MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE

STEPAN GZHYTSKYI NATIONAL UNIVERSITY OF VETERINARY MEDICINE AND BIOTECHNOLOGIES LVIV

Department of Normal and Pathological Physiology named after S. V. Stoianovskiy

ANIMAL PHYSIOLOGY. MANUAL

Lviv 2022

УДК 619:616:612(07)
Коло 61

Фізіологія трваин. Навчальний посібник: навч. посібник / укл. І.А. Коломієць, І.І. Ковальчук, ред. І.А. Коломієць, М.В. Подоляк; ЛНУВМБ ім. С.З. Гжицького. – Львів, 2022.– 190 с.

Редактор:

Ірина Коломієць	к.вет.н., доцент кафедри нормальної та патологічної фізіології імені С.В. Стояновського Львівського національного університету ветеринарної медицини та біотехнологій імені С.З. Гжицького.

Літературний редактор:

Михайло Подоляк	к.пед.н., доцент, завідувач кафедри української та іноземних мов імені Я.Яреми Львівського національного університету ветеринарної медицини та біотехнологій імені С.З. Гжицького

Рецензенти:

Олексій Данчук	д.вет.н., професор, професор кафедри фізіології, патофізіології та біохімії Одеського державного аграрного університету
Дмитро Масюк	д.вет.н., професор, професор кафедри фізіології та біохімії сільськогосподарських тварин Дніпровсього державного аграрно-економічного університету
Микола Жила	д.вет.н., доцент, завідувач кафедри нормальної та патологічної морфології і судової ветеринарії Львівського національного університету ветеринарної медицини та біотехнологій імені С.З. Гжицького

Рекомендовано Львівським національним університетом ветеринарної медицини та біотехнологій імені С.З. Гжицького навчальний посібник «Animal Physiology» (укладачі: І.А. Коломієць, І.І. Ковальчук; за ред. І.А. Коломієць, М.В. Подоляка) для студентів спеціальності 211 «Ветеринарна медицина» другого (магістерського) рівня вищої освіти (Наказ №317 від 24 грудня, 2021).

В навчальному посібнику представлені основні розділи фізіології тварин, структуровані до лекційного матеріалу, адаптовані для іноземних студентів відповідно до навчальної дисципліни «Фізіологія тварин» для студентів спеціальності 211 «Ветеринарна медицина» другого (магістерського) рівня вищої освіти. Посібник буде корисним також для іноземних здобувачів медичних та біологічних спеціальностей.

UDK 619:616:612(07)
Kolo 61

Animal Physiology. Manual: manual / comp. I.A. Kolomiiets, I.I. Kovalchuk, ed. I.A. Kolomiiets, M.V. Podoliak; LNUVM named after S.Z. Gzhytskyi. – Lviv, 2022.– 190 p. – a – il.

Editor:

Iryna Kolomiiets	PhD, Associated Professor of Department of Normal and Pathological Physiology named after S. V. Stoianovskiy, Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv

English language editor:

Mykhailo Podoliak	PhD, Associated Professor, Head of Department of the Ukrainian and Foreign languages named after Ya. Yarema, Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv

Reviewers:

Oleksii Danchuk	Doctor of Veterinary Sciences, Professor, Professor of Department of Physiology, Pathophysiology and Biochemistry, Odesa State Agrarian University
Dmytro Masiuk	Doctor of Veterinary Sciences, Professor of Department of Physiology and Biochemistry of Agricultural Animals, Dnipro State Agrarian and Economic University
Mykola Zhyla	Doctor of Veterinary Sciences, Associated Professor, Head of Department of Normal and Pathological Morphology and Forensic Veterinary, Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv

Recomended by Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv Manual «Animal Physiology. Manual» (comp. I.A. Kolomiiets, I.I. Kovalchuk, ed. I.A. Kolomiiets, M.V. Podoliak) for students of the speciality 211 «Veterinary medicine» of the second educational level (Order №317 as of 24th December, 2021)

In the manual are represented the main parts of animal physiology, lectures, in particular, handout for foreign students, which correspond to the syllabus of the educational discipline «Animal Physiology» for foreign students of the speciality 211 «Veterinary medicine» of the second educational level. It will be also useful for foreign students of medical and biological high schools.

CONTENTS

PREFACE

This manual has been developed from a series of lectures given to second-year students at the Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv, reading for a degree in Veterinary Sciences. It is intended to provide an accessible introduction to animal physiology at the second-year university level. At this level, students want to build on and develop the knowledge base they have gained prior to entering University and during the first year university level. However, at this stage, they do not wish to be inundated and confused with detailed knowledge about the minutia of physiological processes. It is hoped that this manual will fall between these two areas and serve as a suitable introductory text.

This manual is not for a casual reader. The recent trends in biological research promise to understand the integrated function of animals and human biological systems to improve human beings' health. The development of medical sciences recently stimulates the study of animal physiology as it holds many chemical and physical principles. Since the discovery of the cell structure and tissues, the science of physiology has undergone rapid development. It includes studying vital activities in cells, tissues, and organ processes such as contractility of muscle tissue, coordination through the nervous system, feeding, digestion, respiration, circulation, reproduction, and hormone secretion. Virtually every specialized field in the biological functions involves some consideration of the physiological aspect. In contrast to anatomy, which deals primarily with structure, physiology is the study of the integrated functions of the body and the functions of all its parts (systems, organs, tissues, cells, and cell components), including biophysical and biochemical processes. In the physiology laboratory, the student studies the response of whole animals, isolated organs, or individual cells to changes in their environment (both internal and external).

Making an excellent manual on Animal Physiology more relevant and even more appealing in the Ukrainian context is a challenge and an opportunity. This is a book for all students who are passionate about studying the normal functioning of animals' body organs during life and the actions by which life is maintained and transmitted. Writing this manual has been an enjoyable learning experience in itself. Any errors or omissions remain my fault alone, and I would be pleased to learn of any. Equally, if you have enjoyed the manual, I would like to hear from you.

I am grateful to the Head of the Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv, Doctor of Veterinary Sciences, Professor Volodymyr Stybel, and the administration of the University for their help and advice. Thanks must also go to the colleagues at the Department of Normal and Pathological Physiology named after S.V. Stoianovskiy. However, I would like to thank specifically the following colleagues within the Department of Normal and Pathological Morphology and Forensic Veterinary of the Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv, Department of

Physiology, Pathophysiology, and Biochemistry at Odesa State Agrarian University, Department of Physiology and Biochemistry of Agricultural Animals at Dnipro State Agrarian and Economic University, Department of Biochemistry and Physiology of Animals named after Academician M. F. Gulyi at the National University of Life and Environmental Sciences of Ukraine, for their many and varied contributions, who made helpful comments on draft versions of the text.

Iryna Kolomiiets
PhD, Associated Professor,
Department of Normal and Pathological Physiology
named after S.V. Stoianovskiy,
Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies
Lviv
email: kolomieciryna@gmail.com

CHAPTER 1. INTRODUCTION TO ANIMAL PHYSIOLOGY

Contents and objectives of discipline «Animal Physiology». Subject of animal physiology.

Physiology – is part of biology that studies the basic processes that occur in the body in a healthy relationship with each other and with the impact of regulatory factors endogenous and exogenous nature. **Physiology** (physis – nature, logos – science) – is the science about general laws of functioning of living organisms and their parts. Physiology is the subdivision of biology that deals with the various functions of living organisms. There are many different species of living organisms in the nature, which functioning is significantly different. Therefore, the physiology is divided into several independent sciences: plant physiology, physiology of microorganisms, animal physiology and human physiology. Animal (or mammalian) physiology is the oldest branch of this science. Animal physiology is the study of animal function—the study of "how animals work" *(work her heart, how she breathes, how digested nutrients and how energy is produced).*

This scientific branch covers a big diversity of functions, ranging from the cellular and the interaction of organ systems which maintain for the smooth running of the highly complex biological mechanisms.

Physiology studies the functions of the living organism, functions of its organs and systems of organs, its connection with each other, adaptation to environment. Physiological patterns of functioning of living organisms based on data about macro- and microscopic structure of organs and tissues, biochemical and biophysical processes that are carried out in cells, tissues and organs. Therefore, the physiological mechanisms are based on the anatomy, histology, biochemistry, biophysics and other disciplines. Physiology synthesizes the knowledge of other disciplines, combining them into a unified system of knowledge about the body. On the other hand, the physiology is the basis for the study of other health sciences such as pathological physiology and clinical disciplines.

Physiology of farm animals not only reveals the basic mechanisms that ensure the existence of the whole organism of animals, but also manages them useful for human direction. By studying the physiological laws of the body, can be scientifically significantly increase the production of meat, milk, eggs and other animal products, light industry to provide the necessary raw materials. *For example: the concentration of animals in relatively small areas leads to inactivity, reducing resistance, the emergence of various diseases. In this regard, there is a need for deeper study of the physiological functions of animals (resistance to stress factors), as well as individuals who have a high immune system.*

Physiology of farm animals is the theoretical basic discipline in the education system of veterinary medicine professionals. It is the theoretical basis of pathophysiology, clinical diagnosis, care, feeding, zoohygiene, breeding, and obstetrics and so closely related to the anatomy, histology, biochemistry, biophysics,

genetics. *Most diseases are manifested primarily by the dysfunction, because without knowledge about the functioning of a healthy body can not diagnose illness, identify ways of treatment, preventive measures, to correct and prevent disease.* A thorough understanding of the physiological processes of the animal body can help future doctors of veterinary medicine correct diagnosis and take timely preventive measures.

The guiding principle of physiology is the principle of unity of structure and function. So, physiology studies connection between the structure and function of organs. Although anatomy and physiology are commonly pursued as more or less independent disciplines, they are both facets of the study of the animal body. A thorough knowledge of structure imparts much information about its function. However, a mere description of structure without describing function would be of little practical value. Conversely, it is impossible to gain a thorough understanding of function without a basic knowledge of structure.

Function – is a form of living structure. *For example, the function of muscle tissue is contraction, function of nervous tissue - the generation of impulses, etc.*

The functional unit – is the smallest group of cells, united to perform a specific function (nephron, motor unit, etc.).

Physiological systems – the union of the organs for a specified function (blood system, circulatory system, the system of external respiration, etc.).

A functional state – the state of biological structures and functions of the organism as a whole at a particular time.

For practical purpose physiology can be divided into such main sections**:**

General physiology studies the basic properties that are common to most cells, organs and system of organs of the whole organism, the main life processes, the effect of all living organisms, and their functional changes due to the influence of external conditions.

Special physiology studies processes of digestion, circulation, respiration, metabolism, reproduction in a healthy body, their relationship, the interaction of the organism as a whole with the environment. Scientists also observe and investigate how certain body systems, like the circulatory, respiratory, and nervous systems, work independently and together to maintain life.

Comparative physiology studies the function of certain organs in different groups of organisms. It reveals the functional processes of different living organisms. It explores the similarities and differences between living things and how they function.

Another important aspect of comparative physiology is the relationship between organisms and their environment, or ecophysiology. Ecological physiology, reveals how animals developed or evolved specific biological mechanisms to cope with a particular environment. The same physical setting may exercise very different effects on divergent organisms. *A fish, for example, will have a much bleaker outcome in a desert environment than in its home habitat of water. In contrast, a land-dwelling lizard acclimated to harsher climates would be ill-equipped to deal with an aquatic setting due to its anatomical makeup.* As such, ecophysiology and its

study of aspects of adaptation can offer enhanced understanding of all animal groups in comparative physiology.

One particular area of comparative physiology has received increased attention over time: the use of phylogenic comparative methods. Scientists utilize these methods to examine potential evolutionary relationships between diverse living organisms and to document any significant changes a particular animal group may have undergone since its inception. Researchers may study the physical resemblances between certain organisms or how certain organisms have developed similar functional parts, like lungs or gills for breathing purposes. As a result, the study may uncover common ancestors among different species and solidify an evolutionary link. Examination of fossil remains and other archaeological evidence may also help comparative physiologists understand how an animal group has changed and adapted from ancient times until the present era.

Age-old physiology – proper comparisons can only be achieved when the scientist understands how each organism's physical body allows it to carry out the actions essential for day-to-day living.

Methods of physiological research.

Physiology is an experimental science, the source of knowledge is experience. Physiological experiments conducted in laboratory and domestic animals, cells and subcellular structures with modern devices (electronic, optical, etc.).

The experiments are:

1. Observing the behavior of the animal. This is an easy way, which shows the physiological state of the animal.

2. Acute (vivisection). Animal dopes and conduct surgery, operating on separate bodies of electric shock, chemicals and so on. Sometimes certain body isolated. Sometimes experiment selected individual tissues.

3. Chronic (long-term) experiments. Is usually carried out on a specially trained animals. To this end, the gastrointestinal tract or impose certain cancer fistula, isolated loop of intestine. Often removing a particular gland.

4. Transplantation of organs. It can be from one animal to another. It also can be from one place to another in the same organism (*for example glands*).

5. Formation of conditional reflexes thanks to cerebral cortex. It is way to research animal behavior.

6. Using of electrical current to some tissue and observing its reaction or response.

7. Telemetry. It means investigation at a distance.

8. Modeling functions. Sometimes simulate electronic circuits functioning of an organ. Yes, there were attempts to simulate the function of the stomach, the rumen, the heart, but these models are schematic and do not account for the fullness of natural body functions. Therefore, this solution can solve the problem only simplified.

9. Clinical methods, such as to research blood pressure, etc.

Living organism and its contact with the environment.

It is always interesting and surprising that how the different components of living organisms adjust to maintain a constant internal environment.

Organism – a living anatomical and histological structure which functionally is a single unit. Living organisms, as opposed to inanimate bodies, remain relatively stable internal environment, whereas in inanimate bodies under the influence of various factors changing the chemical composition, structure, comes from balancing their environment.

The body is a unit, in which organs, systems of organs and functional systems perform a single function of maintaining and developing the life of the body in a continuously changing world around them. The body support relative dynamic constancy of the functions of internal organs and biochemical composition of the internal environment. It is because of homeostasis, adaptation, feedback mechanisms.

The concept of homeostasis was explained by Claude Bernard in 1865. The term «homeostasis» was obtained from Greek (homoios,= similar and stasis = standing still). The word «homeostasis» was coined by Walter Bradford Cannon in 1926. **Homeostasis** – is the constancy of internal environment, the process of internally constancy of living organisms. Homeostatic processes act at the level of the cell, the tissue, and the organ, as well as for the organism as a whole. So, animals have constant body temperature, constant pH of Blood, glucose level, water balance, sustainability of the chemical and gas composition. The tendency of all living organisms or cell to adjust its internal conditions, such as the chemical composition of its body fluids, so as to maintain health and functioning, regardless of external conditions. Its regulation involves a receptor, a stimulus and an effector.

Adaptation – the ability to be alive and healthy under different environmental conditions. That balance help to maintain by the nervous and endocrine systems.

Feedback mechanism is a process in which the body senses a change and activates mechanisms that increase or reduce that change. It consists of reducing the production or activity of any organ or system back to its normal range of functioning. It involves an action that directly opposes a variation from normal limits. Hormones, negative and positive feedback loops, the nervous and endocrine systems all help to maintain that balance. An increase or decrease in the variable (ex. blood pressure) causes responses that tend to push the variable in opposite direction (negative feedback mechanisms). Positive feedback is a process in which the body senses a change and activates mechanisms that accelerate or increase that change. This can also aid homeostasis, but in many cases it produces the opposite effect and can be life threatening. It is rarely used by body.

During the evolution of the body gained the properties to withstand environmental changes. With a large supply of potential (chemical) energy, the body actively prevents large fluctuations in temperature, humidity, radiation.

Basic functional properties of the body.

The basic condition of life – a constant exchange of substances between the body and the outside world. Metabolism and energy between the organism and the

surrounding environment is a phenomenon that is the basis of life. With the termination of this exchange the organism dies. Metabolic process consists of two opposite and yet inseparably interrelated processes: assimilation and dissimilation. Assimilation – the process of absorption of substances with subsequent formation of cells, intercellular fluid fabrics. Dissimilation – a disintegration, destruction of organic matter. It is associated with the conversion of chemical energy to others – thermal, mechanical, electrical, radiation. Consequently, assimilation leads to accumulation and dissimilation – to matter and energy costs.

Associated with metabolism there are another properties of a living organism. These properties ensure the existence of the individual, its species:

- ✓ irritability (reactivity) – ability to respond to environmental influences. The inherent plant and animal organisms and is found primarily in changing metabolism. Thanks irritability organism adapts to its environment;
- ✓ excitability – the ability of living cells respond to stimulation, it is ability of biological structures to excitation. The most exciting – nerve and muscle tissue, where excitement quickly transferred from one cell to another. Excitability associated with the occurrence of bioenergy action;
- ✓ excitation – energetic state of tissues, organs, body. Muscle excitation in decreasing gland secretes some secret nervous system sends impulses. Under normal conditions of excitation precedes the emergence of electric potential.
- ✓ growth – an increase in the mass of the developing organism;
- ✓ development – the process of formation of an adult organism from zygotes This physiological property provides self-healing;
- ✓ reproduction – the property of self-reproduction, that is birthday like myself organisms.

Nervous and humoral regulation of functions in the body.

Living organism has self-regulation – is the body's ability to carry out the regulation of physiological functions. As a system of self-regulation that maintains constant internal environment (homeostasis) for 60-70 years with large fluctuations in either direction. Regulation of all processes carried out by the nervous and humoral. These two regulatory systems are so closely linked that often have common links. In the process of historical development of the nervous system of living organisms acquired the leading role, as it brings together the work of all systems and determines the behavior of the organism in the environment, its resistance to environmental influences. The nervous regulation coordinates its voluntary and involuntary actions and transmits signals between different parts of its body.

The nervous regulation is carried out by the central nervous system and the peripheral nervous system including the autonomic nervous system, comprising the sympathetic nervous system and the parasympathetic nervous system.

The nervous regulation is carried out by reflexes – the body's response to irritation with the involvement of the central nervous system.

The humoral regulation is carried out by means of chemicals dissolved in body fluids – hormones biologically active substances and metabolic products. The main

role belongs to Hormones. Hormones have many different functions and modes of action; one hormone may have several effects on different target organs, and, on the other hand, one target organ may be affected by more than one hormone.

So, along with nervous system humoral regulation controls and coordinate the body functions and maintains a homeostasis. So both endocrine and nervous systems collectively called neuro-endocrine system.

Table 1. Continuance of life and pregnancy of animals

Kind of animal	Life, years	Farm using	Pregnancy
Horse	30-40	15-20 years	11 months
Cattle	20-30	8-12 years for milk 2 years for meat	9 months
Sheep, goat	10-15	6-7years	150 days
Pig	10-15	1 years	114 days (3 months, 3 weeks, 3 days
Rabbit	2-6	6-8 months	30 days

Table 2. Continuance of incubation of poultry eggs

Kind of bird	Days	Kind of bird	Days
Hens	21	Goose	29-30
Ducks	28	Quail	17
Turkey	28-29	Ostrich	42-44

So, physiology is the study of how the body functions. Cause and effect occurrences are the focus of physiology. Our bodies are kept internally balanced even though our outward atmosphere is always changing. This process of constancy is known as homeostasis. Homeostasis is a concept used throughout this book to explain how the internal environment is maintained at a level favorable to healthy functioning within the body compartments. Each organ has a specific function. An independent body is relative, since it is part of the system of its activity is regulated by the body as a whole. Bodies are divided into permanent functioning throughout life, and temporary formed at a certain stage of development of the individual and then through the various periods of time dying. Bodies are combined into systems that perform specific functions, such as the nervous, cardiovascular, respiratory, digestive, excretory, and others. In the process of ensuring the unity of the body and the conditions of his life selectively combines the activity of several organ systems. These temporary associations called functional organ systems. Functional systems are different from the systems of the fact that they are involved in the various activities of the body, depending on the changes it needs.

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.

2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.
5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.
7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.
14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

CHAPTER 2. PHYSIOLOGY OF EXCITABLE TISSUES

Physiological characteristics of excitable tissues, their common properties.

To excitable tissues that we will study belong the nervous, muscule, glandular tissue. All of them can be in the same functional states. These states are:

Physiological rest – is state without any reaction or excitation process what can be physiologically displayed.

Excitation – is the response of biological structures to the action of the stimulus, energetic state of tissues, organs, body.

Inhibition (braking) – decrease or stopping of excitability

Let me make a brief discussion on their characteristics. The common properties of all excitable tissues are:

An irritability (reactivity) – the ability of biological structures to move from a state of calm in the active state under the influence of various factors (irritants).

Excitability – is ability of biological structures to excitation (is an ability of a tissue to respond to stimuli (an irritation) specially, singlemindedly and with the maximal velocity).

Excitation – is a complex (complicated) biological process expressing by response reaction to an irritation,

Concept about irritant, classification of irritants.

During evolution gradual differentiation of tissues participating in adaptive organism activity has taken place. The irritability in these tissues has reached the best expression and has received the name Irritation.

Irritation – the process of effect of the stimulus on the biological structure.

Irritant – is a factor that causes the transition of the biological structure from physiological rest in active status.

Classification of the irritants:

By the nature of power:

- ✓ physical – mechanical, temperature, light, sound and electrical ones- osmotic pressure, pH, ion structure changing;
- ✓ chemical – acid, alkalis, medicines;
- ✓ biological – hormones, vitamins and others, biologically active substances;

By the biological features:

- ✓ adequate – stimuli to which the biological structure is adapted (*for example, a light to the eye, the sound to the ear)*;
- ✓ inadequate – stimuli to action of which biological structures are not adapted.

(*for example, the effect of mechanical factors (impact) on the receptors of the eye, the effect of chemicals on tactile skin receptors*).

By the power, the intensity of the action:

- ✓ sub-threshold – stimuli that do not cause biological reactions;
- ✓ threshold – stimuli that are beginning to cause a biological response;
- ✓ suprathreshold – stimuli whose power exceeds the power threshold stimuli.

Description of tissue excitation and conditions of excitation.

The excitation is the response of biological structures to the action of the stimulus. Excitable structures – is structure which is characterized by excitability. They include:

- ✓ nerve cells and nerve fibers;
- ✓ muscle fibers;
- ✓ some types of glandular cells.

There are such types of biological reactions:

- ✓ local (biological reaction that occurs at the site of irritation and does not extend to adjacent biological structures);
- ✓ common (biological response that extends to adjacent structures).

The nonspecific description of excitation of all excitable tissues are changes of metabolic processes in their cells, almost increase, changes in the chemical composition of cells, the emergence of energy.

The specific description of excitation of nervous tissue is generation and conduction of the electrical impulses, the formation of signaling substances (neurotransmitters, neuromodulators, neurohormones). The specific description of excitation of muscle tissue is contraction. The specific description of excitation of glandular tissue is synthesis and allocation of biologically active substance.

Conditions of appearance of excitation.

1.First of all it should be any irritant.

2. The irritant has to cause during some time (duration of the stimulation). This time is called useful time. Useful time – the smallest time at which an the irritant of the threshold power can cause excitation.

3.By the power the irritant has to be not less than certain thresholds. In physiology it is called the law of power. The minimum stimulus power, able to cause minimal reaction – irritation threshold. For excitable structures characteristic of this pattern: the higher excitability of the tissue needs the smaller threshold force of irritation.

4. The law "All or Nothing". On the effect of subthreshold stimulus biological structure does not answer ("nothing"). On the effect of stimulus of the threshold power occurs once the maximum response ("all"). Further increase in stimulus force did not cause increased biological response. *For example, if is greater power of the stimulus, then is greater biological response. Really, in some cases maximum power of the stimulus can cause the biggest reaction. On the other hand the answer of the biological structures can be the intensity of biological response is reduced; the biological structure is destroyed, any response is absent.*

Bioelectric phenomena in the body. Classification of potentials.

The cell is an elementary biological unit. Most of the physiological processes in the cell occur involving the cell membrane. There are significant differences in chemical composition of intracellular environment and extracellular fluids. These differences are reflected in Table 3.

Table 3. Constant exchange through the cell membrane of substances between the intracellular and extracellular sectors.

	Extracellular fluid	**Intracellular fluid**
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{2+}	2,4 mEq/L	0,0001 mEq/L

Mg^{2+}	1,2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/ L
HCO_3^-	28 mEq/L	10 mEq/L
PO_4^{3-}	4 mEq/L	75 mEq/L
SO_4^{2-}	1 mEq/L	2 mEq/L
Proteins	5 mEq/L	40 mEq/L
Glucose	90 mg%	from 0 to 20 mg%
Amino acids	30 mg%	200 mg%
pO_2	35 mm Hg	20 mm Hg
pCO_2	46 mm Hg	50 mm Hg
pH	7,4	7,0

Bioelectric phenomena in the body – exchange of electric potentials between the inner and outer surfaces of the plasma membrane of all cells. The basis of this exchange is the mechanisms of transport of substances through the cell membrane.

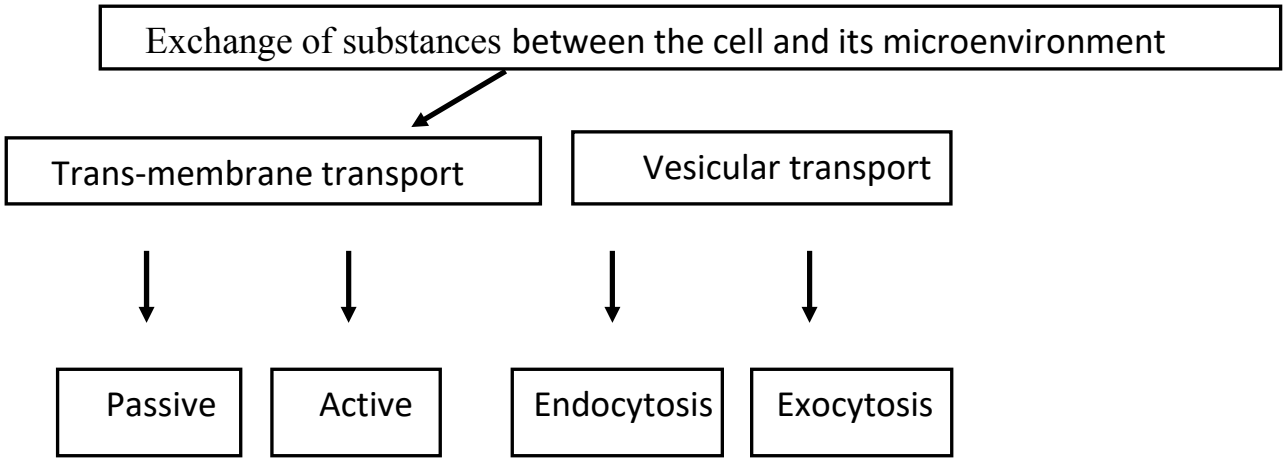

Figure 1. Exchange of substances between the cell and its microenvironment

There is a difference of electric potentials between the inner and outer surfaces of the plasma membrane of all cells. To understand the phenomenon, imagine a cell in which the cytoplasm is replaced by the electrolyte solution, which consists of small particles of cations (e.g. potassium ions) and anions of larger particles (e.g. protein). Small particles of cations can easily diffuse through the pores of the membrane while the cell membrane is impermeable to anions. It is called the membrane potential.

Membrane potential (MP) – is a trans-membrane potential difference that exists between the inner and outer surfaces of the plasma membrane. Cell membrane (membrane) has a positive charge (+), and the cytoplasm is negative (-). In excitable cells membrane potential is called– resting potential.

Resting potential (RP) – is a membrane potential of excitable cells that are at rest. In other words, RP – is a special case of membrane potential. In physiological resting conditions the inner side of membrane is charged negatively and the outside one, positively, i.e. the living cell membrane is polarized. The physiological importance of resting potential. The presence of the RP on the membrane of cells determines their rice such as anxiety, i.e. the ability to be excited in response to stimulus. In terms of electrophysiology, this means that the presence of RP is a prerequisite for the emergence of the action potential (AP).

Action potential (AP) – is a rapid change of membrane potential that occurs in excitable structures in response to stimulus. Excited area has a negative (-) charge, not excited has a positive charge (+). Series of the AP (impulses), which are distributed along the cell membrane, are "signals" that provide the transmission of information along nerve and muscle fibers. Actually the ability to generate the AP is the main feature which distinguishes the excitable structures (nerve, muscle and some types of secretory cells) from others. AP is caused by interaction of stimulus with the exciting cell. The stimulus is actually the cause of the AP in this interaction, and the properties of cells determine the conditions of its occurrence. The main characteristic of cells that determines the conditions of the AP is its excitability.

In damaged tissue membrane potential is called the potential damage. There is potential difference between intact and damaged areas of tissue. **Potential damage**– is a membrane potential of damaged cells. The damaged area has (-), but undamaged (+).

For the first time bioelectric phenomena (the theory of “animal electricity”) in the body was invented and was proved by the Italian physiologist Luigi Galvani in his experiments on the frog. He worked out on the frog the method of practical realization his invention and explanation to it. His first experiment (1791) is the example of the action potential. His second experiment (1794) is the example of the potential damage.

Hypothesis about the origin of resting potential.

Ionic hypothesis (ionic mechanisms for the origin of resting potential). The first hypothesis about ionic mechanisms of the origin of the membrane potential was proposed in 1896 by a representative of the Ukrainian school of physiologists Chagovets V.Y., who was the head of the physiology department at Kiev University of St. Vladimir. He said that after influence of any irritant in excitable tissues dissociation of H2CO3 is observed. As a result $HCO^{-}3$ and H+ is formed. H+ transits through the cell membrane. Difference of the potential (i.e. the membrane potential) arises between the inner and outer surfaces of the membrane and resting potential appears.

Membrane hypothesis, was formed by Bernstein (1902). He said that after influence of any irritant the cell membrane become penetrable to anions. The transition of the anions from cells in the extracellular environment leads to what is on the inner surface of the membrane and creates an excess of + ions ("+"sign appears), on the outer surface exactly the same number of anions increases (sign "-"). In other words, difference of the potential (i.e. the membrane potential) arises between the inner and outer surfaces of the membrane.

Nernst's hypothesis was proposed in 1909. He said that after influence of any irritant on the inner and outer surface of the membrane accumulates the number of ions and resting potential appears. This means that the number of K+ ions which comes from the cell by concentration gradient is equal to the number of K+ ions which enters the cell by the electrical gradient. Membrane potential value at which occur states of equilibrium is called the equilibrium potential for this ion. In other words the equilibrium potential - is a level of electric potential on the membrane that completely stops the flow of ion diffusion by concentration gradient. Substituting in the Nernst's formula the value of the concentration of K+ ions inside the cell (140 mEq/L) and in the extracellular environment (4 mEq/L), we obtain the value of potassium equilibrium potential which is equal to – 94 mV.

Today, it is finally proved that the occurrence of membrane potential is associated with the diffusion of ions. It is known as the **Na+, K+-pump or hypothesis of Hodgkin, Huxley and Katz (1952).** This is because there are not one but several types of ions in the cell (e.g. potassium, sodium, chlorine) that penetrate through the membrane. They said that after influence of any irritant through a cell membrane some proteins carry out active transport of Na+ and K+ against their concentration gradients. It takes place a passive entry of Na+ ions into the cell. In this case the share of cations (K+) under the laws of diffusion will leave the cells in the environment by the concentration gradient and anions will remain in the cell because the membrane is impermeable to them. The transition of the cations from cells in the extracellular environment leads to what is on the inner surface of the membrane and creates an excess of K+ ions ("+"sign appears), on the outer surface exactly the same number of anions increases (sign "-"). Permanent passive entry of Na+ into the cell reduces its membrane potential. In other words, difference of the potential (i.e. the membrane potential) arises between the inner and outer surfaces of the membrane and resting potential appears.

Changes in excitable tissues during excitation.

Excitability of cells and tissues is a basic function of life. It is the ability of cells to respond to stimuli. Excitability is necessary for the functioning of nerves, muscles, and hormones, among other things. The basis for the excitability of cells is their ion distribution, and the distribution of ions and molecules is determined by transport mechanisms associated with their plasma membrane structure. This structure permits and regulates various forms of ionic and molecular transport mechanisms associated with their plasma membrane structure. During and immediately after the influence of irritant cell excitability changes. There is a certain relation between the action potential phases and excitability. There are 5 periods:

1. The latent period. It is associated with the chemical and all the other molecular changes of which the actual contraction is but can not be visible.

2.Period of absolute refractory. During this period, the cell is not exciting – no stimulus is can not cause AP. During an action potential, a second stimulus will not produce a second action potential (no matter how strong that stimulus is).The existence of absolute refractory is because in this period all sodium channels are in

the inactivated state. To excitability recovered necessary transition of sodium channels inactivated state to the resting state. This is achieved by closing and opening of the activation gate inactivated protein channels. The duration of this period for large nerve fibers - from early AP and for some time after its completion, approximately 2 msec. Therefore, the duration of the absolute refractory is for skeleton muscle – 0,005s, cardiac muscle – 0,3–0,4 s.

3.Relative refractory period. Occurs immediately after the absolute refractory period. It is characterized by an increasing the threshold depolarization. This means that during the period in AP may occur, but under the influence of stimuli greater force than usual depolarization is described as the reversal of the resting membrane potential, because during this period the membrane potential is closer to zero. (Another action potential can be produced, but only if the stimulus is greater than the threshold stimulus). AP which occurs during this period is characterized by changes in shape – reduced amplitude and steepness of the rise, increasing the duration.

The possibility of AP during the relative refractory is because at this time a number of sodium channels has regained its initial state (state of rest), but a significant number of them is still in the inactivated state. In addition, potassium channels are not fully closed, so potassium current output prevents AP that appears in response to a strong stimulus to the relative refractory period. The duration of this period for large nerve fibers is 0,001–0,01 s, for muscle – 0,03 s.

4. Period of exaltation or supernormal excitability. It is characterized by increasing of excitability, since the membrane potential is closer to the critical level, than in the resting state. In this phase the tissue can respond to the subthreshold stimulus.

5. Period of subnormal excitability. In contrast, it is characterized by the decreased excitability, because of the deviation of the membrane potential from the critical level (Figure 5, e). In this phase the tissue can respond to the superthreshold stimulus.

The law «Power of Time». Concept about rheobase, chronaxie, lability.

Among the stimuli that can cause AP, is the most important electrical current. During laboratory classes we use electrical current for nerves and muscles of frogs. From the frog we make muscle-nerve preparation and do a few experiments. A muscle-nerve preparation of the frog usually consists of the muscle with the sciatic nerve with a portion of the femur. The basis of electric current is it's the ability to cause stimulation, and the electrical current acting as a stimulus. In order to cause excitement, an electrical impulse is to be sufficient (threshold or above threshold) duration. Threshold power (or threshold voltage) of electric current is used as a measure of excitability of nerves and muscles.

Between the threshold force and threshold of electric current electrical pulse duration is the reciprocal dependence. In the physiology is it won the called of the «law of hyperbole» or curve «power – time», the law «Power of Time»).

The excitability curve demonstrates the exact relationship between the strength and the duration of a stimulus (fig. 2.).

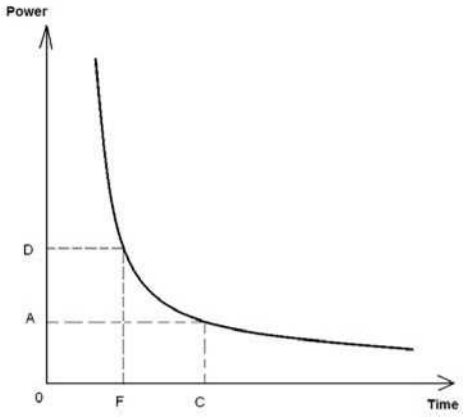

Figure 2. Curve "power-time"

The shape of the curve is similar in almost all excitable tissues. The greater power of the stimulus, the less time is needed so that there was a biological reaction. Following are some of the important points to be studied in the excitability curve:

a) **Rheobase** (OA) – minimum direct current power, can cause excitability (threshold stimulation). This is the least possible, i.e. minimum, strength (voltage) of stimulus which can excite the tissue. The voltage below this cannot excite the tissue, whatever may be the duration of stimulus.

b) **Chronaxie** (OF) – the smallest time during which any stimulus must act largest two rheobase to cause excitement.

This figure is easier to determine than the useful time, so practice using research rheobase and chronaxie. Threshold or above threshold is steepness of increase electrical pulse. The value of chronaxie is used to compare the excitability in different tissues. The measurement of chronaxie determines the excitability of tissue. Longer the chronaxie, lesser is the excitability. Chronaxie in human skeletal muscles varies from 0.08 milliseconds to 0.32 milliseconds. In frog's skeletal muscle, it is about 3 milliseconds. Chronaxie is 10 times more in skeletal muscles of infants than in the skeletal muscles of adults.

Chronaxie is shortened by increased temperature and prolonged in cold temperature. It is shorter in homoiothermic animals than in poikilothermic animals. Chronaxie is shorter in red muscles than in white muscles. In physiology they determine one more property of excitable tissues, which has received the name a **lability.** It is a functional mobility of tissues, its parameter is the potentials action maximal number, which the excitable tissue is capable to generate per 1 second according to a rhythm of a submitted boring (irritation). The normal size of a lability, e.g., for a nervous tissue makes 500-1000 impulses per second, and for skeletal muscles - 150-200 impulses per second. There is a skeletal muscles lability rising with ageing. It is shown in augmentation of irritation frequency, at which the gear (incomplete) tetanus turns in smooth. In newborn’s muscles it occurs at a stimulus frequency 4-20 per second, at adulthood - 50-100 impulses per second.

Thus, the frequency of discharge of motor nerve fibers with random movements typically is less than 50 per second. While in sensory nerve fibers (e.g., auditory or optic nerve) with a strong stimulation it can reach 1000 per second or more. The maximum number of action potentials ("maximum rhythm"), which is

capable of exciting the structure generated for 1 second in accordance with the rhythm of stimulation.

Doctrine of parabiosis by H. E. Vvedensky.

First attention to the various ability excitable structures played a different number of stimuli turned N.E. Vvedensky (1901). Vvedensky Nikolay Evgenyevich (1852– 1922) – the Russian physiologist. H. E. Vvedensky for the first time studied and described special state on nerves and muscles and gave to it the term «parabiosis». This doctrine is stated in the monograph «Excitement, Braking and Anaesthesia» (1901). **Parabiosis** (parabiosis; Greek para near + biosis life) – the condition of excitable tissue, especially nerve, under the influence of strong irritations and which is characterized by disturbance of conductivity and excitability. The state of the nerve between life and death. The item develops at action on excitable tissue of the most various irritants (nervous impulses, poisons, drugs in high doses, mechanical, electric and other incentives) as is normal, and in pathology.

The parabiosis continues during 3 stages which are consistently replacing each other: transforming, paradoxical and braking. Each phase is characterized by various parameters.

The 1st stage – transforming is characterized by decrease in excitability and increase in lability of nerve. It means that strong, frequent and moderate irritations cause the same reaction (excitation).

The 2nd stage paradoxical – is characterized by the perverted reaction: strong irritations cause smaller effect, than moderated. In the II phase excitability reaches a maximum, and lability begins to decrease.

The 3rd stage – braking is characterized by decreasing in parallel excitability and lability. The strong, moderate irritations do not cause visible reaction: braking develops in nerve.

Vvedensky used drugs in high doses (curare). *Curare - extract that is obtained from the plant Strychnos i Chondodendron, growing in South America (the poison used since ancient times, such as for the treatment of Indians arrows)*. He applied drug on the nerve and observed 3 stages. After a brake stage at action of strong irritants there can occur total loss of excitability and conductivity (block), and further and dying of nerve. H. E. Vvedensky compared parabiosis of a nerve to the stopped excitation wave and designated such state as local not oscillatory excitement. However the parabiosis of nerve can be removed. Using drugs during short time or washing the nerve with physiological solution after drugs can occur excitability and conductivity of the nerve.

The doctrine about a parabiosis is the large achievement of domestic science which exerted impact on development of various fields of physiology and theoretical medicine. Nowadays doctrine about a parabiosis can be called anesthesia. These are substances that are used in medicine as local anesthetics in dentistry (Novocain, Procaine, and others). These drugs make it difficult or even stop the spread of AP along nerve fibers. After some time excitability and conductivity of the nerve returns.

Classification of nerve fibres.

Nerve fibre is the axon of the neuron, which diameter makes up 10-20 μm and length above 1 m. The main function of the nerve fibre is the transduction of a nerve impulse. The nerve fibres can perform the transporting function realizing the convey of mediators, enzymes from the soma to the nerve ending, or in the opposite direction, from periphery to the soma.

Nerve fibres are divided into two groups: myelinated and unmyelinated ones. The unmyelinated fibre consists of an axis cylinder, which encloses axoplasm with microtubules, neurofilaments, mitochondria and so on. The myelinated nerve fibre has the same structure, but its axis cylinder is covered by the myelin sheath, which is produced by Schwann cells. Schwann cell wraps itself in many times around the cylinder. But the myelin sheath is interrupted at regular intervals, leaving uncovered some parts of the axis cylinder membrane, which are called Ranvier's nodes.

In 1937 Erlanger and Gasser classified the nerve fibres into 3 types by their excitability, impulse conduction velocity, duration of the action potential, diameter: A, B and C.

- ✓ All the nerves of A type are myelinated. They are divided into 4 groups: Aα, Aβ, Aγ and Aδ Aα is the motor nerve fibre, innervating the skeletal muscle (d=12-22μm, velocity of 35 impulse conduction, v= 70-120m/sec). Aβ, Aγ and Aδ are the afferent fibres, which start from the pressure-, pain- and thermo- receptors.
- ✓ B type fibres are slightly myelinated and serve as preganglionic fibres of the vegetative nervous system. Their conduction velocity is 3-18 m/sec, diameter is 1- 3μm. A distinctive feature of these fibres is the absence of the after-depolarization phase: the repolarization phase of the action potential passes directly to the after-hyperpolarization.
- ✓ C type fibres are unmyelinated fibres (d=1 μm, v=0.5-3 m/sec.). These fibres are the postganglionic fibres of the sympathetic nervous system. They have a long-lasting after-depolarization, accompanied by still more prolonged after hyperpolarization.

Laws of conducting impulses along nerve fibers

The basis of the spread AP in nerve and muscle fibers are local electric currents that occur between depolarized area fibers and not polarized (quiet) portions of the membrane. In myelinized nerve fibers myelin is an excellent isolator, so the impedance of the membrane AP is very high and can spread through the covered areas of myelin fibers. In Myelinated Fibers electrical current flows through the surrounding extracellular fluid outside the myelin from node Ranvier to node Ranvier.

Laws of conducting impulses along nerve fibers.

1. Anatomical and physiological continuity of fibers. There is a prerequisite conducting excitement. Violation of anatomical continuity occurs when nerve section or injury. In violation of physiological continuity understand changes in functional characteristics of nerve fibers that conducting impulses determined – reduction factor

of safety (e.g. drying nerve).

2. Bilateral conducting (two-way conduction). AP spread to both sides of the place of origin of excitation, as well as branching nerve fibers. If irritate nerve electric current area, the pulses propagate in both afferent and efferent directions.

3. Isolated conducting. In peripheral nerve impulses spread on each fiber separately, i.e. not moving from one fiber to parallel along located. Consequently, the pulses have an effect only on those cells contacted the end of the nerve fibers. This fact is important in view of the fact that each peripheral nerve contains a large number of nerve fibers – motor, sensory, autonomic – that innervate different in structure and function of cells and tissues.

4. Nondecremental conducting. That is conducting no damping, in which the AP does not change its characteristics during spread in fiber.

5. Not relative fatigue nerve fibers. The impulse does not cause fatigue fibers.

Mechanisms of muscle contraction. Stages of muscle contraction.

Human interaction with the environment can not be made without reducing its muscles. Vertebrates and humans have three types of muscles: skeletal muscle (about 50 per cent of the body), cardiac muscle and smooth muscles of the internal organs, vessels and skin (perhaps another 10 per cent).

Muscle fiber, as each cell has a membrane – sarcolemma, endoplasmic reticulum – sarcoplasmic reticulum, mitochondria, sarcoplasm. His special feature is the presence of myofibrils. Myofibrils consist of bundles of «threads» – myofilaments (thin – actin filaments and thick – myosin filaments) (fig.3). The portion of the myofibril (or of the whole muscle fiber) that lies between two successive Z discs is called a sarcomere. Myosin filaments – are thick filaments length of 1.6 micrometers. They consist of a protein myosin (molecular weight 500 000). Actin filaments – are long thin filaments 1 mm and a thickness 7.5 nm. They consist of three proteins: actin, tropomyosin, troponin.

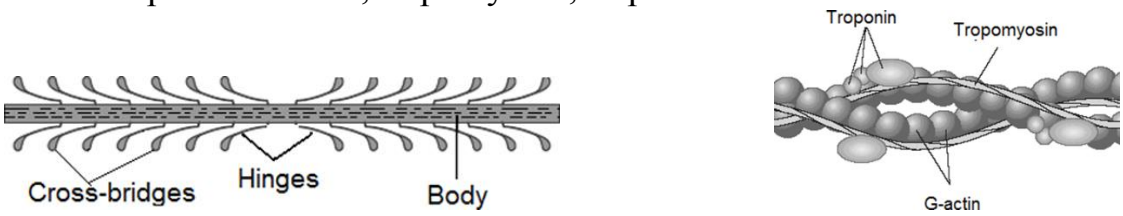

Figure 3. Structure of the myosin filaments (left) and the actin filaments (right)

Molecular mechanisms of muscle contraction explains the theory of Huxley-Hanson – the theory of «sliding» myofibrils (Huxley H.E., Hanson J., 1954). The main provisions of this theory:

- ✓ The process of contraction is a result of sliding actin filaments along myosin filaments.
- ✓ During the contraction the length of "thin" actin and "thick" myosin filaments does not change.

✓ Contraction of myofibrils is due to contraction of a large number of sarcomere. The process of muscle contraction requires energy of ATP.

There are three phases in single muscle contraction (fig. 4).

Stage 1. Latent period – time from start of the stimulus to the contraction of muscles). It lasts 0.01s. It is characterized by excitation of the membrane of muscle fibers and spread the AP along membrane. Electromechanical coupling – is a transmission signal about contraction from sarcolemma to myofibrils. In this period the muscle is in refractory period, during which the processes of preparing contraction, excitation conduction and physicochemical alterations of the muscle occur.

Stage 2. Actually contraction. It lasts 0.04 s. With the opening of the actin active centers begins the process of contraction - sliding actin filaments along miosyn filaments to the center of sarcomere with using ATP. The muscle is in the phase of exaltation (increased excitability).

Stage 3. Relaxation. It lasts 0.05 s.

Totally the single contraction duration is 0.1 sec.

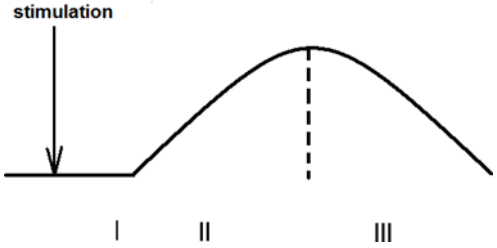

Figure 4. Single contraction curve: I - latent period; II - the period of contraction, III- the period of relaxation.

Types of the muscle contraction. Work, power, fatigue of the muscle.

Depending on the type of load there are 3 contraction models of isolated muscle:

✓ isotonic in which myofibrils are shortened, but the tension is not changed. This type of contraction occurs when the muscle moves the cargo. One end of the muscle fixed, the other free, bound with a cargo;

✓ isometric contraction in which the length of myofibrils remains constant, but their tension increases. This type of contraction occurs when both ends of the muscle are fixed. This static type of contraction provides the contraction to support the posture of the body.

Isotonic contraction	Isometric contraction
During the contraction decreases the length of muscle	During the contraction of muscle length does not change
Muscle tension does not change	Muscle tension increases
Running external work (moving cargo in space)	Exterior work not implemented

Altogether natural contractions in the organism are never purely isotonic or purely isometric. Exceptionally the isometric is the contraction of the heart ventricles. When the issue is not isolated muscle, but the muscle that functions in the body, then distinguish the following type of contraction:

✓ axotonical contraction – mixed type of contraction. This is type of contraction, in which both reduces the length of muscle and increasing its tension. This type of reduction provides a dynamic moving body in space and some of its parts in respect to each other; can be concentric, when the muscle length is reduced, while its tension is increased; and excentric, that is characterized by increase of length and tension.

By the duration the contraction are single (rare) and tetanus.

The single muscle contraction – contraction under stimulation of the muscle or the motor nerve fibre by a single stimulus. Isolated contraction occurs under the condition where one muscle fiber affects one stimulus. But the muscle reacts to the individual stimulus not immediately. Single contraction includes latent period, the period of contraction, the period of relaxation(fig. 4). .

In natural conditions in the organism a skeletal muscle usually receives number of impulses from the nervous system. Stimulation of the muscle by rhythmic stimuli leads to a strong and long-term contraction, known as tetanic contraction or tetanus.

Tetanic contraction (tetanus) – long and strong muscle contractions associated with increased frequency of stimulation. For the occurrence of tetanus each successive stimulus must act on the muscle, which has not finished a cycle of contraction-relaxation.

The basis of tetanus is the phenomenon of summation (imposing a contraction on the other). To place summation, it is necessary that the interval between incentives was no less than the refractory period of muscle fibers.

Depending on the frequency of stimulation distinguishes two types of tetanus (fig. 5):

incomplete, occurs at low frequency stimulation (5-50 Hz) when every to account for the phase relaxation of the previous contraction; If the second stimulus is applied when the muscle has already begun to relax after the first contraction, the peak of the second contraction will be separated from that of the first (incomplete summation, toothed tetanus).

complete, occurs when high frequency stimulation (50 Hz) when every successive incentive to account for the contraction phase of the previous phase of contraction (Figure 9.13). If the second stimulus is applied before the first contraction has reached its peak, the second contraction will fully merge with the first, forming a single summation peak (so-called complete summation, smooth tetanus).

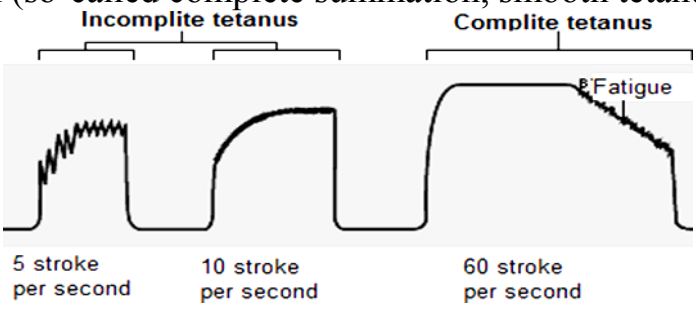

Figure 5. Types of tetanus.

At complete summation the interval between the first and second stimuli must be less than 0.05 sec, while for the second type (incomplete summation), it must be longer than 0.05sec. To produce tetanus artificially the muscle is subjected to a great

number of stimuli following one another at the frequency required for summation. Generally tetanus can be observed if the interval between stimuli is longer than the refractory period and shorter than the whole duration of the contraction response, so that the second stimulus will act on the muscle before it has relaxed after the first stimulation. After termination of the tetanic stimulation muscle fibres do not relax completely and their initial length recovers but some time later. This phenomenon is called post-tetanic or residual contraction.

The work of muscle measured by the product of weigh of the lifted load on the size of shortening of the muscle. There are 2 types of muscle's work:

- ✓ external (dynamic)
- ✓ internal (static).

Dynamic work – is a work of moving cargo body or its parts in space. She is performed in experimental conditions in isotonic mode of contraction, in a body at axotonical contraction. Dynamic work depends on speed and load of the contraction. The maximum dynamic work performed at medium speed and load.

Static work - a work in which muscle fibers develop tension, but not change its length. It is in isometric mode (for example, work with containment of the cargo). Inner work is associated with the processes developing in the same muscle fiber (mechanical work to overcome friction, osmotic work on moving ions, etc.) 6.

The power developed by muscle during contraction is the sum of the powers of individual muscle fibers.

There are maximum and absolute power of contraction.

The maximum power in the isotonic mode is determined by the maximum weight of cargo, which raises the muscle during the contraction, in isometric mode - load, which develops muscle, is expressed in kg. The maximum power depends on the structure of muscle, its functional state. For example, dog jaw muscles can lift cargo, times greater than its mass. However, the maximum force does not allow comparing the strength of various muscles. This is another indicator.

Absolute power of contraction – is the ratio of maximum isometric contraction power to physiological cross-sectional area of muscle, is expressed in kg/cm2. Physiological cross-section of a muscle is cross-sectional area of fibers that make up this muscle.

Fatigue – temporary reduction in muscle performance that occurs as a result of the work and disappears after rest. Fatigue finds himself by the reducing of the contraction power (amplitude), increasing latency period and duration of relaxation phase.

Factors that cause fatigue:

At the cellular level (in conditions in vitro in isolated muscles):

- ✓ reduction of inventories of ATP (occurs due to decreased glycogen reserves, interruption resynthesis of ATP and creatinephosphate);
- ✓ accumulation of metabolic products. Acidic metabolic products (lactic acid, pyruvic acid, phosphoric acid, etc.) is diffuse into the around cell space and

reduce the excitability of muscle fibers, inhibit glycolysis and ATP formation, competitively bind to troponin C, displacing calcium.

It should be noted that isolated skeletal muscle fatigue in his direct irritation is the laboratory phenomenon. In a body to muscle constantly enters the blood, which supplies the necessary nutrients and takes away the metabolic products.

On the organ level (in the in vivo condition):

- ✓ fatigue related motor nerve centers;
- ✓ fatigue of the neuro-muscular synapses.

Proof that the lower efficiency of muscles primarily is concerned with the fatigue of nerve centers, there are Sechenov's experiments in which he proved that rehabilitation of human hands tired muscles faster if other hand or muscles of lower extremities work in the rest period. Sechenov I.M. called this relaxation as active.

Proved that the muscles that perform static work, tired faster than muscles that perform dynamic work. For example, a person is harder to stand than to walk. To study muscle fatigue in humans in laboratory conditions using ergographs – devices to record mehanohramms with rhythmic movements that are performed by the muscle group. Record fatigue curve called ergogramme.

Skeletal muscle fibres. Functions and properties of skeletal muscle fibres.

Skeletal muscle is anchored by tendons to bone and is used to effect skeletal movement. They are multi nucleated. They work under the will of organism or central nervous system. • An average adult male is made up of 42% of skeletal muscle and an average adult female is made up of 36% (as a percentage of body mass).

Skeletal muscles constitute an active part of the supporting system and ensure the following functions:

- ✓ posture support;
- ✓ provide movements of separate parts of the body relative to each other;
- ✓ owing to them the body movement occurs in a space;
- ✓ heat production (they produce 60% of the organism's total heat).

Skeletal muscles possess three very important properties:

1.Excitability. Skletal muscles can be excited by the impulse of motor nerve. In comparison with the motor nerve fibre the skeletal muscle fibre excitability is less. So the excitation threshold (40 mV) in muscle fibres is higher than in nerve ones (20 mV).

2.Conductivity.They have the ability to coduct the excitation along the length of muscle fibre at the rate of 3-5 meters/second.

3.Contractility. Skletal muscles can do the single and tetanic contraction.

Force summation. The muscle consists of separate muscular fibres of different excitability and as the stimulus strength grows up more amounts of myofibrils involve into the contraction process. In result the muscle response gradually increases.

Smooth muscle fibres. Properties of smooth muscle fibres.

It is therefore called smooth muscle because of this lack of striation. They found within the walls of many organs and are involved in their function (stomach, intestine, gall bladder, urinary bladder, uterus, bronchi, eyes, etc.) and the blood vessels, where it plays an important role in circulatory control). Smooth muscle is uninucleated. It has no sarcomeres. It is rich in intermediate filaments that contain two specific proteins, desmin and vimentin (In comparison with the skeletal muscles - troponin – tropomyosin complex). During the muscle contraction the actin and myosin interaction is provided by phosphorylation of the myosin head through the calcium - calmoduline complex. The energy expenditure here is about 300 times less than that in the skeletal muscles. The ratio of thin to thick filaments is much higher in smooth muscle (~15:1) than in skeletal muscle (~6:1). Smooth muscle fibers are much smaller (2-10 m in diameter) than skeletal muscle fibers (10-100 m).

Some peculiarities of smooth muscles:

1.Excitability. Unlike skeletal muscle, smooth muscle is not under conscious control. They do not work under the will of organism. They are innervated with autonomous nervous system. In skeletal muscle there is only one initiator reduction - an electrical nerve impulse. A smooth muscle is excited by external stimuli. The smooth muscle of the initiators can be 5:

- ✓ nerve stimulation (smooth muscles have sympathetic and parasympathetic innervations);
- ✓ hormonal stimulation (serotonin, histamine, angiotensin, vasopressin, oxytocin);
- ✓ mechanical stretching of muscle fibers;
- ✓ hanges in the chemical composition of interstitial fluid (lack of oxygen, excess CO_2, excess acidic foods and H+ ions in blood);
- ✓ spontaneous initiation (action potential generated in some so-called pacemaker).

2.Conductivity. Speed reduction is much less than in skeletal muscle.

