Case 28

Essential Calculations in Renal Physiology

This case will guide you through some of the basic equations and calculations in renal physiology. Use the data provided in Table 4-1 to answer the questions.

**TABLE 4-1  Renal Physiology Values for Case 28**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td>1 mL/min</td>
</tr>
<tr>
<td>Pu</td>
<td>100 mg/mL</td>
</tr>
<tr>
<td>Uu</td>
<td>12 g/mL</td>
</tr>
<tr>
<td>RAPAH</td>
<td>1.2 mg/mL</td>
</tr>
<tr>
<td>RVPAH</td>
<td>0.1 mg/mL</td>
</tr>
<tr>
<td>UPAH</td>
<td>650 mg/mL</td>
</tr>
<tr>
<td>PA</td>
<td>10 mg/mL</td>
</tr>
<tr>
<td>Ua</td>
<td>2 g/mL</td>
</tr>
<tr>
<td>Pb</td>
<td>10 mg/mL</td>
</tr>
<tr>
<td>Ub</td>
<td>10 mg/mL</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*PAH, para-aminobipiric acid; A, Substance A; B, Substance B.*

**QUESTIONS**

1. What is the value for the glomerular filtration rate (GFR)?

2. What is the value for the "true" renal plasma flow? What is the value for the "true" renal blood flow? What is the value for the "effective" renal plasma flow? Why is effective renal plasma flow different from true renal plasma flow?

3. What is the value for the filtration fraction, and what is the meaning of this value?

4. Assuming that Substance A is freely filtered (i.e., not bound to plasma proteins), what is the filtered load of Substance A? Is Substance A reabsorbed or secreted? What is the rate of reabsorption or secretion?

5. What is the fractional excretion of Substance A?

6. What is the clearance of Substance A? Is this value for clearance consistent with the conclusion you reached in Question 4 about whether Substance A is reabsorbed or secreted?

7. Substance B is 30% bound to plasma proteins. Is Substance B reabsorbed or secreted? What is the rate of reabsorption or secretion?
ANSWERS AND EXPLANATIONS

1. GFR is measured by the clearance of a glomerular marker. A glomerular marker is a substance that is freely filtered across the glomerular capillaries and is neither reabsorbed nor secreted by the renal tubules. The ideal glomerular marker is inulin. Thus, the clearance of inulin is the GFR.

The generic equation for clearance of any substance, X, is:

\[ C_x = \frac{U_x \times V}{P_x} \]

where

- \( C_x \) = clearance (mL/min)
- \( U_x \) = urine concentration of substance X (e.g., mg/mL)
- \( P_x \) = plasma concentration of substance X (e.g., mg/mL)
- \( V \) = urine flow rate (mL/min)

The GFR, or the clearance of inulin, is expressed as:

\[ \text{GFR} = \frac{U_{\text{inulin}} \times V}{P_{\text{inulin}}} \]

where

- \( \text{GFR} \) = glomerular filtration rate (mL/min)
- \( U_{\text{inulin}} \) = urine concentration of inulin (e.g., mg/mL)
- \( P_{\text{inulin}} \) = plasma concentration of inulin (e.g., mg/mL)
- \( V \) = urine flow rate (mL/min)

In this case, the value for GFR (clearance of inulin) is:

\[ \text{GFR} = \frac{12 \, \text{g/mL} \times 1 \, \text{mL/min}}{100 \, \text{mg/mL}} = \frac{12,000 \, \text{mg/mL} \times 1 \, \text{mL/min}}{100 \, \text{mg/mL}} = 120 \, \text{mg/mL} \]

