

Settings

1

2

3

4

Item 1 of 4

Question Id: 757

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

A

A

A

Text Zoom

Biologists investigating the morphologic changes associated with reversible cellular injury perform a procedure on anesthetized mice to assess the effects of transient hepatic ischemia. During the experiment, they clamp the hepatic artery and obtain liver biopsy samples at varying intervals. The samples are then examined by electron microscopy. Cells that are exposed to longer ischemic periods are found to have reduced numbers of ribosomes attached to the endoplasmic reticulum. This structural change is most likely to impair which of the following cellular functions?

A. ATP production

B. Drug detoxification

C. Synthesis of cell membrane proteins

D. Synthesis of cytosolic proteins

E. Synthesis of steroid hormones

Submit

Block Time Remaining: 00:00:03

TUTOR

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0

Feedback

II

Suspend

End Block

Windows

Search

Taskbar

5:12 PM

2/13/2019

Settings

1

2

3

4

Item 1 of 4

Question Id: 757

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Biologists investigating the morphologic changes associated with reversible cellular injury perform a procedure on anesthetized mice to assess the effects of transient hepatic ischemia. During the experiment, they clamp the hepatic artery and obtain liver biopsy samples at varying intervals. The samples are then examined by electron microscopy. Cells that are exposed to longer ischemic periods are found to have reduced numbers of ribosomes attached to the endoplasmic reticulum. This structural change is most likely to impair which of the following cellular functions?

☐ A. ATP production [3%]

☐ B. Drug detoxification [3%]

☒ C. Synthesis of cell membrane proteins [64%]

☐ D. Synthesis of cytosolic proteins [24%]

☐ E. Synthesis of steroid hormones [4%]

