

# Multiple-Choice Questions in Medical Physiology

*For Postgraduate Medical Entrance Examinations*

[Revised May 2013]

**E.S.Prakash, MBBS, MD**

---

Written and Published May 2013 by E.S.Prakash.

**Copyright © 2013, all rights reserved by E.S.Prakash.** Except as permitted under the United States Copyright Act of 1976, no part of this publication may be reproduced or distributed in any form or by any means or stored in a database or retrieval system without prior written permission from the author.

**This version has not yet been peer reviewed.**

**150 Pages**

*Please avoid using previous editions of this book.*

**Disclaimer:** Science and medicine constantly change and while I have tried to check information presented here with sources known to be reliable, I cannot guarantee that this book is error free. I encourage you to crosscheck information contained herein with other sources. This book is not written to be used to directly guide the care of patients. Therefore, I cannot accept any responsibility for any consequences that may arise from the use of information contained here in the care of patients – *E.S.Prakash*

## ***2 minutes please***

Think of this book as a tool to help you assess how well you have learnt medical physiology. It was written primarily for use in revision courses for doctors who are preparing for competitive postgraduate (PG) medical entrance examinations in India, but undergraduate medical students and postgraduate physiology students may find this helpful.

The intent here is to use multiple-choice questions (MCQ) as a means to help the reader revise some key facts, test understanding of concepts and the ability to apply them, and thereby improve one's understanding of human physiology and its relevance to clinical medicine. Thus, besides the traditional *select the single best response type* of MCQ which is the question type used in most entrance exams, I have frequently included questions solely intended for learning and practice and so these may not be equivalent in standard to questions commonly appearing in entrance examinations. Also, the *difficulty level* of questions vary across entrance exams and I've attempted to simulate it here.

As MCQs with multiple correct answers enable more material to be revised with fewer questions, I have also frequently used such questions; further, this helps us get into and sustain the important habit of carefully reading all options in a question. Some entrance exams use the *select all correct answers (multiple true-false)* type of MCQ, so some practice with this type of question is needed.

In general, a significant fraction of the questions that I have seen appear on PG entrance examinations test conceptual understanding and meaningful learning. However, some test knowledge of facts that are not of significance to a primary care physician, and while this can be partly rationalized, an undesirable backwash effect of this on students is it tends to encourage rote learning over indepth learning of important concepts. I have focused on the immediate *'learning needs'* of the target audience, as well as to exemplify the relevance of medical physiology in clinical practice.

For the purpose of preparing and revising for PG entrance examinations, I recommend ***Ganong's Review of Medical Physiology*** (abbreviated as WFG in the rest of this book), published by Mc Graw Hill.

For ***more practice questions in physiology***, I recommend the following sources:

- Self-Study Questions in WFG
- *National Medical Series for Independent Study. Physiology*. Eds. Bullock J, Boyle J, Wang MB. Williams & Wilkins, 2001 (or a newer edition)
- Ryan JP and Tuma RF. PreTest – Physiology, 13<sup>th</sup> ed. Mc Graw Hill.
- Questions from previous PG entrance exams, if they are publicly available.

***Clarifications, Follow-up Notes, Some more practice questions:*** I'll post them on my website at <http://esprakash.wordpress.com/mcqmedphy/>

***Images and Schematic Diagrams*** accompanying this book: You can download them from the above webpage; these figures render better on PowerPoint Slides rather than on a 2-column Word Document.

I've greatly benefitted from review of this book by students who used it in the past, and I welcome suggestions for improving this book. If you spot an error, please let me know. I dedicate this book to the memory of Dr William F Ganong.

**E.S.Prakash**, MBBS, MD

Associate Professor of Physiology  
Mercer University School of Medicine,  
Macon, Georgia, USA

**E-mail:** dresprakash@gmail.com

**Website:** <http://esprakash.wordpress.com>

Editor & Publisher, Medical Physiology Online [ISSN 1985-4811]

<http://www.medicalphysiologyonline.org>

## ***Table of Contents***

<b><i>Topic</i></b>	<b><i>Page</i></b>
<i>2 minutes please</i>	2
General Physiology	4
Cell Physiology; Intercellular Communication	11
Physiology of Nerve and Muscle	14
Central Nervous System	24
Endocrinology and Reproduction	39
Gastrointestinal Physiology	48
Circulating Body Fluids	52
Cardiovascular Physiology	56
Pulmonary Physiology	68
Renal and Acid-Base Physiology	82
Critical Care Physiology	93
<b><i>Self-Scorers</i></b>	
1 – General Physiology	98
2 – Physiology of Nerve and Muscle	99
3 – Central Nervous System	101
4 – Endocrinology and Reproduction	104
5 – Gastrointestinal Physiology	108
6 – Cardiovascular Physiology	110
7 – Pulmonary Physiology	112
8 – Renal and Acid-Base Physiology	114
<i>Blast from the Past</i>	116
More Questions for Self-Study	131

## 1. General Physiology

In each of the following questions, select the **single best** response unless instructed otherwise.

1. ECF volume is determined by:

- A. plasma [Na]
- B. plasma protein concentration
- C. the amount of sodium in the ECF

2. The chief determinant of plasma osmolality is

- A. plasma [Na]
- B. plasma [glucose]
- C. blood [urea]
- D. plasma [albumin]

3. The volume of distribution of intravenously administered sucrose in a healthy 70-kg man is about:

- A. 3.5 liters
- B. 10.5 liters
- C. 14 liters
- D. 28 liters

4. Which of the following markers administered intravenously distributes exclusively in intracellular fluid?

- A. Evans blue dye
- B. Heavy water
- C. Sucrose
- D. None of the above

5. Which compartment does the term “sucrose space” refer to?

- A. Extracellular fluid (ECF)
- B. Interstitial fluid (ISF)
- C. Intracellular fluid (ICF)
- D. Plasma

6. 100 mg of sucrose is injected intravenously into an adult male weighing 70 kg. The plasma concentration of sucrose after mixing is 0.01 mg/ml. If 5 mg of sucrose has been metabolized during this period, the ECF volume in this individual is approximately:

- A. 6 liters
- B. 9.5 liters
- C. 14 liters
- D. 17.5 liters

7. In a healthy adult weighing 70 kg, plasma volume was estimated to be 3000 ml. His hematocrit was 40%. His blood volume would be about:

- A. 5000 ml
- B. 5200 ml
- C. 5400 ml
- D. 5600 ml

8. The water content of lean body mass is:

- A. 30 ml/100 g
- B. 50 ml/100 g
- C. 70 ml/100 g
- D. highly variable

9. The following values are obtained on a sample of plasma from a child that has clinical evidence of dehydration.

Plasma [Na] = 135 mmol/L  
Plasma [glucose] = 400 mg/dL  
Blood urea nitrogen = 100 mg/dL.

The osmolality of plasma is expected to be close to:

- A. 290 mOsm/kg H<sub>2</sub>O
- B. 310 mOsm/ kg H<sub>2</sub>O
- C. 330 mOsm/kg H<sub>2</sub>O
- D. 350 mOsm/kg H<sub>2</sub>O

10. What percentage of osmolality of plasma in a healthy, well hydrated individual is attributable to sodium and its accompanying anions?

- A. 30 %
- B. 50 %
- C. 70 %
- D. 90 %

11. Which of the following contributes **least** to the osmolality of plasma?

- A. Glucose
- B. Proteins
- C. Sodium
- D. Urea

12. In the *steady state*, the value of which of the following variables is the same in ICF and ECF?

- A. pH
- B. osmolality
- C. concentration of proteins

D. number of osmoles

13. The body fluid compartment that contains more osmotically active particles (in relation to other fluid compartments in the same individual) is:

- A. intracellular fluid
- B. plasma
- C. interstitial fluid

14. Normal red blood cells from a healthy individual were placed in each of the following solutions and observations made after 1 hour.

Cells would have most likely have lysed in red blood cells placed in:

- A. 0.3% NaCl
- B. 0.9% NaCl
- C. 1.2% NaCl

15. Which of the following solutions is hypertonic?

- A. 0.9 % NaCl
- B. 5% dextrose
- C. 20% mannitol
- D. Distilled water

16. Two liters of 0.9% NaCl is administered to a 12-year old boy with moderate isotonic dehydration. What is the expected change in ICF volume after NaCl administration?

- A. No change
- B. Increase by 0.5 liter
- C. Increase by 2 liters
- D. Decrease by 0.5 liter
- E. Decrease by 2 liters

17. ICF volume decreases when dehydration is:

- A. isotonic
- B. hypertonic
- C. hypotonic

18. If the intent is to replenish total body water in a dehydrated individual which one of the following should be administered intravenously?

- A. 0.9% NaCl
- B. 5% dextrose solution
- C. Albumin
- D. 10% glucose solution
- E. Distilled water

19. Which of the following exerts the greatest osmotic effect on a mole-mole basis?

- A. Dextran
- B. Hydroxyethyl starch
- C. Albumin
- D. Fibrinogen

20. Connexins **do not** allow the passage of:

- A. polypeptides
- B. Na ions
- C. Ca ions
- D. inositol trisphosphate
- E. amino acids

21. Of the following substances, the lipid bilayer per se (i.e., without proteins) is most permeable to:

- A. sodium ions
- B. urea
- C. glucose
- D. water

22. The rate of diffusion of a substance across the cell membrane is inversely proportional to:

- A. concentration gradient for the substance
- B. diffusion coefficient
- C. surface area available for diffusion
- D. thickness of the membrane

23. Which **one** of the following is an example of passive transport?

- A. Calcium efflux by calcium pump
- B. Na-Ca exchanger
- C. Potassium efflux through potassium leak channels
- D. Calcium sequestration in sarcoplasmic reticulum

24. Most of the ATP generated in nerve cells is utilized to energize the:

- A. Na-Ca exchanger
- B. H-ATPase in the cell membrane
- C. Na-K ATPase
- D. synthesis of proteins

25. Which of the following is **incorrectly** matched?

- A. Na-K ATPase: antiport
- B. H-ATPase: uniport
- C. SGLT: symport

D. Ca-ATPase: biport

26. The core body temperature of an experimental animal is raised from 98°F to 106°F by passive heating. Eventually, it dropped back to 99°F. What is the gain of the temperature regulation system in this instance?

- A. Zero
- B. One
- C. -7
- D. Infinity

27. Which of the following is **not** true about negative feedback control systems?

- A. Output is one of the inputs to the system
- B. It is based on a 'set-point' for the controlled variable.
- C. The system corrects "errors"
- D. The 'set point' of the system cannot be changed by inputs other than the controlled variable

**Answers: General Physiology**

1C	2A	3C	4D	5A
6B	7A	8C	9C	10D
11B	12B	13A	14A	15C
16A	17B	18B	19C	20A
21D	22D	23C	24C	25D
26C	27D			

**Answer Explanations:**

1. Children and adults have the same concentration of sodium in plasma. Yet their ECF volumes are greatly different. Thus, ECF volume is proportional to the amount of sodium in ECF.

2. The concentration of sodium in ECF is quantitatively the most important determinant of plasma osmolality.

$$\text{Plasma osmolality (mosm/Kg H}_2\text{O)} = 2 [\text{Na}^+] + [\text{glucose}] / 20 + [\text{BUN}] \times 18/50$$

(mmol/L)      (mg/dL)      (mg/dL)

**Blood urea and urea nitrogen:**

The formula of urea is NH<sub>2</sub>CONH<sub>2</sub>

Molar mass of urea is 60 g; each molecule of urea has 2 nitrogen atoms.

The mass of nitrogen in urea is 2 × 14 = 28 g

Thus, urea concentration of 60 mg/dL corresponds to a [BUN] of 28 mg/dL.

Normally, plasma osmolality is chiefly due to Na and its accompanying anions Cl and HCO<sub>3</sub>.

Normally, serum osmolality ranges from 280–295 mOsm/Kg H<sub>2</sub>O.

4-6. Intravenously administered sucrose distributes throughout ECF (plasma + interstitial fluid). ECF volume in a 70-kg healthy adult is about 14 L (20% of body weight). The volume of interstitial fluid is about 10.5 L (75% of ECF volume) and plasma volume is about 3.5L (25% of ECF volume). Heavy water distributes throughout body water. Sucrose, inulin and mannitol distribute exclusively in the ECF. Evans blue dye stays in the plasma.

Typical values in a healthy adult male weighing 70 kg are as given below:

Compartment	Volume	Marker
Total body water	42 L	D <sub>2</sub> O
ICF	28 L	-
ECF	14 L	Sucrose
Interstitial fluid	10.5 L	-
Plasma	3.5 L	Evans blue

**Indicator-dilution principle:**

Volume of distribution of the indicator equals the amount injected (A) divided by the concentration (C) in plasma (of the indicator) after mixing.

In the above example,

First, sucrose distributes throughout ECF.

Amount of sucrose injected = 100 mg

Amount metabolized = 5 mg

Amount remaining in ECF = 95 mg

Concentration after mixing = 0.01 mg/ml

Volume of distribution of sucrose

$$= 95 \text{ mg} / 0.01 \text{ mg/ml} = 9500 \text{ ml} = 9.5 \text{ L}$$

7. Blood volume

$$= \text{plasma volume} \times [100 / (100 - \text{Hct})]$$

8. Body mass = fat mass + lean body mass.

The water content of lean body mass (fat-free mass) is relatively constant and is about 70 ml/100 g. For example, in an individual weighing 70 kg

and whose total body water is measured to be 42 L (= 42 kg), lean body mass =  $42 / 0.7 = 60$  kg, and fat mass is 10 kg. Fat is relatively anhydrous. Body fat % =  $10/70 \times 100 = 14\%$ . Body fat percentage is greater in women compared to men.

12. ICF is much more acidic than ECF. For example, in muscle cells the pH is about 6.8. The steady state osmolality (i.e., concentration of osmotically active particles) of all body fluid compartments must be the same. The fact that, in a healthy adult, ICF volume is twice as large as ECF volume should indicate that the absolute number of osmoles is much greater in the ICF.

### 13-16. What is osmosis?

Osmosis is the movement of water across a semipermeable membrane permeable to water but not to solutes, from a solution with lesser concentration of osmoles to a solution with a greater concentration of osmoles. This continues until osmotic equilibrium (i.e., the osmolality of either compartment is equal) is attained.

#### What is an osmole?

An osmole (effective osmole) is an osmotically active particle potentially capable of causing osmosis. Examples include sodium ion, chloride ion, protein anions, and phosphate ion. A solute to which the cell membrane is not as freely permeable as it is to water will function as an *effective osmole*. For example, in comparison to water, the cell membrane is relatively impermeable to sodium and chloride ions, mannitol. The amount of ions crossing the cell membrane through channels and transporters is much smaller relative to osmotically driven water fluxes.

#### What is an ineffective osmole?

If the cell membrane is permeable to a solute (for example, urea), the substance will move across the membrane until its concentration is exactly the same on both sides of the membrane. In such an instance, osmosis (net movement of water) does not occur. However, note that urea does indeed function as an effective osmole in the renal medullary interstitium.

**Osmotic pressure** is the pressure that would be required to stop water flux (osmosis) across a semi permeable membrane.

Osmotic pressure  $P = CRT$  (Van't Hoff equation), where,

C = concentration of osmoles

R = a constant

T = temperature in Kelvin

In the steady state, the osmolality of all body fluids is identical; that is, osmotic pressure across the plasma membranes of cells in the steady state is zero and there would be no net water flux (osmosis) across the cell membrane.

Osmolality is a *colligative property* that depends upon the number of solute particles, and not the size of the particles. To illustrate, the contribution of 1 Na ion and 1 albumin molecule toward osmolality of plasma is the same. Since the molar concentration of proteins in plasma is very low (60 g/L) compared to that of Na (140 mM) and Cl (100 mM), one can understand why plasma proteins contribute very little to the osmolality of plasma compared to Na and its accompanying ions.

**Colloid osmotic pressure of plasma:** While proteins are present in plasma at a concentration of 60-80 g/L, they are not normally present in significant concentrations in the interstitium. Thus, the osmotic pressure of plasma proteins (called *colloid osmotic pressure* or *oncotic pressure*) is much greater than the osmotic pressure of proteins in the interstitium. This oncotic pressure gradient across the capillary restrains fluid filtration and favors reabsorption of fluid into the capillary.

Hemolysis begins when normocytes are placed in 0.5% NaCl and is complete in 0.3% NaCl. In contrast, when RBCs are placed in hypertonic saline, they lose water and diminish in size.

#### Why is 0.9% NaCl called an isotonic solution?

0.9% (precisely 0.85%) NaCl has the same osmolality as normal human plasma (about 290 mOsm/kg H<sub>2</sub>O, please see the calculation below); further, when it is infused into a normal human

(i.e., one with an ECF osmolality of 290 mOsm/kg H<sub>2</sub>O), it does not cause any change in the *steady state* volume of red blood cells or other cells; i.e. because it does not change the steady state osmolality of normal human plasma, it is an *isotonic* solution.

**Calculate the osmolality of 0.85% NaCl.**

0.85% NaCl contains 0.85 g of NaCl per deciliter of the solution.

= 8.5 g/ L of the solution

Molar mass of NaCl = 58.5 g

1 mol of NaCl = 58.5 g

8.5 g = 8.5/58.5 mol = 0.145 mol = 145 mmol/L

Each Na is accompanied by 1 chloride ion

Therefore, total concentration of osmoles

(osmotically active particles) = 2 × 145 = 290

mOsm/L

**16-17. ECF volume changes**

When the terms dehydration and overhydration are used without further qualification, they are typically used to refer to ECF volume contraction and ECF volume expansion respectively. The term dehydration can be used to refer to a reduction in total body water as well. However, hypovolemia and dehydration are not synonymous. Hypovolemia specifically refers to a reduction in blood volume. Blood volume is more critically regulated than ECF volume.

**Classification of dehydration\*:**

Type	Example of a cause
Isosmotic	Blood loss
Hyperosmotic	ADH deficiency
Hypoosmotic	Adrenocortical insufficiency

\*Overhydration is classified likewise.

**Changes in ICF volume in various types of dehydration:**

Type	ECF volume	ICF volume
Isosmotic	Decreases	No change
Hyperosmotic	Decreases	Decreases
Hypoosmotic	Decreases	Increases

18. The key phrase here is ‘body water’ which includes ICF as well as ECF. In the steady state, hypertonic dehydration is associated with a reduction in ECF as well as ICF volume. So therapy must be aimed at replenishing total body water, not merely ECF volume.

**Is 5% dextrose isotonic or hypotonic?**

Molar mass of dextrose (D-glucose, C<sub>6</sub>H<sub>12</sub>O<sub>6</sub>) is 180 g

5% solution contains 50 grams of dextrose per liter of the solution

50g = 50/180 mol = 0.277 mol = 277 mmol = 277

mOsm/L ~ 270–280 mOsm/kg H<sub>2</sub>O

As 5% dextrose has approximately the same osmolality as normal human plasma, it is an isosmotic solution. However, when dextrose is infused, it is metabolized and the net effect (over a period of time, especially when large volumes are infused) is that of adding water to plasma. This “excess” water can enter cells. Thus, 5% dextrose is of value in replenishing ICF volume in intracellular dehydration. Also, note 5% dextrose is **hypotonic** because it dilutes plasma in the steady state.

In well hydrated individuals, the hypo-osmolality that occurs when hypotonic dextrose solutions are infused is sensed by osmoreceptors and secretion of antidiuretic hormone is promptly inhibited to excrete ‘excess’ water.

To summarize, *tonicity* of a solution refers to the effect of an administered solution on the steady state osmolality of normal human plasma.

**19. Starling’s law of filtration**

**Starling** described forces that affect fluid flux across capillaries.

Fluid movement = Kf [(Pc + πi) – (Pi + πc)], where,

Kf = capillary filtration coefficient

Pc = hydrostatic pressure in the capillaries

Pi = hydrostatic pressure in the interstitium

πc = capillary colloid osmotic pressure

πi = colloid osmotic pressure in the interstitium

Normally, Pc is the principal force favoring filtration. The osmotic pressure of plasma is normally about 25 mm Hg higher relative to the osmotic pressure of interstitium because ‘plasma’ proteins (colloids) are limited to plasma; proteins

in plasma restrain fluid filtration into the interstitium.

Albumin is quantitatively the most important contributor to the colloid osmotic pressure of plasma. 1 g of albumin in 100 ml of plasma exerts an osmotic effect of 6 mm Hg; the same concentration of globulins will exert a pressure of only about 1.5 mm Hg.

**22. Fick's law of diffusion:**

Diffusion rate (J) = DA dc/dx

D: Diffusion coefficient

A: Area available for diffusion

dc: concentration gradient

dx: thickness of membrane

The diffusion coefficient is affected by factors such as temperature, and the permeability of the membrane to the molecule/ion in question. Permeability of a membrane to an ion/molecule is in turn affected by the number of ion channels or transporter molecules available to transport the species in question.

23. Ion flux through ion channels is a passive process; i.e. it occurs down a concentration gradient and requires no input of free energy.

24. A large fraction of ATP (nearly 70%) synthesized in neurons is used to energize the Na-K ATPase and maintain ion gradients across the nerve cell membrane.

25. Ca-ATPase is a *uniport* because it transports one species. It is a primary active transport process as it uses ATP as the source of energy.

26. Gain = correction / error; in this example, the correction is 7 degrees i.e. from 106°F down to 99 °F, and the error (deviation from the original value of 98°F) is 1°F. The gain of a negative feedback control system is negative. If the error is zero, gain is infinite. Guyton and colleagues suggested that the renal 'pressure-natriuresis' mechanism for controlling body fluid volumes has infinite gain.

27. As far as biological systems are concerned, the application of control system theory is a means to

understanding but there is some risk of teleologic fallacies.

Take temperature regulation as an example. The 'controller' is the hypothalamus. The fact that a rise in body temperature leads to a fall in temperature back toward 98.6°F suggests that temperature is the controlled variable, and this operates as a *negative feedback control system*. This means that there must be a 'sensor' for temperature. The hypothalamus is in fact able to sense core body temperature.

When there is an infection, often the release of cytokines as part of the immunologic response act on the brain to raise the 'set-point' of the temperature regulation system to a higher level so that a higher than normal body temperature is maintained and results in fever. The control system is then said to be 'reset' to a higher operating level. However, once the infection and the immune response resolve and the concentration of cytokines and prostaglandins that reset the temperature set point upward resolve, the set point returns to 98.6°F indicating that resetting of a control system is not necessarily permanent.

\*\*\*\*\*

**Supplement: Classification of mechanism of transport across cell membranes:**

Mechanism	Examples
Simple diffusion	Diffusion of oxygen, carbon dioxide, anesthetic gases, nitric oxide through lipid layer
Facilitated diffusion	Glucose entry into cells through GLUT 1-5; passage of ions through ion channels*
Primary active transport	Na-K ATPase, H-K ATPase, Ca-ATPase, H-ATPase
Secondary active transport	Na-glucose cotransporter (SGLT), Na-amino acid cotransport, Na-H exchanger, Na-Ca exchanger

**Simple diffusion**, by definition, is diffusion occurring through the lipid bilayer. **Facilitated diffusion** occurs through protein molecules in the cell membrane (ion channels or transport

proteins). Some authors consider ion flux through ion channels also as an instance of “simple diffusion” – this distinction is a matter of taste.

By definition, a **primary active transport** process is driven by hydrolysis of ATP.

**Notes about the Na-K ATPase:**

- It is a primary active transport process
- The pump is present in the cell membrane
- It is ubiquitous i.e., present in all cells
- It pumps 3 Na out of the cell and 2 K ions in. Thus it makes the inside of the cell negative with respect to exterior; i.e. it contributes to a small extent (about 4 mV) to the genesis of RMP.
- It plays an important role in maintaining cell volume. If the pump is inhibited as can happen when ATP is limiting or pharmacologically (with digoxin) intracellular Na increases also increasing the size of cells.
- Digoxin, a cardiac glycoside inhibits this pump. Inhibition of the pump leads to an increase in cytosolic Ca and this augments the force of contraction of cardiac muscle cells.
- About 70% of the ATP generated in nerve cells is used to energize the Na-K ATPase.

A **secondary active transport** process utilizes an ion gradient as a source of energy rather than ATP. The Na-Glucose cotransporter (SGLT) utilizes the energy of the Na gradient (Na battery) to drive the uphill transport of glucose from ECF to ICF. Note that the species that is actively transported by SGLT is glucose. The Na-amino acid symporter is similar. The term ‘secondary’ refers to the fact that the energy source (the sodium ion gradient), which drives this process, depends upon normal operation of a primary active transport process – the Na-K pump that generates a Na ion gradient. If the Na-K pump fails due to lack of ATP or any other reason, then the Na gradient will be gradually reduced and all secondary active transport processes powered by the Na gradient will also be affected.

**Nomenclature of transporters based on the direction of movement and the number of species of transported.** *Note:* this is **not** a classification of *mechanism* of transport.

Name	Definition	Example
Uniport	1 species transported	Ca-ATPase, GLUT*
Symport (also cotransport)	2 species transported in the same direction	Na-glucose cotransport, Na-K-2Cl cotransport
Antiport (also countertransport)	2 species transported in opposite directions	Na-K ATPase, Na-H exchanger, Cl-HCO <sub>3</sub> exchanger.

\*GLUT – glucose transporter

**Carrier mediated transport** – this term refers to transport processes in which the transport species physically attaches to a carrier molecule, and is *carried* by it. Carrier mediated transport processes can be active or passive. Na-K ATPase (an active transport process) and glucose transport via GLUT (a passive transport process) are both examples of carrier-mediated transport.

Different authors use the word *transport* in this context differently. Some do not use the word transport to refer to ion movement through ion channels; for them transport entails physical attachment of the transported species to the transporter molecule.

**Other modes of transport:** Exocytosis, endocytosis, transcytosis (vesicular transport). Exocytosis is triggered by a rise in intracellular calcium. Proteins injected into the circulation often have been endocytosed into vesicles by endothelial cells to be exocytosed as vesicles into the interstitium. This process called transcytosis or vesicular transport requires an input of free energy.

\*\*\*\*\*

## 2. Cell Physiology; Intercellular Communication

### Types of intercellular communication:

Type	Mediators
Neurocrine	Neurotransmitters acting across synapses
Endocrine	Hormones acting on target cells located at distant sites
Paracrine	Hormones acting locally without entering the general circulation
Gap junctions	Cells are electrically coupled by gap junctions which allow passage of ions and small molecules
Juxtacrine	Cells linked to adjacent cells through cell adhesion molecules and cell adhesion molecule receptors in extracellular matrix

### Components of signal transduction pathways and their functions:

Components	Functions
Hormone / neurotransmitter	Signal
Receptor	Recognizes the signal
Signal coupling proteins	Coupling ligand binding to intracellular signaling
Second messengers	Intracellular molecules that amplify extracellular hormonal (first messenger) signals several fold
Effector molecules	Enzymes, channels, transporters, that mediate the physiologic effects of the hormone

### Signal transduction cascades and second messengers:

Signal transduction cascades	Second messenger(s)
Adenylate cyclase cascade	cAMP
Phosphatidyl inositol pathway	Inositol trisphosphate (IP <sub>3</sub> ), DAG, and Ca
Guanylyl cyclase	cGMP
Hormones acting upon intracellular receptors	Hormone-receptor complex

### Drugs / toxins used in G-protein research:

Drug/toxin	Mechanism of action
Cholera toxin	ADP-ribosylation of $\alpha$ subunit of Gs, activation of adenylate cyclase
Pertussis	Inhibition of $\alpha$ subunit of Gi

toxin	
Forskolin	Directly activates adenylate cyclase

### Some notes on G-proteins:

1. They have 3 subunits ( $\alpha$ ,  $\beta$ ,  $\gamma$ );
2. Each subunit is distinct (heterotrimeric)
3. They are guanylyl nucleotide (GTP / GDP) binding proteins
4. The  $\alpha$  subunit has inherent GTPase activity
5. The  $\beta$  and  $\gamma$  subunits are coupled to effectors molecules like adenylyl cyclase, ion channels.
6. G proteins couple hormone binding to the receptor to an intracellular signaling pathway. In essence, they are signal coupling proteins.
7. Hormone receptors that are coupled to G-proteins are called G-protein coupled receptors (GPCR)
8. GPCR have seven transmembrane domains; thus they are often called seven-helix receptors or serpentine receptors
9. There are several types of G proteins; Gs is stimulatory G protein and it activates adenylyl cyclase; Gi is inhibitory G protein and it inhibits adenylyl cyclase; activation of Gq leads to activation of the membrane bound enzyme phospholipase C.
10. Other families of proteins such as *ras* resemble G-proteins in structure and function.
11. Mutations in G proteins are implicated in the development of cancer.

### Select the single best response.

1. How many transmembrane domains do G-protein coupled receptors have?
  - A. 2
  - B. 3
  - C. 7
  - D. 12
2. How many subunits do G proteins have?
  - A. One
  - B. Two
  - C. Three
  - D. Four
3. Which G protein activates adenylyl cyclase?
  - A. Gs
  - B. Gq
  - C. Gi

D. Gi

4. Which subunit of G protein has intrinsic GTPase activity?

- A. Alpha
- B. Beta
- C. Gamma
- D. Delta

5. Which of the following hormones does **not** act via a G-protein coupled receptor?

- A. TRH
- B. Angiotensin II
- C. ADH
- D. Thyroxine

6. Which toxin inhibits the function of Gi?

- A. Cholera toxin
- B. Pertussis toxin
- C. Forskolin
- D. Saxitoxin

7. Which receptor does **not** span the cell membrane seven times?

- A. Rhodopsin
- B. *Beta*-adrenergic receptor
- C. Insulin receptor
- D. M<sub>2</sub> receptor

8. The second messengers in the phosphatidyl inositol cascade are:

- A. IP<sub>3</sub>, DAG and calcium
- B. protein kinases A (PKA) and C
- C. cAMP and cAMP dependent PKA
- D. cGMP and calcium

9. Most of the calcium in the endoplasmic reticulum (ER) is sequestered by:

- A. calmodulin
- B. caldesmin
- C. calbindin
- D. calsequestrin

10. Cytosolic calcium concentration in unexcited cells is about:

- A. 2.5 mM
- B. 10 mM
- C. 150  $\mu$ M
- D. 100 nM

11. Which one of the following stimulates the release of calcium from the endoplasmic reticulum?

- A. IP<sub>3</sub>
- B. PTH
- C. 1, 25 (OH)<sub>2</sub> – D<sub>3</sub>
- D. DAG

12. Protein kinase C is activated by:

- A. IP<sub>3</sub>
- B. diacylglycerol (DAG)
- C. cAMP
- D. guanylyl cyclase

13. All of the following chemical messengers act via receptor tyrosine kinases **except**:

- A. insulin
- B. ANP
- C. epidermal growth factor
- D. platelet derived growth factor

14. Guanylyl cyclases are activated by:

- A. CO, NO and ANP
- B. NO, ANP and ET1
- C. AII, NO and ANP
- D. ANP, ET1 and AII

15. Which of the following hormones mediate(s) its effects by activating nuclear / cytosolic receptors? (*select all correct answers*)

- A. Thyroxine
- B. Retinoic acid
- C. Estradiol
- D. Progesterone
- E. Aldosterone
- F. Cortisol
- G. 1, 25 (OH)<sub>2</sub> D<sub>3</sub>

16. Which of the following is matched **incorrectly**?

- A. Microfilaments: actin, myosin
- B. Intermediate filaments: vimentin, keratin
- C. Microtubules: clathrin
- D. Cytoskeleton: spectrin, ankyrin

17. Which intercellular junctions directly allow the passage of small molecules and ions between the cytosol of one cell and its neighbor without movement into interstitial fluid?

- A. Gap junctions

- B. Focal adhesions
- C. Zonula occludens
- D. Desmosomes

18. Which of the following statements regarding regulation of cell cycle is **incorrect**?

- A. This serves to regulate transition of the cell from one phase of the cell cycle to the next.
- B. At restriction points, cyclins always promote transition from G0 to S phase.
- C. Defects in DNA synthesis normally allow progression from G2 to M phase.
- D. Deficiency of p53 allows progression to M phase.

ventricle of the heart contracts as one unit because gap junctions electrically couple all muscle fibers in the ventricle. However, connexins do not allow large molecules such as proteins to pass between cells.

18. Deficiency of the tumor suppressor protein p53 allows entry into M phase and facilitates the growth of tumors, and a number of cancers are associated with deficiency of p53.

\*\*\*\*\*

**Answers: Cell Physiology; Intercellular Communication**

1C	2C	3A	4A	5D
6B	7C	8A	9D	10D
11A	12B	13B	14A	15all
16C	17A	18C		

**Explanations:**

10. ECF  $[Ca^{2+}] = 2.5 \text{ mM}$   
 Cytosolic  $[Ca^{2+}]$  in unexcited cells = 100 nM  
 $ECF [Ca^{2+}] / \text{cytosolic } [Ca^{2+}] = 25000$   
 A transient increase in intracellular calcium is used as a signal to activate or inactivate intracellular processes such as exocytosis, muscle contraction.  $[Ca^{2+}]_i$  is quickly normalized by the sarcoplasmic-endoplasmic reticulum calcium pump (SERCA pump) and a Na-Ca antiporter (also called the Na-Ca exchanger, NCX) in the cell membrane. Sustained increases in intracellular calcium trigger apoptosis, culminating in cell death.

16. Microtubules have a 9 + 2 fibrillar structure. They are made up of tubulin, dynein, and kinesin. The mitotic spindle is made up of microtubules. Colchicine arrests cells in metaphase by inhibiting polymerization of microtubules.

17. Gap junctions (electrical synapses; connexons) are made up of a protein called connexin; these are large diameter channels that allow the passage of ions and other small molecules such as amino acids and glucose. Thus, they electrically couple adjacent cells. They are found in visceral smooth muscle and heart and between some neurons. The

### 3. Physiology of nerve and muscle cells

**Resting membrane potential (RMP)** refers to the transmembrane potential (i.e., the potential difference across the cell membrane) in the steady state (unexcited state). RMP is present across all cells.

#### Origin of RMP:

1. The cell membrane is impermeable to organic anions and proteins present in ICF.
2. In neurons for example, in the resting state, the cell membrane is quite permeable to K, (about 50 times more permeable to K than Na). K exits the cell down its concentration gradient, making the inside of the cell negative with respect to exterior.
3. Charge separation occurs across the membrane (a thin capacitor) leaving the inside of the membrane negative with respect to outside.
4. Additionally, the Na-K ATPase mechanism contributes a small extent to making the inside of the cells negative.

#### Magnitude of RMP in different tissues

Cell / tissue	Magnitude of RMP (inside negative)
Nerve cells	- 70 mV
Skeletal muscle	- 90 mV
GI smooth muscle	Variable; - 40 to - 60 mV
Cardiac muscle	- 90 mV
SA node	- 70 mV
Red blood cells	- 10 mV

**Driving forces for ion fluxes** across membranes are the electrical and chemical (concentration) gradients.

**Equilibrium potential:** the membrane potential at which net transmembrane flux of a particular ion is zero because the electrical gradient counterbalances the chemical gradient.

Example, Na flux across the membrane would stop when the membrane potential reaches + 60 mV.

Equilibrium potential (given by Nernst equation) of Na:

$$E_{Na} = - 61 \log [Na]_i / [Na]_o$$

$$= - 61 \log [10/140] = + 61 \text{ mV}$$

Similarly, for K:

$$E_k = - 61 \log [K]_i / [K]_o$$

$$K_i = 140 \text{ mM}, K_o = 5 \text{ mM}, E_K = - 92 \text{ mV}$$

#### Equilibrium potentials for various ions across nerve cell membranes:

	ICF (mM)	ECF (mM)	Equilibrium potential (mV)
Na	10	140	+ 60
K	140	5	- 90
Cl	10	120	- 70
Ca	100 nM	2.5	+ 130

#### Excitability:

Excitability is the response to a threshold stimulus with a propagated action potential. Nerve and muscle are excitable. Other tissues are not.

**The physiologic basis of excitability:** high potassium permeability at rest (and therefore an RMP in the range of -50 to -90 mV) and presence of voltage gated Na channels are essential.

#### What is the effect of hyperkalemia on RMP of cardiac muscle cells?

Normally, when plasma  $[K^+] = 5 \text{ mM}$ , RMP of cardiac muscle cells = - 90 mV.

When plasma  $[K^+] = 10 \text{ mM}$ ,  
RMP = - 61 log  $[140/10] = - 70 \text{ mV}$

That is, hyperkalemia makes RMP less negative. SA node has an RMP of -70 mV. In this situation, ventricular cells would be expected to compete with SA node to pace the heart.

This clearly increases the risk of cardiac arrhythmias.

#### Functional organization of neurons:

##### Each neuron has the following zones:

**Receptive zone:** afferent input converges on the dendrites and soma.

**Integrator:** all afferent input is integrated by the soma (cell body) and if the axon hillock is depolarized to threshold, a full-fledged action potential occurs.

The **axon transmits the nerve impulse** (action potential) down to the nerve terminal where neurotransmitter is released for synaptic transmission. The action potential also sweeps back through the cell body wiping it clean of all input and rendering it refractory to all input for a short time.

**Nerve conduction speed** is increased several fold by myelination of axons.

If the nerve is stimulated with the cathode (using a subthreshold stimulus), it produces small depolarizations (called *catelectrotonic potentials*). These small depolarizations are *local responses*; i.e. they are not propagated through the nerve fiber. The stimulus that is just adequate to result in a propagated action potential is called *threshold stimulus*.

The membrane potential at which voltage gated Na-channels open all at once to result in a full fledged action potential is called *firing level* or *threshold level* and it is about -55 mV in nerve fibers. Within a millisecond of opening, Na channels get deactivated; i.e. close and cannot be opened until the membrane potential comes back down to firing level. On the other hand, voltage gated K channels open allowing rapid efflux of K. This repolarizes the membrane; i.e., brings it back to RMP.

**Differences between local & action potentials:**  
**Local potentials** (also called *electrotonic potentials*) may be depolarizing (also called **catelectrotonic potentials**) or hyperpolarizing (also called **anelectrotonic potentials**). Excitatory postsynaptic potentials and motor end plate potentials are examples of catelectrotonic responses. Inhibitory postsynaptic potentials are anelectrotonic responses. Electrotonic potentials are *graded responses* (i.e. proportional to stimulus intensity) that occur with subthreshold stimuli, and their magnitude is typically a few mV. They undergo spatial and temporal summation. They are not propagated.

In contrast, action potentials are propagated responses that occur with “threshold stimuli”.

They are all-or-none; i.e., they occur with a constant size.

**Excitability during various phases of the action potential:**

**Absolute refractoriness:** No matter how strong the stimulus, a nerve is absolutely refractory to stimulation during the action potential until repolarization brings the membrane back to firing level. The basis for absolute refractoriness is voltage and time inactivation of voltage gated Na channels.

**Relative refractory period:** In this period, only a suprathreshold stimulus would trigger an action potential. The reason why a stronger stimulus is required for excitation is because the stimulus has to overwhelm the repolarizing current.

**Supernormal phase:** a weaker stimulus would trigger an action potential.

**Subnormal phase:** during afterhyperpolarization, a stronger stimulus would be required to bring the membrane to threshold.

**Stimulus:** a transient change in one of the parameters of the environment.

**Stimulus types:** electrical, chemical, mechanical

**Stimulus parameters:**

1. **Intensity:** subthreshold, threshold, suprathreshold
2. **Duration:** typically (in milliseconds)
3. **Frequency:** 1-100 Hz
4. **Rise time:** time in which stimulus intensity rises to its maximum value.

**Threshold stimulus:** The minimum stimulus intensity that will elicit an action potential in an excitable tissue under a given set of conditions.

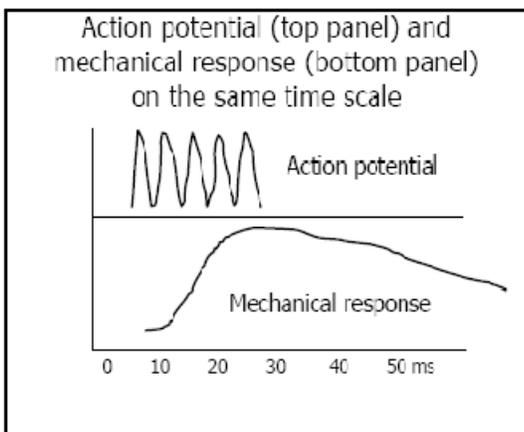
**All or none law:** If a stimulus sufficiently intense as to bring the membrane to threshold, the intensity of the stimulus has no bearing on the size of the action potential.

**Physiologic basis of the all-or-none law:**

Action potential occurs only when the firing level is reached because the voltage-gated sodium channels that allow a massive influx of Na open only at the firing level.

**Effect of stimulus intensity on electrical response of nerve and muscle (all-or-nothing):**

<i>Stimulus Intensity</i>	<i>Electrical response in nerve / muscle</i>
Subthreshold	No action potential
Threshold	Action potential
Suprathreshold	Action potential of the same strength



The figure above depicts action potential in a muscle fiber (top panel) and mechanical response (bottom panel) on the same time scale in skeletal muscle. Whereas the duration of the action potential is only about 5 ms, the duration of the mechanical response is much longer. Thus, it is possible to summate the mechanical responses to successive stimulation of muscle. In cardiac muscle, this is not possible.

**Muscle twitch:** A muscle twitch is contraction followed by relaxation occurring in response to a single stimulus.

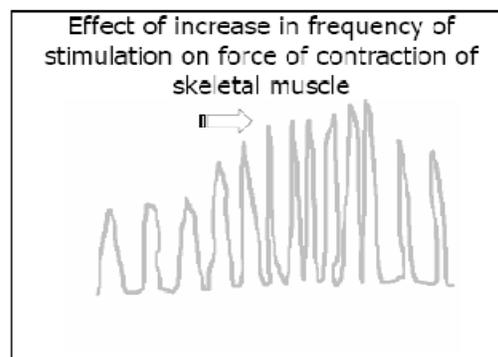
Twitch duration = contraction time + relaxation time. Twitch duration is quite variable and skeletal muscle is classified as fast or slow, depending upon twitch duration. The duration of muscle twitch in fast muscle could be as short as

10 ms. In contrast, in slow skeletal muscle, twitch duration is typically greater than 100 ms.

In cardiac muscle, when average heart rate is 75 beats per minute, average twitch duration is 800 ms; i.e., cardiac muscle is “slower” than skeletal muscle. The twitch duration in the smooth muscle of sphincters is longer. Smooth muscle is thus the ‘slowest’ of three muscle types.

**Tetanzing stimulus frequency:** In skeletal muscle, with high frequency stimulation, it is possible to summate the effects of multiple stimuli and increase the force of muscle contraction. Tetanus is the most forceful and sustained muscle contraction (i.e. with no relaxation in between). To tetanize skeletal muscle, it must be stimulated at a minimum frequency called the tetanizing frequency that depends on the duration of contraction. The minimum stimulus frequency required for tetanizing the muscle is the reciprocal of the contraction period expressed in seconds.

For example, if the contraction period is 100 ms (0.1 s), tetanizing frequency is  $1/0.1 = 10$  Hz.



The figure above depicts the effect of an increase in the frequency of contraction of skeletal muscle on force. With increasing frequency of stimulation at a given intensity, the force of successive contractions increase because of the beneficial effect of previous contractions; more calcium is available for later contractions than earlier ones. This is called the **staircase phenomenon**, *Treppe* or **Bowditch effect**. With a decrease in frequency of stimulation, a gradual decrease in force of contraction is also observed.

**Axoplasmic transport:** This refers to transport of molecules in the cytoplasm of the axon. This is

not to be confused with conduction of the nerve impulse, which is much faster.

Fast anterograde transport (i.e., from the cell bodies to axon terminals) is brought about by microtubules (kinesin and several other proteins are involved).

Axoplasmic transport	Speed (mm/day)
Fast anterograde transport	400
Slow anterograde transport	0.5–10
Retrograde transport	200

**Most if not all of the Questions in this Section have only one correct answer.**

1. Fast anterograde transport occurs at a rate of about:

- A. 40 mm/day
- B. 400 mm/day
- C. 1 mm/day
- D. 10 mm/day

2. The resting cardiac muscle cell is most permeable to:

- A. Na
- B. K
- C. Ca
- D. Cl

3. The membrane potential of cardiac muscle cells is most affected by even a small change in plasma concentration of:

- A. Na
- B. K
- C. Cl
- D. Ca

4. Hypokalemia would be expected to result in:

- A. increased neuronal excitability
- B. a more negative RMP
- C. no change in RMP
- D. a decrease in firing level of neurons

5. The number of Na channels per square micrometer of membrane in myelinated mammalian neurons is maximum in the:

- A. Cell body
- B. Dendritic zone

- C. Initial segment
- D. Node of Ranvier

6. The site of origin in the nerve of conducted impulses is the:

- A. dendritic zone
- B. axon hillock
- C. node of Ranvier
- D. terminal buttons

7. In motor neurons, the portion of the cell with the lowest threshold for the production of a full-fledged action potential is:

- A. initial segment
- B. soma
- C. dendritic zone
- D. node of Ranvier

8. Action potential conduction velocity is influenced by:

- A. axon diameter
- B. temperature
- C. myelination

9. In the CNS, the membranes that wrap around myelinated neurons are those of:

- A. Schwann cells
- B. oligodendroglia
- C. endothelial cells
- D. astrocytes

10. The duration of action potential in a skeletal muscle fiber is typically:

- A. 5 ms
- B. 25 ms
- C. 200 ms
- D. 250 ms

11. When heart rate is about 75 beats per minute, what is the mean duration of action potential in ventricular muscle cells?

- A. 5 ms
- B. 25 ms
- C. 200 ms
- D. 250 ms

12. The force of muscle contraction cannot be increased by:

- A. increasing the frequency of activation of motor units

- B. increasing the number of motor units activated
- C. increasing the amplitude of action potentials in motor neurons
- D. recruiting larger motor units

13. An excitable cell has an RMP of -70 mV and a firing level of - 50 mV. This cell would be inexcitable when its membrane potential is:

- A. - 30 mV
- B. - 55 mV
- C. - 70 mV
- D. - 90 mV

14. For the same conditions (as in the above question), the cell would be most excitable when its membrane potential is:

- A. - 30 mV
- B. - 55 mV
- C. - 70 mV
- D. - 90 mV

15. Although the equilibrium potential of Na is + 60 mV, the membrane potential does not reach this value during the overshoot because:

- A. the concentration gradient of Na is reversed
- B. Na channels undergo rapid inactivation
- C. K efflux commences immediately after the upstroke
- D. the membrane is impermeable to Na

16. Which one of the following statements about electrotonic potentials is **incorrect**?

- A. They are graded responses
- B. They are local (non-propagated) responses
- C. They may be depolarizing or hyperpolarizing
- D. They are produced by a threshold stimulus.

17. Thin filaments do **not** contain:

- A. actin
- B. myosin
- C. troponin
- D. tropomyosin

18. The ATPase activity of which of the following proteins is altered to regulate skeletal muscle contraction?

- A. Actin
- B. Myosin
- C. Troponin
- D. Tropomyosin

19. The activity of which contractile protein is altered to regulate smooth muscle contraction?

- A. Actin
- B. Myosin
- C. Calmodulin
- D. Tropomyosin

20. Smooth muscle lacks:

- A. actin
- B. myosin
- C. troponin
- D. tropomyosin

21. An example for nonsyncytial smooth muscle is:

- A. iris
- B. sphincter of Oddi
- C. vas deferens
- D. uterus

22. The twitch duration in fast type skeletal muscle fibers is about:

- A. 10 ms
- B. 50 ms
- C. 100 ms
- D. 250 ms

23. The major source of calcium for contraction of skeletal muscle is:

- A. ECF
- B. cytosol
- C. mitochondria
- D. sarcoplasmic reticulum (SR)

24. Ryanodine receptor is located in the:

- A. sarcolemma
- B. T-tubule
- C. terminal cisterns of sarcoplasmic reticulum
- D. cytosol

25. Which of the following blocks the ryanodine receptor?

- A. Dantrolene
- B. Curare
- C. Cocaine
- D. Hexamethonium

26. Which of the following slow the relaxation process in skeletal muscle?

- A. Slow myosin ATPase
- B. Inhibition of Ca-Mg ATPase
- C. ATP depletion

27. Rigor mortis is due to:

- A. damage to actin & myosin
- B. rapid sequestration of Ca in ER
- C. increased myosin ATPase
- D. ATP depletion

28. Staircase phenomenon (*Treppe*) is due to:

- A. increased availability of intracellular calcium
- B. summation
- C. tetanus
- D. increased excitability

29. Which of the following statements regarding type I muscle fibers is **incorrect**?

- A. They are rich in myoglobin
- B. Their oxidative capacity is high
- C. Their myosin ATPase activity is high
- D. Their glycolytic capacity is moderate

30. Which of the following is **incorrect** about type II muscle fibers?

- A. They are called slow fibers
- B. Their myosin ATPase activity is high
- C. They contain little myoglobin
- D. They are rich in glycolytic enzymes

31. Which of the following statements is **incorrect**?

- A. Contraction against a constant load with approximation of the ends of the muscle is called isotonic contraction.
- B. Contraction can occur without an appreciable decrease in the length of the muscle.
- C. Isometric contractions do work whereas isotonic contractions do not.
- D. Muscles can lengthen while doing work.

32. The smallest amount of muscle that can contract in response to excitation of a single motor neuron is:

- A. 1 muscle fiber
- B. a muscle fasciculus
- C. the entire muscle
- D. all muscle fibers supplied by that neuron

33. The size of the motor unit is smallest in:

- A. type II muscle fibers
- B. single-unit smooth muscle
- C. orbicularis oculi
- D. soleus

34. Gradation of force in skeletal muscle is **not** achieved by:

- A. increasing intracellular calcium
- B. recruitment of motor units
- C. asynchronous firing of motor units
- D. varying release of calcium from SR

35. Regarding the ionic basis of action potential in cardiac muscle cells, which **one** of the following is **incorrect**?

- A. Phase 0: Na influx
- B. Phase 1: K influx
- C. Phase 2: Ca influx
- D. Phase 3: K efflux

36. When heart rate is about 75 beats/min, the duration of absolute refractory period of cardiac muscle is:

- A. 50 ms
- B. 100 ms
- C. 200 ms
- D. 300 ms

37. When heart rate is about 75 beats/min, the duration of ventricular systole is about:

- A. 0.1 s
- B. 0.2 s
- C. 0.3 s

38. Which of the following muscle types is the 'fastest'?

- A. Skeletal muscle
- B. Smooth muscle
- C. Cardiac muscle

39. Which of the following characteristics is exhibited **only** by skeletal muscle?

- A. Gradation of force production
- B. Refractoriness
- C. Beneficial effect
- D. Staircase phenomenon
- E. None of the above

40. Non-linearity of length-tension relationship is most evident in:

- A. skeletal muscle
- B. smooth muscle
- C. cardiac muscle

41. In adults, intravesical pressure rises suddenly when intravesical volume reaches about:

- A. 100 ml
- B. 200 ml
- C. 300 ml
- D. 400 ml

42. The latch-bridge mechanism in smooth muscle is responsible for:

- A. fast muscle twitch
- B. sustained muscle contraction
- C. excitation-contraction coupling
- D. unstable membrane potential

43. The minimum stimulus strength that produces a compound action potential in nerve or muscle is:

- A. rheobase
- B. chronaxie
- C. twice rheobase
- D. twice chronaxie

44. Which of the following accelerates contraction as well as relaxation of heart muscle?

- A. Norepinephrine
- B. Calcium
- C. Digoxin
- D. Potassium

45. Which of the following statements about cardiac muscle is **incorrect**?

- A. Summation cannot occur
- B. It is a 'fast' muscle
- C. Slow myosin ATPase activity
- D. It contains myoglobin

46. Which nerve fiber type is **most** susceptible to conduction block by local anesthetics?

- A. Type A
- B. Type B
- C. Type C

47. Nociceptors (nerve endings signaling pain) signal through:

- A. A $\alpha$  fibers
- B. A $\beta$  fibers
- C. A $\delta$  fibers

- D. A $\gamma$  fibers
- E. C fibers

48. The nerve fiber type **most** susceptible to conduction block by pressure is:

- A. type A
- B. type B
- C. type C

49. Neuromuscular transmission is impaired in conditions listed below (in List A), however, the pathogenesis of muscle weakness is different in each. Match items in List A with those in List B.

**List A**

- A. Cobra venom intoxication
- B. Myasthenia gravis
- C. Botulism
- D. Lambert-Eaton syndrome

**List B**

1. Antibodies to nicotinic Ach receptors in the motor end plate
  2. Toxin inhibits Ach release from presynaptic nerve terminals in skeletal muscle neuromuscular junction
  3. Competitive blockade of nicotinic AchR in skeletal muscle motor end plate
  4. Antibodies to voltage-gated calcium channels in presynaptic terminals
50. Denervation hypersensitivity:
- A. is due to upregulation of neurotransmitter receptors in the denervated structure
  - B. does not occur in smooth muscle
  - C. partly explains the *release phenomenon* that occurs in neurological diseases

**Answers: Physiology of Nerve & Muscle Cells**

1B	2B	3B	4B	5D
6B	7A	8all	9B	10A
11D	12C	13A	14B	15BC
16D	17B	18B	19B	20C
21A	22A	23D	24C	25A
26all	27D	28A	29C	30A
31C	32D	33C	34D	35B
36C	37C	38A	39E	40B
41D	42B	43A	44A	45B
46C	47CE	48A	49	50AC

49: 1B, 2C, 3A, 4D

**Answer Explanations:**

1. Fast anterograde transport from the cell bodies to axons is brought about by kinesin. It occurs at a speed of 400 mm/day.

4. You can predict this by using the Nernst equation. Hypokalemia makes cells less excitable by reducing RMP (i.e. making it more negative).