3.Contractility. Molecular mechanisms of reduction are the same as in skeletal muscle – actin filaments are slide along myosin. But smooth muscle can shorten much more than striated muscle. Cycle duration of contraction-relaxation in smooth muscles to 30 times greater than in skeletal muscle. Smooth muscle may be able to reduce hours and days, the so-called state of prolonged muscle tone, use less ATP, have a low fatigue.

BIBLIOGRAPHY

1. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
2. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.

3. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
4. Mazurkevich AY, Trokoz VO, editors. Physiology of farm animals. Workshop. 2nd ed. Kyiv: Center for Educational Literature; 2015. (Ukrainian).
5. Mazurkevich AY, Trokoz VO, Karpovsky VI, et al. ; edited by A.Y. Mazurkevich, V.O Trokoz. Physiology of agricultural animals. Textbook. 2nd ed. Kyiv; 2014. (Ukrainian).
6. Moyes CD, Schulte PM. Principles of Animal Physiology 3rd ed. Don Mills, Ontario: Pearson; 2016.
7. Papachristodoulou D, Snape A, Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 6th ed. Oxford, UK: Oxford University Press; 2018.
8. Pineda MH, Dooley MP, editors. McDonald's Veterinary Endrocrinology and Reproduction. 5th ed. Ames, Iowa: Iowa State Press; 2003.
9. Pollard TD, Earnshaw WC, Lippincott-Schwartz J, Johnson GT, editors. Cell Biology. 3rd ed. Elsevier. 2016.
10. Reddy PB. Text book of Animal Physiology. Andhra Pradesh, India: IMRF Publications; 2015.
11. Reece WO, Functional Anatomy and Physiology of Domestic Animals. 4th ed. Baltimore: Wiley-Blackwell; 2009.
12. Rhoades RA, Pflanzer RG. Human Physiology. 4th ed. Pacific Grove, Calif.: Brooks/Cole; 2003.
13. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
14. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.
15. Smith BP. Large Animal Internal Medicine. 3rd ed. St. Louis, Missouri: Elsevier Mosby; 2015.
16. Tortora GJ, Derrickson BH. Principles of Anatomy and Physiology. Atlas and Registration Card. 11th ed. Hoboken, NJ: John Wiley & Sons; 2005.

CHAPTER 3. PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM

The evolution and general characteristic of organization of nervous systems.

The nervous system is the part of an animal's body. Nervous systems are found in most multicellular animals, but vary greatly in complexity. All nervous systems share similar characteristics, although they vary in the complexity of their organization and of their behavioral output. Nervous system is absent in unicellular protozoans and multicellular sponges, placozoans, and mesozoans.

The nervous systems of the radially symmetric organisms' jellyfish which consist of a diffuse nerve net. It is called diffuse type of the nervous system. These organisms don't have bilaterally symmetrical type of the body. Their nervous system

doesn't have structural organization and neurons are not collected into integrating areas. The nervous system formed of nerve cells whose numerous processes are interconnected in different directions to form a network, thats why irritation in one part of the body conduct into another part.

The evolution of nervous systems in the bilaterally symmetrical animals has two major trends characterize: centralization and cephalization. Centralization of nervous systems refers to a structural organization in which integrating neurons are collected into central integrating areas rather than being randomly dispersed. It is called ganglionic nervous system. Aspects of the organization of a ganglionic nervous system are present in molluscs, arthropods. In arthropods, the central nervous system (CNS) consists of a chain of segmental ganglia. Ganglia (singular ganglion) is aggregation of nerve cell bodies. The CNS of an arthropod such as a cockroach (тарган) consists of an anterior brain and a ventral nerve cord. The nerve cords of arthropods have connectives between central ganglia. Between right and left sides of a bilaterally symmetrical ganglion it is a commissure.

The evolution of nervous systems in the bilaterally symmetrical animals has cephalization. It is the concentration of nervous structures and functions at one end of the body, in a spinal cord and a brain. It is called vertebrate nervous system. Vertebrate central nervous systems, in contrast to those of arthropods, are classed as columnar because they consist of a continuous column of neural tissue, with cell bodies and synaptic areas intermingled. For the 1st time the vertebrate CNS is present in lancelet (animal of Cephalochordata) (latin-Branchiostoma lanceolatum). It has a spinal cord. The vertebrate CNS develops from a neural tube that invaginates from the dorsal surface of the embryo. Most animal species have a nervous system which consists of the brain, the spinal cord, and the peripheral nerves, which connect the various parts of the body to either the brain or spinal cord (tabl.4). The size of the nervous system ranges from a few hundred cells to around 100 billion cells (humans).

Table 4. The organization of nervous system.

Components	Brain	Centeral part of nervous system, Controls all body functions
	Spinal Cord	Long and thin bundle of nervous tissue extending from lower part of brain, transmits neural signals between brain and rest of the body
	Nerves	A bundle of peripheral axons enclosed by connective tissue. Carries nervous signals from nervous system to body and from body to nervous system
	Nerve Endings (receptors)	Motor and sensory neurons end in special type of structures depending on their function.

Divisions	Central Nervous System (CNS)	Brain and Spinal Cord
	Peripheral Nervous System (PNS)	Autonomic nervous system (the sympathetic and the parasympathetic nervous system)
		Somatic nervous system
		cranial nerves and spinal nerves going to and from somatic (body) structures

The functions of CNS. The leading role of CNS in regulatory processes of the body.

It is known that the main condition for existence and for providing integrity of the organism and environment is the organism's ability to be adapted to the external medium conditions. The important role in this providing belongs to the nervous system. In general, the main functions of CNS are:

- ✓ the regulation and coordination of all the organs' and systems' functions (activity);

initiate and/or regulate movement of body parts by initiating and/or regulating the contraction of skeletal, cardiac, and smooth muscles;
regulate secretions from glands;

- ✓ gather information about the external environment and about the status of the internal environment of the body, using senses (sight, hearing, touch, balance, taste) and mechanisms to detect pain, temperature, pressure, and certain chemicals, such as carbon dioxide, hydrogen, and oxygen;
- ✓ the organism's effective adaptation to the continuously altering external medium conditions and, as a result, the living organisms' aimed behaviour formation;
- ✓ maintain an appropriate state of consciousness;
- ✓ stimulate thirst, hunger, fear, rage, and sexual behaviors appropriate for survival.

The nervous system owing to its neuronal principle of the structure and the reflector mechanism of activity differs from other regulatory systems by the rapid reactions.

The leading role of CNS in regulatory processes of the body. CNS coordinates its voluntary and involuntary actions and the rapidly transmits signals between different parts of its body – from one cell to others or from one part of the body to others and to receive feedback.

Neuron as the structural unit of the CNS, classification of neurons. The theory of the neurons structure of CNS.

A variety of cell types are found within the nervous system, but the primary functional cell is the neuron. The nervous system contains two main categories or types of cells: neurons and glial cells.

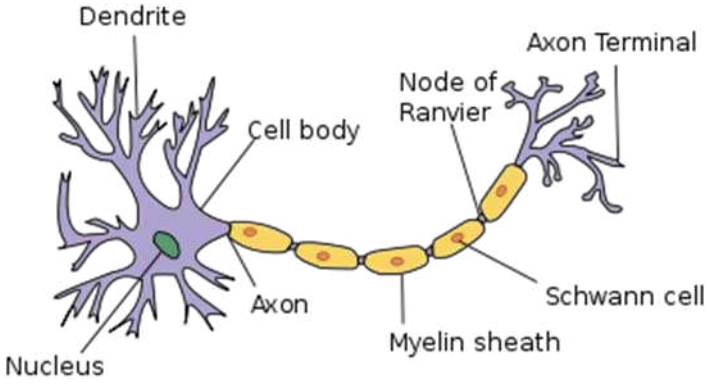

Figure 6. Structure of neuron

Neurons are electrically excitable cells. It is composed of a single soma (cell body), a single axon and one or more axon terminals, one or more dendrites. A soma, or cell body, is the central part of the neuron and contains the nucleus (Fig. 6). Axon hillock (the site of its origin from the soma) and the initial part of the axon, which over the 50-150 μm has no myelin sheath. The specific feature of this segment is its high excitability and an ability to generate the action potential. Immediately after the axon hillock is the axon. An axon can extend tens, hundreds, or even tens of thousands of times the diameter of the soma in length. The axon is specialized for the conduction of a particular electric impulse, called the action potential, which travels away from the cell body and down the axon.The axon is insulated by a myelin sheath. Myelin is composed of either Schwann cells (in the peripheral nervous system) or oligo dendrocytes (in the central nervous system). These nodes of Ranvier can be considered to be "mini axon hillocks", as their purpose is to boost the signal in order to prevent significant signal decay. At the extreme end axon divided into several axon terminals called presynaptic terminals or synaptic boutons. They contain synaptic vesicles which produce neurotransmitters.The junction between the axon of one neuron with another neuron or target cell is the synapse.

Dendrites are cellular projections whose primary function is to receive synaptic signals. The dendrites extend from the soma, which houses the nucleus, and many of the "normal" eukaryotic organelles.

Nerve endings are called receptors. It is a specialized cell or cell part, which distinguishes natural stimuli and transmit information about them to the CNS. They are devided by factor that contributes to stimulation: mechanoreceptors, chemoreceptor, thermoreceptors, photoreceptors. By location they are exteroreceptors (the external surface of the body), interoreceptors (the internal surfaces and organs of the body), proprioreceptors (provide information about body position in muscles, tendons, and joints throughout the body -the locomotor system), visceroreceptors (vessels).

A major function of the other cell types (the glia), which outnumber neurons ten to one, appears to be to maintain the cellular environment to support the activity of the neurons.Although glial cells are not involved with the transmission of electrical signals, they communicate and provide important biochemical support to neurons, provide nutrition, maintain homeostasis, destroy pathogens and remove dead neurons;

generates layers of a fatty substance called myelin that wraps around axons and provides electrical insulation that allows them to transmit action potentials much more rapidly and efficiently. *In the human brain, it is estimated that the total number of glia roughly equals the number of neurons, although the proportions vary in different brain areas.*

Classification of neurons. Neurons are classified by their different properties.

- ✓ By shape they can be round, oval, multangular, pyramidal, etc.
- ✓ By size they vary from 5 μm to 150 μm.
- ✓ Morphologically according to their number of nerve processes they can be unipolar, bipolar, and multipolar. Unipolar neurons have one process; true unipolar neurons are seen only during development. Bipolar neurons have one dendrite and one axon; these are common in sensory systems. Multipolar neurons have a number of dendrites in addition to their single axon. Most neurons are multipolar in nature.
- ✓ By their significance (physiological role) they are subdivided into: 1) afferent, or sensory, or receptory neurons; 2) efferent or motor neurons, 3) intercalated, or contact, or interneurons.

The afferent neurons in vertebrates are represented in the spinal ganglia, ensure the signal perception and conduction from periphery to the centres. Damage of these neurons causes loss of sensitivity. The efferent neurons give rise to an axon that goes out of the CNS and finishes in the effector structures (for example muscles, glands), ensure the signal perception and conduction from the centres to periphery. Damage of these neurons causes flaccid paralysis (a total lack of movement and muscle tone of the affected muscle). The intercalated neurons are characterized by a huge number (90% of all neurons) and small sizes. They are located between the afferent and the efferent neurons. The characteristic feature of the interneurons is their ability to rhythmical and spontaneous activity.

Systemic interaction of all the mentioned neuronal populations provides the regulation, coordination and realization of motor acts in a living organism.

The base of the present conception of the nervous system structure and function is **the neuronal theory of Ramon Cajal and Charles Sherrington.** This theory considers the brain as a functional unity of neurons that are separate structures and only contact to each other. So, the morphofunctional unit of this system is the neuron. The main function of neurons is perception of the afferent signals, their elaboration, and transmission to other neuronal cells and to the executive organs. The action potential is transmitted from site of its origin along the length of the nerve fibre in a particular direction from one neuron to another or from one neuron to some other type of cell (notably, muscle cells) through the synapses.

All functions of the nervous system require the rapid transmission of information from one site within the body to another. This transmission is possible because neurons have the property of excitability. This property permits neurons to develop action potentials and rapidly propagate them along their individual cellular processes (axons). When an action potential reaches the end of an axon, the

information encoded in the action potential is transmitted to another neuron or some other type of cell (notably, muscle cells). This transmission is accomplished at specialized junctions known as synapses. If the nerve fibres are located in parallel or across and don't have synapses they nether conduct signals or transmit to other neuronal cells.

The concept of synapses, their classification. The mechanism of conduction of excitation through chemical synapse. Neurotransmitters.

Information in the form of impulses (AP) is spreads along nerve fibers eventually have to get to the cells in which it is intended. The term «**synapse**» means connection (junction). This term was proposed by Sherrington. A synapse, as we have noted, is a specialized site of contact of a neuron with another neuron or a neuron with an effector. Synapses – transmission of information from nerve fibers by means of cell-cell contacts, which conducts excitation in the cell that it perceives.

All synapses are classified:

- ✓ depending on structure are divided into axosomatic, axodendritic, dendrodendritic, axoaxonic, etc.;
- ✓ depending on functional specialization chemical synapses are divided into excitatory (postsynaptic membrane depolarization, which may lead to AP) and inhibitory (hyperpolarization of the postsynaptic membrane, which hinders the emergence of AP);
- ✓ depending on the mechanism of transmission of nerve fibers per cell they are divided into electrical, chemical and mixed (that combine both chemical and electrical synaptic elements). The electrical synapses in general are represented in invertebrates and partly in vertebrates, but the chemical synapses compose the main part of synapses in the CNS in the human and animals body (tabl. 4).

Table 4. Comparative characteristics of chemical and electrical synapses

Electrical synapse	***Chemical synapse***
The synaptic cleft is 2-4 nm	The synaptic cleft is 10-20 nm
Are functioning without chemicals	Information transfer is carried out by transmitter (mediator)
Synaptic delay is absent	Synaptic delay is 0.2-0.5 msec
Excitation is conducted on both sides	Excitation is conducted in the same direction
Conducted only excitation	Conducted excitation and inhibition
Almost did not undergo modulation	are subject for modulation
Almost sensitive to temperature changes	High sensitivity to temperature, hypoxia and chemical factors.

The mechanism of chemical synapse function can be represented by the following sequence of events:

1. Conduction of impulses (AP) along nerve fibers to nerve endings - presynaptic membrane.
2. Releasing nerve endings in the synoptic cleft mediator (neurotransmitter).
3. Effect of mediator on the postsynaptic membrane. The interaction with specific neurotransmitter receptors for him postsynaptic membrane.
4. Electrophysiological effects of interactions with neurotransmitter receptors in the postsynaptic membrane.

Neurotransmitter – a chemical compound that is released nerve endings in the synoptic cleft in response to stimulation. In 1936 Dale demonstrated, that in chemical synapse this transmitter was acetylcholine. Most neurotransmitters can be classified as amino acids, monamines (modified amino acids), or polypeptides.

Types of neurotransmitters.

1.Excitatory Neurotransmitters that make membrane potential less negative and tend to 'excite' or stimulate the postsynaptic membrane.

Acetylcholine (derived from the amino acid choline) is the neurotransmitter released at the neuromuscular junction on skeletal muscle by some peripheral neurons of the autonomic nervous system (ANS) and found at many synapses throughout the central nervous system (CNS). Neurons releasing acetylcholine are classified as cholinergic, and this term is also applied to synapses for which acetylcholine is the neurotransmitter. The enzyme acetylcholinesterase is responsible for rapidly degrading acetylcholine and thus terminating its action at cholinergic synapses.

Norepinephrine (noradrenaline) is the neurotransmitter used by most peripheral neurons in the sympathetic division of the ANS and at synapses at several sites in the CNS. Presynaptic neurons and synapses using noradrenaline are termed adrenergic, and this term is also applied to cell membrane receptors that bind adrenaline. They are both classified as catecholamines because of their chemical structure and because they are derived from the amino acid tyrosine.

Dopamine is another catecholamine that functions as a neurotransmitter within the central and peripheral nervous systems, and specific dopamine receptors also exist.

Glutamate is the predominant excitatory neurotransmitter in the CNS, and several subtypes of glutamate receptors have been identified. One subtype of glutamate receptor, the NMDA receptor (named for the agonist Nmethyl-D-aspartate), are found in high concentrations in areas within the brain that are involved with memory and learning. Stimulation of NMDA receptors is believed to bring about long-term potentiation of transmission in neural pathways in these areas.

2. Inhibitory. Neurotransmitters that make membrane potential more negative and tend to 'inhibit' (or make less likely) the transmission of an impulse.

γ-Aminobutyric acid (GABA) is the most prevalent inhibitory amino acid neurotransmitter in the CNS. Binding of GABA to its receptor produces neuronal

hyperpolarization (inhibition). Several agents that act as sedatives, tranquilizers, and general muscle relaxants have part of their effect via promoting GABA's effects on the CNS. These include alcohol, barbiturates, and the benzodiazepines (e.g., diazepam and chlordiazepoxide) betaendorphin.

Conduction and peculiarities of excitation through the neuromuscular synapse.

To chemical synapses belongs neuromuscular synapse – the structural formation ensuring the transmission of impulses from the axons of motor neurons to the skeletal muscle fibers. Each nerve fiber branches out many times and may have synapses with many muscle fibers – from 3 to several hundred. Typically, each muscle fiber forms a single synapse nerve endings located in the middle – about the same distance from both ends of the muscle fibers (Fig. 7).

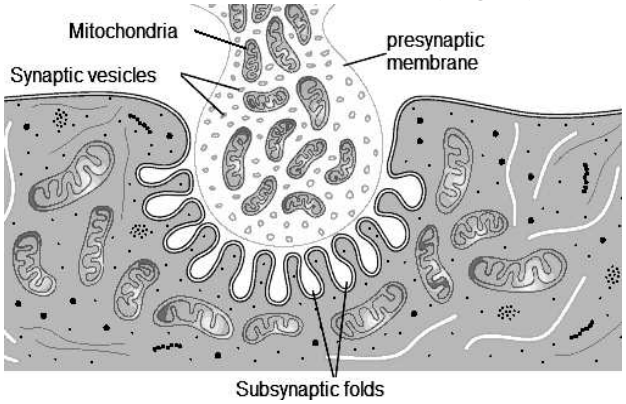

Figure 7. Conduction through the neuromuscular synapse.

The set of all elements of the neuromuscular synapse is called the motor end-plate or end-plate. The structural elements of the end-plate are:

1.Presynaptic part (presynaptic membrane of the nerve fiber ending perceiving the excitement). The formed nervous terminal that is free from myelin nerve endings of the motor nerve. Each nerve fiber due to the fact that it is at the end of a branched, has a large number of terminals. Nerve terminal structural elements are: plasma membrane; acsoplasm (contains ions (ion composition is the same as in the nerve fiber), organic compounds (precursors of neurotransmitter, enzymes, its synthesis); synaptic vesicles (this structure with a diameter of 40-50 nm is containing neurotransmitter acetylcholine, in one nerve terminal contains about 300 thousand of these vesicles); dense bodies (this formation which are attached microfilaments engaged exocytosis (release content vesicle outside); mitochondria. Externally terminal plate is covered by one or more Schwann cells, which provide end-plate relative isolation from the surrounding fluid.

2.Postsynaptic part (postsynaptic cell membrane). The formed plasmatic membrane of muscle fibers, which creates a lot of numerous folds (subsynaptyc fold), which greatly increases the total area of the postsynaptic membrane. At the beginning of each fold in the membrane is embedded proteins specific to perceive the action of neurotransmitter – acetylcholine.

3.Synaptic gap (synaptic cleft). This is the distance (narrow space) between the presynaptic and postsynaptic membranes, which is 20-30 nm and full basal

membrane consisting of thin layer reticular fibers. These fibers form a sponge-like structure which diffuses through the extracellular fluid and neurotransmitter that is released into the synaptic cleft. In the basement membrane matrix has a large number of acetylcholinesterase molecules – an enzyme that breaks down acetylcholine.

Transmission of information through the neuromuscular synapse is associated with the following sequential events.

1. Synthesis and depositing of acetylcholine (ACh). It is carried out in the cytosol of the nerve terminal and is transported into the synoptic vesicles. Each vesicle contains about 10 thousand molecules of ACh.
2. The release of ACh in the synaptic cleft. There is spontaneous and induced action potential release. The action potential arriving at the presynaptic ending evokes presynaptic membrane depolarization, in result of which Ca-channels become open and Ca ions enter the nerve ending.
3. The action of acetylcholine on the postsynaptic membrane. Due to the interaction of the vesicles and the presynaptic membrane acetylcholine is released into the synaptic cleft and interacts with the choline-receptors. Owing to this interaction the chemo-sensitive channels become open and sodium ions pass into the muscle, evoking the depolarization of the postsynaptic membrane and formation of so-called end-plate potential (EPP) or excitatory postsynaptic potential (EPSP). The properties of EPP are similar to the local response: it depends on the amount of a linked acetylcholine (the more the acetylcholine the more open channels are and the more is the membrane depolarization level); it could be summed; it is not propagated.
4. Completing of ACh. Normally, the effect of ACh on the postsynaptic membrane continues to 1-2 msec.
5. Recycling hydrolysis products of ACh and ratio of the number synaptic vesicles. Hydrolysis products ACh-choline and acetate are reabsorbed from the synaptic cleft into nerve terminals. So they re-used for the synthesis of ACh.

After the release of ACh synaptic vesicle membrane becomes part of the presynaptic membrane. A few seconds after starting endocytosis: from the presynaptic membrane retraction mechanism of forming "edging" vesicles. Involvement of the membrane due to reduced protein attached to the inner surface of the membrane. "Edging" vesicles fuse that leads to the formation of tanks. Gradually, from cisterns begin gemmating synaptic vesicles that are filled acetylcholine.

Basic peculiarities of excitation through the chemical synapses. All the chemical synapses, including the neuromuscular synapse, have the following properties:

- ✓ conducting unilateralism (one-way conduction). Unlike the nerve fibers which conduct is bilateral, chemical synapse signal is always transmitted from presynaptic to postsynaptic membrane. That synapse functions like a valve;
- ✓ a small rate of carrying. Compared to the nerve fibers synapse through the excitation conducted with a relatively small velocity;
- ✓ synaptic delay. It makes up 0.2-0.5 msec, which is connected with the low mobility of chemical processes, occurred in the synapse;

- ✓ conducting of each signal coming. Each impulse conduction across the synapse is easier, than the previous one, because each impulse leaves a trace both on the presynaptic- and postsynaptic membrane, exactly on the ion channels. It is called synaptic facilitation;
- ✓ rapid fatigue. Unlike the nerve fibers which practically do not tired to synapses characteristic rapid fatigue, which is explained by weakening of acetylcholine resources and decrease of acetylcholine receptors' sensitivity.
- ✓ rhythm transformation. It is conditioned by the fact, that the lability of the synapse (100 imp/sec) is less, than that in the motor nerve (500 imp/sec).

Reflex – the basic act of nervous activity. Classification of reflexes. The reflex arc, its main elements, classification and functions.

The connection between organs through the neurons provides by the reflex and the reflex arc. It is the basis most fundamental reaction of the nervous system. A reflex action is an automatic, or unconscious, response to an appropriate stimulus.

The reflex is a regular reaction of the organism to a change in its external or internal environment effected through the CNS.

Reflexes can be classified according to a number of attributes:

- ✓ according to biological importance (nutritional, defence, sexual, orientation);
- ✓ according to the location of the reflexogenic receptors (exteroceptive, interoceptive, proprioceptive);
- ✓ according to the character of response, or organs involved (motor, secretor, vasomotor), etc;
- ✓ by origin (according to Pavlov): unconditional and conditional.

The reflex arc is morphological basic way of the reflex. The main elements of reflex arc involves (Fig. 8):

- ✓ receptors- distinguishes natural stimuli and transmit information;
- ✓ afferent nerve fibre – conducts the signal from periphery to the centres;
- ✓ nervous centre-the area within the CNS where afferent information is integrated to produce the efferent activity or reflex response;
- ✓ efferent nerve fibre-conducts the signal from the centres to periphery;
- ✓ effector organ.

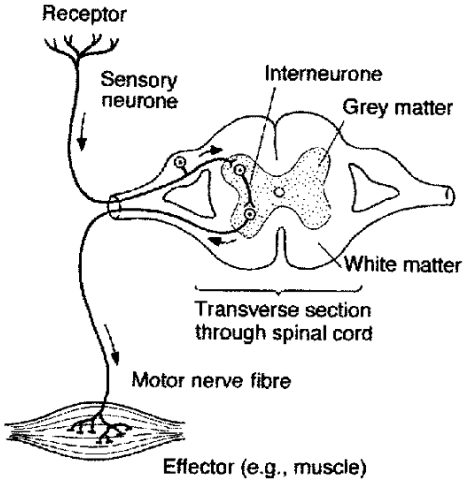

Figure 8. The main elements of reflex arc.

The classification of the reflex arcs:

- ✓ monosynaptic, are formed by two neurons only, an afferent and an efferent, with a synapse between them. The simplest reflex arc can be represented schematically. Very few reflexes are monosynaptic; they may be exemplified by myotatic reflexes (knee jerk, Achilles-tendon reflex, etc);
- ✓ polysynaptic - include two or more neurons (afferent and efferent) and also one or more interneurons.
- ✓ according to the segments or parts of the CNS that are required to complete the reflex, reflex arcs can be classified as spinal (that can be completed within segments of the spinal cord), bulbar, mesencephalic, diencephalic, cortical.

The main function of the reflex arcs is to conduct nervous signals or reflexes. It can be only if all the elements of the reflex arc are not damaged.

The properties of nervous centers.

Groups of nerve cell bodies within the CNS are generally called nuclei, while groups of nerve cell bodies in the PNS are called ganglia. Do not confuse a nucleus of the CNS with the nucleus of an individual cell. **The nervous center** is integrity of neurons, which implies a definite reflex or regulates a particular function. It is a collection of nerve cells that organize a reflex or regulate specific physiological function. It is located in a certain part of the CNS. The localization of nervous centers is determined through experiments with stimulation, or with limited destruction, extirpation, or section of different parts of the brain or spinal cord. Since in the nervous center neurons are interconnected to each other by means of synapses, the nervous centers first are to have all that properties intrinsic to the synapses particularly. They are the following.

1. One-way conduction of stimuli. It can be illustrated by the following experiment. At stimulation of the dorsal roots of the spinal cord (the afferent nerve fibers) the action potentials will be registered in the ventral roots (the efferent nerve fibers). On the other hand, if the ventral roots are stimulated in the dorsal roots no action potential will be registered.

2. Central delay. Excitation is conducted considerably more slowly in the neuronal centers than in nerve fibers, which accounts for the relatively long duration of reflex time, i.e. the period between stimulation and response. Slow transmission of excitation is consequent to the peculiarities of the impulse conduction across the synapses. The more synapses are involved in the reflex response; the more is the central delay.

3. Fatigue of the nervous centers. In prolonged and more frequent stimulation of the nervous centre, considerably weakened responses or gradually ceased responses will be registered on the efferent way of the reflex. The reason is that the intensive stimuli cause the mediator resources full consumption, as well as decrease of the postsynaptic receptors' sensitivity. The definite time period is required for the mediator resynthesis and the energetic resources recovering.

4. Transformation of rhythm excitation. In response to an isolated stimulus applied to an afferent nerve the centre sends along efferent nerve fibres a series of

impulses following each other in a definite rhythm. Figurally said, they respond to "an isolated rifle shot with a burst of machine–gunfire". In certain cases it is due to the EPSP long duration, which triggers the second, third, etc. action potentials after the termination of the first.

5. Summation of excitation. Its essence is that a combination of two or more stimulations of peripheral receptors of afferent nerves arises a reflex, whereas each taken separately is not sufficient to elicit the response.

6. Occlusion. It is like to be contradictory to the summation phenomenon represented above. It consists in simultaneous stimulation of two afferent nerve fibres (each of which gives a strong response), producing an effect which magnitude is less than the arythmetical sum of those taken separately. Reason for this phenomenon is the summation bringing about the process of cathodal depression.

7. Posttetanic potentiation. It is a phenomenon of response increase of production in case of preliminarily given tetanic impulses. For example, we give stimuli in time interval of 2-3 sec. and take responses accordingly to this rhythm. The following intensifying of stimuli brings about intensified responses. It can be continued up to 200-600 impulses per second. But in case of immediate returning to the initial rate of stimuli, the intensified responses will be kept. The reason is that the presynaptic ending acquires a property to cumulate much more amount of the mobilized mediator.

8. After-action. Essence of this is the following. Reflex acts do not end simultaneously with the cessation of the stimuli causing them, but after a certain, sometimes comparatively long interval. This phenomenon can be explained by the circulation of nerve impulses through the closed neuron chains of the reflex centre. With links of that kind between neurons excitation of one is conveyed to another (or others) and returns again to the first cell, through the collateral's of their axons, and so on. Owing to existence of such circular connections the excitation can circulate in a nerve centre for some time until the onset of fatigue in one of the synapses or the neuronal activity arrest by the arrival of an inhibitory impulse.

9. Tone of nervous centers. Electrophysiological researches have shown that the nervous centers are constantly in state of limited excitation, in tone. It is sustained by the afferent impulses continuously conveyed from peripheral receptors to the nervous centers, as well as by various humoral stimulants (hormones, CO_2, etc). The role of afferent impulses in maintaining the tone of neuronal centres is demonstrated by Bronjest's experiment. Section of the sensory roots of the spinal cord innervating the hind leg of a frog causes a decline of the muscular tone, almost identical with that seen with damage of the motor nerve. In result the leg with decreased tone becomes longer than the other one.

10. High sensitivity of the neuronal centers to oxygen supply and to certain poisons. The brain cells are marked by intensive consumption of oxygen (twice more than the skeletal muscles). Because they consume large amount of oxygen, neurons are highly sensitive to its deficit (hypoxia), so a decrease in oxygen supply to the CNS leads to functional disturbances in the nervous centres. That is why complete or

partial cessation of the cerebral circulation (e.g. in thrombosis) entails severe impairments in the neuronal system and the death of nerve elements. Besides, nervous centres possess a selective sensitivity to certain poisons, which are known as nerve poisons. For example, strychnine serves as an inhibitor of the central inhibitory synapses, thereby causes a sharp increase in the excitability of the CNS, particularly of the spinal cord; apomorphine stimulates excessively the vomiting centre; lobeline acts on the respiratory centre and abruptly stimulates it, etc.

11. Irradiation. Impulses arriving at the CNS can induce excitation not only in the neurons of a given reflex centre but also in those of other centres. It occurs mostly in case of strong and prolonged stimulation. To illustrate this phenomenon let us consider the results of the following experiment. A weak stimulus applied to the pads of the animal's hind leg causes flexion of that leg only, at the talocrural joint. Intensified stimulation causes flexion at the knee joint, in addition, and still stronger stimulation at the hip joint. Further increase in stimulus strength entails in addition to the above mentioned flexion, the extension of the hind leg on the opposite side. Irradiation could be endless and strong if the inhibitory synapses don't exist. Irradiation is obstructed by numerous inhibitory neurons in various reflex centres. Importance of inhibition is clearly illustrated by injecting 0,1% solution of strychnine. Strychnine blocks the inhibitory synapses and evokes hyperexcitation. Even insignificant touch or another stimulus can induce the most intensive general excitation of the CNS accompanied by convulsions of all the skeletal muscles.

Principles of coordination in the CNS.

Every reflex is a reaction of the entire central nervous system and is realized by the definite nervous center. It depends on the CNS condition at the given moment and on the whole aggregation of intercentral relationships and interactions, which in turn encounter through the neuronal and synaptic chains. The same reflex could have a number of components – motor, secretor, vascular and so on; and all these centres act in a coordination way.The main principles of coordination are the following.

1. Convergence (come together). Impulses reaching the central nervous system along various afferent fibers may converge upon the same inter- and effector neurons. In the spinal and medullar centers convergence is comparatively limited; only stimuli coming from the same reflexogenic field can converge. In contrast, in the higher parts of the CNS (e.g. in subcortical nuclei and the cerebral cortex) there is a convergence of impulses issuing from different receptive zones, for instance, acoustic, optic, the smell and skin receptors.

2. Divergence (come separate). It is an opposite phenomenon to convergence. The afferent nerve entering into the nervous center can form synaptic contacts with several neurons.

3. Reciprocal innervations (excitation of some neurons is accompanied by inhibition of others). Flexion reflex is accompanied by inhibition of extension reflex, simultaneously the contraction of the extensor muscle and the relaxation of the flexor muscle of the opposite side are observed. This phenomenon is explained as stimulation of the flexion center causing inhibition of the extensor centre. Afferent

nerve exciting the flexor motor centre simultaneously sends the impulses by collateral branch to Renshaw's cell. The latter being excited brings about the extensor α-motoneuron inhibition. The flexor centre could evoke an excitatory influence on the extensor centre of the opposite side (opposite leg), as well as an inhibitory influence on the flexor centre.

4. Principal of the dominant. Activity of the nervous system is characterized in the natural conditions of the organism by the existence of dominant force of excitation, which change the action of all other nerve centers and subordinate them to themselves. If during the act of defecation a strong pain stimulus is applied, the flexion reflex of the leg that is normally evoked by this stimulation will not occur.
Instead, the defecation reflex will be quicken and intensified. Dominant centers fulfil the most important for that moment reflex. Dominant foci are characterized by the following basic peculiarities: a) increased excitability; b) stability of the excitation; c) capacity to summate excitation; d) inertia, capacity to remain excited for a period after the stimulus has ended.

5. The common final pathway. The same reflex may be caused by a great number of different stimuli acting on various receptors. For example, the scratching reflex may be caused by stimulation of the skin receptors, of the flexor muscle proprioceptors, of the extensor muscle proprioceptors on the contrary side, or even by acoustic or visual action, if they have been previously combined with the scratching reflex (conditional reflex). So, in this experiment stimuli from different reflector arcs get the same motoneuron (final common pathway). Reflexes which arcs have a final common pathway may be divided into allied and antagonistic. Reflexes coming to compete for the final common path are antagonistic ones.

6. Inhibition is an independent nervous process, which is caused by excitation and manifested by the suppression of another excitation. In distinct from the excitation process, which is manifested in a view of the local potentials and spreading action potentials, the inhibition process is manifested only in a local form that never spreads. The inhibition is a result of special inhibitory synapses activation (primary inhibition). The inhibition arisen in the neuron is secondary as a sequence of its excitation. This type of inhibition appears in a high rate (pessimal rate) stimulation of the cell or it may be connected with the hyperpolarization processes followed by excitation.

7. The excitation replacement by inhibition, and vice versa (induction). Inhibition is always followed by excitation and this is called consecutive positive induction. Similarly, excitation is followed by inhibition (that will be negative consecutive induction). It is shown, that if the animal's skin is excited by a weak stimulus, a weak scratching reflex will be produced, which in turn will be inhibited if at this moment the strong electrical stimulus is applied at that site of the skin. But,
if we remove that strong stimulus, the scratching reflex will be expressed more intensively. Pavlov studied induction interrelations during the functioning of the conditional reflex, and named these phenomena as the cerebral positive and the negative induction.

8. The «rebound» phenomenon. It consists in the following: one reflex could be replaced by another reflex of the contrary meaning. Termination of stimulation causing a strong flexion reflex is followed by a sharp extension of the flexed leg. The reason is that, the extensor center being in reciprocal relations with the flexor center becomes excited now. Actually, the flexor center excitation brings to the extensor center inhibition, and vice versa. All this is connected with realization of the successive rhythmic reflex.

9. The principle of «feedback» (secondary afferentation). Not only basic stimuli, but also the so-called secondary afferent stimuli come into the CNS. Any motor act induced by an afferent stimulus is accompanied with the stimulation of the receptors of the muscles, tendons, etc., i.e. of the proprioceptors, from which nerve impulses are conducted to the CNS. When a movement is being performed by a human being under the guidance of vision, or hearing, the proprioceptor impulses are joined by visual or acoustic signal. The significance of secondary afferent impulses for reflex realization and of its coordination is very great. It is successfully shown both by experiments on animals and by clinical observations of patients who have lost one or other of the senses. Patients with impaired proprioceptive sensibility no longer have smooth and accurate movements (their movements become abrupt, uncoordinated). Section of afferent nerve fibers, deafferentiation, results in abnormal reflex performing. In this case intensified irradiation of the nerve impulse will be also observed.

Spinal cord, structure and functions.

The spinal cord is phylogenetically the oldest part of the CNS. It is logged in the vertebral canal. The typical feature of the spinal cord is its segmental structure, which reflects the segmental structure of the vertebrate body.The spinal cord (Fig. 9) is the caudal continuation of the medulla oblongata. Unlike that of the cerebrum, the spinal cord's gray matter is found at the center of the cord, forming a butterfl y shape on cross-section. Fiber tracts, the white matter, surround this core of gray matter. In general terms, aggregates of neuronal cell bodies form the gray matter of the CNS, whereas regions characterized primarily by tracts are white matter. A spinal cord segment is defined by the presence of a pair of spinal nerves – dorsal and ventral roots, which come together and enter the vertebral canal. The dorsal and ventral roots unite to form the spinal nerve close to the intervertebral foramen between adjacent vertebrae.

The dorsal roots form afferent inputs of the spinal cord. The dorsal root constitute the processes that extend from the spinal nerve to the spinal cord. It consists of sensory neuronal cell bodies, which give rise to processes that enter the dorsal horn of the spinal cord and others that unite with motor fi bers from the ventral horn neurons to become the spinal nerve extending into the periphery. They are formed by central processes of the fibres of first afferent neurons which bodies are located on the periphery in the spinal ganglia.

The ventral root of the spinal nerve consists of motor fibers that arise from the nerve cells primarily in the ventral horn of the spinal cord. The ventral roots form

efferent outputs of the spinal cord. They contain axons of the α- and γ-motoneurons. This distribution of afferent and efferent roots is known as Bell-Magendie's law.

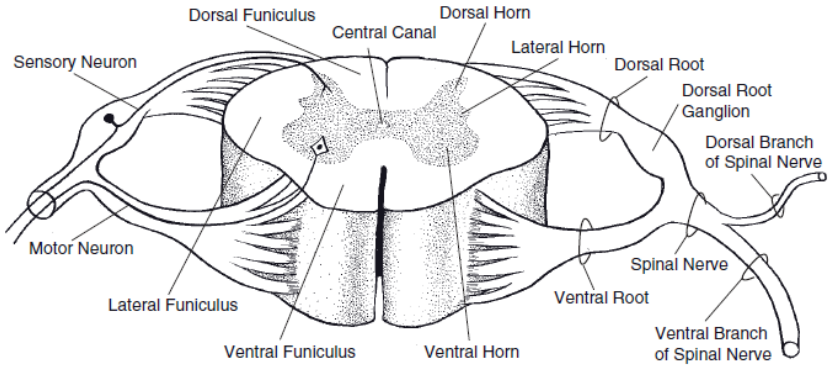

Figure 9. Structure of spinal cord.

Motor neurons are located in the anterior horns. The α-motoneurons innervate skeletal muscle fibres (so-called extrafusal fibres) and ensure muscle contraction. The γ - motoneurons innervate muscle intrafusal fibres, contraction of which causes the excitation of muscle stretch receptors. Combined activity of these two types of neurons provides the motor coordination.

The spinal cord performs the following functions: conducting, reflectory and elementary analysis.

Reflex activity of the spinal cord. The centres of number of reflexes are located in the spinal cord. The tendon and stretch reflexes are the simplest spinal reflexes. Among these reflexes the patellar, the Achilles reflex, the knee reflex are the most important. The spinal cord also plays a major role in the reflex regulation of the internal organs and contains of the centres of numerous visceral reflexes. The centres of defecation and diuresis are also located in the spinal cord.

The conducting tracts of the spinal cord.

As is noted above, the spinal cord contains neurons, which give rise to long ascending pathways to various brain structures. Bundles of nerve processes within the CNS are frequently called tracts, or fasciculi, and bundles of processes in the PNS are called nerves. A tract is a bundle of functionally related axons in the CNS.

Tracts that carry sensory information are ascending tracts, whereas those carrying motor commands are descending tracts. The white matter of the spinal cord in which the tracts are found can be roughly divided into three columns on each half of the cord: a dorsal funiculus (often called the dorsal column), a lateral funiculus, and a ventral funiculus.

Sensory Tracts(ascending tracts). The main ascending pathways of the spinal cord are the fasciculus of Goll and the fasciculus of Burdach (the dorsal funiculi). They are included in the composition of the posterior funiculus of the white matter andend in the medulla oblongata. These pathways are responsible for the perception of skin mechanical stimuli. The dorsal funiculi contain afferent tracts that carry information about body position from joints, tendons, and muscles. This type of sense is called proprioception. Injury to this pathway produces uncoordinated, inaccurate movements, as the cortex lacks some of the information it needs to make ongoing

adjustments in the planning and execution of voluntary movements. Such incoordination is sensory ataxia.

Proprioceptive information also ascends the spinal cord in several spinocerebellar tracts, located superficially on the lateral funiculus. As the name suggests, these tracts are headed for the cerebellum, where the proprioceptive information is used to help shape voluntary movements so that they are accurate and smooth.

Information about pain is carried by a large number of described pathways, but these are often grouped under the names spinothalamic tract or anterolateral system. The other ascending pathways begin from the neurons of the grey matter of the spinal cord. Since these neurons are supplied by the synaptic inputs from the first afferent neurons, it was accepted to designate them as the secondary afferent neurons. The main bulk of secondary afferent fibers pass as part of the lateral funiculus of the white matter. The axons of the spinothalamic neurons are decussated and through the medulla oblongata and midbrain reach uninterruptedly the thalamic nuclei to form synapses with the thalamic neurons. This large group of fibers is found in a wide band through the lateral and ventral funiculi. Some of these tracts terminate in the brainstem, where they mediate reflexes associated with painful stimuli. Others make connections that alert the entire cortex and initiate aversive behaviors. Still others are relayed directly to the parts of the cortex that create conscious awareness of the painful stimulus. Like pain, touch and temperature sense information is carried in a variety of ascending tracts. This tract transmits the impulses from skin receptors. Some of these are found in the dorsal columns and others in the anterolateral system.

The lateral funiculi contain fibers of the spinocerebellar, posterior and anterior tracts, which transmit impulses from the skin and muscle receptors to the cortex. The pathway of pain sensation is located in the anterior funiculi.

The posterior, lateral and anterior funiculi contain propriospinal tracts which provide the functional integration and reflex activity of the spinal cord centers.

Motor Tracts (descending tracts). The spinal cord also receives many descending pathways, which are formed by the axons of nerve cells located in the cerebral cortex, mid-brain and medulla oblongata. Motor systems are often functionally grouped into two main categories: a ventromedial motor system, largely located in the ventral funiculus, and a dorsolateral motor system, found in the dorsal part of the lateral funiculus. The ventromedial motor system primarily is responsible for activity in the axial and proximal limb muscles, especially extensors and antigravity muscles. Activity in the tracts of this system assists with the support phase of gait, when limbs are in weight-bearing position with joints extended. A particularly noteworthy tract of the ventromedial motor system is the lateral vestibulospinal tract, which originates in the region of the pons and medulla. The dorsolateral motor system is in many ways complementary to the ventromedial system. The vestibulospinal tract is composed by the axons of the neurons of the lateral vestibular nucleus, Deiters nucleus. Dorsolateral tracts tend to control the muscles of the distal limb, especially the flexors. Activity here is important in the

flexion or swing phase of gait, when limbs are lifted from the ground and advanced while flexed.

In quadrupeds, the most prominent tract in the dorsolateral motor system is the rubrospinal tract, which arises from the midbrain. The evolutionary younger rubrospinal tract begins from the red nucleus of the mid-brain. After decussating, the rubrospinal tract is included in the composition of the lateral white funiculi.

The reticulospinal tract is formed by axons of the brainstem reticular formation neurons, which terminate on the neurons of the grey matter, including motoneurons.

In primates, and most especially humans, the corticospinal tracts arising from the motor cortex of the cerebrum are especially well developed. The neurons of corticospinal or pyramidal tract (evolutionary the youngest) lie in the motor cortex. The fibers of this tract decussate and as a part of the dorsolateral funiculi pass above the rubrospinal tract. Pyramidal axons make direct contacts with motor neurons.

CNS, subdivisions: the cerebrum.

The gross subdivisions of the adult brain include the cerebrum, cerebellum, the diencephalon, and brainstem with parts: midbrain, hindbrain (Fig. 10). The cerebrum develops from the embryonic telencephalon.

The cerebrum, comprises the two cerebral hemispheres, including the cerebral cortex, the basal nuclei, and other subcortical nuclei, and an aggregate of functionally related structures called the rhinencephalon. The telencephalon encloses the cavities of the lateral ventricles.

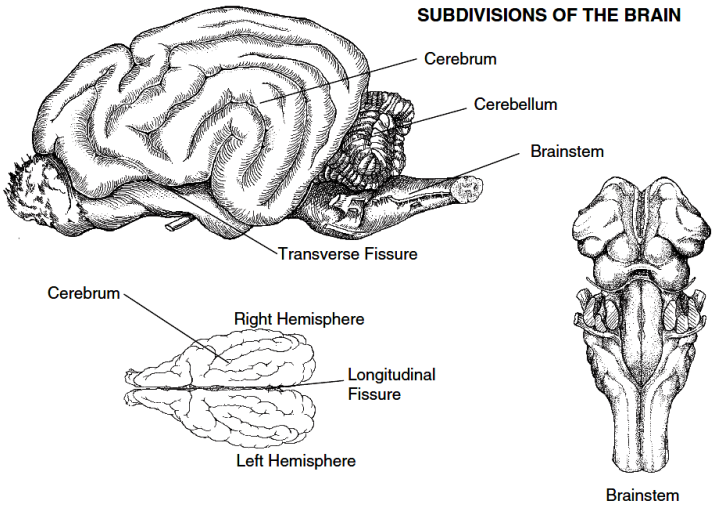

Figure 10. Subdivisions of the brain.

The surface area of the cerebrum in domestic mammals is increased by numerous foldings to form convex ridges, called gyri (singular gyrus), which are separated by furrows called fissures or sulci (singular sulcus). A particularly prominent fissure, the longitudinal fissure, lies on the median plane and separates the cerebrum into its right and left hemispheres. Unlike the spinal cord, in the cerebrum most of the neuronal cell bodies (i.e., the gray matter) are on the exterior. This layer of cerebral gray matter is called cerebral cortex. Cerebral cortex and its functions is studied in the next topic – higher nervous activity.

Deep to the cerebral cortex are aggregates of subcortical gray matter called the basal nuclei (an older term, basal ganglia, is discouraged, as the word ganglion usually refers to an accumulation of cell bodies outside the CNS). The basal nuclei are important in initiation and maintenance of normal motor activity. The rhinencephalon is, from an evolutionary standpoint, one of the oldest parts of the cerebrum. It comprises a series of ventral and deep cortical structures associated primarily with the sense of smell (olfaction). The rhinencephalon has prominent connections to the parts of the brain that control autonomic functions, emotional behaviors, and memory, a fact that accounts for the striking ability of odors to affect these functions.

CNS, subdivisions: the cerebellum.

The metencephalon includes the cerebellum dorsally and the pons ventrally. The cerebellum features two lateral hemispheres and a median ridge called the vermis because of its resemblance to a worm. The surface of the cerebellum consists of many laminae called folia. In the cerebellum, like the cerebrum, the white matter is central, and the gray matter is peripheral in the cerebellar cortex. The pons is ventral to the cerebellum, and its surface possesses visible transverse fibers that form a bridge from one hemisphere of the cerebellum to the other. Many other fiber tracts and cranial nerve nuclei make up the remainder of the pons. The cerebellum is located posteriorly to the cerebral hemispheres, above the medulla oblongata and the pons. The cerebellar hemispheres consist of anterior and posterior lobs, which are covered by cortex. The cerebellum is connected with other parts of CNS by three pairs of peduncles.

Neuronal organization of cerebellum. The cerebellar cortex consists of three layers. The superficial or molecular layer has ramifications of the flask-like or Purkinje cells, which are inhibitory neurons. It has been established that one Purkinje cell forms nearly 200000 synapses due to a huge amount of dendrites. The molecular layer has also parallel fibers, which are the axons of intercalary neurons. The lower part of the molecular layer contains basket cell bodies, the axons of which make synapses with Purkinje cell bodies. The molecular layer also contains a certain number of stellate cells.The second layer is ganglionic layer, which is represented by Purkinje cell bodies. The third layer is granular layer, which contains intercalary neuron bodies. Axons of these cells ascend to the molecular layer where they divide in a T– pattern. The Golgi cells, which axons project to the molecular layer, are also located in the granular layer.

The cerebellar cortex receives only two types of afferent fibres: climbing and mossy. They supply the cerebellum with all sensory influences. Two types of afferent fibres (climbing and mossy) enter the cerebellar cortex, but only one type of efferent fibres, i.e. axons of the Purkinje cells, leave it.The cerebellum receives information from various sensory systems. Afferent signals reach the cerebellum from the spinal cord, vestibular receptors, inferior olive and reticular formation of the hind-brain. The spinocerebellar tract supplies the cerebellum with information about the muscular apparatus, skin and deeper lying tissues. Neurons of the nucleus interpositus (the

globosus and emboliform nuclei) send fibres to the cells of the red nucleus.Synapses formed by these fibres on the rubrospinal neurons are excitatory. Thus, responses arising in spinal motor neurons on stimulation of the nucleus interpositus resemble those arising on stimulation of the red nucleus. Neurons of other nuclei of the cerebellum establish excitatory synapses on the reticulospinal neurons of the medulla oblongata and the pons.Thus, the whole information supplied to the cerebellum is transmitted to the Purkinje cells, which, in turn exert inhibitory influences on the cerebellar nuclei, as well as on the neurons of the lateral vestibular (Deiters) nucleus. Therefore, Purkinje cells through cerebellar nuclei inhibit the activity of the reticulospinal and rubrospinal neurons.Thus, the cerebellum can effectively control most signals transmitted to the spinal cord via the main descending tracts.

Functions of cerebellum. The cerebellum is critical to the accurate timing and execution of movements; it acts to smooth and coordinate muscle activity. The cerebellum receives much of the afferent information about body position and ongoing movements from proprioceptors. It also receives information about movements initiated in the cerebral cortex. After integrating this and other information, the cerebellum sends efferent information to multiple sites in the brain, including the motor cortex, to coordinate ongoing movements. The cerebellum does not initiate movements, but it is essential for normal coordination of voluntary movements.

Clinical manifestations attendant to disturbances of the cerebellum as well as the effects caused by its stimulation or extirpation testify to the important role played by the cerebellum in static and statokinetic reflexes and other processes involved in the control of motor activity. Their main manifestations are impaired equilibration and muscle tone, tremor, ataxia, asynergy and astasia. Muscular atonia is an inability to maintain posture. The tremor is characterized by small amplitudes of oscillations, which occur synchronously in various body segments. Ataxia is described by less precise of movement range, speed and direction. Motor reactions lose their smoothness and steadiness. The goal-directed movement (e.g. an attempt to take an object) becomes rough and jerky. In asynergy, the interaction between motor centres of various muscles is deranged. In astasia movements are swinging and jerky. Total excision of the cerebellum or its anterior lobe in animals increases the tone of extensors; on stimulation of the anterior lobe, the tone decreases.

The cerebellum performs a significant role in the regulation of the vegetative functions due to its numerous synapses with the brainstem reticular formation.

CNS, subdivisions: the diencephalon.

The diencephalon consists of the thalamus, epithalamus, hypothalamus, and the third ventricle.

The thalamus is an important relay center for nerve fibers connecting the cerebral hemispheres to the brainstem, cerebellum, and spinal cord.

Neuronal organization of thalamus. The number of thalamus nuclei is forty. They are classified topographically into the following main groups: anterior, intralaminar, medial and posterior. According to their function, non-specific and

specific nuclei are distinguished. Neurons of the non-specific nuclei first transmit signals into the subcortical structures from where impulses pass to different cortical areas. The non-specific nuclei are a continuation of the reticular formation of the midbrain and by nature they resemble the functions of reticular formation.

Fibres of various ascending tracts end on the neurons of the specific nuclei. Axons of these neurons make direct monosynaptic contacts with the neurons of the sensory and association cortex. Cells of the nuclei of the lateral group of the thalamus receive impulses from receptors of the skin, motor apparatus, and from the cerebellothalamic tract. The other group of the specific nuclei is a component of the posterior group and forms the medial and lateral geniculate bodies. The neurons of the lateral geniculate body receive impulses from the primary visual centre of the anterior quadrigeminal bodies.The medial geniculate body neurons receive signals from the auditory nuclei of posterior quadrigeminal bodies.

Functions of thalamus. All sensory signals, except those arising in the olfactory tract, reach the cerebral cortex only via the thalamocortical projections. The thalamus may be regarded as a kind of a gateway through which the main information about the external and internal environment and status of the body passes to the cortex. Thalamic neurons are relay stations for the afferent signals on the way to the cerebral cortex. In turn, the thalamus receives inhibitory signals from the cortex.

The ascending activating influences from the brainstem reticular formation enter the cerebral cortex through the nonspecific thalamic nuclei. The system of non-specific thalamic nuclei is involved in the control of rhythmic activity of the cerebral cortex and performs as the intrathalamic integrative system. The cortex reaction is marked by prolonged latent period and intensifies on repeated stimulation. This reaction differs from specific responses of the cerebral cortex by generalized pattern, when extensive cortical areas become activated. Damage of non-specific thalamic nuclei causes disorders of consciousness and emotions. Pain signals cause strong activation of the thalamic nuclei. The thalamus is the higher centre of pain sensitivity. Certain thalamic nuclei (dorsal group) exert regulatory influences on the subcortical structures. Thus, the thalamus can play a significant role of a suprasegmentary centre of reflex activity. The talamus is responsible for the locomotion and complex motor reflex control (swallowing, chewing, sucking, etc.).

The hypothalamus, ventral to the thalamus, surrounds the ventral part of the third ventricle and comprises many nuclei that function in autonomic activities and behavior. Neuronal organization of hypothalamus. The hypothalamic nuclei are the higher subcortical centres of the vegetative nervous system and governing all vitally important body functions. The preoptic, anterior, medial lateral and posterior areas are distinguished. The preoptic area comprises the medial and lateral preoptic nuclei. The anterior part includes the supraoptic, suprachiasmatic and paraventricular nuclei. The lateral area consists of lateral groups of nuclei. The posterior hypothalamus has the posterior hypothalamic and a large group of mamillary nuclei.The hypothalamus is characterized by extensive and highly complicated afferent and efferent connections. Afferent signals are supplied from the cerebral cortex, thalamic

structures and basal ganglia. Main efferent pathways pass to the midbrain and thalamic and subthalamic areas. Attached to the ventral part of the hypothalamus is the hypophysis, or pituitary gland, one of the most important endocrine glands. The neuronal connections between the hypothalamus and the hypophysis constitute a critical point of integration of the two primary communication systems of the body, the nervous and endocrine systems.

Functions of hypothalamus. The lateral and dorsal groups of hypothalamic nuclei increase the tone of the sympathetic nervous system. Stimulation of the medial nuclei decreases the sympathetic tone. Experimental evidence suggests the existence of sleep and wakefulness centres in the hypothalamus. The hypothalamus plays a significant role in the thermoregulation. Stimulation of the posterior part causes hyperthermia due to increased heat production (intensification of metabolism). It is the center of chemical thermoregulation. The anterior part of the hypothalamus is responsible for the physical thermoregulation.

The medial area is considered as the centre of satiety and the lateral one, hunger. The activity of these areas is stimulated or inhibited by changes in the chemical composition of the supplied blood. It has been established that the emotional and pleasure centres are located in the hypothalamus.The posterior hypothalamus, which is connected with the anterior pituitary, regulates the secretion of adenohypophyseal hormones by means of liberins and statins. There is a direct connection between anterior hypothalamus and posterior pituitary, which provides the transport of synthesized hormones (oxytocin and ADH).

The epithalamus, dorsal to the thalamus, includes the pineal gland, which is an endocrine organ in mammals. Its primary secretion, melatonin, appears to be important in circadian (daily) rhythms and sleep cycles. In addition, activity of the pineal gland is likely to be important in species with markedly seasonal reproductive cycles.

CNS, subdivisions: the brainstem.

The components of the brainstem are defined in a number of ways; for our purposes, we include midbrain, hindbrain as parts of the brainstem.

The mesencephalon, or midbrain, lies between the diencephalon rostrally and the pons caudally. Neuronal organization of midbrain. The midbrain consists of two main parts:

- ✓ the dorsal part known as the tegmentum of the midbrain-four colliculi (four small bumps (colliculus is Latin for little hill) on the dorsal side of the midbrain) are the most prominent features; colliculi consist of right and left rostral colliculi and right and left caudal colliculi. The rostral colliculi coordinate certain visual reflexes(the primary optic centre), and the caudal colliculi are relay nuclei for audition (hearing)-the primary auditory centre;
- ✓ the ventral part – the two cerebral peduncles also called crura cerebri (singular crus cerebri)- are large bundles of nerve fibers connecting the spinal cord and brainstem to the cerebral hemispheres.

