Glomerular Filtration: An Overview

Mary Jo Holechek

Editor’s Note: This article continues a renal physiology continuing education series to run in the Nephrology Nursing Journal. The articles, which are updates of manuscripts that previously appeared in the journal, are written by experts in nephrology and contain the most up-to-date information and research available.

Glomerular filtration is the first step in the complex process of urine formation. For filtration to occur, a rapid renal blood flow (RBF) at a consistent pressure is essential. There are many factors that can alter RBF and, thus, the rate of glomerular filtrate generation. At any given time, especially under the condition of stress, multiple factors act and counteract to maintain a normal glomerular filtration rate (GFR) despite changes in RBF. This article will examine the unique characteristics of the renal circulation, describe the physiology of glomerular filtration, review the extrinsic and intrinsic factors that can alter renal hemodynamics, and discuss a clinical situation in which multiple factors are interacting in an effort to maintain the RBF and GFR despite systemic pressure changes.

Renal Circulation

Blood flows into the kidneys at a rate of about 1,000-1,200 ml per minute, representing approximately 20%-25% of the cardiac output. This rapid blood flow rate exceeds the metabolic and oxygen needs of the kidneys but facilitates efficient clearance of metabolic waste products.

To understand glomerular filtration, it is essential to consider the special characteristics of the renal circulation. Figure 1 illustrates the gross renal circulatory anatomy.

The renal artery pressure is approximately 100 mmHg. This high pressure is maintained up to the afferent arteriole, the location of the first major point of vascular resistance. Across the afferent arteriole, the arterial pressure falls to about 40-60 mmHg. Although this is a significantly lower pressure than present in the systemic circulation, this pressure is higher than that in the glomerular capillary bed. This pressure is referred to as hydrostatic pressure. Maintaining a hydrostatic pressure of about 50 mmHg is the key to glomerular filtration, as it is needed to overcome other opposing pressures present in the glomerular capillaries and Bowman’s space.

The glomerulus is a bundle of capillaries that are highly porous compared to systemic capillaries. The portion of the blood that is not filtered across the filtration barriers in the glomerulus is a significantly lower pressure than present in the systemic circulation, the renal arteriole. The filtration of blood occurs in the glomerulus, and the filtrate is then transported into the Bowman’s capsule and ultimately into the collecting ducts, where it is modified to produce urine.

The formation of urine is a process that begins with glomerular filtration and is greatly influenced by changes in renal hemodynamics. Selective filtration of the blood is possible because of the unique characteristics of the glomerulus and renal circulation. Many factors interact to maintain a consistent blood flow allowing filtration and urine formation to continue despite systemic changes in blood pressure. Factors that impact on renal hemodynamics include the autoregulatory mechanism, the renin-angiotensin mechanism, eicosanoids, kinins, the sympathetic nervous system (SNS), catecholamines, antiuretic hormone, endothelin, nitric oxide, atrial natriuretic peptide, and dopamine. Knowledge of the effects of these factors will allow the nephrology nurse to predict, identify, and assist in the treatment of clinical conditions that can alter renal hemodynamics and glomerular filtration.

Goal:
Discuss the principles of glomerular filtration and renal hemodynamics and provide nephrology nurses with the ability to predict, identify and assist in the treatment of clinical conditions that can alter glomerular filtration and renal hemodynamics.

Objectives:
1. Define and explain the process of glomerular filtration.
2. Identify factors that can influence the glomerular filtration process.
3. List methods to measure or estimate glomerular filtration rate (GFR).

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The Nephrology Nursing Certification Commission (NNCC) requires 60 contact hours for each recertification period for all nephrology nurses. Forty-five of these 60 hours must be specific to nephrology nursing practice. This CE article may be applied to the 45 required contact hours in nephrology nursing.
glomerular capillaries returns to the central circulation via the peritubular capillary (PTC) network. (See the first article in the physiology series for a discussion of the PTC network.)

### Glomerular Filtration

#### Glomerular anatomy.

The porous glomerular capillaries rest between the afferent and efferent arterioles (see Figure 2). Their function is to filter large quantities of water and solutes from the plasma. As blood flows through the glomerulus a portion is sieved through the filtering layers of the glomerular capillaries into the Bowman’s space. The filtration barrier is composed of three layers that allow for the filtration of solutes (e.g., blood urea nitrogen, creatinine, electrolytes) and water, but prevent the loss of blood components such as red and white blood cells and plasma proteins. The three layers are the glomerular capillary endothelium, glomerular basement membrane, and visceral layer of Bowman’s capsule (epithelial cell layer) (see Figure 2).

