Glomerular Filtration Rate(GFR) Physiology and Measurement

The **glomerular filtration rate (GFR)** refers to the rate at which plasma is filtered through the glomerular capillaries into the Bowman's space. It represents the total ultrafiltration rate of all functioning nephrons and serves as a critical measure of renal excretory function.

Since GFR is a rate, it is expressed in units of volume over time, typically **milliliters per minute (mL/min)** or **liters per day (L/day)** . It reflects how effectively the kidneys are filtering blood and removing waste products.

GFR is proportionate to body size, and the standard reference value for adults is approximately **120 ± 25 mL/min/1.73 m²** after adjustment for body surface area.

A reduction in GFR may lead to the accumulation of metabolic waste products and disturbances in fluid, electrolyte, and acid-base balance, potentially disrupting homeostasis across multiple organ systems.

Direct and Indirect Measurement of GFR

GFR can be measured **directly** using substances like **inulin** or **radiolabeled ethylenediamine tetraacetic acid (EDTA)** . These compounds are freely filtered at the glomerulus and neither reabsorbed nor secreted in the tubules.

In clinical practice, GFR is more commonly **estimated indirectly** using **urea** or **creatinine clearance** , which are easier to assess but less accurate due to partial tubular reabsorption or secretion.

Determinants of GFR

There are two main physiological determinants of glomerular filtration:

1. **Hydrostatic pressure**
2. **Oncotic pressure**

1. Hydrostatic Pressure

The glomerular capillary wall is composed of fenestrated endothelium, a basement membrane, and podocytes. This structure determines the capillary's selective permeability, allowing free passage of small molecules such as sodium, potassium, creatinine, glucose, and water. Larger molecules, particularly those above 5,000 Daltons and negatively charged substances like albumin, do not cross the barrier.

The **net pressure gradient between the glomerular capillaries and Bowman's space** is the primary driving force for filtration and is determined by the balance between hydrostatic and oncotic pressures.

The standard formula for GFR is:

GFR = Kf × (P_gc ? P_bs ? ?_gc)

Where:

- **Kf** is the filtration coefficient (product of capillary permeability and surface area)
- **P_gc** is the glomerular capillary hydrostatic pressure
- **P_bs** is the Bowman's space hydrostatic pressure
- **?_gc** is the glomerular capillary oncotic pressure

The **afferent and efferent arterioles** play a crucial role in regulating glomerular hydrostatic pressure. Afferent arteriole dilation and efferent arteriole constriction increase pressure within the glomerular capillaries, thereby increasing GFR. In contrast, afferent constriction and efferent dilation reduce glomerular pressure and GFR.

Unlike most capillary beds, glomerular capillaries maintain a **relatively constant hydrostatic pressure** , averaging around **45 mm Hg** . This is significantly higher than the hydrostatic pressure in systemic capillaries, where it typically falls from 40 mm Hg to below 15 mm Hg.

In the urinary (Bowman's) space, the pressure is generally low, around **10 mm Hg** , resulting in a strong filtration gradient that favors the movement of fluid from the capillary lumen into the nephron.

On average, about **120 mL/min or 180 liters/day** of plasma is filtered into the Bowman's space. Considering a typical **renal plasma flow (RPF)** of 625 mL/min, approximately **20 percent** of the plasma volume is filtered, a ratio known as the **filtration fraction** .

The filtration fraction is calculated as:
Filtration fraction = GFR ÷ [(1 ? hematocrit) × renal blood flow]

2. Oncotic Pressure

In peripheral capillary beds, oncotic pressure increases only slightly due to the low volume of fluid filtered. However, in the glomerulus, filtration of a high proportion of plasma leads to a **significant increase in oncotic pressure** within the capillary lumen.

Although water and small solutes are filtered, plasma proteins such as **albumin** are retained due to their large size and negative charge. As more fluid is filtered out along the capillary loop, the concentration of proteins increases, which elevates the **oncotic pressure** from approximately **23 mm Hg at the afferent end** to around **40 mm Hg at the efferent end** .

This rising inward pressure eventually balances the outward hydrostatic pressure, leading to a state called **filtration equilibrium** , at which point further filtration ceases.

Estimating GFR in Clinical Practice

1. Creatinine Clearance (CrCl)

Creatinine is an endogenous substance that is freely filtered at the glomerulus. It is not significantly reabsorbed or secreted under normal conditions, making it a practical surrogate for estimating GFR.

The amount of creatinine excreted in a **24-hour urine sample** approximates the amount filtered, as long as the renal function is stable.

The formula is:
CrCl = (Urine creatinine × Urine volume) ÷ Serum creatinine

Although convenient, CrCl slightly **overestimates GFR** due to minor tubular secretion of creatinine. It can also be **influenced by certain drugs** such as **trimethoprim** and **cimetidine** , which inhibit tubular secretion.

2. Estimated GFR (eGFR)

The most widely used equations for estimating GFR include:

- **Modification of Diet in Renal Disease (MDRD) equation**
- **CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation**

These formulas use **serum creatinine** , **age** , **sex** , and **race** to estimate GFR without the need for urine collection. However, they can be inaccurate in individuals with **abnormal muscle mass** , including the elderly, bodybuilders, or individuals with muscle wasting.

Steady-state conditions must be present for these estimates to be valid. This means the rate of creatinine production must equal the rate of excretion. If the serum creatinine is rising or falling rapidly (as in acute kidney injury), the estimates may be misleading.

3. Cystatin C

Cystatin C is an emerging biomarker that may provide a **more accurate estimate of GFR** than creatinine, particularly in non-steady-state conditions or individuals with abnormal muscle mass.

Regulation of GFR

The kidneys maintain a **stable GFR** through both **intrinsic autoregulatory** and **extrinsic hormonal** mechanisms.

A. Intrinsic Regulation

1. **Myogenic mechanism** – Afferent arterioles constrict in response to elevated blood pressure to prevent overfiltration and dilate when pressure drops to preserve filtration.
2. **Tubuloglomerular feedback** – The **macula densa** detects changes in sodium chloride delivery and signals afferent arteriole tone accordingly. Low NaCl delivery stimulates renin release and afferent vasodilation. High NaCl delivery triggers vasoconstriction to reduce GFR.

B. Extrinsic Regulation

1. **Renin-Angiotensin-Aldosterone System (RAAS)** – Angiotensin II constricts efferent arterioles, maintaining glomerular pressure and GFR during hypotension.
2. **Sympathetic nervous system** – Stimulates afferent and efferent arteriolar constriction in response to low blood pressure or stress, with ?1-receptor activation on juxtaglomerular cells promoting renin secretion.
3. **Atrial Natriuretic Peptide (ANP)** – Released from atrial myocytes in response to high volume. It dilates afferent arterioles and constricts efferent arterioles, increasing GFR.

High-Yield Points

- GFR reflects the kidney's filtration capacity and is a key marker of renal function.
- It is driven by the balance between hydrostatic and oncotic pressures across the glomerular capillary.
- Autoregulation via the myogenic response and tubuloglomerular feedback maintains stable filtration rates.
- CrCl and eGFR estimates are useful in practice but have limitations, especially in acute conditions.
- GFR declines in chronic kidney disease and acute kidney injury and must be monitored to guide clinical management.