The midbrain contains also the substantia nigra, the quadrigeminal bodies, the red nucleus, the nuclei of the cranial nerves, and the reticular formation. Various ascending pathways pass through the midbrain to the thalamus and cerebellum; the descending pathways from the cerebellum hemispheres, corpus striatum and hypothalamus run to the midbrain neurons and to the nuclei of the medulla oblongata and the spinal cord.

The red nucleus contains cells of different sizes. The thickest and having higher conduction velocity axons of the rubrospinal tract arise from the large neurons, which receive signals from the motor area of the cerebral cortex, the nucleus interpositus of the cerebellum and from the nerve cells of the subtantia nigra. The red nucleus gives rise to cells, which axons innervate the spinal centres controlling the upper and lower limb musculature.

The substantia nigra is the integrity of nerve cells containing pigment melanin, which imparts the typical dark color to this nucleus. These neurons are dopaminergic. They are lodged in the zona compacta. The other part of the substantia nigra is zona reticulata, which consists of target cells for the projections of the basal ganglia. The latters in turn form synaptic inhibitory contacts with the nuclei of the thalamus, pons, and superior colliculus.

Functions of midbrain nuclei. The arcs of orientation, visual and auditory reflexes are closed in the midbrain (rostral and caudal colliculi). The nuclei of the quadrigeminal bodies participate in the performance of the guarding reflex. The substantia nigra participates in the complex coordination of movements. The dopaminergic neurons of the substantia nigra send axons to the nuclei of the corpus striatum, where the dopamine controls the complicated motor acts. Damage to the substantia nigra leads to degeneration of dopaminergic fibres causing disorders of movements of fingers and development of muscular rigidity and tremor (Parkinson's disease).

Trans-section of the brainstem below the red nucleus in animals causes significant changes in the distribution of muscle tone of the body. The tone of the extensor muscles is sharply increased. The animal's limbs are strongly extended, the head is tilted back, and the tail is raised. This condition is known as decerebrative rigidity. This phenomenon is explained by the activity of the vestibulospinal system, which increases the tone of the motor neurons of the extensor muscles, becomes dominating.

The hindbrain consists of the medulla oblongata and the pons varolii. The medulla oblongata is the cranial continuation of the spinal cord, from which it is arbitrarily distinguished at the foramen magnum. The medulla oblongata (often simply called the medulla) contains important autonomic centers and nuclei for cranial nerves.

The nuclei of the fifth-twelfth (5-12) pairs of cranial nerves are located in the hindbrain. Similar to the spinal cord, it has efferent neurons, interneurons, neurons of ascending and descending tracts, primary sensory fibers and fibers of conducting

tracts passing through the hindbrain in the ascending (rostral) and descending (caudal) directions.

Nuclei of the cranial nerves receive afferent impulses from the periphery and send efferent impulses to the muscles, organs thus resembling the spinal neuron centres. The eleventh pair (n.accessorius) and twelfth pair (n. hypoglossus) nerves are purely motor nerves. The tenth pair (n. vagus) and ninth pair (n. glossopharyngeus) nerves are mixed. The eighth pair of nerves is sensory (n. vestibulocochlearis). It consists of two branches, the vestibular and cochlear nerves. The vestibular neurons give rise to the vestibulocerebellar and vestibulospinal tracts.

The reticular formation is situated in the medial part of the medulla oblongata. Cells of the reticular formation give rise to theascending and descending tracts, which form numerous collaterals whose endings make synaptic contacts with various nuclei of the CNS.

The pons varolii, which is a continuation of the medulla oblongata, connects the medulla with the midbrain. It consists of nuclei of the seventh pair (n. facialis), sixth pair (n.abducens) and fifth pair (n. trigeminus) nerves. The facial and trigeminal nerves are mixed. The abducent nerve is motor.The medial nuclei of the reticular formation of the pons give rise to the ascending fibres to the midbrain and diencephalons.

The hindbrain performs reflectory and conducting functions. Reflex activity of hindbrain. The hindbrain is responsible for numerous functions, such as respiration, heart activity, digestion, vasomotor activity, etc., which are vitally important for the body. The hindbrain realizes static reflexes, which are subdivided into the postural and righting reflexes and statokinetic ones. The postural reflexes ensure changes in the muscle tone, when the body position in space is changed. The righting reflexes govern the redistribution of the muscle tone, owning to which the natural posture can be restored in case it has been changed. The vestibular afferent fibres and neurons of the lateral vestibular nucleus, whose axons pass to the spinal cord as a component of the vestibulospinal tract, take part in the performance of these reflexes. The excitation of vestibular receptors causes postural reflexes, i. e. the activation of extensor muscles and inhibition of flexor muscles.

The righting reflexes are responsible for the normal position of the head.
The statokinetic reflexes are the most complex. They provide the maintenance of posture and orientation in space when the speed of movements is changed. For example, during the sudden halt of bus or car, the muscles contract to overcome the force acting on a human body. The statokinetic reflexes involve almost all body musculature. They are pronounced in the muscles of the eye. Movement of eye muscles mediates the normal visual orientation during acceleration or slowing down of movement. Along with motor reflexes, activation of the vestibular apparatus causes excitation of the autonomic centres, including the nucleus of the n. vagus. The formation of vestibuleautonomic reflexes cause changes in respiration, heart rate, gastro-intestinal activity, etc. In turn, many motor reflexes are associated with the food intake, chewing and swallowing.

Damage to other parts of the CNS may have no symptoms due to great compensatory capacities of the brain, while a minor trauma to hindbrain immediately has a grave or even fatal consequence.

The medulla oblongata and the pons send fibres to the spinal cord, which cause more diffuse non-specific influence on the spinal cord motor centres. Electrical stimulation of the medulla oblongata medial reticular formation causes inhibition of all the spinal motor reflexes owning to the development of postsynaptic inhibition with the help of inhibitory interneurons. It has been concluded that this zone functions as a non-specific inhibitory centre.

The hindbrain reticular formation can have a positive effect on the cerebral cortex, which is associated with involvement of the reticular formation not only of the hindbrain but of the midbrain and the diencephalon. This complex of the reticular nuclei and pathways makes up a functionally united system.

The Autonomic Nervous System (ANS)*. *Sympathetic nervous system.

The Autonomic Nervous System (ANS) is the the part of the peripheral nervous system includes the nerves and ganglia outside the CNS, that regulates activity in viscera, regulates involuntary functions, and the enteric nervous system, which functions to control the gastrointestinal system. Its purpose is to convey sensory information to the brain and spinal cord and to produce movement of muscle and secretion from glands via its motor nerves. The peripheral nervous system includes motor neurons, mediating voluntary movement.

The common representation of the ANS as a motor subdivision of the peripheral nervous system ignores the facts that (1) sensory fibers from viscera make up a large proportion of the fibers in autonomic nerves and (2) some CNS tracts and nuclei integrate and control visceral activity. Nonetheless, for purposes of this introduction, we consider only the peripheral motor components of the ANS. These are the nerves that influence activity in smooth muscle, cardiac muscle, and glands.

In motor nerves to voluntary muscle, the cell bodies of neurons directly innervating the target are found in the gray matter of the CNS, and the telodendria of these neurons make direct contact with the target. Motor nerves of the ANS, in contrast, consist of a series of two neurons. The first has its cell body in the CNS, and its axon extends into the periphery, where it synapses on the cell body of a second neuron. It is the axon of the second neuron that contacts the visceral target. Because of this twoneuron arrangement, autonomic nerves are characterized by the presence of autonomic ganglia, peripheral collections of the cell bodies of the second neurons. Using the autonomic ganglion as a point of reference, the first neuron is called preganglionic, and the second, postganglionic. The preganglionic neurons of the ANS make up a special group of efferent neurons of the spinal cord. They are located in the lateral horns of the gray matter. Axons of these neurons pass to the ganglion cells of the sympathetic chain, where they are interrupted forming synapses with the second neurons. The latters innervate the internal organs.

The motor output of the ANS is concerned with homeokinesis, the dynamic process of regulating the internal environment to meet the needs of the organism.

As a consequence, the motor limb of the ANS is functionally and anatomically divided into two parts. The sympathetic division of the ANS prepares the organism to meet a stress by producing a combination of physiologic changes that increase available fuel molecules, blood flow to muscle, and cardiac output while simultaneously decreasing digestive processes. The parasympathetic division of the ANS is in many respects the opposite of the sympathetic division. Parasympathetic activity leads to digestion and storage of fuel molecules and acts to bring the organism to a state of rest.

Sympathetic nerve fibers arise from thoracic and lumbar segments of the spinal cord, thus the sympathetic division is sometimes called the thoracolumbar division. Preganglionic sympathetic neurons have their cell bodies in a small lateral horn of the spinal cord gray matter, between dorsal and ventral horns. The myelinated axons of these fibers leave via the ventral root, enter the spinal nerve, and then leave it just outside the intervertebral foramen to join a longitudinal chain of autonomic ganglia. One string of these ganglia lies on each side of the vertebral column. Each receives preganglionic fibers from the spinal nerves only in thoracic and lumbar regions, although the chains themselves extend from the cranial cervical region to the most caudal parts of the vertebral column. The ganglia, together with the nerve fibers that link them longitudinally, are called the sympathetic trunk. The ganglia themselves are most correctly called the ganglia of the sympathetic trunk, although they are also called paravertebral or sympathetic chain ganglia. Cell bodies of many of the postganglionic sympathetic neurons are found here. From the sympathetic trunk ganglia, the unmyelinated axons of postganglionic neurons reach their targets either following spinal nerves or via unique autonomic nerves. In some cases, preganglionic axons pass through the trunk without synapsing and instead synapse on other sympathetic ganglia outside the sympathetic trunk. This second group, collectively known as prevertebral or collateral ganglia, tends to be associated with the large, unpaired arterial branches of the abdominal aorta, after which they are usually named.

No sympathetic preganglionic cell bodies lie cranial to the thoracic spinal cord, so sympathetic innervation to head structures (e.g., the pupil, sweat glands, salivary glands) arrives at its targets by traveling cranial in right and left bundles of fibers in the ventral neck. These are the cranial continuation of the sympathetic trunks in the thorax. These preganglionic sympathetic fibers are bound in a connective tissue sheath with fibers of each vagus nerve (cranial nerve X); the combined fibers are therefore called the vagosympathetic trunk, readily identifyed dorsolateral to and parallel with the trachea (windpipe). Sympathetic fibers in the vagosympathetic trunk synapse in the cranial cervical ganglion, found ventral to the base of the skull, and from this ganglion the postganglionic fibers spread to the glands and smooth muscle of the head.

No sympathetic preganglionic cell bodies exist caudal to the midlumbar region, so sympathetic innervation to pelvic organs (rectum and urogenital organs) arrives via the right and left hypogastric nerves, a continuation of the caudal parts of the

sympathetic trunk. The fibers of the hypogastric nerve become admixed with parasympathetic fibers in a diffuse network of autonomic nerves on the lateral surface of the rectum called the pelvic plexus.

The sympathetic innervation to the adrenal gland is unique in that preganglionic sympathetic fibers synapse directly on the chromaffin cells of the adrenal medulla without an intervening ganglion. Sympathetic stimulation causes this tissue to release catecholamines (epinephrine and norepinephrine) into the bloodstream, producing a widespread, pronounced, and prolonged fight-or-flight response. This is another physiologically important site at which the rapid communication system of the body (the nervous system) is integrated with the slow, more lingering communication system of the body (the endocrine system).

Parasympathetic nervous system. The ANS functions.

The parasympathetic division of the autonomic nervous system arises from cranial nerves and sacral segments of the spinal cord; for this reason, it is sometimes called the craniosacral division. Fibers of the cranial portion are distributed via four cranial nerves: the oculomotor, facial, glossopharyngeal, and vagus nerves. The first three of these supply parasympathetic fibers to smooth muscle and glands of the head. The vagus nerve supplies parasympathetic fibers to the viscera of the thorax and neck and to nearly all of the abdominal viscera. The distal part of the digestive tract (including the transverse colon and the area caudal to it) and the pelvic viscera are innervated by parasympathetic fibers from the sacral portion of the parasympathetic nervous system. These pelvic fibers intermix with sympathetic nerves to form the pelvic plexus.

The ANS functions to maintain a relatively stable internal body environment, that is, to maintain a state of homeokinesis (homeostasis). It does so by regulating the activity of cardiac muscle, smooth muscle, and glands. The distribution of ANS nerves is widespread, including all viscera. Normally, the regulation of ANS activity occurs below the level of consciousness. However, emotional reactions (such as fear or excitement) and input from the cerebral cortex also affect ANS activity. Most organs that are innervated by the ANS have both sympathetic and parasympathetic innervations, and in most cases the effects of the two divisions are antagonistic. For example, parasympathetic stimulation of the heart reduces heart rate, while sympathetic stimulation increases heart rate. The antagonistic actions are controlled to bring about appropriate overall regulation of the innervated organ. In the case of the heart, relatively high parasympathetic nerve activity to the heart in an animal at rest maintains a low resting heart rate. During rest there is little sympathetic nerve activity to the heart. To increase heart rate, such as during exercise, parasympathetic nerve activity is first reduced to permit an increase in heart rate, and sympathetic nerves to the heart are activated if a further increase in heart rate is necessary for more intense exercise.

Changes in ANS nerve activity can occur as a result of discrete reflexes. For example, the diameter of the pupil of the eye is controlled by an ANS reflex initiated by changes in the amount of light detected by the retina. The circular smooth muscle

fibers of the iris constrict the pupil and are under the control of parasympathetic nerves. Changes in the amount of light reaching the retina initiate a reflex response to achieve a precise and proper pupil diameter.

Arterial blood pressure, salivary secretion, secretion of hydrochloric acid by the stomach, urination, and defecation are among functions regulated in part by ANS reflexes. The reflex centers for various ANS refl ex arcs are found throughout the CNS. For example, the brainstem has several centers regulating blood pressure, and the refl ex center for urination is in the sacral region of the spinal cord. ANS reflexes may use sympathetic nerves, parasympathetic nerves, or both. For example, the ANS reflex regulation of blood pressure uses sympathetic nerves to blood vessels and both parasympathetic and sympathetic nerves to the heart.

The sympathetic division of the ANS is primarily responsible for the fight-or-flight response that is associated with fear, anxiety, rage, and other strong emotions. The outcomes of this response can be predicted by imagining what changes would favor skeletal muscle activity for either fighting or running away.

Outcomes include increases in heart rate, blood pressure, blood glucose, and blood flow to skeletal muscle; dilation of airways in the lungs (e.g., bronchi); dilation of the pupils; and decreased activity of the digestive tract.

The fight-or-flight response is a short-term event characterized by high levels of sympathetic nerve activity throughout the body. This widespread sympathetic activation is not the result of a discrete reflex but is a more general sympathetic activation initiated in response to fear, anxiety, stress, and so on. The hypothalamus and amygdala in the brain appear to be especially important sites in the initiation of the sympathetic response, but it is not clear how feelings of fear, stress, and so on affect these centers to initiate the response. In addition to widespread increases in sympathetic nerve activity, the fight-or-flight response includes an increase in the release of epinephrine and norepinephrine from the adrenal medullae. Chromaffin cells of the adrenal medullae are innervated by preganglionic sympathetic neurons, and these cells release their catecholamines when stimulated. In most species the primary catecholamine released by chromaffi n cells is epinephrine. Epinephrine and norepinephrine in the circulation bind to adrenergic receptors throughout the body to amplify the general effects of increased sympathetic nerve activity. The blood levels of these catecholamines are relatively low and functionally insignificant when animals are not undergoing a strong sympathetic response.

The list of events in the fight-or-flight response includes dilation of the pupil of the eye. The control of pupil size was earlier described as also being controlled by a parasympathetic reflex based on light reaching the retina. This is an example of how circumstances may affect which division of the ANS dominates the regulation of an organ or gland. If an animal is not undergoing a strong sympathetic response, the parasympathetic nerves are the primary regulator of pupil size, but during times of intense stress, sympathetic stimulation may dilate the pupil in spite of the animal being in a brightly lit environment.

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.
2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.
5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.
7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.
14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

CHAPTER 4. PHYSIOLOGY OF HIGHER NERVOUS ACTIVITY

Structure of cerebral cortex.

Higher nervous activity – part of the central nervous system, that is provided with functions of the only cerebral cortex. The cerebral cortex is the site at which voluntary movements are initiated, sensations are brought to consciousness, and higher functions, such as reasoning and planning, take place. Organisms that do not have cerebral cortex do not have higher nervous activity. The basis of higher nervous activity in higher vertebrates and in man is conditional reflexes formed in the higher centers of the central nervous system (predominantly in the cerebral cortex). Phylogenetic evolution of the cerebral cortex from monostratified to polystratified (from amphibian to reptilian, avian, mammalian, and higher mammalian cortical layer structure).

In humans and some animals, the cortical areas have been extensively mapped to localize specific sensory and motor functions. The cerebral cortex (plural cortices), also known as the cerebral mantle, is the outer layer of neural tissue of the cerebrum of the brain in humans and other mammals. It is separated into two cortices, by the longitudinal fissure that divides the cerebrum into the left and right cerebral hemispheres. The two hemispheres are joined beneath the cortex by the corpus callosum. The cerebral cortex is the outer covering of gray matter over the hemispheres. Anatomic regions defined by consistent gyri (звивини) and sulci and general function are referred to as lobes. This is typically 2- 3 mm thick, consists of six layers and contains between 10 and 14 billion neurons.

The six layers of this part of the cortex are numbered with Roman numerals from superficial to deep:

- ✓ layer I is the molecular layer, which contains very few neurons;
- ✓ layer II the external granular layer;
- ✓ layer III the external pyramidal layer;
- ✓ layer IV the internal granular layer;
- ✓ layer V the internal pyramidal layer;
- ✓ layer VI the multiform, or fusiform layer.

Each cortical layer contains different neuronal shapes, sizes and density as well as different organizations of nerve fibers. This is the process that connects with other brain regions by extending through the white matter deep to the cortex.

The conception of higher nervous activity. The ways of studying of higher nervous activity.

The conception of higher nervous activity was first suggested by Pavlov distinct from the lowest neuronal activity and is represented by the brain hemisphere cortex activity, as well as the closest subcortex, which together provide normal complex interrelations of the whole organism and the internal and external media.

By I. P. Pavlov, «the activity of the higher centers of the central nervous system of animals and man which ensures the normal and complex relations between the entire organism and the external environment» (I. P. Pavlov, Poln. sobr. trudov, vol. 3, 1949, p. 482), as opposed to the activity of the central nervous system in integrating different parts of the organism. The term «higher nervous activity» was introduced into science by I. P. Pavlov, who considered it synonymous with «psychic activity». Thus, according to Pavlov, all forms of psychic activity, including human thought and consciousness, are components of higher nervous activity. A direct precursor of Pavlov in the study of higher nervous activity was I. M. Sechenov, who, in his work Reflexes of the Brain (1863), developed materialistic ideas on the reflex nature of psychic activity.

According to Pavlov, complex unconditioned reflexes (instincts, emotions, and the like) arise mainly in the subcortical nuclei. Moreover, the cortex and the subcortical nuclei of the cerebrum, each with their specific functions, are in continual communication and interaction and work together as an integral mechanism.

Perfect adaptation of an organism to its environment depends on the formation and extinction of various conditional reflexes. Conditioned reflexes permit the organism, on the basis of certain often indirect signals functioning as conditioned stimuli, to prepare in time for favorable events and avoid unfavorable ones. They also help the organism to broaden its perception of objects and events in the surrounding world and its scope of activity. It is well known that Pavlov, having discovered the conditioned reflex, found it necessary to utilize the meager neurophysiology of his time. At the present time neurophysiology has completely changed in character but is still based on his invention – conditioned reflexes.

The ways of studying of higher nervous activity.

- ✓ observing the behavior of the animal. This is an easy way, which shows the physiological state of the animal;
- ✓ resection of the cerebral cortex or part of it. This method allows to determine the functions of different areas in the cortex;
- ✓ Pavlov's work on higher nervous activity has been continued by his students and followers in the USSR and abroad. The principal phenomenon of higher nervous activity— conditioned reflexes—is the object of current research in world neurophysiology and experimental psychology.
- ✓ higher nervous activity is studied not only with the help of the diverse modifications of classical Pavlovian methods but also with the most recent macro- and microelectro-physiological and cytochemical methods – electroencephalography. This opens up the possibility of studying both the cortical and the deep brain structures and of discovering the laws of the functions of individual nerve cells and the molecular basis of their activity.

Localization of functions in the cortex according to its structure.

Of vital importance for higher nervous activity is the dynamic nature of the specialization and localization of functions in the cortex of the cerebral hemispheres, which plays an important role in the reliability of its activity (Fig. 11).

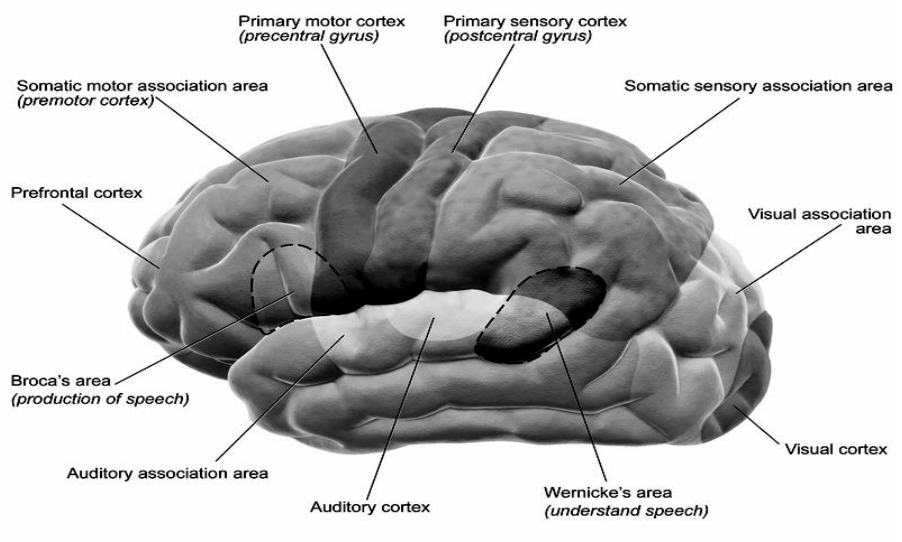

Figure 11. Regions of the cerebral cortex.

Sensory Cortices (Somatosensory Cortex). Primary somatosensory cortex is located in the post central gyrus. Very sensitive areas such as the lips and the fingertips have a huge representation. Neurons within each cortical site (particularly layer IV) are arranged in columns representing specific body regions. If a region is amputated (such as a finger) there is reorganization with neurons responding to stimulation of adjacent body parts. Damage to the sensory cortex results in decreased sensory thresholds, an inability to discriminate the properties of tactile stimuli or to identify objects by touch. The secondary somatosensory cortex is in the lower parietal lobe.

The somatosensory association cortex is directly posterior to the sensory cortex in the superior parietal lobes. This receives synthesized connections from the primary and secondary sensory cortices. Damage can affect the ability to recognize objects even though the objects can be felt (tactile agnosia). Cortical damage, particularly in the area of cortex where the posterior parietal lobe meets the anterior occipital and the posterior, superior temporal lobe, can cause neglect (ignore) of the contralateral side of the world. Therefore, neglect usually involves the left side and can be so severe that the individual even denies that their left side belongs to them.

Visual cortex.The primary visual cortex also called the striate cortex, surrounds the calcarine sulcus. This area has a large granular layer with dense columns of neurons, called ocular dominance columns. The macula, the most sensitive portion of the center of the retina, is represented at the posterior tip of the occipital lobe. Lesions of the occipital lobe would cause cortical blindness and difficulty tracking objects.The primary visual cortex projects to cortical areas surrounding it, called the visual association areas, where signals are interpreted and form is recognized. Selective lesions of these association areas will produce an inability to recognize objects even when they may be seen. There are additional aspects of visual function that are represented in other regions of adjacent cortex, which resides in the posterior part of the middle temporal gyrus is responsible for recognizing movement and color recognition.

Auditory Cortex.The primary auditory cortices are on the transverse temporal gyri, extending into the lateral fissures. These gyri are situated on the upper part of the superior temporal gyri. Unilateral cortical lesions do not effect hearing because of completely bilateral sound representation. There are auditory association areas surrounding the primary auditory cortex. These areas are involved in the interpretation of sound. Damage to this area can produce inability to understand language, including written language. In the nondominant hemisphere this may be involved in understanding the tone of voice.

Language Cortex.There are areas of particular importance of the cerebral cortex. The receptive language area, Wernicke's area is in the upper temporal lobe, extending back to the supramarginal and angular gyri. Lesions produce receptive aphasia with problems understanding spoken and written language. Lesions of the opercular and triangular portions of the inferior frontal gyrus, called Broca's area in the dominant hemisphere, produce expressive or motor aphasia. These patients have difficulty in generating spoken or written language.

The prefrontal cortex is extremely well developed in humans. It is primarily involved in executive functions (working memory, judgment, planning, sequencing of activity, abstract reasoning and dividing attention).

Motor Cortex.The primary motor cortex is in the precentral gyrus. This is the origin of most of the corticospinal tract and a large number of cortical bulbar fibers, particularly those controlling motor cranial nerves. This also has projections to the thalamus and basal ganglion. Specific movements tend to be represented (such as elbow flexion) rather than specific muscles. Lesions produce spastic contralateral weakness, which is most prominent in the distal extremities. The premotor cortex is immediately anterior to the motor cortex and has many of the same connections as the motor cortex. The supplementary motor area is a part of the premotor cortex that extends onto the medial side of hemisphere. Lesions of this area can cause inability to initiate motions, called abulia.

Taste.Taste is detected in the inferior part of the post central gyrus, bilaterally, extending into the lateral fissure, including the insula. Vestibular afferent sensations are processed in the superior temporal or inferior parietal gyri.

The frontal lobes connect to all other cortical regions through association fibers. It receives particularly strong input from limbic cortex, amygdala and septal nuclei, areas involved in emotional responses. Patients with lesions in this area are often referred to as having a changed personality.

Conditioned and uncconditioned reflexes: differences, classification.

According to Pavlov the whole integrity of reflector reactions is the convention to divide into the conditioned and unconditioned reflexes.

Comparative characteristics of conditioned and unconditioned reflexes:

Unconditioned reflexes are congenital; genitive, generic and strictly connected with the structure and are functioning from the birth moment. Unconditioned reflexes become stable during phylogenesis, are constant; afterwards depending on the given structure maturation and have an adaptation significance to

the environment constancy. Unconditioned reflex arc closes at lower parts of CNS. Unconditioned reflexes are typically, simple. Unconditioned turned on the effect of specific adequate stimulus.*Some well-known examples are the knee-jerk reflex, in which sudden muscle stretch causes the muscle to contract, the flexion withdrawal reflex in which a painful stimulus to the skin elicits rapid withdrawal, the pupillary reflex in which a flash of light causes the iris to contract*

Conditioned reflexes are being obtained during ontogenesis and are connected with acting stimulus, formed on the basis unconditioned. Conditioned reflexes arise during ontogenesis, are temporary, unstable. Conditioned reflex arc closes at the level of the cerebral cortex. Conditioned reflexes are individual. Conditioned reflexes turned on the effect of any stimulus, the environment changes, conditional stimulus is not adequate. *For example-the salivary reflex in which the taste of food triggers salivation, and the startle reflex in which a loud sound elicits widespread muscle contraction.*

Classification of reflexes. According to their biological significance the whole totality of unconditioned reflexes are divided into: feeding, defence, sexual, orientation reaction („what is it?'' reflex) and parental reflexes Conditioned reflexes are divided into natural (that are worked out on the natural stimulus action, smell and other natural features), artificial (light, bell ringing, geometrical figures, i.e. features not intrinsic to the acting stimulus).

Rules for building conditioned reflexes:

- ✓ conditioned and unconditional signals have to cohere (accord) in time;
- ✓ conditioned reflex can be produced in time when the beginning of the indifferent (conditional) signal precedes the beginning of unconditional stimulation;
- ✓ stimulus, which will become conditional must not produce a significant unconditional reaction, i.e. physical strength of conditional one must not exceed the strength of unconditional stimulation;
- ✓ the cortex must be active;
- ✓ the cortex must be free from other types of activity;
- ✓ motivation;
- ✓ the animal has to be healthy.

Mechanisms of conditioned reflex producing.

According to Hasratyan, any unconditioned reflex is multistage and each unconditional reflex has a cortical representation. With the cortex removal the unconditional reflex does not disappear, but changes in its character take place. In case of acting of two signals having similar strength and producing feeding and defence reflexes, then altering them timely we can work out doubled conditional reflex: upon the feeding reflex not only saliva excretion, but also paw's pulling off take place. So, between two unconditional reflexes a connection arises. But decortications interrupt this connection.

In the conditioned reaction forming, e.g. on light signal, first the orientation reaction arises, and on reply to alimentary signal the feeding reflex produces.

Multiple combinations in time of these signals create a temporary functional connection between the visual and the feeding centres. Closing of this connection takes place by the dominant principle. Stronger feeding centre (there is a feeding motivation) being excited more impulses attract from the visual centre, and the summation expense becomes more intensive. Now just in case of conditional signal acting (e.g. light) impulses through the existing pathway will arrive from the visual centre to the feeding centre, exciting the latter.

Ecckles considered that repeated passing of impulses through the neuron system enhances effectiveness of synapses and intensifies the synaptic transmission (synaptic relief).

Pavlov previously suggested that the conditional reflector connection was realized transcortically: cortex-cortex. But Hasratyan and other researchers showed, that the vertical dissection of the grey matter does not affect on the conditional reflex producing. Hasratyan proposed the vertical closing of connection: cortex-subcortex-cortex. The afferent impulses arrive by specific and non-specific pathways to the sensory zone of the cortex, and after being worked off there they return to the reticular formation by the efferent ways, and then to the cortical centre of the unconditional reflex. Afterwards this version was ascertained electro-physiologically.

An issue of long-term keeping of the worked out conditional reflexes even nowadays remains not solved. The short-term memory is considered to be connected with the neurons functional characteristics augmentation, as well as with the neuronal traps. As for the long-term memory the version of morphological changes in the neurons is suggested: the development of the presynaptic terminals, increasing in number of synapses, changes in the nucleic acids, particularly in RNA contents. But the update knowledge level does not allow submitting a certain hypothesis regarding the memory problem.

Components of unconditioned and conditioned reflexes. Each reflector reaction is accompanied by vegetative and motor components. For example, unconditional defence reflex on the pain stimulation is manifested by defence motor reaction, changes in breathing, cardiac activity, arterial pressure, blood content, etc. The conditioned reflex produced on the unconditioned base also serves as a multi component reaction. Herein they differentiate the main specific and secondary non-specific components. In the defence reaction the main component is the movement component, the vegetative changes are secondary. In feeding the main component will be secretion and motor activity of the digestive tract; whereas all the rest components will be secondary ones and they have just a serving role, forming optimal conditions for the main component realization.

Biological and economic importance of conditioned reflexes. Dynamic stereotype, its biological and economic significance.

Use of the method of conditioned reflexes has been determined by the historical principles of the development of the general physiology of the nervous system.

The conditioned reflex is an integrated behavioral act. conditioned reflexes have an adaptation significance to the constant environment. Conditioned reflexes have adaptation significance to the altering environment. Conditioned Reflex play important Role in Adaptive Behavior. Consequently the dynamic equilibrium between the inner forces of the animal system and the external forces in its environment has become elemental as compared with the exquisite adaptability of the normal animal, and the simpler balance is obviously inadequate to life. Efforts of many laboratories studying the behavior of animals and man, especially laboratories associated with psychiatric clinics, are devoted to the study of conditioned reflexes.

Conditioned reflexes increase productivity of animals.

Dynamic stereotype – a system of conditioned reflexes which were formed as conditioned signal place related, not signal quality relatedrelated. The basis of habits and professional skills formation. Dynamic stereotype increase productivity of animals. Dynamic stereotype – a type of integral activity performed by the cerebrum of higher animals and man and manifested by a fixed, or stereotyped, succession of conditioned reflexes.

The dynamic stereotype is influenced by external factors that are repeated in a certain order. If the conditions that engendered and maintained the stereotype are altered, the stereotype may change or disappear. The dynamic stereotype is the most vivid manifestation of the extremely subtle analyzing and synthesizing activity of the cerebral cortex and is the product of very complex interactions between the areas of the cortex. The dynamic stereotype is the physiological basis for the automation of skills. It aids in the efficient performance of tasks and in rapid adaptation to the conditions of existence. Human habits and simple labor skills are expressions of dynamic stereotyping.

The development of a dynamic stereotype places a significant burden on the central nervous system. However, once a stereotype is established, it becomes automatic and inert. Thus, the reconstruction of a dynamic stereotype places a great strain on the neural elements of the cerebral cortex. The strain sometimes overburdens the capacities of these elements and often leads to disturbances in higher nervous activity and to the development of neurotic states. The mental crises and emotional turmoil experienced by people upon changing their familiar way of life often have a physiological basis – the disruption of a former dynamic stereotype and the difficulty in establishing a new one. The degree of difficulty in reconstructing a dynamic stereotype depends on the nature of the stimuli and the specific characteristics of the nervous system, as well as on the age and condition of the organism.

Types of inhibition of conditioned reflexes. Analysis and synthesis.

No conditioned reflex is possible to work out just by stimulation. Herein inhibition is necessary and very important. The orientation is the reaction previously arisen by the light stimulation then inhibited and lets the feeding reflex be produced. Without inhibition the existing excitation will irradiate over the whole cortex.

Inhibition is characterized by ceasing or weakening of that or other reflector activity. There are two types of cortical inhibition: conditioned and unconditioned.

Unconditioned inhibition arises since the first display: the feeding reflex becomes inhibited and the orientation reaction arises. This inhibition is called external, because it is formed under the influence of external, non-significant for the given reflector activity stimuli from the other neuronal centres, out of the given reflector arc.

In multiple repetitions the orientation reaction disappears and the signal's inhibitory influence weakens. Such stimuli were called by Pavlov «extinguishing inhibitors». External inhibition is explained by the negative spatial induction. Another type of unconditional inhibition is the transmarginal inhibition. The excessive increase in strength or in action duration of conditional stimulus gives an opposite result, leading to weakening and inhibition of the conditional reflex. It has a protective significance and protects neuronal cells from the exhausting influence of strong and prolonged stimuli. Both of these types of inhibition are connected with the neuronal system's natural congenital properties.

Conditioned inhibition is based on the conditional reflex and appears in those neuronal structures, which participate in the given conditional reflex realization, i.e. within the given reflector arch. So, it is called an internal inhibition. Conditioned inhibition arises during ontogenesis and needs processing. There are 4 types of internal inhibition, depending on conditions expediting the conditional reflex to be not sustained.

- ✓ Extinguishing inhibition. A conditional signal is accompanied and reinforced by an unconditional stimulus, but if a conditional reflex is used alone and is not reinforced by an unconditional stimulus, the stable conditional reflex, previously established, gradually weakens after several applications and finally extinguishes.
- ✓ Differential inhibition. If a conditional reflex is developed to the note „re'', similar sounds (do, re, mi) will also be capable of eliciting a conditional positive reaction. But in case of reinforcing only the „re'' note, generalization of the conditional reflex declines and differentiation of stimuli takes place. The closer parameters of stimuli, the more difficult to develop a conditional reflex.
- ✓ Conditioned inhibitor. It develops in case, when the stimulus A (light) is constantly sustained, but A+B (light + sound) - not. Previously both A and (A+B) combination evoke a conditional reflex. Further, the (A+B) combination loses its positive significance. „B'' serves as a conditional inhibitor. It contributes additional information to the conditional stimulation and obtains an inhibitory significance.
- ✓ Delayed conditioned reflex. If the unconditioned stimulus (food) is constantly delayed for a short span after the beginning of the conditional stimulus (1-5 sec), the secretion begins just after the conditional stimulus action onset. If the reinforcement lags behind for 2-3 min, the secretion is delayed by 1-3min.

The conditional stimulus first has really an inhibitory significance, but afterwards- a positive one. Deeply delayed stimulus loses its positive significance.

The role of internal inhibition is:

a) to divide all conditional signals into 2 categories: the positive, which evokes conditional reflex reactions and the negative, causing inhibition;

b) to have an adaptation importance making the organism's reactions more economic and purposeful;

c) to bring to inhibition and excitation processes underlying the analysis and synthesis of the cortex activity.

Analysis and synthesis. **Analysis** is an investigation of specific discrete sides of a whole process. In physiological meaning it is a reaction of the organism to discrete components of a complex stimulus and consists in discrimination between different signals and divisions of (complex phenomenon) its components. Analysis is achieved through the internal inhibition. **Synthesis** is a common reaction of the organism on several stimuli, and is expressed in the association, generalization and unification of excitations. Synthesis is manifested by the formation of a temporary connection on which every conditional reflex is built.

Mutual induction of excitation and inhibition Excitation and inhibition may intensify each other, which is called induction. First this phenomenon was discovered by Vvedensky in the spinal cord. Then it was studied by Sherrington, and finally, Pavlov, who found out induction in the cortex. After the concentration of excitation or inhibition, they induct contrary phenomenon on the periphery. Pavlov differed two phases of induction:

1) positive (inhibition intensifies excitation);

2) negative (excitation intensifies inhibition).

The first, second signal system.

The first signal system – system of conditioned reflexes to certain stimuli (light, sound, others), is common for animals and people.

The second signal system – system of conditioned reflexes to abstract stimulus – a word and its meaning, is characteristic only for people.

According to Pavlov, the higher nervous activity of animals, even those at a high level of development (for example, dogs and monkeys), is, on the whole, a result of the complexity of diverse and heterogeneous conditioned reflexes of the first signaling system which is common both to man and to animals. In spite of the gradual development of speech, the conditioned reflexes of the first signaling system still continue to constitute the basic fund in the higher nervous activity of children in the first years of life and occupy a specific place in the higher nervous activity of humans at subsequent stages of growth. To this type of conditioned-reflex activity, Pavlov attributes sensations, ideas, and impressions derived by man from the external environment, including the social environment, which are formed without the use of verbal (i.e., word) signals.

But in the case of man, along with the development of social forms of labor activity, «signals of a second order, symbols of those primary signals – in the form of words pronounced, heard, and seen – appeared, developed, and became highly perfected». This qualitatively new, higher, and more perfect second signaling system of reality, also based on conditioned-reflex mechanisms, is characteristic only of the higher nervous activity of man, exists in close interaction with the first signaling system, and plays a leading role in his conscious life, providing the basis for generalization and thought. While continually emphasizing the fundamental, qualitative difference between these two kinds of higher nervous activity, Pavlov at the same time also pointed to the organic connection between them, to the fact that the basic laws established in the working of the first signaling system must also govern the second system.

Types of higher nervous activity, their relationship with farm animal performance.

Integrity of the main individual properties of the neuronal system is called the type of the higher nervous activity. It's a combination of inborn and acquired properties of nervous system – genotype + phenotype.

In Pavlov's laboratory it was revealed, that being in the same conditions not in all animals it was possible to develop conditional reflexes, which depended on individual peculiarities of the higher nervous activity. As a criterion of the higher nervous activity assessment the force mobility and balance of the excitation and inhibition processes were elected.According to these criteria Pavlov elected 4 types of higher nervous activity:

- ✓ I type is strong-balanced- flexible – lively (sanguinic);
- ✓ II type is strong- balanced-inert (phlegmatic);
- ✓ III type is strong-unbalanced – unrestrained (choleric);
- ✓ IV type is weak (melancholic).

Pavlov's this classification coincides with the temperaments submitted by Hippocrates: sanguine, phlegmatic, choleric, melancholic. There are many other intermediate types of higher nervous activity, making variants of these main ones.

Type of higher nervous activity is built up based on congenital and acquired characteristics during all life. The integrity of the congenital characteristics is named as genotype; of the acquired ones as a result of life experience – as phenotype. In man the significance of genotype and phenotype in forming higher nervous activity are approximately equal, since man is a social being. Different conditions during life may change not only behaviour, but all the psychological habits. In any type of higher nervous activity it is possible to work out socially useful features of character. Thus, even a weak type being in favourable conditions can attain much and become a more useful member of a society, than a representative of a strong type deprived of constant purpose (e.g. outstanding composer Chaykovsky was melancholic). In Pavlov's laboratory puppies from the same family were taken and placed into two different conditions – with a poor care and with a good one. They respectively were grown up of a weak and a strong types of higher nervous activity. Excessive

guardianship and limitation of independence lead to weak, noninitiative people's appearance.

BIBLIOGRAPHY

1. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
2. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
3. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
4. Mazurkevich AY, Trokoz VO, editors. Physiology of farm animals. Workshop. 2nd ed. Kyiv: Center for Educational Literature; 2015. (Ukrainian).
5. Mazurkevich AY, Trokoz VO, Karpovsky VI, et al. ; edited by A.Y. Mazurkevich, V.O Trokoz. Physiology of agricultural animals. Textbook. 2nd ed. Kyiv; 2014. (Ukrainian).
6. Moyes CD, Schulte PM. Principles of Animal Physiology 3rd ed. Don Mills, Ontario: Pearson; 2016.
7. Papachristodoulou D, Snape A, Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 6th ed. Oxford, UK: Oxford University Press; 2018.
8. Pineda MH, Dooley MP, editors. McDonald's Veterinary Endrocrinology and Reproduction. 5th ed. Ames, Iowa: Iowa State Press; 2003.
9. Pollard TD, Earnshaw WC, Lippincott-Schwartz J, Johnson GT, editors. Cell Biology. 3rd ed. Elsevier. 2016.
10. Reddy PB. Text book of Animal Physiology. Andhra Pradesh, India: IMRF Publications; 2015.
11. Reece WO, Functional Anatomy and Physiology of Domestic Animals. 4th ed. Baltimore: Wiley-Blackwell; 2009.
12. Rhoades RA, Pflanzer RG. Human Physiology. 4th ed. Pacific Grove, Calif.: Brooks/Cole; 2003.
13. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
14. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.
15. Smith BP. Large Animal Internal Medicine. 3rd ed. St. Louis, Missouri: Elsevier Mosby; 2015.
16. Tortora GJ, Derrickson BH. Principles of Anatomy and Physiology. Atlas and Registration Card. 11th ed. Hoboken, NJ: John Wiley & Sons; 2005.

CHAPTER 5. PHYSIOLOGY OF SENSE ORGANS

General characteristics of sense organs, classification.

All sense organs have 3 main parts:

1.sensory, or afferent, systems are the means by which the nervous system receives information about the external, the internal environment and the position and movement of the body. The body uses sensory information to generate reflex movements (e.g., a blink of the eye when it is touched, withdrawal of a limb from a hot surface, contraction of the bowel when it is stretched) without the participation of the conscious parts of the brain.

2.afferent pathway, intermediate (pathways and subcortical structures, which transmitte nerve impulses to brain).

3. central part (brain, cerebral cortex) Much (but not all) sensory information is also directed to the cerebral cortex for conscious perception. Cerebral cortex is the highest area where there is a feeling - the result of complex interaction of nerve cells.

Classification. To sensory systems belongs: somatosensation (pain, touch, temperature, and position) sense (proprioception). Special senses include smell (olfaction), vision, taste (gustation), hearing (audition), and equilibrium (vestibular sensations).

Depending on the perception of the stimulus sense organs:

- ✓ contact – sensory systems whose receptors are excited by direct contact with a stimulus. This includes taste (gustation), touch;
  distant – sensory systems whose receptors come into activity under the influence of stimuli located at a certain distance from the body. These include the vision, hearing (audition), smell.

Sensory receptors, classification.

Sensory experiences begin at receptors, specialized cells or nerve endings that detect a particular aspect of the internal or external environment. They are the mechanism by which the nervous system changes some sort of environmental energy (e.g., heat, pressure, light) into the electrical activity of neurons, a process called transduction. Sensory receptors may be described by the origin of the stimulus:

- ✓ exteroceptors (external environment);
- ✓ interoceptors (visceral organs);
- ✓ proprioceptors (position and movement sense).

They may also be described on a structural basis as:

- ✓ encapsulated, which vary widely in structure, are primarily concerned with touch sensations; these receptors are invested with specialized connective tissue capsules that impart modality specifi city to the receptor;
- ✓ nonencapsulated or free (naked) nerve endings are widely distributed and are sensitive primarily to painful stimuli.

The most functionally relevant classification scheme for receptors is based on the type of stimulation to which a receptor best responds. In this system, there are five general types of receptors:

- ✓ mechanoreceptors, which respond to physical deformation;
- ✓ thermoreceptors, which respond to both heat and cold;
- ✓ nociceptors, which respond to stimuli that are potentially injurious to tissue (noxious stimuli);
- ✓ photoreceptors, which are the light receptors of the retina;
- ✓ chemoreceptors, which respond to chemical changes associated with taste, smell, blood pH, and carbon dioxide concentrations in the blood.

In normal circumstances, each receptor is preferentially sensitive to one type of stimulus; is called the adequate stimulus for that receptor. Receptors transduce environmental energy into changes in membrane potential. The adequate stimulus produces a local change in membrane potential of the receptor, a voltage change known as the receptor potential or generator potential. The receptor potential is usually depolarizing, brought about by the opening of cation channels permeable to Na^+ and K^+.The receptor potential is a graded event that spreads passively over the local membrane of the receptor; the amplitude of the potential change and the distance along the membrane that the receptor potential travels are proportional to the strength of the stimulus. When the change in membrane potential reaches a critical level, the threshold, an action potential begins in the trigger zone of the sensory neuron's peripheral process. This signal is conducted along the axon into the CNS.

Many encapsulated receptors exhibit a physiologic characteristic called **adaptation**. With sustained stimulation, the receptors cease firing after their initial burst of activity. When the stimulus is withdrawn, the receptor again responds with a volley of action potentials. In doing so, the adapting receptor signals the beginning and end of the stimulus, rather than fi ring throughout its duration. Typically, touch receptors adapt rapidly; naked nerve endings – nociceptors – as a rule do not adapt but fire continuously throughout application of a noxious stimulus.

Sensation: somatosensation, visceral sensations.

Sensation (feeling) is the conscious perception of sensory stimuli. It is impossible to know exactly what an animal (or another person, for that matter) sees, feels, hears, or smells. We infer what sensations an animal may experience by observing its reaction to various stimuli, by identifying homologies between human and animal sensory systems, and by imagining what we might feel in similar situations. The experience of a given sensation as it is perceived at the cortical level has qualities that make it distinct from other types of sensations. This perceptual distinction defines the sensory modality. *For example, the stimulus for the photoreceptors of the retina is light; the sensory modality that is experienced when photoreceptors are stimulated is vision.* Certain animals have sensory systems that have no homology in human beings. For instance, migratory birds and some insects are able to sense geomagnetism of the earth, information they use for navigation. A number of species of fish can detect and generate electric fields; domestic animals

can sense an impending earthquake through a sensory experience unavailable to humans.

Somatic sensation or somatosensation describes modalities thatarise primarily from innervation of body surfaces and musculoskeletal elements; it includes pain, touch, temperature, and position sense (proprioception). In somatosensory systems, the receptor is usually a specialized peripheral terminal of the primary afferent neuron (the sensory neuron extending from the CNS to the periphery); for the special senses, the receptor is usually a separate specialized neural cell that synapses with the primary afferent.

Pain is the conscious perception of noxious stimuli. A noxious stimulus is one that is capable of producing tissue damage; it can be thermal, chemical, or mechanical. The receptor for noxious stimuli is the nociceptor, a naked (not encapsulated) nerve ending. As a rule, axons transmitting noxious information are smaller and less myelinated than those carrying tactile or body position information. Activation of pain fibers of medium diameter and myelination (so-called Aδ fibers) is associated with a sharp, pricking quality of pain as reported by human beings. Activation of the smallest diameter C fibers, which are unmyelinated, produces a dull, burning type of pain.

The preponderance of C fibers in visceral sensory fibers explains the burning, aching quality of visceral pain. A number of ascending spinal cord tracts transmit information about noxious stimuli to brain structures. In addition to projecting to the cerebral cortex for conscious perception, pain pathways typically have strong connections to autonomic centers in the brainstem and parts of the brain that produce increased mental alertness and behavioral and emotional responses to painful stimuli. These connections are responsible for producing signs of sympathetic stimulation (e.g., increased heart and respiratory rates, dilation of pupils), emotional responses, and escape behaviors.

The ability of a given noxious stimulus to produce a perception of pain is a highly mutable property that can be modified in the periphery, in the spinal cord, and in the brainstem.The threshold of nociceptors in the periphery is not a constant. Importantly, many substances released by injured tissues and infl ammatory cells stimulate or lower the threshold of nociceptors.

Thus, in damaged or inflamed tissue, stimuli that would normally be below threshold for detection may produce activity in nociceptive afferents. These events contribute to the development of primary hyperalgesia, a phenomenon wherein the perception of pain in injured tissues is increased. A dramatic example of this is made by sunburned human skin; the inflammation of the injured skin lowers threshold of nociceptors so that even a light touch (for instance, contact with clothing) can activate them.

Proprioception is the nonvisual perception of body position. It is a complex sensory modality that is created through the input of a variety of specialized receptors called proprioceptors. These include joint receptors (providing information on tension and pressure within joints), muscle spindles (signaling changes in muscle length),

Golgi tendon organs (signaling tension in tendons), and skin mechanoreceptors (which report contact with the environment).

Ascending proprioceptive pathways project both to the cerebral cortex and the cerebellum.The cerebral cortex uses proprioception to help formulate voluntary motor plans; the cerebellum uses it to adjust ongoing motor movements so that they are smooth and accurate. The information carried in the separate tracts to these targets arise from the same peripheral receptors and primary afferent neurons; it is only the ultimate destination (and therefore use) that is different. For the cerebral cortex and cerebellum to make effective use of feedback on body position to guide movements, the proprioceptive information must be delivered very rapidly to these brain regions. In fact, the very fastest (up to 120 m/second) axons of the entire nervous system transmit proprioceptive information. We, and presumably animals, are generally not aware of proprioception, but it is critically important in the execution of accurate, wellcoordinated movements. Injury to the proprioceptive pathways results in awkward, inaccurate, uncoordinated gait and movement. The incoordination typical of proprioceptive deficits is referred to as ataxia.

Touch is the modality associated with nonnoxious mechanical contact with the body. Touch receptors are encapsulated, and the axons that transmit touch information to the brain are typically medium in diameter and degree of myelination. Spinal cord tracts associated with touch are found in all the funiculi of the cord.

Visceral sensations involve structures within the body cavities. Most visceral afferent information is not available to consciousness but is instead important in directing the autonomic activity in viscera. Receptors of the viscera are confined to mechanoreceptors and chemoreceptors. The latter as a rule do not project to cortical levels, so perceived sensations are primarily limited to pain and pressure. Since unmyelinated C fibers are the predominant type of sensory fiber innervating the viscera, visceral pain has a burning, aching quality. Remarkably, the viscera tend to be relatively insensitive to stimuli such as crushing, cutting, and thermal injury. Surgical manipulation, therefore, tends to produce very little activity in sensory systems. Visceral afferents do respond vigorously to stretch, dilation, tension, and ischemia (reduced blood flow), however. For this reason, cramping (increased muscular tension in the wall of a viscus) and stretching due to gas accumulation are quite painful. The cramping, stretching, and/or ischemia that occur when the equine large intestine twists or is displaced can produce severe abdominal pain, called colic, in horses.

Chemical Senses (gustation (taste) and olfaction (smell). Features of structure and functions.

Chemical senses are those that detect particular molecules in the external or internal environment. Chemical senses that detect molecules outside the body include gustation (taste) and olfaction (smell). Within the body, the chemical senses include the detection of blood pH and carbon dioxide concentration. These latter afferents are associated with autonomic reflexes and do not project to the cerebral cortex for perception.

Taste, or gustation, is the modality associated with dissolved substances contacting specialized receptor cells on the tongue and throat region. The receptors, simply called taste cells, are arranged in a group with supporting cells, a cluster that constitutes the taste bud. Taste buds are not distributed evenly on the surface of the tongue; they are confined to specific forms of papillae (tiny projections), the vallate, foliate, and fungiform papillae, which are found on the tongue (the greatest number), soft palate, parts of the pharynx, and epiglottis of the larynx.

The tongue is covered with thick keratinized stratified squamous epithelium. The surface is characterized by a large number of projections, the papillae, which are particularly well developed on the dorsal surface. Filiform,fungiform, and vallate papillae are found in all domestic animals, and foliate papillae are present in the horse, pig, and dog, but not in ruminants. Ruminants additionally have large conical papillae. The filiform and conical papillae do not bear taste buds (cells specialized for gustation), but all other types of papillae do. Taste buds may also be found on the epiglottis, larynx, pharynx, and soft palate.

The filiform papillae look somewhat hairlike. In the ox, they consist of a connective tissue core covered by a highly cornifi ed epithelial layer. These papillae are shorter and softer in the horse than in other domestic animals, giving the tongue of the horse its velvety feel. Interspersed amongst the filiform papillae are fungiform papillae, so called because of their resemblance to tiny mushrooms. Foliate papillae resemble the foliage or leaves of plants. They are found in the horse and pig (and only rarely in cattle) on the lateral margin adjacent to where the root of the tongue is connected to the soft palate by a mucous membrane fold, the palatoglossal arch. Vallate papillae are large, circular projections surrounded by a deep groove. These papillae are arranged in a V shape on the caudal part of the tongue and demarcate the morphologic division between the body and the root of the tongue. The body of the ruminant tongue has a prominent dorsal bulge, the torus lingua, which is thickly covered with prominent conical papillae. Similar cornifi ed projections cover the inside of the lips and cheeks.

Sensory nerve fibers subserving taste are distributed to the rostral two-thirds of the tongue by a branch of the facial nerve, the chorda tympani. Taste in the caudal third of the tongue is conveyed by f bers of the glossopharyngeal nerve. Somatic sensations (heat, cold, touch, pain) from the tongue are conveyed by branchesof the trigeminal and glossopharyngeal nerves.It is likely that taste buds on areas other than the tongue are innervated by the vagus nerve.

Traditionally, four basic taste sensations have been identified. These are sweet, salt, bitter, and sour. Individual taste cells have membrane receptor physiology designed to detect the chemical substances associated with these tastes. The more complex sensory experiences that we normally associate with taste (for example, the flavors that we detect when we distinguish between an apple and a carrot) are created primarily from stimulation of olfactory (smell) receptors in combination with the basic taste modalities. For them to stimulate taste cells, chemicals must be in

solution. Dissolution of substances so that they can be tasted is an important function of saliva.

In addition to the four basic tastes, a fifth taste modality with its own specific taste cell receptor has been identified. This taste, experienced when the amino acid glutamate is present, imparts a savory quality to foodstuffs. Because this taste modality was first described by Japanese researchers, it is known by the Japanese word for savory or delicious: umami. It is the presence of the umami taste receptor that explains the enhanced flavor of foods when monosodium glutamate is added.

Olfaction is the sense of smell. Olfactory sensory neurons are scattered among supporting cells throughout the olfactory mucosa in the dorsocaudal part of the nasal cavity. The apex of each olfactory neuron bears a single dendrite with a tuft of several fine hairlike projections, which bear the chemical receptors for the sense of smell. An axon from each olfactory neuron passes through the cribriform plate of the ethmoid bone; the mass of fine fibers thus entering the cranial vault collectively constitutes the olfactory nerve. These fibers synapse within the olfactory bulb on neurons whose central processes make up the olfactory tracts of the brain.

Neural connections within the olfactory parts of the brain are complex. Olfaction is the only sensory modality that is not routed through the thalamus before reaching conscious perception at a primary sensory cortex. Olfaction is also known to have profound connections to the limbic lobe, the part of the brain that generates emotional and autonomic behaviors. Smells, therefore, are uniquely capable of eliciting emotions and behaviors. There is a subset of olfactory sensory neurons outside the olfactory epithelium that innervate the mucosa of the vomeronasal organ, a diverticulum of the nasal cavity in the hard palate. These olfactory neurons appear to be receptors for pheromones, chemical substances that can influence the behavior of other individuals. Pheromones are likely especially important in reproductive behaviors. In spite of vigorous research efforts, no human pheromones have yet been unequivocally identified.

Vision. Features of structure and functions.

The eye is an elaborate organ whose primary function is to collect and focus light upon the photosensitive retina. It lies within a coneshaped cavity of the skull, the orbit, which houses the eyeball (globe) and a number of other soft tissue structures, the ocular adnexa (e.g., muscles, glands), that act upon the eyeball in service of its light-collecting function. Unlike the human orbit, which is a complete bony cone, the ventral portion of the orbit of domestic species is bounded by soft tissues, notably the pterygoid muscles (Fig. 12).

The part of the environment from which light will enter the eyes and stimulate the retinas is the visual field. In predators and arboreal animals, such as birds and primates (for whom accurate depth perception is essential), the eyes are placed so that the visual fields overlap to varying degrees. This region of overlap, where objects are simultaneously viewed by both eyes, is the binocular field; the visual cortex evaluates the slightly different view from each eye and uses the information to provide depth perception. Prey animals, on the other hand, have lateral eyes with a much smaller

binocular field. Such eye placement increases the peripheral vision so that the combined visual field is nearly completely panoramic. Such vision is monocular (seen only with one eye) and therefore lacks very accurate depth cues, but the clear advantage of this wide field of view for a prey animal needs no explanation.