Omitted

Correct answer C

64%

Answered correctly

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09/18/2018

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Explanation

Protein targeting

Ribosomes initiate translation

Mitochondrion

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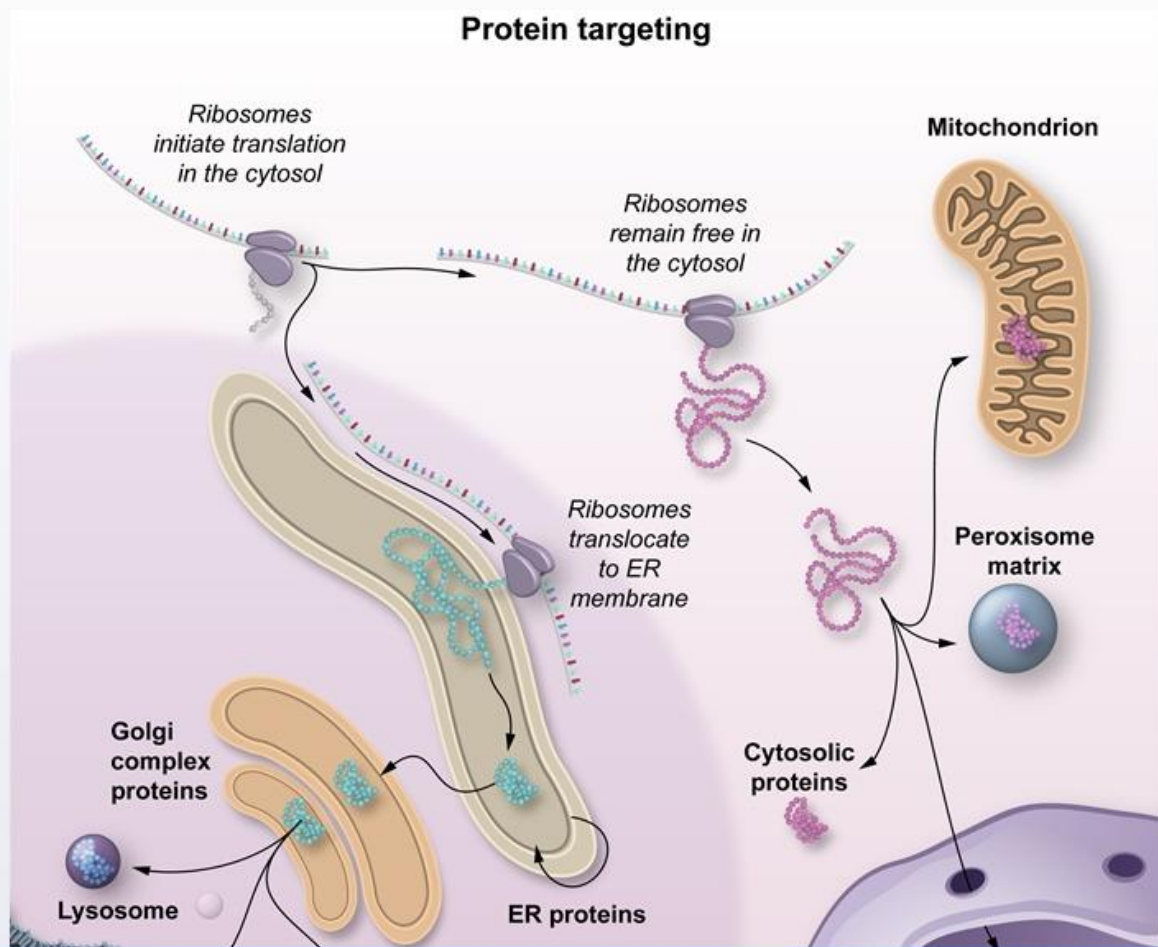
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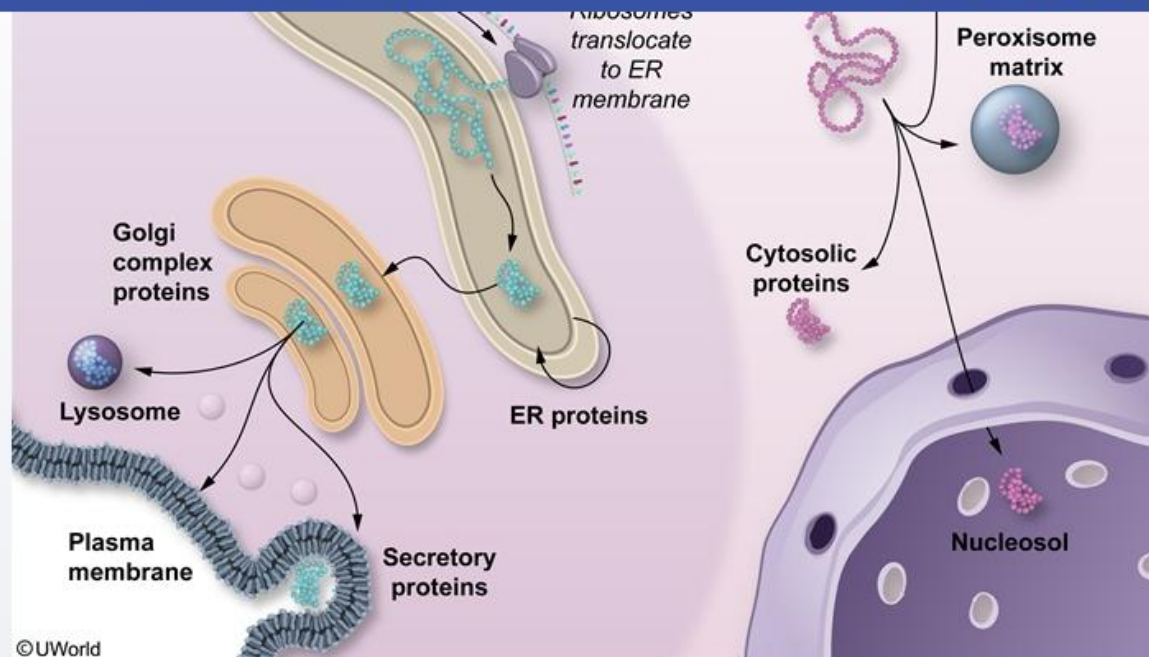
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5:13 PM

2/13/2019





Ribosomes are cellular organelles that synthesize proteins. Each ribosome consists of 2 subunits. The small ribosomal 40S subunit is responsible for binding mRNA (the protein synthesis template) and tRNA (carries amino acids). The larger 60S subunit contains peptidyl transferase, the enzyme that catalyzes peptide bond formation between amino acids. All ribosomes begin protein translation in the cytoplasm, but some translocate to the **rough endoplasmic reticulum** (RER) during protein synthesis depending on the protein's target destination.