The first layer of the filtration barrier is the capillary endothelium, which has large fenestrations that allow the free filtration of substances with diameters up to 100 nm, thus excluding blood cells and large plasma proteins. The surface of the endothelial cells has a negative charge that inhibits the movement of negatively charged substances such as plasma proteins, as like-charges repel each other.

The second layer, the glomerular basement membrane, represents the major barrier to the filtration of macromolecules. The glomerular basement membrane is made of fibrous proteins such as collagen, fibrin, and laminin, which intertwine to form a meshwork. As the fibers cross each other, small openings are created through which selective filtration occurs. The crossed fibers act as a size barrier and restrict the filtration of large molecules. This layer also contains anionic sialoproteins that further inhibit filtration by repelling other negatively charged ions.

The third layer, composed of epithelial cells, is the visceral layer of the Bowman’s capsule. These epithelial cells, called podocytes, are attached directly to the exterior surface of the basement membrane. The podocytes branch into multiple finger-like projections called foot processes. These foot processes, which cover the outer surface of the basement membrane, are in close proximity to each other forming narrow elongated, slit-type openings about 25-60 nm wide. These openings, called slit pores, are covered by thin diaphragms. The foot processes have anionic sialoproteins on their borders that form the slit pores, generating a highly negatively charged region through which the filtrate must pass. These negative charges assist in preventing plasma proteins from entering the tubular fluid since plasma proteins carry negative charges. These narrow slits combined with the negative charges of the podocytes provide the final barrier to molecule movement through the glomerular membrane.

The glomerulus is a selective filtration membrane. The factors that determine which molecules are filtered are molecular size, electrical charge, protein binding, configuration, and rigidity. Small molecules with molecular weights [MW] less than 7,000 Daltons (e.g., water, MW 18; and all ions...
including sodium, potassium, chloride, phosphate, magnesium, and calcium) are filtered without restriction. Larger molecules, such as myoglobin with a MW of 17,000 Daltons, are filtered to a lesser degree. Very large molecules, such as plasma proteins with molecular weights approaching 70,000 Daltons, are restricted from passing through the normal glomerulus.

As the filtration barrier has a net negative electrical charge, the movement of large negatively charged molecules is restricted more than molecules with a positive or neutral charge. As a result, proteins, which are negatively charged, are not freely filtered by the glomerulus. Likewise, drugs, ions, or small molecules bound to protein are not filtered. Round molecules do not filter as easily as ellipsoid molecules. The more rigid a molecule, the less easily it filters. Normal glomerular filtrate is essentially protein free but contains crystalloids (e.g., sodium, chloride, creatinine, urea, uric acid, and phosphate) in the same concentration as plasma.

A final anatomical aspect of the glomerulus is the mesangial cells, which are located between the capillary loops. They support the capillary structures and carry out some phagocytic activities. They also demonstrate contractile properties and can alter the total filtration surface area. Mesangial cells contract when exposed to vasoconstrictive substances, such as angiotensin II, thus decreasing the effective filtration surface area and glomerular filtration rate. The special filtering characteristics of the glomerulus coupled with the unique renal circulation allow for effective glomerular filtration to occur.

**Glomerular Filtration Rate and Filtration Fraction**

Glomerular filtrate moves into the Bowman’s space and then into the tubular component of the nephron. In the average 70 kg adult, glomerular filtration rate (GFR) is approximately 125 ml/minute. This means that about 180 L of glomerular filtrate is produced in a 24-hour period, which is more than 30 times the average total blood volume. All but one to two liters are reabsorbed from the nephron into the peritubular capillary
and vasa recta network. The formation of such a large amount of filtrate assures adequate filtration of plasma, but requires very efficient reabsorptive processes to prevent volume and electrolyte depletion.

GFR, which indicates the volume of filtrate moving from the glomerular capillaries into Bowman’s space per unit of time, is calculated by determining the renal clearance of a marker substance. Clearance (Cl) is defined as the volume of plasma from which a substance is completely removed or cleared by the kidneys per unit of time. The ideal marker for measuring Cl does not bind to proteins, is freely filtered at the glomerulus, and is neither reabsorbed, secreted, synthesized, nor metabolized by the tubules. Substances that do not meet these requirements can result in falsely elevated or decreased values of GFR. As there is no naturally occurring ideal marker, endogenous creatinine (Cr) often is used to measure clearance; however, since a small amount of creatinine is secreted into the tubule, GFR measured with creatinine clearance (CrCl) will be overestimated. Since individual GFRs vary widely, a change in GFR over time is more important than the absolute value of the GFR. Thus, if the CrCL method is used, it should be used for all measurements of GFR to allow for comparison of values over time.