5. *Reference:* Ch 2, p 59 In: WFG 22<sup>nd</sup> ed.

12. The reason is action potentials are all or none and occur with a constant magnitude.

21. Gap junctions are absent from nonsyncytial smooth muscle (example, smooth muscle of iris). This makes possible fine graded contractions of the iris and regulation of pupil diameter.

23. Skeletal muscle depends on the SR as the major source of calcium. Cardiac muscle and smooth muscle depend on influx of calcium from ECF and Ca-induced calcium release for contraction.

27. Note that ATP is required for muscle contraction as well as relaxation.

28. At or above threshold intensity, an increase in the frequency of stimulation (successive stimulation rather) produces a gradual increase in the amplitude of successive contractions. This is called staircase phenomenon or *Treppe* or Bowditch effect. It occurs in skeletal as well as cardiac muscle. In cardiac muscle, it is attributed to increased availability of intracellular calcium (beneficial effect of previous contractions).

**29. Classification of skeletal muscle fibers**

	<b>Type I</b>	<b>Type II</b>
Other names	Slow, oxidative, red	Fast, glycolytic, white
Myosin ATPase rate	Slow	Fast
Ca-pumping capacity of SR	Moderate	High
Oxidative capacity (myoglobin, content of	High	Low

mitochondria, capillary density)		
----------------------------------	--	--

Fast muscle fibers (type II) have high myosin ATPase activity and their twitch duration is short, whereas slow fibers (type I) have slow myosin ATPase activity, and the twitch duration is correspondingly longer.

**31. Types of muscle contraction**

<b>Isotonic contraction</b>	<b>Isometric contraction</b>
Tension developed is constant; muscle shortens	Tension developed; Muscle does not shorten
External work is done	“External work” is not done
Example: Walking, bending, running	Trying to lift a heavy weight, sustained handgrip

$W = \text{Force} \times \text{displacement}$ ; since the muscle ends are fixed in an isometric contraction, no ‘external work’ is done in an isometric contraction.

32. A motor unit is the smallest amount of muscle that can contract in response to excitation of a single motor neuron.

33. **Motor unit:** an alpha motor neuron and all muscle fibers innervated by it.  
**Innervation ratio (IR):** number of muscle fibers in a motor unit.  
 In small motor units: IR 3-10  
 In large motor units: IR >> 100

**Motor point:** point where nerve enters muscle (anatomical)

According to the size principle, small motor units are recruited first and large motor units that consist of large rapidly conducting axons are recruited for more forceful contractions.

<b>Slow motor unit</b>	<b>Fast motor unit</b>
------------------------	------------------------

Small, slow conducting axons	Large, rapidly conducting axons
Innervate slow muscle fibers (type I)	Innervate fast fatigable muscle fibers (type II)

34. Gradation of force in skeletal muscle is achieved by:

- recruitment of motor units
- ↑ the frequency of stimulation of motor units
- asynchronous firing of motor units
- variations in preload.

Gradation of force is not achieved by varying calcium release from the sarcoplasmic reticulum because each action potential that enters the T tubule releases a constant amount of calcium from the terminal cisterns of the SR.

36. Cardiac muscle fibers are refractory during the upstroke of the action potential and until at least repolarization is half complete. This is called *effective (or absolute) refractory period*, and the heart cannot be excited during this time no matter how strong the stimulus is. In the *relative refractory period*, a supranormal stimulus can evoke an action potential. Because of the long duration of absolute refractory period, diastole commences before the heart is reexcitable. Thus, summation of the type seen in skeletal muscle cannot occur in cardiac muscle and why cardiac muscle cannot be tetanized. This is a *safety* feature since the heart has to fill with blood between successive contractions.

### 37. Events in the cardiac cycle

- Electrical (depolarization and repolarization) are followed by mechanical events (systole and diastole)
- Cardiac cycle time: RR interval (variable)
- Action potential duration: variable
- If average HR is 75 bpm, then average cardiac cycle time =  $0.8 \text{ s} = 800 \text{ ms}$
- Average action potential duration ~ 250 ms
- Duration of absolute refractory period ~ 200 ms
- Relative refractory period ~ 50 ms

- *Note:* Refractory period length depends upon the duration of the action potential. For example, when HR is about 150 bpm, the duration of the action potential is definitely shorter.

38. Note that the terms slow and fast are applied to muscle based on twitch duration. Twitch duration is the duration of a single contraction followed by relaxation. In slow type skeletal muscle fibers, it could be as long as 100 ms. The twitch duration in cardiac muscle is normally 800 ms (at a HR of 75 beats/min). The twitch duration could be as short as 10 ms as it is in 'fast' skeletal muscle. The minimum twitch duration in the heart is about 300 ms (at a heart rate of 200/min). Smooth muscle is perhaps the slowest. It is capable of sustained contraction (tonic contraction).

### 40. Some important definitions:

**Preload:** the load on a muscle before it contracts. In the ventricle, the preload (end-diastolic fiber length) varies with the end-diastolic volume.

**Afterload:** the load which contracting muscle has to overcome before it shortens.

Within physiologic limits, an increase in end-diastolic fiber length increases tension developed (force of ventricular contraction). This is the *Frank-Starling law of the heart*.

Similarly, in skeletal muscle, there is a linear relationship between preload and force of contraction when other factors such as recruitment are held constant.

However, in smooth muscle, length-tension relationships are nonlinear over the physiologic range. Consider for example the smooth muscle of the bladder. Refer to the cystometrogram in a normal human (*Fig 38-25, p. 727, Ch 38, WFG, 2005*). Note that an increase in intravesical volume from 0 to 50 ml is accompanied by an increase in intravesical pressure. However, an increase in intravesical volume from 50 up to 380 ml is not accompanied by an increase in intravesical pressure. This means that the bladder is not 'shortening' in this range because if the

bladder shortened, the intravesical pressure would have increased.

Second, in a hollow viscus, wall tension  $T = Pr$ . i.e.,  $P = T/r$ . When intravesical volume increases from 50 to 350 ml, the bladder is stretched and its radius increases. Stretch (the stimulus) elicits some tension (the response) in the wall of the bladder. This is called *passive tension* because it does not cause the radius to decrease but merely enables it to withstand the distending pressure. On the other hand, when intravesical volume is increased to 400 ml, the bladder wall has been *adequately* stretched and a strong reflex contraction of the bladder occurs leading to shortening (*active tension*) of the detrusor and emptying of the bladder

Total tension = active + passive tension.

As far as this question is concerned, this discussion is intended to emphasize the fact that the relation between length (in this example, intravesical volume) and tension is quite unpredictable in smooth muscle.

42. The twitch duration in sphincters and smooth muscle is particularly longer. Latch bridges are actomyosin complexes that detach slowly; this is made possible by a slow myosin ATPase. In turn, this enables maintenance of tension for longer periods without consumption of more ATP.

43. The strength-duration curve is a plot of the strength of the electrical stimulus required to elicit compound action potentials in nerve or muscle against the duration of the stimulus. Rheobase is the minimum stimulus strength that will produce a response. Chronaxie has been defined as the minimum stimulus duration at which twice the rheobasic current will produce a response.

44. Norepinephrine has a positive chronotropic (increases rate of contraction), inotropic (increases force of contraction), and lusitropic effect (i.e., it accelerates relaxation) on the heart.

45. Cardiac muscle is “slow” (i.e., its twitch duration is longer compared to fast skeletal

muscle). The average twitch duration in the heart is 800 ms when HR is 75 bpm.

47. Fast pain is transmitted through myelinated A-delta fibers, and ‘slow pain’ is the result of transmission through unmyelinated C fibers.

\*\*\*\*\*

## 4. Functions of the Central Nervous System

**Most of the questions in this section have only one correct answer**, as should be apparent from the stem of the question; however, some questions may have more than one correct answer – *please read all options!*

- Which of the following types of cells work as scavenger cells in the CNS?
  - Microglia
  - Oligodendroglia
  - Ependymal cells
  - Astrocytes
- Which is the commonest type of synapse in the CNS?
  - Axosomatic synapse
  - Axodendritic synapse
  - Axoaxonal synapse
- Excitatory postsynaptic potentials (EPSP) are **not** produced by:
  - opening of Na channels
  - closure of K channels
  - opening of calcium channels
  - opening of chloride channels
- Inhibitory postsynaptic potentials (IPSP) may be produced by:
  - closure of Na channels
  - closure of Ca channels
  - opening of K channels
  - opening Cl channels
- The minimum time for transmission across one synapse is:
  - 0.5 ms
  - 1 ms
  - 1.5 ms
  - 2 ms
- Inhibitory postsynaptic potentials are an example of:
  - postsynaptic inhibition
  - presynaptic inhibition
  - direct inhibition
  - indirect inhibition
- Presynaptic inhibition occurs at:
  - axoaxonal
  - axosomatic
  - axodendritic synapses
- Renshaw cell inhibition of alpha motoneurone is an example of:
  - negative feedback inhibition
  - feedforward inhibition
  - presynaptic inhibition
  - postsynaptic inhibition
  - indirect inhibition
  - direct inhibition
- Which of the following **is/are** examples of ligand-gated ion channels?
  - Nicotinic Ach receptor
  - GABA-activated Cl channels
  - IP<sub>3</sub> receptor
  - Glycine receptor
- Which of the following statements about synaptic potentials is **incorrect**?
  - They are propagated down the postsynaptic neuron
  - They undergo spatiotemporal summation
  - They are analogous to generator potentials and end-plate potentials
  - IPSP hyperpolarize the postsynaptic neuron
  - They are proportional to the amount of transmitter released by the presynaptic neuron.
- Is conduction of nerve impulse in motor axons unidirectional or bidirectional? Explain.
- Most excitatory neurotransmission in the brain is believed to be mediated by:
  - glutamate
  - glycine
  - GABA
  - GnRH
- The inhibitory amino acid neurotransmitters in the CNS are:
  - glutamate and glycine
  - glutamate and aspartate
  - GABA and glycine
  - aspartate and glycine
- The GABA-A receptor is a:

- A. Na channel  
B. Cl ion channel  
C. Ca channel  
D. cation channel
15. IPSPs due to chloride influx are produced by:  
A. acetylcholine  
B. GABA  
C. glutamate  
D. substance P
16. Which of the following neurotransmitters has both excitatory and inhibitory effects?  
A. Glycine  
B. GABA  
C. Aspartate  
D. Glutamate
17. Which of the following is an excitotoxin?  
A. Glutamate  
B. Glycine  
C. Acetylcholine  
D. Substance P
18. Inhibitory interneurons in the spinal cord release:  
A. glycine  
B. GABA  
C. substance P  
D. neuropeptide Y
19. Neurons mediating direct inhibition in the spinal cord usually secrete:  
A. glycine  
B. GABA  
C. substance P  
D. glutamate
20. Tetanospasmin inhibits the release of:  
A. GABA  
B. glutamate  
C. glycine  
D. acetylcholine
21. "No matter where a particular sensory pathway is stimulated along its course to the cortex, the conscious sensation produced is referred to the location of the receptor". This is:  
A. the law of projection  
B. Weber-Fechner law  
C. Muller's law of specific nerve energies  
D. Bell-Magendie Law
22. The relation between the magnitude of sensation and stimulus intensity is given by the:  
A. law of specific nerve energies  
B. labeled line principle  
C. Weber-Fechner law  
D. law of projection
23. A single sensory axon and all of its peripheral branches constitute a:  
A. receptive field  
B. sensory unit  
C. dermatome  
D. sensory nerve
24. Intensity of a sensory stimulus (whether threshold or subthreshold) is encoded by all of the following **except**:  
A. size of generator potentials  
B. frequency of action potentials in sensory neurons  
C. recruitment of sensory units  
D. size of action potentials
25. Which of the following is a rapidly adapting sensory receptor?  
A. Muscle spindle  
B. Carotid sinus  
C. Pain receptor  
D. Pacinian corpuscle
26. A typical example of a monosynaptic reflex is:  
A. stretch reflex  
B. superficial abdominal reflex  
C. withdrawal reflex  
D. light reflex
27. The receptor for the stretch reflex is the:  
A. muscle spindle  
B. Golgi tendon organ  
C. Pacinian corpuscle
28. In the stretch reflex, the afferents are:  
A. I a fibers  
B. I b fibers  
C. II fibers  
D. A delta fibers

29. The term 'small motor nerve system' refers to:
- Ia afferents from muscle spindle
  - $\alpha$ -motor neurons
  - $\gamma$ -motor neurons
30. In the stretch reflex, relaxation of antagonist muscles is due to:
- reciprocal innervation
  - presynaptic inhibition
  - Ia fiber stimulation
  - antidromic conduction
31. The muscle spindle is made to contract by stimulation of:
- $\alpha$ -motor neurons
  - $\gamma$ -motor neurons
32. A muscle can normally be made to contract by stimulation of which of the following neurons innervating that muscle?
- $\alpha$ -motor neurons
  - $\gamma$ -motor neurons
  - Either one of the above
33. The Jendrassik's maneuver facilitates stretch reflexes by:
- exciting alpha motor neurons
  - increasing gamma efferent discharge
  - releasing glycine
34. The Hoffmann reflex (H reflex) is typically recorded from:
- soleus
  - orbicularis oculi
  - diaphragm
  - thenar muscles
35. The receptor for the inverse stretch reflex is:
- muscle spindle
  - Golgi tendon organ
  - C fiber
  - delta fibers
36. Impulses from Golgi tendon organ pass to inhibitory interneurons in the spinal cord via:
- I a
  - I b
  - II a
  - C fibers
37. All neural influences affecting muscle contraction ultimately funnel through:
- $\alpha$ -motor neurons
  - $\gamma$ -motor neurons
  - corticospinal tract
  - basal ganglia
38. Which of the following is the best example of a polysynaptic reflex?
- Stretch reflex
  - Axon reflex
  - Inverse stretch reflex
  - Withdrawal reflex
39. In humans, spinal shock is characterized by:
- hypertonia
  - hyperreflexia
  - spastic paralysis
  - loss of autonomic function
40. Which of the following is **not** a feature of *lower motor neuron* lesions?
- Muscle atrophy
  - Fasciculations
  - Fibrillations
  - Denervation hypersensitivity
  - Spastic paralysis
41. Locomotion generators in spinal cord are turned on by pattern generators in the:
- suppressor strip
  - midbrain
  - medulla
  - pons
42. The *crossed extensor response* is seen in:
- healthy humans
  - the phase of spinal shock
  - chronic paraplegia
43. The *mass reflex*:
- is a sign of a central inhibitory state
  - occurs in the decerebrate animal
  - is due to irradiation of afferent impulses
  - is a manifestation of 'release of spinal reflexes' from inhibitory control by higher centers
44. Which of the following fibers has the greatest threshold?

- A. Touch  
B. Pain  
C. Pressure  
D. Cold
45. The gate theory of pain was proposed by:  
A. Charles Sherrington  
B. Wall and Melzack  
C. Weber-Fechner
46. Anterolateral cordotomy does **not** interfere with perception of:  
A. pain  
B. pressure  
C. temperature  
D. fine touch
48. Joint position sense is transmitted by:  
A. anterior spinothalamic tract  
B. lateral spinothalamic tract  
C. dorsal column-medial lemniscal system
49. Which of the following is/are termed 'synthetic senses'?  
A. Vibratory sensibility  
B. Fine touch  
C. Joint position sense  
D. Stereognosis  
E. Two-point discrimination
50. Impaired stereognosis in the absence of a detectable defect in touch and pressure sensation points to a lesion in:  
A. the dorsal column  
B. the medial lemniscus  
C. the parietal lobe posterior to the postcentral gyrus  
D. any of the above
51. Ablation of somatosensory area (SI) does **not** significantly impair:  
A. joint position sense  
B. touch localization  
C. two-point discrimination  
D. pain perception
52. Which **one** of the following neural pathways is predominantly an uncrossed pathway?  
A. Somatosensory pathway  
B. Gustatory pathway  
C. Visual pathway  
D. Auditory pathway
53. Axons of ganglion cells in the retina terminate in the:  
A. lateral geniculate nucleus  
B. pretectal nucleus  
C. suprachiasmatic nucleus  
D. superior colliculus
54. The light reflex is integrated in the:  
A. midbrain  
B. frontal eye field  
C. medulla  
D. primary visual area
55. Which **one** of the following is **not** a component of the near response?  
A. Pupillary constriction  
B. Convergence of the visual axes  
C. Increase in convexity of the lens  
D. Ciliary muscle relaxation
56. Which of the following statements about Argyll-Robertson pupil is **incorrect**?  
A. Light reflex is absent  
B. Accommodation reflex is present  
C. The lesion is in the Edinger-Westphal nucleus  
D. It occurs in neurosyphilis
57. Central visual fields are mapped with:  
A. tangent screen (campimeter)  
B. perimetry
58. Impedance matching is a function of:  
A. scala media  
B. endolymph  
C. ear ossicles and tympanic membrane  
D. cochlear nucleus
59. What is the amplification provided by the lever action of the auditory ossicles and the large size of the tympanic membrane compared to the oval window?  
A. 5 times  
B. 10 times  
C. 22 times  
D. 45 times
60. Endolymph is produced by:

- A. stria vascularis  
 B. inner hair cells  
 C. sustentacular cells  
 D. outer hair cells
61. Which of the following structures is involved in the spatial localization of sound?  
 A. Spiral ganglion  
 B. Hair cells  
 C. Superior olivary complex  
 D. Cochlear nerve
62. Which of the following functions as a frequency analyzer in hearing?  
 A. Reissner's membrane  
 B. Tectorial membrane  
 C. Basilar membrane  
 D. Middle ear ossicles
63. Inner hair cells in the organ of Corti are depolarized by:  
 A. K influx  
 B. Na influx  
 C. Ca influx  
 D. closure of K channels
64. Hyperpolarization of receptor cells activates:  
 A. phototransduction  
 B. auditory signaling  
 C. gustation  
 D. olfactory signaling
65. Which of the following changes occur in rod cells when rhodopsin is activated by light?  
 A. Increase in cGMP  
 B. Deactivation of phosphodiesterase  
 C. Depolarization of rod cells  
 D. Decreased release of neurotransmitter
66. Linear acceleration in the vertical plane is signaled by hair cells in:  
 A. anterior semicircular canal  
 B. saccule  
 C. posterior semicircular canal  
 D. utricle
67. Taste projection area is located in the:  
 A. foot of the postcentral gyrus  
 B. precentral gyrus  
 C. cingulate gyrus
68. Which of the following reflexes is always absent in the blind?  
 A. Vestibulo-ocular reflex  
 B. Nystagmus  
 C. Visual accommodation  
 D. Light reflex
69. Saccades are programmed in the:  
 A. medial longitudinal fasciculus  
 B. frontal cortex  
 C. hypothalamus  
 D. superior colliculus
70. In which layer of the cortex do specific thalamic afferents end?  
 A. Layer VI  
 B. Layer IV  
 C. Layer I  
 D. Layer II
71. In which layer of the cerebral cortex do non-specific thalamocortical projections end?  
 A. Layer I-IV  
 B. Layer II  
 C. Layer IV  
 D. Layer VI
72. *Alpha block* is produced by:  
 A. mental arithmetic  
 B. stimulation of ascending reticular activating system  
 C. opening one eye only
73. A 4–7 Hz rhythm normally occurs in:  
 A. hypothalamus  
 B. hippocampus  
 C. parieto-occipital area  
 D. frontal area
74. A low-frequency, high amplitude, synchronized cortical rhythm occurs during:  
 A. stage 1 & 2 slow-wave sleep  
 B. stage 3 & 4 slow-wave sleep  
 C. REM sleep  
 D. narcolepsy
75. Delta waves (0.5-4 Hz) are seen in:  
 A. stage 1 sleep  
 B. stage 4 sleep

- C. an awake adult with eyes open
- D. an awake adult with eyes closed

76. Which of the following is **not** a characteristic of REM sleep?

- A. Slow waves
- B. Hypotonia
- C. Dreaming
- D. PGO spikes

77. Gamma oscillations in EEG, which occur when an individual is aroused and focuses attention on something, occur at a frequency of:

- A. 0–0.4 Hz
- B. 4–7 Hz
- C. 0–12 Hz
- D. 30–80 Hz

### Control of Posture and Movement:

78. Guarding is an example of:

- A. stretch reflex
- B. flexor withdrawal reflex
- C. clasp knife effect
- D.  $\alpha$ - $\gamma$  linkage

79. The procedure in which the hindbrain and the spinal cord are separated from the rest of the brain by transection at the superior border of pons is called:

- A. decortication
- B. decerebration
- C. deafferentation
- D. rhizotomy

80. Which of the following is pathognomonic of decerebration?

- A. Exaggerated standing
- B. Babinski sign
- C. Absence of saccades
- D. Relief of spasticity by cerebellectomy

81. Which type of rigidity is clinically more common?

- A. Decorticate rigidity
- B. Decerebrate rigidity
- C. Extensor rigidity
- D. Cog-wheel rigidity

82. Which of the following is **absent** in decorticate animals?

- A. Gross movements
- B. Temperature regulation
- C. Hopping and placing reaction
- D. Vestibulo-ocular reflex

83. Which of the following is **not** a feature of corticospinal tract disease?

- A. Cogwheel rigidity
- B. Spasticity
- C. Plantar extensor response
- D. Exaggerated deep tendon reflexes

84. All neural influences affecting muscle contraction ultimately funnel through:

- A.  $\alpha$ -motor neurons
- B.  $\gamma$ -motor neurons
- C. corticospinal tract
- D. basal ganglia

85. Lesions of the ventral corticospinal tract result in:

- A. difficulty with balance
- B. deficits in skilled voluntary movements

86. Righting reflexes are integrated for the most part in the:

- A. medulla
- B. midbrain
- C. spinal cord
- D. cerebral cortex

87. The cerebellum receives sensory input from the:

- A. labyrinth
- B. proprioceptors
- C. eyes
- D. all of the above

88. Climbing fiber input to the cerebellum comes from:

- A. superior olivary complex
- B. red nucleus
- C. inferior olivary complex
- D. locus ceruleus

89. Feedforward inhibition has been well described in neural circuits in the:

- A. spinal cord
- B. cerebellum
- C. stretch reflexes

- D. nociceptive pathway
90. The *doll's eye reflex* is integrated in the  
 A. cerebral cortex  
 B. medial longitudinal fasciculus  
 C. thalamus  
 D. medulla
91. Hypothalamus does **not** play a prominent role in the regulation of:  
 A. food and water intake  
 B. temperature  
 C. respiration  
 D. osmolality
92. Lesions of ventromedial hypothalamus typically result in:  
 A. anorexia  
 B. obesity  
 C. hypersexuality  
 D. amnesia
93. The circadian rhythm generator in the hypothalamus receives inputs chiefly from:  
 A. retina  
 B. superior colliculus  
 C. thalamus  
 D. medial geniculate nucleus
95. When ambient temperature is about 20°C, body heat is lost chiefly by:  
 A. radiation and conduction  
 B. vaporization of sweat  
 C. respiration  
 D. urination and defecation.
96. Which of the following is a heat conserving mechanism?  
 A. Panting  
 B. Sweating  
 C. Curling up in a ball  
 D. Insensible water loss
97. The process of; i.e., the conversion of short-term memories to long-term memories occurs in the:  
 A. hippocampus  
 B. amygdala  
 C. cerebral cortex  
 D. hypothalamus
98. Which of the following is/are an example(s) of associative learning?  
 A. Habituation  
 B. Sensitization  
 C. Classical conditioning  
 D. Avoidance responses
99. Intercortical transfer of memory occurs via:  
 A. corpus callosum  
 B. anterior commissure  
 C. posterior commissure  
 D. each of the above
100. A long lasting facilitation of transmission in neural pathways following a brief period of high frequency stimulation is termed  
 A. long-term potentiation (LTP)  
 B. post-tetanic potentiation (PTP)  
 C. sensitization  
 D. habituation
101. Which receptor is directly involved in long-term potentiation?  
 A. Cholinergic receptors  
 B. P2 receptor  
 C. NMDA receptor  
 D. GABA-B receptor
102. Emotional responses often outlast the duration of the stimulus because:  
 A. limbic cortex is made up of three layers  
 B. neocortex cannot modify emotional behavior  
 C. limbic circuits have prolonged afterdischarge
103. Disinhibition is a striking feature of disease of:  
 A. frontal lobe  
 B. temporal lobe  
 C. occipital lobe  
 D. parietal lobe
104. The categorical hemisphere is chiefly concerned with:  
 A. language  
 B. recognition of faces  
 C. stereognosis  
 D. spatiotemporal relations

105. The representational hemisphere is concerned with:

- A. spatiotemporal relations
- B. stereognosis
- C. recognition of faces
- D. recognition of musical themes

**Answers: Functions of the CNS**

1A	2B	3D	4all	5A
6AC	7A	8ADF	9all	10A
11	12A	13C	14B	15B
16A	17A	18A	19A	20C
21A	22C	23B	24D	25D
26A	27A	28AC	29C	30A
31B	32C	33B	34A	35B
36B	37A	38D	39D	40E
41B	42C	43CD	44B	45B
46D		48C	49ADE	50C
51D	52B	53all	54A	55D
56C	57A	58C	59C	60A
61C	62C	63A	64A	65D
66B	67A	68C	69BD	70B
71A	72ABC	73B	74B	75B
76A	77D	78B	79B	80A
81A	82C	83A	84A	85A
86B	87D	88C	89B	90B
91C	92B	93A		95A
96C	97A	98CD	99D	100A
101C	102C	103A	104A	105all

**Answer explanations:**

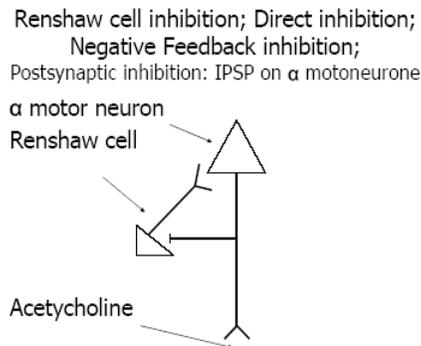
- 2. 98% synapses in the CNS are axodendritic.
- 3. Opening of chloride ion channels in postsynaptic membrane would produce hyperpolarization of postsynaptic neurons.

**6. Classification of synaptic inhibition:**

Direct Inhibition	Postsynaptic inhibition	Glycine producing IPSP on postsynaptic neurons
Indirect inhibition	Presynaptic inhibition	GABA producing inhibition at axoaxonal synapses

**Classification of synaptic inhibition based on structure of neural circuits:**

**Negative feedback inhibition:** Renshaw cell inhibition is a classic example of negative feedback inhibition. Renshaw cells are inhibitory interneurons in the spinal cord.



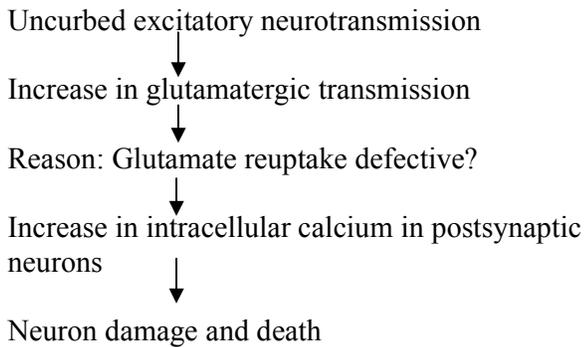
**Feedforward inhibition** occurs in cerebellar circuits.

11. In the intact human, the action potential is initiated at the axon hillock and propagates through the axon membrane to the nerve terminal. However, if we stimulated axons at the median nerve with a threshold stimulus applied through electrodes at the elbow, action potential in excited axons would travel orthograde to the nerve terminal as well as retrograde into the cell body located in the spinal cord. In a motor axon, it is anterograde transmission to the axon terminal that can release neurotransmitter. Retrograde conduction of the impulse to the cell body depolarizes it *sweeping it clean*, and rendering it refractory to stimulatory input for a definite period of time.

16. Glycine, an inhibitory neurotransmitter in the spinal cord, also has excitatory actions on NMDA receptors. In the absence of glycine, glutamate cannot exert its excitatory effects on the NMDA receptor. *See p. 110, Ch 4, WFG, 2005.*

17. Classification of glutamate receptors:

- Metabotropic
- Ionotropic
- NMDA receptor (Na & Ca channel)
- AMPA receptor



18. Golgi bottle neurons and Renshaw cells are two classic interneurons in spinal cord. Both release glycine. Both cause direct inhibition of postsynaptic neurons.

20. Tetanospasmin produces spastic paralysis by preventing the release of glycine from inhibitory interneurons in the spinal cord.

Botulinum toxin causes flaccid paralysis by inhibiting the release of Ach from the neuromuscular junction.

Strychnine blocks glycine receptors.

22. Weber-Fechner Law (Power law):  
 Magnitude of the sensation felt (R) =  $KS^A$  where S is stimulus intensity.

**Muller’s law of specific nerve energies (the labeled line principle):**

Each sensory pathway starting from the receptor up to the cortex is *labeled* for transducing a particular sensory modality.

**Bell Magendie law:** In spinal nerves, dorsal roots are sensory and ventral roots are motor.

**25. Touch receptors:**

Rapidly-adapting touch receptor	Pacinian corpuscle Meissner’s corpuscle
Slowly-adapting touch receptor	Merkel’s disks Ruffini endings

**Touch:** Pacinian corpuscle

**Vibration:** Pacinian corpuscle

Pressure is sustained touch. Vibration is repetitive touch stimuli. Pressure is presumably coded by slowly adapting touch receptors.

In a teleological sense, if the carotid sinus adapted permanently to an increase in arterial pressure, it wouldn’t play a role in the long term control of arterial pressure. It is important to note that adaptation can occur at the level of receptors (peripheral resetting) as well in the neural circuits in the CNS processing information from the receptor (this is called central resetting).

26. Even in the stretch reflex, an interneuron is interposed between the Ia afferent and the alpha motoneurone innervating the antagonist muscle; however, this is perhaps the best answer for the question.

31, 32. Muscle spindle is a stretch receptor. Contraction of the intrafusal fibers stretches the central portion of the intrafusal fiber (muscle spindle). The afferents from the muscle spindle pass via Ia and II fibers. The stretch reflex operates to regulate muscle length.

**A-γ motor neurons** innervate the intrafusal fibers whereas the extrafusal fibers (the regular contractile units of skeletal muscle) are made to contract by stimulation of alpha motor neurons.

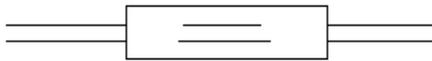
**A-α motor neurons** constitute the final common path for all neural influences causing muscle contraction.

**Monosynaptic stretch reflex** (example: knee jerk)

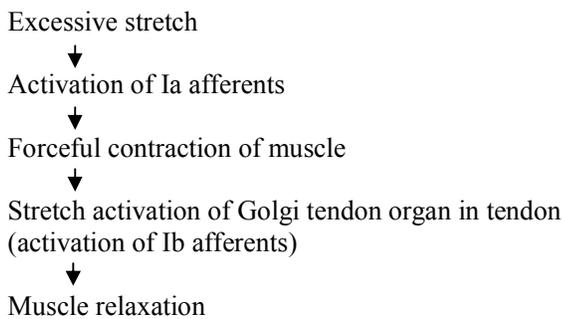
Stimulus	Stretch of muscle
Receptor	Muscle spindle
Afferents	Ia and II fibers
Integration	Spinal cord
Response	Contraction of muscle
Latency	20 ms
Significance	It assesses the integrity of the reflex arc and higher influences upon it
Diminished or lost in	Lower motor neuron type disease, phase of spinal shock, deafferentation,
Exaggerated in	With Jendrassik’s maneuver and conditions increasing gamma motor neuron discharge, upper motor neuron type disease, chronic spinal animals / humans
H reflex	The pathway for this reflex is the same as any monosynaptic

	reflex (MSR); it is a sensitive means of assessing integrity of MSR when reflexes are not clinically elicitable, as can occur in acute onset weakness. However, it is recorded only from soleus (by EMG). The H reflex is absent in Guillain-Barre syndrome.
--	--

**35. Golgi tendon organ** is a stretch receptor located in series with collagen fibers in the muscle tendon; it is innervated by Ib fibers



**Inverse stretch reflex (autogenic inhibition)**



**38. Characteristics of withdrawal reflexes:**

Stimulus:	Noxious stimulus
Integration:	Spinal cord
Control:	Normally suppressed by higher centers
Response:	Withdrawal of affected body part
Exaggerated in	Chronic spinal animals as a result of "release" from inhibitory control from higher centers. Thus the crossed extensor component of the response is seen only in chronic paraplegics (i.e. following recovery from spinal shock)

The **crossed extensor response**, which occurs due to irradiation of afferent stimuli, occurs only in spinal animals that have recovered from spinal

shock. It is a sign of release of spinal lower motor neurons from the inhibitory control of higher centers.

39. Spinal shock is presumably due to sudden loss of tonic bombardment of  $\alpha$ -motor neurons by supraspinal neurons.

40. Spasticity is a release phenomenon. It occurs as a result of release of brain stem motor neurons from inhibitory control by higher centers (i.e. the cerebral cortex and the basal ganglia)

43. The mass reflex is a sign of a central excitatory state; it is presumably a manifestation of release of spinal lower motor neurons from inhibitory control by higher centers. Denervation supersensitivity may contribute to the occurrence of the mass reflex.

45. The gate theory of pain posits that there is a mechanism to facilitate or inhibit transmission of nociceptive impulses at the level of the spinal cord. The putative gate is thought to be located at the substantia gelatinosa of the spinal cord. Higher centers exert influences on this gate. For example, serotonin released from raphe spinal neurons inhibits onward transmission of nociceptive inputs (endogenous analgesia system).

46 and 48. Ascending pathways and the sensory modalities they code:

Dorsal column – lemniscal system	Fine touch, touch localization, two-point discrimination, vibration, joint position sense
Anterior spinothalamic tract	Pressure, crude touch
Lateral spinothalamic tract	Pain, temperature

49. Synthetic senses are synthesized in the sensory association area in the brain (posterior parietal cortex) from component senses. Stereognosis is a good example of a synthetic sense.

50. Since touch and pressure are both intact, one could presume that all sensory pathways right up

to the somatosensory cortex are intact. Impaired stereognosis must therefore be due to a defect posterior to the somatosensory area (i.e. in the posterior parietal cortex).

51. Ablation of somatosensory area does not result in impairment of pain perception since the mere perception of pain does not require the cortex. Cortical processing is concerned primarily with finer aspects of information processing including discrimination of subtle differences in stimulus intensity, localization of stimulus.

**53. Visual pathway:** Retina >> Ganglion cells >> Lateral geniculate nucleus >> Primary visual cortex (V1), Area 17

**Pathway for accommodation:**

Retina >> Ganglion cells >> Lateral geniculate nucleus >> Primary visual cortex (V1), Area 17 >> Frontal eye field (Area 8) >> Edinger-Westphal nucleus (preganglionic parasympathetic neurons) >> Ciliary ganglion (parasympathetic postganglionic neurons) >> Iris, ciliary muscle

**Pathway for entrainment of circadian rhythms:**

Ganglion cells >> Suprachiasmatic nucleus (SCN) >> other relays in the hypothalamus >> brain stem reticular formation >> autonomic efferents

56. Light reflex absent; accommodation reflex present – Argyll Robertson pupil; lesion in the pretectal nucleus of the midbrain where light reflex is integrated.

Light reflex present; accommodation reflex absent – Wernicke’s pupil. In this situation, the lesion could be present anywhere beyond the exit of the fibers from the optic nerve to the pretectal nucleus.

59. Amplification by lever action of ear ossicles = 1.3. Ratio of surface area of tympanic membrane and oval window = 17; total amplification =  $17 \times 1.3 = 22$

60. Endolymph is rich in K like ICF; Perilymph is rich in Na; like ECF; Endolymph and perilymph do not mix.

63. Hair cells are depolarized by K influx because the endolymph is rich in K.

66.

<i>Stimulus</i>	<i>Sensory receptor</i>
Linear acceleration in the vertical plane	Saccule
Linear acceleration in the horizontal plane	Utricule
Rotational acceleration	Semicircular canals in the plane of the rotation

67. There is no separate taste area in the brain as there is for other special senses. Impulses from taste buds finally reach the foot of the postcentral gyrus.

68. Think about how the accommodation reflex is elicited. We ask a person to look at an object placed nearby after he looks at an object placed farther away. Obviously, this is integrated in the multiple areas in the cerebral cortex (visual cortex followed by the frontal eye field) and then projects to the Edinger-Westphal nucleus in the midbrain. Thus, a person who is blind (on both eyes) because of a defect in the visual pathway anywhere beyond the optic chiasm will not have this reflex.

**70, 71. Types of thalamocortical projections:**

**Specific:** function to transmit information to specific areas in the cortex; results in sensory perception; they end in layer IV of the cortex  
**Nonspecific:** function to arouse the individual; end in layers I-IV of the cortex.

**70-75. Notes on EEG:**

In an adult human at rest with mind wandering and eyes closed, the most prominent component of the EEG is a fairly regular pattern of waves at a frequency of 8-12 Hz, and amplitude of about 50 microvolts when recorded from the scalp. This pattern is the **alpha rhythm**. It is most prominent in the parieto-occipital area.

The alpha rhythm is replaced by a fast irregular low voltage beta rhythm (18–30 Hz). This phenomenon is called **alpha block**. A breakup of

the alpha rhythm is produced by any kind of sensory stimulation such as mental arithmetic.

Large amplitude, regular 4–7 Hz waves called the **theta rhythm** occurs in children and is generated in the hippocampus in experimental animals.

**Stages of sleep:** Stages I – IV of NREM (slow wave sleep) followed by rapid eye movement (REM) sleep

**Sleep spindles** (occur in stage II sleep)  
Frequency: 10–14 Hz; amplitude: 50 microvolts.

EEG waves	Frequency
<i>Delta</i>	0.5–4 Hz
<i>Theta</i>	4–7 Hz
<i>Alpha</i>	8–13 Hz
<i>Beta</i>	14–30 Hz
<i>Gamma</i>	30–80 Hz

Delta waves occur in deep sleep (stages III and IV).

REM sleep is called **paradoxical sleep** because it is marked by rapid, low voltage, irregular EEG activity. The threshold for sensory arousal from REM sleep is sometimes greater than NREM sleep presumably because the brain is actively processing information during REM sleep (dreams).

**EEG during sleep:**

Stage	Characteristics
Stage 1	Alpha rhythm
Stage 2	Sleep spindles and K complexes (beginning of slowing; reduction in alpha content)
Stages 3 & 4	Characterized by slow waves (theta and delta)
REM sleep	High frequency, low amplitude rhythm similar to the wakeful state

**Ponto-geniculo-occipital (PGO) spikes**

**Origin:** Pons

**Termination:** Occipital cortex

**Neurotransmitter:** Acetylcholine

**Function:** Generation of dream imagery?

**Overview for Questions 78-88**

**An overview of control of posture and movement**

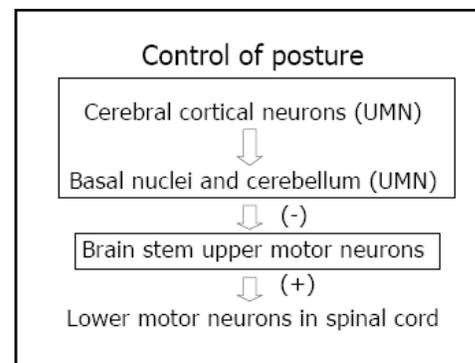
- What is meant by ‘posture’
- What is meant by ‘movement’
- What are the posture regulating pathways?
- What are the movement regulating pathways?

**Animal preparations used to study the regulation of posture:**

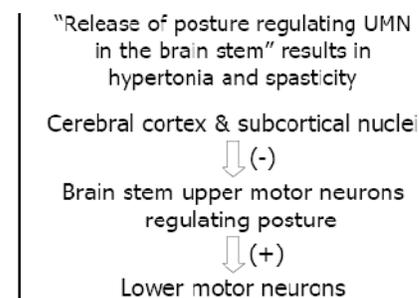
- **Spinal preparation:** spinal cord transection at midthoracic level
- **Decerebrate preparation:** transection of the neuraxis at the superior border of pons
- **Midbrain preparation:** transection of the neuraxis on top of the midbrain
- **Decortication:** removal of cerebral cortex alone leaving subcortical structures intact

**What does each of the following mean?**

- Upper motor neuron (UMN)
- Lower motor neuron (LMN)
- Pyramidal pathway
- Extrapyramidal pathway
- Lateral system pathways
- Medial system pathways



**The mechanism of decerebrate rigidity:**



**Classification of upper motor neurons:**

- Posture regulating upper motor neurons
- Movement regulating upper motor neurons

**Posture regulating upper motor neurons:**

<b>Origin:</b>	Brain stem
<b>Termination:</b>	On alpha and gamma motor neurons in spinal cord
<b>Controlled by:</b>	Inhibitory inputs from cerebral cortex (suppressor strip – 4s) in the anterior edge of the precentral gyrus and basal ganglia.

**Movement mediating / regulating upper motor neurons:**

<b>Origin:</b>	Corticospinal tract (layer V, pyramidal cell axons) from primary motor cortex, sensory cortex, and premotor area.
<b>Termination:</b>	On <i>alpha</i> -motor neurons / interneurons innervating alpha motor neurons in spinal cord
<b>Lesions:</b>	limited to the corticospinal and corticobulbar tracts produce “weakness” rather than paralysis and the affected musculature is generally “hypotonic”. Isolated involvement of corticospinal tract is not clinically common.

**Level of integration of principal postural reflexes:**

Level	Postural reflexes
Spinal cord	Stretch reflexes, withdrawal reflexes
Medulla	Labyrinthine righting reflexes, tonic neck reflexes
Midbrain	Righting reflexes
Cerebral cortex	Hopping and placing reactions, optokinetic reflexes

**Classification of movements:**

Reflexive movements	All reflexes
Rhythmic movements	Swallowing
Voluntary movements	Writing, talking, skilled movements

**Descending motor pathways:**

**Lateral system pathways**

- Lateral corticospinal tract
- Rubrospinal tract

**Medial system pathways:**

- Ventral corticospinal tract
- Reticulospinal tract
- Vestibulospinal tract
- Tectospinal tract

**Lateral system pathways** are movement regulating pathways. If we could manage to cut only lateral corticospinal tract axons (for example, by sectioning pyramids in monkeys), posture would not be affected but the animal would lose its ability to perform fine skilled movements. The affected muscles would become hypotonic.

**Medial system pathways** are posture-regulating pathways.

**Other descending monoaminergic pathways**

- Raphespinal pathways
- Ceruleospinal pathway

One way of classifying descending motor pathways is to classify them as *lateral system pathways* and *medial system pathways*.

The lateral system pathways include the lateral corticospinal tract and the rubrospinal tract (which originates in the red nucleus). The neurons of the lateral corticospinal tract typically (though not necessarily) end straight on alpha-motor neurons innervating skeletal muscles of the distal musculature used for fine, skilled voluntary movements; otherwise, they end on interneurons that regulate the alpha-motor neurons innervating these muscles. The lateral system pathways also course laterally (i.e., in the lateral funiculus) in the spinal cord.

The medial system pathways course medially in the spinal cord and end (at various levels) typically on interneurons in the medial aspect of the ventral horn of the spinal cord. Furthermore, these interneurons, on which the medial system pathways end, connect with their counterparts on the contralateral aspect of the spinal cord contributing to balance and posture. They mainly control axial muscles. The ventral corticospinal

tract, the tectospinal tract, the reticulospinal tract and the vestibulospinal tracts are all medial system pathways.

**Functional divisions of the cerebellum**

<b>Division</b>	<b>Function</b>
Spinocerebellum (midline & paravermal zone)	Maintenance of posture
Vestibulocerebellum (flocculonodular lobe)	Maintenance of posture and equilibrium
Neocerebellum (lateral cerebellar hemispheres)	Coordination of voluntary movement

- Output from the Purkinje cells to the deep cerebellar nuclei is always inhibitory.
- Output from the deep cerebellar nuclei to the thalamus is excitatory.
- Cerebellum facilitates stretch reflexes and usually hypotonia occurs in cerebellar lesions.
- Selective ablation of the flocculonodular lobe of the cerebellum has been shown to abolish the symptoms of motion sickness. The symptoms of motion sickness occur due to excessive stimulation of the vestibular system via its connections to the brain stem and the flocculonodular lobe of the spinal cord. *See p.184, Ch 9, WFG, 2005.*

88. The only source of climbing fiber input to the cerebellum is the inferior olivary complex. There is evidence that this pathway is activated when a new motor task is learnt.

90. This is the vestibulo-ocular reflex, used as a test of brain stem integrity, in patients who are comatose. The absence of the doll's eye reflex in comatose patients is a grave prognostic sign.

**92. Hypothalamus and food intake:**

*Satiety center works by inhibiting feeding center*

Feeding center located in	Lateral hypothalamus
Satiety center located in	Ventromedial hypothalamus
Lesions in ventromedial nucleus lead to	Obesity
Lesions in lateral hypothalamus lead to	Anorexia

93. Circadian rhythms are 24-h biological rhythms entrained by the light-dark cycle. They are paced in the suprachiasmatic nucleus (SCN) in the hypothalamus. The SCN receives neural input from retina. In blind individuals, circadian rhythms are “free running” and have a periodicity of about 25 hours.

**97. Notes on memory:**

Memory is retention and storage of learnt information.

- **Implicit** memory is reflexive (nondeclarative). It is nondeclarative in that one is not aware of its execution. Examples include skills one has perfected.
- **Explicit** memory, (which is declarative), requires conscious recall of events or facts. It requires processing in the hippocampus.
- **Working memory** is a form of short term memory used to plan actions; example, dialing a phone number one has just seen on the phone book. It is stored in prefrontal cortex.
- **Consolidation** refers to the formation of new long term memories from short-term memories, and it occurs in the hippocampus. The hippocampus is rich in NMDA receptors. NMDA receptors are a type of glutamate receptors.
- Short-term memory is prone to erasure; long-term memory (“true memory”) is resistant to erasure.

**Mechanisms implicated in memory:**

- ❖ Post-tetanic potentiation
- ❖ Long-term potentiation
- ❖ Changes in synaptic strength
- ❖ Increases in synaptic contacts
- ❖ Formation of new neurons from stem cells in the olfactory bulb and hippocampus may play a role.

**Post-tetanic potentiation:** Enhanced postsynaptic potentials after a brief tetanizing train of stimuli in the presynaptic neuron.

**Long-term potentiation:** Long-lasting facilitation of transmission in neural pathways following a brief period of high-frequency stimulation. This process is important for

**consolidation**, i.e. the formation of long term memories.

**Conditions which influence consolidation (formation of new LTM from STM)**

- Repetition of stimulus (facilitates)
- Sleep facilitates consolidation
- Convulsions, ECT (inhibit)
- Anesthetics, tranquilizers (inhibit)
- Hypoxia (inhibits)
- Inhibitors of protein synthesis (inhibit)

**98. Types of learning:**

Associative learning	Nonassociative learning
Associating a conditioned stimulus with a neutral stimulus	Learning about a single stimulus
Examples include classical (Pavlovian) conditioning, and operant / instrumental conditioning	Examples include habituation and sensitization

**Classical conditioning**

(Pavlovian conditioning)

- *Conditioned stimulus* (food)
- *Conditioned response* (salivation)
- *Conditioned reflex*
- *Neutral stimulus* (bell ringing)
- Pairing the neutral stimulus with the conditioned stimulus several times...
- The neutral stimulus (bell ringing) eventually elicits the same response as the conditioned stimulus (food).
- **Conditioned reflexes** (or behavior) are classic examples of associative learning.

**Instrumental conditioning**

(Synonymous with operant conditioning)

- This phenomenon was described by B.F. Skinner.
- Here the animal learns by operating on the environment.
- The main learning point here is that animal behavior is determined by the likely consequences of that behavior. From experiments conducted with the Skinner box arose concepts such as the presence in the

limbic system of “**reward centers**” and “**punishment centers**”

- “We may apply this concept to reform society” – Skinner

**Habituation:** The response to a benign stimulus repeated over and over gradually decreases. This is due to decreased release of excitatory neurotransmitter from the presynaptic neuron. The opposite response where the response to a noxious stimulus repeated over and over gradually increases is termed *sensitization*.

Both habituation and sensitization are examples of nonassociative learning because the organism learns about a single stimulus.

**99. Limbic system:**

- The seat of emotions
- It is three layered
- It is phylogenetically older compared to neocortex
- It has reciprocal connections with cortex making it possible to control emotions.
- It has connections with reticular activating system; thus, emotions can impact upon visceral function.
- There may be considerable reverberation of impulses in limbic circuits (Papez circuit); this may be why emotions last longer and are memorized.

\*\*\*\*\*

## 5. Endocrinology & Reproduction

- Which of the following hormones is **not** a glycoprotein?
  - TRH
  - FSH
  - LH
  - hCG
- Which of the following is **not** synthesized from prepro-opiomelanocortin (pre-POMC)?
  - MSH
  - ACTH
  - Endorphin
  - Dynorphin
- Which of the following hormones does **not** act through G-protein coupled receptors?
  - Dopamine
  - Epinephrine
  - Angiotensin II
  - ACTH
  - Retinoic acid
  - Thyroxine
- The group of chemical messengers whose actions are known to be mediated by receptor tyrosine kinases includes:
  - angiotensin II, ANP and ET 1
  - EDRF, ANP and AVP
  - FSH, LH and GHRH
  - insulin, EGF, IGF 1, PDGF
- Selective section of the pituitary stalk in an experimental animal usually increases the secretion of which of the following hormones?
  - Growth hormone
  - FSH
  - LH
  - Prolactin
- The term 'neurohormone' is applied to:
  - oxytocin and vasopressin
  - NO and CO
  - glycine and glutamate
  - FSH and LH
- Growth hormone secretion is increased by all of the following **except**:
  - cortisol
  - hypoglycemia
  - exercise
  - protein meal
- Which of the following hormones has intrinsic lactogenic activity?
  - TSH
  - MSH
  - GH
  - dopamine
- A human growth hormone variant (hGH-V) is expressed primarily in:
  - liver
  - spleen
  - kidney
  - placenta
- Check **all** correct statements.
  - The beta cell releases equimolar amounts of insulin and C-peptide
  - NSILA is due to circulating C-peptide
  - C-peptide has a shorter half-life compared to insulin
  - C-peptide level in plasma provides an index of B-cell function in patients receiving exogenous insulin.
- Which of the following increases insulin / glucagon molar ratio the most?
  - A large carbohydrate meal
  - Intravenous glucose
  - Overnight fast
  - A small protein meal
  - Low carbohydrate diet
- Arrange the following steps in the order in which they occur in the thyroid gland.
  - Coupling reaction
  - Iodination
  - Endocytosis of thyroglobulin
  - Oxidation of iodine
  - Iodine uptake
  - Cleavage of thyroglobulin
  - Secretion of T4
  - Iodide trapping
- Bone resorption is induced by abnormally elevated levels of:
  - IGF-1
  - insulin

- C. estrogens  
D. glucocorticoids
14. Check all correct statements regarding oxytocin.  
A. It is essential for milk ejection  
B. It increases uterine contractility  
C. It facilitates ejaculation of semen  
D. It facilitates sperm transport in the uterus
15. Calcitonin inhibits the activity of:  
A. osteoblasts  
B. osteoclasts  
C. parafollicular cells  
D. thyroid
16. Somatostatin inhibits the secretion of:  
A. insulin  
B. glucagon  
C. growth hormone  
D. gastrin
17. Hans Selye defined “stressors” specifically as stimuli that increase the secretion of \_\_\_\_\_ in healthy humans or laboratory animals.  
A. CRH  
B. ACTH  
C. TSH  
D. cortisol
18. Which of the following organelles is a major site of steroidogenesis?  
A. Peroxisomes  
B. Ribosomes  
C. Smooth endoplasmic reticulum  
D. Rough endoplasmic reticulum
19. Which of the following hormones has the highest mineralocorticoid activity?  
A. Cortisol  
B. Corticosterone  
C. Deoxycorticosterone  
D. Cortisone
20. Which of the following hormones has maximum glucocorticoid activity?  
A. Cortisol  
B. Corticosterone  
C. Deoxycorticosterone  
D. Cortisone
21. In humans, the most abundant adrenocortical hormone is:  
A. cortisol  
B. corticosterone  
C. deoxycorticosterone  
D. DHEA sulfate
22. The major adrenal androgen is:  
A. etiocholanolone  
B. testosterone  
C. dihydrotestosterone  
D. DHEA sulfate  
E. androstenedione
23. In which zones is corticosterone converted to aldosterone?  
A. Zona glomerulosa  
B. Zona fasciculata  
C. Zona reticularis
24. The hormone that is synthesized only in the zona glomerulosa is:  
A. DHEA  
B. aldosterone  
C. corticosterone  
D. deoxycorticosterone
25. Injection of pharmacologic doses of ACTH in healthy experimental animals is **least likely** to produce an increase in:  
A. cortisol  
B. lymphocyte count  
C. skin pigmentation  
D. aldosterone secretion
26. Glucocorticoids decrease the number of circulating:  
A. eosinophils  
B. lymphocytes  
C. platelets  
D. red blood cells
27. Which of the following does **not** occur as a consequence of adrenalectomy?  
A. Decreased ability to excrete a water load  
B. Glucose intolerance  
C. Increased vulnerability to hypotension  
D. Reduced alertness  
E. Dextrose fever

28. Insulin sensitivity is **not** reduced in:
- glucagon-secreting tumors
  - tumors of adrenal medulla
  - tumors of adrenal cortex
  - hypopituitarism
29. Which of the following peptides has been shown to have significant incretin effects?
- Vasoactive intestinal polypeptide
  - Somatostatin
  - Glucagon like polypeptide
  - Pancreatic polypeptide
30. Which of the following is the first of a new class of incretin mimetics approved for use in the treatment of type II diabetes?
- Exenatide
  - Adiponectin
  - Resistin
  - Leptin
31. Which of the following hormone peaks during the mid-luteal phase?
- Inhibin B
  - FSH
  - LH
  - GnRH
32. Which of the following causes luteolysis?
- PGF<sub>2</sub> alpha
  - Progesterone
  - Inhibin B
  - Relaxin
33. With a sensitive radioimmunoassay, hCG can be detected in the blood of a pregnant woman as early as \_\_\_ days post conception.
- 2 days
  - 6 days
  - 10 days
  - 14 days
34. Human chorionic gonadotropin is structurally and functionally similar to:
- LH
  - FSH
  - growth hormone
  - inhibin

35. The *fetal zone of the adrenal cortex* in the fetus predominantly secretes:
- progesterone
  - androstenedione
  - DHEA
  - DHEA sulfate

36. The principal estrogen secreted by the fetoplacental unit is:
- estriol (E3)
  - estradiol (E2)
  - estrone (E1)

37. 21 hydroxylase deficiency results in:
- congenital adrenal hyperplasia
  - testicular feminization syndrome
  - male pseudohermaphroditism

38. The enzyme deficiency that accounts for most instances of the virilizing form of congenital adrenal hyperplasia is:

- 21 hydroxylase
- 17 $\alpha$  hydroxylase
- 11 $\beta$  hydroxysteroid dehydrogenase
- 3 $\beta$  hydroxysteroid dehydrogenase

39. The hypertensive form of congenital adrenal hyperplasia is due to a deficiency of:

- 11 $\beta$  hydroxylase
- 21 hydroxylase
- 3 $\beta$ -hydroxysteroid dehydrogenase
- DHEA sulfokinase

40. Which of the following almost guarantees 'maleness'?

- Presence of Y chromosome
- Functional embryonic testes
- Absence of Barr body in neutrophils
- Well developed male external genitalia

#### Answers: Endocrinology & Reproduction

1A	2D	3EF	4D	5D
6A	7A	8C	9D	10AD
11A		13D	14all	15B
16all	17B	18C	19C	20A
21D	22D	23A	24B	25B
26AB	27B	28D	29C	30A
31A	32A	33B	34A	35D
36A	37A	38A	39A	40D

### Answer explanations:

1. TRH is a tripeptide

2. Pre-proopiomelanocortin (POMC) derivatives are:

- Beta-endorphin
- MSH (alpha, beta and gamma)
- ACTH
- Beta-lipotropin (LPH)
- CLIP

3. Retinoic acid, thyroxine, steroid hormones act mainly through receptors located in the cytosol or nucleus of target cells. However, recent evidence suggests that at least some of the physiologic effects of steroid hormones like estrogens, aldosterone are mediated via receptors located in the cell membrane. These actions have come to be therefore called 'nongenomic actions' of steroid hormones.