- **Free ribosomes** remain floating in the cytosol throughout protein synthesis. They are responsible for translating proteins found within the cytosol, nucleosol, peroxisome matrix, and nuclear-encoded mitochondrial proteins (**Choice D**).
- **Attached ribosomes** bind to the RER after protein translation begins. They synthesize most secretory proteins, the integral membrane

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Feedback



Suspend



End Block

Block Time Remaining: 00:00:05

TUTOR

Settings

1

2

3

4

Item 1 of 4

Question Id: 757

Mark

Previous

Next

?

Tutorial

Lab Values

Notes

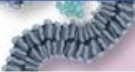
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Text Zoom

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Ribosomes are cellular organelles that synthesize proteins. Each ribosome consists of 2 subunits. The small ribosomal 40S subunit is responsible for binding mRNA (the protein synthesis template) and tRNA (carries amino acids). The larger 60S subunit contains peptidyl transferase, the enzyme that catalyzes peptide bond formation between amino acids. All ribosomes begin protein translation in the cytoplasm, but some translocate to the **rough endoplasmic reticulum** (RER) during protein synthesis depending on the protein's target destination.

- **Free ribosomes** remain floating in the cytosol throughout protein synthesis. They are responsible for translating proteins found within the cytosol, nucleosol, peroxisome matrix, and nuclear-encoded mitochondrial proteins (**Choice D**).
- **Attached ribosomes** bind to the RER after protein translation begins. They synthesize most secretory proteins, the integral membrane proteins of the nucleus and cell membrane, and proteins within the ER, Golgi network, and lysosomes.

The RER is particularly well developed in protein-secreting cells (eg, pancreatic and plasma cells). Ribosomes attach to the RER via the **translocon**, a protein complex containing ribophorins that bind the large 60S subunit.

(Choice A) ATP is produced in the cytosol during glycolysis and in the mitochondria during oxidative phosphorylation. The proteins in both of these cellular compartments are synthesized by free ribosomes in the cytosol.

(Choices B and E) Steroid hormone synthesis and drug detoxification are performed by various proteins found within the smooth ER (SER). The SER does not bind to ribosomes as it lacks the translocon complex.

Educational objective:

The rough endoplasmic reticulum (RER) is covered with ribosomes and is involved in the transfer of proteins to the cell membrane and extracellular space. The RER is well developed in protein-secreting cells. The smooth ER lacks surface ribosomes and functions in lipid synthesis, carbohydrate metabolism, and detoxification of harmful substances.

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Block Time Remaining: 00:00:05

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0

Feedback

Suspend

End Block

5:13 PM

2/13/2019

2

Settings

1

2

3

4

Item 1 of 4

Question Id: 757

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Exhibit Display

Rough & smooth endoplasmic reticulum

Nucleus

Nuclear envelope

Rough ER

Smooth ER

Ribosomes

Transport vesicles

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Zoom Out

Reset

Add To Flash Card

Block Time Remaining: 00:00:05

TUTOR

Feedback

Suspend

End Block

5:13 PM

2/13/2019

A 23-year-old man who lives at sea level is attempting to climb to the top of a mountain with an elevation of approximately 4,200 m (14,000 ft). While hiking, he develops dyspnea, lightheadedness, headache, and fatigue. He is able to reach a high-altitude camp 2 days later, where he is evaluated by medical personnel. The patient has no current medical problems but did have an uncomplicated appendectomy at age 12. He has never smoked and has no family history of pulmonary disease. An arterial blood gas performed at this time would most likely reveal which of the following sets of values?

	pH	pCO ₂	pO ₂
<input type="radio"/> A.	7.27	31 mm Hg	54 mm Hg
<input type="radio"/> B.	7.29	31 mm Hg	75 mm Hg
<input type="radio"/> C.	7.30	54 mm Hg	72 mm Hg
<input type="radio"/> D.	7.37	40 mm Hg	72 mm Hg
<input type="radio"/> E.	7.46	29 mm Hg	57 mm Hg
<input type="radio"/> F.	7.54	31 mm Hg	75 mm Hg