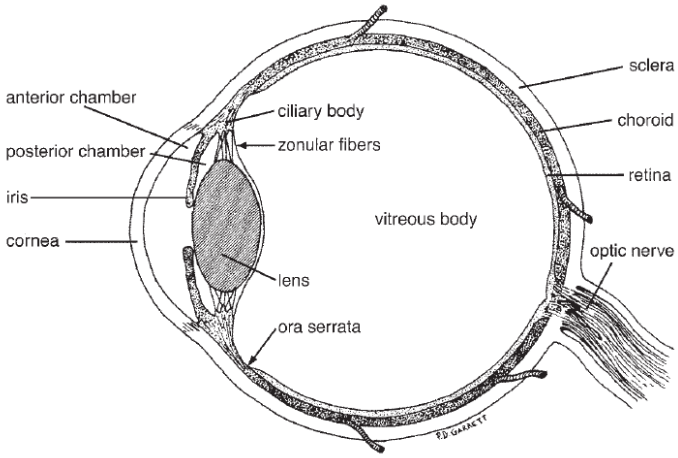

Figure 12. Structure of the eye.

Light traveling from the visual field to the retina passes through a series of transparent media that refract and focus it on the lightsensitive retina of the posterior part of the globe. These dioptric media include the cornea, the aqueous, the lens, and the vitreous body. As indicated before, the cornea is actually the most refractive medium of the eye, but the lens is the only part of the light path with the ability to change its refractive index. This property makes it the organ of accommodation for focus on near objects. Light entering the vitreous chamber of the eye is bent by the more anterior parts of the eye in such a way that the image that is focused on the retina is inverted and reversed.

The site where the ganglion cell axons leave the eye (the optic disk) has no photoreceptors and is therefore considered the blind spot of the retina. In primates, a region dorsolateral to the optic disk is relatively free from large blood vessels and especially densely packed with photoreceptors (particularly cones). This is the region of greatest visual acuity, the macula. Domestic animals lack a macula.

Visual pathways of the brain. The electrical information generated by exposure of photoreceptors to light undergoes initial neural processing within the retina. This information ultimately leaves the eye via the optic nerve, the fibers of which are the axons of the ganglion cells of the retina. Most of the axons of the optic nerve synapse in the thalamus, and from there visual information travels to the primary visual cortex in the occipital lobe of the brain (the most caudal part of the cerebral cortex) for conscious perception.

A smaller subset of ganglion cell axons project to other destinations in the brain. Some reach the rostral colliculi of the mesencephalon, where visual stimuli induce refl ex movements of the eyes and head. Others project to the pretectal nuclei, also in the region of the mesencephalon; these nuclei communicate with the

oculomotor nuclei to coordinate the reflex constriction of the pupils in response to light. Finally, a very small number of ganglion cell axons project to a specific group of cells of the hypothalamus, the suprachiasmatic nucleus. The suprachiasmatic nucleus is the biologic clock, the part of the brain that sets circadian rhythms. Circadian rhythms are physiologic processes that vary regularly on a daily basis; prominent circadian rhythms include sleep–wake cycles, melatonin secretion, and body temperature fluctuations. The suprachiasmatic nucleus has an intrinsic rhythmicity that closely approximates 24 hours, but the projections from the retina keeps the nucleus's cycle entrained to the actual photoperiod of the day.

Many domestic species are seasonal breeders, meaning that their reproductive cycles are determined by the season. The most powerful determinant of the onset and cessation of breeding cycles in these species is the length of the day. The retinal projections to the suprachiasmatic nucleus are the brain's record of day length, and they therefore determine the reproductive cycles via their influence on the autonomic functions of the hypothalamus. It is common agricultural practice to alter breeding behavior by exposing animals to artifi cial light. For instance, in the horse industry, in which an early foaling date is desirable, mares are commonly exposed to artificially increased day length in the winter so as to cause these spring breeders to begin fertile estrous cycles earlier than they would if exposed only to natural light. There is a widely repeated myth among horse trainers that states that visual information from one side of the body is processed strictly on the opposite side of the brain and vice versa.Horse trainers have often cited this «fact» as a rationale for schooling horses from both sides of the body. While it is true that herbivores like horses process a majority of visual information from each half of their visual fi eld in the contralateral visual cortex, there are three reasons why this idea is not neurobiologically sound. One is that not all of the visual information from each eye crosses to the contralateral cortex; some is processed on the ipsilateral (same) side. Secondly, a small portion of the equine visual field is binocular, that is, is seen simultaneously by both eyes. And finally, the caudal part of the corpus callosum (the large bundle of axons connecting right and left cerebral hemispheres) connects the visual cortices of each side so that information is shared between the hemispheres. Trainers must look elsewhere for an explanation of why horses benefit from training on both sides.

Hearing (audition). Features of structure and functions.

The ear can be divided into three main parts: the external, middle, and inner ears. The external ear extends from the exterior as far as the tympanic membrane (eardrum). The middle ear begins at the tympanic membrane; it is an air-filled space within the temporal bone. The inner ear is housed entirely in the temporal bone, forming an elaborate fluid-filled system of chambers and canals.

The environmental energy detected in audition is air pressure waves produced by vibration. These pressure waves can be described in terms of their frequency, the time between peaks of pressure waves, measured in hertz (Hz, cycles per second). Frequency determines the perceived pitch of sounds, with higher frequencies producing sounds of higher pitches. Air pressure waves are also described in terms of

their amplitude, a property that reflects the energy and consequently the loudness of these waves. Amplitude is expressed in decibels (dB), the units by which loudness is measured. The decibel scale is logarithmic, so that the loudest sounds that can be heard without discomfort (around 100 dB) are a million times as energetic as the faintest audible sounds. The cochlear portion of the osseous labyrinth resembles a snail shell (cochlea is Latin for snail). The space on the inside of the cochlea is full of perilymph, and it spirals around a central bony core, the modiolus. The corresponding part of the membranous labyrinth is the cochlear duct, which extends throughoutthe coiled length of the cochlea. The duct is stretched transversely from the modiolus to the outer wall of the bony cochlea, effectively dividing this perilymph-filled space into two: the scala vestibuli above and the scala tympani below the duct. The scala vestibuli originates in the region of the vestibular window, and by this association, the perilymph within it receives pressure waves from the vibration of the auditory ossicles.

At the apex of the cochlea the scala vestibuli is continuous with the scala tympani at a connection called the helicotrema. The scala tympani receives pressure waves from the fluid in the scala vestibuli (but more importantly, through vibrations transmitted through the intervening cochlear duct); these waves are dissipated at the termination of the scala tympani, the cochlear (round) window, which abuts the air-fi lled space of the middle ear. The receptor cells of the auditory system are within the cochlear duct as components of the spiral organ (organ of Corti). The spiral organ contains the receptor cells of the internal ear, mechanoreceptors called hair cells for the bundle of cilia on their apex. The cilia of the hair cells in the spiral organ are embedded in a relatively stiff overlying membrane, the tectorial membrane. The walls between the cochlear duct and the scalae vestibuli and tympani are called the vestibular and basilar membranes, respectively. Cross-sectional views of the cochlea give the impression that the components within are arrayed as repeating separate units, but they are longitudinally continuous throughout the extent of the spiraled cochlea.

The hair cells synapse with peripheral processes of primary afferent neurons whose cell bodies lie within the spiral ganglion. The spiral ganglion is housed in the modiolus, and the axons of the afferent neurons within it gather to form the cochlear nerve. Transduction of the mechanical energy of air pressure waves into the electrical impulses of neurons in the auditory system takes place in the following manner. Air pressure waves captured by the pinna are funneled down to the tympanic membrane, and they put that membrane into vibratory motion. This motion is carried across the airfilled cavity of the middle ear by movements of the auditory ossicles. These ossicles transfer the vibrations to the vestibular window via the foot of the stapes. The perilymph in the osseous labyrinth receives the pressure waves transmitted to it by the vibrations of the vestibular window. These are carried into the cochlea by the scala vestibuli. The vestibular membrane between scala vestibuli and cochlear duct vibrates in response to the pressure waves and transfers those vibrations across the cochlear duct to the basilar membrane and underlying perilymph of the scala

tympani. Movement of the basilar membrane results in movement of the hair cells in the spiral organ that rests upon it, and this produces bending of the hair cells' cilia against the more rigid tectorial membrane. It is the bending of the cilia that results in adepolarization within the hair cells. When this depolarization reaches sufficient intensity, it initiates an action potential in the primary afferents of the spiral ganglion.

The ability to discriminate one pitch from another has its basis in a number of anatomic and electrical features of the spiral organ. Most simply, the basilar membrane varies in width from the base of the cochlear duct, where it is most narrow, to the apex, where it is widest. This difference in width means that each portion of the membrane has a different frequency at which it preferentially vibrates, with the widest part of the membrane vibrating at low frequency and the narrow part at high. The axons of the cochlear nerve enter the brainstem with the vestibular nerve at the junction of the medulla and pons and terminate in cochlear nuclei on the lateral side of the medulla. From this first synapse, multiple pathways produce auditory-mediated refl exes and conscious perception of sound. Auditory information destined for the cortex ascends bilaterally in the medulla, pons, and midbrain. The pathways for conscious perception of sound continue on to the thalamic relay nucleus for audition, and from there fi bers project to the primary auditory cortex on the lateral aspect of the cerebrum. The result of bilaterality of the pathways is that auditory information from both cochleae reaches both left and right auditory cortices.The bilaterality of auditory representations in the brain means that for a brain lesion to produce complete deafness, it must affect both sides of the pathway. Such brain injuries are often incompatible with life; therefore, most deafness is peripheral (associated with the cochlear nerve or internal ear rather than the brain itself). In animals, incomplete loss of hearing is difficult to detect.

Disease processes that affect the ability of the tympanic membrane or auditory ossicles to transmit vibrations to the vestibular window produce conduction deafness. Those that affect the spiral organ or more proximal components of the auditory system (including the cochlear nerves, brainstem, and auditory cortices) produce sensorineural deafness. Most inherited deafness is sensorineural, brought about by degeneration of cochlear hair cells. Congenital deafness has been associated with white hair coats or the merle or piebald color genes in a variety of species, including dogs (most notably the Dalmatian), cats, and horses. In these individuals, lack of pigment-containing cells inside the cochleae appears to be linked to degeneration of cochlear hair cells within a few weeks of birth.

Equilibrium (vestibular sensations). Features of structure and functions. Mechanisms of balance.

The *vestibular system* is a complex neurologic system that is concerned with maintaining a stable orientation in relation to gravity and while in motion. Its influence is widely distributed throughout the nervous system; vestibular input is responsible for the refl exposition of eyes, neck, trunk, and limbs in reference to movement or position of the head. The receptor organs of the vestibular system are housed in the part of the membranous labyrinth known as the vestibular apparatus.

These receptor organs are the maculae of the utriculus and sacculus and the cristae ampullares of the semicircular ducts. Afferent information from these structures gives rise to motor reflexes that maintain stabile visual images on the retinae during movement of the head, to keep the head level with respect to gravity through neck movements, and to produce trunk and limb movements to counteract displacements of the head. The utriculus and the smaller sacculus each posses a macula, a thickened oval plaque of neuroepithelium. The maculae consist of a population of hair cells very like those of the spiral organ. These are covered by a gelatinous sheet, the otolithic membrane, into which project the cilia of the hair cells. The surface of the otolithic membrane is studded with crystals of calcium carbonate, the otoliths, or statoconia, which increase the inertial mass of the otolithic membrane. When the head accelerates in a straight line, the individualsenses linear acceleration. The inertia of the otolithic membrane causes it to lag behind the head under conditions of linear acceleration (including the always present acceleration due to gravity); this dragging of the otolithic membrane bends the cilia of the underlying hair cells with shearing vectors dependent on the direction of acceleration. Attached to the utriculus are three halfcircular extensions of the membranous labyrinth, the semicircular ducts. The ducts lie in three planes at approximately right angles to one another and are designated anterior, posterior, and lateral to describe their orientation. As an extension of the membranous labyrinth, each duct is fi lled with endolymph and surrounded by perilymph. One end of each duct is dilated to form an ampulla, within which are housed the receptor organs of the semicircular ducts. One wall of the ampulla features a transverse ridge of connective tissue, the crista ampullaris, which supports a neuroepithelium of hair cells. Attached to the crista is a gelatinous cupula; this extends across the ampulla, forming a flexible barrier to the fl ow of endolymph. The cilia of the hair cells are embedded in the cupula and are therefore bent by movements of it. The semicircular ducts detect angular acceleration (rotation), and their planes of orientation roughly correspond to the X-, Y-, and Z-axes of three-dimensional space. When the head rotates, the semicircular duct lying in that rotational plane moves with it. The endolymph inside the duct, however, must overcome its inertia at the start of rotation and, as a consequence, briefly lags behind the movement of the head. The flexible cupula, acting as a dam across the ampulla, bulges in response to the endolymph's push, and in doing so, bends the cilia of the embedded hair cells. With three pairs (right and left) of semicircular ducts detecting movement in the three planes of space, complex rotational movements of the head are encoded in the firing patterns of the six cristae ampullares. Primary afferent neurons synapse with the hair cells of the vestibular apparatus. Their cell bodies are in the vestibular ganglion, and their axons constitute the vestibular nerve, which joins the cochlear nerve to become the eighth cranial nerve. Most axons in the vestibular nerve synapse in the large vestibular nuclei of the pons and rostral medulla.

Vestibular reflexes. If there were no mechanism to keep the eyes fixed on a target when the head moved, visual images would continually slip across the retina during head movement, and focusing on the visual field would be difficult or

impossible while the head was moving. The vestibular nuclei use information about acceleration to coordinate extraocular muscle movements with movements of the head and thereby fix the visual image in one place on the retina as long as possible. When the excursion of the moving head carries the fixed image out of visual range, the eyes dart ahead in the direction of movement to fix upon a new image. This new image is held on the retina while the head continues turning until a compensatory jump ahead is again needed. This mechanism results in a cycle of slow movement opposite the direction of turn (eyes fixed on target) followed by a rapid readjustment in the same direction as the turn. This oscillatory reflex eye movement is called nystagmus. Nystagmus is a normal reflex, generated in response to movement of the head. Nystagmus is considered abnormal when it occurs in absence of head movement; this resting (spontaneous) nystagmus is a sign of vestibular disease.

Axons of some neurons in the vestibular nuclei project caudad in a motor tract that influences activity in cervical and upper thoracic spinal cord segments. These motor connections activate neck musculature and forelimb extensors, producing the vestibulocollic reflex, which generates neck movements and forelimb extension to help keep the head level with respect to gravity and movement. Some fibers from the vestibular nuclei form an ipsilateral descending motor tract that extends the length of the spinal cord. This lateral vestibulospinal tract is part of the ventromedial motor system. Its activity has the primary effect of increasing tone in antigravity muscles (proximal limb extensors and axial muscles). This vestibulospinal reflex uses vestibular information to produce limb and trunk movements that counteract the displacement of the head that elicits it. This mechanism is designed to prevent tilting or falling with shifts in head position.

Animals and people with injury to one side of their vestibular system express the vestibular refl exes in the absence of appropriate stimuli. These individuals commonly have resting nystagmus, a head tilt, and a tendency to lean, circle, or fall to one side.

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.
2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.
5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.

7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.
14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

CHAPTER 6. PHYSIOLOGY OF THE ENDOCRINE SYSTEM

General characteristics of the endocrine glands. Classes of hormones. Properties of hormones.

As with the nervous system, the basic functions of the endocrine system are communication and regulation. Along with nervous system it controls and coordinate the body functions and maintains a homeostasis. So both endocrine and nervous systems collectively called neuro endocrine system.

The endocrine system consists of several glands, all in different parts of the body that secrete hormones directly into the blood rather than into a duct system. Hormones have many different functions and modes of action; one hormone may have several effects on different target organs, and, on the other hand, one target organ may be affected by more than one hormone.The classic endocrine system consists of a group of ductless glands that secrete **hormones** (chemical messengers that function in extremely small concentrations). The hormones circulate throughout the body to bring about physiologic responses. However, this classic description does

not account for other types of chemical messengers involved in other types of cell-to cell communication and regulation. For example, normal endothelial cells of blood vessels release prostacyclin, a prostaglandin (discussed later) that acts locally to inhibit the adhesion of blood platelets. This action helps prevent platelets from forming inappropriate blood clots in normal vessels. When prostacyclin diffuses away from its site of production or is washed away by blood flow, it rapidly degrades, so it has no systemic effect. A local effect such as this is termed a paracrine effect. Many types of compounds, including proteins, small peptides, amines (derivatives of amino acids), derivatives of fatty acids, and even a gas (nitric oxide), have been found to function as paracrine agents. The objective of this chapter is to introduce the basic concepts of endocrinology, including the relationships between the nervous and endocrine systems.

Types of hormones on the basis of function:

- ✓ local Hormones, also known as parahormones or tissue hormones. They are secreted at one place and work upon adjacent tissue. They reach by diffusion. *Ex. Acetyl choline;*
- ✓ synergistic hormones, when hormones work together they are known as synergestic hormones. *Ex: FSH and LH, Insulin and gluco corticoids.*
- ✓ antagonistic Hormones, these hormones work against each other. *For example insulin decreases the sugar in the body while glucagon increases.*

The classic hormones can be grouped according to their chemical structure as peptides, steroids,or amines. The amines are biochemical modifications of a single amino acid, tyrosine.The synthesis of steroid hormones begins with cholesterol as a substrate. Cholesterol has carbon atoms arranged in adjoining four rings, and this ring structure is common to all steroid hormones.

Eicosanoid is a general term for compounds that are chemical derivatives of long-chain fatty acids. Prostaglandins, thromboxanes, and leukotrienes are eicosanoids that function as chemical messengers. Arachidonic acid, a component of cell membranes, is the precursor fatty acid in most cases. While these agents are not classic hormones, they are important chemical messengers involved in the regulation of vastly different physiologic functions. In most cases, prostaglandins, thromboxanes, and leukotrienes act as paracrine agents, for they function near their site of origin and are rapidly metabolized after entering the bloodstream. This rapid metabolism in the blood is true for many paracrine agents and is a factor that contributes to their characteristic localized effect.

Prostaglandins have been isolated from nearly every tissue of the animal body, although they derive their name from the prostate gland from which they were originally isolated. There are a number of prostaglandins. Each has a slight difference in chemical structure, and each may have multiple regulatory functions in a variety of tissues. Furthermore, one prostaglandin may have opposite physiologic effects in different organs. In general terms, prostaglandins are implicated in regulation of blood vessel diameter, inflammation, blood clotting, uterine contraction during parturition, and ovulation, among many others.

Leukotrienes are similar in structure to prostaglandins, being produced from arachidonic acid via a different enzymatic pathway. There are several families of related leukotrienes, each with specific functions. Leukotrienes are produced primarily by monocytes and mast cells and are usually associated with allergic reactions. Release of leukotrienes increases vascular permeability and induces constriction of airways; in humans, these substances have been implicated in producing some of the most prolonged manifestations of asthmatic attacks. Because of the prominent role of prostaglandins as mediators of inflammation, drugs that inhibit prostaglandin synthesis are anti-inflammatory. These are the nonsteroidal anti-inflammatory drugs, or NSAIDs, of which aspirin and ibuprofen are widely used overthe-counter varieties. The side effects of these drugs (e.g., gastric ulceration and kidney injury) occur due to the indiscriminate inhibition of both undesirable effects (i.e., inflammation) and important desirable effects (e.g., maintenance of blood flow to stomach and kidneys). Most NSAIDs also inhibit the formation of thromboxanes, because some of the same enzymes are involved in the synthesis pathways for prostaglandins and thromboxanes. Aspirin reduces the synthesis of thromboxanes for blood clotting, and this is part of the rationale for their use in animals and people to reduce the potential for clot formation. Newer NSAIDs have been developed to inhibit only the production of prostaglandins associated with inflammation.

Properties of hormones:

- ✓ they are secreted by endocrine glands;
- ✓ they are known as chemical messengers or information molecules;
- ✓ they have excitory or inhibitory action on target organs;
- ✓ hormones are released in blood (humoral) and reach the target organs through circulatory system;
- ✓ hormones act by binding to specific receptors in the target organ;
- ✓ hormones increase cellular activity and work indirectly by activating the genes;
- ✓ they coordinate physical, mental and development of secondary sexual characters;
- ✓ they maintain homeostasis;
- ✓ chemically they are different in nature;
- ✓ they have low molecular weight and act in very low concentration;
- ✓ they are non antigenic;
- ✓ they are short lived;
- ✓ they are quick in action (adrenalin) while some are very slow (estrogens);
- ✓ they vary widely in their specificity. *For example TSH acts only on thyroid while thyroxine acts on variety of target cells;*
- ✓ they are used up after their action.

Hormones and their receptors. Action mechanism of hormones.

Only certain specific populations of cells respond to an individual hormone. The term target organ is used to identify the tissue whose cells will be affected by a given hormone. Some hormones have multiple target organs, for they affect cells in several sites. For example, both skeletal muscle and liver are among the target organs

for insulin. Cells within target organs are capable of recognizing and responding to a given hormone because they contain specific receptors capable of binding, or forming a chemical union, with the hormone. These cellular receptors may be components of the cell membrane and have a binding site exposed to the extracellular fluid, or they may be contained within the cytoplasm or nucleus of cells.In either case, a receptor for a specific hormone must be present for a cell to respond to the hormone.

The presence and number of receptors within target cells may change in certain conditions. Such changes are one way that the biologic effect of a given hormone can be regulated. For example, levels of estrogen, a reproductive hormone, increase in circulation shortly before birth (parturition), and this stimulates an increase of oxytocin receptors in the smooth muscle of the uterus. The increase in oxytocin receptors prepares the uterus so that oxytocin can promote uterine contractions when released during parturition. Without the increase in oxytocin receptors stimulated by estrogen, oxytocin release itself would not provide adequate uterine contractions for normal parturition. An increase in receptors on target cells is termed up-regulation, and a decrease is termed down-regulation.

Cellular effects of peptide hormones.

The receptors for peptide hormones are found in the cell membrane. Peptides cannot freely diffuse through the lipid bilayer of the cell membrane, so their receptors must be in the outer cell membrane to be available to the hormones in the extracellular fluid. The binding of the hormone with the membrane receptor is the first step in a series of events that brings about changes in the target cell. The subsequent events, which vary with the participating peptide hormones, include changing the permeability of membrane channels, stimulating or inhibiting the activity of membrane-bound enzymes, and stimulating or inhibiting the activity of intracellular enzymes.

When enzymatic activity is increased by a hormone–receptor interaction, the intracellular concentration of the product of the action of that enzyme increases. For example, many peptide hormones activate the enzyme adenylylcyclase, which increases the intracellular production of cyclic AMP (cAMP) by its action on adenosine triphosphate (ATP). The cAMP activates other intracellular enzymes that ultimately bring about the characteristic biologic response to the hormone (e.g., cellular secretion, cellular contraction, protein synthesis).

The term second messenger is a general term for the intracellular compounds, such as cAMP, that function as an intermediate in the sequence of steps leading to the biologic response. Two other common second messengers involved in the cellular response to peptide hormones are diacylglycerol and inositol triphosphate. These second messengers are formed by the action of a membrane-bound enzyme, phospholipase C, on phospholipids in the cell membrane. Ionic calcium (Ca^{2+}) concentration in the cytosol is normally lower than that in typical extracellular fluid, but some cells accumulate even higher concentrations of Ca^{2+} within their endoplasmic reticulum. Increases in cytosolic Ca^{2+} concentrations may result from the entry of extracellular Ca^{2+} through membrane channels or by Ca^{2+} diffusing from

within the endoplasmic reticulum into the cytosol through channels within the membrane of the endoplasmic reticulum. Increases in intracellular free Ca^{2+} above the typical low levels may also act as a second messenger for certain hormones. The increase in Ca2+ begins a series of events that ultimately results in changes in intracellular enzymatic activity and a biologic response.

In many cases the biologic response to peptide hormones is rapid and relatively quickly reversed. For example, the action of antidiuretic hormone on cells in the kidney to change their permeability to water can occur within a matter of minutes. Such rapid effects are possible because pathways leading to the biologic effects may only require activation of enzymes (proteins) that are already in the cell. When the hormone is removed or degraded, the effects are reversed by the inactivation of these enzymes. In some cases, the biologic response to peptide hormones is longer lasting because the intracellular pathways lead to an increase in DNA transcription and the formation of messenger RNA (mRNA). In these cases, the effect is prolonged by the presence of newly synthesized intracellular proteins. The general term for agents that directly influence DNA transcription is transcription factor. So peptide hormones may bring about changes in transcription factors within cells.

Cellular effects of steroid and thyroid hormones.

Receptors that bind steroid and thyroid hormones are found either in the cytosol or in the nucleus. Steroid and thyroid hormones are lipid soluble and can reach these intracellular receptors by diffusing into the cell through the cell membrane. The receptor with its bound hormone acts as a transcription factor for specific genes within the DNA to increase or decrease the formation of mRNA that corresponds to the specific gene. Ultimately, the change in mRNA results in a change in protein production, and this brings about the biologic response. Biologic responses to steroid and thyroid hormones typically develop more slowly but last longer than responses to peptide hormones. In part, this is because all effects are related to changes in protein synthesis. The synthesis of new protein or the degradation of protein already present requires more time than the activation or inactivation of enzymes already present.

Negative and positive feedback regulation.

Assuming that adequate numbers of functioning receptors are available, the biologic effect of any hormone is directly proportional to the concentration of the hormone in the body fluids available to bind to the receptors. This concentration is primarily determined by two factors: the rate of hormone release from endocrine cells and the rate of elimination from the body fluids. In normal conditions, the concentration is typically determined by the rate of release. Peptide hormones and amines are stored in secretory granules by endocrine cells so that they are readily available for release. Steroid hormones are not stored and must be synthesized just prior to release. The release, and thus the plasma concentration, of most hormones is controlled by some type of negative feedback regulation. In this type of regulation, the rising levels of the hormone bring about a biologic response that inhibits further hormone release. For example, β-cells in the pancreatic islets are directly affected by

the concentration of glucose in the body fluids. An increase in glucose concentration causes the β-cells to increase their release of insulin. One effect of insulin is to promote the uptake of glucose by skeletal muscle cells. As glucose is removed from the body fluids, the stimulus for insulin release is removed, and this has a negative effect on insulin release. This negative feedback regulation of insulin release is a major factor in determining a normal plasma concentration of glucose. The negative feedback regulation of insulin by changes in plasma glucose is a relatively simple and straightforward feedback loop. The plasma constituent, glucose, being regulated by the hormone, insulin, has a direct effect on the cells releasing the hormone. However, negative feedback loops can be quite complex and have multiple organs in the loop. Some of the more complex loops involve the hormones regulating reproduction in domestic animals and the hypothalamus, the anterior pituitary gland, and the gonads.

A second type of feedback regulation, that is seen much less frequently than negative feedback, is positive feedback regulation. In this case, the hormone brings about a biologic response that produces a further increase in the release of the hormone. This type of regulation is unusual, and it is not designed to maintain a stable or homeostatic level of some activity or blood constituent. One of the few examples of this type of regulation is the relationship between oxytocin release and dilation of the uterine cervix. An increase in oxytocin release is associated with dilation of the uterine cervix during parturition (details in chapters on reproduction), and oxytocin acts on the smooth muscle of the uterus to increase uterine contractions. When the cervix dilates during parturition and oxytocin is released, the contractions of the uterus move the fetus out of the uterus through the cervix. This further dilates the cervix, providing a greater stimulus for secretion of oxytocin. The overall effect is to expel the fetus when the cervix is dilated.

The hypothalamus and the pituitary gland (hypophysis), connections, functions.

The hypothalamus, containing 32 pairs of nuclei conditionally is divided into 3 parts: anterior, medial, posterior. The hypothalamus is a part of the brain between the pituitary gland and thalamus, that has a vital role in controlling many bodily functions including the release of hormones from the pituitary gland. It plays an important role in hormone production and helps to stimulate many important processes in the body. The hypothalamus acts as the connector between the endocrine and nervous systems to achieve this.

Hypothalamopituitary axis.The hypothalamus works with the pituitary gland, which makes and sends other important hormones around the body. Together, the hypothalamus and pituitary gland control many of the glands that produce hormones of the body, called the endocrine system. The hypothalamus is ventral to the thalamus. The pituitary gland, or hypophysis cerebri, is attached to its base by the infundibulum, a stalk of nervous tissue (primarily axons). Cell bodies of neurons whose axons form the infundibulum are found in the hypothalamus, and their termini abut on the capillaries in the neural part of the pituitary gland (neurohypophysis, posterior pituitary, or pars nervosa). Associated with the infundibulum is a unique

system of arterioles and capillaries called the hypothalamohypophysial portal system. This system is a true vascular portal system in that blood from a capillary network in the hypothalamus flows through portal vessels (similar to veins) to the glandular portion of the pituitary (adenohypophysis, anterior pituitary, or pars distalis), where it enters a second capillary network.

The neurotransmitters of hypothalamic neurons.

The neurotransmitters released by hypothalamic neurons whose termini end in the neurohypophysis enter the blood and are carried to distant sites to function as systemic hormones. These peptides are manufactured by the neuronal cell bodies within the hypothalamus, transported via axons into the neurohypophysis, and released directly into blood vessels when action potentials arrive at the telodendria. Other hypothalamic neurons release neurotransmitters that are carried from the hypothalamus to the adenohypophysis via the hypo thalamohypophysial portal system. There, these neurotransmitters act on endocrine cells either to stimulate or to inhibit the release of other hormones . While these neurotransmitters do not travel to a distant site to stimulate target cells, they are transmitted via the blood from their site of origin to their site of action. Thus, these neurotransmitters may be considered hormones, but they are also referred to as inhibiting or releasing factors. All of these neurotransmitter hormones except dopamine are small peptides, and the small peptides are rapidly degraded after passing through the hypothalamohypophysial portal system and entering the general circulation. The unique portal system permits the delivery of a relatively high concentration of the releasing or inhibiting factors to the adenohypophysis so that a biologic effect is possible.

The different cell types of the adenohypophysis exhibit different histologic staining characteristics, depending on the hormone they produce. As a consequence, cells are characterized as basophils, acidophils, or chromophobes, among other specifi c types. These endocrine cells are arranged in cords or clusters around blood-filled sinusoids, in keeping with their role as an endocrine organ. The neurohypophysis has the typical microscopic appearance of nervous tissue, consisting of unmyelinated axons and supportive glial cells. Historically, the pituitary gland was known as the master gland because of the large number of hormones secreted and their wide-ranging effects. Several hormones from the adenohypophysis stimulate distant endocrine glands to increase production of their own hormones. These stimulatory adenohypophyseal hormones are often called trophic or tropic hormones.

The hypothalamus functions as a crucial interface between the nervous and endocrine systems, where sensory information is integrated and used to regulate the endocrine output of the pituitary gland. Much of this information is related the status of the internal environment in question (e.g., extracellular fluid osmolality, blood glucose concentration, body temperature and metabolic rate). Release of adenohypophyseal hormones can also be regulated through more direct negative feedback loops based on the blood concentrations of the hormones involved. The hormone produced by the target endocrine gland of a specific trophic hormone can act on (1) the hypothalamus to reduce the production of its releasing factors and (2)

the adenohypophysis to reduce its release of the tropic hormone. The tropic hormones of the adeno- hypophysis may also reduce hypothalamic releasing factors via a short negative feedback loop. A synopsis of the hormones released into the general circulation by the hypophysis, the factors that regulate their release, and their general functions is presented here. Further details on these functions will be given in subsequent chapters when the function of their target organs is covered. All of these hormones are peptide or protein hormones based on their chemical structure.

The hypothalamus also directly influences hormones. It commands the pituitary gland to either increase or decrease their presence in the body The neuronal connections between the hypothalamus and the hypophysis constitute a critical point of integration of the two primary communication systems of the body, the nervous and endocrine systems. In the mediobasal shallow cell nuclei and the posterior hypothalamus regions produce substances or factors, which stimulate or inhibit the release of the hypophysial tropic hormones. Correspondingly these parts are named hypophysotropic zones, and the hormones released there releasing factors. Herein the hormone production releasing factors of adenohypophysis are called **liberins**, and the factors, inhibiting the production – **statins**.

Liberins are the followings:

- ✓ thyroliberin, stimulates the thyrotropic (or thyrotropin) hormone production (according to some data the prolactin production too) by adenohypophysis;
- ✓ corticoliberin, stimulates the adrenocorticotropic hormone (ACTH) secretion;
- ✓ gonadoliberin, stimulates the luteinizing and the follicle stimulating hormone secretion;
- ✓ somatoliberin, stimulates the growth (somatotropic) hormone (STH) secretion;
- ✓ prolactoliberin, stimulates the prolactin secretion;
- ✓ melanoliberin, stimulates the melanocytestimulating hormone secretion.

Statins are the followings:

- ✓ somatostatin, inhibits the STH secretion;
- ✓ melanostatin, inhibits the melanocytestimulating hormone secretion;
- ✓ prolactostatin, inhibits the prolactin secretion.

The pituitary gland (hypophysis), its functions.

Hormones secreted from the pituitary gland help control the following body processes:

- ✓ growth;
- ✓ blood pressure;
- ✓ some aspects of pregnancy and childbirth including stimulation of uterine contractions during childbirth breast milk production;
- ✓ sex organ functions in both males and females;
- ✓ thyroid gland function;
- ✓ the conversion of food into energy (metabolism);
- ✓ water and osmolarity regulation in the body;
- ✓ water balance via the control of reabsorption of water by the kidneys;
- ✓ temperature regulation;

- ✓ pain relief;
- ✓ sleeping patterns (pineal gland).

The pituitary gland is about the size of a pea weighing 0.5g and is located at the bottom of the hypothalamus at the base of the brain and rests in a small, bony cavity (sella turcica) of sphenoid bone. It is considered the master gland as it secretes hormones regulating homeostasis. It is composed of three lobes: anterior (adenohypophysis), intermediate, and posterior (neurohypophysis). In many animals, these three lobes are distinct. However, in humans, the intermediate lobe is but a few cell layers thick and indistinct; as a result, it is often considered part of the anterior pituitary.

The intermediate lobe synthesizes and secretes the following important endocrine hormone: melanocyte–stimulating hormone or «intermedins».

Hormones of the adenohypophysis, their physiological effects.

Endocrine cells of the anterior pituitary are controlled by regulatory hormones released by hypothalamus. This vascular relationship constitutes the hypothalamo-hypophyseal portal system.The anterior pituitary synthesizes and secretes **6 hormones**. All releasing hormones (-RH) referred to, can also be referred to as releasing factors (-RF).

Growth hormone (GH) (also called somatotropin or somatotropic hormone). The release of GH, from the adenohypophysis is regulated by hypothalamic factors that either stimulate (GHreleasing hormone) or inhibit (GH release–inhibiting hormone or somatostatin) release. GH levels are highest in young, growing animals, but adult animals continue to secrete it. Increases in GH secretion in adults occur in response to a variety of stimuli, but probably the most important physiologic stimulus is a reduction in plasma glucose. In adults, GH functions as a regulator of metabolism during starvation, defi cits in plasma glucose, or hibernation. It acts to reduce protein breakdown and the use of glucose for energy in skeletal muscle and to increase the mobilization of fatty acids from adipose tissue.

The role of GH is in the determination of body stature in growing animals. As was discussed earlier, GH itself has little direct effect on cartilage proliferation and bone growth in young animals. Its growthpromoting effects are mediated by other peptides, somatomedins (primarily insulin-like growth factors 1 and 2 (IGF-1 and IGF-2), which are released by the liver and cells in the area of growth plates in bone when stimulated by GH. The somatomedins are the direct stimulators of chondrocytes within the growth plates. Somatomedins also have negative feedback effects on the hypothalamus and adenohypophysis to regulate the release of GH. In addition to GH, the secretion of somatomedins by the liver of young growing animals is regulated in part by nutrition. Inadequate nutrition may retard growth in part because of a suppression of somatomedin secretion. Small dogs have lower blood levels of IGF-1 than large dogs, suggesting that within a species body size and IGF-1 levels are correlated. Excessive GH in young animals leads to gigantism *(*occurs due to hyper secretion in childhood, characterized by abnormal increased height and long bones). Increases in body size are not possible in older animals where growth plates

are closed. Excessive GH (with associated IGFs) in mature animals leads to acromegaly (occurs due to hypersecretion, abnormal elongation of limbs and lower jaw, gives gorilla like appearance, protruding bony ridges over the eyes). Further increases in stature are not possible in mature animals, but cartilage proliferation around joints and other skeletal locations produces enlargements in these areas and a characteristic coarseness of facial features. Affected adults also have derangements of carbohydrate and lipid metabolism (increased blood levels of glucose and fatty acids) because of the metabolic effects of excessive GH. Disorders: dwarfism, characterized by retarded growth in children, occurs due to hypo secretion; acromicria, occurs due to hypo secretion in adult, charecterized by smaller hands, feet and face. The amino acid sequence of GH varies among mammalian species, and thus GH produced by one species is not always biologically effective in a different species. Recombinant DNA technology has been used to produce both human recombinant GH and recombinant bovine somatotropin. The human product is used clinically to prevent certain types of human pituitary dwarfism, and the bovine product is used to increase both lactation and food efficiency.

Functions of GH: increased absorption of calcium, lipolysis, protein synthesis, cell division.

Thyrotrophins or thyroid-stimulating hormone (TSH) is released under the influence of hypothalamic thyrotropin-releasing hormone and is inhibited by somatostatin. Effects of TSH: its role is to regulate the production of hormones by the thyroid gland.

Adrenocorticotropic hormone (ACTH). The primary target cells of ACTH are the cells of the adrenal cortex (outer region of the adrenal glands) that produce glucocorticoids. Corticotropins: ACTH and Beta-endorphin are released under the influence of hypothalamic corticotrophin-releasing hormone. Effects of ACTH: its key function is to stimulate the production and release of cortisol from the cortex (outer part) of the adrenal gland.

Lactotrophins. Prolactin (PRL), also known as 'Luteotropic' hormone, whose release is inconsistently stimulated by hypothalamic TRH, oxytocin, vasopressin, vasoactive intestinal peptide, angiotensin II, neuropeptide Y, galanin, substance P, bombesin-like peptides (gastrin-releasing peptide, neuromedin B and C), and neurotensin, and inhibited by hypothalamic dopamine. Effects of PRL: its main physiological functions include the induction and maintenance of milk production, breast enlargement during pregnancy, inhibition of hypothalamic gonadotrophin-releasing hormone, and maintenance of proper ovarian function and of progesterone-secreting structures.

Gonadotropins. Luteinizing hormone (LH) (also referred to as 'Lutropin'), follicle-stimulating hormone (FSH), both released under influence of gonadotropin-releasing hormone. These hormones are released from the anterior pituitary under the influence of the hypothalamus. Hypothalamic hormones are secreted to the anterior lobe by the hypothalamic-hypophysial portal system. Physiologic effects of the gonadotrophins are known only in the ovaries and testes. Together, they regulate

many aspects of gonadal function in both males and females. In both sexes, LH stimulates secretion of sex steroids from the gonads. In the testes, LH binds to receptors on Leydig cells, stimulating synthesis and secretion of testosterone. Theca cells in the ovary respond to LH stimulation by secretion of testosterone, which is converted into estrogen by adjacent granulosa cells. In females, ovulation of mature follicles on the ovary is induced by a large burst of LH secretion known as the preovulatory LH surge. Residual cells within ovulated follicles proliferate to form corpora lutea, which secrete the steroid hormones progesterone and estradiol. Progesterone is necessary for maintenance of pregnancy, and, in most mammals, LH is required for continued development and function of corpora lutea. The name luteinizing hormone derives from this effect of inducing luteinization of ovarian follicles.

As its name implies, FSH stimulates the maturation of ovarian follicles. Administration of FSH to humans and animals induces «superovulation», or development of more than the usual number of mature follicles and hence, an increased number of mature gametes. FSH is also critical for sperm production. It supports the function of Sertoli cells, which in turn support many aspects of sperm cell maturation.

Hormones of the neurohypophysis, their physiological effects.

The posterior pituitary (neurohypophysis) stores and secretes (but does not synthesize) the 2 following important endocrine hormones: oxytocin and antidiuretic hormone, are released by the neurohypophysis.

Oxytocin is produced by the neurons of the paraventricular nucleus of the hypothalamus. When released into the bloodstream by their axon terminals, it induces contraction of target smooth muscle fi bers of the mammary gland and the uterus. As a result of its actions in the mammary gland, oxytocin aids in the phenomenon of milk let-down, wherein suckling stimulates ejection of milk from the duct system of the gland. Physical stimulation of the mammary gland (e.g., suckling) is a strong stimulus to secretion of oxytocin, but it is common for other sorts of stimuli to condition a refl ex release of the hormone. For example, dairy cows frequently learn to associate the milking parlor and the preparations for milking with milk let-down. Even before the mammary gland is handled in any way, oxytocin is released and milk may be seen dripping from the teats. In the pregnant uterus, oxytocin acts on the myometrium (muscle of the uterus) to produce uterine contractions for expulsion of the fetus at parturition. Stretching of the cervix by the fetus stimulates further secretion of oxytocin, which then stimulates greater uterine contractions. Oxytocin is sometimes administered by injection at parturition to enhance uterine contractions.

Effects of oxytocin:

- ✓ contraction of smooth muscles of myometrium of uterus;
- ✓ it induces child labor contractions during delivery;
- ✓ induces milk secretion during sucking. Hence also called as milk ejection hormone.

Antidiuretic hormone (ADH) (vasopressin or arginine vasopressin, the form found in most mammals) is produced by neurons of the supraoptic nucleus in the hypothalamus and released from the neurohypophysis in response to increases in blood osmolality (concentration of dissolved substances) or severe decreases in blood pressure, both of which are infl uenced by the animal's hydration status. The water-retaining effects of ADH on the kidney. ADH also produces constriction of blood vessels, an effect that gives the hormone its other name,.

Effects of ADH:

- ✓ contraction of smooth muscles of arteriole;
- ✓ controls the permeability of wall of collecting tubule and DCT;
- ✓ controls the osmoregulation;
- ✓ controls the blood pressure;
- ✓ deficiency causes diabetes insipidus.

Hormones of the thyroid gland, their physiological effects.

The thyroid gland is associated with the proximal part of the trachea near the thyroid cartilage of the larynx. It is the largest endocrine gland and weighs about 25 gms. It is single lobed in reptile but bilobed in bird and mammals. Both lobes of thyroid are connected by a transeverse tissue called Isthmus. Its appearance varies widely among species, with the thyroid gland of most animals possessing two distinct lobes, variably connected across the midline by a strip of thyroid tissue called the isthmus. In pigs, the bulk of the gland lies primarily on the ventral aspect of the trachea rather than being clearly divided into lateral lobes. A connective tissue capsule covers the gland and gives rise to septa that divide the substance of the thyroid and support the vasculature of the gland. Arterial blood supply to the thyroid and the associated parathyroid glands (discussed later) arrives as branches of the common carotid artery. Histologically it consists of 3 million, small, oval or rounded follicles, spheres lined by a simple epithelium of cells that ranges from cuboidal to columnar. Thyroid follicles are filled with the product of the follicular lining cells, a gel-like substance called colloid, which consists of a protein–iodine complex, thyroglobulin.Each follicle is lined by cuboidal epithelium and surrounded by a gelatinous material called thyroglobulin. In between thyroid follicles parafollicular cells are present. They are scattered in the connective tissue.

The hormones **triiodothyronine (T3)** and **thyroxine (tetraiodothyronine) (T4)** are stored in the colloid as iodinated tyrosine residues that are part of thyroglobulin molecules. This type of storage is a unique among endocrine glands. Scattered among the follicular lining cells and adjacent to them are a small subset of thyroid cells, the C cells (parafollicular cells). The C cells produce calcitonin, a peptide hormone that lowers the blood level of calcium by inhibiting the action of osteoclasts. Calcitonin release is directly regulated by the negative feedback of serum calcium concentration on C cells, not by TSH. The physiologic importance of calcitonin in the overall regulation of serum calcium concentration is minimal compared with the role of parathyroid hormone (discussed later).

Both T4 and T3 are biologically active (bind to thyroid hormone receptors), and most of the circulating hormones are bound to plasma proteins. The T4 and T3 in the body fluids that are not protein bound are the biologically active molecules, but they are also subject to degradation. In many species, the plasma levels of T4 are much higher than those of T3 because the affi nity of T4 for plasma proteins is greater than T3. The intracellular receptors for the thyroid hormones bind both T4 and T3, but they have a higher affi nity for T3. Because of the intracellular receptor affi nity for T3 and the potential for T4 to be converted to T3 after it enters target cells, many consider T3 to be the more biologically important of the two hormones. Secretion of T4 and T3 from the thyroid is a complex series of events that begins with the phagocytosis of thyroglobulin by follicular cells. Endocytotic vesicles containing thyroglobulin then fuse with lysosomes that contain enzymes necessary to degrade the thyroglobulin and release free T4 and T3 from their storage form as part of thyroglobulin molecules. The free T4 and T3 are then secreted into the blood. TSH from the adenohypophysis stimulates follicular cells to synthesis thyroglobulin and to secrete T4 and T3 into the blood. Thus, the overall effect of TSH is to increase blood levels of the thyroid hormones. Plasma levels of thyroid hormones are relatively stable in adult animals; unlike many other hormones, they do not show a signifi cant diurnal rhythm. These stable levels are primarily maintained by negative feedback of T4 and T3 at the level of the pituitary. The thyroid hormones have direct effects on cells in the adenohypophysis to inhibit TSH synthesis and release. Thyrotrophin-releasing hormone from the hypothalamus is always present and acts to promote TSH synthesis and release, but its levels do not respond to feedback regulation by T4 and T3.

Almost all tissues of the body are target tissues for thyroid hormones, for almost all have receptors for them. In mature animals the most general effect of thyroid hormones is to increase overall oxygen consumption and heat production. The basal metabolic rate is a measure of oxygen use in resting conditions, so thyroid hormones are said to increase it. The exact intracellular mechanisms responsible for these general effects are not known, but the effects are known as the calorigenic action of the thyroid hormones. The calorigenic action is associated with an overall increase in the metabolism and use of carbohydrates and lipids, which is consistent with the increased use of oxygen and heat production.

Chronic exposure of some animals to cold is associated with an increase in TSH, T4, and T3. The increased calorigenic effect of the thyroid hormones should work to maintain normal body temperature in the cold environment. The response to the cold appears to be a result of an increase in TRH release by the hypothalamus. The hypothalamus is known to be the refl ex center for other reflexes involved with the regulation of body temperature on a short-term basis (e.g., peripheral vasodilation or vasoconstriction). Thyroid hormones are essential for normal growth and development in young animals. Two systems of special importance are the skeletal and nervous systems.

The target cells for TSH, also called thyrotropin, are endocrine cells of the thyroid that produce and release T4 and T3 when stimulated by TSH. Both are considered amine hormones, for each consists of a linkage of two iodinated tyrosine residues. The 3 and 4 refer to the number of iodine atoms in their molecules. These hormones are necessary for normal growth and development in young animals, and they regulate basal metabolic rate in the adult.

The thyroid produces its own hormones including thyroxine (T4) and triiodothyronine (T3) which regulate the rate of metabolism and affect the growth and functional rate of other systems in the body. T3 and T4 secretions are controlled by the TSRH of hypothalamus and TSH of pituitary gland. The synthesis of thyroxine (T4) in the thyroid gland takes place in the follicular cells and involves a number of steps:

1) The import of iodine into the cell: The import of iodine across the cell membrane takes place by an active transport mechanism (ATP dependent). The thyroid cells are the only cells in the body that will absorb iodine.

2) The iodination of tyrosine: The tyrosine in the thyroid cells is found in thyroglobulin; Tg. Thyroglobulin is a protein which is contained in the lumen of the thyroid cell which includes 140 tyrosines. However only two to five of these tyrosines will be converted to T3 or T4. The iodination occurs using thyroid peroxidase enzymes whilst the tyrosine is still attached to the rest of the thyroglobulin by peptide bonds.

3) The release of the thyroid hormones: TSH stimulates the release of T3 and T4 from thyroglobulin. The ratio of T4 to T3 produced in the thyroid is 4:1. Although all the bodies T4 is produced in the thyroid T3 can be derived from deiodination of T4 in other tissues such as the liver or the kidney, this process releases iodide back in to the body. Once released the thyroid hormones must be transported to the target cells throughout the body. T3 and T4 both have poor solubility in water. Hence most of these hormones are bound to a carrier protein such as thyroxine-binding globulin when being transported in the blood. For the hormones to enter the cells, however, they must be free so they are released ready for target cell uptake.

Bound forms of T3 and T4 remain in the blood. The rate of uptake into cells determines the rate at which T3 is produced from T4 this in turn causes effects such as a change in oxygen consumption and a change in the rate of burning of proteins, carbohydrates and lipids.The disorders associated with the thyroid tend to be either under or over activity.

Hypothyroidism or under activity (animals with thyroid hormone deficits (hypothyroidism) do not attain normal stature and have a variety of central nervous system abnormalities. In humans with severe deficits at birth, mental development remains impaired throughout life, even if replacement therapy is begun when the person is 4 to 5 years of age. It causes following disorders:

- ✓ cretinism: It is a disease of infants. Cretinism is the term for the human condition caused by a congenital lack of thyroid hormone and characterized by arrested physical and mental development and lowered metabolic rate.An

underactive thyroid gland). Charecterized by decreased BMR,stunted growth, retarded mental development, low IQ,delayed puberty,pigeion chest (chest bulging forward in sterna region). It may be due to genetic of lack of iodine in the diet;

- ✓ myxodoema: It is most common in adults (women). Low BMR, low body temperature, reduced heart rate, low sugar etc. are the main characters. Face and hands become swollen due to deposition of albuminous tissue. It can be corrected by thyroxine administration;
- ✓ endemic or Simple Goitre: Occurs due to lack of iodine in the diet. It is non genetic. Characterized by enlargement of thyroid gland. Can be rectified by by adding iodine in the table salt;
- ✓ hashimoto's Disease: Also called as auto immune thyroiditis and occurs due to age factor or injury. When thyroxine level is low antibodies are formed which destroy the thyroid gland.

Hyperthyroidism or Over activity. It is also more common in women than in men and usually occurs in people between twenty and sixty. Hyperthyroidism can make people tired, nervous and irritable and can cause sufferers to have an enlarged thyroid. Patients with disorder will find that despite a large appetite they will lose a lot of weight. A major cause of hyperthyroidism is Graves' disease where antibodies can stimulate the thyroid. Others include an excess of iodine, production of T3 rather than T4, pituitary disorders and cancer of the thyroid. Exophthalmia goiter: Enlarged thyroid gland, increased BMR, increased heart beat and pulse rate, reduced body weight due to rapid oxidation are the major symptoms. Bulging of eyeballs with starring looks and less blinking is peculiar. It can be corrected by removing a part of the gland.

Thyrocalcitonin (TCT) is long peptide and non iodized hormone secreted by parafollicular cells of thyroid gland. It lowers the calcium level in the blood and increases calcium excretion. It is antagonistic to parathormone. It prevents osteoporosis and increases deposition of calcium on bone. So bones become stronger and longer.

Physiology of the parathyroid glands.

These are 4 in number and partially embedded in the dorsal surface of thyroid gland.They are small and yellow colored. The important hormone is a poly peptide **parathyroid hormone** and is regulated by calcium in blood. It is also called as Collip's hormone (After Philips Collip). Its main function is to raise blood calcium level. It is secreted by parathyroid glands, causes bone to release Ca^{2+} in the kidneys. Parathyroid hormone also stimulates the kidneys to activate vitamin D, promoting intestinal uptake of Ca2+ from food. Deficiency causes osteoporosis and bones become week.

Characteristics of the adrenal glands in animals and birds. Hormones of the adrenal medulla of the adrenal gland, their physiological effects.

Adrenal gland (supra renal gland) are paired, yellowish, and star-shaped glands present on the upper surface of the kidneys. It is ecto- mesodermal in origin. The

basic function of this gland is to protect the organism against the acute and chronic stress. This has also been popularized as the fight or flight response for medulla and alarm reaction for cortex. In humans, the right adrenal gland is triangular in shape, whereas the left adrenal gland is semi lunar in shape. The combined weight of the adrenal glands in an adult human ranges from 7 to 10 grams. They are surrounded by an adipose capsule and renal fascia. Each adrenal gland has two distinct structures, the outer adrenal cortex and the inner medulla, both of which produce hormones.

The two adrenal glands are located close to the kidneys (*ad*, toward; *ren*, kidney). Shape, size, and exact location vary from one species to another. Each gland consists of an outer region, the adrenal cortex, and an inner region, the adrenal medulla. These parts of the adrenal gland come from separate embryonic precursors and have distinctly different functions, in spite of their close physical association within a single connective tissue capsule. The blood supply to the adrenal gland varies, but in general, small arteries enter the capsule surrounding the gland. These arteries are derived directly from the aorta or from its branches, including the renal, intercostal, and lumbar arteries. Veins from the adrenal gland drain to the caudal vena cava. Three zones or regions of the adrenal cortex can be identified by light microscopy in most mammals, and each zone is the source of different hormones. From outermost to innermost, the three layers or zones are zona glomerulosa, zona fasciculata, and zona reticularis._All hormones secreted from all three zones are steroid hormones, so cells of all zones have ultrastructural characteristics of steroid-secreting cells.

The adrenal medulla is embedded in the centre of the cortex of each adrenal gland. It is small, making up only about 10 percent of the total adrenal weight.The adrenal medulla is composed of chromaffin cells. These cells migrate to the adrenal medulla from the embryonic neural crest. Indeed, the adrenal medulla is an integral part of the sympathetic nervous system, a major subdivision of the autonomic nervous system. The sympathetic nervous system and the adrenal medulla are collectively known as the sympatho adrenal system. The chromaffin granules produce the hormones of the adrenal medulla, which include **dopamine, nor epinephrine, and epinephrine** (adrenaline and noradrenaline). When stimulated by sympathetic nerve impulses, the chromaffin granules are released from the cells and the hormones enter the circulation by exocytosis.

The hormones secreted by the adrenal medulla (epinephrine and norepinephrine) are amines and are stored in secretory granules prior to release. These endocrine cells are termed chromaffin cells because of their affinity for chromium stains. As was described in the section on the autonomic nervous system, epinephrine and norepinephrine are released from the adrenal medulla in times of stress, and this release is regulated via the autonomic nervous system. A tumor of chromaffin cells is termed a pheochromocytoma, and this neoplasia typically results in excessive secretion of epinephrine and norepinephrine. The resulting clinical signs are those of excessive stimulation of the sympathetic nervous system (e.g., increased heart rate and blood pressure and increased metabolic rate).

Hormones of the adrenal cortex of the adrenal gland, their physiological effects.

The cortex is regulated by ACTH of pituitary hormones.The adrenal cortex is vital to the synthesis of corticosteroid hormones from cholesterol. The source of cortisol and corticosterone synthesis is the hypothalamic-pituitary-adrenal axis. Under normal unstressed conditions, the human adrenal glands produce the equivalent of 35–40 mg of cortisone acetate each day. They also have other functions which include producing androgens (like testosterone) and regulating water and electrolyte concentrations via secretion of aldosterone. The adrenal cortex is regulated by neuroendocrine hormones secreted by the pituitary gland reninangiotensin system, and hypothalamus. The adrenal cortex is meso dermal in origin. It is formed of three distinct regions:

- ✓ zona glomerulosa is the site for production of mineralocorticoids which affect the body's sodium homeostasis;
- ✓ zona fasciculata produces glucocorticoids in humans. Cortisol secretion is simulated by adrenocorticotropic hormone (ACTH) from the anterior pituitary. In the absence of ACTH, zona fasciculata secretes a basal level of cortisol;
- ✓ zona reticularis produces mainly androgens, dehydroepiandrosterone.

The zona glomerulosa secretes **mineralocorticoids** (primarily aldosterone) that function in the regulation of sodium and potassium balance. The regulation of balance is primarily accomplished by controlling the loss of sodium and potassium in urine. Mineralocorticoid secretion is not regulated by ACTH but rather by the serum potassium concentration and the renin–angiotensin system, another group of chemical messengers.

Glucocorticoids are steroid hormones that function in the regulation of metabolism (discussed later). Glucocorticoids (primarily cortisol and corticosterone) are the major secretory product of both the zona fasciculata and zona reticularis, and ACTH is the major regulator (stimulator) of their secretion. Without ACTH the fasciculata and reticularis both atrophy, but the glomerulosa remains intact. The inner zones of the adrenal cortex are also a source of adrenal sex hormones (androgens and estrogens), but the rates of secretion in normal adult animals are very low and not necessary for normal reproductive behavior and function. The secretion of ACTH from the adenohypophysis is stimulated by a hypothalamic hormone, corticotropin-releasing hormone, and this is the most important regulator of ACTH release. However, the regulation of corticotropin-releasing hormone, hence ACTH release, is extremely complex and affected by a wide variety of stimuli. ACTH increases are considered to be a classic sign of stress, and plasma levels of ACTH or cortisol are often used in experimental settings to evaluate the overall stress placed on an animal by any type of physical or emotional stimulus (e.g., restraint, starvation, presence of a predator). Both ACTH and glucocorticoids have negative feedback effects on the pituitary and the hypothalamus to maintain normal resting blood levels of ACTH and glucocorticoids, but stressful stimuli can override these effects.