5. Normally, dopamine from the hypothalamus inhibits the release of prolactin.

6. Neurohormones are hormones synthesized and secreted by neurons into the general circulation

10. Non-suppressible insulin like activity (NSILA) is insulin activity that is not suppressed by anti-insulin antibodies. It is due to insulin-like growth factors IGF-I (somatomedin C) and IGF-II.

12. *Steps in thyroid hormone synthesis:*

1. Iodine uptake (Iodide trapping)
2. Oxidation of iodine
3. Iodination of tyrosine residues
4. Coupling of iodotyrosines
5. Endocytosis of thyroglobulin
6. Cleavage of thyroglobulin
7. Secretion of T4

14. Functions of oxytocin:

- Milk ejection
- Uterine contractions at the time of labor
- Uterine contractions at the time of sexual intercourse promote sperm transport in the uterus

- Contraction of vas deferens and propulsion of sperm toward urethra (during ejaculation)

17. Hans Selye defined stress as any stimulus that increases the release of ACTH in experimental animals or normal humans.

21. DHEA levels peak in the third decade of life and decline thereafter. Thus, it has been looked upon as a marker of aging. There is no evidence at the moment that DHEA supplementation reverses changes associated with aging. However, the most abundant adrenocortical hormone in plasma is DHEAS. Thus, it is appropriate to use plasma DHEAS level as an index of functioning adrenocortical mass.

26. Glucocorticoids decrease the number of eosinophils, basophils and lymphocytes in the circulation.

Glucocorticoids, particularly in pharmacologic doses suppress cell-mediated immunity by multiple mechanisms including:

- inhibiting IL-2 gene transcription
- inhibiting T cell proliferation
- inducing apoptosis in lymphocytes

27. Mechanism of **dextrose fever** in adrenocortical insufficiency:  
Suppose large amounts of 5% dextrose (an isoosmotic solution) is administered,

↓

Dextrose is metabolized

↓

The water added dilutes plasma; however water excretion is defective

↓

Plasma osmolality decreases

↓

Water enters cells

↓

Water influx into temperature-sensitive neurons disrupts function of the hypothalamic thermostat

↓

Fever

Based on the same mechanism (entry of water into cells), cerebral edema can occur as a complication of a reduction in osmolality in this condition.

28. Diabetogenic hormones (hormones which when present in excess reduce insulin sensitivity and thus increase plasma glucose levels):

- Epinephrine
- Norepinephrine
- Glucagon (especially in individuals with DKA)
- Growth hormone
- Cortisol
- Thyroxine (particularly in individuals predisposed to either type 1 or 2 diabetes)

29. Incretins are gastrointestinal hormones that increase insulin secretion in response to an oral glucose load.

*Examples:*

- Glucose dependent insulinotropic polypeptide (GIP) is the most important incretin
- Glucagon-like polypeptide (GLP) has also been shown to have incretin effects.

30. Exenatide is an incretin mimetic. It is a GLP analog and has been approved for use in type 2 diabetes.

31. Inhibin from the ovary inhibits the release of FSH from the pituitary.

34. HCG is a glycoprotein with 2 subunits  $\alpha$  &  $\beta$ . The  $\alpha$  subunit is identical with that in TSH, LH & FSH. The  $\beta$  subunit confers specificity. When [hCG] is high, stimulation of TSH receptors could result in mild hyperthyroidism. HCG maintains the corpus luteum of pregnancy; it is luteotropic in contrast to LH which is luteinizing; indeed both HCG and LH act upon the same receptor.

35. WFG, 2005, pp. 450, Fig 23-37

40. The Y chromosome contains the testis-determining gene (or SRY); this gene encodes a transcription factor that is essential for the development of embryonic testes. Presence of Y chromosome merely dictates the formation of embryonic testes.

Testosterone, one of the hormones produced by embryonic testes, induces the formation of male internal genitalia but not external genitalia.

Mullerian inhibiting substance from the embryonic testes causes regression of Mullerian ducts.

Development of the male external genitalia requires the presence of significant amounts of dihydrotestosterone (the biologically most active androgen) and normal androgen receptors.

Barr bodies are visible as drumstick chromosomes in only about 1-15% of neutrophils. Barr bodies are absent in individuals with Turner's syndrome. However, patients with Turner's syndrome are not male.

Gender is assigned at birth on the basis of external genitalia. The presence of well-developed male external genitalia at birth signifies that genetic sex is male, testes are functional, and dihydrotestosterone was present in adequate amounts. The purpose of the question is to clarify the difference between the terms genetic sex, Gonadal sex and phenotypic sex.

Note the exact meaning of these terms:

Genetic sex	44 XY (male)	44XX (female)
Gonadal sex	Testes (male)	Ovaries (female)
Phenotypic sex (at birth)	Male external genitalia	Female external genitalia

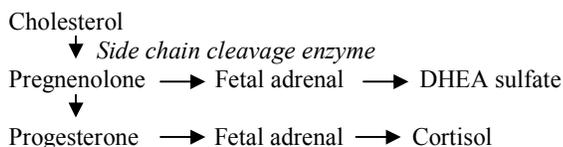
### ***Supplement on steroidogenesis***

**Biosynthesis of steroid hormones** – The best way to learn this is to use the figure on Steroidogenesis in *Ganong's Review of Medical Physiology* in the chapter on the *adrenal cortex*. You can think of the scheme operating in the zona fasciculata as the *basic scheme*. Other cells in which steroidogenesis occurs differ from this *basic scheme* in some way: ZG, ZR, theca interna cell, granulosa cell (follicular phase, luteal phase); Leydig cell; fetal zone of the adrenal cortex; adipose tissue; aldosterone sensitive distal nephron etc. Some notes are below.

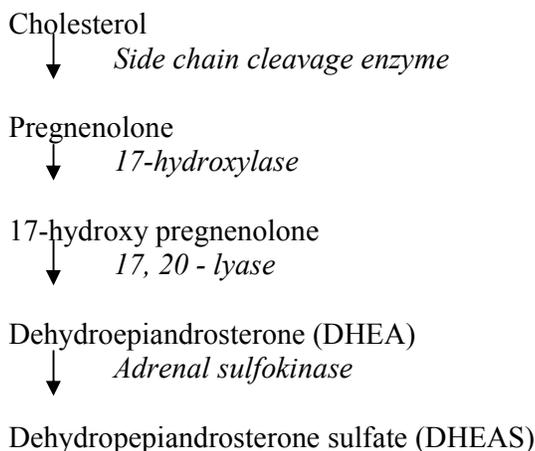
### **What happens in the placenta?**

Placenta's *priority* is to make enough

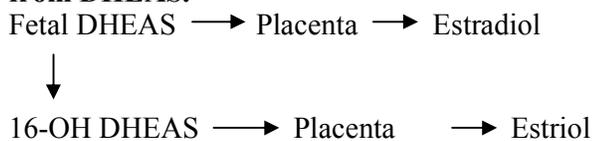
progesterone, thereby taking over the function of the corpus luteum and maintaining pregnancy.



**What happens in the fetal zone of adrenal cortex?** – This zone is recruited to produce DHEAS and 16-OH DHEAS, and it sends this back to the placenta.



**Placenta makes estradiol and estriol starting from DHEAS.**

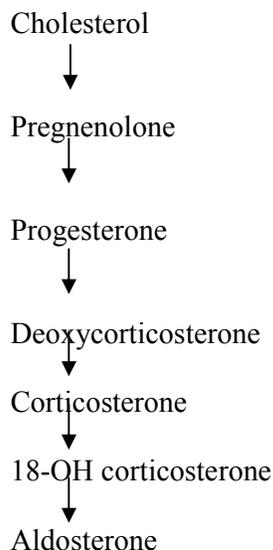


The *fetal zone* of the adrenal cortex in the fetus, which constitutes about 80% of the gland, degenerates at the time of birth. The major function of the *fetal zone* is to produce DHEAS. The placenta synthesizes estradiol and estriol from DHEAS and maintains pregnancy. Excretion of estriol in the urine of a pregnant woman is one integrated index of the health of the **fetoplacental unit**. For more information on this topic, see WFG.

**What happens in zona glomerulosa?**

Aldosterone synthase is normally expressed only in the zona glomerulosa. 17-*alpha* hydroxylase is not expressed in this zone. Angiotensin II and changes in plasma [K] are the principal regulators

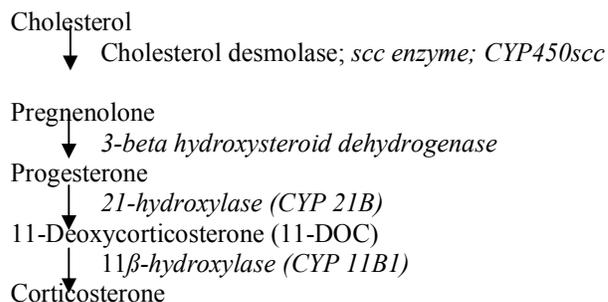
of aldosterone synthesis and secretion by the ZG. The stimulatory effects of ACTH on the ZG are transient if at all. However, with ACTH deficiency from longstanding hypopituitarism, the ZG may also diminish in size.



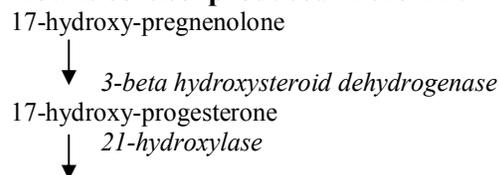
The last three steps are catalyzed by a single enzyme **aldosterone synthase** (aldo synthase; CYP aldo; CYP 11B2) – this is an enzyme with 3 enzyme activities – 11 beta-hydroxylase, 18-hydroxylase and 18-oxidase .

**What happens in zona fasciculata (ZF) and zona reticularis (ZR)? (Fetal as well as adult)**

ACTH is the principal trophic hormone for the ZF and ZR.



**How is cortisol produced in the ZF?**



11-Deoxycortisol  
 ↓ *11β-hydroxylase (CYP 11B1)*  
 Cortisol

Below is the other pathway that is particularly prominent in the ZR (under the stimulatory influence of ACTH) – the synthesis and secretion of DHEA sulfate and androstenedione (adrenal androgens). Both of them function as *prohormones* - precursors to the synthesis of more potent androgens testosterone and DHT, as well as estrogens.

Cholesterol *to*  
 Pregnenolone *to*  
 17-hydroxypregnenolone *to*  
 Dehydroepiandrosterone (DHEA) *to*  
 Dehydroepiandrosterone sulfate (DHEAS)

Normally, DHEAS (and not cortisol) is the **most abundant** adrenocortical hormone in the circulation.

**Why does virilization occur in CAH due to 21 hydroxylase deficiency?**

This can be predicted using the steroidogenesis pathway in the adrenal cortex, and based on the fact that cortisol is the most potent negative feedback regulator of ACTH release from the pituitary.

*Abnormality* - 21-hydroxylase deficiency

Loss of *negative feedback effect* of cortisol on ACTH secretion from the pituitary and CRH release by hypothalamus



Excess progesterone & excess 17-hydroxy-progesterone, which are diverted to the synthesis and secretion of



DHEA sulfate and androstenedione (large amounts)



Masculinizing effects in XX fetuses and females when present in large concentrations. Note,

however, that DHEA sulfate and androstenedione *are in themselves biologically weak as androgens*. They need to be converted to testosterone and or dihydrotestosterone or they must be present in very high concentrations to have effects on the androgen receptor. Note that all androgens exert their effects via the *same* androgen receptor.

***Congenital adrenal hyperplasia (CAH)***

The two most important causes include:

- *21 hydroxylase* deficiency (commonest)
- *11-beta hydroxylase 1* deficiency

***Pathogenetic sequence:***

1. Block in synthesis of glucocorticoids and or aldosterone
2. Increase in ACTH (as a result of loss of negative feedback effects of cortisol)
3. Compensatory bilateral adrenal hyperplasia
4. The *block* remains
5. Increased synthesis of adrenal androgens

Salt loss and Addisonian crises with severe deficiency of 21 hydroxylase (***salt losing form of CAH***) accompanied by adrenogenital syndrome in newborns (males as well as females). Screening a newborn for possible congenital adrenal hyperplasia is done by estimating serum 17-hydroxyprogesterone. If it is elevated then it should be confirmed by estimating aldosterone and cortisol.

***Manifestations in males:***

- Accentuation of male characteristics
- Precocious pseudopuberty

***Manifestations in females:***

- With mild deficiency of 21 hydroxylase, the main consequence of clinical significance may be virilization at the time of birth (***simple virilizing form of CAH***)
- Precocious pseudopuberty
- ***Nonclassic CAH (late onset):*** virilization in postpubertal females

**Clinical presentation depends on severity of deficiency:**

1. Salt losing form – with possible Addisonian crises

2. Ambiguous genitalia at birth in genetic females (*female pseudohermaphroditism*); adrenogenital syndrome
3. Precocious pseudopuberty in males
4. Virilization in postpubertal females

**Summary of Consequences of deficiencies of some enzymes involved in steroidogenesis in the adrenal cortex:**

<i>Enzyme</i>	<i>Consequences of deficiency</i>
Cholesterol desmolase (side-chain cleavage enzyme)	Fatal in utero as no steroid hormones can be synthesized
Steroidogenic acute regulatory protein (STAR)	This enzyme is not expressed in the placenta, and its deficiency has been described to be in some cases compatible with life. STAR is expressed in the adrenal cortex, testes and ovaries and is needed to transport cholesterol to the inner mitochondrial membrane in these tissues. STAR deficiency results in congenital lipid adrenal hyperplasia.
3-beta hydroxysteroid dehydrogenase (type 2)	Rare; this isoform is expressed in the fetal zone of the adrenal cortex and the gonads but not in the placenta. It is characterized by deficiency of cortisol, aldosterone and neither estrogens nor testosterone can be synthesized. In genetic males, the result is development of female external genitalia. Affected infants typically present with <i>salt losing crises</i> .
17 $\alpha$ -hydroxylase (CYP17)	Rare, no sex hormones, female genitalia develop regardless of genetic sex, characterized by an increase in plasma corticosterone, hypertension & hypokalemia
21 hydroxylase (CYP21)	95% congenital adrenal hyperplasia is due to deficiency of this enzyme; however, manifestations vary depending on severity of enzyme deficiency. Three types of presentations are

<i>Enzyme</i>	<i>Consequences of deficiency</i>
	described: classic (salt-losing form) of CAH; simple virilizing form of CAH; and non-classic (late onset) form of CAH.
11 $\beta$ -hydroxylase (CYP11B1)	Cortisol deficiency; virilization due to excessive synthesis of adrenal androgens; hypertension due to mineralocorticoid activity of high levels of 11-deoxycorticosterone

**Principles of diagnosis of disorders of sexual differentiation:** These are the most important facts one needs to know in order to understand and diagnose disorders of sexual differentiation.

1. For our purposes, it is reasonable to think of development of female internal and external genitalia as a *default* genetic program in intrauterine development regardless of genotype.

2. However, the development of normal ovaries from the bipotential gonad requires the presence of 2 normal X chromosomes and the absence of the sex-determining region of the Y-chromosome (SRY). Several genes are required for the development of ovaries – therefore, development of ovaries should not be thought of as a default pathway.

3. If the SRY gene is present, whether on the Y chromosome (normal), or hiding in a X chromosome, it dictates the formation of embryonic testes.

4. The differentiation of the gonadal ridge may be limited by deficiency of factors such as steroidogenic factor (SF-1), a nuclear receptor involved in transcriptional regulation of many genes including those need for steroidogenesis in the ovary and the testes.

5. Embryonic testes may or may not be functional. *Functional embryonic testes* secrete testosterone (Leydig cells) and Mullerian Inhibiting Substance (or Polypeptide, MIS or MIP, from Sertoli cells).

6. Like in the adrenal cortex, **steroidogenic acute regulatory protein (STAR)** is expressed in the gonads and is required for normal synthesis of steroid hormones. As for intrauterine development, this is particularly important in males because embryonic testes produce testosterone.

7. Placenta does not normally express STAR and still synthesizes progesterone. Since STAR deficiency, at least, in some cases is compatible with life, it is likely because some of the progesterone from the placenta is channeled into other sites of steroidogenesis (fetal zone of the adrenal cortex, definitive adrenal cortex, testes and ovaries) and progesterone may serve as the starting point for steroidogenesis in these tissues in this particular condition. This does not mean STAR is not necessary, but is a mechanism that potentially provides partial compensation for STAR deficiency.

6. With normal androgen receptors, testosterone (T) induces the development of 'male internal genitalia' (epididymis, vas deferens, seminal vesicles) from the Wolffian duct (mesonephric duct).

7. MIS (MIP) acts in a paracrine fashion and induces regression of *ipsilateral* Mullerian duct. In the absence of MIS (MIP), the Mullerian ducts develop into Fallopian tubes, uterus, uterine cervix and the upper third of the vagina. In contrast, the lower 2/3rd of vagina is formed by septation of the urogenital sinus.

8. Dihydrotestosterone (DHT), formed from T by the action of testosterone 5-alpha reductase (type 2), is required for the development of male external genitalia from the urogenital sinus into (growth of the male phallus, urethra, complete fusion of labioscrotal swellings to form the scrotum). Of course, the concentration of androgen receptors (AR) and their sensitivity to androgens should be normal for this to happen. The formation of DHT occurs inside *target cells*.

Normally, the *type 2* 5-alpha reductase predominates in the genital tract, and the isoform of the enzyme in the pilosebaceous unit is *type 1*.]

Finasteride is a more potent inhibitor of the type 2 5-alpha reductase; however, finasteride has also been used in the management of hirsutism in females.

9. T and DHT mediate their effects via the same AR. DHT-AR complexes are more stable. This explains why DHT is biologically the most potent androgen.

10. The embryonic ovary **does not** produce any hormones, and estrogens are not required for intrauterine development of female internal or external genitalia.

11. The *critical period* of differentiation of genitalia in intrauterine life is **8-12 weeks**. T synthesis by the Leydig cell during this time is under the control of hCG (LH receptor). After mid-gestation, fetal pituitary LH modulates fetal T synthesis and affects the growth of the differentiated penis.

12. **Genetic sex** - male (46 XY), female (46 XX); **gonadal sex** (male - if testes are present; female - if ovaries are present); **phenotypic sex** - based on external genitalia - male, female, ambiguous.

13. Gender assignment at birth is based on external genitalia (male; female; ambiguous)

14. **Gender identity**: Identification of self as male or female. This is affected by one's perception of his/her genitalia in comparison to others, how the child is raised (as female or male). The size of the phallus is a particularly important determinant.

15. Remember applications of knowing the basic scheme of steroidogenesis, and feedback responses to a defect somewhere in the pathway.

When you consider all of this along with mechanisms involved in puberty and the actions of sex hormones, then we have most of the factual premises needed for understanding the phenotype in most disorders of sexual differentiation and therefore diagnosing them.

**Learning Activity:** Using these principles, describe how you would suspect and diagnose

each of the following conditions, as well as evaluate a female presenting with amenorrhea. As you describe, note each of the following: genetic sex, gonadal sex, internal genitalia, external genitalia, how the child is likely to be raised (as male or female). Consider: changes at the time of puberty; gender identity; the possibility of malignancies; reproductive life; genitourinary function, as well as ethical issues that may arise in management.

- CYP21 (21 hydroxylase) deficiency;
- Klinefelter's syndrome  
Turner's syndrome;
- Complete resistance to androgens;
- Complete deficiency of testosterone 5-alpha reductase;
- Defect in embryonic testes;
- Selective deficiency of MIP;
- Aromatase deficiency (CYP 19);
- 17-beta HSD deficiency

\*\*\*\*\*

## 6. Gastrointestinal Physiology

*In each of the following questions, select the **single best** response.*

1. Motor neurons in the myenteric plexus that stimulate the contraction of smooth muscle in the gastrointestinal tract release:
  - A. acetylcholine
  - B. vasoactive intestinal polypeptide
  - C. nitric oxide
  - D. somatostatin
  - E. enkephalins
2. Postganglionic parasympathetic neurons innervating the gastrointestinal smooth muscle are located in:
  - A. myenteric plexus
  - B. submucosal plexus
  - C. paravertebral ganglia
  - D. prevertebral ganglia
3. The term “brain of the gut” is used to refer to the:
  - A. autonomic ganglia
  - B. enteric nervous system
  - C. migratory motor complex
  - D. interstitial cells of Cajal
4. Which of the following hormone(s) is/are normally released by the stomach into the systemic circulation?
  - A. Ghrelin
  - B. Gastrin
  - C. Pepsinogen
  - D. Secretin
  - E. Vasoactive intestinal polypeptide
5. Which of the following **inhibits** gastric acid secretion by parietal cells in the stomach?
  - A. Prostaglandin E<sub>2</sub>
  - B. Gastrin
  - C. Acetylcholine
  - D. Histamine
6. Enterocytes are replenished by mitotically active undifferentiated cells located in:
  - A. Brunner's glands
  - B. crypts of Lieberkuhn
  - C. Peyer's patches

- D. gut associated lymphoid tissue
7. The pattern of electrical and motor activity in the gastrointestinal tract during periods of fasting is called:
- basic electrical rhythm
  - migrating motor complex (MMC)
  - peristalsis
  - segmentation
8. The major humoral mediator of meal-stimulated enzyme secretion is:
- secretin
  - CCK
  - GIP
  - gastrin
9. The major humoral mediator of pancreatic duct cell secretion of bicarbonate rich juice is:
- secretin
  - CCK
  - somatostatin
10. The major humoral mediator of gall bladder contraction in response to a fat meal is:
- CCK
  - gastrin
  - secretin
  - somatostatin
11. The most potent stimulus for release of secretin from the duodenum is:
- a reduction in duodenal lumen pH to  $< 4.5$
  - peptides
  - fatty acids with  $> 8$  carbons
  - carbohydrates
12. Which of the following statements regarding somatostatin is **incorrect**?
- It inhibits release of growth hormone
  - It inhibits release of insulin
  - It decreases blood flow to the intestine
  - It stimulates gastric acid secretion
13. Which is the most important cholagogue?
- Secretin
  - CCK
  - Gastrin
  - GIP
14. Physiologically, the most important choleretic(s) is/ are:
- bile salts
  - CCK
  - secretin
  - gastrin
15. Bile salts are essential for absorption of fat because they:
- solubilize dietary lipids in micelles
  - increase surface tension
  - are hydrophobic
  - contain cholesterol
16. Micelles in bile are formed by:
- bile salts and phospholipids
  - bile acids and bile salts
  - cholesterol and bile salts
  - cholesterol and phospholipids
17. The total circulating bile salt pool is approximately:
- 35 mg
  - 3.5 g
  - 150 mg
  - 30 g
18. In which of the following segments in the splanchnic circulation is pressure **least** in a healthy individual at rest?
- Hepatic arteriole
  - Hepatic sinusoid
  - Hepatic vein
  - Terminal branches of portal vein in the liver
  - Venule in the small intestinal mucosa
19. Quantitatively, the most important enzyme in the digestion of fat is:
- lingual lipase
  - gastric lipase
  - pancreatic lipase
  - lipoprotein lipase
20. Which of the following is a bile acid synthesized by the hepatocyte?
- Sodium taurocholate
  - Chenodeoxycholic acid
  - Deoxycholic acid
  - Lithocholic acid

21. Which of the following transporters is present only in the sinusoidal membrane of hepatocytes?
- Bile Salt Export Pump
  - LDL-cholesterol receptors
  - MDR 3 (Flippase)
  - Multidrug Resistance associated Protein - 2 (MRP-2)
22. The Oral Rehydration Solution is helpful in rehydration in diarrheas because:
- Na-glucose symporter is unaffected in toxigenic diarrheas
  - 1Na-1K-2Cl symporter is located only in the basolateral membrane
  - cAMP regulated Cl secretion is reduced
  - toxins inhibit facilitated glucose transport
23. Normally, the rate-limiting step in the metabolism of bilirubin is:
- uptake by ligandin
  - conjugation with glucuronic acid
  - secretion into bile
24. Which of the following is absorbed in the intestine independent of sodium?
- Glucose
  - Amino acids
  - Galactose
  - Fructose
25. The type(s) of contraction that normally occur(s) only in the colon is/are: (*choose one or more answers*)
- peristalsis
  - antiperistalsis
  - segmentation
  - mass action contraction
26. The most frequent type of movement in the small intestine in the digestive state is:
- peristalsis
  - antiperistalsis
  - slow wave
  - segmentation contraction
27. The pattern of intestinal motility that hastens transit in the small intestine in the digestive state is:
- peristalsis
  - segmentation contraction

- tonic contraction
  - migrating motor complex
28. Normally, there is a net secretion of which ion in the colon?
- Sodium
  - Potassium
  - Chloride
  - Calcium
29. In clinically significant diarrhea, typically, the most abundant anion in stool is:
- acetate
  - bicarbonate
  - butyrate
  - chloride
30. Normally, most of the water in the GI lumen is absorbed from:
- stomach
  - duodenum
  - jejunum
  - colon

#### Answers – Gastrointestinal Physiology

1A	2A	3B	4AB	5A
6B	7B	8B	9A	10A
11A	12D	13B	14A	15A
16A	17B	18C	19C	20B
21B	22A	23C	24D	25BD
26D	27A	28B	29B	30C

#### Explanations:

4. Ghrelin is released from the stomach during the fasting state and it stimulates food intake by an action on the hypothalamus (it is an orexigenic signal unlike leptin which signals satiety). Ghrelin is also a stimulator of the growth hormone secretagogue receptor (GHS-R) in the anterior pituitary, a receptor that mediates growth hormone release.

7. The migrating motor complex (MMC) sweeps secretions from the mid-stomach through to the terminal ileum. The MMC presumably serves to prepare the gut for the next meal; i.e. it is the “housekeeper of the small intestine”. It is augmented by motilin.

13 and 14. Cholagogues stimulate secretion of bile; since this is osmotically driven, bile salts are themselves amongst the most potent cholagogues. Cholagogues (e.g. cholecystokinin) increase flow of bile from the liver or gallbladder into the duodenum. CCK enhances bile flow into the intestine by stimulating contraction of the gall bladder.

17. The total bile salt pool of 3.5 g recycles repeatedly via the enterohepatic circulation six to eight times per day.

18. Blood flows down a pressure gradient from: venule in small intestinal mucosa → portal vein → branches of portal vein in the liver → hepatic sinusoid → hepatic vein.

19. This is evident from the fact that chronic pancreatic exocrine insufficiency results in steatorrhea. In contrast, fat digestion and absorption is not significantly affected by deficiency of the other lipases as long as pancreatic lipase is available in adequate amounts.

20. Cholic and chenodeoxycholic acids are primary bile acids; deoxycholic acid and lithocholic acids are formed in the intestine (secondary bile acids) by the action of bacteria on primary bile acids.

**25-27. Gastrointestinal motility:** You can build your ideas along the following three lines:

- Digestive vs. interdigestive motility
- Propulsive movements vs. mixing movements
- Anatomical: stomach, duodenum, proximal colon, sigmoid colon etc.

<i>Digestive motility</i>	<i>Interdigestive motility</i>
Peristalsis	MMC
Segmentation	
Haustration	

<i>Propulsive movement</i>	<i>Mixing movement (fosters digestion &amp; absorption)</i>
Peristalsis	Segmentation Haustral shuttling
MMC	

There are regional variations in the frequency of the basic electrical rhythm (BER); for example in the stomach the pacemaker is located in the middle of the body of the stomach, and its frequency is 3-4 per minute.

**Rate of peristalsis:** The rate of peristalsis is quite variable (2–25 cm/min). Each peristaltic wave is propagated usually for a short distance (4–5 cm). On the other hand, the rate of MMC is about 5 cm/min. The MMC operates from mid stomach until the terminal ileum. It is not propagated any further.

Antiperistalsis occurs as part of the vomiting response. But otherwise, normally, antiperistalsis is observed only in the ascending colon. It is actually a sequence of peristalsis-antiperistalsis sequences; the antiperistalsis is said to be 'weak' and eventually the peristaltic wave overrides and sweeps content aborally. Like segmentation contractions do, peristalsis-antiperistalsis sequences in the ascending colon allow more Na and Cl and water to be absorbed in the colon. Normal antiperistalsis in the colon cannot propagate across a competent ileocecal valve.

28. The secretion of K in the distal colon is stimulated by aldosterone. Hypokalemia can result from diarrheal losses of K in individuals with chronic diarrhea or those with severe acute diarrhea. The diarrhea of VIPoma may be accompanied by hypokalemia.

30. Digestion and absorption of nutrients normally occur mainly in the jejunum. Active absorption of amino acids, glucose is coupled to a Na-gradient, and since we know that the intestine cannot maintain an osmotic gradient across its epithelium and water movement follows osmotically - it can be deduced that most of the water in the intestine is absorbed in the jejunum. There is experimental evidence in support of this. In a healthy adult, about 5.5 liters of water is absorbed in the jejunum (out of 9 liters absorbed from the GI lumen).

\*\*\*\*\*

## 7. Circulating Body Fluids

### Red blood cell indices

- What are the RBC indices?
- How are they derived?
- Mention normal values for each.
- How are they used in the differential diagnosis of anemias?
- Calculate RBC indices given that RBC count = 5 million/mm<sup>3</sup>, blood Hb = 15 g/dL, and PCV = 45%

RBC Index	Derivation	Normal values
MCH	$\frac{\text{Hb in g/dL} \times 10}{\text{RBC in millions/mm}^3}$	29–32 pg
MCV	$\frac{\text{PCV} \times 10}{\text{RBC in millions/mm}^3}$	80–95 fL
MCHC	$\frac{\text{Hb in g/dL} \times 100}{\text{PCV}}$	32–35 g/dL

MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; fL, femtoliter; pg, picogram.

I use this 'trick' below to recall the right formula for each index, in case I forget them. Normally,

MCH = 30	= 450 / 5 = 45 × 10 / 5	= $\frac{(\text{PCV} \times 10)}{\text{RBC}}$
MCHC = 33	= 1500 / 45 = 15 × 100 / 45	= $\frac{\text{Hb} \times 10}{\text{RBC count}}$
		= $\frac{\text{Hb} \times 100}{\text{PCV}}$

And then one can use these formula to plug in values at hand.

MCHC = MCH/MCV;

15 g of Hb is present in 100 ml of blood  
 15 g of Hb is present in 45 ml of PRBC  
 30 g of Hb is present in 90 ml of PRBC  
 33 g of Hb is present in 100 ml of PRBC

MCHC is the amount of Hb present in 100 ml of packed red blood cells.

RBC indices are useful in the differential diagnosis of anemias. Anemias may be classified as macrocytic, microcytic or normocytic based on MCV, and normochromic or hypochromic based

on MCHC. Hyperchromia is uncommon but it may occur in hereditary spherocytosis.

### Working definitions:

Normocytes	MCV WNL
Macrocytes	MCV > 95 fL
Microcytes	MCV < 80 fL
Hypochromia	MCHC < 25 g/dL

In each of the following questions, select all correct answers.

1. Macrocytes have an MCV > than:
  - A. 80 fL
  - B. 95 fL
  - C. 90 fL
  - D. 85 fL
2. Each red blood cell contains approximately:
  - A. 20 pg
  - B. 25 pg
  - C. 30 pg
  - D. 35 pg of hemoglobin
3. The most reliable RBC index is:
  - A. MCV
  - B. MCH
  - C. MCHC
  - D. mean cell diameter
4. The amount of hemoglobin present in 100 ml of red blood cells is called:
  - A. MCH
  - B. MCHC
  - C. Hb index
  - D. Price Jones index
5. MCHC does not usually exceed:
  - A. 30 g/dL
  - B. 33 g/dL
  - C. 37 g/dL
  - D. 25 g/dL
6. Primary hemostasis refers to cessation of bleeding due to:
  - A. formation of a definitive clot
  - B. clot retraction
  - C. formation of a temporary platelet plug.
7. Platelet aggregation is stimulated by:
  - A. thromboxane A<sub>2</sub>

- B. fibrinogen  
C. ADP  
D. thrombin  
E. epinephrine
8. Platelet aggregation is inhibited by:  
A. ADP  
B. 5-HT  
C. PG I<sub>2</sub>  
D. TX A<sub>2</sub>
9. Which of the following clotting factors is **not** vitamin K dependent?  
A. Factor II  
B. Factor V  
C. Factor VII  
D. Factor IX  
E. Factor X
10. The extrinsic pathway is triggered by the release of:  
A. factor VII  
B. tissue factor  
C. tissue factor pathway inhibitor  
D. contact factor
11. The enzyme that ultimately lyses fibrin is:  
A. plasminogen  
B. TPA  
C. urokinase  
D. plasmin
12. The extrinsic pathway is inhibited by:  
A. tissue factor  
B. thromboplastin  
C. tissue factor pathway inhibitor (TFPI)  
D. contact factor
13. The test that screens the extrinsic pathway is:  
A. prothrombin time (PT)  
B. activated partial thromboplastin time (aPTT)  
C. thrombin time  
D. urea solubility test  
E. clot lysis time
14. Prolongation of prothrombin time does **not** occur when there is a deficiency of only:  
A. factor VIII  
B. factor IX  
C. factor VII
- D. vitamin K
15. Mutations in which of the following have been implicated in the pathogenesis of hypercoagulable states?  
A. Protein C  
B. Protein S  
C. Factor V  
D. Antithrombin III
16. Factor V Leiden:  
A. is a mutated form of factor IX  
B. is inactivated by protein C  
C. is present in a large subset of patients with venous thromboembolism
17. Which condition(s) is / are characterized by an increase in both bleeding time and clotting time?  
A. Afibrinogenemia  
B. Hypoprothrombinemia  
C. Hemophilia A  
D. von Willebrand's disease
18. Red cell antigens A and B are chemically:  
A. phospholipids  
B. glycosphingolipids  
C. glycopeptides  
D. polypeptides
19. Red blood cell antigens A and B are also present in:  
A. saliva  
B. semen  
C. amniotic fluid  
D. pancreas
20. The red blood cells of a person with the Bombay blood group do **not** have  
A. GLUT  
B. H substance  
C. spectrin  
D. ankyrin
21. CO is formed as an end product of:  
A. heme metabolism  
B. arginine metabolism  
C. oxidation of acetoacetate
22. Heme is converted to bilirubin mainly in the:  
A. kidneys

- B. liver
- C. spleen
- D. bone marrow

23. The protein that binds extracorporeal hemoglobin is:

- A. hemin
- B. haptoglobin
- C. hemopexin
- D. haptopexin

24. Which of the following is **not** synthesized in the liver?

- A. IgG
- B.  $\alpha_2$  macroglobulin
- C. Albumin
- D. Angiotensinogen

25. Which of the following plasma proteins are protease inhibitors?

- A.  $\alpha_1$  antitrypsin
- B. Transferrin
- C. C-reactive protein
- D. Antithrombin III

26. Which of the following is a negative acute phase reactant?

- A. Albumin
- B. C-reactive protein
- C.  $\alpha_2$  macroglobulin
- D. Transferrin

27. ESR is increased in:

- A. anemia
- B. hypofibrinogenemia
- C. spherocytosis
- D. each of the above

28. The protein content of lymph draining from the \_\_\_\_\_ is highest.

- A. choroid plexus
- B. skeletal muscle
- C. liver
- D. gastrointestinal tract

29. Osmotic fragility of red blood cells is decreased in:

- A. sickle cell anemia
- B. hereditary spherocytosis
- C. microcytic hypochromic anemia

D. macrocytic anemia

30. When a serum sample is electrophoresed, which one of the following bands is absent?

- A. Albumin
- B.  $\alpha_1$  globulin
- C.  $\alpha_2$  globulin
- D. Fibrinogen
- E.  $\gamma$ -globulin

31. Erythropoietin is produced by:

- A. interstitial cells surrounding peritubular capillaries in the renal cortex;
- B. endothelial cells in peritubular capillaries in the renal cortex
- C. perivenous hepatocytes
- D. Kupffer cells of liver

32. Hereditary spherocytosis occurs due to mutations in genes coding for:

- A. spectrin and ankyrin
- B. Na-K ATPase
- C. glucose 6 phosphate dehydrogenase
- D. pyruvate kinase

33. The average half-life of neutrophils in the circulation is:

- A. 6 hours
- B. 5 days
- C. 2 weeks
- D. 1 month

34. Most of the iron in the body is present in:

- A. hemoglobin
- B. myoglobin
- C. ferritin
- D. transferrin

#### Answers: Circulating Body Fluids

1B	2C	3C	4B	5C
6C	7all	8C	9B	10B
11D	12C	13A	14AB	15all
16C	17ABD	18B	19all	20B
21A	22C	23B	24A	25AD
26A	27A	28C	29AC	30D
31ABC	32A	33A	34A	

#### Answer Explanations:

3. MCHC is the most reliable index because it does not depend on the RBC count. This is

because the estimation of RBC count is more error prone than the estimation of Hb or PCV.

8. ADP, TXA<sub>2</sub>, thrombin, serotonin, and epinephrine stimulate platelet aggregation. Prostacyclin inhibits platelet aggregation. Aspirin therapy lowers TXA<sub>2</sub>/PGI<sub>2</sub>.

9. Vitamin K dependent clotting factors are factors II, VII, IX and X and Protein C and Protein S. Protein C and protein S inhibit clotting.

10. The extrinsic pathway is called so because it is triggered by a factor extrinsic to plasma (tissue thromboplastin). Simply, it is triggered by “tissue injury”. The extrinsic pathway is also the fastest limb of the clotting cascade. Normally, PT = 12 – 14 seconds.

11. Fibrinolytic system:  
Plasminogen to plasmin  
Enzyme: *Tissue plasminogen activator* (TPA)  
Fibrin to fibrin degradation products  
Enzyme: *Plasmin* (fibrinolysin)

12. TFPI is tissue factor pathway inhibitor.

13. Prothrombin time screens the extrinsic limb and the final common pathway of the clotting cascade. APTT screens the intrinsic limb of the clotting cascade.

<i>Test</i>	<i>Assessing</i>	<i>Factors</i>
Bleeding time	Platelets and vessel wall	
Clotting time	Intrinsic & Extrinsic pathway	
Prothrombin time	Extrinsic pathway & common pathway	VII, X, Prothrombin, Fibrinogen
Activated partial thromboplastin time	Intrinsic pathway & common pathway	VIII, IX, X, XI, XII

15. Loss-of-function mutations in protein C, protein S, antithrombin III and mutations in factor V resulting in resistance to inactivation to protein

C have all been implicated in hypercoagulable states.

16. Factor V Leiden, a mutated form of Factor V, resists inactivation by protein C and is present in a large subset of patients with venous thromboembolism.

17. Fibrinogen is essential for platelet aggregation. Also fibrinogen is a clotting factor. Von Willebrand’s factor mediates the attachment of platelets to subendothelial collagen. Also vWD binds factor VIII and prolongs its half-life in the circulation. When there is a deficiency of vWF, more factor VIII spills over into the urine. Thus, bleeding time and clotting time are both increased in hypofibrinogenemia and VWD. Thrombin is a potent stimulator of platelet aggregation. At least, theoretically, prothrombin deficiency would be expected to delay platelet aggregation.

19. If red cell antigens are also present in exocrine secretions, such individuals are called secretors. In some, they are not secreted. The significance of this is unknown.

20. H substance is absent in persons with the Bombay phenotype. Normally, if an individual has H substance, his blood group would be O. An individual lacking H substance will have anti H antibodies in plasma and can receive transfusions only from a person with the Bombay blood group.

22. Heme oxygenase activity is highest in the spleen. Second, the spleen is much more sensitive to red cell injury. [*Wintrobe’s Clinical Hematology, Lee GR et al, 10<sup>th</sup> ed, Lippincott Williams and Wilkins, volume 1, p 280.*]

23. Haptoglobin binds extracorporeal hemoglobin. Hemopexin binds heme. Haptoglobin binds extracorporeal hemoglobin and prevents it from being filtered and excreted by the kidney. Serum haptoglobin levels are reduced in hemolytic anemias.

26. Albumin is a negative acute phase reactant; i.e., its synthesis is reduced during the acute phase response.

27. Presumably, the increase in ESR in anemia has little to do with rouleaux formation; ESR may be high because both PCV and viscosity are low which in turn reduce the resistance to sedimentation of cells. By the same reasoning, ESR is reduced in polycythemia since the viscosity (and therefore the resistance to sedimentation) is high. However, if blood is more viscous because of an increase in plasma levels of globulins and fibrinogen, ESR is higher since these proteins facilitate rouleaux formation.

29, 30. Osmotic fragility increases when the RBC cytoskeleton is abnormal, as in hereditary spherocytosis.

*Normal range:* 0.5 - 0.3% NaCl

*Increased in:* hereditary spherocytosis

*Decreased in:* microcytic anemia & sickle cell anemia.

Sickle cells and microcytes show greater resistance to osmotic lysis by virtue of their smaller size and normal cytoskeleton.

30. There is little fibrinogen in serum if at all.

31. *See p. 459, Ch 24, WFG, 2005.*

32. Hereditary spherocytosis occurs due to mutations in cytoskeletal proteins spectrin, ankyrin, Band 3. Defects in ankyrin are reported to be commoner.

34. 70% of iron in the body is present in Hb. Under abnormal circumstances, a large amount of iron may be present in hemosiderin.

\*\*\*\*\*

## 8. Cardiovascular Physiology

### List of acronyms that are used in this section:

HR – heart rate

SBP – systolic blood pressure

DBP – diastolic blood pressure

PP – pulse pressure

MAP – mean arterial pressure

RPP – rate-pressure product

BPM – beats per minute

RR – RR interval

Q – cardiac output

TPR – total peripheral resistance

TBF – tissue blood flow

### Electrical properties of the heart

1. The heart continues to beat even after all nerves to it are sectioned. This property is called:

- A. excitability
- B. conductivity
- C. automaticity
- D. contractility

2. Prepotentials are normally absent from:

- A. P cells in the SA node
- B. AV nodal cells
- C. Purkinje fibers
- D. working myocardial cells

3. What is the effect of vagal stimulation on the membrane potential of the SA node?

- A. It increases an inward calcium current
- B. It increases the slope of the prepotential
- C. It activates a hyperpolarizing potassium current
- D. It increases intracellular cAMP

4. Intrinsic heart rate can be determined by:

- A. vagotomy
- B. administration of atropine
- C. beta adrenergic receptor blockade
- D. IV administration of atropine and atenolol

5. The ST segment is elevated in acute myocardial infarction because of:

- A. flow of current into the infarct during diastole
- B. TP segment depression
- C. late depolarization of infarct
- D. early repolarization of infarct

6. Hypocalcemia is associated with QT prolongation because:

- A. it is invariably associated with bundle branch block
- B. it increases ventricular activation time
- C. it lengthens the duration of ventricular repolarization
- D. it accelerates opening of potassium channels

7. AH interval is normally:

- A. 30–50 ms
- B. 60–125 ms
- C. 100–200 ms
- D. 80–120 ms

8. The ability of the AV node to generate its own impulses when the sinus node is “sick” is due to:

- A. a constant phase 4 membrane potential
- B. slow calcium entry during phase zero
- C. spontaneous diastolic depolarization
- D. the absence of prepotentials

9. The AV node does not conduct more than:

- A. 180
- B. 230
- C. 280
- D. 330 impulses / minute

#### Cardiac cycle; systolic time intervals

10. Which of the following need to be recorded in order to determine systolic time intervals?

- A. ECG, ECHO, PCG
- B. ECG, PCG and carotid artery pulse (CAP)
- C. ECHO, CAP and PCG
- D. ECG, CAP and apexcardiogram

11. Which of the following is **not** essential to determine  $QS_2$ , left ventricular ejection time (LVET) and pre-ejection period (PEP)?

- A. Pulse transducer
- B. Electrocardiograph
- C. Phonocardiogram
- D. Swan-Ganz catheter

12. The dicrotic notch is absent from:

- A. radial arterial pulse tracing
- B. pulmonary arterial pulse tracing
- C. aortic pulse tracing
- D. none of the above

13. The maximum pressure rise in the ventricle occurs during:

- A. ejection
- B. isovolumetric contraction
- C. protodiastole
- D. diastasis

14. During the cardiac cycle, aortic valve closes at the end of:

- A. isovolumetric systole
- B. rapid ejection
- C. diastasis
- D. protodiastole

15. The cardiac output of a 50 year old man at rest is 6 L / min; mean HR is 75 BPM. Left ventricular end-diastolic volume (LVEDV) is 120 ml. What is the mean ejection fraction?

- A. 35 %
- B. 50 %
- C. 66 %
- D. 75 %

16. During exercise, a man consumes 2 liters of oxygen per minute. His arterial  $O_2$  content is 200 ml/L and the oxygen concentration of mixed venous blood is 120 ml/L. His cardiac output is:

- A. 16 L/min
- B. 25 L/min
- C. 32 L/min
- D. 40 L/min

17. Venous return is transiently increased during:

- A. strain phase of Valsalva maneuver
- B. positive end-expiratory pressure
- C. intravenous bolus of frusemide
- D. deep inspiration

18. If blood  $[Hb A] = 15$  g/dL and Hb is fully saturated with oxygen, average stroke volume = 70 ml, average HR = 72/min, calculate whole-body oxygen delivery; i.e., the amount of oxygen delivered to the tissues per minute assuming Hb is fully saturated with oxygen.

- A. 1 L/min
- B. 0.5 L/min
- C. 2 L/min
- D. 2.5 L/min

#### The Microcirculation; Dynamics of blood flow

19. Windkessel vessels are represented by the:

- A. aorta
- B. internal jugular v.
- C. arterioles
- D. muscular arteries

20. The stopcocks of the circulation are:

- A. arterioles
- B. capillaries
- C. valves
- D. venules

21. Across which site in the circulation is the pressure drop maximum?

- A. Arterioles
- B. Venules
- C. Capillaries
- D. Aortic valve

22. Which of the following structures are **not** innervated?

- A. Arterioles
- B. Postcapillary venules
- C. AV anastomoses
- D. Precapillary sphincters

23. At any time, the greatest fraction of blood volume is present in the:

- A. heart
- B. arteries
- C. veins
- D. capillaries

24. What fraction of total blood volume is present in the capillaries at any given time?

- A. 5%
- B. 20%
- C. 15%
- D. 1%

25. The term “capacitance vessels” is applied to:

- A. pulmonary capillaries
- B. thoroughfare channels
- C. shunts
- D. veins and venules

26. Hydraulic conductivity of capillaries is highest in:

- A. glomeruli
- B. intestinal villi

- C. skin
- D. brain

27. Rank the hydraulic conductivity of capillaries in various parts of the body.

- A. GIT > glomerulus in kidney > lung > brain
- B. Glomerulus in kidney > brain > skin
- C. GI mucosa > heart > brain
- D. GI mucosa > circumventricular organs > lung

### **Biophysics of the circulation:**

28. Turbulence is almost always present when Reynolds number is more than:

- A. 2000
- B. 2500
- C. 3000

29. The average arm-to-tongue circulation time is:

- A. 5 seconds
- B. 10 seconds
- C. 15 seconds
- D. 20 seconds

30. Thin walled capillaries do not burst when intracapillary pressure is increased because:

- A. they lack smooth muscle cells
- B. the blood flow rate is less
- C. they have a small radius
- D. capillary hematocrit is less than whole-body hematocrit.

31. That capillaries can withstand high internal pressures without bursting is explained using:

- A. Bernoulli’s principle
- B. Laplace’s law
- C. Poiseuille Hagen law
- D. Fahraeus-Lindquist effect

33. Bernoulli’s principle could be applied to explain why:

- A. intravesical pressure does not change with increase in intravesical volume
- B. mean pressure in the femoral artery is greater than that in the brachial artery
- C. coronary blood flow is compromised in aortic stenosis
- D. tissue blood flow ceases below critical closing pressure

### **Regulation of cardiovascular function:**

34. Quantitatively, the most important means of increasing flow to an actively metabolizing tissue is:
- increasing cardiac output
  - increasing peripheral resistance
  - increasing blood pressure
  - decreasing local vascular resistance
35. Which one of the following is **not** a vasodilator metabolite?
- Adenosine
  - Potassium ions
  - Endothelin-1
  - Hydrogen ions
  - ADP
36. What is the chemical identity of endothelium-derived relaxing factor (EDRF)?
- Nitrous oxide
  - Nitric oxide
  - Potassium
  - Carbon monoxide
37. Which one of the following does not have vasodilator actions?
- NO
  - CO
  - Potassium
  - Angiotensin III
38. Blood flow to exercising skeletal muscle is increased by all of the following **except**:
- K<sup>+</sup>
  - norepinephrine
  - ↑ in P<sub>CO<sub>2</sub></sub> in muscle
  - adenosine
39. The most potent vasoconstrictor is:
- endothelin 1
  - angiotensin II
  - norepinephrine
  - vasopressin
40. Check whether the following statements about the arterial baroreflex mechanism are true or false.
- Baroreceptors are free nerve endings responsive to stretch.
  - Application of suction force with a neck chamber loads the arterial baroreceptors.
3. The effect of head-up tilt would be to unload arterial baroreceptors in the carotid sinus.
4. Herring's nerve terminates in the *nucleus tractus solitarius*.
5. Activity in the arterial baroreceptors reflexly excites vagal outflow to the heart and inhibits sympathetic outflow to resistance vessels.
6. The reflex effect of arterial baroreceptor loading is a decrease in HR and MAP.
7. The reflex response to baroreceptor unloading is a decrease in sympathetic outflow to the heart and blood vessels.
41. Intravenous injection of norepinephrine to a normotensive healthy adult human leads to:
- an increase in BP & HR
  - a decrease in BP & HR
  - an increase in HR & decrease in BP
  - an increase in BP & decrease in HR
42. The first reflex response to an increase in arterial pressure produced by intravenous injection of phenylephrine is:
- increase in RR interval
  - increase in heart rate
  - decrease in cardiac output
  - decrease in total peripheral resistance
43. Which of the following maneuvers evokes an increase in vagal discharge to the heart?
- IV infusion of phenylephrine
  - Carotid massage
  - Pressure on the eyeball
  - Irrigation of the ear canals
44. On rising from the supine position:
- central blood volume increases
  - heart rate decreases
  - central venous pressure decreases
  - discharge from arterial baroreceptors decreases
  - stroke volume decreases by about 40%
45. Marey's law states that:
- when BP increases, HR decreases
  - when BP decreases, HR increases
  - when BP decreases, HR decreases
  - when BP increases, HR increases

46. An increase in whole body oxygen demand is met chiefly by:

- A. increasing cardiac output
- B. increasing oxygen content of arterial blood
- C. increasing oxygen extraction from arterial blood
- D. increasing blood pressure

47. During severe exercise, a well-trained athlete may be able to achieve a cardiac output of:

- A. 15 liters
- B. 25 liters
- C. 35 liters
- D. 45 liters

48. Vasomotor ischemia triggers an increase in sympathetic outflow increasing BP and thereby facilitating restoration of cerebral blood flow.