Inulin is a marker that meets all the requirements of an ideal marker for measuring GFR, but is not often used because it is an exogenous substance that must be infused for several hours at a constant rate making it both impractical and costly.

A more practical method to determine the CrCl involves the collection of a 24-hour urine and midpoint plasma Cr (P_Cr). CrCl is calculated using Equation 1 where U_Cr is the urine creatinine concentration, mg/dl; U_v is the average urine flow rate, ml/min; and P_Cr is the plasma creatinine concentration, mg/dl.

**Equation 1**

\[
CrCl = \frac{U_Cr}{U_v - \frac{P_Cr}{\Pi}}
\]

Another method for determining CrCl involves the intravenous injection of a radioactive marker. Clearance of the radioactive marker is assessed by serial scans. The results using this method correlate closely with inulin clearance. The CrCl estimates the GFR and gives a gross indication of how well the kidneys are functioning based on their ability to remove a marker substance.

As using inulin is impractical, urine collections are often inaccurate, and renal scans are costly and require special equipment, the use of alternative methods to estimate GFR have been proposed. The National Kidney Foundation, in its Kidney Disease Outcome Initiative guidelines, recommends the use of the Cockcroft-Gault formula (see Equation 2) or the more complicated Modification of Diet in Renal Disease (MDRD) study formula (available at www.kidney.org).

**Equation 2: Cockcroft-Gault Formula**

\[
GFR = \frac{(140 - \text{Age}) \times \text{Body weight (kg)}}{72 \times \text{Serum creatinine (mg/dl)}} \times \text{(X 0.85 for females)}
\]

Both consider the effects of age, gender, and body weight on creatinine, but no special lab or diagnostic tests are required. The MDRD formula also factors in the effects of race, albumin, and serum urea nitrogen. There are hand-held personal data assistant programs and Web-based calculators with these formulas that easily complete the calculations after the raw data has been entered. Use of one of these standardized formulas with a programmed calculator ensures accurate, consistent results when tracking a GFR over time.

The glomerular filtrate is derived from the plasma portion of whole blood. The term filtration fraction (FF) describes the percentage of the plasma that becomes glomerular filtrate. Since plasma volume is about 55% of total blood volume, normal renal plasma flow (RPF) is approximately 660 ml/min (1200 ml/min x 0.55 = 660 ml/min). The FF can then be determined using Equation 3.

**Equation 3**

\[
FF = \frac{GFR}{RPF} = \frac{125 \text{ ml/min}}{660 \text{ ml/min}} = 19\%
\]

Thus, almost 20% of the plasma passing through the glomerulus becomes glomerular filtrate in the average adult.

Pressures influencing normal glomerular filtration. Glomerular filtration is controlled by four pressures, the algebraic sum of which defines the net filtration pressure. These pressures are:

1. Glomerular capillary hydrostatic pressure (P_0), which is the pressure exerted against the capillary wall by fluid within the capillary lumen. This pressure is generated by the blood pressure. This value ranges from 40-60 mmHg and favors the movement of fluid from the capillary lumen to the Bowman’s space (see Figure 3).
2. Glomerular capillary colloid osmotic pressure (P_π), which is about 18 mmHg. This force, generated by plasma proteins within the capillaries, retards the movement of fluid out of the capillary lumen.
3. Bowman’s space hydrostatic pressure (P_σ), which is the pressure exerted against the outer layer of the capillary walls by fluids within Bowman’s space. This value is about 10 mmHg and also retards the movement of fluid out of the capillary lumen.
4. Bowman’s space colloid osmotic pressure (P_π), which is normally 0 mmHg because normal filtrate is void of protein.

Net filtration pressure (NFP), which is the sum of these negative and positive pressures, can be calculated with the following formula (see Equation 4). An average P_0 of 45 mmHg is used.

**Equation 4**

\[
NFP = (P_{GC} - P_{BS}) \cdot (\Pi_{GC} \cdot \Pi_{BS})
\]
These pressures are based on animal models but are thought to be similar to those in humans. Therefore, for adequate filtration to occur, an NFP of approximately 17 mmHg is required to produce approximately 125 ml/min of glomerular filtrate.