2. Renal plasma flow is measured with an organic acid called para-aminohippuric acid (PAH). The properties of PAH are very different from those of inulin. PAH is both filtered across the glomerular capillaries and secreted by the renal tubules, whereas inulin is only filtered. The equation for measuring "true" renal plasma flow with PAH is based on the Fick principle of conservation of mass. The Fick principle states that the amount of PAH entering the kidney through the renal artery equals the amount of PAH leaving the kidney through the renal vein and the ureter. Therefore, the equation for "true" renal plasma flow is as follows:

\[ \text{RPF} = \frac{U_{\text{PAH}} \times V}{R_{\text{PAH}} - R_{\text{PAH}}} \]

where

- \( \text{RPF} \) = renal plasma flow (mL/min)
- \( U_{\text{PAH}} \) = urine concentration of PAH (e.g., mg/mL)
- \( R_{\text{PAH}} \) = renal artery concentration of PAH (e.g., mg/mL)
- \( R_{\text{PAH}} \) = renal vein concentration of PAH (e.g., mg/mL)
- \( V \) = urine flow rate (mL/min)

Thus, in this case, the "true" renal plasma flow is:

\[ \text{RPF} = \frac{650 \, \text{mg/mL} \times 1 \, \text{mL/min}}{1.2 \, \text{mg/mL} - 0.1 \, \text{mg/mL}} \]
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\[
RPF = \frac{650 \text{ mg/min}}{1.1 \text{ mg/mL}} = 591 \text{ mL/min}
\]

Renal blood flow is calculated from the measured renal plasma flow and the hematocrit, as follows:

\[
RBF = \frac{\text{RPF}}{1 - \text{Hct}}
\]

where

- \( RBF \) = renal blood flow (mL/min)
- \( \text{RPF} \) = renal plasma flow (mL/min)
- \( \text{Hct} \) = hematocrit (no units)

In words, \( RBF \) is \( \text{RPF} \) divided by one minus the hematocrit. **Hematocrit** is the fractional blood volume occupied by red blood cells. Thus, one minus the hematocrit is the fractional blood volume occupied by plasma. In this case, \( RBF \) is:

\[
RBF = \frac{591 \text{ mL/min}}{1 - 0.45} = 1075 \text{ mL/min}
\]

Looking at the equation for "true" renal plasma flow, you can appreciate that this measurement would be difficult to make in human beings—blood from the renal artery and renal vein would have to be sampled directly! The measurement can be simplified, however, by applying two reasonable assumptions. (1) The concentration of PAH in the renal vein is zero, or nearly zero, because all of the PAH that enters the kidney is excreted in the urine through a combination of filtration and secretion processes. (2) The concentration of PAH in the renal artery equals the concentration of PAH in any systemic vein (other than the renal vein). This second assumption is based on the fact that no organ, other than the kidney, extracts PAH. With these two assumptions (i.e., renal vein PAH is zero and renal artery PAH is the same as systemic venous plasma PAH), we have a much simplified version of the equation, which is now called "effective" renal plasma flow. Note that "effective" renal plasma flow is also the clearance of PAH, as follows:

\[
\text{Effective RPF} = \frac{U_{PAH} \times V}{F_{PAH}} = C_{PAH}
\]

For this case, effective RPF is:

\[
\text{Effective RPF} = \frac{650 \text{ mg/mL} \times 1 \text{ mL/min}}{1.2 \text{ mg/mL}} = 542 \text{ mL/min}
\]

Effective RPF (542 mL/min) is less than true RPF (591 mL/min). Thus, the effective RPF underestimates the true RPF by approximately 10% \( [(591 - 542)/591 = 0.11, \text{ or } 11\%] \). This underestimation occurs because the renal vein concentration of PAH is *not exactly* zero (as we had assumed), it is *nearly* zero. Approximately 10% of the RPF serves renal tissue that is not involved in the filtration and secretion of PAH (e.g., renal adipose tissue). The PAH in that portion of the RPF appears in renal venous blood, not in the urine.

Naturally, you are wondering, "When should I calculate true RPF and when should I calculate effective RPF?" Although there are no hard and fast rules among examiners, it is safe to assume that if you are given values for renal artery and renal vein PAH, you will use them to calculate true RPF. If you are given only the systemic venous plasma concentration of PAH, then you will calculate effective RPF.