Glucocorticoids have many target tissues throughout the body. In general their effects on these target tissues would seem an appropriate response to counteract stressful stimuli. For example, glucocorticoids increase the rate of gluconeogenesis (glucose formation) by the liver and increase the rate of fatty acid mobilization from lipid tissue. In skeletal muscle protein synthesis is reduced and protein degradation is increased, which means that more amino acids are available for gluconeogenesis by the liver. These metabolic effects are particularly important during starvation. Glucocorticoids are often used therapeutically to inhibit infl ammatory and immune responses. The doses used for these effects produce blood levels that are much higher than those seen in normal animals, even when they are responding to stress. Such levels and effects are described as supraphysiologic or pharmacologic. Among the many components of the inflammatory process that are inhibited by glucocorticoids are the synthesis pathways for prostaglandins, leukotrienes, and thromboxanes.

The pancreas as endocrine gland, physiological effects of its hormones. Pancreatic islets.

The pancreas of domestic animals is a bilobed gland adjacent to the proximal part of the duodenum (small intestine). The pancreas is an important exocrine gland whose enzymatic secretions are delivered to the lumen of the duodenum by one or two ducts. Scattered throughout the substance of the pancreas are small masses of endocrine tissue called pancreatic islets (formerly the islets of Langerhans). The pancreatic islets are clumps of palestaining cells, arranged in irregular cords separated by capillaries (Fig. 12-10). Special stains are used to demonstrate the types of epithelial cells found in the pancreatic islets. The known number of distinct kinds of cells is still growing, but the two best characterized are the α-*cells* and β-*cells*.

The β-cells are the more numerous (about 75% of all cells in the islet), and they produce the hormone **insulin**. α-Cells produce the hormone **glucagon**. β-Cells are sensitive to increases in blood glucose (sugar), such as occur after a meal containing digestible carbohydrates, and they release insulin in response to such increases in blood glucose. Insulin lowers blood glucose by stimulating the uptake of glucose by many cells of the body, including skeletal muscle. Insulin also stimulates skeletal muscle and liver cells to synthesize glycogen, the storage form of glucose. It affects the metabolism of amino acids and lipids, for it stimulates protein synthesis in skeletal muscle and liver and the deposition of lipids in adipose tissue. Insulin is the major endocrine stimulus for the state of anabolism that exists after a meal is digested and nutrients are absorbed. When blood glucose decreases (such as during fasting), the stimulus for insulin secretion is lost and insulin levels are extremely low.

Glucagon causes liver cells to break down glycogen to release glucose, stimulates adipocytes to release fatty acids, and increases the synthesis of glucose in the liver from substrates other than carbohydrates, such as amino acids. The stimulus for glucagon release is a decrease in blood glucose to levels associated with fasting. α-Cells detect such decreases and respond by secreting glucagon in proportion to the reduction in blood glucose. Insulin is necessary for the uptake of glucose by many cells, including skeletal muscle, which makes up most of the body mass. Without

suffi cient insulin, glucose accumulates in the blood after a meal, for it cannot be transported across cell membranes into cells where it can be used for fuel. The metabolic consequences of insufficient insulin (or of resistance to its effect) create the condition called diabetes mellitus.

There are other endocrine cells in pancreas. The δ-cell accounts for four percent of the islet cells and secretes the peptide hormone **somatostatin**. Recall that somatostatin is also released by the hypothalamus, and the stomach and intestines also secrete it. An inhibiting hormone, pancreatic somatostatin inhibits the release of both glucagon and insulin.

The PP-cell accounts for about one percent of islet cells and secretes the **pancreatic polypeptide hormone**. It is thought to play a role in appetite, as well as in the regulation of pancreatic exocrine and endocrine secretions. Pancreatic polypeptide released following a meal may reduce further food consumption; however, it is also released in response to fasting.

The epiphysis cerebri (pineal gland), physiological effects of its hormones.

The epiphysis cerebri (pineal gland or pineal body) is a midline structure on the dorsocaudal aspect of the diencephalon. In fish, amphibians, and some reptiles, it possesses photoreceptors, and its proximity to the thin calvaria makes it literally a third eye, the function of which is thought to involve setting daily and yearly biologic cycles based on photoperiod. In mammals, including humans and domestic animals, the pineal has no photoreceptors, and its location deep inside the braincase renders it incapable of detecting photoperiods directly. The epiphysis nonetheless does receive information about light and dark cycles indirectly from a nucleus of the hypothalamus. The cells of the epiphysis, although neuronal by lineage, are secretory, and they are supported by neuroglia and receive axonal input. These specialized cells are called pinealocytes. The pinealocytes manufacture serotonin and an enzyme that converts this peptide to **melatonin**, a hormone. Manufacture of melatonin exhibits a profound diurnal rhythm, with releases into the blood peaking during darkness. It is likely, therefore, to be intimately involved in regulating sleep–wake cycles. It appears, too, to be linked to reproduction, inasmuch as the onset of puberty is associated with a profound fall in production of melatonin.

Early discoveries about the link between melatonin and sleep and reproduction have spawned a wave of enthusiastic speculation about its possible use as a cure for insomnia, an aphrodisiac, a treatment for jet lag, and an antiaging drug, among others. To date, however, no controlled studies have supported any of these claims.

The thymus, physiological effects of its hormones.

The thymus gland is a small organ behind the breastbone that plays an important function both in the immune system and endocrine system. Though the thymus begins to atrophy (decay) during puberty, its effect in «training» T lymphocytes to fight infections and even cancer lasts for a lifetime. The thymus gland is very active from before birth until puberty, and it functions as both a lymphatic organ and an endocrine organ (an organ of the endocrine system that produces

hormones). In order to understand the role the thymus gland plays in immunity, it's helpful to first distinguish between T lymphocytes and B lymphocytes.

T cells (also known as T lymphocytes or thymus-derived lymphocytes) mature in the thymus gland and play a central role in cell-mediated immunity, meaning that the cells themselves are active in fighting off foreign invaders such as bacteria, viruses, cancer cells, and more. In contrast, B lymphocytes are part of the humoral immune system and produce antibodies directed at specific invaders.

The thymus produces several polypeptides, which induce lymphocyte differentiation in vitro and in vivo. Several of these polypeptides have been chemically characterized, and three of them have been sequenced and synthesised (alpha 1 thymosin, thymopoietin and the serum thymic factor). The thymus gland produces several hormones including:

- ✓ **thymopoietin and thymulin**, hormones that assist in the process where T cells differentiate into different types;
- ✓ **thymosin** accentuates the immune response as well as stimulating pituitary hormones such as growth hormone;
- ✓ **thymic humoral factor** acts similarly to thymosin, but increases the immune response to viruses in particular.

The thymus gland may produce small amounts of some hormones produced in other areas of the body, such as melatonin and insulin. Cells in the thymus gland (such as epithelial cells) also have receptors through which other hormones can regulate its function. Thymic hormones do not act identically on all T-cell subsets: they alter preferentially post-thymic precursor cells, and among mature T cells cytotoxic cells and suppressor cells. Their mode of action at the cellular level involves binding to specific cellular receptors and interaction with adenyl cyclase. it has been realized that the thymus and its products, the thymus-derived cells (T cells) play a central role in the generation of effector cells in cell-mediated immunity and in the regulation of the various categories of immune responses. It will be the aim of these few pages to review critically the various factors reported in the literature, giving particular emphasis to their pharmacology and their potential use in the modulation of immune responses.

The sex glands (gonads), physiological effects of its hormones.

This section briefly discusses the hormonal role of the gonads – the male testes and female ovaries – which produce the sex cells (sperm and ova) and secrete the gonadal hormones. The roles of the gonadotropins released from the anterior pituitary (FSH and LH) were discussed earlier.

The primary hormone produced by the male testes is **testosterone**, a steroid hormone important in the development of the male reproductive system, the maturation of sperm cells, and the development of male secondary sex characteristics such as a deepened voice, body hair, and increased muscle mass. Interestingly, testosterone is also produced in the female ovaries, but at a much reduced level. In addition, the testes produce the peptide hormone **inhibin**, which inhibits the secretion of FSH from the anterior pituitary gland. FSH stimulates spermatogenesis.

The primary hormones produced by the ovaries are **estrogens**, which include estradiol, estriol, and estrone. Estrogens play an important role in a larger number of physiological processes, including the development of the female reproductive system, regulation of the menstrual cycle, the development of female secondary sex characteristics such as increased adipose tissue and the development of breast tissue, and the maintenance of pregnancy. Another significant ovarian hormone is **progesterone**, which contributes to regulation of the menstrual cycle and is important in preparing the body for pregnancy as well as maintaining pregnancy. In addition, the granulosa cells of the ovarian follicles produce inhibin, which – as in males – inhibits the secretion of FSH.During the initial stages of pregnancy, an organ called the placenta develops within the uterus. The placenta supplies oxygen and nutrients to the fetus, excretes waste products, and produces and secretes estrogens and progesterone. The placenta produces human chorionic gonadotropin as well. It promotes progesterone synthesis and reduces the mother's immune function to protect the fetus from immune rejection. It also secretes human placental lactogen, which plays a role in preparing the breasts for lactation, and relaxin, which is thought to help soften and widen the pubic symphysis in preparation for childbirth.

BIBLIOGRAPHY

1. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
2. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
3. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
4. Mazurkevich AY, Trokoz VO, editors. Physiology of farm animals. Workshop. 2nd ed. Kyiv: Center for Educational Literature; 2015. (Ukrainian).
5. Mazurkevich AY, Trokoz VO, Karpovsky VI, et al. ; edited by A.Y. Mazurkevich, V.O Trokoz. Physiology of agricultural animals. Textbook. 2nd ed. Kyiv; 2014. (Ukrainian).
6. Moyes CD, Schulte PM. Principles of Animal Physiology 3rd ed. Don Mills, Ontario: Pearson; 2016.
7. Papachristodoulou D, Snape A, Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 6th ed. Oxford, UK: Oxford University Press; 2018.
8. Pineda MH, Dooley MP, editors. McDonald's Veterinary Endrocrinology and Reproduction. 5th ed. Ames, Iowa: Iowa State Press; 2003.
9. Pollard TD, Earnshaw WC, Lippincott-Schwartz J, Johnson GT, editors. Cell Biology. 3rd ed. Elsevier. 2016.
10. Reddy PB. Text book of Animal Physiology. Andhra Pradesh, India: IMRF Publications; 2015.
11. Reece WO, Functional Anatomy and Physiology of Domestic Animals. 4th ed. Baltimore: Wiley-Blackwell; 2009.

12. Rhoades RA, Pflanzer RG. Human Physiology. 4th ed. Pacific Grove, Calif.: Brooks/Cole; 2003.
13. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
14. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.
15. Smith BP. Large Animal Internal Medicine. 3rd ed. St. Louis, Missouri: Elsevier Mosby; 2015.
16. Tortora GJ, Derrickson BH. Principles of Anatomy and Physiology. Atlas and Registration Card. 11th ed. Hoboken, NJ: John Wiley & Sons; 2005.

CHAPTER 7. PHYSIOLOGY OF THE BLOOD SYSTEM

The concept of the blood system. The internal environment of the body (blood, interstitial fluid, lymph). The functions of blood.

Higher forms of animals have developed circulating blood, and the fluids derived from it, as a means of maintaining a relatively constant environment for all cells. Blood system consists of four parts: blood proper, hemopoietic organs, organs of blood destruction, and regulatory neurohumoral mechanisms. Blood, lymph and Interstitial fluid compose the internal medium of the organism.

Blood is liquid which consists of cells and a fluid called plasma.

Hematopoiesis is the formation and development of all formed elements of blood (erythrocytes, leukocytes, and platelets), and all of these have a common ancestor, pluripotent stem cells. Hemopoietic organs – the medulla of the bone (bone marrow), spleen, thymus, (Fabricius bursa in birds). Organs of blood destruction – the spleen and liver. Organs of blood keeping (conserving) – the liver, the spleen, capillaries of skin, capillaries of pulmonary circulation.

Lymph is a clear, colorless liquid somewhat similar to blood plasma, from which it is derived, normally taken up by a system of small lymphatic vessels.

Interstitial fluid – fluid outside of cells but not within vessels, is the other subdivision of the extracellular fluid, compartment, similar to blood plasma. Intercellular liquid is serous fluids in the body cavities include peritoneal, pleural, and pericardial fluid. The primary difference between interstitial fluid and plasma is that plasma contains a much higher concentration of proteins that cannot easily diffuse through the walls of capillaries.

Most of the functions of blood are included in the following list:

- ✓ transport (including respiratory) – transport of oxygen from the lungs to cells throughout the body; transport of carbon dioxide from metabolizing cells to the lungs;
- ✓ nutritional – distribution of nutrients absorbed from the digestive tract;
- ✓ excretory – transport of waste products from metabolizing cells to the kidneys for excretion;

- ✓ regulation: humoral regulation – transport of hormones from endocrine glands to target cells; thermoregulation – assistance in body temperature control by transporting heat from deeper structures to the surface of the body;
- ✓ creator connections – assistance in maintaining a constant pH of body fluids by providing chemical buffers Assistance with the prevention of excessive loss of blood from injuries by providing proteins and other factors necessary for blood coagulation;
- ✓ body defense – immune system, assistance with the defense of the body against disease by providing antibodies, cells.

The composition of blood.

Blood consists of the formed elements (40-45%) suspended in a fluid called plasma (55-60%). Blood and plasma have slightly higher specific gravities than water, primarily because of the blood cells and proteins, but the slight difference is usually disregarded when estimating blood or plasma volumes based on body weight.)

The formed elements of the blood include erythrocytes (red blood cells) (4.5-6 mln/mm3), leukocytes (white blood cells) (4000-20000/mm3), and thrombocytes (also called platelets) (200000 - 400000/mm3).

Plasma – fluid portion of the blood, is about 92% water and 8% other substances. The main organic substances are: proteins (albumin – 4%, globulins – 2.8%, fibrinogen – 0.4%), carbohydrates (glucose – 0.08-0.12%), lipids (cholesterine – 0.7%). The inorganic micro- and macro-elements are distinguished: NaCl (0.8%), Ca (9-11 mg%), P (3.00 – 4.00 mg%). There are also some anions: HCO_3^-, HPO_4^{2-}. The microelements are Co, Ni, Cu, Mg, Mn, etc.)

The plasma proteins consist of two major types: albumin and globulins. Albumin is the most prevalent plasma protein and is the predominant protein synthesized by the liver.Many small compounds and electrolytes (e.g., calcium ions) bind to albumin and circulate in plasma in this bound form. This prevents their rapid loss in the urine. Because albumin and other large proteins do not readily pass through capillary walls, they also provide an effective osmotic force to prevent excessive fluid loss from capillaries into the interstitium.

The globulins in serum or plasma may be classified according to their migration (separation) by electrophoresis. α-globulins and β-globulins are classes that are synthesized in the liver. Members of these classes have a variety of functions, including transport in a manner similar to albumin, body defense, and blood clotting. The γ-globulins are synthesized by cells of the immune system. Most of the known circulating antibodies are included in the γ-globulin fraction.The γ-globulin content of the blood therefore increases following vaccination and during recovery from disease. Immune serum or hyperimmune serum can be produced by repeatedly inoculating an animal with a specific antigen.

The significance of plasma proteins is multiform: 1) they are responsible for oncotic pressure, the level of which is important for regulating water exchange between blood and tissue; 2) they maintain the acid-base balance of blood; 3) they ensure a definite viscosity; 4) they prevent sedimentation of erythrocytes; 5) proteins participate in blood coagulation; 6) they provide an immunity; 7) proteins are carriers of a number of hormones, mineral and organic substances; 8) they serve as a reserve

for building up tissue proteins; 9) accomplish intercellular or creative interactions, i.e. transmission of information influencing the genetic cell apparatus and ensuring processes of growth, development, differentiation, and maintenance of the body structure (the nerve growth factor, erythropoietins, etc.).

Serum is plasma minus the plasma proteins responsible for producing the clot. Serum from that animal can then be injected into an animal susceptible to the same disease to provide passive protection for as long as the antibodies remain in the susceptible animal. This provides merely temporary immunity.

The properties of blood.

Blood volume is the total amount of blood in an animal's body, including formed elements and plasma. Typical values given as a percentage of body weight are 7–9%. The total amount of blood in the body of an adult is normally 6 to 8 % of the body weight, i.e. 4.5-6 l.

The composition of blood is relatively constant. The relative constancy of internal medium of the organism is called homeostasis**.** The mechanisms supporting the homeostasis are called homeokinesis.

The main constants of blood are the followings: osmotic pressure (7.6 atm.), oncotic pressure (25-30 mm Hg, which is a 1/200 part of osmotic pressure), temperature (37oC), viscosity (5 in relation to distilled water), typical pH range for blood is 7.35 to 7.45, hematocrit (percentage of the volume of a blood sample occupied by cells, 40-45%).

Osmotic pressure is the pressure by which the molecules of dissolved substance act on the unit surface of the semipermeable membrane, or the force, which provides the entering of dissolvent through semi permeable membrane from the medium with less concentration to the medium with the high concentration. The osmotic pressure is conditioned mainly by inorganic substances (salts).

The oncotic pressure is the part of osmotic pressure. It is conditioned by the plasma proteins (albumin and globulins).

Taking the viscosity of distilled water as unity, the viscosity of whole blood is about 5.0, the viscosity of plasma is 1.7-2.2.

The kidneys are responsible for maintaining constant proportions of water and other constituents of the plasma by the selective filtration and reabsorption of water and other substances from the blood plasma. Osmolality is a measure of the number of osmotically active particles (not the mass of the particles) per unit of solute. The total osmolality of plasma at normal body temperature is about 290 mOsm/kg. The two predominant particles in plasma are sodium and chloride ions, and these contribute the most to the total osmolality of plasma or serum.

A typical pH range for blood is 7.35 to 7.45, just slightly on the alkaline side of neutral. The pH of blood is kept within rather narrow limits by a variety of mechanisms that include contributions by the kidneys and the respiratory system. A shift of the normal pH in man even by 0.1-0.2 may be fatal. (as a value higher than 7.8 or lower than 6.8 can lead to death). During metabolism blood is continuously supplied with carbon dioxide, lactic acidand other metabolites which change the concentration of hydrogen ions. During the life of the organism are formed as acidic and alkaline products of metabolism (that may be produced by cellular metabolism or

absorbed from the gastrointestinal tract) and first formed nearly 20 times greater than the second.

The buffer systems. Regulation of acid-base balance.

The pH of blood plasma and other extracellular fl uids is maintained relatively constant within a narrow range (about 7.35 to 7.45). It is important to maintain this constancy because enzyme activity and metabolic processes require close control of pH for optimal function. Three major mechanisms function together to prevent the development of an abnormal pH. These are:

- ✓ extracellular and intracellular chemical buffers;
- ✓ ventilatory control of plasma carbon dioxide;
- ✓ urinary excretion of bicarbonate or an acid urine as needed.

Extracellular and intracellular buffers.

Acids and bases are produced by normal cellular metabolism and are constantly being added to the ECF. Acids and bases are also added to the ECF by gastrointestinal absorption. Normally, these additions are balanced by the actions of the urinary and respiratory systems so that extracellular fluid pH and the status of body buffer systems, including intracellular proteins, remain stable. However, the ability of these mechanisms to maintain a normal pH can be overwhelmed during metabolic disturbances or after the absorption of large amounts of acids or bases from the gastrointestinal tract. When any acidic or alkaline substance enters the bloodstream, there must be substances which neutralize them. However, blood pH is supported at a constant level owing to the buffer systems.

The most active is **the hemoglobin buffer system** (HHb/KHb) (the oxyhemoglobin and hemoglobin), in order to maintain blood pH, which accounts for 75% of the buffer capacity of blood. Hemoglobin proteins in erythrocytes are a major contributor to the total buffering capacity of whole blood. In the body, there exists another equilibrium between hydronium and oxygen which involves the binding ability of hemoglobin. An increase in hydronium causes this equilibrium to shift towards the oxygen side, thus releasing oxygen from hemoglobin molecules into the surrounding tissues/cells. This system continues during exercise, providing continuous oxygen to working tissues.

Several chemical buffer systems in the plasma also contribute to the control of blood pH.

A chemical buffer system acts to maintain a constant pH by either donating or removing free hydrogen ions in a solution. Quantitatively the most important chemical buffer in blood plasma and other extracellular fluids is **the bicarbonate buffer system** ($H_2CO_3/NaHCO_3$). It consists of carbonic acid (H_2CO_3) and bicarbonate anion (HCO3-) for ex. $NaHCO_3$). The bicarbonate ion is the second most prevalent anion in plasma and is the base in this system. The acid is carbonic acid. In this buffer, hydronium and bicarbonate anion are in equilibrium with carbonic acid. Furthermore, the carbonic acid in the first equilibrium can decompose into CO_2 gas and water, resulting in a second equilibrium system between carbonic acid and water. Because CO_2 is an important component of the blood buffer, its regulation in the body, as well as that of O2 , is extremely important. Note that free hydrogen ions and bicarbonate ions can be excreted in the urine, while carbon dioxide is excreted via the respiratory system. Bicarbonate is the base in this system, and the acid is carbonic

acid. However, because carbonic acid is difficult to measure and in body fluids it is in equilibrium with carbon dioxide, the levels of carbon dioxide are routinely used as indicators of carbonic acid levels. The bicarbonate buffer system is the most important body buffer system from a physiologic standpoint, because the concentrations of the components of the system can be rapidly adjusted by changes in either renal excretion of bicarbonate or pulmonary ventilation to remove carbon dioxide. Bicarbonate is avidly reabsorbed by renal tubules, but a renal threshold value permits rapid excretion of excess bicarbonate. Also, plasma carbon dioxide levels are normally the primary regulator of ventilation, so these levels are also under constant control. Note that free hydrogen ions and bicarbonate ions can be excreted in the urine, while carbon dioxide is excreted via the respiratory system. Because carbon dioxide is a potential acid (it is in equilibrium with carbonic acid) and can be excreted in expired air, it is termed a volatile acid. The respiratory system is responsible for excreting this potential volatile acid produced by cellular metabolism. Other acids in body fluids, such as lactic acid, are not volatile, and the kidneys are responsible for excreting these non-volatile acids. the anion of non-volatile acids (e.g., lactate) may be produced by cellular metabolism or absorbed from the gastrointestinal tract.

The bicarbonate buffer system is the most important body buffer system from a physiologic standpoint, because the concentrations of the components of the system can be rapidly adjusted by changes in either renal excretion of bicarbonate or pulmonary ventilation to remove carbon dioxide.

Both intracellular and extracellular proteins function as buffers; that is, these proteins are capable of accepting excess hydrogen ions or donating free hydrogen ions to assist in the maintenance of a stable pH. Because of the large quantity of intracellular proteins in organs such as skeletal muscle, intracellular proteins account for a large percentage of the total buffering capacity in the body. However, intracellular buffers cannot be as easily regulated as the bicarbonate buffer system in the extracellular fluid, and hydrogen ions from the extracellular fluid must enter cells to be buffered by the intracellular proteins.

The phosphate buffer system (NaH_2PO_4/Na_2HPO_4). Phosphate buffer system is contained in both the blood and cellular fluids of other tissues, particularly in the kidneys. In cells, it is represented by KH_2PO_4 and K_2HPO_4. In blood plasma, and intercellular space it is represented by NaH_2PO_4 and Na_2HPO_4.

Proteins buffer system. Plasma proteins play the role of a buffer system due to their amphoteric properties, because it is composed of COOH and NH_2 groups of aminoacids.

The constancy of the acid-base equilibrium, as it is known, is one of the basic conditions of normal activity of organism. From pH depends on the stability of membranes, enzymes, dissociation of electrolytes, neuromuscular excitability and conductivity, complexation, etc. processes. **Acid-base system** represents the ratio between the concentration of the active masses of hydrogen and hydroxyl ions (major). It is characterized by using a Ph-negative decimal logarithm of the hydrogen ion concentration. Shift the pH ± 0.1 compared to physiological norm leads to respiratory and circulatory disorders, at ± 0.3, loss of consciousness, and in the range of ± 0.4- the death of the body. During the life of the organism are formed as acidic and alkaline products of metabolism, and first formed nearly 20 times greater than the

second. Therefore, mechanisms to ensure the maintenance of the constancy of the acidbasic body systems are aimed at neutralizing and removing, especially acidic products of metabolism.

There are 2 variants of acid-base balance:

- ✓ acidosis – a typical pathological process characterized by an absolute or a relative increase in the body burden of acid and alkaline substances. Gas acidosis occurs when increasing the pCO_2 in arterial blood (for example, with alveolar hypoventilation), non-gaseous acidosis-during the accumulation in the body acidic foods woven metabolism (e.g., diabetes mellitus). Ruminal or lactic acidosis is seen in ruminants that ingest large amounts of carbohydrates, usually grain, over a short period. The sudden ingestion of the concentrated carbohydrates alters the microbial population in the rumen, favoring the rapid growth of organisms that produce lactic acid. The rapid increase in lactic acid absorption into the blood overwhelms the ability of the pH regulatory systems, and systemic acidosis develops.
- ✓ alkalosis is a typical pathological process characterized by an absolute or a relative increase of alkaline in the body or lower acidic substances. Gas alkalosis develops excessive allocation of carbon dioxide (e.g. altitude sickness), non-gas alkalosis, excessive flow of alkaline or acidic substances allocation (for example, uncontrollable vomiting).

Mechanisms of regulation of the acid-basic body systems are very efficient and are able to compensate for the significant changes in pH. Maintaining the acid-basic body systems is ensured by buffer systems, blood and tissue and the physiological mechanisms of compensation: the lungs, kidneys, liver, blood, bone, and skin. Therefore, study of acid-base equilibria, and buffer systems is relevant. In acidosis or acidemia the blood pH is abnormally low, and in alkalosis or alkalemia the pH is abnormally high.

Formed elements of blood: erythrocytes. Forms of hemoglobin.

Erythrocytes or red blood cells (RBC) range from about 5 to 7 μm in diameter. They are biconcave disks with a thickcircular margin and a thin center The biconcave shape provides a relatively large surface area for gas exchange across the cell membrane. Erythrocytes have no nuclei and few organelles. Immature forms in the bone marrow do have nuclei, but these are lost during the latter stages of development. In birds and reptiles, nuclei normally persist in the red cells throughout the life of the cells.

Erythrocytes of humans and mammals perform the following functions: 1) gas transport; 2) they are ideal carriers realizing intercellular or creator connections; 3) formation of blood groups and Rh-factor due to localisation of agglutinogenes on the erythrocyte membrane.

Total erythrocyte counts are expressed as number of cells per microliter of whole blood, and most domestic animals have about 5,0 – 12,7 million per microliter. Cows – 5,0–7,5, horses – 6–9, pigs –6-7,5, sheep – 7,0–12,0, rabbits 5-7,5 birds – 2,5–4,5 (Table 5). Typically, erythrocytes circulate for only 3 to 4 months after their release from the bone marrow.

The protein hemoglobin is the major intracellular constituent of erythrocytes. Hemoglobin is a complex molecule containing fouramino acid chains (globin

portion) held together by noncovalent interactions. Each amino acid chain contains a heme group (red porphyrin pigment), and each heme group contains an atom of iron. Hemoglobin concentration is measured in grams per 100 mL of blood, and typical values for normal hemoglobin concentrations range from about 11 to 13 g/100 mL in domestic mammals. Hemoglobin functions in the transport of both oxygen and carbon dioxide.

Forms of hemoglobin. Oxygen binds to the ferrous iron in the heme group to form **oxyhemoglobin** (HbO_2); this process is termed oxygenation (not oxidation). The amount of oxygen that can be bound is proportional to the amount of iron present, with one molecule of oxygen combining with each atom of iron. Because of the binding to hemoglobin, blood can contain about 60 times as much oxygen as would be dissolved in a similar quantity of water in the same conditions.

Carbon dioxide also binds to hemoglobin at a different site on the molecule. Carbon dioxide binds to α-amino groups of peptide chains to form **carbaminohemoglobin ($HbCO_2$).** Binding of oxygen and carbon dioxide to hemoglobin is readily reversible. Blood arriving at the lungs from the peripheral circulation contains carbaminohemoglobin and is exposed to air with a relatively high concentration of oxygen and a relatively low concentration of carbon dioxide. In the lungs, carbon dioxide dissociates from carbaminohemoglobin, resulting in the formation of hemoglobin, which can bind oxygen to become oxyhemoglobin. When the blood containing oxyhemoglobin returns to the peripheral tissues that are relatively deficient in oxygen, the bound oxygen is released to the tissues. Carbon dioxide can then bind to hemoglobin to continue the cycle.

Methemoglobin is a true oxidation product of hemoglobin that is unable to transport oxygen because the iron is in the ferric (Fe^{3+}) rather than the ferrous (Fe^{2+}) state. Certain chemicals, such as nitrites and chlorates, produce methemoglobinemia (methemoglobin in the blood). Nitrate poisoning has been reported in cattle grazing on highly fertilized plant growth. In these cases, nitrates in the plants are converted to nitrites in the rumen and cause the formation of methemoglobin when absorbed into the blood.

Carboxyhemoglobin (HbCO) is a more stable compound formed when carbon monoxide combines with hemoglobin. The affinity of hemoglobin for carbon monoxide is 210 times that of its affinity for O_2. The carboxyhemoglobin is unable to carry oxygen, and the animal essentially suffocates, although the blood is typically cherry red. This causes hypoxia, intoxication and is dangerous for life.

Myoglobin. Mioglobin is present in muscles and myocardium. Its hem is identical to blood hemoglobin hem, but globin has a lower molecular mass. Myoglobin binds up to 14% of the total oxygen, which is important for the supply of oxygen to the working muscles. When the blood capillaries are compressed in contracted muscles, blood flow either decreases or ceases. However, owing to the presence of oxygen combined with myoglobin oxygen to the muscles is maintained for some time.

Erythrocyte formation, called erythropoiesis, is regulated by the hormone erythropoietin,

Formed elements of blood: leukocytes. Functions of different types of leukocytes. Differential white blood cell counts.

Leukocytes or white blood cells (WBC) (from the Greek word «leuco», white) differ considerably from erythrocytes in that they are nucleated and are capable of independent movement to exit blood vessels. Leukocytes may be classified as either granulocytes or agranulocytes based on the presence or absence of cytoplasmic granules that stain with common blood stains, such as Wright's stain. These stains contain an acid dye, eosin, which is red, and a basic dye, methylene blue, which is bluish. Granulocytes are named according to the color of the stained granules (i.e., neutrophils, which have granules that stain indifferently; eosinophils; and basophils). The nuclei of granulocytes appear in many shapes and forms, leading to the name polymorphonuclear leukocytes. However, the term is commonly used to indicate neutrophils, because they are normally the most prevalent granulocyte. Monocytes and lymphocytes are the two types of agranulocytes.

Neutrophils, a first line of defense against infection, constitute a large percentage of the total leukocyte number (Table 5). Upon tissue injury or microbial invasion, neutrophils rapidly accumulate within the interstitial fluids of the injured or invaded area. The active movement of neutrophils and other leukocytes out of intact blood vessels and into the interstitial fluid is diapedesis. Chemical messengers known as chemotactic factors attract neutrophils to these sites. Chemotactic factor is a general term for a variety of compounds that are capable of attracting neutrophils and in some cases other leukocytes. These factors may be produced by invading microorganisms, by leukocytes after interacting with microorganisms, or by damaged tissue.

Neutrophils are phagocytes; they engulf invading bacteria to destroy them. The destruction involves the action of enzymes in the intracellular granules of the neutrophils and cell membrane–bound enzymes that are activated when phagocytic vesicles are completely formed. During phagocytosis, neutrophils may also release enzymes that contribute to the local inflammation. In the process of responding to the potential infection, many of the attracted neutrophils are destroyed. Pus, the semiliquid material that results from the collective responses to a microbial invasion, may contain neutrophils and cellular debris.

Neutrophilia is an increase in the number of circulating neutrophils in the blood that occurs with bacterial infections. Circulating neutrophils can increase as a result of an immediate release of existing neutrophils from the bone marrow and an increase in neutrophil production. Neutropenia refers to an abnormally low number of circulating neutrophils. The word endings -philia and -penia can be combined with the root names of the other leukocytes to indicate similar conditions (e.g., eosinophilia is an increase in eosinophils).

Eosinophils contain red-staining cytoplasmic granules. Normally, eosinophils are less than 10% of total leukocytes, but they may increase in number with allergic conditions and parasitism. Eosinophils are ameboid and somewhat phagocytic. Their primary function seems to be the regulation of allergic responses and tissue responses to parasites. They act by removing antigen–antibody complexes, which stimulate allergic responses, and by inhibiting some of the mediators of allergic responses, such as histamine.

Basophils contain blue-staining granules and are rarely seen in normal blood. The granules of basophils contain multiple compounds, including heparin, which prevents blood clotting, and histamine, which relaxes smooth muscle of blood vessels and constricts smooth muscle in airways. Cells that are very similar but distinct, mast cells, are found in many sites throughout the body but are especially prevalent in connective tissue below an epithelial lining exposed to the external environment (e.g., dermis, wall of airways, and wall of gastrointestinal tract). Basophils and mast cells release the contents of their granules during allergic responses, and these chemicals contribute to the characteristic tissue responses. The release of the granules is mediated in part by the binding of specifi c antibodies and the associated allergen (antigen).

Monocytes are the largest of the circulating leukocytes. They are phagocytic and develop into even larger macrophages when they exit vessels and enter the tissues. Like neutrophils, monocytes are attracted by chemotactic factors to areas of tissue injury and microbial invasion. In addition to phagocytosis of tissue debris and microbes, macrophages have a major role in the overall initiation and regulation of infl ammatory and immune responses. During their response to tissue injury or microbial invasion, macrophages release numerous chemical messengers that coordinate the function of other cells responding to injury or invasion.

Lymphocytes. In most species, lymphocytes are the second most prevalent circulating leukocyte after neutrophils, but they are more prevalent than neutrophils in ruminants. In blood smears, lymphocytes vary in size, with a relatively large nucleus surrounded by a small amount of cytoplasm. Lymphocytes are the essential leukocytes that develop a specific immune response and immune surveillance. Based on their functions, three general types or groups of lymphocytes have been identified:

- ✓ B-lymphocytes=bursa-dependent, are the lymphocyte subtype associated with the production of antibodies or the humoral component of a specific immune response;
- ✓ T-lymphocytes=thymus-dependent, T cells have various subtypes, each with its specific functions: include T-helper, T-killer, T-supressor, memory T cells;
- ✓ NK, or natural killer cells, but these types cannot be identified by differences in appearance.

Necessary steps in the initiation of specific immune response in the processing of antigens include cooperation of B-lymphocytes, T-lymphocytes, macrophages, cytokines (as the chemical messengers (proteins). B-lymphocytes functions in this response include (1) antigen recognition, (2) antibody production, (3) cytotoxic attack on infected cells, (4) immunologic memory, and (5) regulation of the specific immune response. An individual lymphocyte does not perform all of these functions, but rather subpopulations or subtypes of lymphocytes are responsible for different aspects of the specific immune response.

The first step in the humoral response is recognition of a foreign antigen by B cells. The development of B memory cells and plasma cells and the secretion of antibodies are modulated by numerous cytokines. Cytokines, as the chemical messengers (proteins) secreted by a variety of cells in response to injury or microbial invasion, modulate the activity of cells of the immune system.

Immunoglobulin (Ig) is a general term for a protein that can bind to an antigen; it includes both antibodies (circulating immunoglobulins) and those found in the cell membranes of B cells. Immunoglobulins fall into five major classes, Ig G is the predominant circulating immunoglobulin. IgE is the class of immunoglobulins associated with most allergic responses.

Differential white blood cell counts indicate the percentage of each type of white cell in the blood sample (Table 5). The various types of leukocytes have different functions and respond differently to various types of infections or diseases, so differential counts can be useful for diagnosis. Differential counts taken over time can also be used to evaluate the response of an animal to infection or disease.

Formed elements of blood: blood platelets (thrombocytes).

Blood platelets, also called thrombocytes, are fragments of megakaryocytes, large cells formed and residing in the bone marrow. Thrombocytes are the smallest of the formed elements in the blood at 2–4 mkm. They are surrounded by a plasma membrane and contain some organelles, but not nuclei. Thrombocytes range from 150,000 to 500,000 per microliter of blood in most mammalian species. Platelets reduce loss of blood from injured vessels. By adhering to vessel walls and to each other in the area of the injury, platelets may form a plug upon which a thrombus (clot) forms to occlude the opening in the vessel and prevent further blood loss. Substances released by platelets and lodged on their surface membranes stimulate clotting and help cause local constriction of the injured blood vessel.

Table 5. Representative values for blood cell and platelet numbers per microliter of blood in selected domestic animals

Blood Element	*Horse*	*Cow*	*Dog*	*Chicken*
Erythrocytes	8–11[a]	6–8[a]	6–8[a]	2.5–3[a]
Total leukocytes	8–11[b]	7–10[b]	9–12.5[b]	20–30[b]
Neutrophils	4–7[b]	2–3.5[b]	6–8.5[b]	5–10[b]
Lymphocytes	2.5–4[b]	4.5–6.5[b]	2–3.5[b]	11–18[b]
Monocytes	400–500	350–500	450–600	2–3[b]
Eosinophils	200–500	150–500	200–500	600–2,000
Basophils	<100	<100	<100	200–900
Platelets	150–450[b]	300–500[b]	300–500[b]	25–40[b]

[a]Millions
[b]Thousands

Hemostasis and coagulation.

Hemostasis, the stoppage of bleeding, may involve three basic reactions:

- ✓ constriction by the smooth muscle of the injured vessel to reduce the opening;
- ✓ formation of a platelet plug (clot or thrombus) to occlude the opening;
- ✓ clot (or thrombus) formation to complete occlusion of the opening.

Platelets and the endothelium. When a vessel is injured and the endothelial cell lining is damaged so that the underlying connective tissue is exposed, platelets adhere to collagen and other proteins in the connective tissue. This platelet adhesion results from binding between platelet cell membrane proteins and the connective tissue. The cell membrane of adhered platelets undergoes alterations, and secretory granules are also released. Platelets that have undergone these reactions are termed activated platelets. The presence of activated platelets stimulates other platelets to adhere to those already present. The collection of platelets forms a platelet plug that may be sufficient (together with local vasoconstriction) to occlude extremely small openings in damaged vessels and bring about hemostasis. Platelet aggregation is the term

applied to the overall sequence of events responsible for the formation of the platelet plug. Platelet aggregation is also subject to regulation by two different eicosanoids, thromboxane A2 and prostacyclin. Thromboxane A2 is a stimulant of platelet aggregation, and prostacyclin inhibits platelet aggregation. Thromboxane A2 and serotonin (also released by adhered platelets) are both vasoconstrictors, stimulating smooth muscle contraction to assist with hemostasis. Aspirin inhibits the formation of eicosanoids. However, platelets do not have nuclei and cannot synthesize new enzymes, while nucleated endothelial cells can synthesize additional cyclooxygenase. Thus, with larger sites of injury, more platelets aggregate and more stimulants of clotting are present in the local area.

Coagulation – the formation of a clot. Injuries to vessels do not require the coagulation if hemostasis can be achieved by the first two reactions. Coagulation is initiated when the local concentration of these substances reaches some critical level. Platelets are required for normal coagulation in response to vascular damage. There are intrinsic and extrinsic coagulation.

The ultimate product of blood coagulation is a relatively solid gel plug (clot or thrombus). This plug may be red or somewhat clear. The color varies with the number of erythrocytes and other blood cells trapped in the clot. Erythrocytes and leukocytes are not necessary for coagulation, and they may or may not be present in a clot. A clot is relatively solid because of interlacing strands of fibrin (a protein polymer) that are covalently cross-linked. Thus, the most basic explanation of coagulation is that it is a series of biochemical reactions to produce and stabilize a protein polymer, fibrin.

The series or chain of biochemical reactions that links initial exposure to collagen or a surface other than normal endothelium (e.g.,glass surface of a blood draw tube) to a stabilized fibrin network is the intrinsic clotting pathway, or intrinsic cascade. It is intrinsic because all substances necessary for the cascade are present in the circulation (Table 6). This pathway includes several proteolytic enzymes (clotting factors) normally in the plasma in an inactive form. When one of these inactive forms converts to an active form, it activates the next enzyme in the cascade.

The first step in the intrinsic cascade is the activation of factor XII. This could occur when a vessel is damaged and the underlying tissue is exposed or when blood is drawn into an untreated glass tube. Coagulation can also be initiated when a protein from interstitial fluid (tissue factor or tissue thromboplastin) forms an active complex with an inactive plasma protein, factor VII. Tissue thromboplastin is a component of cell membranes of various cell types and apparently may be released from injured cells.The factor VII–tissue factor complex activates factors X and IX. Factor X is a component of the intrinsic cascade, so from this point on, the pathway to fibrin formation and linkage is the same as in the intrinsic cascade.

Table 6. International nomenclature of coagulation factors with synonyms.

I	Fibrinogen
II	Prothrombin
III	Tissue thromboplastin
IV	Calcium
V	Proaccelerin; labile factor
VII	Proconvertin; stable factor

VIII	Antihemophilic globulin; antihemophilic factor A
IX	Christmas factor; antihemophilic factor B
X	Stuart-Power factor
XI	Plasma thromboplastin antecedent; antihemophilic factor C
XII	Hageman factor
XIII	Fibrin stabilizing factor

The cascade that is initiated by tissue thromboplastin is the extrinsic cascade, or extrinsic pathway. The final product of both the extrinsic and intrinsic cascades is a fibrin clot. Clot formation at the site of injury reduces blood loss and occludes the opening in the damaged vessel.

In many cases, the damage to small vessels can be repaired so that normal blood flow can again occur. These repair mechanisms include removal of the clot and proliferation of endothelial cells to reestablish normal vascular lining. A key element in clot removal is the activation of the fibrinolytic system. This system is similar to the clotting cascade in that an inactive plasma protein or proenzyme, plasminogen, is activated to plasmin, which converts fibrin to soluble fragments. There appear to be several different pathways by which plasminogen can be activated to plasmin, but these are not as well understood as the activation of clotting factors. However, the presence of fibrin may stimulate several of these pathways. It seems that as fibrin is generated, it also begins to initiate its own ultimate destruction. Plasminogen is also activated by tissue plasminogen activator, an enzyme secreted by normal, intact endothelial cells.

Calcium ions are required as cofactors at various steps in both cascades, and several anticoagulants used to prevent blood clotting outside the body do so by binding calcium ions. Two additional plasma proteins, protein C and antithrombin III, prevent coagulation from continuing inappropriately. Protein C circulates in an inactive form that is activated by thrombin. Thrombin forms as part of both the intrinsic and extrinsic pathways and is also responsible for one of the final steps in both, the production of fibrin from fibrinogen. Antithrombin III is also inactive by itself, but when bound to heparin (present on normal endothelial cell membranes), the heparin–antithrombin III combination inactivates thrombin.

The majority of the plasma factors for both the coagulation and fibrinolytic cascades are synthesized in the liver, and this synthesis is vitamin K dependent. (*Dicumarol is a toxic form of a general class of compounds known as coumarins. Dicumarol, found in spoiled sweet clover hay or silage, inhibits the clotting of blood. Warfarin is another coumarin and vitamin K antagonist that is used commercially in rodent poisons.)*

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.
2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.

5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.
7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.
14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

CHAPTER 8. PHYSIOLOGY OF CARDIOVASCULAR SYSTEM

The functions of cardiovascular system. Evolution of cardiovascular system.

The cardiovascular system consists of the heart and the many vessels through which blood flows. The functions of cardiovascular system:

- ✓ transport of oxygen, nutrients, hormones to organs and tissues;
- ✓ transport of carbon dioxide and metabolic products to the organs of excretion;
- ✓ thermoregulation.

Evolution of cardiovascular system

Jellyfish has open circulatory system, where the blood (called hydrolymph) is present.

In arthropods (e.g., insects and crustaceans) and non-cephalopod mollusks (e.g., clams, snails and slugs) is open circulatory system, where the blood (called hemolymph) empties from a contractile heart and major supply vessels into the body cavity (termed a hemocoel), where it directly bathes the organs. Hemolymph returns to the heart either through ostia in the ventricle (arthropods) or via the atrium (mollusks).

In insects, the open circulation is not responsible for delivering oxygen. Oxygen delivery is carried out by an elaborate, highly branched tracheal system (like a heart), which facilitates diffusion to each and every cell of the body.

Closed circulatory systems occur in a wide variety of invertebrates including annelids, cephalopods (e.g., octopus and squid) and non-vertebrate chordates, as well as in vertebrates. In closed systems, the blood remains inside distinct channels or chambers, where it is physically separated from the intercellular fluid, body cells and coelom. In other cases (e.g., in cephalopods), chambered hearts have evolved to promote fluid movement.

In vertebrates, the closed vascular system consists of a series of closed vessels Most vertebrates have a lymphatic system, which collects and recycles interstitial fluid back to the circulation.

Fish have a single circulatory system, consisting of an undivided heart with a single atrium and single ventricle in series with oxygen-exchanging gills.

In amphibians and reptiles the heart is not completely divided.

Birds and mammals have a double circulatory system in which the heart is completely divided into right and left sides, resulting in separation of deoxygenated and oxygenated blood.

The structure of the heart. The function of the blood circulation: pulmonary and systemic circulations.

The heart is a cone-shaped hollow muscular structure surrounded by a serous membrane called the pericardium. The heart wall consists of three layers: an outer serous covering called epicardium, an inner endothelial lining called endocardium, and athick muscular layer called myocardium.

Whether or not the blood is oxygenated, vessels that carry blood away from the heart are called arteries, and vessels that carry blood toward the heart are called veins.

The heart is divided into right and left sides. Each side has two chambers: an atrium, which receives blood by way of large veins, and a ventricle, which pumps blood from the heart through a large artery. The myocardium between the two chambers is the ventricular septum. There are 4 valves in the heart. Between the atrium and the ventricle of each side is an atrioventricular valve, or A-V valve. The left atrioventricular valve A-V valve is occasionally called the bicuspid because in humans it has two distinct flaps, or cusps. Another more commonly used synonym is mitral valve.

The right atrioventricular valve called the tricuspid valve because in humans it has three flaps or cusps. These 2 valves ensures blood flows only from the atrium into the ventricle and not in the opposite direction. There are 2 the semilunar valves – the aortic valve lies at the junction of the left ventricle and aorta; the pulmonary valve is at the junction of the right ventricle and pulmonary trunk. They ensures blood flows only from the ventricle into the artery and not in the opposite direction.

There are 2 blood circulations – pulmonary (circulation to the lungs) and systemic (circulation to the rest of the body). Functionally pulmonary circulation is separate from systemic circulation. Conceptually, it is therefore useful to regard the heart as two separate pumps housed within the same organ; one is a low-pressure pump that directs blood returning from the body to the lungs (i.e., the pulmonary

circulation), and the other is a high-pressure pump that distributes blood to the systemic circulation.

The function of the pulmonary circulation refers to the movement of deoxygenated blood to the lungs and the return of oxygenated blood to the heart.It begins from the right ventricle where pulmonary trunk divides into right and left pulmonary arteries, carrying deoxygenated blood to the respective lungs. In the arterioles of the lungs gaseous exchange takes place. Oxygenated blood returns from the lungs to the left side of the heart, to left atrium by right and left pulmonary veins. In the adult the pulmonary circulation is the only place where deoxygenated blood is found in arteries (which, by definition, carry blood away from the heart) and oxygenated blood is found in veins (returning blood to the heart).

The function of the systemic circulation refers to the movement of oxygenated blood to all areas of the body and the return of deoxygenated blood to the heart.It begins from the left ventricle where blood past the aortic valve into the aorta. The deoxygenated blood returns from the systemic circulation in the right side of the heart to the right atrium where the cranial and caudal venae cavae are situated.

The loop design means that all components of the system must function together in a highly coordinated and integrated fashion to maintain blood flow throughout the system. If the right side of the heart cannot pump an adequate amount of blood into the pulmonary circulation, the left side of the heart will not receive enough blood to maintain flow into the systemic circulation.

The functional peculiarities of the heart muscle (myocardium).

Definitely, the vital peculiarity of myocardium is to be in **refractory period.** It means that under normal conditions during the period of hearts systole neither irritants nor any other factors can cause additive contraction. Also, the refractory period in cardiac muscle lasts as long as the systole goes. There is one more inetesting thing concerned refractory period. It devides into absolute and relative period. During the absolute period nothing is occurred. During the relative period different irritants can influence the myocardium and additive systole takes place called extrasystole.

Contraction. It means the capacity to contract. It is caused by the peculiarities of the myocardium structure. The contraction time in cardiac muscle lasts as long as the action potential does. Cardiac muscle has many anatomic characteristics that are similar to those of skeletal muscle fibers. The most striking difference is the tendency for cardiac muscle fibers to branch and join, forming a network. The heart is made up of cells that are separate entities; however, unique structures, found where cardiac muscle cells meet end to end, are the intercalated disks. These disks can be seen with the light microscope and are interposed between muscle cells. The disks represent apposed cell membranes and gap junctions. The gap junctions provide a mechanical attachment between cells and permit mechanical transmission from one cardiac muscle cell to the next.

Excitation It means that the heart muscle can excitate under the conditions of influence of different irritants such as electrical, chemical, thermal, biological. The excitation process is based on the formation of a negative electrical potential in the excitable area of the heart, and is accompanied by an enhanced metabolism. *For example, human medicine is used to apply electric current for somebodys rebirth*

from clinical death. Moreover the calcium Ca2+ binds to regulatory proteins on the actin filaments of myocardium, and contraction occurs. It means that an increase in intracellular Ca^{2+} must occur to bring about cardiac cell contraction. So major drugs used to treat cardiosystem are based on calcium. Some hormones such as adrenaline causes the heart excitation and increases its contraction becouse it causes enhanced metabolism in myocardium such as influence of sympathetic autonomic nerves.

Automatism is the opposite peculiarity to the excitation. It means that the heart muscle can contract autonomically without any external influence. In fact individual cardiac muscle cells do not require nerve or hormone stimulation to contract. But how is it possible that action potentials occur on the cell membrane? The reason is that in the heart, the initial action potential occurs spontaneously in a specialized group of myocardial cells named myocardial pacemaker cells. Action potentials are propagated throughout the heart by a specialized conduction system and from cell to cell via the gap junctions (at intercalated disks).

Conduction. It is the functional peculiarity of the heart muscle to conduct under influence of electrical action potentials. Action potentials can readily spread from cell to cell, causing cardiac muscle to act electrically and mechanically as a functional syncytium, as if it were a single cell mass. Autonomic nerves innervate the pacemaker cells, and these serve to modify the rate of spontaneous action potentials, which in turn determines contraction rate of the entire heart. I underline that action potentials frst occur spontaneously within specialized myocardial pacemaker cells in the heart. It is interesting thing that the cardiac action potential is much slower than that of skeletal muscle. It lasts for hundreds of milliseconds (1 msec = 1/1000 second), as opposed to 5–10 msec in skeletal muscle.

Electrical activity of the heart (the conductive system).

It is something we were talking about. Like skeletal muscle, contraction of each cardiac muscle cell requires an action potential on the cell membrane and the action potential brings about the release of calcium from intracellular stores. However, unlike skeletal muscle, each cardiac muscle cell is not innervated by a motor neuron that is responsible for eliciting an initial action potential. In the heart, the initial action potential occurs spontaneously in pacemaker cells. They are found in the sinoatrial (SA) node of the heart.

1.Thus, **the sinoatrial node** is the first element of the whole conductive system. It is situated in right atrium nearby the cranial and caudal venae cavae. By the way the sinoatrial SA node cells generates just aboute 70–110 action potentials per minute. It is termed the pacemaker of the heart because each action potential that spontaneously develops in the sinoatrial SA node is propagated around the heart to stimulate action potentials in all myocardial cells and produce a contraction. The cell-to-cell propagation in the heart is possible because the intercalated disks provide an electrical connection between myocardial cells. A unique feature of the electrical activity of these cells is that the resting membrane potential is unstable. This instability permits sinoatrial SA node cells to depolarize spontaneously to threshold, where an action potential is generated. Both sympathetic and parasympathetic nerves innervate the sinoatrial SA node. By their actions on cells in the sinoatrial SA node, sympathetic nerves increase the rate of spontaneous action potentials & heart rate in general and parasympathetic nerves reduce it.

2.The second element of the whole conductive system is **the atrioventricular node** (A-V node). It is situated in the intraatrial septum. It generates action potentials just aboute 40-50 per minute. Cells of the atrioventricular A-V node are specialized to conduct action potentials more slowly than other myocardial cells. This characteristic allows enough time for the atria to depolarize completely and contract before action potentials spread into the ventricles to stimulate their contraction. Sympathetic and parasympathetic nerves that increase and reduce conduction velocity, respectively, also innervate the A-V node.

3.The third element of the whole conductive system is the common bundle, or **bundle of His**. It extends from the atrioventricular node A-V node into the ventricle. It extends through the fibrous connective tissue of the cardiac skeleton. The cardiac skeleton separates the cardiac muscle of the atria and ventricles, so the only direct electrical connection is through the A-V node and common bundle of His. The atrial contraction completes the filling of the ventricles so that ventricular contraction can eject a larger volume.

4. The 4th element of the whole conductive system is **the Purkinje fibers**.The common bundle divides into several branches that rapidly propagate action potentials throughout the ventricle. The individual cells that make up these branches are the Purkinje fibers. They are specialized for conducting action potentials.

Examining the situation scientists came to the decision that sinoatrial SA node is the vital node of the whole conductive system. When its work is interrupted contraction of the myocardium slows down until to stop of the heart in a few minutes. In that moment a clinical deadth is diagnosed. Between clinical and biological deadth there are somethere in the region of 5 minutes for doctors to save the life. That's why the atrioventricular node can also generates action potentials, roughly 40-50 per minute. It is enough for a patient to be given a feetback using electric current or hormones. If it is not possible to make sinoatrial SA node work (I mean appearance of action potential in pacemaker cells) doctors diagnose biological deadth.

The cardiac cycle.

The cardiac cycle is one complete cycle of cardiac contraction and relaxation. The events of the cardiac cycle occur in a specific sequence, and for descriptive purposes, the continuous cycle is divided into phases or periods (systole & diastole) marked by different events. **Systole** refers to the contraction of a chamber of the heart that drives blood out of the chamber. **Diastole** refers to the relaxation of a chamber of the heart just prior to and during the filling of that chamber.

Systole of both atriums continues just aboute 0.1 second. Systole of both ventricles goes between 0,3–0,4 second. Diastole of myocardium lasts 0,4 second.

Systole. As the ventricles begin their contraction, blood pressure increases in them. Almost immediately, the pressure within each ventricle exceeds the pressure within their respective atria, and the pressure differences force the A-V valves closed. The ventricles continue to contract and pressure continues to increase during the early part of systole. At this point in the cycle, all four heart valves are closed, and all remain closed until pressure in the ventricles exceeds that in the arterial vessels that they supply (aorta for left ventricle and pulmonary trunk for right ventricle). The period of systole during which all valves are closed is the isovolumetric contraction period, because during it the volume of each ventricle remains constant.

When ventricular pressures exceed those in their respective arterial vessels, the semilunar valves open to permit ejection of blood. An initial rapid ejection phase of systole is followed by a reduced ejection phase, during which ventricular and arterial pressures fall.The elasticity of the aorta and pulmonary trunk maintains blood pressure in these vessels even though the ventricles begin to relax. When the blood pressures in these vessels are greater than the pressures in their associated ventricles, the pressure differences close the semilunar valves.

Diastole. At the beginning of diastole, both the semilunar and A-V valves are closed, so the initial phase is termed isovolumetric relaxation. When ventricular relaxation reaches the point that atrial blood pressures exceed ventricular blood pressures, the pressure differences open the A-V valves. While the A-V valves are closed during systole and early diastole, blood continues to flow into the right and left atria from the systemic and pulmonary circulations, respectively.The accumulation of blood within the atria increases atrial blood pressure.

When A-V valves open, much of the accumulated blood flows rapidly into the ventricles. Most ventricular filling occurs during this period prior to any atrial contraction (Fig. 18-2). Blood continues to flow into the atria throughout diastole, and because the A-V valves are open, blood flows directly through the atria into the ventricles. As mentioned earlier, diastole is the phase of the cardiac cycle that lengthens most with slow heart rates, so slow heart rates provide a long period for ventricular filling. Atrial contraction (atrial systole) occurs during ventricular diastole, forcing an additional volume of blood into the ventricles, but this amount is relatively small (perhaps 15%) compared to the volume already in the ventricles.

The cardiac sounds.

Two distinct heart sounds can be heard during each cardiac cycle in all domestic species, and these are typically described as lub (first sound) and dub (second sound). These sounds are separated by a short interval and followed by a longer pause. The pause increases with slower heart rates.