Submit

Settings

1

2

3

4

Item 2 of 4

Question Id: 12024

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

A

A

A

Text Zoom

A 23-year-old man who lives at sea level is attempting to climb to the top of a mountain with an elevation of approximately 4,200 m (14,000 ft). While hiking, he develops dyspnea, lightheadedness, headache, and fatigue. He is able to reach a high-altitude camp 2 days later, where he is evaluated by medical personnel. The patient has no current medical problems but did have an uncomplicated appendectomy at age 12. He has never smoked and has no family history of pulmonary disease. An arterial blood gas performed at this time would most likely reveal which of the following sets of values?

	pH	pCO2	pO2
<input type="radio"/> A.	7.27	31 mm Hg	54 mm Hg
[6%]			
<input type="radio"/> B.	7.29	31 mm Hg	75 mm Hg
[5%]			
<input type="radio"/> C.	7.30	54 mm Hg	72 mm Hg
[10%]			
<input type="radio"/> D.	7.37	40 mm Hg	72 mm Hg
[5%]			
<input checked="" type="radio"/> E.	7.46	29 mm Hg	57 mm Hg
[47%]			
<input type="radio"/> F.	7.54	31 mm Hg	75 mm Hg
[24%]			

Omitted

47%

3 Seconds

11/14/2018

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Feedback

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End Block

Block Time Remaining: 00:00:08

TUTOR

Windows

Search

Taskbar

System Tray

Settings

1

2

3

4

Item 2 of 4

Question Id: 12024

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

A

A

A

Text Zoom

Explanation

This patient is likely suffering from **high-altitude sickness**, a condition occurring as a result of low partial pressure of oxygen (pO_2) in environments $>2,500$ m (8,000 ft). Common symptoms include headache, fatigue, nausea, dizziness, and sleep disturbances. Most cases subside within 2 days, but progression to life-threatening cerebral and/or pulmonary edema is possible.

The pathophysiologic mechanism behind high-altitude sickness is **hypobaric hypoxia**. Although the fraction of oxygen in inspired air remains constant at different terrestrial elevations, barometric pressure drops with increasing altitude, leading to decreased pO_2 in the air and blood. The resulting tissue hypoxia stimulates peripheral chemoreceptors, causing **hyperventilation** in an attempt to improve oxygenation. This results in decreased partial pressure of carbon dioxide (pCO_2) and increased blood pH (respiratory alkalosis). Renal bicarbonate excretion **compensates** for the alkalosis, stabilizing the pH toward the normal range **within 48 hours**.

(Choices A, B, C, and D) Hyperventilation decreases $PaCO_2$, generating a respiratory alkalosis, not acidosis.

(Choice F) Hyperventilation at high altitude generates a respiratory alkalosis by decreasing $PaCO_2$; however, within 24-48 hours partial renal compensation leads to a near-normal pH via an increase in bicarbonate excretion.

Educational objective:

People traveling to elevations $>2,500$ m (8,000 ft) are at risk for developing high-altitude sickness, characterized by headache, fatigue, nausea, dizziness, and sleep disturbances. Hypobaric hypoxia is the primary cause; it leads to an increased respiratory rate with development of respiratory alkalosis, which is compensated by renal excretion of bicarbonate within 24-48 hours.

References

- Hypoxia-related altitude illnesses

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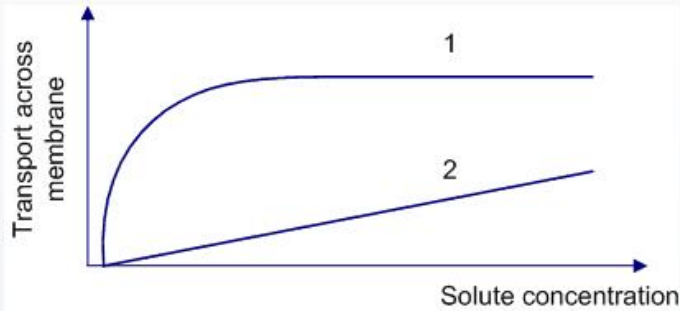
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2/13/2019

Two graphs illustrating the transport of low molecular weight solutes across the plasma membrane are shown on the slide below.



Which of the following best explains the difference in the shape of the curves?