As blood progresses through the glomerulus toward the efferent arteriole, the $\Pi_{GC}$ increases from 18 to approximately 35 mmHg, reflecting the removal of protein free fluid from the glomerular capillary. $P_{GC}$, $P_{BS}$, and $\Pi_{BS}$ remain essentially unchanged along the capillary loop. As a result, NFP decreases along the length of the capillary and in some species is zero before or at the end of the capillary.

The point at which NFP falls to zero is called filtration equilibrium and is the point at which glomerular filtration ceases.

**Conditions altering glomerular filtration rate.** The GFR can be altered by changes in any of the above four pressures or the ultrafiltration coefficient. Theoretically, there is a direct relationship between the renal plasma flow rate (the primary determinant of $P_{GC}$) and the GFR. If $RPF$ increases due to volume expansion or other causes, GFR should also rise. However, a change in RBF rarely occurs in isolation and is usually accompanied by changes in afferent or efferent arteriolar resistance designed to maintain a consistent $P_{GC}$ and, therefore, GFR at normal levels. Through a process called autoregulation, the kidney is adept at maintaining a normal GFR over a wide range of vascular pressures.

Changes in the glomerular colloid osmotic pressure ($\Pi_{GC}$) can also alter GFR. Serum protein is the major determinant in colloid osmotic pressure. If $\Pi_{GC}$ increases due to increased protein concentration, as in hypovolemic states, NFP and, thus, GFR will fall in an effort to prevent further intravascular volume loss. If the $\Pi_{GC}$ decreases due to protein losses, as in severe malnutrition or hypoalbuminemic states, GFR can increase.

When $P_{BS}$ increases, as in urinary tract obstruction, GFR falls. GFR decreases as glomerular filtrate outflow from the tubule is obstructed and the pressure of the increased filtrate volume in the Bowman’s space opposes the forces favoring filtration.
If $P_{m}$ rises above 0 mmHg, as it does in nephrotic conditions where protein is filtered into the Bowman’s space because of changes in the filtering membrane, GFR can increase. The presence of plasma proteins in Bowman’s space favors increased filtration due to the increased colloid osmotic pressure within that compartment.

A final factor that can alter GFR is a change in the ultrafiltration coefficient ($K_f$) of the glomerular capillary membrane. The $K_f$ is the product of the surface area and hydraulic permeability of the glomerular membrane. Vasoactive substances such as angiotensin II can cause the mesangial cells to contract thereby decreasing the available surface area for filtration resulting in a decreased GFR.

Glomerular filtration is the critical initial step in urine formation. In order for adequate solute and water removal to occur, glomerular filtrate must be generated at a constant rate. Changes in RPF, hydrostatic and osmotic pressures, available filtering surface area, and glomerular membrane permeability can upset the internal environment by increasing or decreasing GFR. Fortunately, there exists a complicated system where factors both extrinsic and intrinsic to the kidneys act simultaneously to minimize the effects of these changes.

**Summary**

Glomerular filtration is a complex process that is impacted by numerous intrinsic and extrinsic factors that can alter renal hemodynamics and RBF. These factors interact in an attempt to maintain a consistent glomerular filtration rate under a wide variety of normal and pathologic conditions. If these integrated systems fail, serious problems can develop with renal function and urine production and excretion. Understanding the physiology of glomerular filtration and the interactions of factors altering renal hemodynamics will help the nephrology nurse in predicting, identifying, and assisting in the treatment of clinical conditions that alter glomerular filtration and renal hemodynamics.

**Additional Readings**


Glomerular Filtration: An Overview

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Posttest – 1.7 Contact Hours

Posttest Questions

(See posttest instructions on the answer form, on page 292.)

1. A rapid renal blood flow rate is necessary to assure
   A. the kidneys are oxygenated.
   B. efficient clearance of metabolic waste products.
   C. the metabolic needs of the kidneys are met.
   D. medullary blood flow is maintained.

2. The first point of major vascular resistance in the renal arterial system is the
   A. efferent arteriole.
   B. vasa recta.
   C. afferent arteriole.
   D. peritubular capillaries.

3. The glomerular capillary bed differs from other capillary beds in that it is
   A. a highly porous, high pressure system.
   B. not affected by systemic arterial pressure changes.
   C. freely permeable to blood proteins.
   D. an impermeable, low pressure system.