This is called:

- A. Bainbridge reflex
- B. the CNS ischemic pressor response
- C. Head's paradoxical reflex
- D. Marey's reflex

49. Heart rate is slowed by:

- A. deep inspiration
- B. Bainbridge reflex
- C. increased intracranial tension
- D. carotid massage

50. In a healthy normotensive individual at rest, heart rate is typically increased by:

- A. deep expiration
- B. fear
- C. anger
- D. IV infusion of phenylephrine

51. Which of the following varies from beat-to-beat?

- A. RR interval
- B. Venous return
- C. Stroke volume
- D. Cardiac output
- E. Blood pressure

52. During the strain phase of the Valsalva maneuver (forced expiration with the glottis open and maintaining an expiratory pressure of 40 mm Hg for 15 seconds):

- A. venous return decreases

B. cardiac output decreases

C. blood pressure decreases

D. heart rate increases

E. sympathetic outflow to blood vessels ↑

F. TPR gradually increases

53. Atrial natriuretic peptide is metabolized by:

A. dicarboxypeptidase

B. kininase II

C. neutral endopeptidase

D. kininase I

54. Cardiac output increases during:

A. Valsalva maneuver

B. positive pressure ventilation

C. negative 'g'

D. head-up tilt

55. Which of the following is **least likely** following prolonged space missions?

A. Cardiac hypertrophy

B. Postural hypotension

C. Weight loss

D. Motion sickness

#### **Regional circulation:**

56. The arteriovenous O<sub>2</sub> concentration difference is highest across the:

A. brain

B. heart

C. kidneys

D. liver

57. The mechanism that regulates cerebral blood flow during cerebral compression is the:

A. CNS ischemic response

B. Cushing's reflex

C. Bezold-Jarisch reflex

D. Bainbridge reflex

58. Activity in the noradrenergic nerves to the heart causes / has:

A. coronary vasoconstriction

B. coronary vasodilation

C. no effect on blood flow

59. If the noradrenergic nerves to the heart are stimulated after giving a  $\beta$ -blocker, then what would be the effect on coronary blood flow?

A. Coronary vasodilation

- B. Coronary vasoconstriction
- C. No change
- D. Unpredictable

60. Capillaries empty when mechanically stimulated. This is called the:

- A. axon reflex
- B. white reaction
- C. flare response
- D. red reaction

61. The wheal in the triple response is due to:

- A. contraction of precapillary sphincters
- B. increased capillary permeability
- C. axon reflex
- D. decreased absorption of fluid

62. Which of the following physiologic responses has a neural basis?

- A. Red reaction
- B. White reaction
- C. Flare
- D. Reactive hyperemia

63. Of the following vascular beds, autoregulation of tissue blood flow is least prominent in the:

- A. skin
- B. heart
- C. brain
- D. kidneys

64. When determining BP with a sphygmomanometer, a spuriously high value (of either SBP or DBP) may be recorded when:

- A. there is an auscultatory gap
- B. the cuff is smaller than preferable
- C. the person is obese
- D. the arm is not placed at the level of the heart

**Answers:**

1C	2CD	3C	4D	5all
6C	7B	8C	9B	10B
11D	12D	13B	14D	15C
16B	17D	18A	19A	20A
21A	22D	23C	24A	25D
26A	27C	28C	29C	30C
31B		33C	34D	35C
36B	37D	38B	39A	40
41D	42A	43all	44CDE	45AB
46A	47C	48B	49D	50C

51all	52all	53C	54C	55A
56B	57AB	58B	59B	60B
61B	62C	63A	64all	

40: statement 7 is false; others are true

**Answer Explanations:**

1. The automaticity is attributed to the presence of pacemaker cells that demonstrate spontaneous depolarization in the absence of extrinsic innervation. *See below.*

2. Note that the terms prepotential, pacemaker potential and spontaneous diastolic depolarization are often used interchangeably. They all mean the same. Normally prepotentials are present only in the SA node and AV node which contain pacemaker cells (P cells).

However, in abnormal situations (e.g. hypoxemia) other regions of the heart (e.g. a ventricular focus) exhibit prepotentials. This state is one of “increased automaticity”, and premature ventricular or atrial depolarizations are manifestations of increased automaticity.

3. Stimulation of the right vagus nerve, which predominantly innervates the SA node, decreases the firing rate of the SA node. The effect of acetylcholine on pacemaker cells in the SA node is to activate a hyperpolarizing potassium current.

4. Intrinsic heart rate (IHR) is the rate at which the heart will beat when completely denervated. This is determined, in humans, by intravenous administration of a standard dose of atropine and atenolol. In healthy humans, IHR is about 100-110/min. The magnitude of IHR reflects the automaticity of the SA node. The fact that resting heart rate in healthy humans is around 70 beats per minute indicates that the effects of cardiac vagal tone at rest are greater than the effect of sympathetic outflow to the heart. Patients with transplanted hearts have higher resting heart rates closer to IHR because of cardiac denervation. Also, because of denervation, they are less able to increase their heart rate in response to exercise.

5. The infarct is deprived of blood supply and consequently its RMP becomes less negative. What do you expect the effect of ATP depletion to be on RMP? RMP will become less and less

negative. The other reason why RMP becomes less negative is that potassium is lost from cells as a result of injury. Thus, the infarcted zone loses its surface positivity and consequently it is negative with respect to surrounding normally polarized tissue (surface positive, inside negative).

Therefore, during diastole, extracellularly, current flows into the infarct. This depresses the baseline, i.e., the TP segment is depressed. However, the arrangement in ECG recorders is such that TP segment depression is recorded as ST segment elevation.

Secondly, the infarct depolarizes late with respect to surrounding normal tissue probably due to decrease in conduction velocity in the infarcted tissue; the effect of this late depolarization is to cause ST segment elevation.

Finally, ischemic myocardium repolarizes faster due to accelerated opening of K channels. The effect of early repolarization is also ST segment elevation. Thus, myocardial infarction is characterized by ST segment elevation in leads facing the infarct. See *p 563-4, Ch 28, WFG, 2005*.

7. The AH interval, from the A wave to the start of the H spike is normally 60-125 ms.

**His Bundle Electrogram:**

<i>Interval</i>	<i>Physiologic correlate</i>	<i>Time (ms)</i>
PA interval	Atrial activation time	30
AH interval	AV nodal delay	60-125
HV interval	His Bundle - ventricle	35-50

The AH interval represents AV nodal conduction time. See *p. 554, Ch 28, WFG, 2005*.

8. The AV node, like the SA node, exhibits prepotentials but its rate of discharge is much less compared to the SA node.

9. See *p. 557, Ch 28, WFG, 2005*.

**10, 11, 12. Systolic time intervals (STI)**

**QS2** is the time duration from the beginning of the Q wave to the first high frequency component of the aortic component A2 of the second heart sound. Note that this is an electromechanical interval; QS2 is called electromechanical systole. It is remarkably constant.

**Left ventricular ejection time (LVET)** is the period from the upstroke of the carotid artery pulse to the dicrotic notch (an oscillation on the falling wave of the carotid artery pulse). The dicrotic notch in the carotid artery pulse tracing represents the closure of the aortic valve. Note that ejection is a part of systole.

**Pre-ejection period (PEP)** is calculated as QS2 – LVET. It denotes the time taken for electrical excitation of left ventricle, excitation-contraction coupling and isovolumetric ventricular contraction.

If the duration of ventricular excitation and excitation-contraction coupling can be assumed to be constant, then, PEP can be taken to reflect the duration of isovolumetric ventricular contraction (IVVC).

PEP, which reflects the duration of isovolumetric contraction, is prolonged in heart failure. This is also associated with a decline in left ventricular ejection time. Thus, PEP/LVET ratio is a sensitive index of left ventricular systolic performance. STI cannot be used for diagnosis of specific heart conditions. Of late, STI have been superseded by echocardiography.

13. See *Fig 29-2 on p.566, Ch 29, WFG, 2005*

15. Cardiac output = SV × HR  
 HR = 75/min; cardiac output = 6 L/min.  
 Therefore, average SV = 80 ml.  
 Average LVEDV = 120 ml.  
 Therefore, ejection fraction = SV/LVEDV = 0.66 = 66%.

16. The Fick's principle states that the amount of a substance (X) consumed by an organ per unit time (A) = A-V conc. difference of X across that organ (circuit) × blood flow through that organ (or circuit)

Thus, blood flow (Q) = A / A-V conc. diff  
In this example, O<sub>2</sub> consumption = 2000 ml/min.  
AV O<sub>2</sub> difference = 80 ml/L. Cardiac output =  
2000/80 = 25 L/min.

18. Cardiac output = 5 L/min; Blood Hb = 15 g/dL. Oxygen carrying capacity of blood is approximately 20 ml/dL i.e. 200 ml/L.

Whole body oxygen delivery = cardiac output × oxygen content of arterial blood.

Therefore about 1L of oxygen will be delivered to the tissues per minute.

23. At any time, 54% of blood volume is contained in the veins and venules & vena cava.

26. See *Table 30-2, p. 579, Ch 30, WFG, 2005.*

30. For a cylindrical structure, transmural pressure (P) = T/r (Laplace's law) where T is wall tension and r is radius

Though capillaries are thin walled, they have a smaller radius and consequently need to develop less tension in order to withstand a given distending (transmural) pressure.

The statement in the question should not mislead you into believing that capillaries can withstand a pressure of 100 mm Hg – they will definitely rupture at that pressure. Rather if we compared a larger vessel and a capillary distended by physiologic pressures (say 40 mmHg), one still wonders how the thin walled capillary is able to withstand it. That is because it also has a smaller radius.

**33. Bernoulli's principle:** The greater the velocity of flow in a vessel, the lower the lateral pressure distending its walls.

Note coronary arteries originate virtually at a right angle from the aorta, above the aortic valve. Thus, in aortic stenosis, the lateral pressure at the level of the origin of coronary arteries is reduced, and this in turn reduces coronary blood flow. However, this is only one of many mechanisms

that contribute to the reduction in coronary blood flow in aortic stenosis.

34. Tissue blood flow = BP / local vascular resistance. Quantitatively, changes in local vascular resistance achieved mainly through local autoregulatory mechanisms contribute the most to regulating tissue blood flow.

39. See *p. 599, Ch 31, WFG, 2005*

41. Norepinephrine has a greater affinity for alpha adrenergic receptors than beta adrenergic receptors. So when it is administered intravenously to a healthy individual with normal BP, it elicits a rise in total peripheral resistance because of alpha adrenergic receptor mediated vasoconstriction. The rise in BP elicits a baroreflex mediated lowering of HR that overwhelms the direct cardioacceleratory effect of norepinephrine.

43. Phenylephrine is an alpha adrenergic agonist, so it raises TPR and BP and elicits a baroreflex mediated lowering of HR. Carotid massage mechanically activates the vagus nerve contained within the carotid sheath increasing cardiac vagal outflow.

44. Central venous pressure decreases upon rising due to a decrease in venous return. A decrease in arterial pressure, which occurs on rising from the supine position, also decreases the stretch of arterial baroreceptors (i.e., arterial baroreceptors are said to be 'unloaded') and the firing rate in the carotid sinus nerves decreases. This reflexly inhibits vagal outflow to the heart and increases sympathetic outflow from the brain resulting in an increase in heart rate and a rise in total peripheral resistance.

45. **Marey's law** states that HR (the dependent variable) is inversely related to BP (the independent variable) and that the converse is not true.

Marey's law is only a restatement of negative feedback regulation of BP by the arterial baroreflex; i.e., when BP increases, baroreflex-mediated lowering of HR occurs. When BP

decreases, HR reflexly increases. This is a mechanism to rapidly regulate and maintain BP within a normal range.

There are several exceptions to this:

1. During exercise, BP and HR both increase. The goal here is to allow cardiac output to increase and deliver more oxygen to actively metabolizing tissue, and it is logical to raise BP rather than maintain it at resting levels.
2. Vasomotor ischemia occurring in the face of hypotension triggers an increase in sympathetic outflow (CNS ischemic response) leading to an increase in BP but this is not accompanied by HR lowering.
3. Sometimes, when MAP is less than 50 mm Hg, activation of arterial chemoreceptors leads to a vagally mediated bradycardia.

46. At rest, blood flow through the systemic circulation (i.e., cardiac output) = 5 L/min  
 Assuming that functional Hb A concentration is 15 g/dL and PaO<sub>2</sub> is 100 mm Hg and that Hb is fully saturated with oxygen,  
 Oxygen content of arterial blood = 200 ml/L  
 Whole body oxygen delivery = 1 L/min  
 Whole body oxygen consumption = 250 ml/min  
 Whole body oxygen extraction = 0.25  
 This is sometimes called 'oxygen utilization coefficient (OUC)'.  
 Theoretically, oxygen extraction can increase up to 1. Thus, an increase in oxygen extraction is one mechanism of fulfilling an increase in oxygen demand.

However, in trained athletes, cardiac output can be increased 7 times from its resting value.

47. See Table 29-3, p. 572, Ch 29, WFG, 2005.

48. Vasomotor ischemia stimulates sympathetic outflow. This leads to an increase in BP that in turn serves to restore cerebral blood flow. This is the CNS ischemic pressor response.

**Cushing's reflex vs. CNS ischemic response**

Reflex	Cushing's reflex	CNS ischemic pressor response
--------	------------------	-------------------------------

Reflex	Cushing's reflex	CNS ischemic pressor response
Stimulus	Raised intracranial tension causing vasomotor ischemia as a result of compression of brain cells	Vasomotor ischemia due to any cause (example, hypotension)
Response	Increased sympathetic outflow	Increased sympathetic outflow
Effect	Increase in BP. If the individual had normal BP at baseline, his BP would become higher	Increase in BP & HR toward normal
HR change	If BP increases above normal (say from 120 mm Hg to 140 mm Hg), then a baroreflex mediated bradycardia would occur	Increases (since when MAP is too low the arterial baroreflex mechanism does not operate)
Significance	A mechanism to eventually maintain cerebral blood flow	A mechanism to eventually maintain cerebral blood flow

49. Note that raised intracranial tension (ICT) is not necessarily associated with bradycardia. An individual with raised ICT may be hypotensive due to blood loss. In this instance, hypotension is usually associated with tachycardia.

Rather, if raised ICT leads to hypertension, this usually elicits a baroreflex mediated lowering of heart rate.

**52. Valsalva maneuver:**

Maneuver	Forced expiration against a closed glottis
Stimulus	Decrease in BP due to a decrease in venous return and consequently stroke volume

	(SV)
Response	Immediate increase in HR and a more gradual increase in TPR
Goal	To maintain BP
Immediately after the maneuver	Venous return suddenly increases, SV increases, TPR is already high. Thus BP = SV × HR × TPR 'overshoots'
Response	The BP overshoot triggers a baroreflex mediated lowering of HR
Significance	BP maintained

54. During negative 'g', i.e. acceleration in the long axis of the body from foot to head, there is a headward shift of body fluids and central blood volume, cardiac output and blood pressure increase. When intrathoracic pressure is raised as occurs during the Valsalva maneuver, venous return reduces and cardiac output decreases. Similarly, during positive pressure ventilation, the increase in ITP reduces venous return and decreases cardiac output. Passive head-up tilt is associated with a decreased cardiac output since venous return is reduced.

55. Cardiac atrophy rather than hypertrophy occurs following prolonged space missions since the load on the heart is reduced. This is because skeletal muscles are not regularly used in microgravity conditions. Postural hypotension occurs upon return to earth (where the effects of earth's gravity are again fully manifest) because of autonomic as well as physical deconditioning. Motion sickness in space occurs due to conflicting neural inputs from visual cues and vestibular system and diminished input from muscle proprioceptors.

56. If the arteriovenous concentration difference of a substance (example, oxygen) across a vascular bed is high, it means that the vascular bed extracts a large fraction of this substance. Oxygen extraction ratio across the heart is 0.5-0.7 at baseline, higher compared to other tissues. Cardiac venous oxygen tension is low and little additional oxygen can be extracted from the blood in the coronaries, so increases in myocardial oxygen consumption require increases in coronary

blood flow. If that cannot happen, myocardial ischemia would result with predictable consequences.

At rest, oxygen extraction ratio in the heart = (A-V O<sub>2</sub> difference / arterial O<sub>2</sub> content) × 100 = (114 / 200) × 100 = 0.55

This is based on data in *Table 32-1, p. 612, WFG, 2005.*

58, 59. Activity in the noradrenergic nerves to the heart increases myocardial oxygen demand since it would increase the force as well as rate of cardiac contraction. However, this normally results in coronary vasodilation caused by products of metabolism. The pressor effect of norepinephrine on alpha-adrenergic receptors in the coronary arteries is not manifest therefore. However, the direct effect of norepinephrine on segments of isolated coronary arteries is vasoconstriction. On the other hand, the increase in myocardial oxygen demand (and consumption) during exercise is attenuated in individuals taking beta-blockers because the norepinephrine mediated rise in heart rate and contractility are also diminished, and consequently their ability to exercise is diminished. The learning point here is that the coronary circulation is capable of excellent autoregulation.

#### 60-63. The triple response:

Response	Mechanism
Wheal production	Increased capillary and venular permeability
Red reaction	Venodilation
Flare	Axon reflex

The white reaction is the response to a benign stimulus. It occurs due to contraction of precapillary sphincters.

The triple response is evoked by a noxious stimulus.

With the exception of the flare which is mediated by an axon reflex, the triple response, indeed, is an example of autoregulation.

However, we might say that autoregulation of tissue blood flow is least prominent in the skin;

this is because, cutaneous blood flow is mainly regulated by neural signals from the hypothalamus; this is logical since skin serves as the interface across which heat exchange is regulated to maintain body temperature.

64. All four options are **correct**. When there is an auscultatory gap and the palpatory method is not used, systolic pressure will be underestimated. When there is an auscultatory gap and you use the palpatory method, you will get a correct estimate of systolic pressure (say 210 mm Hg). Sounds will cease at some point (say 160 mm Hg). However, if the cuff is not deflated any further (because sounds disappeared at 160), one may not realize that there is an auscultatory gap with the result that diastolic pressure is overestimated. Something like 210/160 mm Hg will be recorded when the actual pressure is 210/90 mm Hg.

---

### **Supplementary Material:**

#### **Effect of load on muscle contraction:**

Within physiologic limits, the energy of cardiac contraction is directly proportional to preload. This is the **Frank-Starling law** of the heart.

**Preload:** The load on a muscle before it contracts. In the ventricle, the preload (end-diastolic fiber length) varies directly with the end-diastolic volume.

**Afterload:** The load which contracting muscle has to overcome before it shortens. The velocity of shortening varies inversely with afterload. For the left ventricle, the afterload is the total systemic vascular resistance.

**Cardiac output:** The volume of blood ejected by the left or the right ventricle per minute.

Cardiac output = stroke volume  $\times$  heart rate

**Cardiac index** is the cardiac output per square meter of body surface area.

#### **Regulation of stroke volume:**

Stroke volume is influenced by preload, afterload and myocardial contractility.

An increase in stroke volume for a given preload and afterload is due to an increase in myocardial contractility. This is sometimes called 'homometric regulation' (meaning same length). In contrast, heterometric regulation refers to changes in stroke volume brought about by changes in end diastolic volume.

The best index of myocardial contractility is the rate of pressure rise (dP/dt) in the ventricle during isovolumetric contraction. However, clinically, the **ejection fraction** is used as a surrogate of myocardial contractility.

Myocardial contractility is markedly enhanced by sympathetic stimulation, digoxin and depressed by myocardial ischemia, acidosis.

**Inotropic effects:** the term refers to the effect of a stimulus on myocardial contractility.

#### **What is BP determined by?**

BP = cardiac output  $\times$  total peripheral resistance

#### **Blood pressure indexes:**

**Systolic pressure (SBP):** the highest pressure in the arteries during the cardiac cycle.

**Diastolic pressure (DBP):** the lowest pressure in the arteries during the cardiac cycle.

**Pulse pressure:** SBP – DBP

**Mean arterial pressure** = diastolic pressure + 1/3 (pulse pressure). However, this applies only when HR is in the 60-90 BPM range. MAP is actually determined by integrating the arterial pressure curve.

MAP is also equal to (SP + 2DP)/3

**Rate-pressure product (RPP):** It is calculated as the product of SBP and HR and generally divided by 100 to get a smaller number. If SBP is 120 mm Hg and HR is 80 BPM, then RPP is 96 mm Hg BPM  $10^{-2}$

**Physiologic correlates of the blood pressure indexes:**

Diastolic pressure reflects the total resistance offered to peripheral run off of blood (specifically, the resistance offered by the arterioles).

When blood is ejected into the arteries, arterial blood pressure increases from about 80 mm Hg to about 120 mm Hg.

Ejection of blood produces an increment in arterial blood pressure; this is called pulse pressure.

*Pulse pressure depends upon two factors:* Volume of blood ejected (stroke volume) and arterial compliance. If arteries are thick and rigid (and thus less compliant), a given stroke volume produces a greater rise in pulse pressure.

It is often stated that pulse pressure = SBP– DBP. However, conceptually, systolic pressure = diastolic pressure + pulse pressure

RPP is a useful index because it reflects myocardial O<sub>2</sub> demand. Greater the HR, greater the myocardial oxygen demand; to generate a greater systolic pressure, greater wall tension needs to develop (according to Laplace’s law) and this also increases oxygen consumption.

**The arterial baroreflex mechanism for regulating blood pressure:**

<b>Inputs</b>	Mean arterial pressure, pulse pressure
<b>Receptor</b>	Called “arterial baroreceptors”
<b>Location of receptors</b>	Adventitia of the carotid sinus and aortic arch
<b>Receptor type</b>	Free nerve endings
<b>Adequate stimulus</b>	Stretch (both tonic as well as phasic response)
<b>Afferent</b>	Via IX (from the carotid sinuses) and X nerves (from the aortic arch)
<b>Termination of first order neurons</b>	NTS in medulla
<b>Receptor operating range</b>	MAP between 70 and 110 mm Hg
<b>Receptor characteristics</b>	Increase in static (mean arterial pressure) as well as phasic stretch (pulse pressure) increase firing rate; decrease in stretch decreases firing rate. There are presumably

	two subtypes of receptors of which is adapting and the other nonadapting.
<b>Response to an increase in BP</b>	An increase in BP leads to a decrease in cardiac output and TPR through cardiac vagal excitation and inhibition of sympathetic outflow
<b>Response to a decrease in BP</b>	Sympathetic outflow from the medulla is “disinhibited”; and vagal outflow to the heart is disinhibited.
<b>Response time:</b>	It takes only about 1 second for a change in BP to result in a compensatory change in HR; it takes a little longer (about 10 seconds) for changes in TPR to occur following a primary change in BP

**Isotonic versus isometric exercise:**

<b>Isotonic (dynamic) exercise; example, running</b>	<b>Isometric (static) exercise; example, sustained isometric handgrip</b>
BP increases mainly due to an increase in cardiac output	BP increases primarily due to an increase in TPR
TPR may fall in severe exercise because of accumulation of vasodilator metabolites	Cardiac output may reduce or not change significantly from baseline as a result of the baroreflex mechanism.

\*\*\*\*\*

## 9. Pulmonary Physiology

### Respiratory minute volume and alveolar ventilation:

Respiratory minute volume =  $V_T \times$  respiratory rate

Alveolar ventilation =  $(V_T - \text{anatomical dead space}) \times$  respiratory rate

Anatomical dead space is roughly equal to body weight in pounds.

If  $V_T = 500$  ml and respiratory rate = 12 per minute, then respiratory minute volume = 6 liters

If the anatomical dead space = 150 ml, then alveolar ventilation =  $(500 - 150) \times 12 = 4.2$  liters/minute. Note that only alveolar ventilation could contribute to gas exchange.

### Lung volumes and capacities:

Each lung volume is an independent fraction of total lung capacity (TLC). **Lung capacities** are combinations of **lung volumes**. Values given below are for a healthy young adult male weighing 80 kg with a body surface area of about 1.8 m<sup>2</sup>. Values in females are about 10% lower. Note that lung volumes and capacities are greatly influenced by height, weight, body surface area.

Tidal volume $V_T$	500 ml
Inspiratory reserve volume (IRV)	3200 ml
Expiratory reserve volume (ERV)	1100 ml
Residual volume (RV)	1200 ml

Tidal volume is about 5–7 ml/kg body weight;

By definition, the reserve volumes are recruited with effort.

FRC is the resting lung volume or the volume of air present in the lungs at the end of a tidal expiration. It is the lung volume at which the inward elastic recoil of lung parenchyma is balanced by the natural tendency of chest wall to recoil outward.

### Lung capacities in a healthy adult male weighing 70 kg:

Capacity		Volume (ml)
Functional residual capacity (FRC)	RV + ERV	2300
Inspiratory capacity (IC)	$V_T +$ IRV	3700
Vital capacity	$V_T +$ IRV + ERV	4800
TLC	RV + ERV + $V_T +$ IRV	6000

Note that the term expiratory capacity is not used. Unless otherwise stated, vital capacity is the maximum amount of air that can be expelled after a forced inspiration. If measured during inspiration, it is specifically called **inspiratory vital capacity**.

### Testing mechanics of respiration:

What are the factors affecting vital capacity?

1. Strength of muscles of inspiration
2. Lung compliance
3. Strength of muscles of expiration
4. Airways resistance

### Evaluating airways resistance:

Examine the relationship between air flow, airways resistance and airway pressure before you consider evaluating airways resistance.

Air flow = transairway pressure / airway resistance;

Transairway pressure = intrathoracic pressure – pressure at the mouth (which is zero mm Hg with reference to atmospheric pressure)

FEV<sub>1</sub>, the volume of air expelled during the first second of a forced vital capacity maneuver, varies directly with expiratory pressure and inversely with airways resistance. It is normally at least 80% of FVC; FEV<sub>1</sub>/FVC is > 0.8.

Note that if vital capacity is reduced, FEV<sub>1</sub> will be reduced, still FEV<sub>1</sub>/FVC may be normal.

For example, in restrictive lung disease, FEV<sub>1</sub> is reduced because vital capacity is reduced; however, FEV<sub>1</sub>/FVC is normal because airways resistance is normal.

Thus, FEV1/FVC is reduced when airways resistance is increased.

Peak expiratory flow rate (PEFR) is the highest flow rate during forced expiration (vital capacity maneuver). Note that when flows are reduced, flow rates are reduced. Thus, for example, the peak flow rate during tidal expiration is much lower than that during forced expiration. Normally PEFR is about 12 liters/second or 720 liters/minute (values are 10-15% lower in age matched females).

PEFR is dependent upon vital capacity. If vital capacity is reduced, PEFR is also reduced. Thus, it does not make sense to use PEFR as an index of airways resistance in a patient with restrictive lung disease.

So, PEFR must be used as an index of airways resistance only in patients known to have obstructive airways disease (low FEV1/FVC) because FEV1/FVC is normalized for flow whereas PEFR is not.

**Forced expiratory time:** this is a useful bedside index of airways resistance. Auscultate the trachea during forced expiration, if expiratory sounds are heard for longer than 4 seconds, airways resistance is increased.

**Maximum mid-expiratory flow rate (MMEFR):** The first 25% of expired air comes mainly from the major airways; MMEFR is the highest rate at which the middle 50% of VC is expelled; it is also called forced expiratory flow rate (FEF<sub>25-75</sub>). This reflects the resistance of the small airways that are narrowed in bronchial asthma.

**Using vital capacity as an index of pulmonary function:** Vital capacity is always reduced in lung disease; however, total lung capacity may be increased or decreased depending on the cause. However, vital capacity is not a sensitive index of pulmonary function. For example, a person can have a subnormal FEV1/FVC and yet his vital capacity could be normal.

Mechanism of reduction of vital	Disease
---------------------------------	---------

capacity	
Weakness of muscles of respiration	Myasthenia gravis, poliomyelitis
Lung compliance reduced	“Restrictive” lung disease
Increased airways resistance	Major airway obstruction; bronchial asthma

In summary,

	FEV1	FVC	FEV1/FVC	PEFR
OLD*	↓	↓	< 80%	↓
RLD*	↓	↓	Normal or > 80%	↓

\*OLD & RLD are obstructive & restrictive lung disease respectively.

“**Air trapping**” occurs whenever there is expiratory flow limitation. Since flow is driven by pressure and opposed by resistance, air trapping is usually a consequence of an increase in airways resistance. Air trapping occurs in chronic obstructive pulmonary disease. As a result of this, total lung capacity increases, however the vital capacity is subnormal; in other words, patients with obstructive lung disease breathe at a higher FRC compared to normal subjects. The fraction of FRC that increases is the residual volume.

*Below, there are questions here and there that have multiple correct answers.*

**Questions:**

- The volume of air that moves in or out during each tidal breath is called:
  - residual volume
  - expiratory reserve volume
  - functional residual capacity
- The amount of air present in the lungs at the end of a tidal breath is:
  - residual volume
  - inspiratory reserve volume
  - expiratory residual volume
  - tidal volume
- The largest lung volume is:
  - residual volume
  - inspiratory reserve volume
  - expiratory residual volume
  - tidal volume
- By spirometry, one **cannot** determine:
  - vital capacity
  - functional residual capacity
  - residual volume

- D. total lung capacity
5. Functional residual capacity can be determined using:
- spirometer
  - computerized spirometry
  - helium dilution technique
  - whole body plethysmography
6. A person breathes into and from a spirometer (volume 12 liters) containing 10% helium gas mixture. After equilibration, helium concentration of expired gas was found to be 6.7%. His vital capacity is 4.2 liters. What is his residual volume?
- 1000 ml
  - 1200 ml
  - 1500 ml
  - 1800 ml
7. In a healthy individual with a total lung volume of 6 liters, the amount of oxygen present in the lungs at the end of a normal expiration is about:
- 400 ml
  - 1000 ml
  - 100 ml
  - 250 ml
8. The maximum amount of gas that can be exhaled after a full inspiration is called:
- expiratory reserve volume
  - vital capacity
  - total lung capacity
  - functional residual capacity
9. Vital capacity correlates inversely with body surface area. True / false?
10. Vital capacity is greater in the upright posture compared to supine posture. True / false?
11. Residual volume is normally about \_\_\_\_% of total lung capacity.
- 10
  - 20
  - 30
  - 40
12. The largest volume of gas that can be moved into and out of the lungs in 1 minute by voluntary effort is called:
- respiratory minute volume
  - minute ventilation
  - maximal voluntary ventilation
  - vital capacity
13. In a healthy adult male, maximum voluntary ventilation is about:
- 60-80 L/min
  - 125-170 L/min
  - 200-220 L/min
  - 90-100 L/min
14. Which is the major muscle of inspiration?
15. Which muscle does **not** contract during forced expiration?
- Internal intercostals
  - External intercostals
  - Transversus abdominus
  - Rectus abdominis
16. The normal compliance of the human lungs and chest wall is:
- 0.1 L/cm H<sub>2</sub>O
  - 0.2 L/cm H<sub>2</sub>O
  - 0.3 L/cm H<sub>2</sub>O
  - 0.4 L/cm H<sub>2</sub>O
17. Resting lung volume would be lesser than FRC if it were not for the presence of:
- surface tension forces
  - surfactant
  - elastic recoil forces
18. In which pathologic condition is lung compliance increased?
19. Normally, during quiet breathing, intrapleural pressure is negative during inspiration as well as expiration. True/False?
20. The major constituent of surfactant is:
- neutral lipid
  - dipalmitoyl phosphatidyl choline
  - phosphatidylglycerol
  - surfactant proteins A & D
21. Intrapleural pressure is positive during:
- deep inspiration
  - tidal expiration

- C. forced expiration  
D. tidal inspiration
22. Which of the following produce bronchodilation?  
A. VIP  
B. Epinephrine  
C. Leukotriene C4  
D. PAF
23. Bronchodilation is mediated by:  
A.  $\alpha_1$  receptors  
B.  $\alpha_2$  receptors  
C.  $M_2$  receptors  
D.  $\beta_2$  adrenoceptors
24. Bronchial tone is highest at about:  
A. 6 AM  
B. 10 AM  
C. 2 PM  
D. 6 PM
25. Which of the following produces bronchoconstriction?  
A. VIP  
B. PAF  
C.  $LTB_4$   
D. Epinephrine  
E. Nitric oxide
26. Which of the following is **least likely** to produce bronchoconstriction?  
A. NO  
B. Sulfur dioxide  
C. Cool air  
D. Exercise
27. The FEV1/FVC ratio is normally greater than:  
A. 0.8  
B. 0.7  
C. 0.9  
D. 0.5
28. Peak expiratory flow rate (PEFR) is reduced in:  
A. restrictive lung disease  
B. bronchial asthma
29. The most sensitive index of small airways resistance in a patient with bronchial asthma is:  
A. vital capacity  
B. FEV1  
C. FEV<sub>1</sub>/FVC  
D. PEFR  
E. MMEFR
30. In chronic obstructive lung disease:  
A. FRC increases  
B. TLC increases  
C. VC decreases  
D. RV increases
31. Which of the following statements is **correct**?  
A. Normally, ventilation is greater at the apex than at the lung bases  
B. In the upright position, lower lung zones are more compliant compared to upper lung zones  
C. In the upright position, blood flow is greater at the lung bases than at the apices  
D. Positive intrapleural pressures during forced expiration prevent airways from closing.
32. Anatomic dead space is determined using:  
A. whole body plethysmography  
B. spirometry  
C. single-breath nitrogen curve  
D. single-breath carbon monoxide method
33. The pattern of ventilation in lungs is assessed by:  
A. Kety method  
B. inhalation of radioactive xenon  
C. angiography  
D. single breath technique
34. Under basal conditions, the amount of oxygen consumed per minute (in a healthy adult weighing 70 kg) is about:  
A. 100 ml  
B. 250 ml  
C. 350 ml  
D. 500 ml
35. Under basal conditions, the respiratory quotient (i.e., the volume of CO<sub>2</sub> produced / volume of oxygen consumed) is about:  
A. 1  
B. 0.8  
C. 0.7  
D. 1.2

36. Under basal conditions, respiratory exchange ratio is normally:
- 0.7
  - 0.8
  - 0.9
  - 1.0
37. Under basal conditions, in a person on a mixed diet, respiratory quotient is about:
- 0.7
  - 0.8
  - 0.9
  - 1.0
38. Alveolar oxygen tension ( $PAO_2$ ) is influenced by:
- barometric pressure
  - fraction of oxygen in inspired air ( $F_{iO_2}$ )
  - $P_ACO_2$
  - respiratory exchange ratio
39. At rest, the normal diffusing capacity of the lungs for carbon monoxide is about:
- 25 ml/min/mm Hg
  - 50 ml/min/mm Hg
  - 75 ml/min/mm Hg
  - 100 ml/min/mm Hg
40. The mean systemic arterial pressure and the mean pulmonary artery pressure are respectively 90 and 15 mm Hg. Can you tell the ratio of systemic and pulmonary vascular resistances?
- 1
  - 10
  - 6
  - Data inadequate
41. Ventilation-perfusion ratio (whole lung) is normally:
- 1
  - 0.8
  - 0.6
  - 1.2
42. In the upright position, V/Q ratio is highest in the:
- lung apices
  - middle zone
  - lung bases
43. In the upright position, the V/Q ratio at the lung apex is about:
- 1
  - 0.7
  - 0.5
  - 3
44. Arterial blood contains more oxygen than carbon dioxide. True / false?
45. Venous blood is normally 40% saturated with oxygen. True / false?
46. The sigmoid shape of the oxygen-hemoglobin dissociation curve is due to:
- allosteric effects
  - steric effects of oxygen binding on the configuration of Hb
  - the effects of 2,3-BPG on oxygen affinity of Hb
47. The major buffer of carbondioxide in blood is:
- bicarbonate
  - albumin
  - hemoglobin
48. If blood [Hb] were 15 g/dL, how much oxygen is contained in arterial blood?
- Approximately 20 ml/dL
  - Approximately 15 ml/dL
  - Data inadequate
49. If Hb were completely absent, how much plasma would be required to transport oxygen required for basal metabolism?
- 10 liters
  - 27 liters
  - 52 liters
  - 84 liters
50. Which of the following shifts the oxyhemoglobin dissociation curve to the right?
- $CO_2$
  - 2, 3-BPG
  - Increase in tissue temperature
  - Decrease in tissue pH

51. Suppose you administer 100% oxygen at 4 atmospheres, then how much oxygen would be transported in 100 ml of plasma?  
 A. 0.3 ml  
 B. 3 ml  
 C. 6 ml  
 D. 9 ml
52. The decrease in oxygen affinity of Hb when the pH of blood in tissues falls is:  
 A. Bohr effect  
 B. Haldane effect  
 C. Hawthorne effect  
 D. Hamburger effect
53. Which of the following shifts the oxyhemoglobin dissociation curve to the left?  
 A. CO  
 B. Increase in [2,3 BPG] in RBC  
 C. Increase in tissue temperature  
 D. Decrease in tissue pH
54. The commonest cause of arterial hypoxemia is:  
 A. type II respiratory failure  
 B. lactic acidosis  
 C. V/Q mismatch  
 D. anemia
55. PaO<sub>2</sub> is / may be normal in hypoxia due to:  
 A. hypoventilation  
 B. diffusion limitation  
 C. severe circulatory shock  
 D. anemia  
 E. cyanide poisoning
56. Administration of O<sub>2</sub> rich gas mixtures improves tissue oxygenation most in:  
 A. hypoxic hypoxia  
 B. anemic hypoxia  
 C. hypokinetic hypoxia  
 D. histotoxic hypoxia
57. CO<sub>2</sub> is chiefly transported in blood:  
 A. as bicarbonate  
 B. bound to hemoglobin  
 C. as dissolved CO<sub>2</sub>  
 D. in combination with plasma proteins
58. The major stimulus for spontaneous respiration is:  
 A. CO<sub>2</sub>  
 B. O<sub>2</sub>  
 C. lactate  
 D. HCO<sub>3</sub>
59. Central chemoreceptors are chiefly stimulated by:  
 A. an increase in CSF [H<sup>+</sup>]  
 B. a fall in PaO<sub>2</sub>  
 C. a decrease in PaCO<sub>2</sub>  
 D. all of the above
60. The neurons pacing spontaneous breathing are located in:  
 A. pneumotaxic center  
 B. apneustic center  
 C. pre-Bottzinger complex  
 D. dorsal motor nucleus of vagus
61. Systemic arterial chemoreceptors (commonly called peripheral chemoreceptors) are mainly stimulated by:  
 A. a decline in PaO<sub>2</sub>  
 B. an increase in [H<sup>+</sup>] of arterial plasma  
 C. a decrease in blood flow through them  
 D. an increase in PaCO<sub>2</sub>
62. The plasma/CSF ratio of proteins is:  
 A. 3  
 B. 10  
 C. 20  
 D. 300
63. Forced hyperventilation to exhaustion may result in:  
 A. a decrease in serum ionized calcium  
 B. an increase in plasma protein level  
 C. an increase in blood pH
64. Hypocapnia is usually due to:  
 A. hypoxemia  
 B. alkalosis  
 C. decreased CO<sub>2</sub> production  
 D. alveolar hyperventilation
65. Normally, PaCO<sub>2</sub> chiefly depends on:  
 A. total lung capacity  
 B. PaO<sub>2</sub>

- C. alveolar ventilation
- D. rate of CO<sub>2</sub> production

66. Caution needs to be exercised in administering O<sub>2</sub> to patients with:

- A. ARDS
- B. metabolic acidosis
- C. type I respiratory failure
- D. type II respiratory failure

67. Which of the following data suggests type II respiratory failure? (pH, PaCO<sub>2</sub> and plasma [HCO<sub>3</sub>]<sup>-</sup> given below in that order).

- A. 7.4, 60 mm Hg, 30 mmol/L
- B. 7.2, 80 mm Hg, 30 mmol/L
- C. 7.33, 46 mm Hg, 20 mmol/L

68. J receptors are located in:

- A. pulmonary interstitium
- B. alveoli
- C. bronchial mucosa
- D. roof of the fourth ventricle

69. Stimulation of J receptors results in:

- A. apnea
- B. tachypnea
- C. hyperpnea
- D. apnea followed by tachypnea

70. An increase in the duration of expiration produced by lung inflation is due to:

- A. Hering-Breuer deflation reflex
- B. pulmonary chemoreflex
- C. Bezold-Jarisch reflex
- D. Hering-Breuer inflation reflex

71. Which of the following statements regarding Cheyne-Stokes respiration are **correct**?

- A. It is characterized by periods of hyperpnea punctuated by apnea.
- B. It is attributed to increased sensitivity of the respiratory center to CO<sub>2</sub>.
- C. It may occur if lung-to-brain circulation time is prolonged.
- D. It may occur in severe congestive heart failure

72. During mouth-to-mouth resuscitation, what is the oxygen concentration of the resuscitating gas mixture?

- A. 16%

- B. 21%
- C. 28%
- D. 35%

73. Regarding physiologic changes during moderate isotonic exercise in a healthy young adult, which of the following are true and which are false?

1. PaO<sub>2</sub> declines
2. PaCO<sub>2</sub> increases
3. pH of arterial blood decreases (eventually during intense exercise)
4. A-V O<sub>2</sub> difference increases
5. SvO<sub>2</sub> increases
6. Plasma [K<sup>+</sup>] increases
7. The impulse rate from carotid bodies increases.
8. During maximal exercise, O<sub>2</sub> consumption may reach up to 4 L /min, about 16 times basal oxygen consumption.
9. VO<sub>2</sub> max (maximum oxygen consumption during intense exercise) is increased by training.
10. Heart rate may remain elevated for as long as 1 hour after severe exercise.

#### **Are chemoreceptors stimulated in anemia or not?**

For the sake of clarity, let us ask a question like this:

Chemoreceptors are not stimulated in:

- A. anemia
- B. anemic hypoxia

Note the difference between anemia, which simply means that the concentration of hemoglobin is lower than normal, and anemic hypoxia - a consequence of anemia associated with anaerobic metabolism and acidosis.

The effect of acidosis is stimulation of the peripheral chemoreceptors (i.e., those in the carotid bodies) in anemic hypoxia. In an anemic individual who is at rest, and whose arterial pH is normal, peripheral chemoreceptors may not be as stimulated.

“The additional increase in ventilation (during exercise) produced by the acidosis is dependent

upon the carotid bodies and does not occur if they are removed". See *p 682, Ch 37, WFG, 2005.*

**Now take this question:** Systemic arterial chemoreceptors are stimulated in (*check all correct answers*):

- A. anemic hypoxia
- B. hypoxic hypoxia
- C. hypokinetic hypoxia
- D. histotoxic hypoxia

All are correct. The question is whether peripheral chemoreceptors are stimulated or not in various types of hypoxia. It is not how they are stimulated. There are several factors besides a low PaO<sub>2</sub> that could stimulate peripheral chemoreceptors. These are:

A decrease in blood flow through the chemoreceptors as occurs in circulatory shock (stagnant hypoxia) can stimulate them.

Inhibition of oxygen utilization in chemoreceptor cells (by injection of cyanide) also activates chemoreceptors.

Whenever hypoxia is accompanied by acidosis (for example in an anemic individual doing exercise), acidosis activates the receptors and increases minute ventilation. Injection of K<sup>+</sup> has been shown to activate them; this may partly account for exercise induced changes in ventilation.

Thus, in anemic hypoxia, arterial chemoreceptors are not stimulated by hypoxia, but rather by the ensuing acidosis.

**Answers to Pulmonary Physiology:**

	2C	3B	4BCD	5CD
6D	7A	8B	9F	10T
11B	12C	13B		15B
16B	17B		19T	20B
21C	22AB	23D	24A	25BC
26A	27A	28AB	29E	30all
31BC	32C	33B	34B	35B
36B	37B	38all	39A	40C
41B	42A	43D	44F	45F
46B	47C	48C	49D	50all
51D	52A	53A	54C	55DE

56A	57A	58A	59A	60C
61ABC	62D	63AC	64D	65C
66D	67B	68A	69D	70D
71all	72A			

1 Tidal volume; 14 Diaphragm; 18 Emphysema

73. Physiologic changes during exercise:

1F	2F	3T	4T	5F
6T	7T	8T	9T	10T

**Answer Explanations:**

5. FRC (the volume of air remaining in the lungs at the end of a tidal breath) cannot be determined by spirometry.

FRC is determined by:

- 1. helium dilution technique
- 2. whole body plethysmography

**6. Principle:** Indicator-dilution principle

**Indicator:** Helium. This is used because it has a very low molar mass (low density), that it does not dissolve in blood when it is inhaled at 1 atmosphere. Initially, the helium gas is present only in the spirometer. The person breathes from as well as into the spirometer. **The circuit is closed.** After a few breaths, the helium concentration in the spirometer will reduce because it would have also got diluted in lung volume.

Initially,

C1: Helium concentration in spirometer = 10%

V1: Spirometer volume = 12 liters

C2: Helium concentration in spirometer (= lungs) = 6.7%

V2: Volume of distribution is now total lung capacity + spirometer volume.

Very little helium actually dissolves in blood. So it can be neglected.

Applying law of conservation of mass,

$$C1V1 = C2 (V1+V2)$$

Substituting, we get,

$$10 \times 12 = 6.7 (12 + TLC)$$

$$TLC = [10 \times 12 / 6.7] - 12 = 18 - 12 = 6L$$

$$VC = 4.2 L$$

$$\text{So } RV = 6 - 4.2 = 1.8 L = 1800 \text{ ml.}$$

7. FRC = 2300 ml

Because alveolar oxygen is diluted with CO<sub>2</sub>, the fraction of oxygen in alveolar gas is only about 16%.

Thus, the amount of oxygen present in lungs at the end of a tidal expiration =  $(16 / 100) \times 2300 = 370$  ml

10. Intrathoracic blood volume increases by about 400 ml in the supine position compared to standing; the increase in pulmonary blood volume is greater in patients with left ventricular systolic failure and consequently they may be breathless when lying supine.

**16. Lung compliance** is the change in lung volume for a given change in pressure.

$$\text{Compliance} = \Delta V / \Delta P$$

The normal compliance of human lungs and chest wall is about 0.2 L/cm H<sub>2</sub>O. Compliance is reduced in restrictive lung disease.

22. VIP is released by nonadrenergic noncholinergic neurons. VIP relaxes bronchial smooth muscle. VIP deficiency has been implicated in asthma.

**Leukotrienes** are potent bronchoconstrictors.

**Zileuton**, a lipoxygenase inhibitor inhibits the synthesis of leukotrienes. It is used in the management of asthma. **Zafirlukast** is a leukotriene receptor blocker.

25. Inhaled nitric oxide has been shown to produce bronchodilation as well as a decrease in pulmonary artery pressure. Substance P, platelet activating factor (PAF) and leukotrienes are bronchoconstrictors.

28. PEFr is reduced when vital capacity is reduced, and so is reduced in both obstructive and restrictive lung disease. It is used therefore to monitor airways resistance only in individuals who are known to have asthma.

**29. Maximum mid-expiratory flow rate (MMEFR)** is the peak flow rate during expiration. It may not be the same as PEFr. MMEFR is effort independent. It reflects the resistance of small airways affected in asthma.

**Forced expiratory flow rate (FEF 25-75)** is an integrated calculation of the average flow rate during exhalation of the interquartile range (25<sup>th</sup> - 75<sup>th</sup> percent) of vital capacity.

31. *Option B* – upper lung zones are less compliant because of their higher volume at baseline. *Option D* - Positive intrapleural pressures during forced expiration tend to cause compression of small bronchi (dynamic airway compression).

**32. What is a shunt; what is dead space?**

**Shunt:** Perfusion of unventilated alveoli results in shunting of deoxygenated blood across the lungs to the heart, i.e. a right-to-left shunt.

**Dead space:** Ventilation of unperfused alveoli is effectively an extension of anatomic dead space since it cannot contribute to gas exchange.

35-37. At rest, a healthy adult weighing 70 kg uses about 250 ml of oxygen per minute and 200 ml of CO<sub>2</sub> is produced.

Respiratory exchange ratio (RER) is the ratio of the volume of CO<sub>2</sub> to O<sub>2</sub> exchanged across the lungs per minute. At rest, it is normally 200 / 250 = 0.8

Respiratory exchange ratio reflects the average respiratory quotient (RQ) when gas exchange across lungs is normal.

RQ is different for different energy substrates.

Carbohydrate	1
Protein	0.8
Fat	0.7
Average RQ	0.8

The average RQ depends upon the metabolic state.

38. The alveolar gas equation:

$$\text{Alveolar oxygen tension } PA_{O_2} = [(P_B - P_{H_2O}) \times F_{iO_2}] - [(PA_{CO_2})/R]$$

P<sub>B</sub> is barometric pressure (760 mm Hg at mean sea level);

P<sub>H<sub>2</sub>O</sub> is the pressure of water vapor at body temperature (it is 47 mm Hg);

$F_{iO_2}$  is the percentage of oxygen in inspired air; and  $P_{ACO_2}$  is the  $CO_2$  tension in alveolar gas (normally about 40 mm Hg). It is equal to  $P_{aCO_2}$  because  $CO_2$  is highly soluble and readily equilibrates across the alveolocapillary membrane. So you can substitute  $P_{aCO_2}$  for  $P_{ACO_2}$ .

R is respiratory exchange ratio (as defined above, see answer explanation for Questions 35-37); it is assumed to be 0.8 when the alveolar gas equation is used for solving common clinical problems.

Substituting, we get,  
 $P_{AO_2} = [(760 - 47) \times 0.21] - [40/0.8]$   
 $= 150 - 50 = 100 \text{ mm Hg}$

39. When alveolar ventilation is held constant, the amount of  $CO_2$  removed is limited by pulmonary blood flow. However,  $CO_2$  accumulation is invariably due to a decrease in alveolar ventilation.

When alveolar oxygen tension is constant, normally (i.e., at rest), oxygen exchange is limited by perfusion because enough time is available for equilibration across the alveolocapillary membrane. However, during exercise, when blood flow rates are higher, the time available for equilibration is lesser and oxygen exchange is increasingly limited by diffusion (**diffusion-limited**). Thus, impairment in diffusion capacity of the lungs for oxygen causes problems especially during exercise.

#### Testing diffusion capacity of the lungs:

The "single breath technique": The subject inhales a mixture containing 0.01% CO  
 We know that diffusion rate  $J = (P_A - P_c) \times DA/x$   
 In a nonsmoker,  $P_c \text{ CO} = 0 \text{ mm Hg}$  and  $P_A$  is a constant; thus the diffusion rate depends upon  $DA/x$

$DLCO = 25 \text{ ml/min/mm Hg}$

$DLO_2 = 25 \text{ ml/min/mm Hg}$

Since CO exchange is diffusion limited, it is used for assessing diffusion capacity.

40. Since pulmonary and systemic circulations are in series, the flows are identical  
 Cardiac output =  $P / R$ ;

(P is mean arterial pressure and R is vascular resistance)

$P_s / P_p = R_s / R_p$  (s and p refer to systemic and pulmonary vascular beds respectively)

$P_s / P_p = 90 / 15 = 6$

Ratio of systemic and pulmonary vascular resistance = 6

Thus, the pulmonary circulation is a low resistance, low pressure system.

At rest, systolic pulmonary artery pressure is about 25 mm Hg, diastolic pulmonary artery pressure averages 10 mm Hg, mean pulmonary artery pressure is about 15 mm Hg, and pulmonary capillary pressure averages about 10 mm Hg.

**41-43. Ventilation-perfusion ratio** is the ratio of alveolar ventilation to pulmonary blood flow.

For example, at rest, alveolar ventilation =  $12 \times (500 - 150) = 4.2 \text{ L/min}$ ;

Assuming  $V_T = 500 \text{ ml}$ ,  $V_D = 150 \text{ ml}$ ;

At rest, pulmonary blood flow = 5 L/min;

Thus, whole lung V/Q ratio = 0.84;

In the lung apices, V/Q approaches infinity;

In the lung bases, V/Q is lower than 1.

It must however be noted that alveolar ventilation is much higher at the lung bases than the apices because the lower lung zones are less distended at the start of inspiration and therefore more compliant. As a result of regional differences in intrapleural pressure, upper lung zones are already in a more expanded position at the start of inspiration.

#### Lung zones:

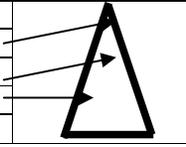
$P_A$  = Alveolar pressure;

$P_a$  = Pressure at the arterial end of the pulmonary capillary;

$P_v$  = Pulmonary venous pressure;

$P_i$  = Pulmonary interstitial pressure.

Zone	Definition
Zone 1	$P_A > P_a > P_v$
Zone 2	$P_a > P_A > P_v$
Zone 3	$P_a > P_v > P_A$
Zone 4	$P_a > P_i > P_A$



**Zone 1:** above the heart; arterial pressure is lower and may be lower than alveolar pressure if the

alveoli are well expanded. Flow may be minimal. V/Q approaches infinity.

**Zone 2:** pulmonary arterial pressure is greater than alveolar pressure and flow is determined by arterial – alveolar pressure difference; however, during inspiration when alveolar pressure becomes more negative, blood flows from the arteries into the pulmonary veins. This is called the ‘**waterfall effect**’.

**Zone 3:** flow is continuous and is driven by pulmonary arterial – venous pressure gradient.

**Zone 4:** it occurs in pulmonary edema (always abnormal). When pulmonary interstitial pressure is > than alveolar pressure, alveolar collapse (atelectasis) would result.

When a Swan Ganz catheter is wedged in the pulmonary capillary to estimate left ventricular end diastolic pressure (LVEDP) in a patient who is on a ventilator with positive end expiratory pressure (PEEP) added, the measured pressure would reflect alveolar pressure rather than LVEDP; thus, the catheter must be placed in Zone 3 conditions (perhaps by momentarily discontinuing PEEP) to reliably estimate LVEDP

### Regulation of pulmonary vascular resistance:

Block ventilation to a lung zone



Perfusion of that lung zone decreases

Hypoxic pulmonary vasoconstriction serves to shunt blood to well ventilated lung zones and optimize oxygen uptake in the lungs. However, chronic alveolar hypoxia leads to a chronic increase in pulmonary vascular resistance and pulmonary hypertension.