- ☐

A. Concentration difference across the membrane [10%]
- ☐

B. Diffusion area [4%]
- ☐

C. Membrane thickness [2%]
- ☐

D. Oil/water partition coefficient [5%]
- ☒

E. Protein carrier [77%]

Omitted
Correct answer
E

77%

Answered correctly

4 Seconds

Time Spent

02/06/2019

Last Updated

Settings

1

2

3

4

Item 3 of 4

Question Id: 1378

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Explanation

The image above illustrates the difference between the rate of transport of solute across the cell membrane in simple diffusion (line 2) and carrier-mediated transport (line 1). The difference in the shape of the graphs is explained by the presence of a carrier protein in the scenario represented by line 1.

There are two types of diffusion:

1. Simple diffusion – molecules move through a membrane without the help of carrier proteins.
2. Facilitated diffusion – requires carrier proteins.

Carrier proteins are typically transmembrane proteins that possess binding sites for the substrate they transport. They bind extracellular ions and molecules forming a carrier-substrate complex. Binding is followed by movement of the complex across the cell membrane to the intracellular space, where the substrate is released into the cytoplasm. Because there is a finite number of carrier proteins in the cell membrane, and these carrier proteins require a discrete amount of time to pass a single molecule or ion through the membrane, saturation is an important property of carrier-mediated diffusion (facilitated diffusion). Once all of the carrier molecules are bound by substrate, no further diffusion can occur until a carrier protein is vacated. This maximum rate of transport is referred to as the transport maximum (T_m) and is similar in principle to the V_{max} in standard enzyme kinetics.

(Choices A – D) The other factors mentioned are not significantly different between simple diffusion and facilitated diffusion.

$$D \propto \frac{\Delta P \times SA \times SOL}{T \times \sqrt{MW}}$$

The difference in the concentration of the substrate across the membrane is called concentration gradient (ΔP). The higher the concentration

Block Time Remaining: 00:00:12

TUTOR

Activate Windows

Go to Settings to activate Windows.

Feedback

Suspend

End Block

5:13 PM

2/13/2019

Settings

1

2

3

4

Item 3 of 4

Question Id: 1378

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

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Text Zoom

Carrier proteins are typically transmembrane proteins that possess binding sites for the substrate they transport. They bind extracellular ions and molecules forming a carrier-substrate complex. Binding is followed by movement of the complex across the cell membrane to the intracellular space, where the substrate is released into the cytoplasm. Because there is a finite number of carrier proteins in the cell membrane, and these carrier proteins require a discrete amount of time to pass a single molecule or ion through the membrane, saturation is an important property of carrier-mediated diffusion (facilitated diffusion). Once all of the carrier molecules are bound by substrate, no further diffusion can occur until a carrier protein is vacated. This maximum rate of transport is referred to as the transport maximum (T_m) and is similar in principle to the V_{max} in standard enzyme kinetics.

(Choices A – D) The other factors mentioned are not significantly different between simple diffusion and facilitated diffusion.

$$D \propto \frac{\Delta P \times SA \times SOL}{T \times \sqrt{MW}}$$

The difference in the concentration of the substrate across the membrane is called concentration gradient (ΔP). The higher the concentration gradient the higher the rate of transport of the molecule or ion across the membrane.

The larger the surface area (SA) the greater the rate of diffusion. If the thickness of the membrane (T) is higher (eg, lung fibrosis) then the rate of diffusion would be slower. High molecular weight (MW) compounds diffuse slowly.

A high oil-water partition coefficient means that a solute is much more soluble in oil than in water. This characteristic is widely used to describe the pharmacokinetic properties of general anesthetics.

Educational Objective:

Carrier-mediated transport includes facilitated diffusion and active transport. Movement of substrate across the cell membrane by these mechanisms depends on the presence of carrier proteins in the membrane. Transport mechanisms utilizing proteins are able to be saturated.

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Block Time Remaining: 00:00:12

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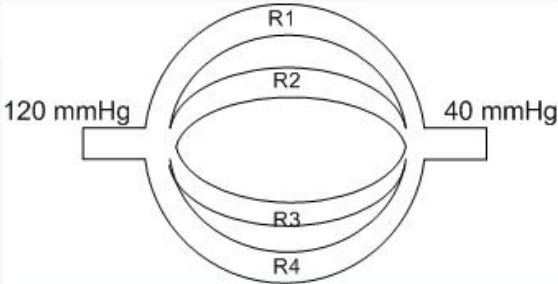
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5:13 PM

2/13/2019

The circuit shown below has an inflow pressure of 120 mmHg and an outflow pressure of 40 mmHg.