The first sound marks the beginning of systole. It is associated with closure of the right and left atrioventricular valve. The first sound is caused by the tension and vibration of the auriculo-ventricular valves. The first sound is owing to the contractions of the large mass of muscle composing the ventricles.

The second sound marks the beginning of diastole. It is associated with closure of the aortic and pulmonary valves of the aortic and pulmonary vessels. There is general agreement in the view that the second sound, the former, owing to their greater tension in consequence of the higher blood-pressure in the aorta, taking much the larger share in the production of the sound, as may be ascertained by listening over these vessels in the exposed heart.

The first and second heart sounds are associated with valve closures, but turbulent blood flow and vibrations of large vessels induced by the closures are believed to be the actual causes of the sounds. Third and fourth heart sounds may be heard in some normal horses and cattle with relatively slow heart rates. The third sound is associated with the rapid ventricular filling phase after the initial opening of the A-V valves, and the fourth sound is associated with atrial contractions. *By the way, there is no sound associated with the* opening *of the semilunar valves.*

First 2 sounds are used clinically to divide the cardiac cycle into two phases, systole (ventricular) and diastole (ventricular). They are studied by means of auscultation (fonendoscope and stethophonendoscope) on the surface of the chest in the area 4-5 of the intercostal space to the left, pushing forward the left front limb and using the method of phonocardiography (graphic recording). The aim of auscultation is to listen to systole and diastole sounds, work of valves and any abnormal heart sound. Abnormalities in heart valves are a common cause of murmurs.

Heart murmur is a general term for any abnormal heart sound. Murmurs may occur when a valve fails to close completely (valvular insuffi ciency) and blood flow goes in the wrong direction at the wrong time. Murmurs may also occur when a valve fails to open completely (valvular stenosis) and blood is forced through a smaller than normal opening.

Electrocardiography.

Electrocardiography is the recording of electrical activity on the surface of the body that reflects the electrical activity in the heart. Recording electrodes are placed on the surface of the body at specific sites, and the recorded electrical activity reflects the summated electrical activity of the heart. An electrocardiogram (ECG) is the actual recording (Fig. 13).

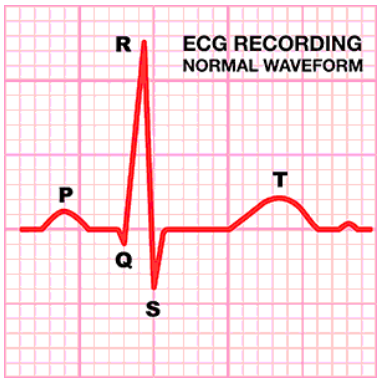

Figure 13. A typical electrocardiogram recorded from a dog.

Major waves are P, Q, R, S, and T. The P wave is associated with atrial depolarization. The QRS complex is associated with ventricular depolarization, and the T wave is associated with ventricular repolarization. The period between the P and Q waves is associated with A-V node delay. Differences in wave shape and size among species are due to normal differences in the pattern of conduction of action potentials around the heart.

Cardiac output. Regulation of cardiac activity.

Cardiac output (minute volume) is the volume of blood pumped by a left ventricle of the heart into its vessel per unit time (1 minute), and it is the product of heart rate (HR) and stroke volume (SV): CO = HR × SV.

The values for cardiac output refer to the output of a single ventricle, but the outputs of the right and left ventricles should be equal. The regulation of heart rate is via autonomic nervous system regulation of the SA node, as described earlier, and this is one means by which cardiac output is regulated. The two major factors that can change stroke volume are ventricular filling and cardiac contractility.

Stroke (systolic) volume is also subject to change and regulation. These changes are associated with stronger contractions until the muscle is overstretched.

The relation between stretching of cardiac muscle and force of contraction is known as Frank-Starling law of the heart. In normal resting animals, the Frank-Starling curve is less than optimal, so increases in end-diastolic volume can produce increases in stroke volume and cardiac output (Table 7).

Table 7. The volume of blood pumped by the heart into its vessel

Animals	Stroke (systolic) volume,l	Cardiac output (minute volume) ,l
Cow	0,7	45
Horse	0,7	23
Sheep	0,07	5
Pig	0,06	4,5
Dog	0,02	2

An indicator of myocardial contractility in the intact heart is the percentage of the end-diastolic volume that is ejected during ventricular systole (i.e., ejection fraction). A typical value for ejection fraction in a resting animal is 40%. With sympathetic stimulation, this increases, while with primary cardiac diseases it may reduce to 15–20%.

In normal animals, blood volume and arterial blood pressure are directly related. Increases or decreases in blood volume tend to produce similar changes in cardiac output and therefore in arterial blood pressure. In light of this relation and the goal of biologic systems to maintain homeostasis, it is predictable that decreases in blood pressure elicit physiologic responses designed to increase blood volume and increases in blood pressure elicit responses designed to reduce blood volume.

The regulatory mechanisms of cardiac activity are divided into intracardiac and extracardiac mechanisms.

Intracardiac regulatory mechanisms of the heart activity are divided into intracellular and mechanisms that are realized by peripheral reflexes. The increased calcium, as well as other changes in intracellular metabolism brought about by the β-adrenergic receptor stimulation, promotes an increase in the force of contraction. Other inotropes use different membrane receptors, but the intracellular events usually involve calcium availability or the affinity of intracellular proteins for calcium.

Extracardiac regulatory mechanisms of cardiac activity. Like the other organs, the heart is submitted to the neuronal and humoral regulation. Both sympathetic and parasympathetic nerves innervate the SA node. This is the means by which sympathetic stimulation increases heart rate and parasympathetic stimulation reduces heart rate.

The contraction force generated by individual myocardial cells can also be changed by a mechanism that is independent of the length to which cardiac muscle is stretched prior to contraction. This phenomenon is a change in cardiac contractility; it typically results from the direct action on myocardial cells of a hormone, neurotransmitter, or drug. Agents that can elicit changes in cardiac contractility are inotropes. Norepinephrine and epinephrine are positive inotropes, because both increase cardiac contractility. Norepinephrine and epinephrine both bind to β-adrenergic receptors on myocardial cells, and subsequent to this binding, both elicit increases in the availability of intracellular calcium in stimulated myocardial cells.

Function of blood vessels.

Vessels that carry blood away from the heart are called arteries and arterioles, and vessels that carry blood toward the heart are called veins. The smallest arteries are arterioles, which are continuous with the smallest blood vessels, capillaries. Capillaries again unite to form small venules that come together to form larger and larger veins.

The arterial side of the circulation provides a ready supply of blood under relatively high hydrostatic pressure. The walls of arteries tend to be thick and elastic, properties that are important in maintaining blood pressure. Smooth muscle in the walls of smaller arteries controls the diameter of these vessels. Because of their relatively thick walls, arteries are not very compliant (i.e., do not distend easily with increases in pressure), so arterial pressure remains high as the heart pumps blood into the arteries.

The arterioles at the end of the branching arterial network function as on-off valves to regulate the rate of blood flow from the arteries into capillary networks. Sympathetic vasoconstrictor nerves innervate the smooth muscle in the wall of most arterioles, and this is one mechanism by which blood flow is regulated. However, the degree of constriction of arteriolar smooth muscle is also subject to regulation by a large number of vasoactive agents.That is, an increase in metabolism brings about an increase in blood flow. The process by which local mechanisms regulate local blood flow is autoregulation.

Capillaries are the site of exchange between blood and the interstitial fluid that surrounds all cells. Capillaries are thin-walled vessels are only large enough in diameter to accommodate a single file of erythrocytes. The wall acts as a selectively permeable membrane that permits water, oxygen, and nutrients to leave the blood for tissue cells and permits waste products from tissue cells to enter the blood. Some fluid remains in the tissues, and excess fluid normally is removed by lymph vessels.In most cases, this exchange is by simple diffusion (i.e., substances move down their concentration gradients though capillary walls.

Gases (oxygen and carbon dioxide) and other lipid-soluble substances freely diffuse though capillary walls, but substances that are not lipid soluble, such as glucose, must diffuse through pores in the capillary wall. Exchange by diffusion does not necessarily require the movement of fluid between the capillary and the interstitial space. Oxygen, for example, can diffuse down its concentration gradient from the plasma to metabolizing cells as blood flows in a capillary past the cells. As stated earlier, the rate of capillary exchange is primarily governed by the rate of blood flow into the capillaries. In resting tissues, blood flow occurs only through a small percentage of the total capillaries at any one time. As metabolism and blood flow increase, the percentage of capillaries being perfused increases.

Typically, there is a small net loss of fluid from the plasma as it flows through most capillary networks. This fluid is recovered via the lymphatics and ultimately returned to the blood where lymphatics enter large veins near the heart. A small number of plasma proteins are similarly lost from capillaries and returned via the lymph. The primary factor that forces fluid out of a capillary into the interstitial space is the blood pressure in the capillary. The primary force that tends to keep fluid in capillaries is the effective osmotic pressure generated by plasma proteins, primarily

albumin. This pressure is also termed oncotic pressure. At the arterial end of a capillary, the blood pressure is higher than the oncotic pressure, so some fluid is lost from the capillary, while at the venous end of a capillary the oncotic pressure is higher, so some fluid moves into the capillary. A slight imbalance between fluid loss and fluid gain by the capillaries gives rise to a net loss and provides fluid for lymph formation.

Like arteries, veins have smooth muscle in their walls, but the walls of veins are much thinner and more compliant. The compliance of venous vessels permits relatively large changes in the volume of blood in the veins with minimal changes in venous blood pressure. Thus, the venous side of the circulation functions as a low-pressure reservoir of blood. Constriction of venous smooth muscle promotes an increase in blood flowing back to the heart and an increase in cardiac filling pressure. Venous blood pressure is typically quite low. Valves, usually consisting of two cusps each, are scattered at irregular intervals throughout the venous and lymphatic systems. A valve frequently is present in veins where two or more veins unite to form a larger vein.

The main principles and velocity of the blood-stream along the vessels.

The main principles and velocity of the blood-stream along the vessels (hemodynamics) are**:**

- ✓ blood continuous to flow and flow should be constant;
- ✓ one-way blood flow;
- ✓ the valves of the heart;
- ✓ the pressure difference between the initial and the terminal parts of the vascular system;
- ✓ contraction of skeletal muscles in the limbs and trunk squeezes the thin-walled veins, assisting the flow of venous blood back toward the heart;
- ✓ the valves in the veins ensure a unidirectional flow of venous blood toward the heart;
- ✓ the sucking property of the atria in diastole and chest, promoting the blood flow in the vena cava, especially during inspiration.

The velocity of the blood-stream along the vessels: in aorta – 0,5 m/s, in the capillaries – 0,5 mm/s, in small veins – 6–14 sm/s, in the larger veins (cranial and caudal) – 20-30 sm/s, arteries – 30-40 sm/s.

Time for 2 circulations – horses 32 seconds (5-6 seconds pulmonary circulation), cows– 28 seconds, goats-14 seconds.

Regulation of arterial blood pressure and blood volume.

Arterial blood pressure (MAP) is a function of cardiac output (CO) and total peripheral vascular resistance (TPR), usually written as MAP = CO × TPR.

The pressure depends on the amount of blood being pumped into the reservoir cardiac output and the rate at which blood is permitted to flow out of the reservoir. Recall also that the resistance of the arterioles, which contribute the most to the total vascular resistance, regulates the rate of blood flow out of the arteries. Thus, the level of cardiac function and the degree of arteriolar constriction are the two determinants of arterial blood pressure. Changes in arterial blood pressure can be brought about by changes in cardiac function, the degree of arteriolar constriction, or some combination of these determinants.

Any chemical regulator (e.g., hormone or paracrine agent) or neural reflex that affects cardiac activity or the smooth muscle of arterioles has the potential to alter blood pressure. The large number of therapeutic chemical agents used to treat high blood pressure in humans and animals, and the different mechanisms by which these agents have their effects, illustrate the diversity of factors that can alter blood pressure.

The organs primarily responsible for bringing about changes in blood volume are the kidneys. Thus, blood volume regulation by the kidneys is one factor in the ultimate determination of arterial blood pressure.

The arterial baroreceptor reflexes are the neural reflexes primarily responsible for the short-term or immediate regulation of arterial blood pressure. Neural receptors in the aorta and carotid arteries respond to changes in arterial pressure in these vessels, and this information is relayed to refl ex centers in the brainstem. The efferent nerves for these reflexes are the autonomic nerves to the heart and the sympathetic vasoconstrictor nerves to both arterioles and veins. Decreases in arterial blood pressure bring about adjustments in these efferent nerves to increase heart rate, increase cardiac contractility, and promote arteriolar vasoconstriction and venoconstriction. Increases in arterial blood pressure above some original level should elicit reductions in cardiac activity and relaxation of the vessels. Inhibition of vasoconstrictor and venoconstrictor nerves is the mechanism by which the reflex permits relaxation of the vascular smooth muscle.

Neural receptors in the atria of the heart respond to changes in the volume of blood filling the atria, and afferent information from these receptors is relayed to brainstem reflex centers. The primary efferents involved in these reflexes are the sympathetic nerves to the kidneys. Increases in atrial filling bring about reductions in sympathetic nerve stimulation of the kidneys, and this permits an increase in the urinary excretion of sodium chloride and water. This tends to reduce blood volume and therefore cardiac filling, cardiac output, and blood pressure. Reductions in atrial fi lling bring about increases in sympathetic nerve activity to the kidneys. This reflex also affects the secretion of renin from the kidneys.

Lymphatic vessels.

The walls of capillaries are thin enough to permit fluid as well as nutrients and gases to escape into spaces between tissue cells. Some of this extracellular fluid does not reenter the vascular space directly but is instead recovered by thin-walled lymphatic vessels. Lymphatic vessels resemble veins in that they contain numerous valves permitting flow only toward the heart. The smallest lymphatic vessels are blind capillary-sized structures that begin in intercellular spaces, where they accumulate extracellular fluid. Fluid within the lymphatic vessels, called lymph, is transported to larger and larger lymph vessels and finally emptied into the cranial vena cava or one of its tributaries.

The tracheal trunks, two large lymph vessels draining the head and neck, usually terminate in the jugular veins. Lymph from the caudal half of the body is delivered to the large thoracic duct (of which there may be one or two), which traverses the thoracic cavity adjacent to the aorta to empty its lymph into the cranial vena cava. Movement of lymph is driven largely by gravity or changing pressures of adjacent structures. The lymph is filtered by nodular structures called lymph nodes

scattered along the course of most lymphatic vessels. Lymphatic vessels begin as blind-ending vessels similar in structure to capillaries, and these join to form larger vessels resembling veins. The direction of lymph flow is from small lymphatics to large ones. The largest of the lymphatic vessels join with large veins just cranial to the heart, and here all lymph returns to the blood.

Lymph usually contains numerous lymphocytes, inorganic salts, glucose, proteins, and other nitrogenous substances. Neutrophilic leukocytes are not normally present in great numbers except during acute infections. Lymph derived from the intestine during digestion may contain large quantities of lipids, giving it a milky appearance. This milky lymph, called chyle, results from the absorption of lipids into the lacteals, the small lymphatics of the intestine.

BIBLIOGRAPHY

1. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
2. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
3. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
4. Mazurkevich AY, Trokoz VO, editors. Physiology of farm animals. Workshop. 2nd ed. Kyiv: Center for Educational Literature; 2015. (Ukrainian).
5. Mazurkevich AY, Trokoz VO, Karpovsky VI, et al. ; edited by A.Y. Mazurkevich, V.O Trokoz. Physiology of agricultural animals. Textbook. 2nd ed. Kyiv; 2014. (Ukrainian).
6. Moyes CD, Schulte PM. Principles of Animal Physiology 3rd ed. Don Mills, Ontario: Pearson; 2016.
7. Papachristodoulou D, Snape A, Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 6th ed. Oxford, UK: Oxford University Press; 2018.
8. Pineda MH, Dooley MP, editors. McDonald's Veterinary Endrocrinology and Reproduction. 5th ed. Ames, Iowa: Iowa State Press; 2003.
9. Pollard TD, Earnshaw WC, Lippincott-Schwartz J, Johnson GT, editors. Cell Biology. 3rd ed. Elsevier. 2016.
10. Reddy PB. Text book of Animal Physiology. Andhra Pradesh, India: IMRF Publications; 2015.
11. Reece WO, Functional Anatomy and Physiology of Domestic Animals. 4th ed. Baltimore: Wiley-Blackwell; 2009.
12. Rhoades RA, Pflanzer RG. Human Physiology. 4th ed. Pacific Grove, Calif.: Brooks/Cole; 2003.
13. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
14. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.
15. Smith BP. Large Animal Internal Medicine. 3rd ed. St. Louis, Missouri: Elsevier Mosby; 2015.

16.Tortora GJ, Derrickson BH. Principles of Anatomy and Physiology. Atlas and Registration Card. 11th ed. Hoboken, NJ: John Wiley & Sons; 2005.

CHAPTER 9.PHYSIOLOGY OF THE RESPIRATORY SYSTEM

Functions of the respiratory system.

Oxygen is a vital requirement of animals. An animal may survive for days without water or for weeks without food, but life without oxygen is measured in minutes.

1.Delivering oxygen and removing carbon dioxide (the product of cellular respiration). The processes involved with these functions related to gases include ventilation (movement of air in and out of the lungs), gas exchange between air and blood in the lungs, gas transport in blood, and gas exchange between blood and cells at the level of the tissues.

2.Assistance in the regulation of the pH of the body fluids (is closely associated with the ability of the respiratory system to remove carbon dioxide. If carbon dioxide accumulates in the blood because the respiratory system cannot remove it, blood pH falls; this is respiratory acidosis. Blood pH rises if the respiratory system removes more carbon dioxide than is appropriate and blood levels of carbon dioxide are lower than normal; this is respiratory alkalosis.

3.Assistance in temperature control.

4.Phonation (voice production).

5.Immune defense against disease by providing antibodies (Ig A).

6.Organs of blood keeping (conserving) – capillaries of pulmonary circulation.

Structure and functions of the upper respiratory tract.

The respiratory system consists essentially of the lungs and upper respiratory tract that conducts air into and out of the lungs.

Upper respiratory tract include nose, the nostrils, nasal cavity, pharynx, larynx, trachea, and bronchi. The nose of domestic animals comprises the parts of the face rostral to the eyes and dorsal to the mouth.The external nares (nostrils) are the external openings of the respiratory tract. Their size and shape are highly variable among domestic farm animals. The pig also possesses a rostral bone in the tip of its flat, disklike nose. This is presumably an adaptation to the rooting habits of the pig. The nasal cavity is separated from the mouth by the hard and soft palates and separated into two isolated halves by a median nasal septum. The pharynx is a common soft tissue conduit for food and air, lying caudal to the oral and nasal cavities. The larynx is the gatekeeper to the entrance of the trachea. The trachea extends from the caudal end of the larynx to the bronchi. It is formed by a series of C-shaped hyaline tracheal cartilages that provide cross-sectional rigidity to resist collapse and are joined one to another by elastic annular ligaments that permit the trachea considerable flexibility to follow movements of the neck. The trachea passes caudad as far as the base of the heart, where it divides into two principal bronchi, one for each lung. The principal bronchi branch into secondary (also called lobar) then tertiary bronchi, subsequent branches becoming smaller and smaller. When the airways divide to the extent that they are less than 1 mm in diameter, the cartilage

disappears, and these airways are called bronchioles. The bronchiole eventually branches into several alveolar ducts. Some terminal bronchioles have alveoli in their walls, hence are called respiratory bronchioles

Functions of the upper respiratory tract.

The upper airways are not sites of gas exchange. These airways are considered to be anatomic «dead space». Physiologic dead space includes the anatomic dead space and any alveoli in which normal gas exchanges cannot occur.

1.The sense of smell (The mucous membrane investing the ethmoidal conchae is the olfactory epithelium. It contains the sensory endings of the olfactory nerve (cranial nerve I).

2.Humidify and warming of inspired air. The hairless region of the most rostral parts of the nose in species other than the horse contains no sebaceous glands but does have numerous sweat glands, which keep the region around the nostrils moist. The vascular mucous membrane covering conchae of the nasal cavity.

3.Protection. (The equine nose lacks a planum, being instead covered with short, fine hairs. The larynx's primary function is to regulate the size of the airway and to protect it by closing to prevent substances other than air from entering the trachea. It is capable of increasing the diameter of the air passageway during forced inspiration (as during heavy exercise) and closing the opening during swallowing or as a protective mechanism to exclude (eliminate) foreign objects.

4.Phonation. It is the production or utterance of speech sounds The walls of the pharynx are supported by striated muscles whose actions assist in deglutition (swallowing) and phonation. The larynx is the organ of phonation (vocalization), hence its common name, voice box. Contraction of muscles in the larynx changes the tension on ligaments that vibrate as air is drawn past them; this vibration produces the voice.

Lungs and surfactant.

Each lung is roughly conical, with the base resting against the cranial side of the diaphragm and the apex in or close to the thoracic inlet.

Lobes of the lungs are defined by the presence of lobar (secondary) bronchi. In ruminants and the pig, the left lung is divided into cranial (apical) and caudal (diaphragmatic) lobes, the right lung in these animals is divided into four lobes. Both right and left lungs of the horse have cranial and caudal lobes, distinguished by the cardiac notch.

The bronchiole eventually branches into several alveolar ducts, which terminate in clusters of air sacs, the alveoli. It is here that the exchange of gases with the blood takes place.

Lung consists of millions of alveolis. Alveoli are the primary site of gas exchange in the lungs. A type I squamous epithelial cell lining the alveoli – gas exchange. Surface tension, a property of fluids, results from the cohesive forces that tend to pull or hold the molecules of a fluid together. Thin layer of fluid lines the microscopic alveoli. The surface tension of this fluid tends to draw the walls of alveoli together and collapse them.

The alveolar fluid contains the pulmonary surfactant – a combination of substances that reduces surface tension. A type II squamous epithelial cell lining the alveoli – produce pulmonary surfactant. The reduction in surface tension promotes

alveolar stability and makes alveolar expansion during inspiration easier. Production of pulmonary surfactant does not begin until late in gestation. Neonates born prematurely may have insufficient amounts of surfactant, which results in labored breathing.

Physiology of respiration. Ventilation.

Ventilation is the process by which air is moved into (inspiration) and out of (expiration) the lungs.

As described earlier, there is no physical connection between the visceral and parietal pleural surfaces (except at the hilus), and the closed pleural cavity between them is a potential space filled with a small amount of fluid. The hydrostatic pressure in the pleural cavity is always slightly negative relative to atmospheric pressure, and this small negative pressure exerts a pulling force to keep the lungs expanded.

During **inspiration**, air moves in through the upper airways and down to the alveoli because of a hydrostatic pressure gradient (i.e., atmospheric pressure) between the outside air and the air passages in the lungs (intrapulmonic pressure). This gradient is generated by lung expansion. Expansion increases the volume of the air passages in the lungs but reduces the pressure in them.

The inverse relationship between volume and pressure of a gas is expressed as Boyle's law. The negative (inspiration) and positive (expiration) values for intrapulmonic pressures are relative to atmospheric pressure (760 mm Hg at sea level), so negative pressure is less than atmospheric and positive is greater than atmospheric. Enlargement of the thoracic cavity is accomplished by contraction and flattening of the dome-shaped diaphragm and a forward and outward movement of the ribcage by the contraction of appropriate thoracic muscles. These are skeletal muscles innervated by somatic motor nerves. After inspiration, the pressure in the pleural cavity remains at its lowest point until expiration begins and the thoracic cavity begins to return to its original volume. Muscles which are involved in the inspiration: dome-shaped diaphragm and thoracic muscles (skeletal muscles innervated by somatic motor nerves). The most important is diaphragm. Paralysis of its nerve causes hypoxia (breathlessness) and death.

Expiration in a resting animal is a passive process that does not require muscle contraction. Relaxation of the muscles contracted during inspiration permits the intrinsic elastic properties of the lungs and the thoracic wall to recoil to their original volume. The return to the original volume increases the intrapulmonic pressure so that it is greater than atmospheric pressure, and air is forced out of the lungs. Forced expiration is an active process that forces more air from the lungs than would occur during a normal passive expiration. Forced expiration requires contraction of abdominal muscles to force viscera against the diaphragm and contraction of other muscles to pull the ribs caudad. Both of these actions reduce the size of the thoracic cavity and permit recoil of the lungs to a smaller volume than typical for resting expiration. This causes a further increase in intrapulmonic pressure and forces more air out than would occur with passive expiration.Muscles which are involved in the expiration: abdominal muscles and muscles to pull the ribs caudad.

Movement of thoracic cavity during inspiration and expiration can be recorded by pneumographia. Actually recording is called pneumogramma.

Types and respiratory (ventilatory) rate in different species of animals.

In normal animals a soft rustling sound associated with air movements may be heard with a stethoscope. Abnormal lungs, for example lungs with abnormal amounts of fluid in the airways, may produce exaggerated sounds termed rales.

Types of respiration:

- ✓ thoracic;
- ✓ abdominal;
- ✓ mixed (in most healthy animals).

Respiratory (ventilatory) rate is the number of breaths (inspiration and expiration) performed by an animal in 1 minute (Table 8).

Table 8. Respiratory (ventilatory) rate per 1 min in domestic animals

Animals	Respiratory rate per 1 min
horse	8-16
cow	12-25
sheep, goat	16-30
pig	12-20
rabbit	50-60

Inspired, expired, alveolar air composition.

The oxygen and carbon dioxide concentrations in air can be described in two ways: partial pressures and percentages. Room air is approximately 21% oxygen and 0.3% carbon dioxide (Table 9).The primary component of room air is the inert gas nitrogen (about 78%). The partial pressure of an individual gas in a mixture of gases is the product of the percentage of the individual gas in the mixture and the total barometric or atmospheric pressure. Thus, at sea level, where atmospheric pressure is 760 mm Hg, the partial pressure of oxygen in room air is approximately 160 mm Hg.

The partial pressure of an individual gas in a mixture is one factor that determines the amount of the gas that will dissolve in a liquid (such as blood plasma). The partial pressure of a gas in a mixture can be viewed as the driving force that moves molecules of an individual gas from the air into the liquid when the liquid is exposed to a gas mixture. Thus, because partial pressures depend on both total atmospheric pressure and the percentages of individual gases, both of these factors also determine the amount of an individual gas that can be dissolved in a liquid. The unit of measurement of the amount of a gas dissolved in a liquid is in millimeters of mercury.

Table 9. Inspired, expired, alveolar air composition

Air	O_2	CO_2	N_2
	%	%	%
Inspired	20,94	0,03	79,03
Expired	16,50	4,00	79,50
Alveolar	14,00	5,30	80,70

Gas exchange in the lungs.

Gas exchange between the blood and alveolar air in the lungs occurs across the walls of alveoli. At its thinnest point, the alveolar wall barrier between blood plasma and alveolar air consists of the endothelial cell of pulmonary capillaries, a type I squamous epithelial cell lining the alveoli, and a fused basement membrane

contributed by both cells. Gases readily move back and forth across this very thin and fragile structure. Any abnormality that thickens this barrier (e.g., pulmonary edema with an accumulation of extracellular fluid in the alveolar wall) can greatly reduce the efficiency of exchange. Oxygen exchange is usually affected first because its solubility is much less than that of carbon dioxide.

Exchange begins as soon as blood enters a pulmonary capillary from pulmonary arterial vessels and continues until equilibrium between alveolar air and plasma is reached. Table 10 shows typical values for partial pressures of oxygen and carbon dioxide in alveolar air and a pulmonary capillary. Plasma entering pulmonary capillaries from the pulmonary arteries contains the highest concentration of carbon dioxide and the lowest of oxygen. Because of the continuous gas exchange in the pulmonary capillaries, alveolar air contains less oxygen and more carbon dioxide than inspired air (PO_2 of 160 mm Hg and PCO_2 of 0.23 mm Hg for inspired air).

Gases exchange in the lungs by diffusion across the walls of alveoli because there are differences in partial pressures of oxygen and carbon dioxide in alveolar air and a pulmonary capillary, gases move from the place with the highest concentration to the place with the lowest concentration.

To be most efficient, the rate of pulmonary artery blood flow into an area of the lung must be balanced with the rate of air movement in and out of the alveoli in the same area. To appreciate the importance of this balancing, consider an extreme case in which one lung is collapsed so that air movement is impossible, but the collapsed lung receives the same amount of blood flow as the inflated normal lung. The lack of airflow in the collapsed lung means that any alveolar air is stagnant and contains high levels of carbon dioxide and low levels of oxygen. Gas exchange in the collapsed lung does not occur, and levels of oxygen and carbon dioxide are the same as those entering. The blood exiting the collapsed lung mixes with an equal volume of blood from the intact lung, so that blood reentering the heart from the pulmonary circulation is deficient in oxygen and has an excess of carbon dioxide.

Within the lungs, a unique type of vascular mechanism functions at the level of small arterial blood vessels to balance blood flow and airflow. This mechanism, local hypoxic (low oxygen) vasoconstriction, produces local vasoconstriction in response to low levels of alveolar oxygen (such as with poor alveolar ventilation).

The vasoconstriction reduces blood flow into the area of poor ventilation and shunts blood into better-ventilated areas of the lungs. It is not clear how low levels of alveolar oxygen are detected and what vasoactive agent or agents are responsible for the vasoconstriction. The hypoxic vasoconstriction mechanism operates well on a local basis to redirect blood flow into different areas of the lungs. However, when both lungs are exposed to low oxygen levels, such as at high altitudes, the mechanism produces a general increase in vascular resistance throughout both lungs. Pulmonary hypertension (high pulmonary circulation blood pressure) results, and the right side of the heart must work harder to pump blood through the lungs. Right heart failure with peripheral edema can result if the right heart cannot compensate for the increased resistance.

Table 10. Typical values for partial pressures of oxygen and carbon dioxide

Gases	Venous blood	Alveolar air	Arterial blood	Extracellular liquid	Cells
O_2	40	102	100	20-40	0-1
CO_2	46	40	40	46	60

Gas exchange in the tissues. Gas transport in blood.

Cells in peripheral tissues consume oxygen and produce carbon dioxide during normal metabolism. This maintains relatively low oxygen and high carbon dioxide concentrations (partial pressures) in the extracellular fluid around capillaries. As arterial blood enters capillaries, partial pressure gradients promote the diffusion of oxygen out of the blood to the interstitial fluid and carbon dioxide from the interstitial fluid into the blood.

Both oxygen and carbon dioxide dissolve in plasma, and the partial pressures of each are a measure of the amount dissolved. However, the quantity of each gas that is transported as a dissolved gas is very small compared with the amounts of each transported in other forms in the blood. Only 1.5% of the total oxygen and 7% of the carbon dioxide are dissolved. Most oxygen in the blood (98.5%) is found chemically bound to hemoglobin in erythrocytes. At partial pressures of oxygen normally found in alveolar air (about 100 mm Hg), hemoglobin is almost completely saturated with oxygen (i.e., hemoglobin molecules cannot bind any additional oxygen). Normally, the hemoglobin in erythrocytes is almost completely saturated with oxygen as blood passes through the pulmonary capillaries. At partial pressures of oxygen typically found in venous blood (40 mm Hg) a great deal of hemoglobin still has oxygen bound to it. Several factors affect the ability of hemoglobin to bind chemically with oxygen. An increase in temperature, a reduction in pH, or an increase in the concentration of carbon dioxide reduces the ability of hemoglobin to bind oxygen. These factors alter the relation between hemoglobin saturation and the partial pressure of oxygen so that the saturation is less for any given partial pressure.

High temperature, low pH, and high carbon dioxide occur in tissues with high metabolic rates (e.g., exercising skeletal muscle). The effects of these factors on the relation between hemoglobin and oxygen is useful, because more oxygen is liberated from hemoglobin and delivered to the metabolizing cells when blood passes through such areas.

Almost all of the carbon dioxide (93%) that enters the blood in the systemic circulation diffuses into erythrocytes. Some of the carbon dioxide (23%) chemically combines with the hemoglobin in the erythrocytes to form carbaminohemoglobin. When the erythrocytes carrying the carbaminohemoglobin reach the pulmonary capillaries in the lungs, the reaction is reversed so that the carbon dioxide can diffuse into alveoli to be expired. Most (70%) of the carbon dioxide that enters the erythrocytes is converted to carbonic acid under the influence of the enzyme carbonic anhydrase. The carbonic acid rapidly dissociates into a hydrogen ion and a bicarbonate ion in the erythrocyte. The hydrogen ion is buffered by hemoglobin in the erythrocyte, and the bicarbonate ion leaves the erythrocyte and enters the plasma. It is in this form (bicarbonate ion in plasma) that most carbon dioxide is transported

from the peripheral tissues by the blood to the lungs. Within the lungs, the reactions are reversed so that carbon dioxide can be reformed and be expired from the alveoli.

Control of ventilation.

Most of the air passages in the lungs have smooth muscle in the walls, and the constriction or relaxation of this smooth muscle determines the resistance to air flow. Much of this smooth muscle has β2-adrenergic receptors that produce smooth muscle relaxation when stimulated. Sympathetic stimulation during exercise reduces resistance to airflow and promotes alveolar ventilation. Airway smooth muscle constricts in response to stimulation by histamine or leukotrienes.These substances are released during allergic reactions from mast cells around airways. The resulting increase in airway resistance makes it more difficult to move air, and a more forceful skeletal muscle contraction is needed to move a given volume of air. This greatly increases the work of breathing.

Contraction and relaxation of skeletal muscle generates the forces to move air in and out of the lungs. Although the skeletal muscles of respiration can be consciously controlled, as illustrated by voluntarily holding the breath, normal ventilation is almost entirely reflexive. The respiratory reflex centers consist mainly of three bilateral groups of nerve cells in the brainstem that have a definite effect on respiration when stimulated electrically. One of these, the medullary rhythmicity area, is responsible for setting respiratory rate, and it consists mainly of an inspiratory center. Neurons in this center are tonically active, fi ring at an inherent rhythmic rate by regular variations of their membrane potentials. Expiratory neurons are also in this area; however, they do not discharge spontaneously and so are normally active only during a forced expiration. Stimulation of the inspiratory center leads to contractions of the diaphragmatic and intercostal muscles via neural connections through the spinal cord and phrenic and intercostal nerves, respectively. Feedback circuits between the inspiratory center and the other two neural centers relax these muscles and allow for passive expiration. The interplay among these three centers provides for regular intermittent rhythmic breathing at rates appropriate for each species during eupnea (normal quiet breathing).

The tonic activity of the inspiratory center is regulated by neural input from a variety of sites. In resting animals, the most important neural input is from central chemoreceptors in the medulla of the brainstem. These receptors respond to hydrogen ion concentration changes in the interstitial fluid of the brain and stimulate the inspiratory center to increase ventilation when the hydrogen ion concentration increases. Because carbon dioxide from the blood readily diffuses into the interstitial fluids of the brain, and in body fluids is in equilibrium with carbonic acid, an increase in blood carbon dioxide increases the hydrogen ion concentration in the brain and stimulates ventilation. The effects of changes in blood carbon dioxide on ventilation are so pronounced that blood carbon dioxide is considered to be the most important regulator of ventilation in most conditions.

Animals sometimes hyperventilate (breathe abnormally rapidly) during the induction of general anesthesia because they are excited. As a result of the hyperventilation, their blood carbon dioxide may be significantly reduced. The low blood carbon dioxide concentration means that the primary stimulus for normal

ventilation is lost. These animals may undergo a period of apnea (cessation of breathing) until blood carbon dioxide levels are restored by metabolism.

Another group of chemoreceptors, the carotid and aortic bodies, also provide neural input to the inspiratory center. These peripheral chemoreceptors detect changes in arterial blood hydrogen ion concentration and oxygen content. Increases in hydrogen ion concentration or reductions in blood O_2 content initiate neural inputs to increase ventilation. However, the effects of these peripheral chemoreceptors are less pronounced than those of the central chemoreceptors, so changes in blood hydrogen ion concentration or oxygen content must be severe to override the effect of blood carbon dioxide.

Further regulating the inspiratory center and breathing rhythmicity is a reflex arc involving stretch receptors in the lung parenchyma, visceral pleura, and bronchioles. These receptors are stimulated as the lung inflates during inspiration, and afferent impulses are transmitted up the vagus nerves into the brainstem, where the inspiratory center is inhibited. This is the Hering-Breuer reflex, which reinforces the action of the other center to limit inspiration and prevent overdistension of the lungs.

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.
2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.
5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.
7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.

14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

CHAPTER 10. NUTRITION AND METABOLISM

Nutrition and metabolism. Essential nutrients.

The nutritional needs of animals vary greatly with their metabolic state. A rapidly growing, active young animal has much different nutritional needs from those of an older, more sedentary animal. Both animals must consume certain essential nutrients (compounds needed for normal growth and/or survival that cannot be synthesized in adequate amounts in the body), but the amounts of these nutrients per unit of body weight and the relative amounts of specific nutrients vary. Some essential nutrients are required in minute quantities and are toxic in large quantities. For example, copper is an essential mineral, but excessive consumption over a short period leads to copper toxicity. Minerals that are needed in small quantities are often termed trace minerals.

The structural make up of all living organisms mainly are made from proteins, carbohydrates and lipids. As these molecules are vital for life, metabolic reactions either focus on making these molecules during the construction of cells and tissues, or by breaking them down and using them as a source of energy. These biochemicals can be joined together to make polymers such as DNA and proteins, essential macromolecules of life. Vitamins function as coenzymes for various biochemical reactions throughout the body and are also typically required in small amounts. Water-soluble vitamins (B complex, biotin, C, folic acid, and niacin) are not stored in the body, but fatsoluble vitamins (A, D, E, and K) are stored in the liver and adipose tissue. Water-soluble vitamins can be consumed in large amounts without significant toxicities because the excess is rapidly excreted in the urine. Because they accumulate in the body, excessive consumption of fat-soluble vitamins can be harmful.

The nutritional and metabolic status of individual animals may be evaluated by determining the balance for a given nutrient or type of nutrient. Balance is determined by comparing the amount consumed by the animal to the amount used or lost from the body.

Metabolism (the word metabolism aroused from Greek which means change). It is the set of life-supporting chemical transformations within the cells of living organisms. These enzyme-catalyzed reactions allow organisms to grow and

reproduce, maintain their structures, and respond to their environments. It can also refer to all chemical reactions that occur in living organisms, including digestion and the transport of substances into and between different cells.

The chemical reactions of metabolism are organized into metabolic pathways, in which one chemical is transformed into another chemical through a series of reactions in the presence of enzymes. So, enzymes are crucial to metabolism because they allow organisms to drive desirable reactions. Enzymes also allow the regulation of metabolic pathways in response to changes in homeostasis or to signals from other cells. Metabolic pathways can have reversible and irreversible steps. Alternative routes may exist that can bypass steps in a pathway. A remarkable feature of metabolism is the similarity of the basic metabolic pathways and components between even greatly different species.

Metabolic pathways involve anabolism and catabolism to provide energy and building blocks. The terms anabolic and catabolic are used to describe the overall metabolic state or status of an animal. **Anabolism** refers to a constructive process=biosynthetic processes=synthetic pathways require the input of energy. (e.g., synthesis of proteins from amino acids), while **catabolism** refers to a destructive process=the breakdown of molecules=pathways that break down molecules usually release energy. (e.g., degradation of proteins into individual amino acids). During catabolism carbohydrates break down to monosaccharides (*for example glucose*), proteins break down to amino acids, and lipids break down to fatty acids and triglycerides (as part of chylomicrons).

Example 1: Muscle proteins are made up of myosin and actin. It consists of many amino acids attached to each other by so-called peptide bonds. Proteins are broken down to the individual amino acids in digestion of dietary protein. This is known as catabolism. In this process, energy that had been stored in the protein molecules is liberated. In contrast, when skeletal muscles are being built up (such as during normal growth in childhood, or the hypertrophy that occurs with weight training), this is anabolism. Individual amino acids are bonded together in specific sequences to form the proteins. Formation of these bonds requires energy that must come from other chemical reactions.

While anabolic and catabolic refer to the overall metabolic status, both processes are usually ongoing at the same time in an animal's body. For example, even in a young, rapidly growing animal that is digesting a meal, absorbing nutrients, and synthesizing body proteins, some body proteins are degrading at the same time. However, in this case, the rate of protein synthesis is greater than the rate of protein degradation, so the animal is in an anabolic state. Several hormones contribute to the regulation of the balance between anabolic and catabolic processes, and the study of the hormones that regulate metabolism is termed metabolic endocrinology. A common feature of such hormones is that blood glucose concentrations participate in regulation of their secretion. This indicates that the maintenance of a minimal and constant source of glucose for energy is a key factor in the overall endocrine control of metabolism.

The food we eat, (carbohydrates, lipids, and proteins), are our only source of energy for doing the biological work of cells. These nutrient molecules have energy

stored in the bonds between their atoms. Metabolic uses for nutrients, it is mainly of three types:

- ✓ used immediately for energy for active processes;
- ✓ synthesized into structural or functional molecules;
- ✓ synthesized as fat or glycogen for later use as energy.

Oxidation-Reduction reactions.

Oxidation – the removal of electrons from a molecule and results in a decrease in the energy content of the molecule. Because most biological reactions involve the loss of hydrogen atoms, they are called dehydrogenation reactions.

Reduction – the opposite of oxidation; the addition of electrons to a molecule, and results in an increase in the energy content of the molecule.

An important point to remember in Oxidation-Reduction reactions is that oxidation is usually an energy-releasing reaction. For normal metabolism, cells of an animal's body need the three major classes of nutrients (carbohydrates, proteins, and lipids) delivered to them via the blood in their simplest forms (monosaccharides, amino acids, and fatty acids).

Absorptive state: anabolism.

To study the endocrine control of anabolism and catabolism, metabolic endocrinologists often contrast the period shortly following a meal, during which nutrients are being absorbed from the gastrointestinal tract (absorptive state), with a period during which there is no net absorption (postabsorptive state). During the absorptive state, blood levels of metabolic products increase. The overall goals of the metabolic processes during this period appear to be to increase the use of these nutrients by cells of the body or store them so that they can be used later. Metabolic periods of ruminants differ from those of other animals, because nutrients are constantly being absorbed from the forestomach and passing from the forestomach down the remainder of their gastrointestinal tract.

Figure 14 summarizes the overall fate of the major nutrients absorbed during the digestion of a meal, and these are described in more detail in the following paragraphs.

Glucose is the predominant product of carbohydrate digestion in most animals, and following a typical meal, blood glucose levels may rise to 150% of fasting levels. The increase in blood glucose is a major stimulus for the release of insulin from the pancreas, but increases in plasma amino acids during the digestion of a high-protein meal can also stimulate insulin release. Insulin affects carbohydrate, amino acid (protein), and lipid metabolism during the absorptive period, and it is considered the primary endocrine regulator of metabolism during anabolism.

Insulin stimulates the uptake of glucose by skeletal muscle cells, where it can be used for energy or stored as glycogen (essentially a polymer of glucose molecules). The liver also stores glucose as glycogen during the absorptive period, and this is also stimulated by insulin. Primarily because the mass of skeletal muscle is greater than the liver, much more glycogen (75% of the total) is formed and stored in skeletal muscle. Blood glucose is also available for use by all cells of the body for energy during this period, but no other organ is capable of significant glycogen storage.

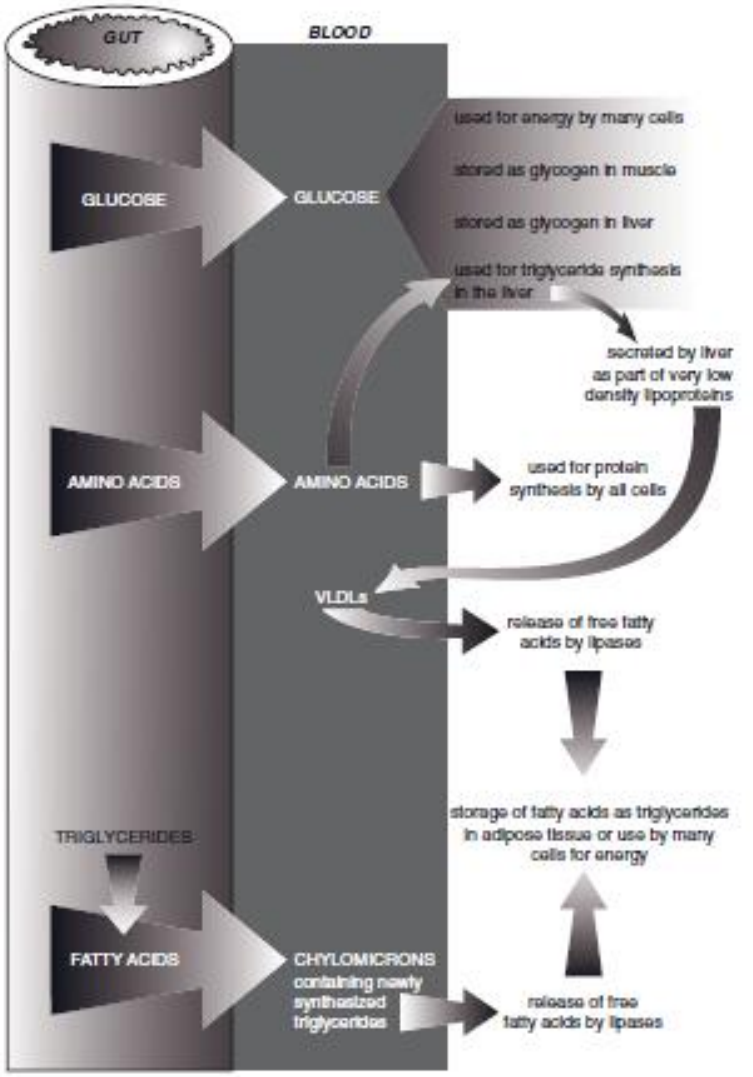

Figure 14. Summarizes the overall fate of the major nutrients absorbed during the digestion of a meal.

Absorbed amino acids are immediately available to all body cells for protein synthesis. Because all of the amino acids necessary for synthesis of a given protein must be available at the time of synthesis, it is imperative that animals have a balanced diet that contains all of the essential amino acids. Protein synthesis in many organs, including liver and skeletal muscle, is stimulated by insulin, so the increase in insulin following a meal also promotes protein synthesis during this period. However, this stimulatory effect on protein synthesis is minor compared to the effects of insulin on glucose metabolism (e.g., the rate of plasma protein production by the liver increases by only a small percentage after a meal). The amounts of amino acids absorbed after a typical meal are more than can be efficiently used by the body for protein synthesis. However, no metabolic pathways permit the various amino acids to be stored for later use the way glucose is stored as glycogen. Many of the excess amino acids are taken up by hepatocytes and enter metabolic pathways that result in triglyceride (lipid) formation. These pathways remove nitrogen-containing amino groups from the amino acids (deamination). Most of the resulting lipids are secreted by hepatocytes into the blood as part of lipoproteins (discussed later).

Deamination of amino acids is also part of a different metabolic pathway by which liver cells use amino acids to produce glucose. However, the hormone

glucagon must be available to stimulate this pathway, and glucagon release from the pancreas is reduced by increases in blood glucose. Thus, during the period that blood glucose is elevated following a meal, the use of amino acids to produce glucose is suppressed.

Gluconeogenesis is the term for the collective metabolic processes by which liver cells produce glucose from non-carbohydrate substrates, such as amino acids and short-chain fatty acids. The liver and kidneys are the only organs that are capable of any signifi cant gluconeogenesis, and the kidneys do so only in states of chronic acidosis.

During the absorptive state, the liver uses both excess glucose and amino acids as substrates for triglyceride (lipid) synthesis, and insulin stimulates these pathways. Some of the newly synthesized triglycerides are stored in the liver, but most are released into the blood in complex particles known as very low density lipoproteins (VLDLs). Lipoproteins are particles that contain lipids, cholesterol, and proteins in various ratios. VLDLs are so named because their lipid content is high relative to their protein content. Because lipids are less dense than protein, the density of VLDLs particles is quite low.

Recall that chylomicrons are also circulating lipoproteins, but the triglycerides in these lipoproteins were absorbed from the intestinal tract. As chylomicrons and VLDLs circulate throughout the body, they encounter lipoprotein lipase, an enzyme bound to endothelial cells that acts on their triglycerides to release free fatty acids. When the triglycerides are released within adipose tissue, the free fatty acids are available to adipose cells for the resynthesis and storage of lipids as triglycerides. In other organs, such as skeletal muscle, cells use the free fatty acids for energy. The synthesis and storage of triglycerides in adipose tissue is stimulated by insulin, which is typically elevated during the absorptive period.

After losing triglycerides by the action of lipoprotein lipase, some VLDLs undergo changes in the circulation and become a different type of lipoprotein, low-density lipoprotein (LDL). LDLs contain a great deal of cholesterol, and cells throughout the body receive cholesterol from the blood by the endocytosis of LDLs. Cholesterol is a necessary component of cell membranes, and all cells need some cholesterol. However, abnormal increases in LDL levels are associated with an increased risk of cardiovascular disease in humans. Recall that the original VLDLs were produced in the liver, so much of the cholesterol in the blood is produced by the liver.

Postabsorptive state: catabolism.

After a meal has been digested and absorbed, blood glucose concentration gradually decreases as glucose is used for energy throughout the body (Fig 15). This drop in blood glucose is the primary event bringing about the changes in endocrine secretions that orchestrate the metabolic changes during the postabsorptive state. Two major endocrine changes are a gradual drop in insulin secretion and a rise in the release of glucagon. Recall that increases in blood glucose stimulate insulin release from β-cells, whereas decreases in blood glucose stimulate glucagon release from α-cells in pancreatic islets.

During the absorptive period, when glucose and amino acids were being absorbed into the blood from the intestinal tract, insulin stimulated the synthesis of glycogen for glucose storage, proteins, and lipids (from any excess glucose and amino acids). As insulin levels decrease, its stimulatory effect on these synthetic

(anabolic) processes is lost, and this is a major factor in changing the overall metabolic balance from anabolism to catabolism. Glucagon stimulates the breakdown of glycogen (glycogenolysis) in the liver to provide glucose that the liver can release into the blood. Glycogenolysis is the initial process by which the liver derives glucose to add to the blood, but later the liver also releases glucose formed by gluconeogenesis, which is also stimulated by glucagon. The amino acids used for gluconeogenesis are derived from the catabolism of body protein.The maintenance of a minimal or fasting blood glucose level during this period has primary importance to neuronal function. Neurons do not have the metabolic processes to permit them to use fatty acids for energy, so they need a ready supply of glucose for cell energy.

During fasting, the catabolism of adipose tissue increases the supply of fatty acids, which are used by cells other than neurons for energy. The increased use of fatty acids by other cells reduces the overall need for glucose and conserves it for use by neurons. This conservation of glucose is termed glucose sparing. The liver also metabolizes the circulating fatty acids to produce ketones, another cellular energy substrate. The ketones produced by the liver include acetone, acetoacetate, and β-hydroxybutyrate.

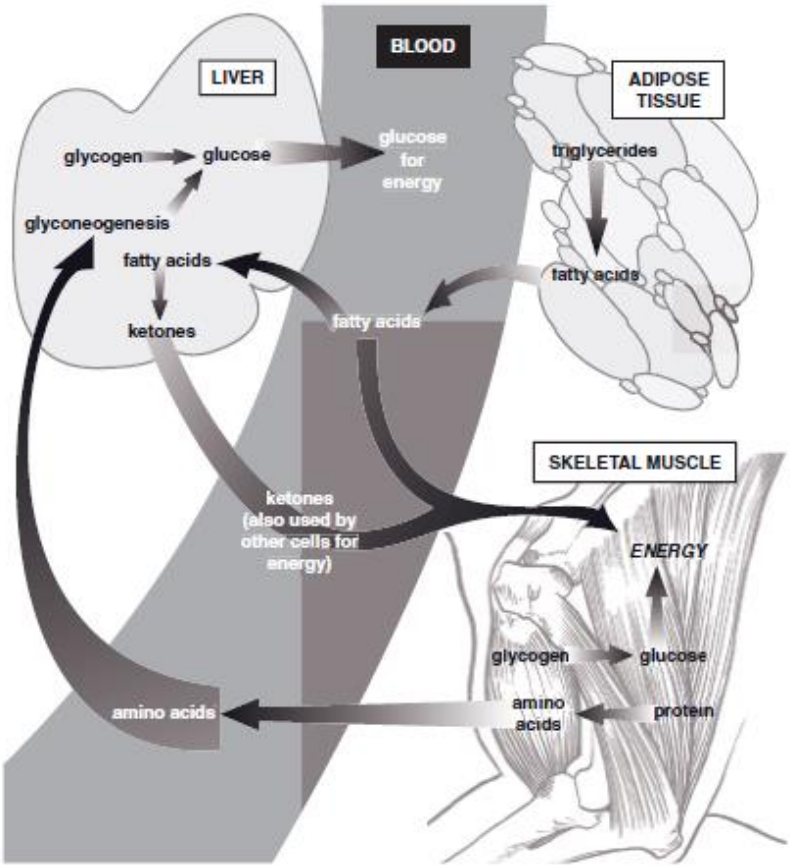

Figure 15. Summary of metabolic organs and mechanisms that maintain blood glucose and provide energy for cells when nutrients are not being absorbed from the gastrointestinal tract.

Two other hormones, growth hormone and glucocorticoids from the adrenal cortex, also contribute to the maintenance of blood glucose and other sources of energy during anabolic periods. Glucocorticoids do not increase in the circulation during a short fast, but a deficit of glucocorticoids reduces the rate of liver gluconeogenesis and mobilization of fatty acids from adipose tissues. The effect of

glucocorticoids on these processes during fasting is a permissive effect. Decreases in blood glucose stimulate the release of growth hormone, which increases the mobilization of fatty acids from adipose (lipolysis). Some tissues (e.g., skeletal muscle) can use the fatty acids for energy (glucose sparing), and the liver can further increase its production of ketones.

Protein metabolism, its regulation. Nitrogen balance, essential amino acids.

Protein metabolism consists of a cycle of breaking down proteins, synthesizing new ones and removing nitrogenous waste products that result from these reactions. The amount of protein needed to balance this cycle changes throughout an individual' life. Growing children who are creating new muscle and bone, for example, have higher protein needs than adults.

During digestion, proteins are hydrolyzed into amino acids, which are then absorbed by the capillaries of villi and enter the liver via the hepatic portal vein. Amino acids, under the influence of human growth hormone and insulin, enter the body cells by active transport. Inside cells, amino acids are synthesized into protein that function as enzymes, transport molecules, antibodies, clotting chemicals, hormones, contractile elements in muscle fibers and structural elements such as hair. They may also be stored as fat or glycogen or used for energy.

Protein catabolism. Before amino acids can be catabolized, they must be converted to substances that can enter the TCA cycle. These conversions involve deamination, decarboxylation, and hydrogenation.Amino acids can be converted into glucose, fatty acids and ketone bodies.

Protein anabolism. Involves the formation of peptide bonds between amino acids to produce new proteins. Protein synthesis is stimulated by human growth hormone, thyroxine, and insulin. Protein synthesis is carried out on the ribosomes of almost every cell in the body, directed by the cells' DNA and RNA.

Nitrogen balance. Balance is determined by comparing the amount consumed by the animal to the amount used or lost from the body. For example, because proteins are the primary nitrogencontaining nutrient, nitrogen balance is often used as an indicator of the status of protein metabolism. Nitrogen is a fundamental component of amino acids, which are the molecular building blocks of protein. Therefore, measuring nitrogen inputs and losses can be used to study protein metabolism. If an animal consumes more nitrogen than it excretes, it is said to be in a positive nitrogen balance, indicating that the animal is synthesizing more body proteins than are being degraded and lost from the body. Young, growing animals are typically in positive nitrogen balance. Positive nitrogen balance is associated with periods of growth, hypothyroidism, tissue repair, and pregnancy. This means that the intake of nitrogen into the body is greater than the loss of nitrogen from the body, so there is an increase in the total body pool of protein. During prolonged starvation, an animal is in negative nitrogen balance, for body proteins are broken down to provide energy, and the resulting nitrogen is excreted in the urine. Negative nitrogen balance is associated with burns, serious tissue injuries, fevers, hyperthyroidism, wasting diseases, and during periods of fasting. This means that the amount of nitrogen excreted from the body is greater than the amount of nitrogen ingested. A negative nitrogen balance can be used as part of a clinical evaluation of malnutrition.

Amino acids. The main amino acids involved are serine, histidine, and aspartic acid. They all play a role in cleaving the peptide bond. These three amino acids are known as the catalytic triad which means that these three must all be present in order to properly function. Metabolic uses of amino acids building blocks for protein synthesis, precursors of nucleotides and heme, source of energy, neurotransmitters, precursors of neurotransmitters and hormones.

Amino acid metabolism is reprogrammed due to its important role in energy metabolism abnormity in tumor cells. Being the most prominent part in tumor-specific amino acid metabolic pathways, glutamine, the second important energy resource of tumor cells, produces abundant ATP for tumor growth. Of the 20 amino acids in your body, 10 are referred to as «essential» amino acids. These amino acids cannot be synthesized by the human body from molecules present within the body. Foods containing these amino acids are «essential» for human growth and must be part of the diet. Non essential amino acids CAN be synthesized by body cells by a process called transamination. Once the appropriate essential and nonessential amino acids are present in cells, protein synthesis occurs rapidly.

