some the taste of urine...You may observe this if you apply a glass lens to your eye for then, when the tubules are compressed, the urine is very clearly seen welling out as if gushing forth from so many little water pipes. From these things we can confidently infer that the substance of the kidney, even though they have called it parenchym, is nothing else than...a mass of caniliculae and capillary spaces through which the urine flows into the pelvis...”
“In all kidneys which up to this time I have been able to get, I have detected a number of very small glands. …a black fluid mixed with spirit of wine should be injected through the renal artery until the whole kidney swells, and the exterior grows black. …when the kidney is sectioned ….longitudinally, between the bundles of the urinary vessels and the narrow space formed by them, one will see these same innumerable glands attached like apples to the blood vessels, the latter swollen with the black liquid and stretched out into the form of a beautiful tree…”

Marcello Malpighi, 1666
WILLIAM BOWMAN, 1842

Bowman using a more powerful microscope and better dyes, was able to describe the afferent and efferent arterioles, the glomerular capillaries enclosed in a capsule and the peritubular capillaries.
In 1844 Ludwig proposed a purely mechanistic theory for urine formation.

Filtration occurs at the glomeruli. Blood pressure pushes fluid through the wall of the glomerular capillaries into the tubules. This fluid carries all the components of plasma except for proteins.

He also proposed that part of the fluid entering the nephron is reabsorbed by an ‘endosmotic force’ due to the presence of protein in the peritubular capillary blood.
ALFRED N. RICHARDS

A.N. Richards and his associates:

Developed the micropuncture technique.

Proved that fluid entering Bowman’s capsule is an ultrafiltrate of plasma.
THE FILTRATION PATHWAY

- Bowman’s space
- Epithelial foot processes
- Slit membrane
- Lamina rara
- Lamina densa
- Lamina rara
- Basement membrane
- Fenestra
- Endothelial cell
- Capillary lumen
**EFFECT OF DISEASE ON GLOMERULAR PERMEABILITY TO LARGE MOLECULES**

<table>
<thead>
<tr>
<th>Macromolecule</th>
<th>Molecular Radius (A)</th>
<th>Fractional Clearance $(U/P)_m/(U/P)_i$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal Values</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neutral Dextran</td>
<td>36</td>
<td>0.19</td>
</tr>
<tr>
<td>Dextran Sulfate</td>
<td>36</td>
<td>0.015</td>
</tr>
<tr>
<td><strong>Experimental Glomerular Nephritis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutral Dextran</td>
<td>36</td>
<td>0.14</td>
</tr>
<tr>
<td>Dextran Sulfate</td>
<td>36</td>
<td>0.24</td>
</tr>
</tbody>
</table>