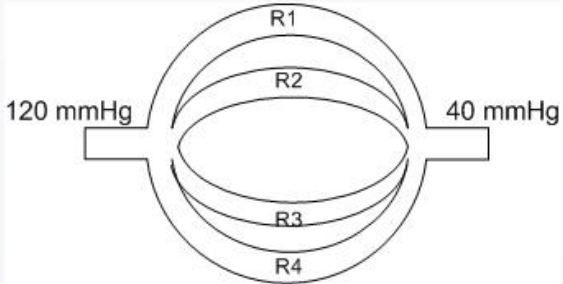


Resistance in each of the four vessels shown is 2 mmHg/mL/min ($R_1 = R_2 = R_3 = R_4 = 2 \text{ mmHg/mL/min}$). What is the total peripheral resistance of the circuit shown on the slide?

- ☐ A. 8 mmHg/mL/min
- ☐ B. 4 mmHg/mL/min
- ☐ C. 2 mmHg/mL/min
- ☐ D. 1 mmHg/mL/min
- ☐ E. 0.5 mmHg/mL/min

Submit

The circuit shown below has an inflow pressure of 120 mmHg and an outflow pressure of 40 mmHg.



Resistance in each of the four vessels shown is 2 mmHg/mL/min ($R1 = R2 = R3 = R4 = 2 \text{ mmHg/mL/min}$). What is the total peripheral resistance of the circuit shown on the slide?

- ☐ A. 8 mmHg/mL/min [13%]
- ☐ B. 4 mmHg/mL/min [4%]
- ☐ C. 2 mmHg/mL/min [30%]
- ☐ D. 1 mmHg/mL/min [2%]
- ☒ E. 0.5 mmHg/mL/min [48%]

Omitted

Correct answer E

48%

Answered correctly

3 Seconds

Time Spent

02/06/2019

Last Updated

Settings

1

2

3

4

Item 4 of 4

Question Id: 1616

Mark

Previous

Next

Tutorial

Lab Values

Notes

Calculator

Reverse Color

A

A

A

Text Zoom

Explanation

The diagram given in the question stem illustrates a set of vessels arranged in parallel. Systemic circulation is often simplified in this way for the purposes of calculating total peripheral resistance (TPR). Each branch of the aorta can be visualized as one of the vessel branches on the above graph. For example, the four vessels above could represent coronary, splanchnic, renal, and cerebral circulation. The formula for calculating the total resistance for parallel circuits is as follows. RT represents total peripheral resistance, and the circuits represent blood vessels.

$$1/R_T = 1/R_1 + 1/R_2 + 1/R_3 + \dots 1/R_n$$

In this calculation, the inverse of the TPR (or RT) is equal to the sum of the inverse of each vessel or system that lies in parallel. The resistance of the vessels are $R_1 = R_2 = R_3 = R_4 = 2 \text{ mmHg/ml/min}$. Therefore

$$1/TPR = \frac{1}{2} + \frac{1}{2} + \frac{1}{2} + \frac{1}{2} = 4(\frac{1}{2}) = 2$$

so $TPR = \frac{1}{2} = 0.5$

Therefore, the $TPR = \frac{1}{2}$ or 0.5 mmHg/ml/min .

(Choice A) Eight (8) mmHg/ml/min would be the resistance if each of the above vessels were arranged in series, rather than in parallel. A series arrangement does not estimate total body circulation well, but is a good way to describe blood flow in an individual organ. To calculate the resistance of a circuit in series, the individual values for resistance are summed as follows:

$$\text{Total resistance in organ} = R_{\text{artery}} + R_{\text{arteriole}} + R_{\text{capillary}} + R_{\text{venule}} + R_{\text{vein}}$$

Educational Objective:

The total resistance for a group of vessels arranged in parallel is equal to one divided by the sum of the inverse values for resistance of each of the contributing vessels as follows: $1/TPR = 1/R_1 + 1/R_2 + 1/R_3 + \dots 1/R_n$. Total body circulation can be best described as a parallel circuit, whereas circulation in an individual organ is often best described by a series arrangement.

Block Time Remaining: 00:00:15

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5:14 PM

2/13/2019