Carbohydrate metabolism, its regulation.

Carbohydrate metabolism, is the whole of the biochemical processes responsible for the metabolic formation, breakdown, and interconversion of carbohydrates in living organisms. Plants synthesize carbohydrates from carbon dioxide and water through photosynthesis, allowing them to store energy absorbed from sunlight internally. When animals and fungi consume plants, they use cellular respiration to break down these stored carbohydrates to make energy available to cells. Both animals and plants temporarily store the released energy in the form of high-energy molecules, such as ATP, for use in various cellular processes. Digestion breaks down complex carbohydrates into a few simple monomers (monosaccharides) for metabolism: glucose, fructose, and galactose. Glucose constitutes about 80% of the products and is the primary structure that is distributed to cells in the tissues, where it is broken down or stored as glycogen. In aerobic respiration, the main form of cellular respiration used by humans and animals, glucose and oxygen are metabolized to release energy, with carbon dioxide and water as byproducts. Most of the fructose and galactose travel to the liver, where they can be converted to glucose. Glucose metabolism helps with energy production, hormone regulation, and energy storage.

Glucose anabolism includes glycogenolysis, glycogenesis, gluconeogenesis. During digestion, polysaccharides are converted to monosaccharides (primarily glucose), which are absorbed through capillaries in villi and transported to the liver via the hepatic portal veins. Glucose is the body's preferred source for synthesizing ATP. If cells require immediate energy, glucose is oxidized by the cells to produce ATP. Glucose can also be used to form amino acids, which then can be incorporated into proteins. Excess glucose can be stored by the liver (25%) and skeletal muscle (75%) as glycogen (how animals store carbohydrate) in a process called glycogenesis. If glycogen storage areas are filled up, (they hold about 1.1 pounds of glycogen), liver cells and fat cells convert glucose to glycerol and fatty acids that can be used for synthesis of triglycerides in a process called lipogenesis.

Glycogenolysis – is the process of breaking down of glycogen, the conversion of glycogen back into glucose. In the liver, muscles, and the kidney, this process occurs to provide glucose when necessary. Glucagon in the liver stimulates glycogenolysis when the blood glucose is lowered, known as hypoglycemia.The glycogen in the liver can function as a backup source of glucose between meals. This process occurs between meals and is stimulated by glucagon and epinephrine. Adrenaline stimulates the breakdown of glycogen in the skeletal muscle during exercise.In the muscles, glycogen ensures a rapidly accessible energy source for movement.

Glycogenesis refers to the process of synthesizing glycogen, the conversion of glucose to glycogen for storage in the liver and skeletal muscle. In humans, excess glucose is converted to glycogen via this process. Glycogen is a highly branched structure, consisting of glucose. Glycogenesis occurs primarily in the liver, skeletal muscles, and kidney. The process is stimulated by insulin.

Gluconeogenesis is the conversion of protein or fat molecules into glucose, the reverse process of glycolysis. It involves the conversion of non-carbohydrate molecules into glucose.This process occurs when there are lowered amounts of glucose. The liver is the primary location of gluconeogenesis, but some also occurs in the kidney. Glycerol from fat can be converted to glyceraldehyde-3-phosphate and some amino acids may be converted to pyruvic acid. Both of these compounds can enter the TCA cycle to provide energy. This pathway is regulated by multiple different molecules. Glucagon, adrenocorticotropic hormone, and ATP encourage gluconeogenesis.Gluconeogenesis is inhibited by AMP, ADP, and insulin.

Glucose catabolism. Glucose oxidation is also called aerobic or cellular respiration. It occurs in every cell of the body (except red blood cells because they lack mitochondria), and provide the cells main source of energy.The complete (aerobic) oxidation of glucose to CO_2, H_2O results in large amounts of energy (ATP) and occurs in successive stages: glycolysis, formation of acetyl coenzyme A, the tricarboxylic acid cycle and the electron transport system. **Glycolysis** is the process of breaking down a glucose molecule into two pyruvate molecules, while storing energy released during this process as ATP and NADH. Nearly all organisms that break down glucose utilize glycolysis. This pathway is common to both anaerobic and aerobic respiration. Glycolysis consists of ten steps, split into two phases.

The pentose phosphate pathway is an alternative method of oxidizing glucose. It occurs in the liver, adipose tissue, adrenal cortex, testis, milk glands, phagocyte cells, and red blood cells.It produces products that are used in other cell processes, while reducing NADP to NADPH.This pathway is regulated through changes in the activity of glucose-6-phosphate dehydrogenase.

Blood glucose in ruminants.

In ruminants: fibrous feeds containing cellulose and hemicellulose and grains rich in starch are the primary carbohydrate sources. Ruminants have most of their dietary carbohydrates (e.g., starch and cellulose) fermented in the rumen by microorganisms, and only 5 to 20% of consumed dietary carbohydrates are digested in the small intestine. The major source of energy to the ruminant is the VFA absorbed from the rumen and other parts of the digestive tract.

Normal ranges for blood glucose levels in mature ruminants are lower than in other animals, even other herbivores (cattle, 45 to 80 mg/dL; dog, 70 to 110 mg/dL; and horse, 60 to 110 mg/dL). The lower normal range for mature ruminants is associated with the relatively small amount of glucose-yielding carbohydrate digestion in their small intestine. Most of the carbohydrates that they consume undergo fermentative digestion in the forestomach and result in the production of short-chain volatile fatty acids, which are absorbed directly from the forestomach.

Without glucose readily available via absorption from the gastrointestinal tract, ruminants must have a continuous and a relatively high rate of gluconeogenesis in the liver to maintain the blood glucose level. Glucagon appears to be an important endocrine stimulant to maintain this rate of gluconeogenesis. Rising levels of amino acids and propionic acid (a volatile fatty acids produced in the rumen) can stimulate glucagon release, so presumably the continual absorption of these from the ruminant gastrointestinal tract can maintain glucagon secretion. Propionic acid is the one of the three major volatile fatty acids produced in the rumen that can be used by the liver for gluconeogenesis.

Ketosis is a metabolic state characterized by an increase in blood ketones, a reduction in urine and blood pH, and ketones in the urine. The increase in the acidic ketones in the blood and urine are responsible for the changes in pH. Ketosis may occur when fatty acid mobilization from adipose tissue is elevated and glucose is deficient. The deficiency in glucose stimulates the release of glucagon and inhibits insulin release, and the increased ratio of glucagon to insulin promotes the formation of ketones by the liver from readily available fatty acids. Ketosis may develop in dairy cattle at the peak of lactation, when the need for glucose to synthesize lactose (milk sugar) is maximal. The rapid use of glucose by the mammary glands reduces blood glucose and brings about these changes in glucagon and insulin. Ketosis may also develop as a result of type I diabetes mellitus, in which the primary problem is a deficiency of insulin. In this case, the dominant effects of glucagon on fatty acid mobilization and ketone synthesis are primarily responsible for the development of the ketosis.

Lipid metabolism, its regulation.

Lipid metabolism is the synthesis and degradation of lipids in cells, involving the breakdown or storage of fats for energy and the synthesis of structural and functional lipids, such as those involved in the construction of cell membranes. In animals, these fats are obtained from food or are synthesized by the liver. Lipogenesis is the process of synthesizing these fats. The majority of lipids found in the human body from ingesting food are triglycerides and cholesterol.Types of lipids found in the body are fattyacids and membrane lipids.

Lipid metabolism is often considered as the digestion and absorption process of dietary fat; however, there are two sources of fats that organisms can use to obtain energy: from consumed dietary fats and from stored fat. Vertebrates (including humans) use both sources of fat to produce energy for organs such as the heart to function. Since lipids are hydrophobic molecules, they need to be solubilized before their metabolism can begin. Lipid metabolism often begins with hydrolysis, which occurs with the help of various enzymes in the digestive system.The second step after the hydrolysis is the absorption of the fatty acids into the epithelial cells of the

intestinal wall. In the epithelial cells, fatty acids are packaged and transported to the rest of the body.

Lipid metabolism entails the oxidation of fatty acids to either generate energy or synthesize new lipids from smaller constituent molecules. Lipid metabolism is associated with carbohydrate metabolism, as products of glucose (such as acetyl CoA) can be converted into lipids. Triglyceride broken down into a monoglyceride A triglyceride molecule (a) breaks down into a monoglyceride (b). Lipid metabolism begins in the intestine where ingested triglycerides are broken down into smaller chain fatty acids and subsequently into monoglyceride molecules by pancreatic lipases, enzymes that break down fats after they are emulsified by bile salts. When food reaches the small intestine in the form of chyme, a digestive hormone called cholecystokinin (CCK) is released by intestinal cells in the intestinal mucosa. CCK stimulates the release of pancreatic lipase from the pancreas and stimulates the contraction of the gallbladder to release stored bile salts into the intestine. CCK also travels to the brain, where it can act as a hunger suppressant.

Together, the pancreatic lipases and bile salts break down triglycerides into free fatty acids. These fatty acids can be transported across the intestinal membrane. However, once they cross the membrane, they are recombined again form triglyceride molecules. Within the intestinal cells, these triglycerides are packaged along with cholesterol molecules in phospholipid vesicles called chylomicrons. The chylomicrons enable fats and cholesterol to move within the aqueous environment of your lymphatic and circulatory systems. Chylomicrons leave the enterocytes by exocytosis and enter the lymphatic system via lacteals in the villi of the intestine. From the lymphatic system, the chylomicrons are transported to the circulatory system. Once in the circulation, they can either go to the liver or be stored in fat cells (adipocytes) that comprise adipose (fat) tissue found throughout the body.

Most proteins are transported in the blood in combination with proteins as lipoproteins. There are 4 classes of lipoproteins:

- ✓ chylomicrons contain triglycerides, cholesterol molecules, and other apolipoproteins (protein molecules). They function to carry these water-insoluble molecules from the intestine, through the lymphatic system, and into the bloodstream, which carries the lipids to adipose tissue for storage. They form in small intestinal mucosal cells and contain dietary lipids. They enter villi lacteals, are carried into the systemic circulation into adipose tissue where their triglyceride fatty acids are released and stored in the adipocytes and used by muscle cells for ATP production;
- ✓ VLDL's (very low density lipoproteins) transport vehicles that carry triglycerides synthesized in hepatocytes to adipocytes for storage;
- ✓ LDL's (low density lipoproteins) carry about 75% of total blood cholesterol and deliver it to cells throughout the body. When present in excessive numbers, LDL's deposit cholesterol in and around smooth muscle fibers in arteries;
- ✓ HDL's (high density lipoproteins) remove excess cholesterol from body cells and transport it to the liver for elimination.

There are two sources of cholesterol in the body: food we eat, and liver synthesis. For adults, desirable levels of blood cholesterol are under 200 mg/dL for total

cholesterol; LDL under 130 mg/dL; and HDL over 40 mg/dL. Normally, triglycerides are in the range of 10-190 mg/dL. Exercise, diet and drugs may be used to reduce blood cholesterol levels.

Fate of lipids:

- ✓ some lipid may be oxidized to produce ATP, where each unit of lipid produces twice the amount of ATP as an equivalent unit of carbohydrate;
- ✓ some lipids are stored in adipose tissue;
- ✓ other lipids are used as structural molecules or to synthesize essential molecules. Examples include phospholipids of cell membranes, lipoproteins that transport cholesterol, and cholesterol used to synthesize bile salts and steroid hormones;
- ✓ triglycerides are stored in adipose tissue, mostly in the subcutaneous layer;
- ✓ adipose cells contain lipases that hydrolyze fats into glycerol and fatty acids.

Lipid anabolism. Lipogenesis – the conversion of glucose or amino acids into lipids.

Lipid catabolis. Lipolysis – triglycerides are split into fatty acids and glycerol. As a part of normal fatty acid catabolism, ketone bodies are formed. An excess of ketone bodies (ketosis), may cause acidosis or abnormally low blood pH.

Metabolism during fasting or starvation.

Fasting means going without food for many hours or a few days. Starvation implies weeks or months of food deprivation or inadequate food intake. Catabolism of stored triglycerides and structural proteins can provide energy for several weeks. The amount of adipose tissue determines the lifespan possible without food. The average person has a 1-2 month energy reserve in adipose tissue. Initially, during fasting and starvation glucose is used for ATP production. During prolonged fasting, large amounts of amino acids from tissue protein breakdown (primarily skeletal muscle) are released to be converted to glucose in the liver by gluconeogenesis. Ketogenesis increases as catabolism of fatty acids rises. The presence of ketones reduces the use of glucose for ATP production which in turn decreases the demand for gluconeogenesis and slows the catabolism of muscle proteins.

Energy metabolism.

An important necessity of all living organisms is to obtain energy and matter. Energy is essential to drive the metabolic activities. Energy metabolism refers to all the reactions involved in generating adenosine triphosphate (ATP) from nutrients, including both aerobic respiration (oxygen present), anaerobic respiration (fermentation) as well as fatty acid and amino acid metabolism. Anabolism and catabolism are the two broad types of biochemical reactions that make up metabolism. Anabolism builds complex molecules from simpler ones, while catabolism breaks large molecules into smaller ones. Metabolism is how a cell gets energy and removes waste. Vitamins, minerals, and cofactors aid the reactions. Normal body temperature is maintained by a homeostatic balance between heat-producing and heat-losing mechanisms.

Metabolic rate – overall rate at which heat is produced. Basal metabolic rate (BMR) = measurement of the metabolic rate under basal conditions. BMR is the measure of the rate at which the quiet, resting, fasting body breaks down nutrients to liberate energy. BMR is also a measure of how much thyroxine the thyroid gland is

producing, since thyroxine regulates the rate of ATP use and is not a controllable factor under basal conditions.

Body temperature homeostasis:

- ✓ if the amount of heat production equals the amount of heat loss, a human maintains a constant core temperature of 98.6 degrees F, (37 degrees C);
- ✓ core temperature refers to the body's temperature in body structures below the skin and subcutaneous tissue;
- ✓ shell temperature refers to the body's temperature at the surface (skin and subcutaneous tissue);
- ✓ too high a core temperature kills by denaturing proteins. Too low a core temperature causes cardiac arrhythmias that can result in death.

Heat and energy balance. Heat Production.

Heat is a form of kinetic energy that can be measured as temperature and expressed in units called calories. A calorie is the amount of heat energy required to raise the temperature of 1 gram of water from 14 degrees C to 15 degrees C. Constancy of the temperature is maintained by two counteracting and predetermining processes: heat production and heat loss.

Heat production takes place in mitochondria of the cells. So, the most heat production occurs in the organs, which are rich in them, the liver, skeletal muscles, kidneys. This process is a result of continuous biochemical reactions**.** It is influenced by metabolic rate and responses that occur when body temperature starts to fall. Factors that affect metabolic rate include exercise, hormones, and the nervous system, and body temperature, ingestion of food, age, gender, climate, sleep, and malnutrition. Heat conservation mechanisms include vasoconstriction, sympathetic stimulation, skeletal muscle contraction (shivering), and thyroid hormone production. The hypothalamus is involved in thermoregulation and several negative feedback loops are involve in raising or lowering body temperature when it is too low or too high.

Chemical and physical thermoregulation.

Thermoregulation, by definition, is a mechanism by which mammals maintain body temperature by tightly controlled self-regulation, no matter the temperature of their surroundings. Temperature regulation is a type of homeostasis, which is a process that biological systems use to preserve a stable internal state to survive. Human beings have a normal core, or internal, temperature of around 37 degrees Celsius, which is equivalent to around 98.6 degrees Fahrenheit. Core temperature is most accurately measured via rectal probe thermometer. This is the temperature at which the human body’s systems work together at their optimum, which is the reason the body has such tightly regulated mechanisms.

Thermoregulation in organisms runs along a spectrum from endothermy to ectothermy. Endotherms create most of their heat via metabolic processes, and are colloquially referred to as “warm-blooded.” Ectotherms use external sources of temperature to regulate their body temperatures. Ectotherms are colloquially referred to as “cold-blooded” even though their body temperatures often stay within the same temperature ranges as warm-blooded animals.

An ectotherm, from the Greek (ektós) “outside” and (thermós) “hot,” is an organism in which internal physiological sources of heat are of relatively small or

quite negligible importance in controlling body temperature. Since ectotherms rely on environmental heat sources, they can operate at economical metabolic rates. Ectotherms usually live in environments in which temperatures are constant, such as the tropics or ocean. Ectotherms have developed several behavioral thermoregulation mechanisms, such as basking in the sun to increase body temperature or seeking shade to decrease body temperature. The common frog is an ecotherm and regulates its body based on the temperature of the external environment.

In contrast to ectotherms, endotherms regulate their own body temperature through internal metabolic processes and usually maintain a narrow range of internal temperatures. Heat is usually generated from the animal's normal metabolism, but under conditions of excessive cold or low activity, an endotherm generate additional heat by shivering. Many endotherms have a larger number of mitochondria per cell than ectotherms. These mitochondria enables them to generate heat by increasing the rate at which they metabolize fats and sugars. However, endothermic animals must sustain their higher metabolism by eating more food more often. For example, a mouse (endotherm) must consume food every day to sustain high its metabolism, while a snake (ectotherm) may only eat once a month because its metabolism is much lower.

A poikilotherm is an organism whose internal temperature varies considerably. Homeotherm, an organism which maintains thermal homeostasis. Poikilotherm's internal temperature usually varies with the ambient environmental temperature, and many terrestrial ectotherms are poikilothermic. Poikilothermic animals include many species of fish, amphibians, and reptiles, as well as birds and mammals that lower their metabolism and body temperature as part of hibernation or torpor. Some ectotherms can also be homeotherms. *For example, some species of tropical fish inhabit coral reefs that have such stable ambient temperatures that their internal temperature remains constant.* Homeotherm vs. Poikilotherm: Sustained energy output of an endothermic animal (mammal) and an ectothermic animal (reptile) as a function of core temperature. In this scenario, the mammal is also a homeotherm because it maintains its internal body temperature in a very narrow range. The reptile is also a poikilotherm because it can withstand a large range of temperatures.

The chemical and physical thermoregulatory mechanisms are distinguished.

The chemical thermoregulatory mechanisms take place by means of changes in the cell metabolism. The chemical one takes place continuously and is most significant, when the temperature of medium becomes lower than 18-20ºC. It is provided in the neuronal and humoral ways. The reflexogenic zone for the neuronal regulation is the skin, where the cold-sensitive and the heat-sensitive receptors are located. When the body surface temperature decreases the coldsensitive receptors are excited, and the impulses go through the sensory nerves towards the posterior part of hypothalamus, where the centre of chemical thermoregulation (heat production) is located. Thereafter, the impulses reach the muscles, bringing them to chaotic involuntary contractions, in a type of shivering. Herein, the metabolic processes intensify markedly, so the heat production increases. Beyond the muscles, the kidneys and the liver participate in thermoregulation as well. In cold-perception the heat production in them increases in reflector way. There is also a humoral way of

thermoregulation. The latter is provided by the hormones, increasing the metabolic processes and hence the heat production: the hormones of thyroid and adrenal glands.

The physical thermoregulation (heat loss) encounters by means of changes in the heat emission intensity.The physical thermoregulation becomes of a special significance in increase of the environmental temperature and is realized by the heat emission changes by the organism. The heat emission takes place in the following ways:

- ✓ radiation heat loss, the body gives off heat into the medium;
- ✓ convection, movement and mixing of air heated by the body;
- ✓ heat conduction, the body gives off heat to objects that are in direct contact with the body surface;
- ✓ evaporation of water from the skin and the lung surface.

In a human being at rest (the air temperature is equal to +200 C) radiation accounts for 66%, evaporation for 19% and convection for 15% of the total heat loss of the body. When the environmental temperature rises to 350 C heats can be lost mainly by evaporation of water from the surface of the skin and lungs. The latter share can increase up to 75% in intensive muscular work. It is calculated that in 1 ml of sweat evaporation 0.56 kcal of heat is released. Evaporation depends on the relative humidity of the air. In the air saturated by water vapours, e. g. in the bath there is excessive sweat production, but it does not undergo evaporation. This sweat production does not contribute to the heat loss.

The centre of physical thermoregulation (heat loss) is located in the anterior part of the hypothalamus. Heat loss process also is regulated by the neuronal and humoral pathways. In the environmental temperature increase the heat-sensitive receptors of the skin are excited, and the impulses are directed to the heat loss centre, due to which the skin vessels are dilated in reflector way and the circulating blood in them increases. This contributes to the heat loss by radiation and convection. Here, blood will be taken by the sweat glands as well, and sweat is going to be produced more. In this case the heat production is inhibited. At cold the cold-sensitive receptors are excited bringing to vasoconstriction of the skin arterioles, so the blood enters the abdominal vessels. In result the cutaneous vessels will get less blood, so the heat loss will decrease. Endocrine glands, mainly adrenals and thyroid gland also take part in the regulation of the body temperature. Beyond the neuronal and humoral regulation the blood temperature itself has a significant regulatory meaning. The blood, having higher temperature than normal, excites the heat loss centre and evokes heat loss. The blood with decreased temperature excites the heat production centre and brings to increase of metabolic processes in the organism and the heat production consequently. The above-described thermoregulatory mechanisms have an important significance in the organisms' adaptation to the altering circumstances of the external medium.

Energy needs during exercise.

The increase in skeletal muscle metabolism during exercise can rapidly deplete the glycogen stores within skeletal muscle cells. In humans these stores are capable of providing energy only for an estimated 2 to 3 minutes of very intense exercise. To sustain exercise, other energy sources must be rapidly mobilized and delivered to working skeletal muscle. Circulating levels of epinephrine and norepinephrine

increase during exercise, and these catecholamines have several actions that mobilize energy stores, including increased glycogenolysis in the liver and nonworking skeletal muscle and lipolysis in adipose tissue. Insulin levels are reduced and glucagon levels are increased during exercise, which promotes liver gluconeogenesis and more lipolysis in adipose tissue. The decrease in insulin is not detrimental to working skeletal muscle, because glucose uptake by working muscle is less insulin dependent.

Anaerobic metabolism, by working skeletal muscles, raises the rate of lactic acid production. The lactate ion can diffuse into the blood from the skeletal muscle, and plasma levels of lactate increase during strenuous and prolonged exercise. The liver can use blood lactate for gluconeogenesis, and glucose can then be returned to the blood to maintain blood glucose levels.

BIBLIOGRAPHY

1. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
2. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
3. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
4. Mazurkevich AY, Trokoz VO, editors. Physiology of farm animals. Workshop. 2nd ed. Kyiv: Center for Educational Literature; 2015. (Ukrainian).
5. Mazurkevich AY, Trokoz VO, Karpovsky VI, et al. ; edited by A.Y. Mazurkevich, V.O Trokoz. Physiology of agricultural animals. Textbook. 2nd ed. Kyiv; 2014. (Ukrainian).
6. Moyes CD, Schulte PM. Principles of Animal Physiology 3rd ed. Don Mills, Ontario: Pearson; 2016.
7. Papachristodoulou D, Snape A, Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 6th ed. Oxford, UK: Oxford University Press; 2018.
8. Pineda MH, Dooley MP, editors. McDonald's Veterinary Endrocrinology and Reproduction. 5th ed. Ames, Iowa: Iowa State Press; 2003.
9. Pollard TD, Earnshaw WC, Lippincott-Schwartz J, Johnson GT, editors. Cell Biology. 3rd ed. Elsevier. 2016.
10. Reddy PB. Text book of Animal Physiology. Andhra Pradesh, India: IMRF Publications; 2015.
11. Reece WO, Functional Anatomy and Physiology of Domestic Animals. 4th ed. Baltimore: Wiley-Blackwell; 2009.
12. Rhoades RA, Pflanzer RG. Human Physiology. 4th ed. Pacific Grove, Calif.: Brooks/Cole; 2003.
13. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
14. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.
15. Smith BP. Large Animal Internal Medicine. 3rd ed. St. Louis, Missouri: Elsevier Mosby; 2015.

16. Tortora GJ, Derrickson BH. Principles of Anatomy and Physiology. Atlas and Registration Card. 11th ed. Hoboken, NJ: John Wiley & Sons; 2005.

CHAPTER 11. PHYSIOLOGY OF DIGESTION

Types of nutrition. Steps in nutrition.

For normal metabolism, cells of an animal's body need the three major classes of nutrients (carbohydrates, proteins, and lipids) delivered to them via the blood in their simplest forms (monosaccharides, amino acids, and fatty acids). Animals consume foodstuffs that contain these nutrients in more complex chemical and physical forms.

The materials required for the growth and metabolism are known as **nutrients.**

The process by which the animal obtains these nutrients is known as **nutrition.**

Most of the animals are heterotrophs (hetero= different, trophic=nutrition). It means that animals depend on others for their food.

Types of nutrition:

- ✓ autotrophic nutrition, in this method, the organism can obtain the food from sun light. *Eg. Euglena (photo synthesis) or from chemicals (chemosynthesis) Eg. Bacteria*;
- ✓ heterotrophic nutrition, in this method, animals depend on other organisms for its food. It is the characteristic feature of animals. On the basis of nature of food it is of following types;
- ✓ herbivores (Herb=plant, vore=to eat), their food mainly consists of plant material. *Ex. Cow;*
- ✓ carnivores (Cornis= flesh), their food mainly consists of flesh. *Ex. Tiger;*
- ✓ omnivores (Omni= all), their food consists of both plant and animal materials. *Ex. Man, Cockroach;*
- ✓ detrivores, they mainly feed upon dead organic matter. *Ex. Eartworm;*
- ✓ predators, they obtain the food by hunting and killing the animal. *Ex. Tiger, Eagle*;
- ✓ scavengers, they mainly feed upon other dead animals;
- ✓ insectivores, they feed on insects. *Ex. Manis (ant eater);*
- ✓ osmotrophic, they feed on pre digested food by diffusion. *Ex.Taenia solium;*
- ✓ parasitic, they depend for the food on their host. *Ex. Ascaris*;
- ✓ larvivorous, they feed upon larvas.*Fishes*;
- ✓ sanguivorous, they feed upon blood. *Ex.Leech,Mosquito*;
- ✓ coprophagous, their food consists of faecal matter. *Ex.rabbit,Pig*.

Steps in nutrition:

1. Ingestion / prehension: intake of the food into the mouth or entry of food in the digestive system.
2. Digestion: breaking of complex and large molecules into simple soluble components. Mastication and the mixing of the water, acids, bile and enzymes in the stomach and intestine to break down complex molecules into simple molecules.

3. Absorption: entry of the digested food from the intestine into blood. The simple molecules (nutrients) from the digestive system enter into the circulatory and lymphatic capillaries through osmosis, active transport, and diffusion.
4. Assimilation: reuse of simple components into complex components in the cell. This process occurs according to the necessity of the cell.
5. Egestion: this is the final step. The elimination of undigested food as faeces is known as egestion. Elimination of solid waste material /Removal of undigested materials from the digestive tract through defecation.

Types of digestion. Functions of the digestive system.

Digestion is the breakdown of food into smaller components that can be more easily absorbed and assimilated by the body.

Types of digestion:

- ✓ intracellular: it occurs inside the food vacuoles of the cell. Digested food diffused into cytoplasm. It is primitive and less efficient;
- ✓ extracellular: it occurs outside the cell or gut lumen. It is found in higher animals. Digested materials are absorbed into the cell. It is more complex but efficient.

Functions of the digestive system. Its primary functions are prehension, mastication, digestion, and absorption of food, and elimination of solid wastes. The digestive system reduces the nutritious constituents of the food to molecular compounds that are small enough to be absorbed and used for energy and for building other compounds for incorporation into body tissues. It is the function of the gastrointestinal tract to reduce the consumed foodstuffs to simpler molecules and to transfer them to the blood so that they can be delivered to the cells for metabolism. Based on how food is broken down it is divided into two types. The processes of physical and chemical breakdown of foodstuffs are termed mechanical and chemical digestion, respectively.

Mechanical digestion. It occurs mainly in oral cavity. It refers to the physical breakdown of large pieces of food into smaller pieces by chewing. **Chemical digestion**. The breakdown of large pieces of food into smaller pieces with help of enzymes. In addition to monosaccharides, amino acids, and fatty acids, the gastrointestinal tract must absorb other essential minor nutrients (e.g., salts, vitamins), so that they are available to the cells of the body.

Organization of the digestive system. Gastrointestinal motility and its regulation.

The digestive system (digestive tract) consists of a muscular tube lined with mucous membrane that is continuous with the external skin at the mouth and at the anus. Elements of the digestive system are the mouth, pharynx, esophagus, forestomach (ruminants), glandular stomach, small intestine, large intestine, rectum, and the accessory glands (salivary glands, liver, and pancreas).

The gastrointestinal tract is essentially a long, smooth muscle tube extending from mouth to anus. The tube has two distinct layers of smooth muscle in its wall (circular and longitudinal layers) and is lined with epithelia that function as selective barriers between the lumen and the body fluids. The anatomic and functional characteristics of the mucosa and its epithelia vary greatly among segments of the intestine. Indigestible substances or items (such as a coin) can pass through the tract

without being altered and without affecting the animal if they are not large enough to impair movement of the other contents.

The smooth muscle in the wall of the gastrointestinal tract provides the force to move digesta through the tract; **gastrointestinal motility** is the general term used to describe the activity of this smooth muscle. Gastrointestinal motility is primarily regulated by three mechanisms:

- ✓ autonomic nervous system;
- ✓ gastrointestinal hormones;
- ✓ enteric nervous system.

Gastrointestinal hormones are released from endocrine cells in the epithelial lining of the gastrointestinal tract (enteroendocrine cells) and may stimulate or inhibit gastrointestinal smooth muscle. The release of these hormones is usually in response to digesta in the lumen of the tract. Thus, these hormones are a means of local regulation that is coordinated with the ingestion and digestion of food. The enteric nervous system consists of neural plexuses between layers of smooth muscle in the wall of the tract. These plexuses contain complete neurons (dendrites, cell bodies, and axons) that can form complete neural and reflex circuits in the wall of the tract so that neural regulation can be independent of external innervation. The presence of food and distension of gastrointestinal tract segments act as stimuli to initiate activity of the enteric nervous system. The three regulatory mechanisms (autonomic nervous system, gastrointestinal hormones, and enteric nervous system) also regulate secretions from glands in the wall of the gastrointestinal tract and the intestinal accessory organs (salivary glands, liver, and pancreas).

All three of these mechanisms may regulate a given intestinal segment or accessory organ, but the relative importance of each varies among the segments of the gastrointestinal tract and the accessory organs. For example, salivary secretion is almost entirely regulated by the autonomic nervous system, whereas gastrointestinal hormones are primary in the initiation of bile secretion.

Regulation of food intake. Two centers in the hypothalamus related to regulation of food intake are the feeding (hunger) center and the satiety center. The feeding center is constantly active but can be inhibited by the satiety center. Stimuli that affect the feeding and satiety centers are: glucose, amino acids, lipids, body temperature, distention of the GI tract and the hormone cholecystokinin.

Digestive hormones.

There are at least five hormones that aid and regulate the digestive system in mammals. There are few variations across the vertebrate group.

- ✓ gastrin: secreted by the gastric glands of stomach. Stimulates the glands to secrete inactive pepsinogen. Secretion of gastrin is stimulated by the presence of food in the stomach. The secretion is inhibited by low pH;
- ✓ secretin: produced in the duodenum and signals the secretion of sodium bicarbonate in the pancreas. It stimulates the bile secretion in the liver. This hormone responds to the acidity of the chime;
- ✓ cholecystokinin (CCK): produced in the duodenum and stimulates the release of digestive enzymes in the pancreas. Also stimulates the emptying of bile in the gall bladder. This hormone is secreted in response to fat in chime;

- ✓ gastric inhibitory peptide (GIP): also produced in the duodenum and decreases the stomach mixing in turn slowing the emptying in the stomach. Another function is to induce insulin secretion;
- ✓ motilin: produced in the duodenum. Increases the gastrointestinal motility and stimulates the production of pepsin.

Pregastric physiology. Organization of the mouth. Prehension and chewing in different animals.

The mouth is used primarily for holding, grinding, and mixing food with saliva but may also be used to manipulate the environment (through grasping of objects) and as a defensive and offensive weapon. The entrance into the mouth is defined by the lips (labia), the appearance and mobility of which vary among species. The external parts of the lips are covered by typical haired skin, which changes to mucous membrane at the mucocutaneous junction of the labial margins. The upper lip of small ruminants is deeply grooved with a midline philtrum. Lips are densely innervated by sensory fibers, making them very sensitive tactile organs. The lips of sheep, goats, and horses are soft and flexible and aid in picking up food, whereas those of cattle and hogs are stiffer and less mobile.

Tongue manipulates food for chewing/swallowing. Moreover, it is the main taste organ, covered in taste buds. The tongue is covered with thick keratinized stratifi ed squamous epithelium. The surface is characterized by a large number of projections, the papillae, which are particularly well developed on the dorsal surface. Filiform, fungiform, and vallate papillae are found in all domestic animals, and foliate (листоподібні) papillae are present in the horse, pig, and dog, but not in ruminants. Ruminants additionally have large conical papillae. The filiform and conical papillae do not bear taste buds (cells specialized for gustation), but all other types of papillae do. Taste buds may also be found on the epiglottis, larynx, pharynx, and soft palate.

Prehension and chewing. The act of bringing food into the mouth is **prehension**. The teeth, lips, and tongue are used as prehensile organs by domestic animals. The lips of the horse, the tongue of the cow and sheep, and the snout of the pig are used extensively in obtaining food.

Teeth help in **chewing** (mastication) of food. The type of teeth, arrangement of jaws, and chewing habits vary with the species and the food. Carnivorous animals have simple teeth and tear their food but do little grinding. Herbivorous animals have at least some hypsodont teeth; the upper jaw is wider than the lower jaw; and chewing of the food is thorough. Chewing can be controlled voluntarily, but the presence of food in the mouth will stimulate reflex chewing.

Salivary glands. Salivary secretion in different animals and its control.

The salivary glands of domestic farm animals comprise three pairs of well-defined glands as well as scattered lobules of salivary tissue (minor salivary glands). The chief salivary glands are the parotid (largest and present in the cheek region near the ear), mandibular (present towards posterior end of the lower jaw), and sublingual (smallest and present beneath the tongue). In man and domestic animals 3 types of salivary glands are present. But in rabbit it is of 4 types.

The minor salivary glands include labial, buccal, lingual, and palatine glands. The salivary glands are classified as serous, mucous, or mixed. Serous glands secrete a watery clear fluid, as compared with mucous glands, which secrete mucus, a viscous material that acts as a protective covering for the surface of mucous

membranes. A mixed gland produces both mucous and serous fluids. The parotid salivary gland secretes primarily serous saliva; mandibular and sublingual glands are classified as mixed glands in domestic farm animals. Most of the minor salivary glands have a mucous secretion.

Saliva keeps oral cavity moist and begins the process of digestion with amylase or ptyalin. Saliva consists of water (99,2-99,4 %), electrolytes, mucus, and enzymes. The water and mucus soften and lubricate the ingesta to facilitate chewing and swallowing. The starch-digesting enzyme amylase is present in the saliva of omnivores (pig) and to a limited degree in horses but absent in ruminants and carnivores (dog). pH is 7,32-8,00. Salivary amylase is the main enzyme that acts upon starch. The breakdown of starch into smaller pieces (glucose) is provided with help of salivary amylase. (*If you chew bread for sometime you feel sweet taste in your mouth)*. Lysozyme is a salivary enzyme with antibacterial actions (kills harmful bacteria).

Adult cattle may secrete up to 90- 180 L of saliva per day as compared to 1–2 L per day for humans, horses— 40 L, pigs — 15 L, sheep – 6-10 L.

This large volume maintains the fluid consistency of the rumen contents, and components of the saliva may also prevent frothing of the rumen fluid. Ruminant saliva has a relatively high pH and contains high concentrations of bases (bicarbonate and phosphate). These bases neutralize acids produced by fermentation in the rumen so that the pH in the rumen does not become too acidic.

Salivary secretion and its control. Salivary secretion is controlled by ANS. Parasympathetic nerves are the efferent limbs of neural reflexes that regulate salivary secretion. Afferent inputs that stimulate salivary secretion include sight and smell of food, presence of food in the oral cavity, and conditioned reflexes, where some event is associated with food and feeding. Conditioned reflex control of salivation was the subject of the classic studies by Pavlov, who conditioned dogs to salivate at the sound of a bell.

Swallowing and its regulation.

Deglutition, the act of swallowing, is arbitrarily divided into three stages. The first stage is passage of food or water through the mouth; the second is passage through the pharynx; and the third consists of passage through the esophagus into the stomach.

The first stage of swallowing is under voluntary control. After the food is chewed and mixed with saliva, a bolus (rounded mass of food) forms and is moved to the upper surface of the tongue. The tongue is raised against the hard palate (tip first) to push the bolus toward the pharynx. At the same time the soft palate is raised, closing the caudal nares. The base of the the bolus through the pharynx. Respiration is reflexively inhibited, and the larynx reflexively closes and pulls up and forward. The base of the tongue folds the epiglottis over the laryngeal opening as it moves back. The pharynx shortens, and a peristaltic (milking) action of the pharyngeal muscles forces the bolus into the esophagus. The third stage of deglutition consists of reflex peristalsis of the esophagus initiated by the presence of food in the esophagus. Peristalsis consists of alternate relaxation and contraction of rings of muscle in the wall coupled with regional contraction of longitudinal muscles in the area of the bolus. Peristalsis carries solid and semisolid food through the esophagus of the horse at 35 to 40 cm/second. Liquids travel about five times as fast by a squirting action of the mouth and the pharynx.

In conclusion: digestion begins in the mouth with the secretion of saliva and its digestive enzymes. Food is converted into a bolus by the mechanical mastication and swallowed into the esophagus.

Vomiting and its regulation.

Vomiting (emesis) is a protective response to remove potentially harmful ingesta from the stomach and upper small intestine. Vomiting is a highly coordinated reflex that is controlled by a refl ex center in the brainstem. Drugs that stimulate this center to produce vomiting are termed emetics. The process begins with relaxation of the sphincter between the stomach and upper small intestine and reverse peristalsis to move intestinal contents to the stomach. The movement of stomach contents into the esophagus and out of the mouth requires relaxation of the upper and lower esophageal sphincters together with an inspiratory movement against a closed glottis and forceful contraction of abdominal muscles. Closure of the glottis and movement of the soft palate prevent regurgitated food from entering the trachea and nasal cavity, respectively.

Gastric physiology. Nonruminant stomach. Gastric glands and secretions.

In nonruminants (horse and pig), the stomach is just caudal to the left side of the diaphragm. It is sometimes described in these species as a simple stomach. The old term monogastric is discouraged because it perpetuates the misconception that ruminants possess more than one stomach, although the ruminant actually has a single stomach with multiple compartments. The simple stomach is grossly subdivided into the cardia (entrance), fundus, body, and pyloric region (out flow); the pyloric region features a dense, palpable sphincter muscle called the pylorus that controls gastric emptying into more distal parts of the digestive tract (Figure 16). The esophagus joins the stomach at the cardia, a part of the stomach so named because of its proximity to the heart. The walls surrounding the cardia (where the lumen of the esophagus becomes continuous with that of the stomach) feature a thickening of the muscle that constitutes a functional sphincter, the cardiac sphincter. This muscle is especially well developed in the horse, where its strength and configuration make it difficult or impossible for the horse to vomit.

The large bulge near the cardia is the fundus. In the horse, the fundus is enlarged to create a blind sac, the saccus cecus, the mucosa of which is stratifi ed squamous and nonglandular. The porcine stomach features a similar albeit smaller outpocketing called the gastric diverticulum; the mucosa of this feature of the pig stomach is of the typical glandular, columnar type. The body of the stomach is the expansile part that is defi ned externally by the greater curvature.

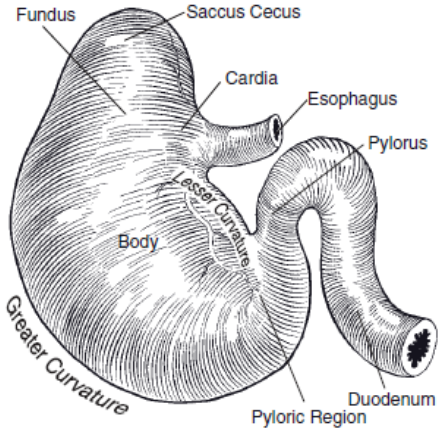

Figure 16. The simple stomach.

The lumen of the simple stomach features several histologically distinct regions whose names are similar to the gross parts of the stomach but that unfortunately do not directly correspond to these. Exclusive of the esophageal region, the mucosa of the simple stomach is glandular. Grossly, the mucosa here is thrown into prominent gastric folds that allow the stomach volume to expand to accommodate meals. On the microscopic level, the columnar epithelium of the tunica mucosa undulates in deep infoldings that create depressions called gastric pits.

The cardiac glands that give this region its name are short, branched tubular glands whose major secretory product is mucus. The equine cardiac gland region is small, but it covers nearly half of the interior of the porcine stomach.The fundic gland region lines much of the interior of the stomach (and certainly more than just the fundus). The typical gland is the fundic gland (also called the gastric gland proper). Fundic glands are simple tubular glands that open into the gastric pits, where they discharge their secretions. The pyloric gland region corresponds more or less to the pyloric region of the simple stomach. The pyloric glands are histologically similar to the cardiac glands, and like them, they secrete mucus.

Enteroendocrine cells are scattered throughout the mucosa of the glandular stomach. These secrete hormones that affect the secretory and muscular activity of the gut and its accessory organs (e.g., liver and pancreas).

Gastric juice. The regulation of gastric juice secretion.

The term gastric juice refers to the combination of substances secreted into the stomach lumen by gastric glands, also termed gastric pits because of their pitlike extension into the wall of the stomach, and epithelial cells of the stomach mucosa. Gastric juice contains water, hydrochloric acid, mucus, intrinsic factor, pepsinogen (an inactive form of pepsin, a proteolytic enzyme), and the enzyme rennin. pH of gastric juice is 0,8- 2,5.

The regulation of gastric juice secretion has three phases:

- ✓ cephalic phase: occurs at the head region. Thought and smell of food stimulate the cerebral cortex which is transferred to the hypothalamus and medulla oblongata. Then after it is routed through the vagus nerve and release of acetylcholine. Gastric secretion at this phase rises to 40% of maximum rate;
- ✓ gastric phase: takes 3 to 4 hours. It is stimulated by expansion of the stomach. Presence of food in stomach and decrease in pH stimulates the secretion of gastric juices;
- ✓ intestinal phase: has two parts, the excitatory and the inhibitory. Partially digested food fills the duodenum. This triggers intestinal gastrin to be released. Enterogastric reflex inhibits acetylcholine of vagus. Pyloric sphincter get tighten to prevent more food from entering, and inhibits local reflexes.

Stimulation of gastric secretions during the cephalic phase is in response to the sight, smell, or taste of food. These induce a neural response that increases parasympathetic (vagal nerve) stimulation to the stomach, and this stimulates gastric secretions. The gastric phase begins when food enters the stomach. The presence of food, especially proteins, stimulates the secretion of the hormones gastrin and histamine from cells in the gastric epithelium. Gastrin and histamine stimulate parietal cells in gastric glands to secrete hydrochloric acid. Acetylcholine (parasympathetic neurotransmitter) also stimulates parietal cells to secrete

hydrochloric acid, but all three regulators (gastrin, histamine, and acetylcholine) must be present for the most efficient hydrochloric acid secretion. The histamine receptors on parietal cells (H2 receptors) are different from those on cells involved in allergic reactions (H1 receptors). The specific H2 receptor antagonists provide a means to reduce acid secretion with few side effects. The antihistamines used for allergies do not bind to H2 receptors and thus do not disturb digestion. The hormones cholecystokinin, gastric inhibitory peptide, and secretin inhibit hydrochloric acid secretion. These hormones are released from the duodenal epithelium in response to the presence of food in the duodenum. The release of these hormones that act to inhibit gastric function is part of the intestinal phase of gastric regulation.

The pH of gastric juice in mammals can be 2 or less. The low pH is protective in that most foreign microbes ingested with food cannot survive such an acidic environment. The low pH inhibits hydrochloric acid secretion to prevent it from becoming too acidic. Pepsinogen (an inactive form of the enzyme pepsin and a component of gastric juice) is activated by the low pH. By its proteolytic activity, pepsin can activate more pepsinogen. The low pH also promotes the activity of pepsin, because the most favorable pH range for its proteolytic activity is 1.3 to 5. Chief or peptic cells secrete pepsinogen to begin protein digestion in the stomach, but protein digestion is completed in the small intestine by other digestive enzymes.

A layer of mucus covers the epithelial lining of the stomach and protects the epithelium from the low pH of the gastric fluids. This mucus is produced by cells in the gastric glands and is secreted from there onto the surface of the epithelium. Mucus secretion is stimulated by prostaglandins, which are also produced locally in the wall of the stomach. Non-steroidal anti-infl ammatory drugs (such as aspirin and phenylbutazone) inhibit the synthesis of prostaglandins, and toxic doses of these agents are associated with gastric ulcers. It is presumed that a lack of mucus secretion contributes to the development of the ulcers.

Rennin is an enzyme in the gastric juice in the abomasum of young ruminants. Its function is to coagulate milk and reduce its rate of passage through the gastrointestinal tract.

Intrinsic factor, a carrier protein for vitamin B_{12}, binds to the vitamin, and the resultant complex passes through the tract to the ileum, which absorbs the B_{12}.

Gastric motility.

Gastric movements mix the ingesta with the gastric juice, continue mechanical digestion (to liquefy the digesta), and pass the digesta into the duodenum at a controlled rate. The stomach regularly produces peristaltic contractions, beginning in the region of the cardia and increasing in force as they travel over the stomach to the pyloric antrum. These mix and grind the food and force some through the pyloric sphincter into the duodenum. However, much of the food (and especially larger particles) is held back to allow for more mixing and grinding. The ingesta forced through the pyloric sphincter, termed chyme, is a mushy, semisolid mixture of food, water, and gastric juice.

Similar to the regulation of gastric secretions, the regulation of gastric motility can be divided into cephalic, gastric, and intestinal phases. Stimulation during cephalic regulation occurs via the parasympathetic nerves, and this increases in response to sight, smell, or taste of food. The hormone gastrin stimulates overall

gastric motility to promote mixing (gastric phase). The hormones cholecystokinin and secretin and gastric inhibitory peptides promote a more forceful contraction of the pyloric sphincter to slow gastric emptying (intestinal phase). The inhibitory effect of the duodenal hormones (released in response to chyme entering the duodenum) prevents the delivery of chyme to the duodenum too fast to be digested normally.

The stomach of a carnivore empties within a few hours, usually before the next meal. Other animals require many hours to empty the stomach. Both the horse and pig require a full day's fast (24 hours) to empty a full stomach. The stomach of a nursing foal empties slowly, but in an adult pony liquid passes from the stomach to the cecum in 2 hours.

In addition to the typical pattern of stomach contraction when food is present, waves of peristaltic contractions may occur over the stomach as a slight ripple. These are produced by spontaneous electrical depolarizations, which sometimes induce action potentials, in the smooth muscle. These begin in the cardia region, and the waves of membrane depolarization are termed gastric slow waves. In prolonged fasting, the magnitude of the contractions becomes greater (hunger contractions). These are apparently a response to an increase in parasympathetic input during prolonged fasting. These reach maximum intensity in humans after about 3 days without food and weaken progressively thereafter. In the horse, hunger contractions may begin as early as 5 hours after eating, when the stomach still contains some food. The intensity of hunger contractions is related to the level of blood sugar. As the blood sugar level decreases, the intensity of hunger contractions increases.

Ruminant stomach.

The ruminant stomach is actually a single stomach modified by marked expansion of the esophageal region into three distinct and voluminous diverticula, the rumen, reticulum, and omasum, collectively known as the forestomach. These are lined with nonglandular stratified squamous epithelium and comprise a series of chambers where food is subjected to digestion by microorganisms before passing through the digestive tract to the smaller glandular portion of the stomach in the ruminant, the abomasum.

Because of their functional and anatomic relatedness, the reticulum and rumen are often collectively called the ruminoreticulum. The opening of the esophagus (the cardia) is about the level of the middle of the seventh intercostal space, and it opens into the dorsal space that is common to both the rumen and reticulum. The mucosa in the region of the cardia forms two heavy muscular folds that together create a groove extending from the cardia to omasum. This is the sulcus ruminoreticularis (variously called the esophageal, gastric, or reticular groove). In nursing ruminants, the act of suckling initiates a reflex contraction of the muscular walls of the sulcus, transforming it from a groove to a closed tube that connects the cardia with the omasum. By this reflex, swallowed milk bypasses the ruminoreticulum and is instead delivered to the more distal parts of the stomach; this ensures that the milk will not be allowed to sour in the forestomach.

The reticulum is the most cranial compartment of the forestomach. Its mucosa is thrown up into intersecting ridges that give the reticulum its common name, the "honeycomb." Foreign objects such as wire or nails that are swallowed typically will fall into and remain in the reticulum; contractions of this part of the forestomach may

drive sharp objects through the wall of the stomach, leading to traumatic peritonitis or hardware disease. The location of the reticulum immediately caudal to the diaphragm places it opposite the heart, with only the muscular diaphragm between, so that these sharp objects may also be driven into pleural and pericardial spaces.

The reticulum and the rumen (colloquially known as the paunch) are divided ventrally by a thick, muscular ruminoreticular fold. The rumen extends from this fold to the pelvis and almost entirely fills the left side of the abdominal cavity; its capacity depends on the size of the individual but in adult cattle ranges from 110 to 235 L (about 30 to 60 gallons).

The rumen is subdivided internally into compartments by muscular pillars, which correspond to grooves visible on the exterior of the rumen. Right and left longitudinal pillars (corresponding to right and left longitudinal grooves on the exterior) together with cranial and caudal pillars (externally,cranial and caudal grooves) form a nearly complete constricting circle in the horizontal plane. These divide the rumen into dorsal and ventral sacs. The dorsal sac is the largest compartment. The dorsal sac is continuous cranially with the reticulum over the ruminoreticular fold so that the two compartments share a dorsal space. Caudally, the dorsal sac is further subdivided by the dorsal coronary pillars, which form an incomplete circle bounding the dorsal blind sac. The caudal part of the ventral sac forms a diverticulum, the ventral blind sac, separated from the rest of the ventral sac by the ventral coronary pillars. As in the rest of the forestomach, the mucous membrane lining the rumen is a nonglandular, stratified squamous epithelium. The most ventral parts of both sacs of the rumen contain numerous feathery papillae up to 1 cm long, but papillae are almost entirely absent on thedorsal part of the rumen.

The omasum is a spherical organ filled with muscular laminae (an estimated 90–130 in the bovine omasum) that lie in sheets, much like the pages of a book (giving the omasum its colloquial name, book stomach). The stratified squamous mucous membrane covering the laminae is studded with short, blunt papillae. Each lamina contains three layers of muscle, including a central layer continuous with the tunica muscularis of the omasal wall. The omasum lies to the right of the ruminoreticulum, just caudal to the liver, and in the ox makes contact with the right body wall. The
omasum of the sheep and goat is much smaller than the bovine omasum and normally is not in contact with the abdominal wall. Food enters the omasum at the reticulo-omasal orifice, between the laminae, and goes on to the omasoabomasal orifice.

The abomasum (true stomach) is the first glandular portion of the ruminant digestive system. Its proximal portion is ventral to the omasum, and its body extends caudad on the right side of the rumen. The pylorus demarcates the muscular junction of the stomach and small intestine, and like the porcine pylorus, it features an enlarged torus pyloricus. The epithelium of the abomasum consists primarily of two glandular regions, equivalent to the fundic gland region (region of the proper gastric glands) and the pyloric gland region. The cardiac gland region in the abomasum is confined to a very small area adjacent to the omasoabomasal orifice.

Ruminant forestomach. Fermentative digestion.

No mammal can directly digest the complex carbohydrates that constitute plant cell walls (cellulose and hemicellulose), because mammals do not produce the

enzyme cellulase, which is necessary to break the unique chemical bonds in these compounds. The ruminant forestomach provides an excellent environment for the growth of bacteria, protozoa, and possibly other microbes that do produce cellulase. The action of cellulase on cellulose and hemicellulose produces monosaccharides and simple polysaccharides, which are available for further microbial digestion.

The microbial digestion in the forestomach occurs in an anaerobic environment and is termed fermentative digestion. Volatile fatty acids (VFAs) are produced by fermentation of carbohydrates consumed by ruminants, including carbohydrates produced by the actions of microbial cellulase. The primary VFAs are acetic acid, propionic acid, and butyric acid.

The VFAs are absorbed directly from the forestomach and are the major energy source for ruminants. VFAs are also used for synthesis of milk fat in lactating animals. Methane and carbon dioxide are produced by fermentative digestion and accumulate as a gaseous layer above the ingesta in the rumen and reticulum. Bloat (acute tympany) results in enlargement of the rumen and reticulum, which in turn press on the thorax, inhibiting function of the heart and lungs. Bloat results from more gas being produced than is eliminated by eructation (belching). Eructation is particularly difficult if foam forms. A stomach tube may be passed into the rumen by mouth to remove the gas. If that is not possible, a trocar (sharp tube) may be passed into the rumen through the left flank.

Dietary protein consumed by ruminants is available first to the microbes in the forestomach. The microbes may use the dietary protein to produce microbial proteins and promote microbial growth or to produce VFAs by fermentative digestion. Microbes can also produce microbial proteins from nonprotein nitrogen sources, such as urea and ammonia. The microbes and by-products of microbial metabolism other than VFAs continue down the ruminant gastrointestinal tract from the forestomach. The microbial organisms, which grew in the forestomach, are a major source of dietary protein for ruminants. When the organisms enter the abomasum (true or glandular stomach of the ruminant) and the remainder of the tract, they are digested in a manner similar to digestion of protein sources in nonruminants. Beneficial by-products of microbial metabolism include many water-soluble vitamins.

Forestomach motility.

The rumen and reticulum of the adult cow normally undergo complicated sequences of contractions that are repeated at varying frequencies up to several times per minute. One pattern of contractions begins in the reticulum and spreads over both the dorsal and ventral sacs of the rumen (see Fig. 20-10). This series of contractions mixes the contents to promote fermentation and provide force to move liquifi ed digesta out of the forestomach and into the abomasum.

A second pattern of contractions begins in the caudal portion of the dorsal sac and moves cranially. These contractions move gases toward the cranial part of the rumen for eructation. Rumen contractions can be felt by forcing the fist into the upper left flank (paralumbar fossa). Pathologic condition of the rumen or morbidity associated with systemic diseases usually results in a decreased rate or complete cessation of rumen movements. Rumination permits an animal to forage and ingest food rapidly and fi nish chewing later. It entails regurgitation of the food (returning it

to the mouth) from the forestomach, remastication (rechewing), reinsalivation (mixing with more saliva), and fi nally reswallowing.

Regurgitation is the only step of rumination that differs markedly from the initial mastication, insalivation, and swallowing. Regurgitation is preceded by contraction of the reticulum, which presumably brings some of the heavier ingesta into proximity to the cardia. The sphincter at the junction of the esophagus and forestomach (lower esophageal sphincter) relaxes as the bolus of food reaches it. An inspiratory movement with closed glottis follows. The negative pressure produced in the thorax by this movement is transmitted to the relatively thinwalled esophagus, dilating the thoracic esophagus and cardia. The lower pressure in the esophagus than in the rumen coupled with reverse peristalsis causes a quantity of material (semifl uid ingesta) to pass through the cardia into the esophagus and up to the mouth. The regurgitated material consists largely of roughage and fluid, with little if any concentrate. It is well known that whole kernels of corn may pass through the entire digestive tract with little change in physical appearance.

Cattle average about 8 hours a day ruminating, with periods of activity scattered throughout the entire day. One rumination cycle requires about 1 minute, of which 3 to 4 seconds is used for both regurgitation and reswallowing. Rumination appears to be largely refl exive, although the process can be interrupted or stopped voluntarily. Both afferent and efferent portions of the reflex are probably carried in the vagal nerves. Contact of roughage with the wall of the reticulum and near the cardia is likely the major stimulus for rumination.

Reticular, or esophageal, groove.

In young ruminants, nursing and afferents from the pharynx appear to stimulate reflex closure of the groove, which causes milk to bypass the rumen and reticulum and pass through the omasum directly to the abomasum. The paunchiness of bucket-fed calves usually is attributed to milk entering the rumen, where it is not properly digested. The use of buckets with nipples tends to prevent appreciable amounts of milk from entering the rumen. After weaning, fluid drunk from open containers largely passes into the rumen and reticulum. The groove has no known function in adult animals, but refl ex closure in adults has been produced with sodium salts in cattle and copper
sulfate in sheep.

The omasum is nearly always found packed tightly with rather dry roughage in animals examined after death. The appearance of the omasal leaves, studded with short horny papil lae, suggests a burr type of grinder. Experimental vagal stimulation elicits strong contractions of the omasal wall, but movement of the leaves is limited.

Physiology of the small intestine.