4. High pressure in the glomerular capillaries is essential to
   A. prevent hypotension.
   B. ensure perfusion of the vasa recta and peritubular capillary network.
   C. overcome other opposing pressures in the glomerulus and Bowman’s space.
   D. prevent the movement of plasma proteins into Bowman’s space.

5. Approximately what percentage of the cardiac output circulates through the kidneys per minute?
   A. 10%-15%
   B. 20%-25%
   C. 30%-35%
   D. 40%-45%

6. The major barrier to filtration of molecules in the glomerulus is
   A. glomerular capillary endothelium.
   B. glomerular basement membrane.
   C. visceral layer Bowman’s capsule.
   D. anionic sialoproteins.

7. Factors that determine which molecules are filtered include
   A. molecular size only.
   B. molecular size and charge only.
   C. molecular size, charge, and protein binding only.
   D. molecular size, charge, protein binding, and rigidity.

8. Constriction of the mesangial cells results in a(n)
   A. decrease in phagocytic activity.
   B. increase in the glomerular filtration rate (GFR).
   C. decrease in the surface area available for filtration.
   D. increase in catecholamine activity.

9. Which of the following would be found in normal glomerular filtrate?
   A. Urea only.
   B. Urea and sodium only.
   C. Urea, sodium, and creatinine only.
   D. Urea, sodium, creatinine, and albumin.

10. The normal GFR for an adult is
    A. 75 ml/min.
    B. 100 ml/min.
    C. 125 ml/min.
    D. 150 ml/min.

11. Efficient reabsorption processes of glomerular filtrate are required to prevent
    A. volume overload.
    B. dehydration.
    C. hypertension.
    D. hyperkalemia.

12. The GFR reveals
    A. how rapidly blood flows through the kidney per unit of time.
    B. the volume of solutes removed from the blood per unit of time.
    C. the rate at which solutes and water are reabsorbed by the peritubular capillary network per unit of time.
    D. the volume of filtrate moving from the glomerular capillaries into Bowman’s space per unit of time.

13. The production of massive amounts of glomerular filtrate is essential to
    A. assure adequate filtration of the complete plasma volume.
    B. maintain a normal systemic blood pressure.
    C. assure efficient removal of blood proteins.
    D. prevent circulatory collapse.

14. What is an ideal marker to measure glomerular filtration?
    A. Creatinine.
    B. Urea.
    C. Inulin.
    D. Potassium.

15. You are seeing Mrs. Sue in the clinic. She is 73 yrs old and weighs 72 kg. Her serum creatinine is 2.3. What is her estimated GFR?
    A. 25 ml/min.
    B. 29 ml/min.
    C. 33 ml/min.
    D. 40 ml/min.

16. A GFR determined using creatinine as the marker should
    A. predict the GFR exactly.
    B. slightly overestimate the GFR.
    C. slightly underestimate the GFR.
    D. not be used to estimate the GFR.

17. The NKF recommends the use of which method to estimate the GFR?
    A. 24 hour urine.
    B. inulin clearance.
    C. prediction equation.
    D. urea clearance.

18. Glomerular filtration is opposed by which of the following forces?
    A. Glomerular capillary hydrostatic pressure.
    B. Bowman’s capsule oncotic pressure.
    C. Glomerular capillary oncotic pressure.
    D. Peritubular capillary hydrostatic pressure.

19. You are seeing a patient in the clinic. The patient is malnourished and hypoalbuminemic. You would predict the GFR to
    A. be decreased.
    B. not be affected.
    C. be increased.
    D. fall to 0 ml/min.
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Goal: Discuss the principles of glomerular filtration and renal hemodynamics and provide nephrology nurses with the ability to predict, identify and assist in the treatment of clinical conditions that can alter glomerular filtration and renal hemodynamics.

Evaluation

1. The objectives were related to the goal.
   Strongly disagree 1 2 3 4 5
2. Objectives were met
   a. Define and explain the process of glomerular filtration.
   b. Identify factors that can influence the glomerular filtration process.
   c. List methods to measure or estimate glomerular filtration rate (GFR).
   Strongly disagree 1 2 3 4 5
3. I verify that I have completed this activity:
   (Signature)
   Comments
   _______________________________________________________________
   _______________________________________________________________
4. Suggest topics for future articles?
   _______________________________________________________________
   _______________________________________________________________