44. It contains more CO<sub>2</sub> since CO<sub>2</sub> is much more soluble than O<sub>2</sub> in blood.

45. It is 75% saturated with oxygen

47. HCO<sub>3</sub> cannot buffer protons formed from CO<sub>2</sub>;  
CO<sub>2</sub> + H<sub>2</sub>O = H<sup>+</sup> + HCO<sub>3</sub>

H + HCO<sub>3</sub> = CO<sub>2</sub> (acid);  
Hb is the major buffer of CO<sub>2</sub>

48. Factors that affect oxygen delivery to the tissues include the following (the *oxygen cascade*):

- Alveolar ventilation
- Pulmonary blood flow
- Ventilation / perfusion balance
- Diffusion capacity of lungs for oxygen
- Cardiac output
- Hb concentration of arterial blood
- Affinity of Hb for oxygen
- Blood flow to each tissue

49. Basal oxygen requirement at rest = 250 ml/min

O<sub>2</sub> carrying capacity of 1L of plasma = 3 ml  
Amount of plasma that would be required to transport 250 ml of oxygen = 83 liters!

This problem illustrates the importance of Hb.

51. O<sub>2</sub> solubility in plasma is limited, hence Hb required for oxygen transport.

O<sub>2</sub> solubility in plasma = 0.003 ml O<sub>2</sub>/100 ml plasma/ mm Hg PO<sub>2</sub>.

Greater the PaO<sub>2</sub>, greater the dissolved oxygen (Henry’s Law)

Calculate the expected PaO<sub>2</sub> using the alveolar gas equation:

$$PAO_2 = [(4 \times 760) - 47] \times 1 - (40/0.8)$$

Expected PaO<sub>2</sub> is approximately 3000 mm Hg.

Thus, about 9 ml of oxygen will be transported in 100 ml of plasma.

That is, in 4 liters of plasma 360 ml of oxygen can be transported. Let us say the requirement is 250 ml O<sub>2</sub>/min. This meets the demand; this is the rationale for use of hyperbaric oxygenation. However, it is resorted to only when the oxygen transport capacity of blood cannot be raised otherwise because oxygen toxicity is also a significant concern.

52. The presence of higher levels of CO<sub>2</sub> and H<sup>+</sup> in the capillaries of metabolically active tissue promotes the release of O<sub>2</sub> from hemoglobin. This is the Bohr effect.

53. CO is a competitive inhibitor of oxygen binding of hemoglobin. Exposure for 1 hour to a

CO concentration of 0.1% in inspired air leads to the occupancy by CO of about 50% of heme sites in Hb, a proportion that is frequently fatal. Apart from being a competitive inhibitor of oxygen binding to Hb, CO also inhibits the dissociation of oxyhemoglobin (prevents unloading of oxygen at the tissues). That is, it shifts the ODC to the left.

54. Ventilation – perfusion imbalance is the commonest cause of hypoxemia. Of course, the hypoxemia in ARDS is also due to ventilation-perfusion match; V/Q mismatch is an umbrella term that illuminates pathophysiology and is the single best answer for this question.

55. Note the difference between the terms hypoxemia (decreased arterial PO<sub>2</sub>) and hypoxia (inadequate tissue oxygenation). While the PaO<sub>2</sub> may be normal in carbon monoxide poisoning, circulatory shock, cyanide poisoning and anemia, the tissues are yet hypoxic. Carbon monoxide inhibits the dissociation of O<sub>2</sub> from HbO<sub>2</sub>.

58. CO<sub>2</sub> in plasma quickly equilibrates across the blood brain barrier. There it is quickly hydrated to form H<sub>2</sub>CO<sub>3</sub>. Carbonic acid is unstable and dissociates at physiologic pH to form H and HCO<sub>3</sub>. The protein content of CSF is extremely low that it cannot buffer H ions formed from carbon dioxide. Thus H ions in CSF stimulate central chemoreceptor neurons which in turn drive the respiratory neurons. Central chemoreceptors are chiefly stimulated by an increase in P<sub>a</sub>CO<sub>2</sub> i.e. an increase in [H<sup>+</sup>] of CSF.

61. In arterial plasma, CO<sub>2</sub> gets buffered by Hb and plasma proteins. Therefore, it is less effective stimulating receptors in carotid and aortic bodies. This would not happen in the CSF because there is very little protein there. Note that the ratio of the concentration of protein in plasma and CSF is normally about 300.

62. Plasma protein concentration = 6000 mg/dL  
CSF protein concentration = 20 mg/dL

64. If minute ventilation reduces, then PaCO<sub>2</sub> increases (hypercapnia). Hypercapnia is a PaCO<sub>2</sub> > 45 mm Hg. Hypercapnia is almost always due to inadequate alveolar ventilation. Conversely,

hypocapnia (PaCO<sub>2</sub> < 35 mm Hg) is almost always due to hyperventilation, i.e. minute ventilation in excess of that required to maintain arterial plasma pH at 7.4

66. In chronically hypercapnic patients, CO<sub>2</sub> depresses rather than stimulates respiration and respiration is driven by hypoxia. Administration of 100% oxygen may remove the hypoxic drive and breathing may stop. Such a patient will require mechanical ventilation to bring down CO<sub>2</sub> a level which would stimulate respiration.

70. The Hering Breuer inflation reflex is an increase in the duration of duration of expiration produced by steady lung inflation and the Hering Breuer deflation reflex is a decrease in the duration of expiration caused by marked deflation of the lung.

#### Nonchemical influences on respiration

Reflex	Stimulus	Response
Hering Breuer inflation reflex*	Lung inflation	Increase in the duration of expiration
Hering Breuer deflation reflex*	Lung deflation	Increase in the duration of inspiration
Head's paradoxical reflex <sup>ε</sup>	Lung inflation	Further inflation

\*Hering Breuer reflexes are probably initiated by considerable changes in lung volume (deep inspiration or deep expiration).

<sup>ε</sup> It may play a role in lung expansion in newborns.

71. Periodic breathing may occur in:

- Severe congestive heart failure
- Uremia
- Sleep
- Brain stem disease
- A normal individual following a bout of voluntary hyperventilation.

73. PaCO<sub>2</sub> changes little because alveolar ventilation also increases.

The impulse rate from the carotid bodies increases possibly because of an increase in body temperature, plasma [K] and [H] formed from lactic acid.

Plasma K increases because K is released from actively metabolizing skeletal muscle.

pH of arterial blood is initially maintained but eventually decreases and that is when one fatigues. A substantial increase in hydrogen ion concentration of arterial blood will accelerate the onset of fatigue.

Arteriovenous O<sub>2</sub> difference increases because oxygen extraction by tissues increases.

Saturation of mixed venous blood with oxygen decreases because oxygen extraction by metabolically active tissue increases.

During maximal exercise, O<sub>2</sub> consumption may increase to as high as 3-4 liters/min, i.e. 12-16 times the oxygen consumption at rest.

Heart rate may remain elevated for as long as 1 hour after severe exercise because the increase in sympathetic nerve activity also persists. This is due to the oxygen debt incurred during exercise. Until the debt is cleared, minute ventilation and cardiac output will be higher compared to preexercise levels.

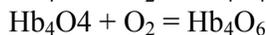
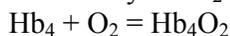
\*\*\*\*\*

### **Supplement: Gas Transport**

#### **Oxygen loading in the lungs:**

*the reaction of Hb with oxygen*

The T (tense) configuration reduces the affinity of Hb for O<sub>2</sub>; the R (relaxed) configuration increases the affinity for O<sub>2</sub>



***These are some facts that you must remember:***

The solubility of oxygen in plasma at body temperature is 0.003 ml / mm Hg PO<sub>2</sub> / 100 ml of blood;

Assuming PO<sub>2</sub> is 100 mm Hg, the amount of oxygen dissolved in blood / plasma ≈ 0.3 ml / dL. However, CO<sub>2</sub> is about 20 times more soluble in blood compared to O<sub>2</sub> and there is much more CO<sub>2</sub> in arterial blood compared to oxygen (see the tables below).

#### **Normal PO<sub>2</sub> and PCO<sub>2</sub> levels in blood:**

PO <sub>2</sub>	Arterial	100 mm Hg
PO <sub>2</sub>	Venous	40 mm Hg
PCO <sub>2</sub>	Arterial	40 mm Hg
PCO <sub>2</sub>	Venous	46 mm Hg

#### **Gas content of blood (in ml).**

	Arterial		Venous	
	Dissolved	Combined	Dissolved	Combined
O <sub>2</sub>	0.3	19.5	0.12	15
CO <sub>2</sub>	2.5	45	3	50

#### **Oxygen transport capacity of blood:**

Assuming all Hb is Hb A, PaO<sub>2</sub> = 100 mm Hg, and that Hb is fully saturated with O<sub>2</sub>, then:

Content of oxygen in arterial blood (CaO<sub>2</sub>) = 19.8 ml/dL of blood; of this, about 0.3 ml is dissolved in plasma and the rest is in combination with Hb A.

**Hypoxia:** The term is often used to denote inadequate oxygenation of tissues (tissue hypoxia).

**Hypoxemia:** a reduction in oxygen tension of arterial blood below 80 mm Hg

#### **Classification of hypoxemia (based on severity):**

Grade	PaO <sub>2</sub>
Mild	61–80 mm Hg
Moderate	41–60 mm Hg
Severe (fulminant)	< 40 mm Hg

#### **Classification of causes of tissue hypoxia:**

Type	PaO <sub>2</sub>	Cause	Treatment
Hypoxic hypoxia	↓	High altitude; defects in gas exchange	Administer oxygen; address cause
Anemic	Normal	Anemia;	Raise oxygen

hypoxia		CO poisoning	carrying capacity of plasma / blood as appropriate; address cause
Hypokinetic hypoxia, <i>alt.</i> stagnant hypoxia, ischemic hypoxia	Normal or ↓	Myocardial hypoxia due to coronary ischemia; circulatory shock	Address cause;
Histotoxic hypoxia	Normal	Cyanide poisoning	Address cause; hyperbaric oxygenation

**Myoglobin (Mb):** an oxygen storage protein; also a heme protein; single subunit; so there is no quaternary structure; so it does not bind 2,3 BPG; it is abundant in red muscle; 1 mol of Mb binds one mol of O<sub>2</sub>; its P50 is about 1 mm Hg (much lesser compared to HbA). **Neuroglobin** may have a similar function in brain.

### Transport of CO<sub>2</sub>

1. CO<sub>2</sub> from tissues diffuses into RBC
2. It is hydrated by the enzyme carbonic anhydrase (CA) present in RBC:  

$$\text{CO}_2 + \text{H}_2\text{O} = \text{H}_2\text{CO}_3$$
The hydration of CO<sub>2</sub> in plasma is much slower because of the absence of CA in plasma.
3. H<sub>2</sub>CO<sub>3</sub> dissociates into H<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>
4. H<sup>+</sup> is buffered by Hb; HCO<sub>3</sub><sup>-</sup> enters plasma in exchange for chloride which enters RBC; this is called **chloride shift** or Hamburger phenomenon (it is mediated by the Cl-HCO<sub>3</sub> exchanger)

### What happens in the lungs?

The high PO<sub>2</sub> in alveolar gas causes Hb to give up CO<sub>2</sub> and take up oxygen.

**Haldane effect:** The high concentration of O<sub>2</sub> in the alveolar capillaries unloads H<sup>+</sup> and CO<sub>2</sub> from hemoglobin; i.e., oxygen dissociation curve of Hb shifts to the left.

### Transport of CO<sub>2</sub> in 100 ml arterial blood:

	Arterial	Venous
Dissolved	2.5 ml	3 ml
Bicarbonate	45 ml	47 ml
Carbamino compounds	2.5 ml	3.5 ml

### How much acid do the lungs excrete per day?

200 ml of CO<sub>2</sub> per minute amounts to 288 liters of CO<sub>2</sub> per day, which is equivalent to 12500 meq of H<sup>+</sup> per day. The kidneys normally excrete about 50 mEq of H ions per day.

**Functions of hemoglobin:** Apart from transporting oxygen, CO<sub>2</sub> and buffering protons, Hb also binds nitric oxide (a vasodilator); this may help match oxygen delivery with increases in tissue blood flow.

\*\*\*\*\*

## 10. Renal and Acid-Base Physiology

### *Abbreviations used here:*

ADH – antidiuretic hormone  
ANG II – angiotensin II  
CCD – cortical collecting duct  
MCD – medullary collecting duct  
MD – macula densa  
DCT – distal convoluted tubule  
GFR – glomerular filtration rate  
MI – medullary interstitium  
PT – proximal tubule  
PCT – proximal convoluted tubule  
PST – proximal straight tubule  
RBF – renal blood flow  
RPF – renal plasma flow  
TAL – thick ascending limb  
TDL – thin descending limb  
OMCD – outer medullary collecting duct  
IMCD – inner medullary collecting duct  
FENa – fractional excretion of sodium

### **Instructions: In each of the following questions, check all correct answers.**

- The 'gold standard' for estimation of glomerular filtration rate is the clearance of
  - inulin
  - creatinine
  - urea
  - mannitol
  - glucose
  - para-amino hippuric acid
- In clinical practice, the urinary clearance of which substance is most frequently used to estimate GFR?
  - Inulin
  - Creatinine
  - Urea
  - Mannitol
- Which of the following substances **should not** be used to measure GFR?
  - Inulin
  - Creatinine
  - Phenol red
- The term filtration fraction is used to refer to:
  - RPF / GFR
  - GFR / RPF
  - RPF  $\times$  GFR
- What fraction of renal plasma flow is normally filtered in the glomerular capillaries?
  - 0.1
  - 0.2
  - 0.3
  - 0.4
- When mean arterial pressure is held constant, selective constriction of glomerular efferent arterioles:
  - increases GFR
  - raises filtration fraction
  - decreases renal plasma flow
- In humans, what percentage of nephrons has long loops of Henle?
  - 5
  - 15
  - 25
  - 85
- Juxtamedullary nephrons constitute about \_\_\_\_\_ % of the total nephrons.
  - 10
  - 15
  - 25
  - 40
- The macula densa is located in the:
  - juxtaglomerular cells
  - extraglomerular mesangium
  - beginning of *early distal tubule*
  - peritubular capillaries
- The 'brush border' is most extensive in cells of the:
  - PCT
  - loop of Henle
  - DCT
  - collecting duct
- Which of the following **increases** renal cortical blood flow?
  - Prostaglandin E2
  - Norepinephrine
  - Angiotensin II
  - Vasopressin

12. The PAH clearance of a 56-year-old male with sustained elevations of blood urea nitrogen, creatinine and potassium was estimated to be 100 ml/min. His PCV is 20. His renal blood flow is approximately:

- A. 25 ml/min
- B. 125 ml/min
- C. 250 ml/min
- D. 600 ml/min

13. Autoregulation of GFR is achieved through changes in:

- A. renal perfusion pressure
- B. renal blood flow
- C. glomerular afferent arteriolar resistance
- D. glomerular efferent arteriolar resistance

14. In a healthy adult human with a resting BP averaging about 110/70 mm Hg who is not on any medication, the earliest MAP at which renal autoregulation of GFR is overwhelmed is when mean arterial pressure falls below:

- A. 30 mm Hg
- B. 50 mm Hg
- C. 70 mm Hg
- D. 90 mm Hg

15. The rate-limiting step in the biosynthesis of angiotensin II is the synthesis of:

- A. renin
- B. angiotensinogen
- C. angiotensin I
- D. angiotensin II

***All about angiotensin II:***

Which of the following statements regarding angiotensin II are true and which are false?

- 1. It is a much more potent vasopressor compared to norepinephrine;
- 2. It stimulates aldosterone release from adrenal cortex;
- 3. It inhibits ADH release;
- 4. It has a dipsogenic effect;
- 5. It reduces Na reabsorption in PT;
- 6. It facilitates norepinephrine release from postganglionic sympathetic neurons;
- 7. It has a greater constrictor effect upon glomerular afferent arterioles;
- 8. It reduces renal plasma flow;

- 9. It causes mesangial cells to contract;
- 10. Normally, it serves to maintain GFR;
- 11. It increases Na and H<sub>2</sub>O reabsorption by a direct action on PT

12. It plays an important role in cardiac remodeling after a myocardial infarction;

13. Angiotensin III has 100% aldosterone-stimulating activity;

14. Angiotensin III is a more potent pressor than angiotensin II;

15. Angiotensin converting enzyme is a dipeptidyl carboxypeptidase.

16. ACE is the only enzyme responsible for angiotensin II synthesis.

16. Which of the following stimulates the release of aldosterone from the adrenal cortex?

- A. Renin
- B. Angiotensin III
- C. ↓ plasma [K<sup>+</sup>]
- D. ANP

17. In the nephron, glucose reabsorption occurs mainly in the:

- A. proximal tubule
- B. loop of Henle
- C. distal convoluted tubule
- D. collecting duct

18. The following data were obtained on a patient: Creatinine clearance = 125 ml/min; plasma [glucose] = 400 mg/dL. If the tubular maximum for glucose were 350 mg/min, what would the glucose excretion rate be?

- A. 50 mg/min
- B. 100 mg/min
- C. 150 mg/min
- D. 200 mg/min

19. Reabsorption of water in the PT:

- A. is chiefly driven by osmotic gradients
- B. occurs through water channels in apical membranes of tubular epithelial cells
- C. is facilitated by vasopressin
- D. all of the above statements are correct

20. Principal cells (P cells) in the cortical collecting duct of the nephron are concerned with:

- A. secretion of protons
- B. potassium reabsorption

- C. ADH-stimulated water reabsorption  
D. reabsorption of sodium and chloride
21. Which ion is both secreted and absorbed by the nephron?  
A. Na  
B. K  
C. Cl  
D. Ca
22. The retention of 'free water' by ADH in the collecting ducts is mediated mainly by which aquaporin in the luminal membrane?  
A. AQP-1  
B. AQP-2  
C. AQP-3  
D. AQP-4
23. The major humoral regulator of the concentration of sodium in plasma is:  
A. aldosterone  
B. vasopressin (ADH)  
C. renin  
D. angiotensin II
24. Plasma potassium concentration is chiefly regulated by:  
A. aldosterone  
B. vasopressin (ADH)  
C. renin  
D. ANP
25. In the presence of vasopressin, most of the water filtered by the kidneys is reabsorbed in the:  
A. proximal tubule  
B. thin descending limb  
C. thick ascending limb  
D. collecting ducts
26. In the absence of vasopressin, most of the filtered water is reabsorbed in the:  
A. PT  
B. loop of Henle  
C. DT  
D. collecting ducts
27. Potassium secretion occurs mainly in:  
A. PT  
B. early distal tubule  
C. late distal tubule  
D. collecting ducts
28. In a euvolemic normotensive healthy adult with, ADH secretion is **most likely** to be stimulated by:  
A. intake of 500 ml water  
B. intake of 30 ml of 10% ethanol  
C. 2.5 mg of enalapril  
D. ingestion of a 400 meal consisting exclusively of simple sugars
29. Which one of the following inhibits ADH secretion?  
A. Hyperosmolality  
B. Exercise  
C. Angiotensin II  
D. Ethanol
30. Water deprivation fails to produce an increase in urine osmolality in:  
A. neurogenic diabetes insipidus  
B. nephrogenic diabetes insipidus
31. The tubular fluid at the end of the PT is \_\_\_\_\_ with respect to plasma  
A. isotonic  
B. hypotonic  
C. hypertonic
32. Which is the 'concentrating segment' of the nephron?  
A. Descending limb of loop of Henle  
B. Thin ascending limb of loop of Henle  
C. Thick ascending limb of loop of Henle  
D. Collecting ducts
33. Which portion of the tubule is **least permeable** to water?  
A. Proximal tubule  
B. Thin descending limb of LOH  
C. Thick ascending limb of LOH  
D. Cortical collecting duct
34. The 'diluting segment' of the nephron is:  
A. proximal tubule  
B. descending limb of loop of Henle  
C. ascending limb of loop of Henle  
D. cortical collecting duct

35. 'Free water' is formed in the:
- descending limb of loop of Henle
  - thin ascending limb of loop of Henle
  - thick ascending limb of loop of Henle
  - collecting duct
36. Na-K-2Cl transporter in the apical membrane of the thick ascending limb of the loop of Henle is an example of:
- primary active transport
  - secondary active transport
  - passive transport
  - countertransport
37. What fraction of filtered water is reabsorbed in the loop of Henle?
- 15%
  - 25%
  - 35%
  - 5%
38. What fraction of filtered Na is reabsorbed in the loop of Henle?
- 15%
  - 25%
  - 35%
  - 5%
39. The fluid entering the early distal tubule is (*choose the best answer*):
- always isotonic
  - always hypotonic
  - isotonic / hypotonic but not hypertonic
  - isotonic / hypertonic but not hypotonic
  - hypertonic when urine is concentrated
  - hypotonic when urine is dilute
40. Which of the following transport mechanisms in the macula densa allows it to sense Na and Cl concentrations in the tubular fluid that flows past this segment?
- Apical chloride channels
  - 1Na-1K-2Cl transporter (NKCC2)
  - Na-Cl cotransporter
  - Na-H exchanger
  - ROMK exchanger
41. Loop diuretics (example, furosemide) inhibit:
- 1Na-1K-2Cl transport in the TAL
  - Na reabsorption in the collecting duct
  - aquaporins in PT
  - carbonic anhydrase in PT
42. Vasa recta receive blood from the:
- afferent arteriole of cortical nephron
  - afferent arteriole of juxtamedullary nephron
  - efferent arteriole of cortical nephron
  - efferent arteriole of juxtamedullary nephron
43. Hypertonicity in the inner medulla is maintained because:
- vasa recta receive 50% of renal blood flow
  - of the low blood flow rate through vasa recta
  - NaCl passively moves into the medullary interstitium from the thin ascending limb
44. The system for the formation of concentrated or dilute urine does **not** include the:
- proximal convoluted tubule
  - loop of Henle
  - collecting ducts
  - vasa recta
  - medullary interstitium
45. 'Free water' formation in the nephron is essential for production of:
- dilute urine
  - concentrated urine
46. What contributes most to the osmolality of the medullary interstitium? Urea / NaCl?
47. Which segment of the nephron is permeable to urea?
- Descending limb of loop of Henle
  - Thin ascending limb of loop of Henle
  - Thick ascending limb of loop of Henle
48. The principal regulator of plasma osmolality is:
- plasma [Na]
  - antidiuretic hormone
  - aldosterone
  - angiotensin II
49. Which is the fundamental mechanism generating hypertonicity in the medullary interstitium?
- Active transport of NaCl in TAL
  - ADH action in the collecting ducts

- C. Passive recirculation of NaCl in MI
- D. Urea permeability of collecting ducts

### Acid-Base Physiology

50. In the nephron, the highest amount of H ions is secreted into tubular lumen in the:

- A. PCT
- B. DCT
- C. collecting ducts
- D. loop of Henle

51. The principal site of ammoniagenesis in the nephron is:

- A. PT
- B. Loop of Henle
- C. Early distal tubule
- D. Late distal tubule
- E. Outer medullary collecting duct

52. The principal mechanism of H<sup>+</sup> secretion in the proximal convoluted tubule is:

- A. Na-H exchange
- B. H-ATPase
- C. H-K ATPase
- D. H-Ca exchange

53. The principal mechanism for acid secretion by type A intercalated cells in the nephron is:

- A. H-ATPase
- B. Na-H exchanger
- C. H-Ca exchanger
- D. H-K ATPase

54. Normally, most of the filtered HCO<sub>3</sub> is reabsorbed from:

- A. PT
- B. distal tubule
- C. cortical collecting duct
- D. loop of Henle

55. The most abundant buffer in proximal tubular fluid is:

- A. bicarbonate
- B. phosphate
- C. ammonia

56. The principle site of acidification of tubular fluid is:

- A. proximal convoluted tubule

- B. loop of Henle
- C. the *aldosterone sensitive distal nephron*
- D. urinary bladder

57. Normally, in urine, most of the H<sup>+</sup> is tied up with:

- A. bicarbonate
- B. phosphate
- C. ammonia

58. Normally, most of the *titratable acidity* of urine is attributable to acid buffered by:

- A. bicarbonate
- B. phosphate
- C. ammonia
- D. uric acid
- E. creatinine

59. Which of the following statements is / are **correct** regarding the role of kidney in acid-base balance?

- A. The kidney can eliminate CO<sub>2</sub> as free H
- B. Acid secretion is a passive process
- C. Most acid secreted in the PCT acidifies urine
- D. Acid secretion in collecting ducts is facilitated by aldosterone

60. Type B intercalated cells in the collecting duct are concerned with:

- A. secretion of protons
- B. controlled bicarbonate secretion
- C. ADH-stimulated water reabsorption
- D. Na reabsorption

61. The [H<sup>+</sup>] of arterial plasma is normally about:

- A. 20 nmol/L
- B. 30 nmol/L
- C. 40 nmol/L
- D. 50 nmol/L

62. Urinary ratio of NH<sub>4</sub><sup>+</sup> to titratable acid ranges from:

- A. 1-2.5
- B. 2-5
- C. 0.1-0.5
- D. 5-7

63. The Henderson-Hasselbalch equation states that when a buffer acid is half dissociated the pH of the solution is equal to:

- A. pKa
- B. 7.0
- C. 2 pKa
- D. 0.5 pKa

64. A buffer is most effective when the pH of the solution is close to:

- a. pKa
- b. 2 pKa
- c. 0.5 pKa

65. Quantitatively, the most important buffer of carbonic acid in blood is:

- A. bicarbonate
- B. plasma protein
- C. phosphate
- D. hemoglobin

66. HCO<sub>3</sub> cannot buffer protons formed from:

- A. lactic acid
- B. sulfuric acid
- C. carbonic acid

67. In a healthy human with an arterial plasma pH of 7.38, and normal levels of electrolytes, the *anion gap* reflects the plasma concentration of:

- A. HCO<sub>3</sub>
- B. chloride
- C. protein anions
- D. phosphates

68. The anion gap may be elevated in:

- A. metabolic acidosis
- B. metabolic alkalosis

**Answers: Renal Physiology**

1A	2B	3C	4B	5B
6ABC	7B	8B	9C	10A
11A	12B	13CD	14C	15D
16B	17A	18C	19AB	20CD
21B	22B	23B	24A	25A
26A	27D	28D	29D	30AB
31A	32A	33C	34C	35C
36B	37A	38B	39B	40B
41A	42D	43B	44A	45AB
46	47B	48B	49A	50A
51A	52A	53A	54A	55A
56C	57C	58B	59AD	60B
61	62	63	64	65
66	67	68	69	70

**All about ANG II:**

1T	2T	3F	4T	5F
6T	7F	8T	9T	10T
11T	12T	13T	14F	15T
16F				

**Answer Explanations:**

1-3. Clearance is the volume of plasma that is cleared of a substance per minute

Clearance of a substance X =  $U_X V / P_X$

$U_X$ : concentration of substance in urine

$P_X$ : concentration of substance in plasma

V: urine flow rate in ml/min

**Inulin clearance** gives the best estimate of GFR since it is neither reabsorbed nor secreted by the nephron; it is nontoxic, freely filtered and does not affect hemodynamics; however, estimation of inulin clearance is impractical. Endogenous **creatinine clearance** is slightly higher than inulin clearance since some creatinine is also secreted by the tubules. Despite this shortcoming, creatinine clearance remains the most common clinical method to estimate GFR. These days, we calculate creatinine clearance inputting age, sex, ethnicity, and serum creatinine, deploying regression equations such as the MDRD equation or the Cockcroft Gault equation. This calculator is available online at [www.nephron.com](http://www.nephron.com)

Phenol red has been used to estimate renal plasma flow. Tubular cells secrete it.

12. Given PAH clearance = 100 ml/min

Effective renal plasma flow (ERPF) = 100 ml/min.

Renal blood flow (RBF) =  $RPF \times (100 / 100 - Hct)$ . In this case PCV = 20; thus RBF = 125 ml/min.

True renal plasma flow actually equals ERPF/PAH extraction ratio. If this problem noted that the PAH extraction ratio was 0.9, then RBF would have been 138 ml/min.

13-14. Renal autoregulation defends changes in GFR and renal blood flow in the face of changes in renal perfusion pressure. As the name suggests, it is essentially independent of extrinsic innervation, although it is influenced by renal

sympathetic activity. The effect of intense stimulation of the renal sympathetic nerves is to reduce GFR.

Renal autoregulation of GFR may be overwhelmed when mean arterial pressure falls below 70 mm Hg. The lower limit of this autoregulatory change depends on an individual's typical resting mean arterial pressure.

When MAP falls rapidly, the reflex increase in sympathetic outflow to the kidneys causes afferent arteriolar constriction, decreases GFR and RPF and acute renal failure may ensue.

15. Synthesis and secretion of renin by juxtaglomerular cells is regulated by renal blood flow as well as by sympathetic innervation of JG cells.

16. The renin-angiotensin-aldosterone axis is a salt and water conserving and blood pressure raising system that is set in motion by stimuli such as hypovolemia, hypotension, a decrease in renal blood flow, and a decrease in GFR.

Ang II stimulates the release of ADH by an action on the subfornical organ (SFO) and the organum vasculosum of lamina terminalis (OVLT). It stimulates Na reabsorption, and proton secretion in the PCT. The glomerular efferent arterioles are more susceptible to the constrictor effects of angiotensin II compared to afferent arterioles. Angiotensin III has only 40% of the pressor activity of angiotensin II but it has 100% aldosterone stimulating activity. There is evidence that there are enzymes other than ACE that convert angiotensin I to angiotensin II although their quantitative importance is not established.

18. Filtered load = plasma [glucose] × GFR  
Amount of glucose filtered per minute = 500 mg  
T<sub>max</sub> for glucose is given to be 350 mg/min  
Thus, glucose excretion rate  
= filtered load – T<sub>max</sub> for glucose  
= 500 – 350 = 150 mg/min.

22. Rapid diffusion of water across cells depends upon the presence of water channels called aquaporins. There are several types of aquaporins.

Vasopressin mediates its antidiuretic effect by increasing the number of AQP-2 channels in the luminal membrane of collecting duct epithelial cells.

23. Changes in water excretion are a commoner cause of changes in plasma Na concentration rather than changes in Na excretion. ADH, being the hormone that regulates water excretion, is an important determinant of plasma Na concentration and osmolality. For example, diabetes insipidus, which is caused by ADH deficiency, is characterized by excretion of large volumes of dilute urine, and plasma [Na] increases.

24. Aldosterone is the hormone regulating secretion of potassium in the collecting ducts, and hyperaldosteronism is typically associated with hypokalemia. However, some patients with primary hyperaldosteronism are normokalemic.

25. 60-70% of the filtered water is reabsorbed in the proximal tubule. This does not depend upon vasopressin. Water reabsorption in the collecting ducts requires vasopressin facilitated aquaporin 2 molecules on the luminal membrane of collecting duct epithelial cells. When vasopressin is absent, 24-hr urine volume may increase to as high as 12% of filtered water load, about 22 liters for a GFR of 180 liters per day.

30. Normally, water deprivation (for say 7 hr) produces a significant increase in ADH secretion. Consequently, urine becomes more concentrated and its osmolality exceeds 700 mOsm/kg H<sub>2</sub>O. In neurogenic diabetes insipidus, urine does not become concentrated because of a deficiency of ADH. In nephrogenic diabetes insipidus, urine does not become concentrated because the kidneys do not respond to ADH. This is usually due to a defect in V<sub>2</sub> receptors or ADH responsive aquaporins (AQP-2) in the collecting ducts. After administration of a vasopressin analog, the osmolality of urine increases significantly in neurogenic diabetes insipidus whereas urine remains dilute in nephrogenic diabetes insipidus.

32. Luminal fluid becomes more and more concentrated in the thin descending limb because

this portion of the nephron is relatively impermeable to solute and freely permeable to water. Water exits the descending limb into the hypertonic medullary interstitium. Thus osmolality of tubular fluid is greatest at the tip of the loops of Henle.

34. The ascending limb of the loop of Henle is impermeable to water and is the diluting segment of the nephron. The fluid emerging from the ascending limb of the loop of Henle is always hypotonic whether the urine excreted is dilute or concentrated.

41. The thick ascending limb of the loop of Henle is impermeable to water. It is permeable only to solute. 25% of the filtered Na is recovered in the loop of Henle. That is why loop diuretics are very efficacious. They inhibit the 1Na-1K-2Cl symporter and increase solute delivery to distal portions of the nephron. The unabsorbed solutes in the tubular lumen retain their water equivalent and a considerable diuresis results because the reabsorptive capacity of the collecting duct is overwhelmed.

46. Both NaCl and urea contribute substantially (and to a similar extent) to the tonicity of the medullary interstitium.

56. Tubular fluid is mainly acidified in the distal portions of nephron (distal convoluted tubule and collecting ducts). Since bicarbonate has been completely reabsorbed by the time fluid reaches this portion of the tubule, secreted H acidifies the tubular fluid. The concentration of phosphate increases however and it buffers some of the secreted H. This allows more H to be secreted without acidifying the urine beneath a limiting pH.

56. The highest amount of acid is secreted in the proximal tubule; however, this contributes mainly to reabsorption of filtered bicarbonate rather than acidification of tubular fluid. In the collecting ducts, the protons secreted acidify tubular fluid.  
57. Normally, the ratio of NH<sub>4</sub> to titratable acid in urine is 1 – 2.5.

58. The amount of alkali required to titrate acidic urine to the pH of arterial plasma is called titratable acidity; normally, most of this is due to protons buffered by phosphate. However, in patients with chronic renal failure, protons buffered by creatinine and uric acid constitute about 20% of titratable acid.

The ammonia-ammonium buffer base system has a pK of 9.0. Thus, at a pH of 7, the ratio of NH<sub>3</sub> to NH<sub>4</sub> is 1: 100, and it does not contribute to titratable acidity. To calculate total acid excretion in the urine, titratable acidity and urinary NH<sub>4</sub> concentrations should be summed.

60. Type A intercalated cells secrete protons (and conserve bicarbonate); acid-secretion by intercalated cells is stimulated by aldosterone. Proton secretion is also affected by transepithelial voltage; a lumen negative transepithelial voltage favors secretion of protons and potassium ions in the collecting duct. Type B intercalated cells have been observed in the context of metabolic alkalosis. They express pendrin, a Cl-HCO<sub>3</sub> exchanger, on the luminal membrane, and secrete bicarbonate in exchange for luminal chloride.

61-70. See *Supplement on acid-base physiology* below.

\*\*\*\*\*

***Supplement on acid-base physiology***

pH = - log [H] in moles/liter  
Suppose [H] = 100 nM, pH = - log [10<sup>-7</sup>]  
= - 7 [-1] = 7

pH	Hydrogen ion concentration corresponding to this pH
7	100 nM
6	1000 nM
5	10000 nM
4	100000 nM

H ion concentration is expressed in logarithmic as well as linear scale. It is expressed on a log scale so that the values become convenient to handle (because hydrogen ion concentration is of the order of nanomoles). However, it must be noted that a unit change in pH say from 6 to 7 represents a ten-fold change in H ion concentration. The table above is meant to emphasize this.

**pH of various body fluids:**

pH	[H] concentration in nanomoles per liter	Compartment / condition
1	100 million	Gastric juice
6.9	120	ICF (muscle); arterial plasma in life threatening acidosis
7	100	Pure water
7.1	80	Inside RBC
7.33	50	Cerebrospinal fluid
7.4	40	Normal arterial plasma
7.7	20	Severe alkalosis
8	10	Pancreatic juice

The Henderson-Hasselbalch equation reads thus:

$$pH = pK_a + \log [\text{salt}] / [\text{acid}]$$

For example, consider the H<sub>2</sub>CO<sub>3</sub> –HCO<sub>3</sub> system

The acid is H<sub>2</sub>CO<sub>3</sub>

The conjugate base is HCO<sub>3</sub><sup>-</sup>



$$pH = pK + \log [HCO_3^-] / [H_2CO_3]$$

If buffer acid were half dissociated, i.e., the concentration of acid and the conjugate base are equal, then, [salt] = [acid], and the pH would be equal to pK. A buffer system works best when the pH of the solution is close to the pK value.

**Buffers in 1 L arterial plasma:**

Buffer	Concentration in plasma (mM)
HCO <sub>3</sub> <sup>-</sup>	24
Hb	9
Protein	15
Total buffer base	48

**What does HCO<sub>3</sub> in ECF buffer?**

HCO<sub>3</sub> in ECF combines with H liberated by the formation of fixed acids (lactic acid, ketoacids).

Lactic acid → Lactate + H

H is buffered by HCO<sub>3</sub> to form H<sub>2</sub>CO<sub>3</sub>

H<sub>2</sub>CO<sub>3</sub> is unstable.

It dissociates to form CO<sub>2</sub> + H<sub>2</sub>O.

CO<sub>2</sub> is volatile. The lungs excrete CO<sub>2</sub>.

The hydrogen ions formed from lactic acid are eliminated as carbon dioxide.

In contrast, bicarbonate cannot buffer protons formed from carbonic acid (see the reaction sequence below).



Thus, the protons formed from carbondioxide can be buffered only by hemoglobin or plasma proteins.

The Henderson-Hasselbalch equation may be modified to read thus:

$$[H^+] \text{ in nM} = \frac{24 \times PaCO_2 \text{ (mm Hg)}}{[HCO_3^-] \text{ mM}}$$

This is the **modified Henderson's equation**.

Substitute normal values of PaCO<sub>2</sub> and plasma HCO<sub>3</sub> and you can easily remember the equation.

Normally, [H<sup>+</sup>] nmol/L = 40 nmol. This is on the left side of the equation.

$$40 = 24 \text{ (a constant)} \times 40 / 24$$

On the right side, 40 = normal PaCO<sub>2</sub> and 24 = normal plasma HCO<sub>3</sub>. The constant 24 has been derived taking into consideration the solubility coefficient of carbon dioxide at body temperature, so that PaCO<sub>2</sub> can be substituted in the equation instead of carbonic acid.

**Anion gap** is calculated as:

$$\{[Na^+] + [K^+]\} - \{[Cl^-] + [HCO_3^-]\}$$

All of them are expressed in mmol/L, and the anion gap normally varies from 8-16 mmol/L

Some authors omit [K<sup>+</sup>] from the above equation. That is OK, but if this is done, then the normal value will be lower by about 4 mmol/L.

*Here is an easy way to understand the anion gap*

- In plasma, the sum of charges of positive ions is equal to the sum of negative charges
- Plasma is thus electroneutral
- Some ions in plasma are routinely measured (measured ions)
- Some are not (unmeasured ions)
- What are the major cations in plasma?

- They are Na and K
- What are the major anions in plasma?
- They are chloride and HCO<sub>3</sub>
- Measured cations are Na and K
- Measured anions are Cl and HCO<sub>3</sub>
- Unmeasured cations are Ca and Mg
- Normally, the unmeasured anions are phosphate, sulfate and protein anions.
- The concentration of unmeasured cations is small that it can be ignored
- In summary, [measured cations] – [measured anions] = [unmeasured anions]

$$\text{Anion gap} = \{[\text{Na}] + [\text{K}]\} - \{[\text{Cl}] + [\text{HCO}_3]\} = [\text{unmeasured anions}]$$

**When does the anion gap increase and why?**

In metabolic acidosis (for example, due to lactic acidosis), pH decreases. The H ions are buffered by HCO<sub>3</sub>. The concentration of lactate (an unmeasured anion) increases. Therefore, anion gap increases. The increase in anion gap reflects an increase in the concentration of one or more unmeasured anions in plasma. This happens in metabolic acidosis. The anion gap may also be increased in metabolic alkalosis; one can plug some chloride, Na and bicarbonate values in and try. However, in practice, the anion gap is used mainly in the differential diagnosis of metabolic acidosis.

**Examples of high anion gap metabolic acidoses and the unmeasured anions:**

Cause of metabolic acidosis	Unmeasured anion(s)
Lactic acidosis	Lactate
Ethylene glycol poisoning	Oxalate
Ketoacidosis	Acetoacetate, beta-hydroxybutyrate
Acute renal failure; end-stage renal disease	Multiple anions include phosphate

**Disorders of Micturition – Summary**

**Definition for Urinary Frequency:** > 8 voids per day (Cecil 24e, pp. 111)

**Urinary incontinence** – inability to voluntarily restrain bladder emptying;

**Stress Incontinence (SI)** – a significant increase in intra-abdominal pressure (called ‘stress’ here) triggers the emptying.

**Urge Incontinence (UI)** – the urge to micturate is perceived, but one is unable to voluntarily inhibit it at bladder volumes an age-matched normal individual can hold.

Some individuals have both SI and UI.

A weakness of the pelvic floor (in females) and the external urethral sphincter (in both males and females) due to any cause (example, denervation) is a basic abnormality underlying both stress and urge incontinence.

*Urge incontinence* is a bit more problematic because “**detrusor instability**” (sometimes known as an **over-reactive bladder** is believed to additionally contribute (Cecil 24e, pp. 110). The over-reactive bladder is often ‘idiopathic’ but may be due to an upper motor neuron type lesion (see under Chronic Spinal Cord Injury below). Note however that an over-reactive bladder is not necessarily one with good contractility; i.e. it may not empty completely. Detrusor hyperactivity may also be associated with a bladder calculus, urethral obstruction.

**Overflow incontinence** – A distended bladder contracts and empties in an individual with no voluntary control of micturition (see below).

**Acute phase of spinal cord injury (spinal shock):**

There is abrupt loss of tonic facilitation of parasympathetic motor neurons from supraspinal influences. **Urinary retention** is due to lack of neural drive for detrusor contraction but is additionally likely to uninhibited contraction of the internal urethral sphincter; the bladder distends (overfills) and empties reflexly (at which the point the IUS relaxes), and no voluntary control is present (“**overflow incontinence**”); nonetheless the contractions of the detrusor are not as forceful and emptying may be incomplete; with risk for UTI. Bladder catheterization is necessary.

### ***Chronic spinal cord injury***

Spinal reflexes below the level of the transection are “**released**” from the inhibitory influences of supraspinal centers.

The basic sacral reflex arc for micturition becomes hyperactive; i.e., the threshold for the micturition reflex is a lower bladder volume (**hyperactive voiding reflex**). Marked by bladder wall hypertrophy; reduced bladder capacity; increased urinary frequency [**collectively called Spastic Neurogenic Bladder**]. Furthermore, neural influences on detrusor and the sphincter may not be coordinated in the absence of supraspinal influences (detrusor-sphincter dys-synergia).

**Deafferentation:** Sacral afferent roots sectioned experimentally; equivalent – tabes dorsalis affecting sacral sensory roots. Here, the brain is slow to perceive bladder filling – therefore, the bladder in the long run becomes **thin walled, distended; it becomes hypotonic** because of loss of afferents in the sacral micturition reflex arc. Contractions of detrusor that occur are an intrinsic response of smooth muscle to stretch.

**Denervation (deafferentation + injury to efferent nerves innervating the bladder)** as with cauda equine tumors compressing on filum terminale. In this case, information about bladder distension does not promptly reach the CNS. Neither is the efferent nerve supply intact. Thus, the bladder is effectively “decentralized”

The bladder becomes flaccid (**flaccid, areflexic bladder**). The muscle becomes active gradually with contraction waves expelling dribbles of urine out of the urethra. Since the spinal reflex arc itself is interrupted, incontinence of the ‘overflow type’ occurs here.

**Lesion of the parasagittal medial frontal micturition center**, as can happen with parasagittal meningiomas, hydrocephalus, or with a stroke of the frontal cortex.

The **medial frontal micturition centers** in the cortex are presumably the origins of descending pathways that activates the voiding reflex.

With a lesion in this region, the voiding reflex per se is normal, but there is no voluntary control. The individual may or may not be aware of the incontinence; commonly called “**frontal-type incontinence**”

The term “Neurogenic bladder” is a nonspecific term – it may refer to flaccid bladder, or a hyperreflexic bladder, and therefore it should be used only with further qualification.

**References:** Ganong’s Review of Medical Physiology (2005); Cecil’s Textbook of Medicine 24e (Ch 25 Incontinence)

\*\*\*\*\*

## 11. Critical Care Physiology

**Instructions: In each of the following questions, select all correct answers. Each question may have one or more correct responses or none at all.**

1. An 8-year-old girl is being treated with mechanical ventilation and other disease-specific therapy for acute respiratory distress syndrome. She is being administered 60% oxygen. Her PaCO<sub>2</sub> and PaO<sub>2</sub> were found to be 20 and 100 mm Hg respectively. Which of the following statements is **correct**?

- A. Gas exchange in the lungs is normal
- B. There is a defect in pulmonary gas exchange
- C. She has alkalosis

2. An eight-year old boy was put on a ventilator after he developed acute respiratory failure. FiO<sub>2</sub> was 60%, and PaCO<sub>2</sub> was found to be 60 mm Hg. What is the expected O<sub>2</sub> tension of arterial blood?

- A. 340 mm Hg
- B. 290 mm Hg
- C. 240 mm Hg
- D. 190 mm Hg

3. During mechanical ventilation, the addition of positive end-expiratory pressure (PEEP):

- A. is helpful in the management of ARDS
- B. may decrease cardiac output
- C. is associated with increased ADH secretion
- D. allows FiO<sub>2</sub> to be reduced

4. A 60-yr old man is being mechanically ventilated after he developed respiratory arrest. The ventilator settings are as follows: V<sub>T</sub> = 500 ml; respiratory rate = 12/min; FiO<sub>2</sub> = 60%; and PEEP = 5 cm H<sub>2</sub>O. His arterial [H<sup>+</sup>] is 20 nM; arterial plasma HCO<sub>3</sub> is 24 mM; and PaO<sub>2</sub> is 200 mm Hg. Which of the following statements is **correct**?

- A. FiO<sub>2</sub> will need to be increased
- B. Intracranial tension is elevated
- C. Minute ventilation needs to be decreased
- D. PEEP could be increased

5. A 70-kg man is breathing through a tube that has a radius of 5 mm and a length of 1 m. The dead space is approximately

- A. 150 ml
- B. 190 ml
- C. 230 ml
- D. 270 ml

6. An (acute) increase in intracranial tension does **not** occur as a result of:

- A. breath holding in full inspiration
- B. ventilation with 20 cm H<sub>2</sub>O PEEP
- C. Valsalva maneuver
- D. decrease in PaCO<sub>2</sub>

7. A 60 yr old man is on mechanical ventilation for management of acute pulmonary edema and renal function is normal.

Results of arterial blood gas analysis are: pH = 7.5, [HCO<sub>3</sub>] = 24 mmol/L; PaCO<sub>2</sub> = 30 mm Hg, PaO<sub>2</sub> = 50 mm Hg. O<sub>2</sub> saturation of Hb is 84%.

Ventilator settings are as follows: tidal volume = 1000 ml, respiratory frequency = 12 breaths per min, and FiO<sub>2</sub>=1.

Which of the following statements is **correct** with regard to management?

- A. Minute ventilation should be increased
- B. PEEP should be instituted
- C. Calcium gluconate must be given
- D. IV infusion of 20% mannitol is required

8. Does any **one** of the following physiological parameters **in itself** indicate that arterial blood oxygenation in a critically ill patient is satisfactory? If so, which one?

- A. (A-a) O<sub>2</sub> gradient = 10 mm Hg
- B. PaO<sub>2</sub> = 95 mm Hg
- C. O<sub>2</sub> saturation of Hb > 90%
- D. Blood [Hb] = 12 g/dL

9. In ventilated patients, oxygenation of arterial blood should be assessed by monitoring:

- A. (A-a) O<sub>2</sub> gradient
- B. PaO<sub>2</sub>
- C. blood hemoglobin concentration
- D. O<sub>2</sub> saturation of Hb

10. The organ that excretes the greatest amount of acid is:

- A. lungs

- B. kidneys
- C. skin
- D. GIT

11. The most common acid-base disturbance in patients on mechanical ventilators is:

- A. metabolic acidosis
- B. metabolic alkalosis
- C. respiratory acidosis
- D. respiratory alkalosis

12. Sodium bicarbonate should **not** be administered to a patient with:

- A. arterial blood pH of 7.1
- B. serum  $[HCO_3^-]$  of 12 mM
- C. a  $PaO_2$  of 50 mm Hg
- D. a  $PaCO_2$  of 68 mm Hg

13. Hyperbaric oxygen therapy is useful in the management of (*tick all that apply*):

- A. cyanide poisoning
- B. carbon monoxide poisoning
- C. diabetic leg ulcers
- D. gas gangrene
- E. decompression sickness

14. Which of the following is **not** required to calculate total dead space using Bohr's equation?

- A. End-tidal  $CO_2$
- B.  $PaO_2$
- C.  $PaCO_2$
- D. Tidal volume

**Answers: Critical Care Physiology**

1B	2A	3all	4CD	5C
6D	7B	8 None	9 All	10A
11D	12D	13 All	14B	

**Answer Explanations:**

1. The approach:

- What is the  $P_{AO_2}$ ?
- What is the expected  $PaO_2$ ?
- Is there a difference between expected  $PaO_2$  and actual  $PaO_2$ ?
- Alveolar–arterial  $O_2$  gradient does not normally exceed 10 mm Hg

**Solution:** Using the alveolar gas equation, we get:

Expected  $P_{AO_2} = 400$  mm Hg;

Expected  $PaO_2 = 390$  mm Hg;

Actual  $PaO_2 = 100$  mm Hg;

(A–a)  $O_2$  difference = 290 mm Hg

This represents a considerable defect in gas exchange. In fact, this is the reason why this girl was ventilated in the first place; acute respiratory distress syndrome is characterized by hypoxemia and normocapnia or hypocapnia (type I respiratory failure). Regarding option C, it is impossible to tell whether she has alkalosis because plasma pH is not known.

2. Use the alveolar gas equation and first determine the oxygen tension of alveolar gas  $P_{AO_2}$ .

$$P_{AO_2} = [(P_B - P_{H_2O}) \times F_{iO_2}] - [(P_A CO_2) / R].$$

Here  $P_B = 760$  mm Hg,  $P_{H_2O} = 47$  mm Hg,  $F_{iO_2} = 0.6$ ,  $R = 0.8$ ].

Since  $PaCO_2 = 60$  mm Hg,  $PACO_2$  will be about the same, since  $CO_2$  rapidly equilibrates across the alveolar capillaries. It is much more soluble than oxygen.

Substituting, we get, alveolar  $PO_2 = 350$  mm Hg. Normally, the (A-a)  $O_2$  gradient is less than 10 mm Hg. So we would expect arterial  $PaO_2$  to be about 340 mm Hg.

Thus, it is clear that alveolar  $PO_2$  is much less than  $PO_2$  of inspired air. This is because it gets saturated with water vapor and then diluted with carbon dioxide in the alveolar gas.

The reason for subtracting  $PACO_2 / R$  is that alveolar  $PO_2$  gets diluted by alveolar  $CO_2$  which is equal to arterial  $CO_2$  (since  $CO_2$  is highly soluble). This is divided by R, the respiratory exchange ratio; i.e., the ratio of the volumes of  $CO_2$  to  $O_2$  exchanged across the lungs per unit time. R is for practical purposes assumed to be 0.8; i.e., 200 ml  $CO_2$  / 250 ml  $O_2$ . Let us say an equal volume of  $CO_2$  and  $O_2$  were exchanged; then the denominator would be 1. Since only a lesser volume of  $CO_2$  is exchanged (i.e. 200 ml) and more  $O_2$  is taken up (i.e. 250 ml), alveolar oxygen gets even more diluted by  $CO_2$ . This is given by R; i.e.  $V_{CO_2} / V_{O_2}$ .

3. In patients who are on mechanical ventilators, intrathoracic pressure (ITP) becomes positive during inspiration, and when PEEP is added,

average intrathoracic pressure becomes even more positive. The beneficial effect of PEEP is believed to stem from the recruitment of previously atelectatic alveoli and consequently an increase in the surface area and time available for oxygenation; furthermore, it keeps fluid from entering the pulmonary interstitium. However, the hemodynamic effect of raised ITP would be to reduce venous return and consequently cardiac output. Note that it is possible that the beneficial effect of PEEP on oxygenation might be offset by a low cardiac output. To prevent this from happening, fluids must be administered, and cardiac output has to be monitored.

One or more of the following means could improve oxygenation:

- Increasing minute ventilation but this has the effect of removing CO<sub>2</sub>; further, there is a risk of 'volutrauma' with higher tidal volumes.
- Increasing FiO<sub>2</sub> but there is a limit to the time for which oxygen rich gas could be administered; i.e., there is a risk of lung damage due to high FiO<sub>2</sub>.
- Administering PEEP; however, this comes with two risks: one, of barotrauma due to overdistended lung zones; and two, reduction in cardiac output due to a decrease in venous return. The risk of barotrauma and consequent pneumothorax is significant because even in patients with lung disease, not all lung zones are affected, and some might be even normal. Lung zones that are normal will be overdistended by the applied PEEP and may rupture.

4.  $[H^+] = 24 [PaCO_2] / [HCO_3^-]$   
 Here  $[H^+] = 20 \text{ nM}$ , and  $[HCO_3^-] = 24 \text{ mM}$ , so  $PaCO_2 = 20 \text{ mm Hg}$

An increase in PaCO<sub>2</sub> raises intracranial tension (ICT) by causing cerebral vasodilation. In this case, ICT cannot be high since  $[H^+]$  is quite low; i.e. it is only 20 nmol/L (normal  $[H^+]$  of arterial plasma is 40 nmol/L). Also  $[HCO_3^-]$  is normal, so the patient has respiratory alkalosis. This is because of hyperventilation.