3. Filtration fraction is the fraction of the renal plasma flow that is filtered across the glomerular capillaries. In other words, **filtration fraction** is GFR divided by RPF:

\[
\text{Filtration fraction} = \frac{\text{GFR}}{\text{RPF}}
\]
In this case:

\[
\text{Filtration fraction} = \frac{120 \text{ mL/min}}{591 \text{ mL/min}} = 0.20
\]

This value for filtration fraction (0.20, or 20%) is typical for normal kidneys. It means that approximately 20% of the renal plasma flow entering the kidneys through the renal arteries is filtered across the glomerular capillaries. The remaining 80% of the renal plasma flow leaves the glomerular capillaries through the efferent arterioles and becomes the peritubular capillary blood flow.

4. These questions concern the calculation of filtered load, excretion rate, and reabsorption or secretion rate of Substance A (Figure 4–1).

An interstitial-type fluid is filtered from glomerular capillary blood into Bowman’s space (the first part of the proximal convoluted tubule). The amount of a substance filtered per unit time is called the filtered load. This glomerular filtrate is subsequently modified by reabsorption and secretion processes in the epithelial cells that line the nephron. With reabsorption, a substance that was previously filtered is transported from the lumen of the nephron into the peritubular capillary blood. Many substances are reabsorbed, including \( \text{Na}^+ \), \( \text{Cl}^- \), \( \text{HCO}_3^- \), amino acids, and water. With secretion, a substance is transported from peritubular capillary blood into the lumen of the nephron. A few substances are secreted, including \( \text{K}^+ \), \( \text{H}^+ \), and organic acids and bases. Excretion is the amount of a substance that is excreted per unit time; it is the sum, or net result, of the three processes of filtration, reabsorption, and secretion.

We can determine whether net reabsorption or net secretion of a substance has occurred by comparing its excretion rate with its filtered load. If the excretion rate is less than the filtered load, the substance was reabsorbed. If the excretion rate is greater than the filtered load, the substance was secreted. Thus, it is necessary to know how to calculate filtered load and excretion rate. With this information, we can then calculate reabsorption or secretion rate intuitively.

The filtered load of any substance, \( X \), is the product of GFR and the plasma concentration of \( X \), as follows:

\[
\text{Filtered load} = \text{GFR} \times P_x
\]

where

- Filtered load = amount of \( X \) filtered per minute (e.g., mg/min)
- GFR = glomerular filtration rate (mL/min)
- \( P_x \) = plasma concentration of \( X \) (e.g., mg/mL)
The excretion rate of any substance, X, is the product of urine flow rate and the urine concentration of X:

\[ \text{Excretion rate} = \dot{V} \times U_x \]

where

- Excretion rate = amount of X excreted per minute (e.g., mg/min)
- \( \dot{V} \) = urine flow rate (mL/min)
- \( U_x \) = urine concentration of X (e.g., mg/mL)

Now we are ready to calculate the values for filtered load and excretion rate of Substance A, and to determine whether Substance A is reabsorbed or secreted. The GFR was previously calculated from the clearance of inulin as 120 mL/min.

\[
\text{Filtered load of A} = \text{GFR} \times P_A
\]
\[
= 120 \text{ mL/min} \times 10 \text{ mg/mL}
\]
\[
= 1200 \text{ mg/min}
\]

\[
\text{Excretion rate of A} = \dot{V} \times U_A
\]
\[
= 1 \text{ mL/min} \times 2 \text{ g/mL}
\]
\[
= 1 \text{ mL/min} \times 2000 \text{ mg/mL}
\]
\[
= 2000 \text{ mg/min}
\]

The filtered load of Substance A is 1200 mg/min, and the excretion rate of Substance A is 2000 mg/min. How can there be more of Substance A excreted in the urine than was originally filtered? Substance A must have been secreted from the peritubular capillary blood into the tubular fluid (urine). Intuitively, we can determine that the net rate of secretion of Substance A is 800 mg/min (the difference between the excretion rate and the filtered load).