Use the alveolar gas equation and determine his PaO<sub>2</sub>.

$P_{A}O_2 = (760 - 47) 0.6 - (20/0.8) = 400 \text{ mm Hg}$   
 His PaO<sub>2</sub> is expected to be at least 380 mm Hg whereas his arterial PaO<sub>2</sub> is only 200 mm Hg. The (A-a) O<sub>2</sub> gradient = 180 mm Hg is quite high and reflects poor gas exchange (a right-to-left shunt).

Increasing FiO<sub>2</sub> alone does not ameliorate hypoxemia due to a shunt because the oxygen administered would not equilibrate with the shunt. In this case, the underlying disease process has to be addressed.

Increasing PEEP in this patient would certainly improve oxygenation if the poor gas exchange, manifest as high (A- a) DO<sub>2</sub>, were due to a generalized process such as ARDS or cardiogenic pulmonary edema. If that happens, FiO<sub>2</sub> could then be reduced. However, cardiac output has to be monitored.

In this patient, it is however important to reduce minute ventilation since it will be difficult to wean him at a later stage if his PaCO<sub>2</sub> is as low as 20 mm Hg. CO<sub>2</sub> is the major stimulus for respiration. If the PaCO<sub>2</sub> is too low, the drive for spontaneous respiration itself is removed.

In ventilated patients, it is not uncommon to vary minute ventilation so that PaCO<sub>2</sub> is around 45 mm Hg (i.e. at the upper end of the normal range) though this represents a trade off from the possibility of better oxygenation. This is called *permissive hypercapnia*. This is usually accompanied by hypoxemia (also called *permissive hypoxemia*). This is an attempt to preserve the drive for spontaneous respiration. This makes it more likely that, as soon as the underlying disease process is fully addressed, the patient could be weaned to start breathing on his or her own.

5. Radius = 0.5 cm  
 Length = 1 m = 100 cm  
 Volume of the tube  
 $= \pi \times (\text{radius squared}) \times \text{length}$   
 $= (22/7) \times (0.5)^2 \times 100$   
 $= 80 \text{ ml}$

This adds to the normal anatomical dead space of about 150 ml (in a 70 kg man) to make it 230 ml.

6. PaCO<sub>2</sub> will gradually rise during breath holding and it will raise intracranial tension (ICT) by causing cerebral vasodilation. Intrathoracic pressure is increased during PEEP and Valsalva maneuver and this will reduce venous return from the skull and raise ICT. A decrease in PaCO<sub>2</sub> per se will produce cerebral vasoconstriction and this in itself cannot cause ICT to increase.

7. This patient, who has acute pulmonary edema, has arterial hypoxemia despite administration of 100% O<sub>2</sub>. The expected PaO<sub>2</sub> can be calculated to be about 650 mm Hg but his arterial PaO<sub>2</sub> is only 50 mm Hg. This represents a formidable defect in oxygen exchange. In this situation, institution of PEEP would improve oxygenation by inflating atelectatic alveoli. Secondly, PEEP would reduce the gradient for filtration of fluid across the pulmonary capillaries. FiO<sub>2</sub> can subsequently be tailored down to an acceptable value; this is important since prolonged administration of high concentrations of O<sub>2</sub> (especially > 24 h) may result in oxygen toxicity. This patient has respiratory alkalosis, a consequence of hyperventilation. Note that CO<sub>2</sub> elimination is hardly of any concern even in the face of severe impairment of oxygen exchange. This is because CO<sub>2</sub> is much more soluble. Patients with respiratory alkalosis may develop hypocalcemia but in this instance the alkalosis can be readily corrected by reducing minute ventilation. The patient also does not require mannitol since there is no evidence from the data provided that ICT is raised. In fact, PaCO<sub>2</sub> is lower than normal.

8. None of these parameters **taken alone** will give us this information.

To illustrate, consider the following situations:  
A (A-a) O<sub>2</sub> gradient of 10 mm Hg only tells us that diffusion capacity of the lungs for oxygen is normal.

*Case 1:* a healthy individual at high altitude

- D (Alveolar – arterial) O<sub>2</sub> gradient = 10 mm Hg
- His P<sub>A</sub>O<sub>2</sub> = 60 mm Hg
- His PaO<sub>2</sub> = 50 mm Hg
- Problem: moderate hypoxemia

- **Conclusion:** D (A-a) O<sub>2</sub> only tells us the efficiency of oxygen exchange

*Case 2:* An anemic patient with a PaO<sub>2</sub> of 95 mm Hg performing mild-moderate exercise

- PaO<sub>2</sub> = 95 mm Hg
- Hb = 7.5 g/dL
- Oxygen carrying capacity is reduced by half
- Significant exercise intolerance due to anemic hypoxia

*Case 3:* A patient who is on a ventilator and has a PaO<sub>2</sub> of 95 mm Hg

- Patient is given 60% oxygen
- His PaCO<sub>2</sub> is 40 mm Hg
- Then, expected PaO<sub>2</sub> is 400 mm Hg
- If actual PaO<sub>2</sub> is 95 mm Hg then, this represents a defect in gas exchange.

*Case 4:* A PaO<sub>2</sub> of 90 mm Hg may occur even in the absence of Hb!

*Case 5:* A person can have a blood [Hb] of 3 g/dL and yet the O<sub>2</sub> saturation of Hb may be > 90%;

The properties of Hb are such that it is 90% saturated with O<sub>2</sub> even if PaO<sub>2</sub> is only 60 mm Hg. While this is a safety characteristic, a decline in PaO<sub>2</sub> below 60 mm Hg is associated with a steady decline in O<sub>2</sub> saturation of Hb (please examine the oxygen dissociation curve for adult hemoglobin). Further, if O<sub>2</sub> saturation of Hb is 90% but blood Hb is only 3 g/dL, then he will definitely be hypoxemic!

*Case 6:* Neither does a blood [Hb] of 12 g/dL by itself guarantee adequate oxygenation.

An individual might have a blood [Hb] of 12 g/dL and still not be able to transport enough oxygen to the tissues if the hemoglobin itself is not pure. For example, with even small amounts of carboxy hemoglobin, the oxygen dissociation curve is shifted to the left. Simple methods of blood Hb estimation cannot distinguish between normal and abnormal hemoglobin derivatives.

9. All of these parameters should be monitored. Furthermore, one should know if hemoglobin itself is normal Hb A or not.

12. Injected  $\text{NaHCO}_3$  dissociates to give Na and  $\text{HCO}_3$ . The  $\text{HCO}_3$  buffers H ions in ECF and becomes  $\text{H}_2\text{CO}_3$

$\text{H}_2\text{CO}_3$  will dissociate to give  $\text{CO}_2$  and  $\text{H}_2\text{O}$ . Normally, the lungs eliminate  $\text{CO}_2$  readily. However, if the  $\text{PaCO}_2$  is already as high as 68 mm Hg, this means that minute ventilation is already inadequate and such a patient would require mechanical ventilation since he very likely has respiratory acidosis (type II respiratory failure). The administration of  $\text{NaHCO}_3$  in this instance will aggravate acidosis. So get the  $\text{CO}_2$  out down to a level that will make him breathe. *Intubate and ventilate!* Sodium bicarbonate is appropriate only for the management of metabolic acidosis – even in metabolic acidosis there are specific clinical guidelines for its use. It depends on what the cause of metabolic acidosis and if that is reversible, the pH and other factors.

13. The principle of hyperbaric oxygenation has been discussed in the chapter on pulmonary physiology. 100% oxygen is administered at pressures exceeding atmospheric (usually 2–3 atmospheres) for brief periods of time. This greatly increases arterial oxygen tension if pulmonary gas exchange is normal.

Hyperbaric oxygenation is generally resorted to only when all other means of increasing oxygen carrying capacity of arterial blood have failed.

High concentrations of oxygen might serve to displace cyanide from cytochrome oxidase. In carbon monoxide poisoning, high concentrations of oxygen help overcome competitive inhibition by carbon monoxide. Diabetic leg ulcers due to obliterative peripheral vascular disease might benefit from an increase in the content of dissolved oxygen content of blood. In gas gangrene, the causative organisms are anerobic and may be killed by high oxygen concentration. In decompression sickness, the rationale is to “recompress” as well as “oxygenate” and this is achieved by hyperbaric oxygenation, and of course, this is followed by slow decompression.

**14. Bohr’s equation for determining total dead space:**  $P_{\text{E}}\text{CO}_2 \times V_{\text{T}} = \text{PaCO}_2 (V_{\text{T}} - V_{\text{D}})$   
If  $P_{\text{E}}\text{CO}_2 = 28$  mm Hg,  $\text{PaCO}_2 = 40$  mm Hg, and  $V_{\text{T}} = 500$  ml, then, dead space = 150 ml

End-tidal carbondioxide is measured by capnometry. Note that  $\text{PaCO}_2$  represents gas equilibrated with perfused alveoli. If there is significant V/Q mismatch,  $\text{PaCO}_2$  will be higher than  $\text{P}_{\text{A}}\text{CO}_2$ .

$V_{\text{D}}$  is an index of dead space ventilation;  $V_{\text{D}}/V_{\text{T}}$  is used as yet another index of dead space ventilation.

\*\*\*\*\*

## SELF-SCORERS

### Self-Scorer 1: General and cellular basis of medical physiology

Select the single best answer unless otherwise instructed.

- 2 liters of Ringer's lactate is administered to a 12-year old boy with isotonic dehydration. What will be the change in ICF volume?
  - No change
  - Increases by 2 liters
  - Increase
  - Decreases by 0.5 liter
- Cell volume and pressure is mainly dependent upon activity of:
  - Na glucose cotransporter
  - Na-K pump
  - glucose transporter
  - Na-Ca exchanger
- Which of the following ions is not transported across the cell membrane by a primary active transport mechanism?
  - Na
  - Cl
  - K
  - Ca
- Which of the following substances can be used as a marker for the ECF compartment?
  - Nonmetabolizable sugars
  - Glucose
  - Radio-iodinated albumin
  - D<sub>2</sub>O
- Sodium-glucose cotransport in the intestine and kidneys is an example of:
  - primary active transport
  - secondary active transport
  - facilitated diffusion
  - passive transport
- Figures A and B given below depict the relationship between transport rates (in Y-axis, in arbitrary units) and concentration gradients (in X-axis, in arbitrary units) of two substances A and B respectively.

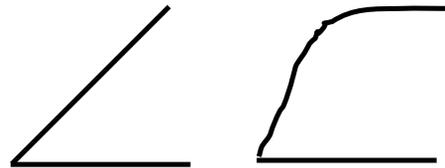


Fig A

Fig B

Which of the following statements is correct?

- B is transported by facilitated diffusion
  - Transport of B may be ATP dependent
  - There is a 'transport maximum' for A
  - Substance A would move in one direction only
- Which of the following mediates ion transport between the cytosols of adjacent epithelial cells?
    - Gap junctions
    - Tight junctions
    - Desmosomes
    - Hemidesmosomes
  - Which of the following transport processes is active? (select all correct answers)
    - Acidification of lysosomes
    - Actin-myosin cross bridge cycling
    - Exocytosis
    - Micropinocytosis
  - Which of the following transport processes is mediated by a carrier protein in the plasma membrane?
    - Glucose uptake through SGLT-1
    - Na influx through Na channels
    - Na-K ATPase
    - Water fluxes through aquaporins
  - The volume of RBC placed in a NaCl solution with an osmolality of 280 mOsm/Kg H<sub>2</sub>O is 100 femtoliters. What will be the steady state volume when they are placed in a NaCl solution with an osmolality of 350 mOsm/Kg H<sub>2</sub>O?
    - 120 fL
    - 80 fL
    - 50 fL
    - Data inadequate

### Answers to Self-Scorer 1: General and cellular basis of medical physiology

1C	2B	3B	4A	5B
----	----	----	----	----

6B	7A	8all	9AC	10B
----	----	------	-----	-----

**Notes:**

1. Ringer's lactate is an isoosmotic solution; however, as lactate is taken up by liver and other cells and metabolized, the infusion of it adds a definite amount of water to plasma that dilutes plasma in the steady state. This will, in turn, cause some water to enter cells. It is hard to tell what the actual increase in ICF volume will be but one would expect ICF volume to increase especially when a large volume of Ringer's lactate is administered.

2. By pumping 3 Na ions out of the cell for every 2 K ions pumped into the cell, the Na-K ATPase effectively removes one osmole (and the corresponding water equivalent) from the cell. Thus, inhibition of Na-K pump would cause cells to swell.

3. Chloride transport across the cell membrane occurs by secondary active transport mechanisms or diffusion but not by a primary active transport mechanism.

4. Examples of substances that distribute exclusively in the ECF include inulin, mannitol, and sucrose. Isotonic solutions of inulin, mannitol and sucrose can all be used to determine ECF volume. Radioiodinated albumin may be used for estimating plasma volume.

5. The complete absorption of glucose from the intestinal lumen (against a concentration gradient) is driven by the electrochemical gradient of sodium. This is a classic example of secondary active transport.

6. B may be transported either by facilitated diffusion or active transport. Both are like enzyme catalyzed reactions and exhibit saturation kinetics. Diffusion rate is proportional to the concentration gradient when other factors affecting diffusion are held constant.

8. All of them are examples of active processes. There are proton translocating ATPases in lysosomes.

9. The term 'carrier-mediated transport' emphasizes the fact that the transported species binds to a transport protein. Glucose *attaches* to the GLUT molecule and a conformational change in GLUT shuttles glucose to the interior of the cell. The transport of Na and K by Na-K ATPase is also an example of carrier-mediated transport because both ions bind to the transporter.

In contrast, aquaporins and ion channels are not carrier proteins; they are channels through which water or the respective ions flow. The ions themselves do not bind to ion channels. This is an example of diffusion facilitated by the presence of proteins in the cell membrane (facilitated diffusion). Some authors also call it "simple diffusion".

10. The following mathematical relationship applies to the situation described in the question.

$$P_i \times V_i = P_f \times V_f$$

$P_i$  and  $P_f$  are initial and final osmolalities and  $V_i$  and  $V_f$  are initial and final volumes respectively

$$280 \times 100 = 350 \times V_f$$

$$V_f = 80 \text{ femtoliters}$$

Thus, there is a decrease in RBC volume in the steady state when it is placed in hypertonic saline.

\*\*\*\*\*

**Self-Scorer 2: Physiology of nerve and muscle cells**

*In each of the following questions, select the single best response.*

1. Which **one** of the following increases excitability of cardiac muscle?

- A. Increase in ECF  $[K^+]$  from 5 to 10 mM
- B. Increase in ECF  $[K^+]$  from 5 to 28 mM
- C. Decrease in ECF  $[K^+]$  from 5 to 1.4 mM

2. The force of skeletal muscle contraction cannot be increased by:

- A. increasing the frequency of activation of motor units
- B. increasing the number of motor units activated
- C. increasing the amplitude of action potentials in motor neurons
- D. recruiting larger motor units

3. Which of the following **is correct** with regard to numbers of each of the following in the CNS?

- A. neurons >> glia > synapses
- B. glia >>> synapses >>> neurons
- C. synapses >> glia > neurons
- D. synapses >> neurons >> glia

4. Na is not included in the assessment of the approximate value of the resting membrane potential of nerve fibers because:

- A. extracellular [Na] is higher than ICF [Na]
- B. Na-K pump extrudes 3 Na for 2 K pumped in
- C. permeability of the resting membrane to Na is low
- D. unexcited cells are equally permeable to Na and K

5. Neuron C responds to stimulation of neuron A with a propagated action potential only when neuron B (which terminates only on neuron C) is also simultaneously stimulated. Which of the following is correct?

- A. Neuron C releases glycine
- B. Neuron B releases an excitatory neurotransmitter
- C. The synapse between A and C is axosomatic
- D. The neurotransmitter released by neuron A opens K channels in neuron C

6. Which of the following nerve fibers is **most** susceptible to hypoxia?

- A. Somatic motor neurons
- B. Nociceptive afferents
- C. Preganglionic autonomic neurons
- D. Fibers transmitting touch sensation

7. The term 'size principle' refers to the fact that:

- A. neurons in small motor units conduct slowly
- B. chronically denervated skeletal muscle decreases in size due to reduced release of growth factors from motor neurons
- C. small motor units are recruited for more forceful contractions
- D. fast motor units are recruited after slow motor units

8. Recruitment and activation of motor units is investigated by:

- A. electromyography
- B. electroencephalography

- C. nerve action potential recordings
- D. clinical examination of tendon jerks

### Answers to self-scoring 2:

#### Physiology of nerve and muscle cells

1A	2C	3C	4C	5B
6C	7D	8A		

#### Notes:

1. Using the Nernst equation (below) to determine the equilibrium potential of K, we get, equilibrium potential for potassium

$$E_k = -61 \log [(K)_i / (K)_o]$$

Case a:  $E_k \approx RMP = -70 \text{ mV}$

Case b:  $E_k \approx RMP = -40 \text{ mV}$

Case c:  $E_k \approx RMP = -122 \text{ mV}$

When RMP is  $-70 \text{ mV}$ , the muscle cell is closest to the firing level, which is about  $-55 \text{ mV}$ . In contrast, when RMP is  $-40 \text{ mV}$ , it has crossed the firing level so it would be absolutely refractory or inexcitable. Hypokalemia makes the RMP more negative, and because at RMP the heart would be filling with blood, it may stop the heart in diastole. Similarly, intense stimulation of the vagus nerve to the heart may stop the heart in diastole because acetylcholine activates an outwardly directed potassium current in SA node; i.e. it hyperpolarizes the SA node and the AV node.

2. There is no "larger" action potential; rather, action potentials are all or none.

3. The ratio of synapses to neurons in the brain is about 1000; glia outnumber neurons by about 50 times. *See p. 51 in Ch 2 and p. 85 in Ch 4 in WFG, 2005.*

4. The resting cell membrane is 50 times more permeable to K than Na. When Na and Cl are removed from the Goldman Hodgkin equation, it becomes the much simpler Nernst equation.

5. It is easy if you draw a schematic diagram. You will see that both neurons A and B have to release excitatory neurotransmitters in order to fire C (i.e., by spatial summation of EPSP). However, repeated stimulation of either A or B may also

elicit an action potential in C by temporal summation.

6. Type B fibers are most susceptible to hypoxia.

7. Slow motor units are activated by slowly conducting axons; fast motor units are innervated by fast conducting axons. Slow units are recruited first in most movements; fast motor units, which are easily fatigable, are recruited for more powerful contractions. *See p. 76, WFG, 2005.*

8. In this technique, compound muscle action potentials (CMAP) are recorded by placing electrodes either on the surface of muscles or within the muscle (when needle electrodes are used); it is much like ECG which represents the compounded potentials generated by heart recorded by placing electrodes on the body surface. CMAP is examined at rest, during mild contraction, and forceful contractions. The pattern of EMG during these maneuvers is useful to distinguish between muscle weakness due to myopathy and neuropathy.

\*\*\*\*\*

### Self-Scorer 3: Functions of the CNS

1. Which of the following cells in the CNS is primarily involved in the reuptake of excitatory neurotransmitters released by neurons?

- A. Astroglial cell
- B. Microglial cell
- C. Oligodendroglial cell
- D. Ependymal cell

2. Which of the following effects is **not** produced by stimulation of  $\mu$  opioid receptor?

- A. Analgesia
- B. Constipation
- C. Miosis
- D. Diuresis
- E. Sedation
- F. Euphoria

3. The phantom limb phenomenon exemplifies:

- A. Bell-Magendie law
- B. the law of projection
- C. Muller's doctrine of specific nerve energies
- D. Weber-Fechner law

4. In which sensory transduction pathway does hyperpolarization of the receptor cell activate transmission in the pathway?

- A. Phototransduction
- B. Auditory signaling
- C. Gustation
- D. Olfactory signaling

5. The muscle spindle is **not** innervated by:

- A. A $\alpha$  fibers
- B. A $\gamma$  fibers
- C. Ia fibers
- D. II fibers

6. The muscle spindle remains capable of responding to stretch even the muscle is contracting. This is because of:

- A. presence of stretch receptors in the tendon
- B. co-activation of  $\alpha$ - and  $\gamma$ -motor neurons
- C. reciprocal innervation
- D. autogenic inhibition

7. Muller's doctrine of specific nerve energies is better known as:

- A. Bell-Magendie law
- B. labeled-line principle
- C. Weber-Fechner law
- D. law of projection

8. The receptor for autogenic inhibition (or the inverse stretch reflex) is:

- A. hair cell
- B. muscle spindle
- C. Golgi tendon organ
- D. glomus cell

9. Proprioceptive information reaches consciousness through the (*choose all correct answers*):

- A. spinothalamic system
- B. dorsal column – medial lemniscal pathway
- C. spinocerebellar pathway
- D. olivocerebellar pathway

10. If light reflex is present and the accommodation reflex absent, then the lesion is most likely in the:

- A. pretectal nucleus
- B. ganglion cells

- C. Edinger-Westphal nucleus  
D. visual association cortex
11. REM behavior disorder is primarily characterized by:  
A. lack of REM sleep  
B. day-time somnolence  
C. absence of hypotonia during REM sleep  
D. absence of PGO spikes during REM sleep
12. Which sensory modality is transduced by free nerve endings?  
A. Vision  
B. Taste  
C. Smell  
D. Sound
13. The fifth taste modality is:  
A. umami  
B. imami  
C. himami  
D. emami  
E. mami
14. Muscle contraction in response to maintained stretch is initiated by sensory inputs from:  
A. nuclear bag fibers  
B. nuclear chain fibers  
C. Golgi tendon organ  
D.  $\gamma$ -motor neurons
15. Rhodopsin has peak sensitivity to light at a wavelength of:  
A. 405 nm  
B. 505 nm  
C. 605 nm  
D. 705 nm
16. Which **one** of the following sensory modalities does **not** have a separate neocortical projection?  
A. Taste  
B. Smell  
C. Vision  
D. Hearing
17. Dark adaptation is nearly maximal in about:  
A. 1 minute  
B. 5 minutes  
C. 20 minutes  
D. 40 minutes
18. Which of the following statements regarding the autonomic nervous system is **incorrect**?  
A. Preganglionic sympathetic neurons are more sensitive to hypoxia compared to postganglionic sympathetic neurons.  
B. Postganglionic fibers are unmyelinated.  
C. Medulla is the highest center for integration of autonomic reflexes.  
D. Stimulation of parasympathetic system usually elicits discrete responses whereas stimulation of the sympathetic nervous system usually elicits widespread physiologic responses.
19. Normally, the total blood flow to the brain is about:  
A. 250 ml/min  
B. 500 ml/min  
C. 750 ml/min  
D. 1200 ml/min
20. Normally, cerebral metabolic rate for oxygen (CMRO<sub>2</sub>) is about:  
A. 2 ml/100 g/min  
B. 3.5 ml/100 g/min  
C. 5 ml/100 g/min  
D. 7 ml/100 g/min
21. Normally, the brain is perfused with what fraction of resting cardiac output?  
A. 5%  
B. 10%  
C. 15%  
D. 20%
22. In which sensory system does excitation of receptor by an adequate stimulus result in hyperpolarization of receptor cells?  
A. Visual pathway  
B. Auditory pathway  
C. Taste pathway  
D. Olfactory signaling
23. Which of the following has been suggested as a possible mediator of analgesia produced by stimulation of the raphespinal pathway?  
A. Substance P  
B. Glutamate  
C. Serotonin

D. GABA

24. Which area is uniquely concerned with color vision?

- A. V1
- B. V3
- C. LO
- D. V8

25. Which eye movements bring new objects of interest onto the fovea?

- A. Saccades
- B. Convergence movements
- C. Smooth pursuit movements
- D. Vestibular movements

26. Kluver-Bucy animals exhibit:

- A. hypersexuality
- B. visual agnosia
- C. bizarre exploratory behaviour
- D. amnesia
- E. all of the above

27. Symptoms of the Kluver-Bucy syndrome have been shown to be reproduced by:

- A. amygdectomy
- B. dorsal rhizotomy
- C. decerebration
- D. lesions in the internal capsule

28. In a majority of lefthanders, the left cerebral hemisphere is the categorical hemisphere.

True/False.

29. The *planum temporale* is an area in the superior temporal gyrus concerned with language-related auditory processing. True/False.

30. Lumbar CSF pressure varies from 70-180 mm CSF. True / False

### Answers to Self-Scorer 3: Functions of CNS

1A	2D	3B	4A	5A
6B	7B	8C	9AB	10D
11C	12C	13A	14B	15B
16A	17C	18C	19C	20B
21C	22A	23C	24D	25A
26E	27A	28T	29T	30T

### Explanations:

1. Indeed, reduced reuptake of excitatory neurotransmitters such as glutamate by astrocytes in ischemic zones is said to contribute to excitotoxicity in stroke.

2. Diuresis is mediated by an action on kappa receptors. See *Table 4-5 on p. 113, Ch 4, WFG, 2005.*

3. When light strikes retina, conformational changes in rhodopsin activate phosphodiesterase, decreasing cGMP, causing closure of Na channels and hyperpolarization of receptor cells and decreased release of neurotransmitter. This triggers response in other neural elements of the retina. See Fig 8-19, p. 159 in WFG 22<sup>nd</sup> ed.

6. Since  $\alpha$ - and  $\gamma$ -motor neurons are coactivated, intrafusal fibers also contract whenever extrafusal fibers contract. Thus, the central portion i.e. the spindle is stretched and fires even while the muscle is contracting; thus the spindle is capable of responding to rate of change of stretch, as well as maintained stretch.

7. The same sensation is perceived no matter how a sensory pathway is excited. Each pathway is labeled to transmit a specific sensory modality. This is the *labeled line* principle or Muller's doctrine of specific nerve energies.

8. Autogenic inhibition is a term that is used interchangeably with inverse stretch reflex. It indicates that the relaxation that occurs when muscle is excessively stretched arises from a receptor located in the muscle itself. This receptor is the Golgi tendon organ.

9. Impulses in the spinothalamic tracts and the dorsal column-medial lemniscus pathways reach consciousness. Impulses in the spinocerebellar pathways terminate in the cerebellar cortex and therefore do not reach consciousness.

10. This is what happens in cortical blindness.

11. In this condition, hypotonia does not occur during REM sleep and the person may act out his dreams. It is treated with benzodiazepines.

14. The nuclear bag fiber is activated whenever the spindle is stretched; i.e. it detects a change in length of the muscle. The nuclear chain fiber, a slowly adapting receptor, fires even during maintained stretch; i.e. it detects the absolute length of the muscle. See *p. 131, Ch 6, WFG, 2005*.

15. Steady state neurotransmitter release from rod cells occurs in the dark. Light causes activation of cGMP - phosphodiesterase, reducing intracellular cGMP, this resulting in closure of Na channels, hyperpolarization of rod cells and reduced release of neurotransmitter from rod cells.

17. Dark adaptation requires synthesis of more rhodopsin.

18. The hypothalamus is the highest center for integration of autonomic reflexes. Charles Sherrington said, "the hypothalamus is the head ganglion of the autonomic nervous system".

20. Mass of the brain = 1400 g  
Cerebral oxygen consumption per minute = 50 ml  
CMRO<sub>2</sub> (i.e. oxygen consumption per minute per 100 g of brain tissue) = 3.5 ml/100 g/min

21. Resting cardiac output = 5 L/min  
Cerebral blood flow = 750 ml/min (this is 15% of cardiac output)

23. Serotonin may act presynaptically on the 'gate' in the dorsal horn of the spinal cord and reduce the efficacy of transmission in the pain pathway. Enkephalins are also implicated in this mechanism. See *p. 146, WFG, 2005*.

25. Saccades are sudden jerky movements and occur as gaze shifts from one object to the other. They are programmed in the frontal eye field (in the cerebral cortex) and the superior colliculus.

26, 27. Kluver & Bucy observed the effects of bilateral temporal lobectomy. However, it is now known that these features could be reproduced by bilateral resection of the amygdalae.

\*\*\*\*\*

## Self-Scorer 4: Endocrinology and Reproduction

*In each of the following questions, choose the single best response.*

1. JAK-STAT pathways mediate the effects of:

- A. transducin
- B. aquaporins
- C. gusducins
- D. growth hormone

2. Men castrated before puberty grow taller because:

- A. release of growth hormone is increased
- B. of androgen resistance
- C. estradiol level in the epiphyseal growth plate takes longer to reach its threshold
- D. of insensitivity to IGF-1

3. Patients with sexual precocity are apt to be dwarf because of:

- A. increased levels of androgens
- B. the estrogen surge during precocious puberty
- C. deficiency of androgen receptors
- D. increased levels of thyroxine

4. The satiety-producing hormone is:

- A. orexin
- B. resistin
- C. adiponectin
- D. leptin

5. Hypophysectomy does **not** immediately affect the secretion of:

- A. zona glomerulosa
- B. zona fasciculata
- C. zona reticularis

6. Which hormone also upregulates its receptors in the adrenal cortex?

- A. Epinephrine
- B. Angiotensin II
- C. Cortisol
- D. Aldosterone

7. In glucocorticoid-remediable aldosteronism:

- A. angiotensin II has no effect on aldosterone synthesis

- B. angiotensin II stimulates whereas angiotensin III inhibits aldosterone synthesis
- C. aldosterone synthase is expressed in the zona fasciculata and exquisitely sensitive to stimulation by ACTH.
- D. administration of glucocorticoids increases ACTH levels
8. What is true about development of a 44 XX, SRY+ zygote?
- A. Female internal and external genitalia develop
- B. Both ovaries and testes develop
- C. Ovaries develop
- D. Testes develop
9. Which of the following zones in the adrenal cortex does not normally express 17 alpha hydroxylase?
- A. Zona glomerulosa
- B. Zona fasciculata
- C. Zona reticularis
10. The blood-testis barrier is formed by tight junctions between:
- A. Leydig cells
- B. primary spermatocytes
- C. spermatogonia
- D. Sertoli cells
11. Human menopausal gonadotropin consists of:
- A.  $\beta$ -subunits of hCG
- B. FSH & LH
- C. prolactin
- D. recombinant GnRH
12. The hormone that is essential for the formation of male external genitalia is:
- A. testosterone
- B. dihydrotestosterone
- C. Mullerian regression factor
- D. SOX factor
13. Testicular feminization syndrome is caused by mutations in genes coding for:
- A. androgen-binding proteins
- B. testosterone 5 $\alpha$  reductase
- C. androgen receptor
- D. inhibin
14. The “penis-at-12” syndrome occurs due to a deficiency of:
- A. 17 $\alpha$  hydroxylase
- B. testosterone 5 $\alpha$  reductase
- C. 11 $\beta$  hydroxysteroid dehydrogenase
- D. CYP 450sc
15. The most abundant androgen in the plasma of both males and females is
- A. androstenedione
- B. dehydroepiandrosterone sulfate
- C. testosterone
- D. dihydrotestosterone
16. In humans, the hormone that is mainly secreted by the adrenal medulla is:
- A. epinephrine
- B. norepinephrine
- C. dopamine
- D. adrenomedullin
17. The major stimulator of PTH release from the parathyroid gland is:
- A. vitamin D
- B. a fall in plasma ionized calcium
- C. calcitonin
- D. a fall in plasma phosphate concentration
18. In postnatal life, thyroid hormones do not increase oxygen consumption in the:
- A. heart
- B. skeletal muscle
- C. brain
- D. liver
19. Which of the following hormones is lactogenic?
- A. Chorionic growth hormone
- B. HCG
- C. Oxytocin
- D. Relaxin
20. Which of the following inhibits lactation?
- A. Prolactin
- B. Chorionic somatomammotropin
- C. Estrogen and progesterone
- D. Growth hormone
21. Which of the following inhibits ovulation?
- A. Prolactin

- B. Human menopausal gonadotropin
- C. Estrogens
- D. Luteinizing hormone releasing hormone

22. Which of the following hormonal combinations in plasma is associated with normal lactation?

- A. Cortisol + prolactin + oxytocin
- B. Estrogen (E) + progesterone (P) + prolactin
- C. E + P + insulin + cortisol + prolactin
- D. Prolactin + oxytocin + E + P

23. During normal pregnancy, which hormone(s) peak during the first trimester? (*select all that apply*)

- A. HCG
- B. HCS
- C. Prolactin
- D. Estradiol
- E. Estriol
- F. Relaxin

**Answers: Self-Scorer 4 - Endocrinology & Reproduction**

1D	2C	3B	4D	5A
6B	7C	8D	9A	10D
11B	12B	13BC	14B	15B
16A	17B	18C	19A	20C
21A	22A	23AF	24	25

**Answer Explanations:**

1. Janus tyrosine kinases (JAK) are enzymes that phosphorylate signal transducers and activators of transcription (STAT). STAT proteins are transcription factors. Growth hormone, prolactin, and erythropoietin act via JAK-STAT pathways.

2. The testes is virtually the only source of circulating testosterone and very little testosterone is synthesized by the adrenal cortex. Thus, orchiectomy prior to puberty will result in a steep fall in testosterone levels in males; consequently the pubertal surge in androgens would be deficient. Thus, the formation of estradiol in the epiphyseal growth plates from circulating testosterone is also greatly reduced. In males as well as females, closure of epiphyseal plates occurs is mediated by estradiol (acting via estrogen receptors) when its level in the growth plate exceeds a certain *threshold* level. This happens following the pubertal growth spurt

4. All you need to know about leptin:

- Leptin is a satiety signal from the adipocytes acting on the hypothalamus to inhibit food intake.
- It presumably signals the amount of fat to the CNS.
- Chemically, it is a polypeptide. It is coded by the *ob* gene.
- Leptin levels increase after a meal
- Leptin receptors are coded by *db* gene.
- Leptin deficiency as well as deficiency of functional leptin receptors have been implicated in the pathogenesis of obesity.
- Leptin increases sensitivity to insulin.
- Adiponectin is another hormone from adipocytes that increases insulin sensitivity.
- Significant weight loss (fat loss) is accompanied by a reduction in serum leptin level.
- When serum levels of leptin are abnormally low, GnRH secretion is eventually downregulated. Low levels of leptin may in part explain amenorrhea that occurs in athletes and individuals with thyrotoxicosis.

5. Although ACTH is trophic to all three zones in the adrenal cortex, the major stimulators of aldosterone synthesis is angiotensin II, and a rise in plasma [K]. In the long run, however, the size of the zona glomerulosa would also decrease.

7. The basic defect in glucocorticoid-remediable aldosteronism (GRA; sometimes called dexamethasone remediable aldosteronism) is a *hybrid* aldosterone synthase gene that has a promoter sensitive to stimulation by ACTH, and this gene is expressed in the zona fasciculata. (Note, normally, aldo synthase is expressed only in the ZG). The ZF is 5 times larger than the zona fasciculata, and therefore aldosterone levels are high even with normal levels of ACTH. The hypertension that occurs as a result of hyperaldosteronism suppresses plasma renin activity. Hyperaldosteronism in this instance is remediable with glucocorticoid therapy ('low dose dexamethasone'); i.e., administered glucocorticoids inhibit ACTH release and consequently reduce aldosterone synthesis.

8. The sex determining region of the Y chromosome dictates the formation of embryonic

testes and inhibits the development of ovaries. Mullerian inhibiting polypeptide from the testes inhibits the growth of Mullerian duct structures. Testosterone induces the development of male internal genitalia.

**13. Testicular feminizing syndrome** (by definition testes are present but external genitalia are female)

<i>Genotype</i>	46XY
<i>Gonad</i>	Testes
<i>Testosterone</i>	Levels normal or increased
<i>Internal genitalia</i>	Male or female
<i>External genitalia</i>	Female
<i>Phenotype</i>	Female
<i>Defects</i>	Loss of function mutations in genes coding for either the androgen receptor <b>or</b> testosterone 5 $\alpha$ reductase (type 2)

This condition is an example of *male pseudohermaphroditism*. Testosterone levels are increased in this condition. When the basic defect is a mutated androgen receptor, there is resistance to actions of testosterone and dihydrotestosterone and the resulting clinical syndrome is called **androgen resistance syndrome**. The resistance can vary from mild (*partial androgen insensitivity*) to severe (*complete androgen resistance*). Both testosterone and DHT act upon the same androgen receptor. DHT is much more potent and is essential for formation of male external genitalia.

Causes of male pseudohermaphroditism:

- Androgen resistance syndrome
- Testosterone 5-alpha reductase (type 2) deficiency
- Deficiency of steroidogenic acute regulatory protein (STAR), rare
- 17 $\alpha$ - hydroxylase deficiency, rare

**14. Pathogenesis of the “penis-at-12 syndrome”:**

- It occurs due to a deficiency of the enzyme testosterone 5 $\alpha$ - reductase (type 2)
- Testosterone (T) and DHT act on the same receptor
- DHT is much more potent than T

- In T 5 $\alpha$ - reductase deficiency, during puberty, surges in LH are *greater* because of the lack of negative feedback effect of DHT on the pituitary and the hypothalamus; thus, induces synthesis of large amounts of T.
- Because of DHT deficiency, feedback inhibition of LH release is lower than normal.
- ‘High levels’ of T via their effects on the androgen receptor (normal in this case) may induce growth of the *clitoris*.
- However, despite high levels of T, labioscrotal fusion does not still occur because androgen receptors are downregulated at this site.
- These individuals have been raised as females and they may prefer to change their *gender identity* at the time of puberty; the management of this condition is complex.

15. DHEA sulfate and androstenedione are biologically very weak androgens if at all. They function mainly as precursors for the synthesis of testosterone in males and estrogens in females. However, when large amounts of adrenal androgens are present and depending on when the level of adrenal androgens is high, it can induce virilization in a female fetus or in postpubertal females.

18. T4 and T3 increase the oxygen consumption of all metabolically active tissues. The exceptions are the adult brain, testes, uterus, lymph nodes, spleen and anterior pituitary.

20. Estrogens stimulate breast growth but antagonize the milk producing effect of prolactin; lactation commences once the placenta is expelled and there is an abrupt decline in circulating levels of estrogens and progesterone.

21. The best answer is prolactin. Prolactin inhibits the release of GnRH from the hypothalamus, inhibits release of FSH and LH from the anterior pituitary and also inhibits the actions of FSH and LH on the ovary. These effects of prolactin constitute the mechanism of *lactational amenorrhea*. However, oral contraceptive pills which inhibit ovulation usually contain a combination of estrogen and progesterone, and the dose is pharmacologic.

\*\*\*\*\*

## Self-Scorer 5: Gastrointestinal Physiology

- Normally, instillation of acid into the duodenum to reduce pH in its lumen to 4:
  - stimulates gastrin release
  - increases output of an enzyme rich pancreatic juice
  - increases activity of Brunner's glands
  - relaxes the pyloric sphincter
- Which of the following statements regarding the actions of gastrointestinal hormones is **incorrect**?
  - Secretin inhibits gastric emptying
  - Gastrin stimulates histamine release in the stomach
  - Somatostatin reduces blood flow to the GIT
  - GIP inhibits the release of insulin from pancreas
- The prokinetic effects of erythromycin are due to its agonist actions on:
  - histamine receptors
  - motilin receptors
  - CCK receptors
  - somatostatin receptors
- Which of the following mechanisms allows complete absorption of glucose from the intestinal lumen into the cytosol of the enterocyte?
  - Simple diffusion through GLUT-5
  - Na-glucose cotransporter-1 (SGLT-1)
  - Na channels in enterocyte membrane
  - Paracellular uptake via gap junctions
- Which of the following strategies would **most likely** be therapeutic in an individual with achalasia?
  - Injection of tetanus toxin into the lower esophageal sphincter
  - Surgical division of the lower esophageal sphincter
  - Administration of a muscarinic receptor agonist
  - Administration of a nitric oxide synthase inhibitor
- In which of the following conditions is a long acting analog of somatostatin of therapeutic value?
  - Acute mesenteric ischemia
  - Bleeding from esophageal varices
  - Cholelithiasis
  - Pancreatic exocrine insufficiency
  - Pernicious anemia
- Which of the following **inhibits** gastric acid secretion by an action on the parietal cell?
  - Acetylcholine
  - Epinephrine
  - Gastrin
  - Histamine
  - Prostaglandin E
- The 'postprandial alkaline tide' is abolished by:
  - antrectomy
  - gastrin
  - parietal cell vagotomy
  - total inhibition of gastric  $H^+K^+$  ATPase
  - truncal vagotomy
- Which pattern of motility **hastens** the transit of chyme in the small intestine in the digestive state?
  - Mass action contraction
  - Migrating motor complex
  - Peristalsis
  - Segmentation contraction
  - Tonic contraction
- Intestinal absorption of which of the following does **not** directly utilize a  $Na^+$  gradient?
  - Fructose
  - Galactose
  - Glucose
  - Phenylalanine
  - Tyrosine
- The release of gastrin from G cells in the antrum of the stomach is **inhibited** by:
  - activation of vagal efferent fibers to the stomach
  - circulating epinephrine
  - blood-borne calcium
  - mechanical distention of the stomach
  - somatostatin

12. Which of the following muscles is subject to control by voluntary as well as reflex mechanisms?

- A. External anal sphincter
- B. Lower esophageal sphincter
- C. Pyloric sphincter

13. From a physiologic standpoint, the advantage of a 'parietal cell vagotomy' over truncal vagotomy for treating duodenal ulcer is that in parietal cell vagotomy:

- A. a gastrojejunostomy is not required
- B. only basal acid output is reduced
- C. G cells are also denervated
- D. pyloric sphincter is also denervated
- E. receptive relaxation is abolished

14. Your patient is a 30-year-old man with recurrent right upper quadrant pain suggestive of biliary pain. There is no clinical evidence of liver cell disease, gallstones in the gall bladder or the bile duct, gastroesophageal reflux, peptic ulcer disease. However, mild and transient elevations in serum transaminases were documented during an episode of 'biliary pain'. Ultrasonography of the hepatobiliary system following an intravenous infusion of cholecystikinin indicated that it caused dilation of the common bile duct. Further, the pancreatic duct dilated during intravenous infusion of secretin. These findings are most consistent with the possibility of:

- A. defective pumping of bile by gall bladder
- B. spasm of the sphincter of Oddi
- C. a defect in secretion of bile by hepatocytes
- D. a defect in processing of bile by cholangiocytes
- E. a defect in processing of pancreatic secretion by pancreatic duct epithelial cells

**Answers: Self-Scorer 5 - Gastrointestinal Physiology**

1C	2D	3B	4B	5B
6B	7E	8D	9C	10A
11A	12A	13A	14B	

1. The acidity of duodenum drives the release of secretin thereby evoking alkaline secretions from the liver, pancreas and intestine.

2. Secretin inhibits gastric emptying by contracting the pyloric sphincter. Gastrin from G cells stimulates acid secretion by two means: one, it stimulates histamine release from ECL cells in the stomach; two, it directly acts on parietal cells to augment acid secretion. Somatostatin reduces intestinal blood flow and secretion.

Glucose-dependent insulinotropic polypeptide (GIP) was previously called gastric inhibitory peptide. However, now it is clear that the physiologic action of GIP is stimulation of insulin secretion. Its inhibitory effects on gastric secretion occur only at pharmacologic doses.

3. Erythromycin is a motilin receptor agonist. It is used in the management of diabetic gastroparesis.

4. Glucose could enter enterocytes from the intestinal lumen by diffusion through GLUT; however, for complete absorption of glucose against a concentration gradient, the active transport mechanism provided by the sodium-glucose cotransporter is required.

8. The  $H^+ - K^+$  ATPase in the parietal cell is the final common pathway for gastric acid secretion by the stomach. The *postprandial alkaline tide* refers to a slight increase in pH of plasma following a meal. It reflects gastric acid secretion by parietal cells since for every proton secreted by the parietal cell, one bicarbonate ion enters the blood stream. Though the liver, pancreas and the small intestine collectively secrete a large amount of alkaline fluid into the GI lumen, this does not produce a postprandial acid tide in plasma because the stomach secretes about 2-2.5 liters of gastric juice per day, and parietal cells concentrate protons a million fold in gastric juice relative to plasma.

10. Fructose is not absorbed by an active transport process. It enters enterocytes down its concentration gradient through GLUT-5.

11. Options A-D are factors that stimulate gastrin release.

13. Option A is correct because the denervation in a parietal cell vagotomy (PCV) involves the

branches that supply the fundic area but not the antrum. As a result antral motility is preserved and a gastrojejunostomy (GJ) is not required.

PCV will reduce BAO as well as meal stimulated acid output.

G cell innervation remains intact in PCV. The innervation of the pyloric sphincter is preserved in PCV.

*Receptive relaxation* is lost after PCV because a vagovagal reflex that requires intact efferent innervation of the fundus mediates it; but the loss of receptive relaxation after PCV is not the reason why it is advantageous over a truncal vagotomy.

14. Based on anatomic and physiologic principles, with the information provided, it can be deduced that there is increased resistance to flow of bile and pancreatic juices into the duodenum following administration of secretin and CCK. Spasm of the sphincter of Oddi is the best explanation, as it regulates the flow of bile as well as pancreatic juice into the duodenum. A diagnosis of sphincter of Oddi dysfunction is established by sphincter of Oddi manometry (performed usually during endoscopic retrograde cholangiopancreatography). Spasm of the SOD is a potential cause of recurrent biliary pain following cholecystectomy, and may underlie pancreatitis that is otherwise unexplained.

\*\*\*\*\*

## Self-Scorer 6: Cardiovascular Physiology

1. What is the primary ionic basis of the prepotential in the SA node?
  - A. Ca influx through transient T Ca channels
  - B. Inwardly directed long-lasting Ca current
  - C. Outward Na current
  - D. Potassium efflux through leak channels
2. Normally, the impulse that excites the left ventricular myocardium originates in the:
  - A. SA node
  - B. Purkinje system
  - C. left bundle branch
  - D. ventricle

3. Conduction speed is slowest in the:
  - A. SA node
  - B. atrial pathways
  - C. bundle of His
  - D. Purkinje system

4. The propagation of repolarization from the ventricular epicardium to endocardium is represented by the:
  - A. QRS complex
  - B. QT interval
  - C. T wave
  - D. TP period

5. T wave inversion occurs when ventricular repolarization occurs from:
  - A. endocardium to epicardium
  - B. epicardium to endocardium
  - C. apex to base of the heart
  - D. base to apex of the heart

6. The most reliable index of AV nodal delay is:
  - A. PR interval
  - B. PR segment
  - C. AH interval
  - D. PA interval

7. Cardiac muscle cannot be tetanized because of:
  - A. accommodation
  - B. its slow rate of repolarization
  - C. calcium influx during phase II
  - D. voltage inactivation of Na channels at membrane potentials  $< 80$  mV

8. When you stand up, pressure falls in:
  - A. carotid arteries
  - B. brachial arteries
  - C. lower limb arteries
  - D. all arteries

9. If QRS deflection is highest and upright in lead I and equiphasic (or null) in lead aVF, then mean electrical axis of the QRS vector in the frontal plane is about:
  - A. 30 degrees
  - B. 0 degrees
  - C. +45 degrees
  - D. +90 degrees

10. What would be the change in blood flow to a tissue if radius of the arterioles in that tissue is doubled and perfusion pressure is halved?

- A. Increase 8 times
- B. Increase 16 times
- C. Increase 4 times
- D. Decreases 4 times

11. Recombinant brain natriuretic peptide (nesiritide) is currently used in the management of:

- A. bronchial asthma
- B. congestive heart failure
- C. bilateral renal artery stenosis
- D. ACE inhibitor induced cough

12. Maximal oxygen consumption ( $VO_2$  max) in healthy active men is about

- A. 10 ml/kg/min
- B. 20 ml/kg/min
- C. 40 ml/kg/min
- D. 80 ml/kg/min

13. The 'last ditch stand' in defense of a falling blood pressure is the:

- A. arterial baroreflex mechanism
- B. arterial chemoreflex mechanism
- C. CNS ischemic pressor response
- D. Bainbridge reflex

14. Which of the following does **not** occur when the body is immersed in water up to the neck?

- A. Increase in central venous pressure
- B. Increase in plasma level of renin

15. Which of the following statements is **correct**?

- A. Pulse pressure is directly proportional to stroke volume
- B. Pulse pressure is inversely proportional to compliance of large arteries
- C. Reflected arterial pulse waves normally serve to increase coronary perfusion during diastole

16. Which of the following is most likely to happen in a normal healthy adult seated in a centrifuge and spun at a force equal to 2 times that of gravity?

- A. Increase in intracranial tension
- B. Increase in BP
- C. Increase in cardiopulmonary blood volume

D. A doubling of pressure in the veins of the foot

17. The blood-brain barrier is formed by:

- A. tight junctions between vascular endothelial cells in the cerebral capillaries
- B. choroidal epithelial cells
- C. ependymal cells
- D. foot processes of oligodendroglia

### Answers to Self-Scorer 6 - Cardiovascular Physiology

1A	2A	3A	4C	5A
6C	7B	8AB	9B	10A
11B	12C	13C	14B	15ABC
16D	17A			

### Answer Explanations:

1. See *p 548, Ch 28, WFG, 2005.*

2. Normally, it is the impulse that originates in the SA node that excites the ventricular myocardium. Such a rhythm is called sinus rhythm.

3. There are two regions in the heart where the inhibitory effect of vagal stimulation on conduction speed is profound. These are the SA and AV nodes. The conduction speed in the SA and AV nodes is about 0.05 m/s. See *p. 549, Ch 28, WFG, 2005.* Compared to the fast conducting Purkinje system, this is about 80 times slower. The conduction speed is slowed even further in disease conditions such as SA node exit block and AV nodal block.

4-5. Depolarization and repolarization are electrically opposite processes. Normally, ventricular depolarization occurs from endocardium to epicardium, and repolarization occurs from epicardium to endocardium. This is why the T wave is upright, i.e. in the same direction as QRS. An inverted T wave indicates that the direction of ventricular repolarization is reversed, i.e. occurring from endocardium to epicardium.

6. PA interval (approximately 30 ms) reflects the time taken for conduction across the atrial pathways to the AV node. PR segment is a combined index of AV nodal delay and conduction in infranodal pathways. PR interval is

a rather poor index of AV nodal delay. AH interval, which is obtained by a His bundle electrogram specifically reflects AV nodal delay. See p. 553-554, Ch 28, WFG, 2005.

7. The long duration of action potential (or the absolute refractory period) in the heart is due to slow repolarization. This is a safety features that ensures that the ventricles relax to fill with blood before contracting again.

10. Tissue blood flow = BP / local vascular resistance. Blood flow is directly proportional to the fourth power of radius.

11. ANP is a natriuretic hormone. It increases blood flow through the kidneys and glomerular filtration rate. ANP levels are increased in heart failure. The action of ANP in heart failure is to increase Na and water excretion by the kidneys. At first sight, this would appear to be a beneficial effect; however, it must be noted that in heart failure, effective arterial blood volume is diminished. Angiotensin II, aldosterone and the renal vasoconstrictive effects of elevated activity in the renal sympathetic nerves counteract the natriuretic effects of ANP.

12. VO<sub>2</sub> max is the maximum amount of oxygen that can be utilized during dynamic exercise; it can be increased by training. See p 635, Ch 33, WFG, 2005.

13. Arterial BP is affected by numerous neural and humoral mechanisms. The arterial baroreflex mechanism buffers BP fluctuations when mean arterial pressure (MAP) is in the 70-150 mm Hg range. But when MAP is lower than 70 mm Hg, baroreceptors are maximally deactivated and the arterial chemoreflex mechanism assumes greater importance in defending against a further fall in BP.

In severe hypotension such as when mean arterial pressure is < 50 mm Hg), ischemia of the vasomotor center in the medulla triggers a powerful increase in sympathetic outflow and MAP. This mechanism, the CNS ischemic pressor response (called the “last ditch stand” in defense

of a falling BP), contributes to restoring cerebral blood flow.

Reflex mechanism	Mean arterial pressure (mm Hg) range in which it operates
Arterial baroreflex	70–110
Arterial chemoreflex	40–70
CNS ischemic response	< 50

14. When a person is immersed in water up to the neck, this functions as an anti-G suit (anti G suits are filled with water or compressed air) – thereby mitigating the effect of gravity. Thus, venous return and central blood volume increase. A rise in CVP due to an increase in central blood volume is accompanied by a reflex decrease in renin release from the kidneys as long as arterial blood pressure, renal blood flow and GFR are normal.

15. The stiffer the arteries, i.e., the less distensible they are, higher the pulse pressure for a given stroke volume. This is the basis of higher systolic pressure in isolated systolic hypertension, the commonest type of hypertension in the elderly.

16. The effect of positive g forces, in an individual standing upright, would be to throw blood into the lower part of the body.

17. While foot processes of astrocytes end on cerebral capillaries and induce the formation of tight junctions, the actual anatomic basis of the blood brain barrier is the tight junctions between endothelial cells in cerebral capillaries. In the circumventricular organs such as area postrema, subfornical organ, this barrier is absent.

\*\*\*\*\*

## Self-Scorer 7: Pulmonary Physiology

*Choose the single best answer*

- The major area of airway resistance during breathing is located in:
  - oropharynx
  - trachea and large bronchi
  - intermediate-sized bronchi
  - bronchioles < 2 mm in diameter

2. Pulmonary capillary wedge pressure must be estimated under:

- A. zone 1 conditions
- B. zone 2 conditions
- C. zone 3 conditions
- D. zone 4 conditions

3. Cardiogenic pulmonary edema occurs when pulmonary capillary pressure exceeds:

- A. 10 mm Hg
- B. 15 mm Hg
- C. 20 mm Hg
- D. 25 mm Hg

4. Apneusis occurs typically after:

- A. damage to phrenic motor neurons
- B. damage to pneumotaxic center
- C. lesions of pneumotaxic center and vagotomy
- D. denervation of peripheral chemoreceptors

5. Which one of the following has been recently postulated to function as a sensor of oxygen levels and a facilitator of oxygen transport in the brain?

- A. Myoglobin
- B. Neuroglobin
- C. Nitric oxide
- D. Cytochrome oxidase c

6. Life is impossible without pressurization at an altitude greater than:

- A. 12000 m
- B. 14000 m
- C. 17000 m
- D. 19000 m

7. The altitude at which body fluids boil is about:

- A. 8800 m
- B. 12400 m
- C. 14500 m
- D. 19000 m

8. Which of the following occurs as a consequence of increased barometric pressure?

- A. Rapture of the deep
- B. Black out
- C. Bends
- D. Air embolism

9. Deep sea divers have been known to offer their mouths to fish! This is because:

- A. of low fat solubility of nitrogen
- B. of nitrogen toxicity
- C. helium impairs intellectual functions
- D. of increased work of breathing

10. Which of the following is used during deep sea diving?

- A. Compressed room air
- B. 100% oxygen
- C. A helium–oxygen mixture
- D. 50% N<sub>2</sub> and 50% oxygen

11. In which of the following situations does decompression sickness **not** occur?

- A. During ascent in an unpressurized cabin of an airplane
- B. At a depth of 100 ft in the ocean
- C. During rapid ascent from a deep-sea dive

12. What is the treatment of choice for air embolism?

- A. Continuous positive airway pressure
- B. Gradual decompression
- C. Hyperbaric oxygenation
- D. Positive pressure ventilation

13. Which of the following combination of arterial blood gas results is most likely in a normal person after a month's residence at 4000-meter altitude?

Arterial pH, PaCO<sub>2</sub> and HCO<sub>3</sub> (mmol/L)

respectively would be:

- A. 7.4, 40 mmHg, 24
- B. 7.36, 36 mm Hg, 30
- C. 7.6, 20 mm Hg, 40
- D. 7.46, 26 mm Hg, 19

14. The amount of oxygen dissolved in plasma relates most closely with:

- A. FiO<sub>2</sub>
- B. PAO<sub>2</sub>
- C. PaO<sub>2</sub>
- D. Blood [Hb]

**Answers: Self-Scorer 7 - Pulmonary Physiology**

1C	2C	3D	4C	5B
6B	7D	8A	9B	10C
11B	12C	13D	14C	

### Answer Explanations:

1. This is because of the high airflow velocity in these segments. Bronchioles less than 2 mm in diameter represent less than 10% of total airway resistance. See *p 282, NMS Physiology, Bullock J et al, 2001.*

3. Normally, pulmonary capillary hydrostatic pressure is about 10 mm Hg. It is considered elevated when PCWP exceeds 18 mm Hg. The osmotic pressure of plasma proteins is normally about 25 mmHg.

4. The effect of afferent vagal input from stretch receptors in the lungs is to inhibit inspiration. The pneumotaxic center in the pons serves to 'switch' from inspiration to expiration. Thus, after vagotomy alone, the depth of respiration would be higher than normal. However, after damage to both pneumotaxic center as well as vagotomy, prolonged inspiratory spasms that resemble breath holding (apneusis) occur. See *p 672, Ch 36, WFG, 2005.*

6. At an altitude of 14000 meters, consciousness is lost despite administration of 100% oxygen. This is because the barometric pressure at this altitude is far too low to permit adequate oxygenation of arterial blood. See *p. 689, Ch 37, WFG, 2005.*

9. The euphoria is attributed to increased solubility of nitrogen in body fluids. This is why a helium-oxygen mixture is used and while increased solubility of helium is associated with impairment of manual dexterity, intellectual function is apparently not significantly impaired. See *p. 694-5, Ch 37, WFG, 2005.*

10. If a diver breathes compressed air, the increased partial pressure of nitrogen can result in a constellation of neurological symptoms known as "rapture of the deep". See *p 694-5, Ch 37, WFG, 2005.*

11. At a depth of 100 ft in the ocean, barometric pressure is about 4 atmospheres, four times greater than at mean sea level. The problems that occur are therefore due to increased solubility of gases in blood and depend on the gas mixture used for breathing. You may want to remember

this as 'compression sickness'. In contrast, decompression sickness (the exact opposite of compression sickness) occurs during rapid ascent following a deep-sea dive or when an airplane cabin loses pressure at high altitude. Gases dissolved in body fluids come out of solution because of the reduction in ambient pressure, forming bubbles and blocking blood flow to tissues.

14. By applying high pressure, solubility of gas (air emboli *in this question*) in plasma is increased. At a constant temperature, solubility of a gas in plasma is directly proportional to partial pressure of gas (Henry's law).

\*\*\*\*\*

### Self-Scorer 8: Renal and Acid-Base Physiology

1. Which of the following substances **cannot** be used for measuring GFR?

- A. Glucose
- B. Iothalamate
- C. Inulin

2. If the glomerular capillary hydrostatic pressure, osmotic pressure of plasma proteins, hydrostatic pressure in the Bowman's space and oncotic pressure in the interstitium are respectively 40, 25, 5, and 0 mm Hg respectively, what is the net pressure driving filtration of fluid into the Bowman's space?

- A. 10 mm Hg
- B. 15 mm Hg
- C. 20 mm Hg
- D. 25 mm Hg

3. In a normal adult human on an average diet, and with an arterial plasma pH of 7.37, which of the following is **least likely** to be present in urine obtained first thing in the morning?

- A. Calcium
- B. Urea
- C. Uric acid
- D. HCO<sub>3</sub>

4. Normally the ratio of PaCO<sub>2</sub> and plasma HCO<sub>3</sub> is:

- A. 1.2

- B. 1.4
- C. 1.6
- D. 1.8

5. If PaCO<sub>2</sub> is 80 mm Hg and arterial plasma [H<sup>+</sup>] is 80 nmol/L, then plasma [HCO<sub>3</sub>]<sup>-</sup> is:

- A. 40 mmol/L
- B. 28 mmol/L
- C. 24 mmol/L
- D. 10 mmol/L

6. In the above situation (*Question 5*), what is the acid-base status?

- A. Compensated metabolic alkalosis
- B. Uncompensated respiratory acidosis
- C. Compensated respiratory acidosis
- D. Uncompensated metabolic acidosis
- E. Normal acid-base status

7. In arterial blood gas analysis, which **one** of the following is calculated?

- A. Arterial pH
- B. Plasma bicarbonate
- C. PaCO<sub>2</sub>
- D. PaO<sub>2</sub>

8. Which of the following is **not** elevated in ethylene glycol poisoning?

- A. Anion gap
- B. Base excess
- C. Osmolar gap
- D. Serum osmolality

9. The severity of acidosis is related to:

- A. anion gap
- B. pH of arterial plasma
- C. pH of ICF and plasma
- D. plasma HCO<sub>3</sub><sup>-</sup>

**Answers:**

1A	2A	3D	4C	5C
6B	7B	8B	9C	

**Answer Explanations:**

1. Glucose is normally not excreted by the nephron. So it cannot be used to measure GFR.

2. Recall Starling's equation describing fluid movement across capillaries. In this instance, the

pressure gradient for filtration across the glomeruli is (40 + 0) – (25 + 5) = 10 mm Hg.

4. Normally, PaCO<sub>2</sub> = 40 mm Hg, and plasma HCO<sub>3</sub><sup>-</sup> = 24 mM and PaCO<sub>2</sub> / [HCO<sub>3</sub>]<sup>-</sup> = 1.6. If this were the case, then the [H<sup>+</sup>] of arterial plasma would be equal to 40 nM (corresponding to an arterial pH of 7.4) as predicted by the modified Henderson equation.

5,6. Using the modified Henderson equation, we get, plasma HCO<sub>3</sub><sup>-</sup> = 24 mM. This is uncompensated respiratory acidosis because there is no compensatory increase in bicarbonate levels.

7. Plasma pH and total CO<sub>2</sub> concentration are measured, and plasma [HCO<sub>3</sub>]<sup>-</sup> is calculated using the Henderson-Hasselbalch equation.

8. Base excess = Observed buffer base – normal buffer base. Normal buffer base is approximately 48 mM. If observed buffer base is 52 mM, then base excess is 4 mM. Base excess is present in metabolic alkalosis. The calculation of base excess does not offer any advantage over assessment of serum bicarbonate if blood Hb and plasma protein concentrations are constant.

Serum osmolality is elevated in ethylene glycol poisoning because of an increase in the serum level of oxalate; thus, the difference between measured and calculated osmolality (osmolar gap) increases.

The elevation of anion gap in this condition is primarily because of an increase in serum oxalate.

9. It is important to understand that it is possible that there might be an acid base disturbance although the pH of arterial plasma may be 7.4 ('normal'). For example, there might be intracellular acidosis before arterial pH drops. See Balakrishnan *et al.* *What is the ultimate goal in acid-base regulation? Advances in Physiology Education.*

\*\*\*\*\*

## *A Blast from the Past*

I believe some of these questions appeared in past PG entrance exams in some form but I have made several editorial changes to the stem and the answer choices in many of them. Needless to say, it is good to use these questions to guide your preparation for future exams.

### Choose the single best answer

1. A substance injected intravenously was found to be distributed through 30% of total body water (TBW). It probably:

- A. did not pass through blood capillaries
- B. was distributed evenly throughout body water
- C. did not enter cells
- D. was excluded from CSF

2. What fraction of total body potassium is present in plasma?

- A. 0.4%
- B. 7.6%
- C. 10.4%
- D. 89.5%

3. A solution contains 1 gram mole of magnesium sulfate per liter. Assuming full ionization, calculate the osmotic pressure of the solution. (1 mOsm/L exerts an osmotic pressure of 19.3 mm Hg)

- A. 19.3 mm Hg
- B. 3.86 mm Hg
- C. 19300 mm Hg
- D. 38600 mm Hg
- E. 57900 mm Hg

4. If potassium chloride concentration of a solution is 39 mg %, then, what is the millimolar concentration of potassium in this solution?

- A. 1 mM
- B. 3.9 mM
- C. 10 mM
- D. 100 mM

5. Emiocytosis requires an increase in the intracellular concentration of:

- A. Na
- B. K
- C. Ca

D. Cl

6. Amongst plasma proteins, albumin makes the greatest contribution to the colloid osmotic pressure of plasma proteins **because** relative to most plasma proteins albumin:

- A. is the most abundant plasma protein
- B. has the longest half-life
- C. has the lowest molar mass
- D. exits the capillary fastest

7. The osmotic pressure of crystalloids is not included in the Starling's equation describing fluid exchange across capillaries **because**:

- A. they were discovered after Starling described the forces
- B. crystalloids carry electric charges
- C. crystalloids diffuse freely across the capillary endothelium
- D. the quantity of crystalloids in plasma is negligible compared to plasma proteins

8. A pole vaulter fell during pole vaulting and paralyzed his arm. Which of the following investigations is most useful to estimate likelihood of recovery?

- A. Electromyography
- B. Muscle biopsy
- C. Strength-duration curve
- D. CPK levels

9. Synaptic conduction is mostly orthodromic because:

- A. dendrites cannot be depolarized
- B. once repolarized, an area cannot be depolarized.
- C. the strength of antidromic impulses is less.
- D. chemical mediator is located only in the presynaptic terminal.

10. The main excitatory neurotransmitter in the CNS is:

- A. glycine
- B. acetylcholine
- C. aspartate
- D. glutamate

11. A 10°C decrease in body temperature decreases cerebral metabolic rate (i.e., cerebral consumption of oxygen) by:

- A. 10%
- B. 30%
- C. 50%
- D. 70%

12. In spinal anesthesia, which of the following is lost first?

- A. Sympathetic tone
- B. Sensation in the lower limbs
- C. Motor function
- D. Proprioception

13. Feedforward inhibition occurs in the:

- A. basal ganglia
- B. thalamus
- C. cerebellum
- D. cerebral cortex

14. Which of the following changes occur in rod cells when rhodopsin is activated by light?

- A. Increase in cGMP
- B. Deactivation of phosphodiesterase
- C. Depolarization of rod cells
- D. Decreased release of neurotransmitter

15. During the dark phase of the visual cycle, which form of vitamin A combines with opsin to make rhodopsin?

- A. All trans retinaldehyde
- B. All trans retinol
- C. 11-cis retinaldehyde
- D. 11-cis retinol

16. In the visual system, the term blobs refers to:

- A. parvocellular pathway from the lateral geniculate nucleus
- B. clusters of axons of ganglion cells in the retina
- C. clusters of amacrine cells in the retina
- D. clusters of cells in layers 2 and 3 of the visual cortex that have high levels of cytochrome oxidase

17. Which of the following phenomena is closely associated with slow wave sleep?

- A. Dreaming
- B. Atonia
- C. Sleep walking
- D. Irregular heart rate

18. Which combination of the following statements **are correct** regarding hypoxia? (choose all correct answers).

- A. When it is severe, causes stimulation of the sympathetic nervous system
- B. It leads to the accumulation of hydrogen and lactate ions in tissues and the circulation
- C. It causes a decrease in cerebral blood flow
- D. Chronic hypoxia is typically associated with a rightward shift of oxyhemoglobin dissociation curve

19. An anterolateral cordotomy relieving pain in the right leg is effective because it interrupts the:

- A. left dorsal column
- B. left ventral spinothalamic tract
- C. left lateral spinothalamic tract
- D. right lateral spinothalamic tract

20. A lesion of the ventrolateral part of the spinal cord is likely to lead to loss (below the level of the lesion) of:

- A. pain sensation on the ipsilateral side
- B. proprioception on the contralateral side
- C. pain sensation on the contralateral side
- D. proprioception on the ipsilateral side

21. Which of the following states does a predominance of *beta* waveforms in an electroencephalogram suggest?

- A. Deep anesthesia
- B. Surgical anesthesia
- C. Light anesthesia, eyes closed, relaxed
- D. Awake, alert state

22. Which of the following is **least likely** to aggravate insult in an injured brain?

- A. Hypercapnia
- B. Hypoxia
- C. Hypotension
- D. Hypothermia

23. Cushing's triad does **not** include:

- A. hypertension
- B. bradycardia
- C. hypothermia
- D. irregular respiration

24. Cell bodies of orexigenic neurons are present in:

- A. locus ceruleus  
 B. dorsal raphe nucleus  
 C. lateral hypothalamic area  
 D. hippocampus
25. Exposure to darkness leads to increased melatonin secretion. It is brought about by:  
 A. decreasing the activity of suprachiasmatic nucleus  
 B. increasing activity of serotonin N-acetyl transferase  
 C. decreasing the hydroxy-indole-O-methyl transferase activity.  
 D. blocking the release of norepinephrine from sympathetic nerve terminals.
26. Stimulation of sympathetic nerves to the pineal gland:  
 A. increases synthesis of melanin  
 B. increases activity of serotonin N-acetyl transferase  
 C. reduces melatonin synthesis  
 D. increases release of serotonin
27. Which of the following statements regarding the thermic effect of feeding is **incorrect**?  
 A. It is most prominent at the time of eating  
 B. It is synonymous with specific dynamic action of food  
 C. It is greater following a protein meal  
 D. It is enhanced by sympathetic neural activity
28. The first physiologic response to high environmental temperature is:  
 A. sweating  
 B. cutaneous vasodilation  
 C. decreased heat production  
 D. nonshivering thermogenesis
29. A 38-year old gentleman reports decreased hearing in the right ear for the last 2 years. On testing with a 512 Hz tuning fork, the Rinne's test (without masking) is negative on the right ear and positive on the left side. With the Weber's test, the tone is perceived as louder in the left ear. The most likely diagnosis is:  
 A. conduction loss in the right ear  
 B. sensorineural hearing loss in the right ear  
 C. sensorineural hearing loss in the left ear  
 D. conduction loss in the left ear
30. Adrenaline, noradrenaline and dopamine act upon membrane receptors that span the membrane:  
 A. 2 times  
 B. 5 times  
 C. 7 times  
 D. 10 times
31. ADH circulates in plasma primarily  
 A. bound to neurophysin I  
 B. bound to neurophysin II  
 C. bound to plasma albumin  
 D. not bound to plasma proteins
32. The following values were obtained from a patient diagnosed to have diabetic ketoacidosis:  $\text{PaO}_2 = 90$  mm Hg,  $\text{PaCO}_2 = 30$  mm Hg, plasma  $[\text{HCO}_3^-] = 10$  mM, the pH of CSF in this patient would be about:  
 A. 7.2  
 B. 7.25  
 C. 7.33  
 D. 7.40
33. A 10 days old neonate is posted for pyloric stenosis surgery. Serum calcium is 6 mg/dL (normally 8.5 – 10.5 mg/dL). What information would you like to have before you supplement calcium to this neonate?  
 A. Blood glucose  
 B. Serum albumin  
 C. Serum bilirubin  
 D. Oxygen saturation
34. The positive feedback effect of estrogen in inducing LH surge is associated with one of the following steroid hormone ratios in the peripheral circulation:  
 A. High estrogen: low progesterone  
 B. Low estrogen: high progesterone  
 C. Low estrogen: low progesterone  
 D. High estrogen: high progesterone
35. The major trophic hormone for Sertoli cells and the major stimulator of aromatase activity of Sertoli cells is  
 A. inhibin  
 B. LH  
 C. FSH

D. Melatonin

36. In a young female of reproductive age with regular menstrual cycles of 28 days, ovulation occurs around the 14<sup>th</sup> day. When is the first polar body extruded?

- A. 24 h prior to ovulation
- B. At the time of ovulation
- C. 48 h after the ovulation
- D. At the time of fertilization

37. A baby girl presents with bilateral inguinal masses, thought to be hernias, but these were found to be testes in the inguinal canals. Which karyotype would you expect to find in the child?

- A. 46 XX
- B. 46 XY
- C. 47 XXY
- D. 47 XYY

38. The enzyme needed for the conversion of androstenedione to estrone in the granulosa cells of the ovarian follicle in the follicular phase of the ovarian cycle is:

- A. cholesterol desmolase
- B. CYP11B1
- C. aromatase (CYP 19)
- D. 17-*beta* hydroxysteroid dehydrogenase

39. The biologically most active androgen is:

- A. testosterone
- B. dehydroepiandrosterone
- C. androstenedione
- D. dihydrotestosterone

40. The laboratory report shows values of gonadotropins and ovarian hormones of the blood sample taken on the 20<sup>th</sup> day of the menstrual cycle of a young woman. Whether her cycle was ovulatory or not may be validly assessed by measuring serum levels of:

- A. FSH
- B. LH
- C. estradiol
- D. progesterone

41. Apoptosis occurs as a result of changes in hormone levels during the ovarian cycle. When the ovum is not fertilized, endometrial cells die because:

- A. the involution of corpus luteum causes estradiol and progesterone levels to fall dramatically.
- B. LH levels rise after ovulation.
- C. estradiol levels are not involved in the LH surge phenomenon.
- D. estradiol inhibits the induction of the progesterone receptor in the endometrium.

42. The conjugation of bilirubin with glucuronic acid in the liver:

- A. converts a hydrophilic compound to a hydrophobic molecule
- B. converts a hydrophobic molecule to a hydrophilic molecule
- C. enables bilirubin to cross the cell membrane
- D. is increased during neonatal jaundice

43. Removal of the liver is fatal because:

- A. blood urea rises
- B. jaundice develops
- C. clotting time is prolonged
- D. progressive hypoglycemia occurs

44. CD-95 has a major role in:

- A. apoptosis
- B. cell necrosis
- C. interferon activation
- D. proteolysis

45. Erythropoiesis is inhibited by:

- A. ACTH
- B. thyroxine
- C. estrogen
- D. prolactin

46. Vagal stimulation (considering all viscera) is **least likely** to:

- A. increase intestinal secretion
- B. contract smooth muscle of intestine
- C. cause bronchodilation
- D. cause an increase in heart rate

47. Saccades are

- A. voluntary, slow eye movements
- B. involuntary, slow eye movement
- C. abrupt, involuntary, slow eye movements
- D. abrupt, voluntary, rapid eye movements

48. In an Rh-negative mother not previously sensitized by the Rh antigen, Rh incompatibility does **not** usually have a serious consequence during the first pregnancy because:
- antibodies are not able to cross placenta
  - the titer of IgG is low during the primary immune response
  - IgG is ineffective against fetal red cells
  - massive hemolysis in the fetus is compensated by increased erythropoiesis

49. Although more than 400 blood groups have been identified, ABO blood group system is one of the most important in clinical medicine because:

- it was the first blood group system to be discovered.
- it has four different groups viz A, B, AB and O
- ABO antigens are present in most body tissues and fluids.
- ABO antibodies are invariably present in plasma when the person's RBC lacks the corresponding antigen.

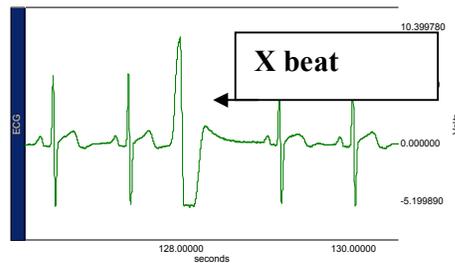
50. A 55-year-old male accident victim in the ED urgently requires a transfusion. His blood group could not be determined as his red cell group and plasma group did not match. Emergency transfusion should be done with:

- RBC corresponding to his red cell group and colloids and crystalloids
- Whole blood corresponding to his plasma group.
- O positive RBC, colloids and crystalloids
- AB negative blood

51. Stimulation of sympathetic nerves to the heart decreases:

- heart rate
- force of cardiac contraction
- speed of conduction
- refractory period

52. Which of the following statements represent the **most appropriate** interpretation of the ECG shown below?



- X beat originated from an atrial focus
- X beat reset the cardiac rhythm
- Both heart sounds would have been present at X beat
- The path of spread of excitation was normal.

53. A dye ABC has been in use for the measurement of blood volume and cardiac output. This was rivaled by the introduction of XYZ, which crossed the capillaries. What difference would the use of XYZ make in this context?

- No change in measured cardiac output & blood volume
- Increase in measured blood volume alone
- Increase in measured cardiac output alone
- Cause an error in the measurement of both

54. The most recent technique for noninvasive measurement of cardiac output is:

- pulmonary artery catheterization
- thermodilution
- echocardiography
- impedance cardiography

55. A cardiologist asked his lab technician to determine the systolic time intervals of a 60 yr old patient with a recent anterior wall infarction. The technician said that the pulse transducer was not working. Which of the following could he then have not determined?

- QS2
- Left ventricular ejection time (LVET)
- Pre-ejection period (PEP)
- Both LVET and PEP

56. Loss of 500 ml of blood over 30 minutes will lead to:

- an increase in HR, fall in BP
- a fall in BP and HR
- a prominent increase in HR and BP
- a slight increase in HR

57. Two students, AB and CD were asked to demonstrate in dogs the role of sinus nerve in hypovolemic shock. AB severed the sinus nerve when the mean blood pressure was 85 mm Hg and CD cut the sinus nerve when the mean arterial pressure (MAP) was 60 mm Hg. On cutting the sinus nerve:

- A. AB recorded an  $\uparrow$  in MAP but CD recorded a  $\downarrow$
- B. AB recorded a  $\downarrow$  in MAP but CD recorded an  $\uparrow$
- C. both recorded an  $\uparrow$  in MAP
- D. both recorded a  $\downarrow$  in MAP

58. As part of a space-research program, a physiologist was asked to investigate the effect of flight-induced stress on blood pressure.

Accordingly, the blood pressures of the cosmonauts were to be measured twice: once before take-off and once after the spacecraft entered the designated orbit around the earth. For a proper comparison, the pre-flight blood pressure should be recorded in (the):

- A. lying down position
- B. sitting position
- C. standing position
- D. any position as long as the post-flight recording is made in the same position.

59. During exercise, an increase in  $O_2$  uptake by exercising muscles does **not occur** due to:

- A. shift of the oxyhemoglobin dissociation curve to the left
- B. decrease in vascular resistance in exercising skeletal muscle
- C.  $\uparrow O_2$  extraction
- D.  $\uparrow$  blood flow

60. In hemorrhaged dogs with marked hypotension (mean arterial pressure  $< 50$  mm Hg), denervation of arterial chemoreceptors would:

- A. increase BP since chemoreceptors reduce sympathetic outflow
- B. produce no change in BP since chemoreceptors do not influence sympathetic outflow
- C. result in a further fall in BP since the arterial chemoreflex is sympathoexcitatory
- D. depend on whether arterial baroreceptors are reset or not

61. Patients with acute cardiac failure may not have edema if:

- A. oncotic pressure of plasma proteins is high
- B. renal compensation occurs
- C. cardiac output is decreased
- D. there is a fall in systemic capillary hydrostatic pressure

62. In which of the following organs is the flow **least** under sympathetic control?

- A. Brain
- B. Heart
- C. Viscera
- D. Skin

63. **Statement:** Blood is a non-Newtonian fluid.

**Reason:** Its viscosity is constant at any flow velocity.

- A. Both (S) and (R) are false
- B. (S) is true and (R) is false
- C. Both (S) and (R) are true but (R) does not explain (S)
- D. Both (S) and (R) are true and (R) explains (S)

64. While introducing the Swan Ganz catheter, its placement in the pulmonary artery (PA) is **best inferred** from which of the following?

- A. Diastolic pressure is lower in PA than in right ventricle
- B. Diastolic pressure is higher in PA than right ventricle
- C. PA pressure tracing has dicrotic notch
- D. Right ventricular pressure tracing for plateau and sharp drop in early diastole.

65. Which of the following is usually associated with turbulence in blood flow?

- A. Reynolds number less than 2000
- B. Decrease in blood flow velocity
- C. Decrease in density of blood
- D. Increase in diameter of blood vessel

66. Filtration at the arterial end of capillary occurs mainly due to:

- A. hydrostatic pressure in capillaries
- B. hydrostatic pressure in interstitium
- C. oncotic pressure in capillaries
- D. oncotic pressure in interstitium

67. Intrapleural pressure is normally negative because:
- intrapulmonary pressure is always negative
  - chest wall and lungs recoil in opposite directions at functional residual capacity
  - surfactant prevents lung collapse
  - transpulmonary pressure determines the negativity
68. Which of the following is **incorrect** about fetal hemoglobin (Hb F)?
- In comparison to HbA, Hb F has greater affinity for 2,3-BPG
  - Its ODC is shifted to left relative to HbA
  - At low PO<sub>2</sub>, Hb F gives up more oxygen to tissues than Hb A.
69. The normal value of P<sub>50</sub> on the oxyhemoglobin dissociation curve in an adult is:
- 1.8 kPa
  - 2.7 kPa
  - 3.6 kPa
  - 4.5 kPa
70. Which of the following conditions leads to tissue hypoxia **without** an alteration of oxygen content of blood?
- Carbon monoxide poisoning
  - Methemoglobinemia
  - Cyanide poisoning
  - Respiratory acidosis
71. The arterial blood gas values, pH 7.58, PCO<sub>2</sub> 23 mm Hg, PO<sub>2</sub> 300 mm Hg and oxygen saturation of hemoglobin 60% are most consistent with a diagnosis of:
- carbon monoxide poisoning
  - ventilatory (type 2 respiratory) failure
  - voluntary hyperventilation
  - methyl alcohol poisoning
72. Intense stimulation of J receptors results in:
- tachypnea
  - hypoxemia
  - pulmonary edema
  - apnea followed by tachypnea
73. If inflation of the lungs induces further inflation, this is the:
- Hering-Breuer inflation reflex
  - Hering-Breuer deflation reflex
  - Head's paradoxical reflex
  - J-reflex
74. One intern calculated the concentration of O<sub>2</sub> in blood as 0.0025 ml/ml of blood. Considering atmospheric pressure as 760 mm Hg, what is the approximate oxygen tension of arterial blood?
- 40 mm Hg
  - 60 mm Hg
  - 80 mm Hg
  - 100 mm Hg
75. A traveling nerve impulse does not depolarize the area immediately behind it because:
- it is hyperpolarized
  - the area immediately behind is refractory
  - it is not self-propagating
  - the conduction is always orthodromic
76. The renal plasma flow (RPF) of a patient was to be estimated through the measurement of para-amino hippuric acid (PAH) clearance. The technician observed the procedures correctly but due to an error in weighing inadvertently used thrice the recommended dose of PAH. The RPF estimated thus is likely to be:
- falsely high
  - falsely low
  - high or low depending on GFR
  - correct and is unaffected by the overdose of PAH
77. Several hormones regulate tubular reabsorption of water and electrolytes at different sites in the nephron. Which of the following combinations is/are **correct**?
- Angiotensin II acts in the DCT
  - Aldosterone acts in the collecting ducts
  - ADH acts in the PCT
  - ANP acts in the loop of Henle
78. A modified neuroepithelial cell is **not** the sensory receptor in the:
- visual pathway
  - auditory pathway
  - gustatory pathway
  - olfactory pathway

79. The hyperkinetic features of the Huntington's disease are due to the loss of neurons in the:
- nigrostriatal dopaminergic system
  - intraatrial cholinergic system
  - GABAergic and dopaminergic system
  - intraatrial GABAergic and cholinergic system
80. Epiphysial closure in humans is caused (mediated) by:
- androgens
  - estrogens
  - growth hormone
  - thyroxine
81. If a genetically male fetus with functional testes is born with male internal genitalia and female external genitalia, which of the following is the **most likely** explanation?
- Loss of function mutation in SRY gene
  - Deficiency of testosterone
  - Deficiency of Mullerian inhibiting peptide
  - Deficiency of testosterone 5 $\alpha$  reductase
  - Complete androgen insensitivity
82. Of those mentioned below, which of the following is **least likely** in a normal pregnancy?
- Increase in heart rate
  - Increase in cardiac output
  - Increase in blood volume
  - Decrease in pulse pressure
83. The SI unit of pressure is:
- mm Hg
  - cm H<sub>2</sub>O
  - Pascal
  - Torr
84. Which method is dependable for measuring cardiac output when cardiac output is low?
- Fick principle
  - Thermodilution method
  - Indicator dilution method
85. Breathing in individuals with restrictive lung disease is typically:
- slow and deep
  - slow and shallow
  - rapid and deep
  - rapid and shallow
86. The mitotic spindle is made up of a protein called:
- tubulin
  - caveolin
  - connexin
  - annexin
87. When a heavy object in hand is lowered, the extension at the elbow is brought about by:
- active shortening of the extensors
  - passive shortening of the extensors
  - active lengthening of the flexors
  - active shortening of the flexors
88. Rod cell excitation by photons results in the conversion of:
- 11-cis-retinal to 11-trans-retinal
  - 11-cis-retinal to all trans-retinal
  - all trans retinal to all cis-retinal
  - 11-trans-retinal to 11-cis-retinal
89. Which of the following is characterized by a hypercontractile, shrunken bladder, increased frequency of urination and incontinence?
- Deafferented bladder
  - Denervated bladder
  - Spastic neurogenic bladder
  - Bladder in acute paraparesis
90. The smooth muscle relaxing effects of endothelium derived relaxing factor nitric oxide are mediated by an increase in intracellular levels of
- cAMP
  - cGMP
  - calcium
  - endothelin
91. Calculate the osmolality of plasma given that plasma glucose is 108 mg/dL, plasma [Na] is 125 mM, and blood urea nitrogen is 140 mg/dL.
- 300 mOsm/Kg H<sub>2</sub>O
  - 306 mOsm/Kg H<sub>2</sub>O
  - 312 mOsm/Kg H<sub>2</sub>O
  - 318 mOsm/Kg H<sub>2</sub>O
92. Which of the following markers is **incorrectly** matched with its volume of distribution?
- Antipyrine - total body water

- B. Inulin - ECF volume  
 C. Evans blue - plasma volume  
 D.  $I^{125}$  albumin - blood volume
93. Which of the following processes does **not** exhibit 'saturation kinetics'?
- A. Facilitated diffusion  
 B.  $Na^+ - Ca^{2+}$  exchanger  
 C. Simple diffusion  
 D.  $Na^+$  coupled active transport
94. Insulin dependent glucose uptake into skeletal muscle and adipose tissue is mainly mediated by:
- A. GLUT 1  
 B. GLUT 2  
 C. GLUT 3  
 D. GLUT 4
95. Insulin secretion from *beta* cells of pancreas in response to a glucose load is mediated by:
- A. GLUT 1  
 B. GLUT 2  
 C. GLUT 3  
 D. GLUT 4
96. Which of the following is **not** true about cerebrospinal fluid?
- A. Its pH is less than that of plasma  
 B. It is formed in arachnoid villi  
 C. It normally does not contain neutrophils  
 D. Leakage of CSF during dural tap causes headache
97. Which of the following mechanisms is currently implicated in learning and memory?
- A. Modulation of release of neurotransmitters in postsynaptic neurons in response to repeated firing of presynaptic neurons  
 B. Modulation of neurotransmitter receptor synthesis in postsynaptic neurons  
 C. Formation of new neurons  
 D. Spatial organization of association areas
98. The first reflex response to reappear during recovery from spinal shock is the
- A. tympanic reflex  
 B. withdrawal reflex  
 C. neck righting reflex  
 D. labyrinthine reflex

99. The concentration of sodium in normal human plasma varies from
- A. 280 – 295 mOsm/Kg  $H_2O$   
 B. 135 – 145 mOsm/Kg  $H_2O$   
 C. 240 – 255 mOsm/Kg  $H_2O$   
 D. 95 – 110 mOsm/Kg  $H_2O$

100. Arterial blood gas analysis of a 5-year-old child at sea level gives the following results: pH 7.41,  $PaO_2$  100 mmHg, and  $PaCO_2$  40mm Hg. The child is being mechanically ventilated with 80% oxygen. What is the (A-a)  $PO_2$ ?
- A. 420 mm Hg  
 B. 470 mm Hg  
 C. 520 mm Hg  
 D. 570 mm Hg

101. Physiologic dead space ventilation is **decreased** by:
- A. upright position  
 B. positive pressure ventilation  
 C. neck flexion  
 D. emphysema

102. What does the macula densa sense?
- A. Na concentration of fluid delivered to it  
 B. Cl concentration of the fluid delivered to it  
 C. Volume of fluid delivered to it

**Answers: Blast from the Past**

1C	2A	3D	4C	5C
6A	7C	8A	9D	10D
11D	12A	13C	14D	15C
16D	17C	18ABD	19C	20C
21D	22D	23C	24C	25B
26B	27A	28B	29B	30C
31D	32D	33B	34A	35C
36B	37B	38C	39D	40D
41A	42B	43C	44A	45C
46C	47D	48B	49D	50C
51D	52C	53D	54D	55D
56D	57A	58A	59A	60C
61D	62A	63B	64C	65D
66A	67B	68A	69C	70C
71A	72D	73C	74C	75B
76B	77AB	78D	79D	80B
81D	82D	83C	84A	85D
86A	87C	88B	89C	90B
91B	92D	93C	94D	95B
96B	97all	98B	99B	100A

101C	102BC			
------	-------	--	--	--

**Answer Explanations:**

1. Volume of distribution of this substance = 30% of total body water (TBW). In a healthy adult male weighing about 70 kg, the volumes of ICF and ECF are 28 and 14 L respectively; i.e., 1/3<sup>rd</sup> of TBW is outside cells. Thus, the substance in question distributed exclusively in ECF.

2. TBW = ICF + ECF volumes = 28 + 14 = 42 L  
 Concentration of potassium in ICF = 140 mM  
 Concentration of potassium in ECF = 5 mM  
 Plasma volume = 3.5 L  
 Volumes of all other fluids combined = 38.5 L  
 Amount of K contained in plasma is about 20 mM.  
 Amount of K in all other fluids = 3980 mM  
 Thus, about 0.4% of potassium is in plasma

3. 1 gram mole of MgSO<sub>4</sub> = 1000 mM MgSO<sub>4</sub>  
 Each molecule of MgSO<sub>4</sub> dissociates to give 2 ions viz., Mg and sulphate.  
 Thus, 1000 mM = 2000 mOsm/L  
 1 mOsm/L exerts a pressure of 19.3 mm Hg  
 Therefore, 2000 mOsm/L will exert an osmotic pressure = 19.3 × 2000 = 38600 mm Hg

4. Concentration of KCl = 39 mg % = 39 mg/dL = 390 mg/L = 0.390 g/L  
 Molar mass of K = 39 g  
 1 mole of K = 39 g/L  
 Thus, 0.39 g of K = 10 mM of K

5. The term emiocytosis based on a limited search appears to be essentially the same as exocytosis, and it is not frequently used in recent literature. Emiocytosis (exocytosis) of secretory granules requires a rise in intracellular calcium – for example, the release of insulin by B cells of the pancreas involves depolarization of the B cell by closure of K channels followed by influx of calcium through voltage dependent calcium channels. The transient rise in intracellular calcium brings about emiocytosis of granules that contain insulin, proinsulin, C-peptide.

6. Osmotic pressure is simply dependent upon the number of particles and not the mass of a substance. Albumin (or plasma proteins) does not

make a significant contribution to the osmolality and osmotic pressure of plasma because they are found in concentrations much lower than Na, Cl – the most effective osmoles in ECF. However, albumin is quantitatively the most important contributor to the *colloid osmotic pressure of plasma (oncotic pressure) because it is restricted to plasma and does not exit the capillary as fast.* Among plasma proteins it is the most abundant and hence it contributes the most to colloid osmotic pressure of plasma.

7. Crystalloids include NaCl, Ringer's lactate; colloids include large molecular weight substances such as plasma proteins, plasma expanders like dextran, gelatin and hydroxyethyl starch.

8. While the strength duration curve can tell us if a nerve is functioning or not or what the degree of impairment is at a point in time, of late, it has been superseded by electromyography which has this capability and a wider range of uses. That is why, perhaps, little mention is made about SD curve these days in textbooks. The only advantage of the SD curve is that it is noninvasive. Electromyography (EMG) can be recorded with surface as well as needle electrodes. The occurrence of reinnervation potentials or denervation potentials (obtainable only with an EMG) may be used for prognostication.

11. A 1°C decrease in temperature reduces cerebral metabolic rate for oxygen by 7%.

12. Type B fibers are more susceptible to blockade by anesthetics compared to type A fibers, which have a larger diameter. Sympathetic preganglionic neurons, which originate in the intermediolateral column of the thoracolumbar segments of the spinal cord, are type B fibers.

15. In the dark, the prosthetic group retinene in retinaldehyde is in the 11-cis configuration. The action of light is to change the shape of this to the all-trans isomer.

17. Sleep walking, bed wetting and night terrors occur during slow wave sleep or, more specifically during arousal from slow wave sleep.

They are not associated with REM sleep See *p* 200-1, *Ch 11, WFG, 2005*.

18. Cerebral blood flow is regulated by local metabolites and hypoxia would cause vasodilation and thereby slightly increase flow. Similarly, hypercapnia produces cerebral vasodilation and an increase in cerebral blood flow.

23. Cushing's triad, which was originally described in some patients with raised intracranial tension, includes hypertension, bradycardia and irregular respiration but it is uncommon to have all signs in a patient.

24. Neurotransmitters that increase food intake are said to be orexigenic. Two neurotransmitters with orexigenic effects are the polypeptides orexin A and orexin B. Orexins are synthesized in neurons located in the lateral hypothalamus. The feeding center is located in the lateral hypothalamus. Ghrelin and neuropeptide Y also stimulate food intake. In contrast, leptin from adipose tissue acts on the hypothalamus signaling satiety and inhibits food intake.

25. Melatonin is synthesized in the pineal gland starting from tryptophan.

26. Postganglionic sympathetic (noradrenergic) neurons innervating the pineal commence in the superior cervical ganglion and reach it via *nervi conarii*.

27. Specific dynamic action (SDA) of food (also called thermic effect of feeding, diet induced thermogenesis) is a physiological phenomenon that represents energy expended on all activities of the body incidental to the ingestion, digestion, absorption, and assimilation of a meal. Metabolic rate starts increasing 30 min after a meal, stays high for about 2 hours and declines to the resting level within 4 hours. The energy expended depends upon the volume, caloric content, consistency, and composition of meal.

28. While cutaneous vasodilation and sweating go together, however, cutaneous vasodilation per se could contribute to heat loss even if it were not accompanied by increased sweating.

29. This question tests if we understand the importance of masking the untested ear when performing the Rinne's test. For example, if we were testing the right ear, how sure are we that the person hears through the right ear and not on the left? To ensure this does not happen, the untested ear is masked using a Barany's noise box. Alternately, we could ask the patient to insert his finger in the left ear and make quick noisy movements during the Rinne's test.

Second, the results of Rinne's and Weber's test must be interpreted together and not in isolation.

In this case, the Rinne's test was negative (called 'false negative') because there is apparently no defect in ossicular conduction on the right side. Furthermore, Weber's test was localized to the left side. Taken together, this is indicative of sensorineural deafness on the right side.

Absolute bone conduction of a test subject could also be compared with a reference subject whose hearing is known to be normal. The results of this test (Schwabach's test) are useful in detecting early sensorineural deafness.

31. ADH is stored in the posterior pituitary bound to neurophysins. However, ADH circulates free in plasma.

33. Using Henderson equation,  $[H^+]$  of blood can be calculated to be 72 nM. That is, the individual has metabolic acidosis. CSF  $[H^+]$  is directly proportional to  $PaCO_2$ . Since  $PaCO_2$  is 30 mm Hg (10 mm Hg lower than it normally is), CSF pH must be higher than normal. Normally, CSF pH is 7.33. From the options given, 7.4 is the only answer one can choose.

34. Normally, total serum calcium ranges from 8-10 mg/dL. Normally, the ratio of protein bound calcium to ionized calcium is approximately 1:1. In this case, total calcium = 6 mg/dL. A decrease in total calcium could be due to:

- Decrease in serum protein
- Decrease in ionized calcium

Thus, it is appropriate to seek to determine if hypoalbuminemia is the cause of hypocalcemia.

36. The 46 XX primary oocyte undergoes meiosis which consists of two phases.

Phase 1: Meiosis (reduction division) results in the formation of secondary oocyte (with a large amount of cytoplasm) and the first polar body (with little cytoplasm). The first polar body is extruded at the end of the first phase of meiotic division. This is immediately followed by ovulation. See WF Ganong, 21<sup>st</sup> Ed, Ch 23, Gonads: development and function of the reproductive system, pp 438. I think that the best answer for the question is “at the time of ovulation”. Ovulation is the release of the secondary oocyte from the ovary.

Phase 2: The 23X secondary oocyte immediately begins a mitotic division but this is arrested in metaphase until fertilization occurs. After fertilization, the mitotic division is completed and the second polar body is extruded.

37. The phenotypic sex is female (it is a baby girl); gonadal sex is male (because the surgeons are telling that the inguinal masses are testes). We are to *predict* chromosomal sex (genetic sex) based on this information. Since testes are present, the sex-determining region (SRY) of the Y chromosome, which encodes a transcription factor that is required for the development of embryonic testes, must be present. This gene is normally located on the Y chromosome. Thus the most likely genotype is 46XY. In contrast the 47XXY genotype does not lead to feminization (the phenotype is that of Klinefelter’s syndrome).

With the information we are given in the problem, we cannot however distinguish whether this baby girl has testosterone 5-alpha reductase (type 2) deficiency or complete androgen insensitivity. If needed see the summary on principles of diagnosis of disorders of sexual differentiation in the earlier chapter on *Endocrinology and Reproduction*.

45. Androgens stimulate erythropoiesis. Estrogens have been noted to have an inhibitory influence on

erythropoiesis. This may be one reason why anemia occurs in hyperestrogenic states; perhaps, the anemia is relative rather than absolute, i.e., due to a greater increase in plasma volume rather than a reduction in total red blood cell volume. High levels of ACTH (via cortisol) stimulate erythropoiesis and polycythemia may be a striking feature of Cushing syndrome. Thyroxine and prolactin also stimulate erythropoiesis.

48. Sensitization of the mother’s immune system with fetal Rh antigens results in the production of anti-Rh immunoglobulin. First, IgM is formed but this is too large to cross the placental barrier.

The major antibody in the primary immune response is IgM. However, over a time period that varies from individual to individual, IgG is also produced as part of this response, although the titer of IgG is usually not sufficient to evoke significant hemolysis in the first pregnancy. On the other hand, in a woman who has been previously sensitized with Rh antigen and anti D IgG titers were significant, significant hemolysis could occur even during the first pregnancy.

52. You can see that the depolarization is from a focus in the ventricle. The beat could not have originated in an atrial focus since it has not reset the sinus rhythm. An atrial premature beat is not usually followed by a compensatory pause; it is conducted to the SA node and it “resets” sinus rhythm. In contrast, a ventricular premature beat is usually not conducted retrograde through the AV node to the SA node, so it does not reset normal sinus rhythm.

The duration of premature ventricular depolarization is longer than a normal QRS complex since it is conducted much slowly through the myocardium rather than through the normal conducting pathway. Thus the resulting ventricular contraction is unlikely to have been really “premature”. So enough ventricular filling would likely have occurred and the beat must have been strong enough for the aortic valve to open (and then close). Thus both heart sounds would most likely have been present at beat X. The learning point here is that a *premature*

*ventricular depolarization* does not always result in a *premature beat*.

53. For correct estimation of blood volume as well as cardiac output, the dye must remain in the blood stream.

55. Without the carotid pulse transducer, LVET cannot be determined. Since  $PEP = QS_2 - LVET$ , PEP cannot also be determined.

56. Note that blood loss occurs over a 30-minute period (a common example is venesection of a healthy adult blood donor). There occurs only a slight increase in HR because of a reduction in central blood volume. BP is maintained in the steady state, and one cannot detect the fall in BP by intermittent sphygmomanometry.

57. When MAP is in the normal range, i.e., between 70 and 110 mm Hg, an increase in BP results in an increase in discharge rate from the carotid sinus. Activity in the buffer nerves inhibits tonic vasoconstrictor discharge from the medulla. Therefore, sectioning of the buffer nerves when MAP is normal would result in acute elevation of BP. This is called **neurogenic hypertension**.

A MAP less than 70 mm Hg is a **hypotensive state**. When MAP is as low as 60 mm Hg, discharge rate in carotid baroreceptors is already minimal and the resulting reflex sympathoexcitation is manifest. Thus, sectioning of afferents from arterial baroreceptors at such a low MAP would not be expected to have further sympathoexcitatory effects.

On the other hand, when MAP is as low as 60 mm Hg, blood flow through the arterial chemoreceptors near the carotid sinus would be reduced. A reduction in either PaO<sub>2</sub> and/or a decrease in flow through the chemoreceptors lead to a reflex increase (via afferents from carotid bodies) in sympathetic outflow that serves to bring BP back into the normal range. Thus, when the buffer nerves are sectioned at a time when MAP is lower than normal, BP would fall further. See p. 628, Ch 33, WFG, 2005.

**Summary:** When MAP is reduced below 70 mm Hg, arterial baroreceptor discharge is maximally inhibited and sympathetic outflow is disinhibited as a result of this; apart from this, activation of the arterial chemoreflex contributes significantly to “increasing” MAP at such low pressures.

61. Why does edema not occur in early stage forward heart failure?

*Follow this sequence from i to vii*

- i. Acute cardiac failure (‘forward failure’)
- ii. By definition, cardiac output (Q) is reduced
- iii. Thus, whole body perfusion (and oxygen delivery is reduced)
- iv. Accumulation of metabolites causes a drop in peripheral resistance (TPR)
- v.  $MAP = Q \times TPR$
- vi. MAP falls (i.e. systemic capillary hydrostatic pressure falls) as a result of a reduction in Q and TPR
- vii. Since capillary hydrostatic pressure falls, edema is unlikely.

Stated in another way, if edema is not observed in an individual who truly has heart failure, then this is the most likely explanation.

62. All organs are capable of autoregulating their blood flows. Although cerebral vessels have noradrenergic innervation, cerebral blood flow itself is not chronically under neural control. Cerebral blood flow is excellently autoregulated in the steady state when mean arterial pressure is between 65 and 140 mm Hg.

Although the heart is also capable of excellent autoregulation, under certain circumstances, neural regulatory mechanisms override local regulatory mechanisms. For example, sudden excessive discharge in the sympathetic fibers to the heart can cause severe coronary vasospasm and a severe reduction in coronary blood flow.

Cutaneous blood flow is most often varied in response to neural signals from the hypothalamus. It is the vascular bed that is most consistently under neural control.

64. If needed, review tracings of pressure and volume in various chambers during various phases of the cardiac cycle, including pulmonary artery pressures.

65. Reynolds number  $Re = \rho DV/\eta$   
 $\rho$  is the density of the fluid;  
 $D$  is the diameter of the vessel;  
 $V$  is the blood flow velocity; and  
 $\eta$  is the viscosity of fluid.  
Flow is turbulent when  $Re$  exceeds 3000;  
See p. 583, Ch 30, WFG, 2005.

66. The major force driving filtration is the capillary hydrostatic pressure, which is normally about 40 mm Hg at the arterial end of the capillary in a capillary that is at the level of the heart. More precisely, transcapillary hydrostatic pressure gradient is the major factor.

67. At functional residual capacity, lungs and the chest wall recoil in opposite directions causing the intrapleural (intrathoracic) pressure to be negative.

68. Hb F binds 2,3 BPG less avidly compared to Hb A and therefore has a greater affinity for oxygen relative to Hb A. This is one reason why it is able to draw O<sub>2</sub> from Hb A.

69. Hey! Here is a professor with a passion for SI units, asking a “you miss – I hit” kind of a question! The question is designed to test whether we know how to convert pressure in mm Hg to Pascals. Here it is:  
1 atm = 760 mm Hg = 100 kPa  
7.6 mm Hg = 1 kPa

70. Methemoglobin cannot transport oxygen. Less than 1% of Hb is in the Fe<sup>3+</sup> state. Methemoglobin cannot also unload oxygen much like carboxyhemoglobin. Thus, there is also a leftward shift of the oxyhemoglobin dissociation curve. Taken together, the oxygen content of blood is reduced in methemoglobinemia and the oxygen unloading capacity of blood is reduced even more.

Carbon monoxide poisoning reduces oxygen content of arterial blood by competing with oxygen to bind heme. Respiratory acidosis is associated with severe hypoxemia.

Methemoglobin binds oxygen but is not capable of unloading oxygen until it is reduced to ferrihemoglobin.

Clinically, respiratory acidosis is always accompanied by arterial hypoxemia (type II respiratory failure).

However, in cyanide poisoning, oxygen content of blood is normal, yet utilization of oxygen in the mitochondria is inhibited because cyanide inhibits cytochrome oxidase, the final donor of electrons to molecular oxygen.

71. The fact that oxygen saturation of Hb is as low as 60% although PaO<sub>2</sub> is as high as 300 mm Hg suggests a diagnosis of carbon monoxide poisoning straightaway.

72. This reflex helps a newborn child inflate its liquid filled lungs.

73. O<sub>2</sub> carrying capacity of blood:  
0.003 ml O<sub>2</sub> per mm Hg O<sub>2</sub> tension per deciliter of blood  
i.e.,  $3 \times 10^{-3}$  ml O<sub>2</sub> per mm Hg O<sub>2</sub> tension per deciliter of blood  
=  $3 \times 10^{-5}$  ml of O<sub>2</sub> per mm Hg O<sub>2</sub> tension per ml of blood  
Here, O<sub>2</sub> carrying capacity = 0.0025 ml.  
Oxygen tension should have been  $2.5 \times 10^{-3}$   
Divided by  $3 \times 10^{-5}$   
= 80 mm Hg

76. PAH clearance gives effective RPF  
Clearance of PAH depends upon its plasma concentration. Secretory and reabsorptive processes have a rate maximum i.e., they can be saturated. When a high dose is used, PAH secretory capacity is overwhelmed and clearance of PAH reflects this secretory capacity rather than RPF. So  $U_{PAH} V / P_{PAH}$  i.e. PAH clearance will be low, and estimated RPF will be falsely low.

80. Estradiol (an estrogen) ultimately terminates linear growth by causing epiphyses to fuse to the long bones (**epiphysial closure**) in males as well as females. In males, this estradiol is **not** from that in the circulation; it is estradiol that is formed

locally in the epiphyseal growth plate by the action of bone aromatase enzyme on testosterone that reaches it from the testes. This is not to say that sex hormones inhibit linear growth. Rather the pubertal growth spurt is due to the synergism between sex hormones and other hormones (GH, IGF-1, thyroid hormones), and when the epiphyseal plate concentration of estradiol reaches a certain threshold, it mediates epiphyseal closure. Patients with sexual precocity are apt to be dwarfed because of premature epiphyseal closure.

82. Pregnancy is a classic example of a hyperdynamic circulatory state in which total peripheral resistance is lowered as a result of opening a new vascular bed (placenta) in the systemic circulation. Blood volume, heart rate and cardiac output are increased. The diastolic pressure drops and pulse pressure increases; MAP is maintained.

84. This is because when flow is reduced, flow velocity is reduced and temperature is quickly dissipated thereby rendering an accurate measurement of pulmonary blood flow difficult.

On the other hand, Fick's principle is dependable when cardiac output is low since arteriovenous oxygen difference is quite high and oxygen uptake across the lungs reduces.

Note that cardiac output (or pulmonary blood flow) equals oxygen uptake across the lungs divided by whole-body arteriovenous oxygen difference.

When there are intracardiac shunts, Fick's method will either overestimate or underestimate cardiac output depending on whether the shunt is left-to-right or right-to-left.