5. The fractional excretion of a substance is the fraction (or percent) of the filtered load that is excreted in the urine. Therefore, fractional excretion is excretion rate \( U \times V \) divided by filtered load \( \text{GFR} \times P \), as follows:

\[
\text{Fractional excretion} = \frac{U_x \times \dot{V}}{\text{GFR} \times P_A}
\]

where

- Fractional excretion = fraction of the filtered load excreted in the urine
- \( U_x \) = urine concentration of X (e.g., mg/mL)
- \( P_A \) = plasma concentration of X (e.g., mg/mL)
- \( \dot{V} \) = urine flow rate (mL/min)
- \( \text{GFR} \) = glomerular filtration rate (mL/min)

For Substance A, fractional excretion is:

\[
\text{Filtration fraction} = \frac{\text{Excretion rate}}{\text{Filtered load}}
\]
\[
= \frac{U_A \times \dot{V}}{\text{GFR} \times P_A}
\]
\[
= \frac{2 \text{ g/mL} \times 1 \text{ mL/min}}{120 \text{ mL/min} \times 10 \text{ mg/mL}}
\]
\[
= 2000 \text{ mg/min}
\]
\[
= \frac{1200 \text{ mg/min}}{1200 \text{ mg/min}}
\]
\[
= 1.67, 167\%
\]

You may question how this number is possible. Can we actually excrete 167% of the amount that was originally filtered? Yes, if secretion adds a large amount of Substance A to the urine, over and above the amount that was originally filtered.
6. The concept of clearance and the clearance equation were discussed in Question 1. The renal clearance of Substance A is calculated with the clearance equation:

\[
C_A = \frac{U_A \times V}{P_A}
\]

\[
= \frac{2 \text{ g/mL} \times 1 \text{ mL/min}}{10 \text{ mg/mL}}
\]

\[
= \frac{2000 \text{ mg/mL} \times 1 \text{ mL/min}}{10 \text{ mg/mL}}
\]

\[
= 200 \text{ mL/min}
\]

The question asked whether this calculated value of clearance is consistent with the conclusion reached in Questions 4 and 5. (The conclusion from Questions 4 and 5 was that Substance A is secreted by the renal tubule.) To answer this question, compare the clearance of Substance A (200 mL/min) with the clearance of inulin (120 mL/min). Inulin is a pure glomerular marker that is filtered, but neither reabsorbed or secreted. The clearance of Substance A is higher than the clearance of inulin because Substance A is both filtered and secreted, whereas inulin is only filtered. Thus, comparing the clearance of Substance A with the clearance of inulin gives the same qualitative answer as the calculations in Questions 4 and 5—Substance A is secreted.

7. The approach to this question is the same as that used in Question 4, except that Substance B is 30% bound to plasma proteins. Because plasma proteins are not filtered, 30% of Substance B in plasma cannot be filtered across the glomerular capillaries; only 70% of Substance B in plasma is filterable. This correction is applied in the calculation of filtered load.

\[
\text{Filtered load of B} = \text{GFR} \times P_B \times \% \text{ filterable}
\]

\[
= 120 \text{ mL/min} \times 10 \text{ mg/mL} \times 0.7
\]

\[
= 840 \text{ mg/min}
\]

\[
\text{Excretion rate of B} = V \times U_B
\]

\[
= 1 \text{ mL/min} \times 10 \text{ mg/mL}
\]

\[
= 10 \text{ mg/min}
\]

Because the excretion rate of Substance B (10 mg/min) is much less than the filtered load (840 mg/min), Substance B must have been reabsorbed. The rate of reabsorption, calculated intuitively from the difference between filtered load and excretion rate, is 830 mg/min.

**Key topics**

- Clearance
- Effective renal plasma flow
- Excretion rate
- Filtered load
- Filtration fraction
- Fractional excretion
- Glomerular filtration rate (GFR)
- Hematocrit
- Reabsorption
- Renal blood flow
- Renal plasma flow
- Secretion