Furthermore, when there is a ventricular septal defect, mixed venous blood must be taken from the right atrium rather than the pulmonary artery, i.e. venous blood must be taken proximal to the shunt. *Harrison's Principle of Internal Medicine, 16<sup>th</sup> ed., vol. 2, p 1329-30.*

87. Take a rather heavy object in your hand and try lowering it toward the ground. When you do

so, you will feel the tension in your biceps, yet the elbow extends; that is, although biceps develops tension, it lengthens. One must understand the difference between contraction of sarcomeres which leads to development of tension, and change in muscle length that depends upon load. Sarcomeres contract and develop force but the muscle can shorten or lengthen depending upon the load. If a muscle lengthens while developing force, external work done is negative.

$$91. \text{Plasma osmolality (mosm/L)} = 2 [\text{Na}^+] + [\text{glucose}] / 20 + [\text{BUN}] \times 18/50$$

(mmol/L)      (mg/dL)      (mg/dL)

97. It is now established that the longheld belief that we do not add brain cells after birth is incorrect. New neurons arise from stem cells in the olfactory bulb and hippocampus and since formation of long-term memories occurs in the hippocampus, it is possible that the two are related; this hypothesis is currently intensely researched. [*p 270, Ch 16, WFG, 2005*]

98. The tympanic reflex, labyrinthine reflex and neck righting reflex are not integrated in the spinal cord.

100. PAO<sub>2</sub>  
 $= [(\text{PB} - \text{PH}_2\text{O}) \times \text{FiO}_2] - [(\text{PACO}_2) / \text{RER}]$ .  
 This is the "alveolar gas equation" that is used to estimate the oxygen tension of alveolar gas. In this problem,  
 PB = 760 mm Hg, FiO<sub>2</sub> = 0.8; PaCO<sub>2</sub> = PACO<sub>2</sub> = 40 mm Hg, and RER is assumed to be 0.8. Substituting we get, PAO<sub>2</sub> = 520 mm Hg  
 Arterial PO<sub>2</sub> = 100 mm Hg  
 Thus, D (A-a) O<sub>2</sub> = 420 mm Hg.  
 This represents a considerable defect in gas exchange as normally the difference between alveolar and arterial oxygen tension is not greater than 10 mmHg.

The learning point here is that a PaO<sub>2</sub> of 100 mmHg is not necessarily reflective of gas exchange function of lungs as it is influenced by the oxygen concentration of inspired gas.

Rather, D (A-a) O<sub>2</sub> is a measure of oxygen exchange function of lungs.

101. Extension of the neck, positive pressure ventilation, and emphysema increase ventilation of dead space.

In the case of positive pressure ventilation, total dead space increases depending on:

- the volume of the tubing used;
- regional differences in lung compliance in patients with lung disease

\*\*\*\*\*

## More Questions for Self-Study: General Physiology

Unless otherwise indicated, choose the single best answer.

1. The philosophy that all vital mechanisms are directed toward maintaining constancy of composition of the internal environment and that this is necessary for the sustenance of life was first propounded by:

- A. Claude Bernard
- B. Walter B Cannon
- C. William Harvey
- D. Alan Hodgkin

2. The term 'homeostasis' was coined by:

- A. Claude Bernard
- B. Walter B Cannon
- C. Homer Smith
- D. William Harvey

3. In adults, ECF volume is about \_\_\_\_\_% of body weight

- A. 10%
- B. 20%
- C. 30%
- D. 40%

4. In a healthy adult male weighing 70 kg, the total volume of fluid present in the transcellular compartment does not exceed:

- A. 1 liter
- B. 3 liters
- C. 5 liters
- D. 7 liters

5. Which of the following statements regarding body fluid compartments is **incorrect**?

In health,

- A. blood volume is about 70-80 ml/kg body weight
- B. the ratio of ICF to ECF volumes is about 2
- C. ICF volume accounts for about 60% of body weight.

6. Radioiodinated albumin is a marker that can be used to measure the volume of:

- A. plasma
- B. interstitial fluid

- C. ECF  
D. red blood cells
7. Which of the following is **not** isosmotic with normal human plasma?  
A. 5% dextrose  
B. 0.85% NaCl  
C. 20% mannitol
8. In the steady state, the value of which of the following variables is the same in ICF and ECF?  
A. pH  
B. osmolality  
C. concentration of proteins  
D. number of osmoles
9. ICF volume does **not** change when dehydration is:  
A. isotonic  
B. hypertonic  
C. hypotonic
10. Which of the following modes of transport is quantitatively more important?  
A. Diffusion  
B. Filtration  
C. Vesicular transport
11. Which of the following is an example of primary active transport?  
A. Ca extrusion from cells by the Na-Ca exchanger  
B. Glucose entry into cells through glucose transporter 2 (GLUT-2)  
C. H<sub>2</sub>O flux across cell membranes through aquaporins  
D. Glucose uptake into intestinal epithelial cells by Na-glucose cotransporter 1 (SGLT-1)  
E. Ca sequestration in sarcoplasmic reticulum by Ca-ATPase
12. Sodium-glucose cotransport in the intestine and kidney is an example of:  
A. primary active transport  
B. secondary active transport  
C. facilitated diffusion  
D. passive transport
13. Which of the following is / are active transport processes? (*Tick all that apply*)

- A. Extrusion of calcium into ECF  
B. Efflux of K during repolarization  
C. Entry of chloride into neurons  
D. Transcytosis (vesicular transport)

14. The most abundant protein in mammalian cells is:

- A. actin  
B. collagen  
C. titin  
D. dystrophin

15. Gap junctions are made up of a protein called:

- A. connexin  
B. clathrin  
C. cadherin  
D. calcineurin

16. The mitochondrial genome is absent from:

- A. sperm cells  
B. ovum  
C. mature red blood cells  
D. white blood cells

#### ***Whatzit***

- The most abundant cation in ECF
- The most abundant anion in ECF
- The most abundant cation in ICF
- The most abundant protein in blood
- The ion that is absorbed as well as secreted by the kidney

#### **Answers (to *Whatzit*):**

- Sodium
- Chloride
- Potassium
- Hemoglobin
- Potassium

#### **Answers for Practice Questions in General Physiology**

1A	2B	3A	4A	5C
6A	7C	8B	9A	10B
11E	12B	13AD	14A	15A
16C				

5. ICF volume constitutes  $\frac{2}{3}$ <sup>rd</sup> of total body water (not body weight). In a healthy adult weighing about 70 kg, ICF volume (28 liters) is about 40% of total body weight.

9. Isotonic dehydration (example, that due to loss of blood or plasma), is the result of proportional loss of NaCl and water (basically a fluid with the composition of plasma minus proteins) from ECF, and there is no change in ECF osmolality. There is thus no drive for movement of water between ICF and ECF, and therefore there is no change in ICF volume. Therapy is aimed at replenishing ECF volume such as with 0.9% NaCl (a solution that is isotonic with normal human plasma) is used. In hypertonic dehydration, steady state ECF osmolality increases; thus, it leads to intracellular dehydration as well. In hypotonic dehydration, steady state osmolality of ECF is decreased and some of this water will enter cells.

11-13. If needed, review the Supplement on *Transport across cell membranes in Chapter 1.*

14. Proteins are translocated from capillaries into the interstitium by transcytosis (vesicular transport). This involves endocytosis of the protein molecules into vesicles in endothelial cells and exocytosis of these vesicles into the interstitium.

18. Actin is present in virtually all cells although most abundant in muscle. Collagen is the most abundant protein in extracellular matrix. Titin is the largest protein in the human body. Dystrophin is a glycoprotein in the muscle cell membrane; it is involved in transmitting the tension generated by shortening of sarcomeres eventually to the tendon.

15. Clathrin is a protein involved in receptor-mediated endocytosis; it is the protein that coats pits that are the sites of aggregation of cell-surface receptors involved in receptor-mediated endocytosis. Cadherin is a cell adhesion molecule. Calcineurin, like calmodulin, is a calcium binding protein found in cells.

16. Mature RBCs do not have mitochondria; these cells exclusively use anaerobic glycolysis to generate ATP.

Although sperm cells contain mitochondria, mitochondria from sperm cells do not enter the

secondary oocyte during fertilization; i.e., mitochondrial DNA in the zygote is exclusively of maternal origin.

\*\*\*\*\*

## More Questions for Self-Study: Nerve & Muscle Physiology

In each of the following questions, select the single best answer.

1. The RMP of some neurons is equal to the equilibrium potential of:

- A. Na
- B. K
- C. Cl
- D. Ca

2. The equilibrium potential of chloride in mammalian spinal motor neurons is about:

- A. + 20 mV
- B. - 40 mV
- C. - 70 mV
- D. - 90 mV (inside negative)

3. The largest known axons are found in:

- A. humans
- B. whales
- C. squids
- D. ostriches

4. The Nernst potential (also called the equilibrium potential) is positive for:

- A. Na and Cl
- B. Na and K
- C. Na and Ca
- D. K and Cl

5. Which of the following statements regarding nerve fibers is **incorrect**?

- A. Large diameter fibers conduct faster than small diameter fibers.
- B. Type C fibers are more susceptible to inhibition by local anesthetics.
- C. Nerves innervating skeletal muscle contain only one type of nerve fiber.

6. Excitation and contraction of skeletal muscle are coupled by:

- A. ATP
- B. myosin

- C. release of calcium into sarcoplasm  
D. calmodulin
7. Which of the following regarding slow skeletal muscle fibers is **false**? They, in comparison to fast muscle fibers:
- have a greater number of mitochondria
  - have higher myoglobin content
  - typically demonstrate oxidative metabolism
  - have the faster isoform of myosin ATPase
8. Which of the following is **not** observed in cardiac muscle?
- Contraction of the ventricle is an all-or-none phenomenon
  - Staircase phenomenon
  - Complete summation of successive contractions
  - Long refractory period
9. Which of the following muscles consists predominantly of *fast* muscle fibers?
- Soleus
  - Diaphragm
  - Orbicularis oculi
  - Detrusor
10. Which of the following proteins is absent from smooth muscle?
- Actin
  - Myosin
  - Troponin
  - Tropomyosin
11. Which of the following statements about visceral smooth muscle is **incorrect**?
- Neighboring cells are electrically coupled by means of gap junctions
  - Force is graded by varying intracellular calcium
  - Stretch of smooth muscle consistently elicits active contraction
12. Oxidative capacity is highest in:
- type I muscle fibers
  - type II muscle fibers
  - type F muscle fibers
13. Which of the following statements about gastrointestinal smooth muscle is **incorrect**?
- Contraction can occur in the absence of extrinsic neural innervation.
  - Within limits, stretch increases tone.
  - It always exhibits linear length-tension relationships.
  - Twitch duration is typically longer when compared to skeletal muscle.
14. The calcium-binding protein that plays a key role in the regulation of smooth muscle cell contraction is:
- dystrophin
  - calmodulin
  - troponin C
  - calcineurin
15. An example for *multi-unit smooth muscle* is:
- stomach
  - myometrium
  - iris
  - vascular smooth muscle
16. Actin is tethered to Z-lines in the sarcomere by:
- actinin
  - titin
  - nebulin
  - dystrophin
17. A stronger than normal stimulus can cause excitation of nerve or muscle during:
- absolute refractory period
  - relative refractory period
  - spike potential
  - overshoot
18. Under basal conditions, which is the predominant energy substrate utilized by cardiac muscle?
- Carbohydrate
  - Amino acids
  - Ketones
  - Fatty acids
19. The gene coding for which of the following proteins is the largest?
- Titin
  - Dystrophin
  - Gigantin
  - Nebulin

20. At a given stimulus intensity, the increase in the force of muscle contraction with increasing frequency of stimulation is referred to as:

- A. tetanus
- B. tetany
- C. staircase phenomenon
- D. summation

**Answers: Self-Study in Nerve-Muscle Physiology**

1C	2C	3C	4C	5C
6C	7D	8C	9C	10C
11C	12A	13C	14B	15C
16A	17B	18D	19B	20C

**Answer Explanations:**

8. Summation of the type seen in skeletal muscle cannot occur in cardiac muscle. That is, a second contraction cannot begin before the previous contraction (systole) is completed and diastole (filling) has commenced. However, a premature depolarization and premature contraction can occur when the ventricle is just filling with blood.

\*\*\*\*\*

**More Questions for Self-Study: Central Nervous System**

*Some quizzical questions*

**Whatzit:**

- 1. The photoreceptor protein in rod cells:
- 2. The organ of hearing:
- 3. The fluid present in the scala media:
- 4. The unit of sound pressure:
- 5. The fluid present in the bony labyrinth:
- 6. The muscles subserving the tympanic reflex:

**Answers to Whatzit:**

- 1. Rhodopsin
- 2. Organ of Corti
- 3. Endolymph
- 4. Decibel
- 5. Perilymph
- 6. Stapedius and tensor tympani

**What is the**

- 1. major excitatory neurotransmitter in the brain
- 2. main inhibitory neurotransmitter in the brain

- 3. neurotransmitter released by small intensely fluorescent (SIF) cells in autonomic ganglia
- 4. neurotransmitter released by Golgi bottle neurons
- 5. neurotransmitter released by Renshaw cells
- 6. major neurotransmitter released by sympathetic postganglionic neurons
- 7. cotransmitter released by sympathetic postganglionic neurons
- 8. major neurotransmitter released by parasympathetic postganglionic neurons
- 9. cotransmitter released by some parasympathetic postganglionic neurons
- 10. neurotransmitter released by all autonomic preganglionic neurons

**Answers:**

1	Glutamate	6	Norepinephrine
2	GABA	7	Neuropeptide Y
3	Dopamine	8	Acetylcholine
4	Glycine	9	Vasoactive intestinal polypeptide
5	Glycine	10	Acetylcholine

**State whether the following statements are true or false.**

- 1. There are no photoreceptors overlying the optic disk.
- 2. Renshaw cell is an inhibitory interneuron.
- 3. Olfactory receptors are free nerve endings.
- 4. Sign of Babinski is an unequivocal sign of a corticospinal tract lesion.
- 5. The muscle spindle is basically a stretch receptor that responds to changes in muscle length.
- 6. The muscle spindle is part of a feedback circuit regulating muscle length.
- 7. The Golgi tendon organ is part of a feedback circuit regulating muscle force.

8. Extrafusal muscle fibres can be made to contract by stimulation of alpha motor neurons.
9. Increased gamma efferent discharge increases the sensitivity of the stretch reflex.
10. If gamma motor neurons innervating a skeletal muscle were cut, tone of that muscle would decrease.
11. If Ia afferents from skeletal muscle were cut, muscle tone would decrease.
12. Botulinum toxin inhibits the release of acetylcholine at the skeletal muscle neuromuscular junction.
13. Strychnine produces convulsions by blocking glycine receptors on *alpha*-motor neurons.
14. Tetanospasmin produces spastic paralysis by preventing the release of glycine from Renshaw cells (inhibitory interneurons) in the spinal cord.

*Answers:* All statements 1-14 are true.

**In each of the following questions, match items in list A with those in list B.**

**Question 1**

**List A (Functional areas)**

1. Satiety center
2. Feeding center
3. Osmoreceptors
4. Chemoreceptor trigger zone

**List B (Location)**

- A. Ventromedial hypothalamus
- B. Anterior hypothalamus
- C. Lateral hypothalamus
- D. Area postrema

**Question 2**

**List A (Brodmann's area)**

1. Areas 3, 1, 2
2. Area 41
3. Area 17
4. Areas 18 and 19

5. Area 4

**List B (Function)**

- A. Visual association area
- B. Primary auditory area
- C. Primary visual cortex
- D. Primary somatosensory cortex
- E. Primary motor cortex

**Question 3**

**List A (Glial cells)**

1. Oligodendroglia
2. Microglia
3. Astrocytes
4. Schwann cells

**List B (Functions)**

- A. Blood-brain barrier
- B. Myelin synthesis
- C. Scavenger cells
- D. Neurotransmitter reuptake

**Question 4**

**List A**

1. Eye movements, stance, and gait
2. Truncal and proximal limb movements
3. Coordination of movements of distal parts of the limbs

**List B**

- A. Vestibulocerebellum
- B. Spinocerebellum
- C. Neocerebellum

**Question 5**

**List A (Circumventricular organ)**

1. Median eminence
2. Organum vasculosum of lamina terminalis (OVLT)
3. Subfornical organ (SFO)
4. Area postrema (AP)

**List B (Function)**

- A. When activated by circulating angiotensin II, signal to the *thirst center* and supraoptic and paraventricular nuclei of the hypothalamus
- B. Chemoreceptor trigger zone
- C. Site where hypothalamo-hypophysial portal vessels originate

### Question 6

#### List A (Cortical Area)

1. Posterior parietal cortex
2. Fusiform gyrus
3. Angular gyrus
4. Posterior end of superior temporal gyrus

#### List B (Effect of lesion in this area)

- A. Prosopagnosia
- B. Anomic aphasia
- C. Wernicke's aphasia
- D. Astereognosis

#### Answers:

1	1A 2C 3B 4D
2	1D 2B 3C 4A
3	1B 2C 3DA 4B
4	1A 2B 3C
5	1C 2A 3A 4B
6	1D 2A 3B 4C

#### State if the following statements are true or false.

1. The dominant EEG rhythm in an adult human at rest with eyes closed and the mind wandering is *beta* rhythm.
2. REM sleep is called *paradoxical sleep* because it is characterized by slow waves.
3. The *alpha* rhythm in EEG is replaced by a faster irregular low voltage activity when a person does mental arithmetic.
4. Impulses in the ascending reticular activating system desynchronize cortical activity producing arousal.
5. Typically, in adults, REM sleep comprises 25% of total sleep time.
6. REM sleep deprivation produces weight loss despite adequate caloric intake.
7. There is more REM sleep in the early hours of morning.
8. Sleep spindles and K complexes are seen in REM sleep.

9. The mechanism that triggers REM sleep is located in the pons.
10. Hyperventilation elicits latent EEG abnormalities by decreasing cerebral blood flow.

#### Answers:

1F	2F	3T	4T	5T
6T	7T	8F	9T	10T

#### Notes on True-False Statements:

1. *Alpha* rhythm
2. REM sleep is called paradoxical sleep because it is characterized by high frequency EEG, similar to that observed in the awake state.
3. *Alpha* rhythm is blocked and is replaced by a high frequency, low voltage *beta* rhythm.
4. This is the function of the ascending reticular activating system.
5. The proportion of REM sleep decreases with age.
8. They are seen in Stage II sleep.
10. The decrease in PaCO<sub>2</sub> as a result of hyperventilation results in cerebral vasoconstriction; the decrease in cerebral blood flow presumably reduces the seizure threshold.

#### Temperature regulating mechanisms:

Classify items 1-8 into:

- Mechanisms that serve to conserve heat
- Mechanisms that serve to dissipate heat
- Mechanisms that serve to generate heat
- Mechanisms that reduce heat production

1. Panting
2. Sweating
3. Curling up in a ball
4. Shivering
5. Rigors
6. Specific dynamic action of food
7. Horripilation
8. The "it's too hot to move reaction"

**Heat loss mechanisms:** Panting and sweating

**Mechanisms that conserve heat:** Curling up in a ball, horripilation

**Mechanisms that generate heat:** Shivering, rigors, specific dynamic action of food (thermic effect of feeding), muscular exercise

**Mechanisms that prevent excessive heat production:** The “it’s too hot to move reaction”

\*\*\*\*\*

### **More Questions for Self-Study: Endocrinology & Reproduction**

**Instruction:** Some questions have more than one correct answer. Please **select all correct answers**.

1. The term hormone was first used to describe the actions of:

- A. secretin
- B. insulin
- C. epinephrine
- D. growth hormone

2. Which of the following is **not** a glycoprotein?

- A. Erythropoietin
- B. TRH
- C. FSH
- D. hCG

3. Which of the following hypophysiotropic hormones is a tripeptide?

- A. TRH
- B. Somatostatin
- C. Dopamine
- D. CRH

4. The three glycoprotein hormones each containing 2 subunits (an alpha and a beta subunit) produced by the pituitary are:

- A. FSH, LH and TRH
- B. TRH, ACTH and LH
- C. TSH, LH and FSH
- D. GH, TSH and LH

5. Histamine released from mast cells in the stomach stimulates the secretion of HCl by the parietal cells. What type of signaling is this?

- A. Endocrine
- B. Paracrine
- C. Autocrine
- D. Juxtacrine

6. Which of the following has the longest biologic half-life?

- A. Insulin
- B. Angiotensin II
- C. Glucagon
- D. Thyroxine
- E. ADH
- F. Nitric oxide

7. The commonest cell type in the anterior pituitary is:

- A. somatotroph
- B. lactotroph
- C. corticotroph
- D. thyrotroph
- E. gonadotroph

8. Growth hormone stimulates the secretion of:

- A. somatostatin
- B. somatomedin (IGF-1)

9. A diabetic woman who is pregnant and who has been taking recombinant insulin during the pregnancy delivered a baby weighing 5 kg. This is most closely related to:

- A. passage of maternal insulin into the fetus
- B. elevated levels of fetal insulin
- C. uteroplacental insufficiency
- D. hyperglycemia in the mother

10. Sertoli cells produce:

- A. androgen-binding protein
- B. inhibin B
- C. Mullerian inhibiting polypeptide

11. Normally, the thyroid gland secretes:

- A. CGRP
- B. PTH related peptide
- C. TSH
- D. calcitonin

12. Which of the following hormones lowers plasma level of ionized calcium?  
 A. Calcineurin  
 B. Calcitonin  
 C. Parathyroid hormone  
 D. PTH related peptide
13. Secretion of TSH is inhibited by:  
 A. dopamine  
 B. TRH  
 C. somatostatin  
 D. T3 and T4
14. For a euthyroid woman who is neither pregnant nor nursing, and taking no medication, the recommended daily dietary allowance of iodine is:  
 A. 75 micrograms  
 B. 150 micrograms  
 C. 225 micrograms  
 D. 300 micrograms
15. In a healthy adult, the thyroid gland predominantly secretes:  
 A. thyroxine  
 B. triiodothyronine  
 C. reverse T3
16. Most of the T3 in the liver is formed from circulating T4 by the action of:  
 A. type 1 deiodinase (D1)  
 B. type 2 deiodinase (D2)  
 C. type 3 deiodinase (D3)
17. Iodine is concentrated in thyroid cells by  
 A. primary active transport  
 B. secondary active transport  
 C. simple diffusion  
 D. facilitated diffusion
18. Most of the circulating T4 is bound to:  
 A. prealbumin  
 B. albumin  
 C. thyroxine-binding globulin
19. Thyroxine does **not** increase O<sub>2</sub> consumption in the:  
 A. heart  
 B. adult brain  
 C. brown adipose tissue  
 D. skeletal muscle
20. The normal basal metabolic rate in a euthyroid adult male is (BSA is body surface area):  
 A. 10-15 kcal/m<sup>2</sup> BSA/hr  
 B. 20-25 kcal/m<sup>2</sup> BSA/hr  
 C. 35-40 kcal/m<sup>2</sup> BSA/hr  
 D. 45-60 kcal/m<sup>2</sup> BSA/hr
21. TSH secretion is stimulated by:  
 A. dopamine  
 B. TRH  
 C. somatostatin  
 D. T3 and T4
22. Which of the following statements is **incorrect**?  
 A. Thyroxine is biologically more active than triiodothyronine.  
 B. The pituitary converts T4 to T3 using type 2 deiodinase  
 C. Type 3 deiodinase in the placenta inactivates T4 and T3  
 D. *Beta*-blockers in pharmacologic doses inhibit type 3 deiodinase
23. Insulin:  
 A. decreases K<sup>+</sup> uptake by skeletal muscle  
 B. increases protein catabolism in muscle  
 C. decreases cell growth  
 D. increases the utilization of ketone bodies
24. Somatostatin is found in:  
 A. pancreas  
 B. GIT  
 C. hypothalamus
25. Worldwide, the commonest preventable cause of mental retardation in the newborn is:  
 A. iodine deficiency  
 B. phenylalanine hydroxylase deficiency  
 C. cystic fibrosis  
 D. urea cycle defect  
 E. Down syndrome
26. The secretion of aldosterone is normally limited to:  
 A. zona glomerulosa  
 B. zona fasciculata  
 C. zona reticularis

27. New cortical cells are formed from reserve cells in the:

- A. zona glomerulosa
- B. zona fasciculata
- C. zona reticularis

28. Which of the following is **not** a catecholamine?

- A. Epinephrine
- B. Norepinephrine
- C. Dopamine
- D. Acetylcholine

29. Normally, androgens are predominantly secreted by the:

- A. zona glomerulosa
- B. zona fasciculata
- C. zona reticularis

30. The hormones produced by the ovary include:

- A. estrogens
- B. progesterone
- C. relaxin
- D. inhibin

31. Circulating norepinephrine has greater affinity for:

- A.  $\alpha$  adrenergic receptors
- B.  $\beta_1$  adrenergic receptor
- C.  $\beta_2$  adrenergic receptor

32. The lipolytic effect of catecholamines is mediated by:

- A.  $\beta_1$  adrenergic receptors
- B.  $\beta_2$  adrenergic receptors
- C.  $\beta_3$  adrenergic receptors
- D.  $\beta_1$  &  $\beta_3$  adrenergic receptors

33. Deficiency of which of the following hormones is not known to result in a clinically significant disorder of regulation of ionized calcium in plasma?

- A. Parathyroid hormone
- B. Calcitriol
- C. Calcitonin

34. *Congenital lipoid adrenal hyperplasia* occurs due to a lack of:

- A. CYP450 scc (desmolase)

- B.  $3\beta$ -hydroxysteroid dehydrogenase
- C.  $17\alpha$  hydroxylase
- D. steroidogenic acute regulatory protein

35. The most abundant cell type in the islets of Langerhans is:

- A. A cells
- B. B cells
- C. D cells
- D. F cells

36. In the management of a child with diabetic ketoacidosis and a plasma pH of 6.9, insulin infusion is typically continued even after plasma glucose is reduced to 250 mg/dL, and glucose is coadministered with insulin. This is done in order to:

- A. replenish glycogen stores in muscle
- B. restore total body potassium stores
- C. completely oxidize ketone bodies
- D. rapidly reduce plasma osmolality to normal

37. Which of the following conditions increases the risk of fasting hypoglycemia?

- A. Adrenocortical insufficiency
- B. Beta-adrenergic receptor blockade
- C. Hyperglucagonemia
- D. Hypothyroidism
- E. Acromegaly

38. Which tissues do **not** require insulin for glucose uptake? (*check all correct answers*)

- A. Red blood cells
- B. Most parts of the CNS
- C. Adipose tissue
- D. Skeletal muscle

39. Which of the following is **not** an energy-releasing hormone?

- A. Growth hormone
- B. Cortisol
- C. Epinephrine
- D. Insulin
- E. Glucagon

40. Which of the following hormones is / are diabetogenic? (*Check all correct answers*)

- A. Epinephrine
- B. Cortisol
- C. Growth hormone

- D. Glucagon
- E. Thyroid hormones

41. Insulin secretion from B-cells in pancreas is inhibited by:

- A. acetylcholine
- B. activation of *beta*-adrenergic receptors
- C. activation of *alpha*-adrenergic receptors
- D. glucagon
- E. somatostatin

42. For the same plasma concentration of glucose achieved, the insulin secretory response to an oral glucose load is greater than the insulin secretory response to an intravenous infusion of glucose.

This is because of the:

- A. potentiation of insulin secretion by glucagon like polypeptide-1 and glucose dependent insulinotropic polypeptide (incretin effect) when glucose is ingested orally
- B. secretion of preformed insulin occurs only when glucose is ingested orally.

43. Glucagon, when present in high concentrations such as in a type I diabetic, facilitates all of the following **except**:

- A. lipolysis
- B. gluconeogenesis
- C. hepatic glycogenolysis
- D. muscle glycogenolysis

44. Which of the following is a potent stimulator of insulin secretion?

- A. Somatostatin
- B. VIP
- C. Glucagon like polypeptide-1 (GLP-1)
- D. Leptin

45. Hypoglycemia does **not** stimulate the secretion of:

- A. epinephrine
- B. cortisol
- C. growth hormone
- D. insulin
- E. glucagon

46. The *hormone of energy storage* (hormone of plenty) is:

- A. growth hormone
- B. thyroxine

- C. insulin
- D. glucagon
- E. epinephrine

47. Which of the following **increase** insulin resistance? (*Tick all that apply*)

- A. Leptin
- B. TNF- $\alpha$
- C. Resistin
- D. Adiponectin
- E. GH secreting tumors
- F. Epinephrine secreting tumor

48. The two drugs that are commonly used to induce diabetes in rats are:

- A. streptozotocin
- B. alloxan
- C. forskolin
- D. capsaicin

49. Which of the following hormones inhibits ovulation and downregulates GnRH release when present in high concentrations?

- A. Prolactin
- B. FSH
- C. LH
- D. Human menopausal gonadotropins

50. The *maternal growth hormone of pregnancy* is:

- A. hGH-N
- B. hCS
- C. estriol
- D. hCG

51. Which of the following is **not** detectable in the blood of a nonpregnant female?

- A. Oxytocin
- B. Relaxin
- C. hCS
- D. Inhibin B

52. Which of the following hormones is **not** detectable in normal females?

- A. Androstenedione
- B. Testosterone
- C. Dehydroepiandrosterone sulfate
- D. Dihydrotestosterone

53. Which of the following hormones is **not** detectable in normal males?
- Oxytocin
  - Estradiol (E2)
  - Estrone (E1)
  - Progesterone
  - Prolactin
54. Complete fusion of labioscrotal swellings does not occur despite exposure to high concentrations of androgens beyond which point in intrauterine life?
- 3 weeks
  - 6 weeks
  - 9 weeks
  - 12 weeks
55. Which of the following is the most sensitive test of pancreatic B-cell insulin secretory reserve?
- Oral glucose tolerance test
  - Fasting plasma glucose
  - Urine glucose excretion
  - Random blood glucose
56. Chronic androgen abuse by otherwise healthy male athletes is **least likely** to result in:
- increased erythropoiesis
  - increased sperm count
  - increased respiratory endurance
  - increased muscle mass
57. Which of the following statements is **incorrect**?
- Somatopause is attributed to a decline in the activity of GH-IGF1 axis
  - Andropause is characterized by an increase in LH and FSH.
  - Menopause is characterized by decreased ovarian responsiveness to pituitary gonadotropins.
  - Adrenopause is characterized by a decrease in plasma DHEA sulfate.
58. The *hormone of darkness* is:
- leptin
  - melatonin
  - serotonin
  - galanin
59. The adrenal medulla does **not normally** secrete:
- epinephrine
  - norepinephrine
  - chromogranin B
  - vasoactive intestinal polypeptide
60. The release of androgens from the adrenal cortex is stimulated mainly by:
- LH
  - FSH
  - ACTH
  - GnRH
61. The biologically most active androgen is:
- testosterone
  - dehydroepiandrosterone
  - androstenedione
  - dihydrotestosterone
62. Which of the following would be **most likely** in an XX female with one mutated androgen receptor gene?
- Incomplete development of breasts
  - Infertility
  - Defective synthesis of dihydrotestosterone
  - Incomplete septation of urogenital sinus
63. Which of the following drugs produces therapeutic effects by downregulating hormone receptors in target cells?
- FSH
  - Long acting GnRH analogs
  - Inhibin
  - Finasteride
64. HCG acts upon the:
- LH receptor
  - PRL receptor
  - GH receptor
  - FSH receptor
65. The testis-determining gene (or the SRY gene) is located normally on/in:
- chromosome 6
  - chromosome 12
  - short arm of chromosome 22
  - Y chromosome

66. The hormone secreted by the pineal is synthesized starting from:
- tyrosine
  - tryptophan
  - phenylalanine
  - lysine
67. In normal healthy adults on a daytime work shift, at what time does pineal hormone peak in blood?
- 2 am
  - 8 am
  - 2 pm
  - 8 pm
68. Which of the following statements about the pineal gland in human beings is **correct**?
- It directly responds to light
  - It is part of the nervous system
  - It is controlled by the hypothalamus
  - It is rudimentary
69. Which of the following cells undergo meiotic division?
- Primordial germ cells
  - Primary spermatocytes
  - Secondary spermatocytes
  - Spermatids
70. The average number of spermatids formed from a single spermatogonium is:
- 16
  - 128
  - 512
71. The formation of mature sperm cells from a primitive germ cell takes an average of:
- 2 days
  - 1 week
  - 74 days
  - 3 months
72. Sperm cells first acquire the ability to move forward (*progressive motility*) in the:
- seminiferous tubules
  - epididymis
  - female genital tract
73. Sildenafil citrate enhances penile erection by:
- activating adenylyl cyclase

- blocking nitric oxide synthase
- activating guanylyl cyclase
- inhibiting cGMP-phosphodiesterase

74. The enhancement of penile erectile function produced by sildenafil citrate is primarily because of inhibition of:

- cGMP-PDE3
- cGMP-PDE4
- cGMP-PDE5
- cGMP-PDE6

75. The transient loss of the ability to discriminate between blue and green following the use of sildenafil is due to inhibition of:

- cGMP-PDE3
- cGMP-PDE4
- cGMP-PDE5
- cGMP-PDE6

### Answers: Self-Study in Endocrinology & Reproduction

1A	2B	3A	4C	5B
6D	7A	8AB	9B	10ABC
11D	12B	13ACD	14B	15A
16A	17B	18C	19B	20C
21B	22D	23D	24ABC	25A
26A	27A	28D	29C	30all
31A	32D	33C	34D	35B
36C	37A	38AB	39D	40all
41CE	42A	43D	44C	45D
46C	47BCEF	48AB	49A	50B
51C	52none	53none	54D	55A
56B	57none	58B	59D	60C
61D	62none	63B	64A	65D
66B	67A	68C	69B	70C
71C	72B	73D	74C	75D

### Answer Explanations:

2. TRH is a tripeptide.

7. 50% of cells in the anterior pituitary secrete growth hormone. See Table 22-1, p.397, WFG, 2005.

8. The somatomedins are insulin-like growth factors 1 (IGF-1) and IGF-2.

9. The best answer is option B. Hyperglycemia in the mother results in fetal hyperinsulinemia. High levels of insulin in the fetus cause it to have effects on insulin as well as IGF-1 receptors, and this causes the macrosomia. Unbound insulin is normally degraded by placental proteases and does not reach the fetus. However, insulin bound to anti-insulin antibodies is known to cross the placenta, and this mechanism is also believed to contribute to fetal macrosomia in women who took animal insulins during pregnancy.

15. The human thyroid releases about 80 micrograms of T4 and 4 micrograms of T3 per day.

16. One third of circulating T4 is normally converted to T3 in humans by the action of 5'-deiodinase in the liver and kidneys. See *p. 322, Ch 18, WFG, 2005*.

18. See *p. 321, Ch 18, WFG, 2005*.

19. T4 and T3 increase the oxygen consumption of all metabolically active tissues. The exceptions are the adult brain, testes, uterus, lymph nodes, spleen and anterior pituitary. See *p. 324, Ch 18, WFG, 2005*.

23. Insulin increases K uptake by muscle probably by stimulating Na-K ATPase. Insulin increases the oxidation of ketone bodies; this is one reason why it is necessary in the treatment of diabetic ketoacidosis.

31. Norepinephrine has a greater affinity for alpha-adrenergic receptors and epinephrine has a greater affinity for beta-adrenergic receptors. For example, when norepinephrine is administered intravenously the blood pressure increases enough to trigger a baroreflex-mediated decrease in heart rate although norepinephrine has a direct chronotropic action on the heart.

38. Red blood cells and most regions of the brain with the exception of cells in the satiety center do not require insulin for glucose uptake.

40. Diabetogenic hormones: epinephrine, norepinephrine, glucagon, growth hormone,

cortisol, and thyroxine. All of them oppose the blood glucose lowering effects of insulin.

41. When acting via alpha 2 adrenergic receptors, epinephrine/norepinephrine inhibit insulin secretion; however, when acting via *beta*-adrenergic receptors, it stimulates insulin secretion. The significance of sympathetically mediated inhibition of insulin secretion is it reduces the likelihood of hypoglycemia during exercise. See *p. 345, Ch 19, WFG, 2005*.

42. The insulin response to an oral load of glucose is greater because of the release of glucose-dependent insulinotropic polypeptide and other hormones from the GIT, which in turn stimulate insulin secretion. This effect, called the incretin effect, is absent when glucose is administered intravenously.

44. GLP-1 (7-36) is glicentin-like polypeptide, a gastrointestinal hormone; it is a potent stimulator of insulin secretion (incretin). See *p. 348, Ch 19, WFG, 2005*.

47. Leptin and adiponectin are adipokines (i.e., hormones from adipocytes) that increase insulin sensitivity. In contrast, TNF- $\alpha$  and resistin decrease insulin sensitivity. Growth hormone in excess causes insulin resistance because it has hyperglycemic effects and facilitates lipolysis. See *p.347-8, Ch 19, WFG, 2005*.

51. Human chorionic somatomammotropin is a placental hormone.

56. Chronic use of pharmacologic doses of androgens suppresses FSH release from the pituitary thereby inhibiting spermatogenesis.

57. The term adrenopause is used to refer to a decline in serum DHEA. Since DHEA is the most abundant adrenocortical hormone, a fall in serum DHEA indicates a decline in functional adrenal cortical mass.

62. Because of random inactivation of X-chromosome, the presence of one mutated androgen receptor (with loss of function) is inconsequential. Furthermore, androgens are not

normally involved in feedback regulation of gonadotropin secretion (and consequently fertility) in females. In contrast, XY zygotes with a loss of function mutation in the androgen receptor gene develop manifestations attributable to androgen insensitivity, and are phenotypically female.

63. Long acting GnRH analogs suppress FSH and LH release by downregulating GnRH receptors in the pituitary, and thereby inhibit ovulation.

\*\*\*\*\*

### More Questions for Self-Study in Gastrointestinal Physiology

1. The term 'hormone' was coined by Ernest H. Starling to describe the actions of:

- A. secretin
- B. insulin
- C. growth hormone
- D. glucagon

2. Which of the following **inhibits** gastric acid secretion?

- A. Pentagastrin
- B. Hypoglycemia
- C. Acetylcholine
- D. PGE<sub>2</sub>

3. Complete inhibition of gastric acid secretion is achieved with pharmacologic doses of:

- A. H<sup>+</sup>-K<sup>+</sup> ATPase inhibitor
- B. H<sub>2</sub> receptor blocker
- C. M<sub>2</sub> receptor blocker
- D. CCK-B receptor blocker

4. Vagally mediated increase in gastric acid secretion is partly mediated by:

- A. gastrin releasing peptide (GRP)
- B. gastric inhibitory peptide (GIP)
- C. vasoactive intestinal polypeptide (VIP)
- D. somatostatin

5. The optimum pH for the activity of pepsin is:

- A. less than 1
- B. between 1.6 and 3.2
- C. between 3 and 5
- D. between 6 and 7

6. Which of the following statements about CCK is **incorrect**?

- A. It causes gall bladder contraction
- B. It relaxes the sphincter of Oddi
- C. It relaxes the pyloric sphincter
- D. It stimulates the secretion of an enzyme-rich pancreatic juice

7. Trypsinogen, a pancreatic proenzyme, is activated by:

- A. enterokinase
- B. hydrochloric acid
- C. HCO<sub>3</sub>
- D. pancreatic trypsin inhibitor

8. Most pancreatic zymogens are activated in the duodenal lumen by:

- A. enterokinase (enteropeptidase)
- B. trypsin
- C. trypsin activator protein

9. Trypsin inhibitor:

- A. inhibits the action of pancreatic enzymes in the lumen of the duodenum
- B. inhibits activation of trypsin in the pancreas
- C. deficiency is implicated in acute pancreatitis
- D. is produced by enterocytes

10. The most abundant bile acid is:

- A. cholic acid
- B. chenodeoxycholic acid
- C. deoxycholic acid
- D. lithocholic acid

11. In healthy humans, active absorption of bile acids and bile salts occurs mainly in the:

- A. duodenum
- B. jejunum
- C. terminal ileum
- D. colon

12. Bile acids are synthesized starting from:

- A. cholesterol
- B. fatty acids
- C. lecithin
- D. bile salts

13. Vitamin B<sub>12</sub> is mainly absorbed in the:

- A. terminal ileum
- B. upper jejunum

- C. duodenum  
D. stomach
14. Calcium absorption from the intestine:  
A. is facilitated by vitamin D  
B. is decreased by phytates and oxalates  
C. occurs mainly in the upper small intestine
15. The protein that transports iron in the plasma from the site of absorption to cells engaged in erythropoiesis is:  
A. hepcidin  
B. transferrin  
C. ferritin  
D. hemosiderin
16. In healthy humans, iron in tissues other than red blood cells is stored principally in combination with:  
A. ferritin  
B. transferrin  
C. hepcidin  
D. hemosiderin
17. Which of the following is an endopeptidase?  
A. Carboxypeptidase A  
B. Deoxyribonuclease  
C. Trypsin  
D. Dipeptidase
18. Which of the following enzymes is located in the brush border of enterocytes in the small intestine?  
A. Lactase  
B. Colipase  
C. Cholesterol ester hydrolase  
D. Lingual lipase
19. Disaccharidases are present in:  
A. pancreatic acinar cells  
B. brush border of enterocytes  
C. D cells of pancreas  
D. Brunner's glands
20. In healthy humans, the maximal rate of glucose absorption from the intestine is estimated to be about:  
A. 10 g/hour  
B. 40 g/hour  
C. 120 g/hour  
D. 180 g/hour
21. The least oxygenated and consequently the zone in the hepatic acinus most vulnerable to ischemia is:  
A. zone I  
B. zone II  
C. zone III
22. In healthy humans, the earliest the first part of a test meal reaches the cecum is in about:  
A. 4 hours  
B. 6 hours  
C. 9 hours  
D. 12 hours
23. Normally, the main function of the colon is absorption of:  
A. Na, Cl and H<sub>2</sub>O  
B. triacylglycerols  
C. secondary bile acids  
D. iron
24. Gastric emptying is slowest after a meal containing:  
A. fat  
B. carbohydrate  
C. protein  
D. indigestible fiber
25. *Slow waves* in the GIT are initiated by:  
A. I cells  
B. K cells  
C. interstitial cells of Cajal  
D. S cells
26. The most alkaline exocrine secretion is:  
A. bile  
B. pancreatic juice  
C. intestinal juice  
D. saliva
27. The odor of feces is partly due to:  
A. stercobilinogen  
B. indole, skatole and sulfides  
C. primary bile acids  
D. secondary bile acids
28. The normal rate of bile salt synthesis is:  
A. 0.05 – 0.1 g/day

- B. 0.2 – 0.4 g/day
- C. 0.8 – 1.2 g/day
- D. 2 – 2.5 g/day

29. Which of the following enzymes is **not** synthesized by the pancreas?

- A. DNAase
- B. Proelastase
- C. Aminopeptidases
- D. Pepsin

30. The basal acid output / maximum acid output ratio is normally less than:

- A. 0.1
- B. 0.6
- C. 0.8
- D. 0.9

31. Which of the following cells sample the antigenic milieu of the gastrointestinal lumen?

- A. P cells
- B. I cells
- C. K cells
- D. M cells (microfold cells)
- E. Mo cells

32. The defecation reflex is integrated in the:

- A. brain stem
- B. pons
- C. medulla
- D. spinal cord

**Answers: Questions for Self-Study in Gastrointestinal Physiology**

1A	2D	3A	4A	5B
6C	7A	8B	9B	10A
11C	12A	13A	14ABC	15B
16A	17C	18A	19B	20C
21C	22A	23A	24A	25C
26B	27B	28B	29D	30A
31D	32D			

3. This is because the H-K ATPase is the final common pathway for acid secretion in the parietal cell. New proton pumps need to be synthesized before parietal cells can overcome the inhibitory effects of H-K ATPase inhibitors.

Vagal neurons ending on G cells in the antrum release gastrin-releasing peptide. Gastrin from G

cells stimulates the release of histamine from enterochromaffin like cells in the stomach, and acid secretion from parietal cells.

Regarding *option B*, glucose-dependent insulinotropic polypeptide (GIP) was previously called gastric inhibitory peptide (also GIP). However, now it is clear that the physiologic action of GIP is stimulation of insulin secretion. Its inhibitory effects on gastric secretion occur only at pharmacologic doses.

5. CCK contracts the pyloric sphincter thereby inhibiting gastric emptying.

7. Activation of trypsinogen requires enterokinase. Enteropeptidase (enterokinase) is an intestinal brush border enzyme that catalyzes the proteolytic activation of trypsinogen to trypsin.

8. Trypsin is the common activator of all pancreatic proenzymes. This ensures that pancreatic proenzymes are activated only when they reach the intestinal lumen. Once trypsin is formed, it catalyzes activation of trypsinogen and other pancreatic enzymes secreted as proenzymes.

\*\*\*\*\*

**More Questions for Self-Study: Renal & Acid-Base Physiology**

1. Which of the following statements about control of micturition is **incorrect**?

- A. Deafferentation of the bladder leads to overflow incontinence.
- B. In healthy adults, the first urge to void is felt at a bladder volume of about 400 ml.
- C. Decentralization of bladder function results in urinary retention accompanied by overflow incontinence.

2. What is the immediate effect of spinal cord transection on bladder function?

- A. Urinary retention
- B. Overflow incontinence
- C. Anuria

3. The substrate for renin is:

- A. angiotensinogen

- B. angiotensin I  
C. angiotensin II  
D. bradykinin
4. Angiotensin converting enzyme is a / an:  
A. dipeptidyl carboxypeptidase  
B. aminopeptidase  
C. aspartyl protease
5. The kidneys do **not** synthesize or secrete:  
A. calcitriol  
B. rennin  
C. erythropoietin  
D. PGE2
6. Renin is released mainly from:  
A. macula densa  
B. juxtaglomerular cells  
C. type I medullary interstitial cells  
D. peritubular capillaries
7. In the kidneys, type I medullary interstitial cells secrete:  
A. renin  
B. PGE2  
C. aquaporins  
D. aldosterone
8. Mesangial cells are similar to:  
A. pericytes  
B. fibrocytes  
C. mast cells  
D. ependymal cells
9. Physiologically, important stimulators of aldosterone production by the zona glomerulosa cells include (*tick all that apply*):  
A. a rise in plasma [K<sup>+</sup>]  
B. angiotensin II  
C. angiotensin III
10. The actions of aldosterone are antagonized by:  
A. angiotensin III  
B. arginine vasopressin (AVP)  
C. ANP
11. Chronic licorice ingestion is characterized by:  
A. low blood pressure  
B. hyperkalemia  
C. metabolic acidosis  
D. a decrease in plasma renin activity
12. Which of the following substances normally has a “clearance ratio” of about 1.2?  
A. Inulin  
B. Creatinine  
C. Urea  
D. PAH
13. Which of the following substances has a clearance ratio close to 1?  
A. Creatinine  
B. Mannitol  
C. Urea  
D. Glucose
14. Which of the following substances is cleared the most by the kidneys?  
A. Inulin  
B. PAH  
C. Creatinine  
D. Urea
15. Arrange the following substances in the descending order of their clearance. [Cr: creatinine]  
A. PAH > Inulin > Urea > Cr > Glucose  
B. Inulin > PAH > Cr > Urea > Glucose  
C. PAH > Cr > Inulin > Urea > Glucose
16. The tubular transport maximum for glucose (T<sub>max</sub> for glucose) in a healthy young man is about:  
A. 100 mg/min  
B. 225 mg/min  
C. 375 mg/min  
D. 500 mg/min
17. When urine is maximally concentrated, the ratio of osmolality of urine to plasma is about:  
A. 3  
B. 4.2  
C. 4.6  
D. 6.7
18. High protein diets increase the likelihood of:  
A. metabolic acidosis  
B. metabolic alkalosis  
C. respiratory acidosis  
D. respiratory alkalosis

19. Which of the following is consistent with hypotonic urine?

- A. A high  $U_{osm} / P_{osm}$  ratio
- B. A urinary pH of 7
- C. Positive free water clearance

20. In a healthy adult, the urge to void urine is first felt at a bladder volume of about:

- A. 50 ml
- B. 150 ml
- C. 250 ml
- D. 350 ml

21. In a healthy adult, the volume of urine in the bladder that initiates reflex contraction of the bladder is about:

- A. 50–100 ml
- B. 100–200 ml
- C. 200–300 ml
- D. 300–400 ml

22. Which of the following is **not** a feature of tabes dorsalis?

- A. Bladder wall hypertrophy
- B. Distended bladder
- C. Urinary retention
- D. Incontinence

23. Arrange the following substances in the descending order of their concentrations in intracellular fluid.

- A.  $K^+ > Ca^{2+} > Na^+ > H^+$
- B.  $H^+ > K^+ > Na^+ > Ca^{2+}$
- C.  $K^+ > Na^+ > Ca^{2+} > H^+$
- D.  $K^+ > Ca^{2+} > H^+ > Na^+$

**Answers: Self-Study in Renal Physiology**

1B	2A	3A	4A	5B
6B	7B	8A	9ABC	10C
11D	12B	13B	14B	15C
16C	17C	18A	19C	20B
21D	22A	23C		

**True or false:**

- 1. Urine volume in an adult may increase to as much as 23L / day in the complete absence of vasopressin.
- 2. 75 % of potassium is secreted in the *collecting ducts*.

- 3. 65% of filtered water is reabsorbed in the proximal tubule.
- 4. Stimulation of renal sympathetic nerves inactivates the renin angiotensin system.

**Answers:** statement 4 is false; others are true.

**Answer Explanations:**

1. In chronic paraplegics, the voiding reflex returns and it may be hyperactive. The hyperactive reflex may be because of release of the spinal mechanism for micturition from the inhibitory effects of higher control. The bladder wall becomes hypertrophied and bladder capacity is reduced. This condition is called spastic neurogenic bladder. See *Summary - Disorders of Micturition* on pp.81 of this book. Also see p 728, Ch 38, WFG, 2005.

2. The immediate effect of spinal cord transection is urinary retention. This is, of course, followed by overflow incontinence; i.e., excessive stretch of the urinary bladder, and local reflex contractions of the detrusor that is not under voluntary control. See p 728, Ch 38, WFG, 2005.

7. One of the effects of renal prostaglandins is mediating redistribution of blood flows within the kidneys.

8. When mesangial cells contract, surface area available for filtration reduces.

9. **Factors stimulating aldosterone release from the adrenal cortex:** Angiotensin II is the most important trophic factor for the zona glomerulosa and one of the two most important stimulators of aldosterone release. Even a 0.5 mM increase in plasma [K] stimulates aldosterone release. In turn, aldosterone regulates plasma [K] by promoting K secretion in the collecting ducts. Angiotensin III has 100% aldosterone releasing activity but only 40% of the pressor activity of aldosterone. ACTH as well as a decrease in plasma [Na] stimulate aldosterone release but the stimulatory effects of acute administration of pharmacologic doses of ACTH on aldosterone release are transient if at all.

11. Licorice contains glycyrrhizinic acid and this inhibits 11-*beta* hydroxysteroid dehydrogenase (HSD) type 2 in the collecting duct cells in the nephron. 11-*beta* HSD type 2 is an enzyme that inactivates cortisol and thereby prevents it from stimulating the mineralocorticoid receptor. [Otherwise, cortisol is capable of binding and activating the mineralocorticoid receptor.] This is why, physiologically, the mineralocorticoid receptor is activated only by aldosterone. With chronic licorice ingestion or with inherited deficiency of 11-*beta* HSD type 2, cortisol activates the mineralocorticoid receptor. The concentration of cortisol is much higher than that of aldosterone; the result is hypertension, hypokalemia and metabolic alkalosis and feedback suppression of plasma renin activity and thereby aldosterone secretion by high BP. This is an instance of pseudohyperaldosteronism. Similarly, hypertension that occurs in 11 *beta*-hydroxylase B1 deficiency is due to the actions of high levels of deoxycorticosterone on the mineralocorticoid receptor.

12. *Clearance ratio* is the ratio of the clearance of a substance by the kidneys to the clearance of inulin. The clearance of substances secreted by the nephron is greater than inulin clearance. In contrast, the clearance of substances (such as glucose) that are reabsorbed by the nephron is less than inulin clearance.

14. The clearance of a substance that is actively secreted by the nephron (example, PAH) is greater than the clearance of a substance that is excreted by filtration alone (example, inulin).

16. In women, it is about 300 mg/min.

17. Maximum urine osmolality = 1400 mOsm/kg H<sub>2</sub>O. Plasma osmolality = 300 mOsm/kg H<sub>2</sub>O. When urine is maximally concentrated, U<sub>osm</sub>/P<sub>osm</sub> = 4.6.

18. The metabolism of sulfur containing amino acids generates hydrogen ions (“fixed acid”) that only the kidneys can excrete.

19. ‘Free water clearance’ is the amount of solute-free water excreted. When urine is concentrated

(i.e. hypertonic compared to plasma), free water clearance is negative. When water is lost in excess of osmoles cleared, free water clearance is positive - as in diabetes insipidus.

20. See p 726, Ch 38, WFG, 2005.

21. Laplace’s law states that pressure (P) in a hollow viscus is directly proportional to wall tension (T) and inversely with radius (r).  
 $P = T/r$

As the bladder is distended with urine, the radius as well as passive tension increases proportionately so there is little change in intravesical pressure. However, at an intravesical volume of about 300-400 ml, any further stretch results in “active contraction” of the smooth muscle of the bladder and a sharp increase in intravesical pressure. This results in emptying of the bladder. See p 727, Ch 38, WFG, 2005.

22. Tabes dorsalis predominantly affects the dorsal roots; thus, the effects observed are those of deafferentation: the bladder becomes distended, thin walled and hypotonic. See *Summary - Disorders of Micturition* in Renal & Acid-Base Physiology. See p 728, Ch 38, WFG, 2005.

\*\*\*\*\*

### ***Bibliography:***

**Barrett KE, Barman SM, Boitano S and Brooks HL.** *Ganong’s Review of Medical Physiology*, 2012, Mc Graw Hill – Lange.  
**Ganong WF.** *Review of Medical Physiology*, 2005, Mc Graw Hill – Lange; called WFG.  
**Longo et al.** *Harrison’s Principles of Internal Medicine*, 18<sup>th</sup> ed.  
**Goldman L et al (eds.)** *Goldman’s Cecil Medicine*. 24<sup>th</sup> ed., 2012, Elsevier - Saunders