The small intestine is the primary site of chemical digestion and absorption of nutrients. The exocrine secretions of the pancreas contain most of the enzymes for chemical digestion in the lumen of the small intestine, but the epi thelial cells that line the small intestine (enterocytes) also have in their cell membranes enzymes that participate in the fi nal steps of chemical digestion. The primary digestive function of the liver is to provide bile salts, which facilitate the enzymatic digestion of lipids. The liver is not a source of digestive enzymes.

Small intestine. The duodenum is the first of three divisions of the small intestine. It is closely attached to the right side of the dorsal body wall by a short mesentery, the mesoduodenum. The duodenum arises at the pylorus of the stomach and receives ducts from the pancreas and liver in this region. The transition between duodenum and the next portion of the small intestine, the jejunum, is defined by the marked increase in the length of the supporting mesentery. The jejunum is the longest part of the small intestine (e.g., as much as 28 m in the horse). Histologically, the jejunum is similar to the duodenum, although lymph nodules at the mucosal–submucosal junction may be more numerous. The ileum is the short last part of the small intestine. It is distinguished from the jejunum by a fold of mesentery between it and the cecum. This ileocecal fold is found on the side of the intestine opposite the attachment of the mesentery (the antimesenteric side). The lumen of the ileum communicates with that of the large intestine at the ileal orifice. The ileal epithelium features numerous goblet (mucous) cells, and aggregates of lymph nodules in this region are more abundant than in other parts of the small intestine. Their especially prominent arrangement in the ileum has led to the use of the term Peyer's patches to distinguish them.

Small intestine secretions and motility. Intestinal juice.

Intestinal juice is derived from intestinal glands in the wall of the small intestine. These include crypts or crypts of Lieberkuhn, scattered throughout the entire small intestine, and duodenal glands, which contribute mucus and are found only in the duodenum. The intestinal juice contains salts and water derived from blood capillaries in the wall of the intestine. The function of the secreted salts is unclear, but the water dilutes the chyme, which is usually hypertonic (higher osmolality than normal plasma). Food in the intestine stimulates secretion by these intestinal crypt glands.

The two primary types of movement by the small intestine are segmentation and peristalsis.Segmentation movements, which occur when food is in the small intestine, are characterized by alternating local areas of contraction and relaxation. These movements mix the digesta with intestinal juice and digestive enzymes and increase the contact between digesta and the epithelial surface of the small intestine. The increased contact provides more exposure to enzymes associated with epithelial cells and to the absorptive surface of the epithelial cells. Strong peristaltic contractions of the small intestine in fasting animals or several hours after a meal propel ingesta down the tract, presumably to clean the small intestine of undigested foodstuffs before the next meal.

Exocrine pancreas. Pancreatic exocrine secretions and its control.

The pancreas is a compound gland that has both endocrine and exocrine portions. The exocrine portion of the pancreas produces sodium bicarbonate and digestive enzymes, which pass through the pancreatic ducts to empty into the duodenum close to the opening of the bile duct. The endocrine portion of the pancreas consists of isolated groups of pale-staining cells scattered throughout the gland. These areas are called the pancreatic islets (formerly islets of Langerhans). They produce the hormones that pass directly into the bloodstream, most notably glucagon and insulin, which are the primary regulators of blood sugar levels. Grossly, the pancreas is an irregularly lobulated organ that lies adjacent to the proximal

duodenum and frequently abuts the stomach, the caudal vena cava, and caudal part of the liver as well. The pancreas has the appearance of aggregated nodules loosely connected to form an elongated gland lying parallel to the duodenum.

During organogenesis in many species, the duct systems of the two lobes intermingle and one of the two original connections to the gut lumen is lost; thus, a single duct is the normal condition of the adult in these species. In those species that possess it, the pancreatic duct opens onto a small elevation within the duodenum in common with the bile duct from the liver. This is the major duodenal papilla. A short distance away, a smaller minor duodenal papilla marks the location of the accessory pancreatic duct. As small ruminants lack the accessory pancreatic duct, they also lack the minor duodenal papilla.

Pancreatic exocrine secretions primarily consist of a variety of digestive enzymes and sodium bicarbonate. Pancreatic acinar cells secrete the enzymes, and cells that line ducts in the pancreas secrete the sodium bicarbonate. These ducts empty into one or two pancreatic ducts, which empty into the duodenum. The sodium bicarbonate raises to an acceptable pH the chyme entering from the stomach. The small-intestinal epithelium is not protected from an acidic solution by a thick layer of mucus, as is the stomach. The higher pH is also better for the action of the pancreatic digestive enzymes. The major stimulus for bicarbonate secretion is the hormone secretin from the small intestinal mucosa. Secretin secretion increases in response to the acid chyme entering from the stomach.

Pancreatic proteolytic enzymes include trypsin and chymotrypsin. Similar to pepsin in the stomach, these are secreted as inactive precursors, trypsinogen and chymotrypsinogen. Trypsinogen is activated by an enzyme, enterokinase, a component of the luminal cell membranes of small intestinal cells (enterocytes). Trypsin can activate chymotrypsinogen and more trypsinogen. The ultimate end products of protein digestion are amino acids, but the pancreatic proteolytic enzymes may stop digestion when the peptides reach a length of two or more amino acids. If this occurs, peptidases associated with enterocyte cell membranes can complete hydrolysis of the peptides to individual amino acids for absorption.

Unlike the proteolytic enzymes, pancreatic amylase and lipase are in the active forms when secreted from the pancreas. Amylase digests starches to oligosaccharides (a carbohydrate composed of a small number of monosaccharides, usually two to four). The enzymes maltase and sucrase, components of enterocyte cell membranes, further digest the oligosaccharides to monosaccharides. Lactase, to digest lactose (milk sugar), is present in enterocytes of young mammals but not in all adults. Lipase hydrolyzes triglycerides into fatty acids and glycerol. This action is most effective after the fats have been emulsifi ed by bile (discussed later).

Control of pancreatic exocrine secretion depends on stimulation by vagal autonomic nerves that innervate the pancreas and on three intestinal hormones, cholecystokinin, secretin, and gastrin. Seeing or smelling food stimulates vagal stimulation, and food in the stomach prompts release of gastrin. The greatest amount of pancreatic exocrine secretion occurs when the acid chyme and food components in the duodenum stimulate the release of cholecystokinin and secretin from cells in the duodenal mucosa (intestinal phase of control). These two duodenal hormones also feed back to the stomach to decrease secretions and slow down the activity and

emptying of the stomach until the duodenal chyme has been degraded by the enzymes and adjusted in pH by the pancreatic bicarbonate.

Liver digestive functions.

The liver is the largest gland in the body, constituting 1–2% of total adult body weight. It varies somewhat in number of lobes and precise intra-abdominal location from one species to another. However, the liver is always located immediately caudal to the diaphragm (in contact with it) and tends to be located on the right side, particularly in ruminants, in whom the large ruminoreticulum pushes everything else to the right. Individual liver lobules of the pig are encircled by rather heavy connective tissue septa, which give a lobulated, "cobblestone" appearance to the surface of the porcine liver. This appearance is less distinctive in other domestic species. Liver tissue is usually a reddish brown, although accumulation of fat (whether due to a high-fat diet or pathology) can give it a pronounced yellow tinge.

The liver receives two blood supplies. To provide oxygen and nutrients, arterial blood from the hepatic artery, a branch of the celiac artery, enters the side of the liver adjacent to the viscera, called the porta (the Latin word for gate). This is the nutrient blood supply. The porta also receives the large portal vein, which carries blood to the liver from the stomach, spleen, pancreas, and intestines. The liver performs metabolic and immunologic functions on this blood returning from the gastrointestinal tract, and so the blood of the portal vein constitutes the functional blood supply. Portal blood is detoxifi ed and modifi ed within the sinusoids (capillaries) of the liver and then leaves the liver by way of the short hepatic veins that empty into the caudal vena cava.

All domestic animals except the horse have a gallbladder for storage of bile. The liver's digestive secretion, bile, leaves the liver through hepatic ducts, which join the cystic duct from the gallbladder to form the common bile duct, which then passes to proximal duodenum into the lumen to which it opens in common with the pancreatic duct on the major duodenal papilla (see above).

Microscopically, the morphologic unit of the liver is the hepatic lobule, a polygonal cylinder of liver cells (the hepatocytes) in the center of which is a central vein. At the angles on the periphery, where adjacent hepatic lobules meet, are the portal triads, consisting of branches of the hepatic artery and portal vein (interlobular vessels), an interlobular bile duct, and lymphatics.

Blood (both arterial and portal) flows from the portal canal through the sinusoids and is gathered by the central vein, the smallest tributary of the hepatic veins. In and around the sinusoids are fixed macrophages, which in this location are called Kupffer cells. Between adjacent rows of liver cells is a tiny bile canaliculus, which is little more than a tube formed by grooves in the surfaces of the apposed liver cells. Bile produced by the hepatocytes is carried toward the periphery of the hepatic lobule by the bile canaliculi to the interlobular bile ducts located at the portal canal (notice that this net fl ow is opposite the direction of blood flow).

Secretion of bile and its control.

Liver cells (hepatocytes) are responsible for bile formation. Bile is a greenish-yellow salt solution consisting primarily of bile salts, cholesterol, phospholipids (lecithins), and bile pigments (bilirubin). Hepatocytes synthesize the bile salts (primarily sodium salts of glycocholic and taurocholic acids) from cholesterol. These

salts assist in digestion and absorption of lipids (triglycerides), and the production and secretion of these salts is the most important digestive function of the liver. In an aqueous solution, such as the duodenal chyme, lipids tend to clump together and form large droplets (recall the appearance of an oil and vinegar salad dressing after shaking the bottle). Such large lipid droplets present a small surface area for the action of the pancreatic lipases. Bile acids act as emulsifi ers to reduce droplet size and make the lipids more accessible to the lipases. Lipases can function without bile salts, but lipid digestion is inefficient without them. Micelle is the term for the small droplets formed in the intestinal chyme that contain lipids, bile salts, and products of lipid digestion.

In all farm animals except the horse, bile is stored in the gallbladder. Since the horse has no gallbladder, the bile passes directly from the liver to the duodenum by way of the bile duct and its tributaries at a fairly continuous rate. The gallbladder stores bile for intermittent discharge into the duodenum and concentrates the bile by reabsorbing water from the stored bile. Cholecystokinin stimulates gallbladder contraction and the release of stored bile. Since food entering the duodenum stimulates the release of cholecystokinin, this coordinates the release of bile with the presence of food.

Most of the bile salts released from the liver remain mixed with the digesta as it passes into the terminal part of the small intestine (ileum). Here, enterocytes reabsorb bile salts, which enter the blood. The reabsorbed bile salts are transported to the liver via the hepatic portal vein, and here hepatocytes take up the bile salts from the portal blood. These bile salts can then be secreted by the hepatocytes into bile for reuse. An increase in bile salts in portal blood, such as during the digestion of a meal, is the primary stimulus for bile salt secretion by hepatocytes. The recycling of bile salts between the digestive tract and the liver is enterohepatic circulation. The liver is capable of synthesizing cholesterol, and the liver makes much of the cholesterol in bile. The liver can also eliminate excessive dietary cholesterol via the bile. Cholesterol is insoluble in water, but the bile salts and lecithin normally change it to a soluble form so that it can exist in the bile. However, sometimes cholesterol precipitates from the bile in the gallbladder or bile ducts, forming gallstones.

Breakdown into nutrients: protein, fat, carbohydrate digestion.

Protein digestion (Figure 17) occurs in the stomach and duodenum in which 3 main enzymes:

- ✓ pepsin is secreted by the stomach and trypsin and chymotrypsin secreted by the pancreas;
- ✓ exopeptidases and dipeptidases convert proteins and poly peptides into amino acids.

The digestive enzymes are mostly secreted as their inactive precursors known as zymogens. *For example, trypsin is secreted by pancreas in the form of trypsinogen, which is activated in the duodenum by enterokinase to form trypsin*. Trypsin then breaks proteins to smaller polypeptides.

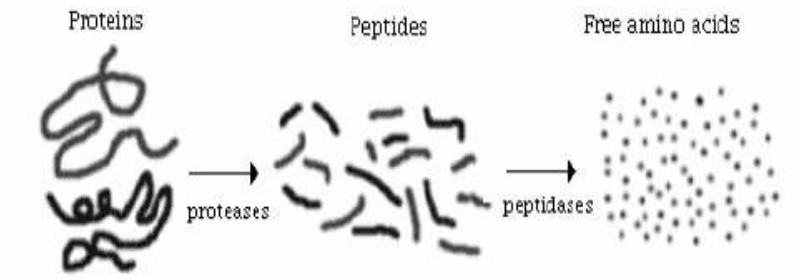

Figure 17. Breakdown into nutrients: protein digestion.

Fat digestion (Figure 18). Digestion of some fats can begin in the mouth. But fats are mainly digested in the small intestine. Small amount of salivary lipase breaks down some short chain lipids into diglycerides. The presence of fat in the small intestine stimulates the release of pancreatic lipase from the pancreas and bile. Bile from the liver helps in the emulsification of fats and absorption fatty acids. Complete digestion of one molecule of fat (a triglyceride) results in 3 fatty acid molecules and one glycerol molecule.

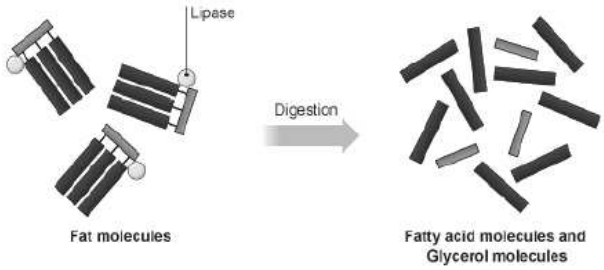

Figure 18. Breakdown into nutrients: fat digestion.

Carbohydrate digestion (Figure 19). Dietary starches are composed of glucose units. During digestion, bonds between glucose molecules are broken by salivary and pancreatic amylase, resulting in progressively smaller chains of glucose. This results in simple sugars glucose and maltose (2 glucose molecules) that can be absorbed by the small intestine. Lactase is an enzyme that breaks down the disaccharide lactose in to glucose and galactose which can be absorbed by the small intestine. Sucrase is an enzyme that breaks down the disaccharide sucrose, commonly known as table sugar. This enzyme breakes the sucrose in to fructose and glucose. They are readily absorbed by the small intestine.

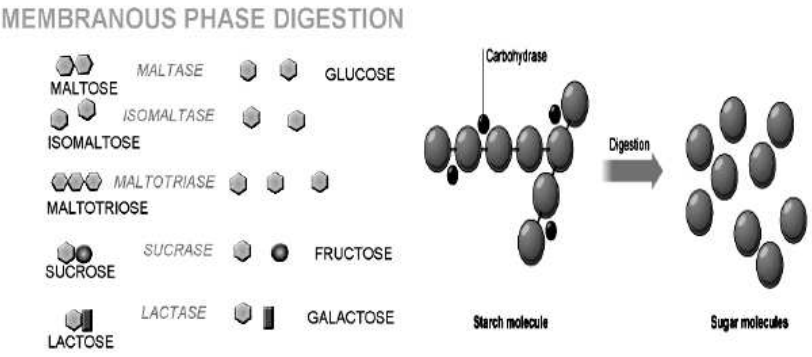

Figure 19. Breakdown into nutrients: carbohydrate digestion.

Nutrient absorption in the small intestine.

The small intestine is the major site of nutrient absorption. Most of the products of carbohydrate, protein, and lipid digestion are absorbed as the digesta pass

through the small intestine. The small intestine is also the primary site of absorption for vitamins, minerals, and water.

The epithelium lining the small intestine has structural features that increase the surface area for nutrient absorption. The mucosa is covered with villi (fingerlike projections) that extend into the lumen, and the individual enterocytes have microvilli on their cell membrane facing the lumen. Individual amino acids and monosaccharides (simple sugars) are the simplest products of protein and carbohydrate digestion, respectively.

The cellular mechanisms of absorptionof amino acids and monosaccharides (primarily glucose) are similar in that the transport across the cell membrane on the luminal surface involves sodium-linked co-transporters. The co-transporters all bind sodium, but different co-transporters are used by glucose and amino acids. At least five cotransporters have been found to transport various amino acids. These are all characterized as secondarily active transport, for they depend on the gradient for sodium between the intracellular fluid of the enterocytes and the fluid in the lumen of the small intestine.

Micelles formed in the lumen of the small intestine contain bile salts, triglycerides, cholesterol, and the products of lipase action on triglycerides (fatty acids and monoglycerides). Intestinal movements (segmentation) bring the micelles into contact with the microvilli of the enterocytes. The lipid-soluble products of lipid digestion and cholesterol can then diffuse from the micelle into the enterocytes. Some long-chain fatty acids are also transported from micelles into the cell by specific sodiumlinked co-transporter proteins in the cell membrane.

Within the enterocytes, absorbed monoglycerides and fatty acids are used to resynthesize triglycerides. The enterocyte packages the triglycerides and absorbed cholesterol together with intracellular proteins into a particle known as a chylomicron. The enterocytes secrete the chylomicrons into the interstitial fluid, where they are absorbed into lymphatics. The smallest of the lymphatic vessels that absorb the chylomicrons are lacteals. The lymphatic drainage from the intestinal tract is ultimately added to the blood, and it is via this pathway that chylomicrons, containing absorbed lipids, reach the blood.

Sodium, potassium, phosphate, calcium, chloride, and other electrolytes are primarily absorbed in the small intestine by both active and passive mechanisms. With the exception of iron and calcium, the absorption of these minerals is not regulated, so that most of what is consumed is absorbed. Iron absorption is reduced at the level of the enterocyte if body iron content is suffi cient. This reduction is primarily accomplished by an increase in an intracellular protein that binds iron in the enterocytes. The iron-containing enterocyte is lost from the body after it sloughs from the epithelial lining. The form of vitamin D produced by the kidneys (calcitriol) increases calcium absorption by increasing calcium transport proteins in enterocytes. Calcitriol formation by the kidneys is increased when blood calcium is low. To be absorbed, minerals such as calcium and phosphate must be in their ionized state. If the ratio of cations to anions is too high or too low, absorption can be reduced. For example, if the dietary content of the phosphate (an anion) is too high relative to calcium (a cation), the excess phosphate binds the available calcium to form calcium phosphate, and calcium absorption is impaired.

The small intestine of some neonatal (newborn) animals can absorb macromolecules, including intact protein molecules from the colostrum. Colostrum, the fi rst milk of the horse, pig, and ruminants, contains the γ-globulins needed to produce passive immunity in the newborns of these animals. This receptive period lasts approximately 1 day in the horse and pig and up to 3 days in the ruminant.

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.
2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.
5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.
7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.
14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

CHAPTER 12. PHYSIOLOGY OF LACTATION

Physiology of lactation. Composition of milk.

Milk contains all of the nutrients necessary for survival and initial growth of mammalian neonates. The nutrients in milk include sources of energy (lipids and carbohydrates), proteins to provide amino acids, vitamins, minerals (ash) for electrolytes, and water. The relative amounts of these nutrients in milk vary among species (Table 11). Diet and the stage of lactation also affect the composition of milk. Diets high in non-fiber carbohydrate sources of energy are associated with increases in the percentage of lipids in the milk. Diets high in protein promote a slight increase in the percentage of protein in the milk, but this effect is much less than the effect of energy on milk lipid content. The amount of carbohydrates in milk (lactose, or milk sugar) does not routinely change with diet. The percentage of lipids and protein in milk is also highest early in lactation. In cattle the percentages are relatively high in the fi rst few weeks after calving and then decrease over the next 3 to 4 months. Later in lactation, the concentrations of lipids and proteins again increase as total daily production (pounds of milk per day) decreases.

Most of the lipids in milk are in the form of triglycerides, and these are the primary source of dietary energy in milk. Triglycerides are composed of three fatty acids and glycerol. The fatty acids for the synthesis of milk triglycerides may be derived from the blood or synthesized within the mammary gland. Nonruminant mammary glands use blood glucose both for energy and as a source of carbon for the synthesis of the fatty acids. The glycerol is derived mostly from glucose catabolism in the process of glycolysis. The mammary glands of ruminants depend on blood acetate and blood hydroxybutyrate to provide carbon for fatty acid synthesis, with acetate being the primary source. The acetate and β-hydroxybutyrate in ruminants are produced as volatile fatty acids by fermentative metabolism by microorganisms in the rumen. These volatile fatty acids are absorbed into the blood and thereby become available for synthesis of milk fat in the mammary gland. Most milk triglycerides have fatty acids with chains 4 to 14 carbon atoms in length – short-chain fatty acids. Such shortchain fatty acids are not generally found in adipose tissue throughout the remainder of the body.

Lactose (milk sugar), the principal carbohydrate in milk, is a disaccharide composed of the two monosaccharides glucose and galactose. Lactose is synthesized in mammary glands and is typically found only in mammary glands and milk. Secretory cells in mammary glands use glucose from the blood to synthesize galactose and then combine the galactose with more glucose to produce lactose, so glucose is essential for lactose synthesis. The extraction of glucose from blood by an actively secreting mammary gland is quite effective, so the glucose concentration of venous blood leaving a mammary gland is relatively low.

Recall that in ruminants blood glucose is primarily derived from gluconeogenesis in the liver using propionic acid, a volatile fatty acid absorbed from the rumen, as a substrate. Thus, propionic acid produced by ruminal microorganisms and fermentative metabolism is the ultimate substrate for the production of lactose in ruminants. Also, blood glucose is relatively low in ruminants compared to other

mammals, in part because ruminants absorb very little glucose from the gastrointestinal tract. At peak lactation of a high-producing dairy cow, the mammary glands use most of the glucose produced by the liver for lactose production. If the need for glucose by the mammary glands cannot be met by gluconeogenesis, and blood glucose levels drop significantly, *lactational ketosis* develops. While blood glucose levels are low, metabolic acids (produced in the liver from fatty acids) accumulate in the blood to produce a metabolic acidosis.

The major milk proteins are the caseins. Blood amino acids are the precursors for direct synthesis of the caseins by secretory cells within mammary glands. Other milk proteins include α-lactalbumin and β-lactoglobulins, which are produced by cells of the mammary gland, and serum albumin and immunoglobulins produced by the liver and lymphocytes, respectively. Rennin (also known as chymosin) is a proteolytic enzyme secreted by gastric epithelial cells of very young mammals. Rennin changes the character of ingested milk from a liquid to a semisolid curd; this process is termed curdling or coagulation. The change in character increases the time that milk is retained in the stomach, and this permits protein digestion to begin. Curdling results when rennin degrades one of the casein proteins responsible for increasing the solubility of micelles, casein protein aggregates in milk (discussed next). Without this specifi c casein, milk proteins precipitate with the calcium in milk to form curds.

Table 11. Typical values for constituents of milk in grams per liter

Species	*Lipids*	*Lactose*	*Protein*	*Total Minerals (ash)*	*Calcium*
Cow	38	48	37	7.0	1.3
Mare	16	50	24	4.5	1.0
Ewe	70	40	60	8.0	1.9
Sow	80	46	58	8.5	2.0
Doe	40	45	35	7.8	1.2

Milk secretion.

The epithelial cells lining the alveoli of mammary glands are the cells primarily responsible for the secretion of milk. The appearance of these cells varies as they synthesize and release the lipids, proteins, and lactose of milk. After the cells actively secrete the constituents of milk and the lumen of the alveoli are fi lled with milk, the epithelial cells shrink and are described as a simple low-cuboidal epithelium (Fig. 20). At this stage, their secretory activity is relatively low. Shortly after the stored milk is removed, the epithelial cells increase their secretory activity and begin to refill the alveoli. Early in the secretory phase the cells assume a more columnar appearance and then gradually reduce to cuboidal as milk fills the alveoli. Small, apparently nonfunctioning alveoli can be found in dry mammary glands, and there is a relative increase in the amount of interstitial loose connective tissue. Milk lipids are synthesized and packaged into secretory droplets, which are extruded from the luminal surface of the cell into the alveoli. As they are released, a membrane covering derived from the cell membrane of the epithelial cell encases the lipid droplets.

The alveolar secretory cells also produce secretory vesicles that contain both milk proteins (caseins) and lactose (Fig. 20). As caseins are synthesized and packaged in these vesicles, they self-aggregate into particles termed micelles. The

inclusion of one specifi c type of casein (κ-casein) in this aggregation increases the solubility of the micelle so that milk proteins remain in solution after their release from the cell. The lactose within the secretory vesicle generates an osmotic force to draw water into the vesicle from the cytosol of the cell. The secretory vesicles, each containing a mixture of micelles, lactose, and water, are transported to the apical surface of the cell and released into the alveoli by exocytosis. Because of the various mechanisms by which lipids, proteins, and lactose are secreted from alveolar cells, milk is considered to be a combination of apocrine and merocrine secretions.

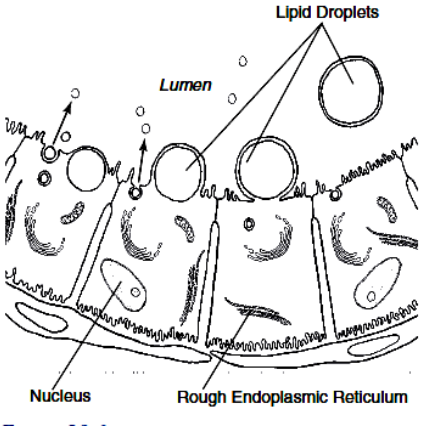

Figure 20. Secretion of milk lipids, milk proteins, and lactose by epithelial cells lining the alveoli of the mam mary glands. Proteins and lactose are together in secretory vesicles that are released by exocytosis *(arrows)*.

Lactogenesis.

Lactogenesis is the establishment of milk secretion, and **galactopoiesis** is the continued production of milk by the mammary glands. Growth and development of the secretory epithelium and the ductile network of the mammary glands must precede lactogenesis. The initial extensive development of the mammary gland is usually associated with puberty (the beginning of sexual maturity) and the subsequent cyclic changes in the ovarian hormones, estrogen and progesterone. Estrogen particularly promotes the growth of the ductile system at each estrus, while progesterone, acting with estrogen, is required for growth and anatomic development of secretory alveoli. Normal secretion of growth hormone and glucocorticoids are also required for complete mammary gland development. During pregnancy, prolonged exposure of the mammary glands to progesterone promotes a more extensive anatomic development of the secretory alveoli. While progesterone stimulates anatomic development, it inhibits the functional development of the secretory epithe-lium. Progesterone also inhibits the production of intracellular enzymes necessary for normal milk secretion. This inhibitory effect of progesterone is lost just prior to parturition, and this is one factor promoting lactogenesis.

Prolactin, a protein hormone, is unique in that its release from the adenohypophysis is primarily regulated by a humoral inhibitor factor from the hypothalamus. In the absence of this inhibitory factor (which is believed to be the catecholamine dopamine), there is a continuous and relatively high rate of prolactin release. In most domestic animals, blood levels of prolactin gradually increase late in gestation, with an abrupt increase at parturition. During late gestation, prolactin receptors in mammary glands also increase under the infl uence of rising estrogen.

Prolactin promotes both anatomic and functional development of the secretory epithelium of mammary glands to promote milk secretion, so the abrupt rise at parturition is appropriate for lactogenesis. Under the influence of prolactin, secretory cells lining alveoli produce intracellular enzymes necessary for milk secretion. The functional development of alveolar secretory cells is also enhanced by glucocorticoids, which increase in the blood prior to parturition in most species.
The placenta of ruminants produces a protein hormone, placental lactogen, or chorionic somatomammotropin, which is similar in structure and function to prolactin. Placental lactogen production increases in late gestation in ruminants and is believed to be more responsible for mammary gland development in these species than prolactin from the adenohypophysis.

Galactogenesis.

The continuation of lactation requires stimuli to promote milk production and removal or inhibition of stimuli that retard milk production. Stimulation of the nipples (teats) by either milking or suckling elicits an abrupt increase in blood levels of prolactin. The increased secretion of prolactin is the result of a neural reflex mediated through the hypothalamus that regulates prolactin release from the adenohypophysis. The increase in prolactin is relatively short in duration (minutes to an hour). This periodic and relatively brief surge of prolactin is essential to maintain normal lactation in most species, but prolactin does not appear to be an essential regulator of lactation in cows. Supplementation with prolactin does not increase milk secretion in cows, and lactation is maintained in cows in spite of severe reductions in blood levels of prolactin.

Growth hormone appears to be especially important in cows, whose blood levels of growth hormone are directly correlated with the maintenance and level of milk production. Growth hormone supplementation increases milk production in cows by 10–40%. Growth hormone supplementation in cattle is associated with a variety of physiologic changes that promote milk production. These include increased mobilization of body energy stores and alterations in overall protein metabolism in other organs to provide substrates for milk secretion, increased food intake, increased nutrient absorption from the gastrointestinal tract, and improved effi ciency of the conversion of nutrients to milk by the mammary gland. It is presumed that many of the effects of growth hormone are mediated via insulin-like growth factors (IGFs), whose production is increased by growth hormone. Even though growth hormone appears to be a primary regulator of milk production in cows, milking or suckling does not produce an immediate release of growth hormone in the lactating cow.

Routine milking or suckling to remove milk from the mammary glands is essential for continued milk production. When milking is stopped abruptly (probably the best way to dry up a cow), a number of changes in the udder occur. At the end of 24 hours, the alveoli become distended to a maximum, and the capillaries are full of blood. Between 36 and 48 hours, there is a decrease in the number of patent (open) capillaries, and the alveoli do not respond to intravenous oxytocin. A protein that inhibits milk production, feedback inhibitor of lactation, is apparently produced in the mammary gland as milk is produced. This protein has a local effect to inhibit milk production. Other components of milk may have similar inhibitory effects, and routine removal of these inhibitory factors promotes the continuation of lactation.

Milk ejection or letdown.

Milking or nursing alone can empty only the cisterns and largest ducts of the udder. In fact, any negative pressure causes the ducts to collapse and prevents emptying of the alveoli and smaller ducts. Thus, the dam must take an active although unconscious part in milking to force milk from the alveoli into the cisterns. This is accomplished by active contraction of the myoepithelial cells surrounding the alveoli (milk ejection, or milk letdown). These myoepithelial cells contract when stimulated by oxytocin, a hormone released from the neurohypophysis of the pituitary as a result of a neuroendocrine reflex. The afferent side of the reflex consists of sensory nerves from the mammary glands, particularly the nipples or teats. Afferent information reaches the hypothalamus, which regulates the release of oxytocin from the neurohypophysis. Suckling the teats by the young is the usual stimulus for the milk ejection reflex, but whether milk is withdrawn from the teat or not, the milk ejection reflex produces a measurable increase in the pressure of milk within the cisterns of the udder.

The milk ejection reflex can be conditioned to stimuli associated with milking routine, such as feeding, barn noises, and the sight of the calf. It can also be inhibited by emotionally disturbing stimuli, such as dogs barking, other loud and unusual noises, excess muscular activity, and pain. Stressful stimuli increase the activity of the sympathetic nervous system, which can inhibit the milk ejection reflex. This inhibition occurs both at the level of the hypothalamus via an inhibition of oxytocin release and at the level of the mammary gland, where sympathetic stimulation can reduce blood flow and directly counteract the effect of oxytocin on myoepithelial cells.

Oxytocin release typically occurs as a surge within a minute or two after initiation of the reflex by some tactile or environmental stimulus, and the plasma half-life of oxytocin (a small peptide hormone) is but a few minutes. Hence, milking or suckling should begin in close association with stimuli known to stimulate oxytocin release, such as washing the udder and stimulation of the teats. If failure to get an adequate stimulus for milk ejection, possibly because of inadequate preparation before milking, becomes habitual, the lactation period may be shortened by excessive retention of milk in the udder. Essentially all the milk obtained at any one milking is present in the mammary gland at the beginning of milking or nursing. However, milking does not usually remove all of the milk in the gland. Up to 25% of the milk in a gland usually remains after milking. Some of this residual milk can be removed after injections of oxytocin, but the routine use of such injections tends to shorten the lactation period.

Colostrum.

Colostrum, the first milk produced upon delivery of the newborn, is important for the survival and vitality of newborn domestic animals. One of the unique differences between colostrum and typical milk is that colostrum contains a high concentration of immunoglobulins produced by the immune system of the dam. These immunoglobulins are concentrated in the milk by selective transport by the epithelial cells lining the alveoli and are needed by the neonate to provide temporary immune protection against infectious agents in the environment.

During the first day or two of life, most domestic neonates can absorb intact immunoglobulins from their gastrointestinal tract into the blood. After this period, immunoglobulins cannot be absorbed intact, and consumed immunoglobulins are digested in a manner similar to other ingested proteins. **Closure** is the term given to the changes that occur in the gastrointestinal tract after the first or secondday of life that prevent the continued absorption of intact immunoglobulins. Colostrum consumption is especially important in domestic farm animals because of limited transfer of immunoglobulins from the dam to the fetus via the placenta. In some mammals, including humans, transfer of immunoglobulins via the placenta occurs to a greater extent, so consumption of colostrum by neonates is less important.

Colostrum is also a source of energy for the newborn, since most are born with limited amounts of body fat and other sources of metabolic energy. The primary sources of energy in colostrum are milk proteins and lipids, because colostrum has a relatively low concentration of lactose. Recall that progesterone inhibits development of enzymes necessary for lactose synthesis until just prior to parturition. The colostrum of most species also has tends to have relatively high concentrations of vitamins A and D and iron, but some species differences in composition do exist.

Cessation of lactation.

Daily milk production reaches a maximal value at some point after lactation begins and then gradually declines over time in most species. The decline in milk production is associated with a gradual decrease in the number of active alveoli and an increase in the relative amount of connective tissue. Mammary gland involution is the term describing the conversion of a milksecreting gland with milk-fi lled alveoli to one characterized by small, nonsecreting alveoli surrounded by an extensive amount of connective tissue. Extending the period of lactation is economically important for some species (e.g., dairy cows), but not all (e.g., piglets may be weaned prior to peak milk production by sows).

BIBLIOGRAPHY

1. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.
2. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
3. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
4. Mazurkevich AY, Trokoz VO, editors. Physiology of farm animals. Workshop. 2nd ed. Kyiv: Center for Educational Literature; 2015. (Ukrainian).
5. Mazurkevich AY, Trokoz VO, Karpovsky VI, et al. ; edited by A.Y. Mazurkevich, V.O Trokoz. Physiology of agricultural animals. Textbook. 2nd ed. Kyiv; 2014. (Ukrainian).
6. Moyes CD, Schulte PM. Principles of Animal Physiology 3rd ed. Don Mills, Ontario: Pearson; 2016.
7. Papachristodoulou D, Snape A, Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 6th ed. Oxford, UK: Oxford University Press; 2018.

8. Pineda MH, Dooley MP, editors. McDonald's Veterinary Endrocrinology and Reproduction. 5th ed. Ames, Iowa: Iowa State Press; 2003.
9. Pollard TD, Earnshaw WC, Lippincott-Schwartz J, Johnson GT, editors. Cell Biology. 3rd ed. Elsevier. 2016.
10. Reddy PB. Text book of Animal Physiology. Andhra Pradesh, India: IMRF Publications; 2015.
11. Reece WO, Functional Anatomy and Physiology of Domestic Animals. 4th ed. Baltimore: Wiley-Blackwell; 2009.
12. Rhoades RA, Pflanzer RG. Human Physiology. 4th ed. Pacific Grove, Calif.: Brooks/Cole; 2003.
13. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
14. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.
15. Smith BP. Large Animal Internal Medicine. 3rd ed. St. Louis, Missouri: Elsevier Mosby; 2015.
16. Tortora GJ, Derrickson BH. Principles of Anatomy and Physiology. Atlas and Registration Card. 11th ed. Hoboken, NJ: John Wiley & Sons; 2005.

CHAPTER 13. PHYSIOLOGY OF THE URINARY SYSTEM

Overview of function of the kidneys.

The urinary system is responsible for maintaining the relatively constant internal environment of the body fl uids. This is accomplished by the formation and excretion of urine of an appropriate volume and composition. Urine formation occurs in the kidneys, and by adjusting the volume and composition of urine in response to changes in dietary intake or metabolism, the kidneys regulate the body balance of water, various electrolytes, acids, and bases. The kidneys also excrete metabolic waste products in the urine, including the nitrogenous waste, urea, and a by-product of skeletal muscle metabolism, creatinine. Signs of kidney diseases include imbalances of water, electrolytes, acids, and bases and increases in blood levels of urea and creatinine.

Kidneys are composite organs that consist of thousands to millions of similar microscopic functional units, the nephrons. Nephrons in all mammalian kidneys are similar in basic structure and function, but the number of nephrons differs among mammals. Large animals have more nephrons per kidney than small animals (e.g., 4 million for cattle and 500,000 for dogs). Nephrons consist of a spherical structure (Bowman’s capsule) that contains a capillary tuft (glomerulus) and a single long tubule connected to Bowman’s capsule. Bowman’s capsule consists of two layers of cells. The inner (visceral) layer closely surrounds the glomerular capillaries, and the outer (parietal) layer is continuous with the first segment of the tubule. A Bowman’s capsule with its contained glomerulus is a renal corpuscle. The single tubule is divided into segments based on differences in histological appearance, location in the kidney, and function. These segments are named the proximal (convoluted) tubule, loop of Henle, and distal (convoluted) tubule. The distal tubules of numerous

nephrons connect to another tubular structure found in the kidney, the ***collecting duct*** (tubule). Collecting ducts begin in the renal cortex, where they connect with distal tubules, and extend into and through the renal medulla.

Stages (steps) of urine formation.

Three processes are involved in urine formation:

- ✓ glomerular filtration;
- ✓ selective tubular reabsorption;
- ✓ selective tubular secretion.

As blood flows through glomeruli, a large quantity of fi ltrate is formed and enters the urinary space of Bowman's capsule. From here the filtrate flows through the tubules and collecting ducts, where tubular reabsorption and tubular secretion alter its volume and composition. Tubular reabsorption is the removal of substances from the tubular fl uid by the tubular cells; these substances are usually returned to the blood in the peritubular capillaries. Tubular secretion is the addition of substances to the tubular fluid by tubule cells. The secreted substances are produced in the tubule cells (e.g., hydrogen ion and ammonia) or taken up by the tubule cells from the blood in the peritubular capillaries (e.g., pharmaceuticals).

The renal microcirculation is unique in that glomerular capillaries are between two arteriolar vessels rather than between an arteriole and a venule. Afferent arterioles lead into glomeruli, and efferent arterioles leave glomeruli. Efferent arterioles from most glomeruli lead into capillary networks that surround tubules in the cortex (peritubular capillaries). Efferents from glomeruli deep in the cortex next to the medulla contribute blood to vessels that extend into the medulla. These vessels (vasa rectae) consist of straight descending branches (descending vasa rectae) that empty into medullary capillaries, which are drained by straight ascending vessels (ascending vasa rectae).

Near glomeruli, the walls of afferent arterioles contain specialized cells termed juxtaglomerular (JG) or granular cells. Secretory granules in these cells contain the enzyme renin. Renin is a component of the renin–angiotensin–aldosterone system, which is involved in the regulation of blood volume and blood pressure. The JG cells are part of a functional grouping of closely related structures, the juxtaglomerular apparatus. The juxtaglomerular apparatus consists of the JG cells, the macula densa, and extraglomerular mesangial cells. The macula densa is a specific region of the wall of the distal tubule where the cellular nuclei appear to be bunched closely together. The segment of the distal tubule found here is part of the same nephron associated with the afferent arterioles. The extraglomerular mesangial cells are between the macula densa and its associated JG cells.

Glomerular filtration. The glomerular filtrate is the fluid and fluid constituents that pass from the blood plasma in the glomerulus into the urinary space of Bowman's capsule. The physical barriers through which the fi ltrate passes include (1) the capillary endothelium of the glomerulus, (2) the inner layer of Bowman's capsule, and (3) a basement membrane (lamina) between these two cell layers. The glomerular endothelium is fenestrated (i.e., has openings or pores in the cells), so this part of the barrier is highly permeable.

Podocytes (cells of the inner layer of Bowman's capsule) have cellular extensions that rest on the glomerular basement membrane, but slitlike pores between

the extensions permit the passage of the filtrate. The glomerular filtration barrier acts much like a sieve, and all substances up to a molecular weight of about 65,000 pass through the barrier. Blood cells are too large to pass, and only a small percentage of plasma proteins pass through the barrier. Most other plasma constituents (e.g., glucose, amino acids, urea, creatinine, sodium, potassium, chlorine, and bicarbonate ions) readily cross the barrier, and their concentrations in the initial filtrate are about the same as in plasma. Proteinuria is the presence of abnormal amounts of protein in voided urine. Kidney diseases that localize in or primarily affect glomeruli are often associated with proteinuria or hematuria (blood in voided urine).

The forces determining the rate of movement of fluid across the glomerular filtration barrier are the same as those that determine fluid movement out of capillaries throughout the body. The effective filtration pressure (the pressure tending to force fluid out of the capillary) is usually considered to be the difference between the blood (hydrostatic) pressure in the capillary and the osmotic pressure generated by the plasma proteins of the blood in the capillaries. The hydrostatic pressure in the urinary space of Bowman's capsule and the osmotic pressure generated by proteins in the fluid in the space can also be factors, and these become important in disease states (e.g., blockage of the urinary tract or renal tubules). In mammals glomerular filtration rate (GFR) and renal blood flow (RBF) remain relatively stable in normally hydrated animals in spite of minor short-term fluctuations in arterial blood pressure (20–30 mm Hg). This stability is maintained by mechanisms intrinsic to the kidney, and this phenomenon is termed renal autoregulation.

Severe dehydration or severe blood loss results in lowering of blood pressure out of the autoregulatory range, and this leads to vasoconstriction of preglomerular vessels, including afferent arterioles. This vasoconstriction is produced by ncreases in sympathetic nerve activity to the kidneys and increases in vasoconstrictors such as angiotensin II. The low blood pressure and renal vasoconstriction can reduce glomerular filtration to the point of renal failure. This type of renal failure is termed prerenal. The GFR of mammals is normally about 100 times that of urine flow rate (typical values for GFR are 3–5 mL/kg body weight per minute). The high GFR relative to urine flow allows for a continuous filtration of the plasma and the rapid removal of unwanted or toxic substances from the body. If such substances can readily pass through the glomerular filtration barrier and are not reabsorbed from the renal tubules, they are rapidly eliminated via the urine.

Proximal tubule transport. The proximal convoluted tubule is the longest of the tubules, and proximal tubules make up most of the renal cortex. Typical proximal tubule cells are cuboidal, with a luminal border that is modifi ed with microvilli (brush border). The length and brush border provide for a large amount of cell membrane surface area, and the proximal tubule does more tubular transport than any other nephron segment. The cellular junctions between proximal tubule cells are also permeable to some substances in the filtrate (e.g. chloride ions) so that some transport can occur between the cells. Glucose and amino acids are examples of essential nutrients that are reabsorbed from the filtrate by cells of the proximal tubule. Normally, 100% of the glucose and amino acids in the initial filtrate are reabsorbed by the proximal tubule. This reabsorption involves secondary active transport using a sodium-linked cotransporter in a manner similar to glucose absorption in the small

intestine. Substances such as glucose that require membrane transporters for reabsorption have limits to the amount that can be reabsorbed as the fluid flows through the tubules. This limit is the tubular maximum, or transport maximum. The blood level at which the amount of a substance presented to the tubules by glomerular fi ltration exceeds the transport maximum is the renal threshold. *For example, animals or people with uncontrolled diabetes mellitus often have blood glucose levels that exceed their renal thresholds for glucose. In these cases, the increased amounts of glucose in the filtrate cannot be completely reabsorbed by the proximal tubules, and glucose is present in voided urine (glucosuria).*

Bicarbonate ions are the predominant base in the plasma and other extracellular fluids throughout the body. Normally, the proximal tubule reabsorbs almost 85–90% of the bicarbonate ions in the initial filtrate to maintain this ready supply of base. The transport of bicarbonate ions from the tubular lumen into proximal tubule cells entails their conversion to carbon dioxide and water under the influence of the enzyme carbonic anhydrase. This reaction requires a hydrogen ion supplied by transport from within the tubule cell. Once inside the tubule cell, the carbon dioxide and water are reconverted to bicarbonate and hydrogen ions, again under the influence of carbonic anhydrase. The bicarbonate ion can then exit the cell, using a membrane transporter, to be added to the blood again. Sodium accompanies the bicarbonate ions, so the electrical neutrality of body fluids is maintained. Sodium and chloride are the two predominant osmolytes in the initial filtrate, and cells of the proximal tubule reabsorb 70–75% of the sodium and chloride in the initial filtrate. The percentage reabsorbed can be increased by the actions of angiotensin II and sympathetic nerves on tubule cells and by vasoconstriction of renal blood vessels. Angiotensin II concentrations and sympathetic nerve activity to the kidneys increase during dehydration or blood loss, when it is appropriate to retain sodium chloride and water. Cells of the proximal tubule also actively secrete organic anions and organic cations into the tubular fluid to be added to the urine. It is by these secretory systems that the kidneys eliminate many pharmaceuticals (that are organic compounds) in the urine.

Concentration and dilution of urine.

To maintain water balance during potentially drastic changes in water intake, the kidneys must be able to excrete urine that is either more concentrated than plasma (hypertonic) or more dilute than plasma (hypotonic). The ability of the kidneys to generate hypertonic or hypotonic urine depends on the functional and anatomic characteristics of both the loop of Henle and the collecting duct. The excretion of hypertonic urine also requires antidiuretic hormone (ADH, or arginine vasopressin) to alter the transport characteristics of the collecting duct.

Loops of Henle are the nephron segments found in the renal medulla. The U-shaped loops extend to variable depths in the medulla, and the terms descending and ascending limbs are applied to the different parts of the loops. The ascending limbs of the loops of Henle are relatively impermeable to water and have a thick portion that is the site of a great deal of sodium and chloride reabsorption. Sodium and chloride transport by the thick ascending limb uses a unique membrane transporter that cotransports sodium, chloride, and potassium into the cell from the lumen. This transport is sodium-linked in that the Na-K-ATPase pump on the opposite side of the cell maintains the low intracellular sodium concentration that permits the

cotransporter to function. The net effect of this cellular transport is continuous addition of sodium and chloride to the interstitial fluid of the medulla without any accompanying water. Sodium chloride is also reabsorbed from the thin ascending limb of the loop, but the mechanism responsible for this transport is controversial. The fluid entering the loop of Henle is isotonic, and the fluid exiting is hypotonic. This change in tubular fluid shows that the net effect of loop of Henle transport is to add more particles than water to the interstitial fluids in the renal medulla.

Transport of sodium and chloride into the interstitium without water is the key factor in generation of hypertonic interstitial fluid in the medulla, and this hypertonic fluid has an essential role in the ability to generate hypertonic urine. The transport of particles without water from the lumen of the loops also creates hypotonic fluid in the tubule, and this is an essential step in the ability to generate hypotonic urine. However, regardless of the tonicity of the final urine, the transport characteristics of the thick ascending limbs of the loops of Henle remain the same, so that hypertonic fluid is generated within the renal medulla and hypotonic fluid is generated within the loop of Henle.

The descending limbs of the loops of Henle are relatively permeable to water but relatively impermeable to particles. As fluid flows into and through the descending limbs, water is removed because of the osmotic gradient between the tubular lumen and the interstitial fluids of the renal medulla.Because the ascending and descending limbs of the loops of Henle are relatively close together in the medulla and because the tubular flows move in opposite directions, the combined effect of transport by ascending and descending limbs produces an osmotic gradient in the interstitial fluids of the renal medulla. Interstitial fluid osmolality increases from the outer zones to the inner zones of the renal medulla.

The **countercurrent mechanism** is any mechanism that depends on streams of flow moving in opposite directions, and these are usually close to each other. The ascending and descending loops of Henle form a countercurrent mechanism that amplifies the osmolyte (sodium chloride) transport properties of the ascending limb of the loop of Henle. This countercurrent mechanism generates the osmotic gradient in the interstitial fluids of the renal medulla. The ascending and descending vasa recta also form a countercurrent exchange mechanism by permitting free exchange of solutes and water between the ascending and descending blood vessels. This exchange allows for blood flow into and out of the medulla without disrupting the gradient. There is a small net gain of both water and particles by the vasa rectae, and some of these are the water and particles that were reabsorbed from the loop of Henle. The maximal osmolality of the osmotic gradient in the renal medulla differs among species, and maximal urine concentration ability is determined by the maximal osmolality of the gradient.

Collecting duct transport. Osmotic regulation of antidiuretic hormone.

Principal cells in the collecting ducts are the target cells for ADH. If ADH is not present, the luminal cell membrane of these cells is relatively water impermeable. ADH stimulates the insertion of water channels into these cell membranes to increase the overall water permeability of collecting ducts. Collecting ducts begin in the renal cortex but extend into and through the renal medulla, where the interstitial fluids are hypertonic. Also, because of the transport in the loop of Henle, the tubular fluid

entering the cortical portion of a collecting duct is dilute or hypotonic, and this is always true regardless of the water balance status of the animal. If ADH is not present, the water permeability of the collecting duct is relatively low, and the hypotonic fluid entering the collecting ducts passes through and is excreted as a hypotonic urine. Because water is not reabsorbed from the water-impermeable collecting duct, the volume is also relatively large. If ADH is present, the water permeability of the collecting duct is increased, and water is reabsorbed because the osmolality inside the duct is less than that outside. As the tubular fluid passes through the medullary portion of the collecting duct, more and more water is reabsorbed, and the osmolality of the tubular fluid increases further. In these circumstances urine volume is low and urine osmolality is high.

ADH (or arginine vasopressin in most mammalian species) release from the posterior pituitary can be regulated by changes in the extracellular fluid osmolality. Specific cells (osmoreceptors) in the hypothalamus monitor the osmolality of the extracellular fluid. In response to increases in ECF osmolality, these cells stimulate increases in ADH release, which results in the excretion of a small volume of a hypertonic urine. The elimination of excess particles and conservation of water dilutes the extracellular fluid, which acts as a negative feedback control to inhibit additional releases of ADH. Reductions in the extracellular fluid osmolality inhibit ADH release, which results in the excretion of a relatively large volume of dilute urine. This eliminates any excess water.

Polyuria is the passage of larger volumes of urine than normal. Animals that cannot generate hypertonic urine when necessary become polyuric. Polydipsia is excessive thirst, and polyuric animals are often able to maintain water balance by increasing water intake. The increased intake is considered to be a sign of excessive thirst. Polyuria and polydipsia may also result when ADH is not available (e.g., pituitary tumor preventing its release) or the kidney does not respond appropriately to ADH. In either case the water permeability of the collecting ducts remains relatively low, and water cannot be reabsorbed from the collecting ducts into the blood. Again, the affected animals must increase water intake to maintain water balance. This condition is diabetes insipidus.

Sodium, potassium, and aldosterone.

Most of the sodium and potassium in the initial glomerular filtrate is reabsorbed by the proximal tubule and the loop of Henle. However, the collecting duct is also capable of sodium and potassium transport, and it is here that the fi nal adjustments are made in the regulation of sodium and potassium balance. Aldosterone, a steroid hormone from the adrenal cortex, functions as a major regulator of sodium and potassium transport in the collecting duct. Aldosterone acts on principal cells of the collecting ducts to promote their reabsorption of sodium when sodium must be retained to maintain sodium balance. The regulation of aldosterone secretion from the adrenal cortex relative to sodium balance is via the renin–angiotensin system. When sodium must be retained (such as with a low-salt diet or after loss of extracellular fluid with sodium), the renin–angiotensin system is activated, and angiotensin II stimulates cells of the adrenal cortex to secrete aldosterone.

The concentration of potassium in plasma and other extracellular fluids also regulates aldosterone secretion. Increases in potassium concentration directly stimulate cells of the adrenal cortex to secrete aldosterone. Aldosterone promotes potassium secretion by principal cells, and this tends to increase the urinary loss of potassium. The increased loss of potassium in the urine reduces plasma potassium, and thus potassium plasma concentration and potassium balance are maintained. Most potassium in excreted urine reaches the tubular fluid by tubular secretion in the collecting duct. Unregulated secretion of aldosterone by adrenal tumors can cause signifi cant reductions in plasma potassium concentrations, and these can threaten life. Such individuals may also have moderate degrees of sodium retention and increases in ECF volume, but this is usually not as severe as the changes in plasma potassium. The more moderate changes in sodium balance are because sodium transport by other nephron segments is regulated by other factors that can counterbalance the sodium-retaining effects of aldosterone.

Urine acidification.

Intercalated cells in the walls of collecting ducts are capable of the active transport of hydrogen ions into the tubular lumen to acidify the urine. This system can generate a difference between blood and urine of about 3 pH units, so if blood pH is 7.4, urine with a pH of 4.4 can be formed. The hydrogen ions to be secreted are generated in intercalated cells by the hydration of carbon dioxide under the influence of carbonic anhydrase. A bicarbonate ion is also generated during this process, and these are secreted into the extracellular fluids at the base of the cell, from where the bicarbonate can diffuse into the plasma. The secretion of hydrogen ions by intercalated cells is regulated in part by the concentrations of carbon dioxide and bicarbonate ions in the plasma and other extracellular fluids. If carbon dioxide concentration increases or if bicarbonate ion concentration decreases, the rate of hydrogen ion secretion accelerates, and urine becomes more acidic. The importance and relevance of this regulation by carbon dioxide or bicarbonate to the regulation of overall acid-base balance is discussed in a later section of this chapter. Some of the secreted hydrogen ions combine with $HPO_4{-}2$ ions in the tubular fluid to form $H_2PO_4{-}$. In this manner, $HPO_4{-}2$ acts as an intratubular buffer to reduce the concentration of free hydrogen ions and prevent the urine pH from dropping too low. The phosphate ions originally entered the tubular fluid as part of the glomerular filtrate. Ammonia may also serve as an intratubular buffer (forming ammonium ions), and it is secreted into the tubular fluid by the collecting duct.

Urinary bladder function. Mechanism and regulation of urination.

The bladder is an organ of the urinary system. The bladder collects and expels urine from the body. As urine is made, it moves from the kidneys and down each ureter to the bladder. The bladder's flexible walls stretch and contract to hold urine until it is expelled from the body through the urethra. It plays two main roles:

- ✓ temporary storage of urine – the bladder is a hollow organ with distensible walls. It has a folded internal lining (known as rugae), which allows it to accommodate up to 400-600ml of urine in healthy adults;
- ✓ assists in the expulsion of urine – the musculature of the bladder contracts during micturition, with concomitant relaxation of the sphincters.

Urinary bladder function is controlled by both voluntary and involuntary nervous pathways. The bladder is the organ that holds urine until it is ready to be released and then helps to expel it from the body. Ureters bring urine to the bladder from the kidneys, passing through an opening to the bladder called the ureterovesical junction. As the bladder fills with urine, nerves send signals to the central nervous system. Somatic and autonomic nerves control the detrusor muscle, which contracts and relaxes along with sphincters in the urethra. When full, the typical adult bladder can hold up to 500 milliliters of urine at a time—or about 2 cups—which must be released every two to five hours.

Urination, or micturition, is a combination of voluntary and involuntary actions regulated by the micturition center—a signal center located in the pons of the brainstem. As the bladder fills and the bladder wall is stretched, sensors send nerve impulses to the micturition center. The result is the relaxing and contracting of the detrusor muscle along with the external and internal urethral sphincters. Infants and young children release urine on reflex, but learn to control the external sphincter and hold their urine longer during potty training.

Composition of urine.

Urine is a liquid byproduct of the body secreted by the kidneys through a process called urination and excreted through the urethra. The normal chemical composition of urine is mainly water content, but it also includes nitrogenous molecules, such as urea, as well as creatinine and other metabolic waste components. Other substances may be excreted in urine due to injury or infection of the glomeruli of the kidneys, which can alter the ability of the nephron to reabsorb or filter the different components of blood plasma.

Normal chemical composition of urine. Urine is an aqueous solution of greater than 95% water, with a minimum of these remaining constituents, in order of decreasing concentration:

Urea 9.3 g/L.

Chloride 1.87 g/L.

Sodium 1.17 g/L.

Potassium 0.750 g/L.

Creatinine 0.670 g/L .

Other dissolved ions, inorganic and organic compounds (proteins, hormones, metabolites).

Urine is sterile until it reaches the urethra, where epithelial cells lining the urethra are colonized by facultatively anaerobic gram-negative rods and cocci. Urea is essentially a processed form of ammonia that is non-toxic to mammals, unlike ammonia, which can be highly toxic. It is processed from ammonia and carbon dioxide in the liver.

BIBLIOGRAPHY

1. Akers RM, Denbow DM. Anatomy and physiology of domestic animals. 2nd ed. Wiley-Blackwell; 2013.
2. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell. 4th ed. New York: Garland Science; 2002.

3. Aspinall V, Cappello M. Introduction to Veterinary Anatomy and Physiology Textbook. 3rd ed. Oxford, UK: Elsevier Science & Technology; 2015.
4. Berne RM, Levy MN. Principles of Physiology. 3rd ed. C.V. Mosby; 2000.
5. Boron WF, Boulpaep EL. Medical Physiology. 2nd ed. Philadelphia, WB: Saunders; 2009.
6. Bullock BL, Henze RL. Focus on Pathophysiology. Philadelphia: Lippincott Williams & Wilkins; 2000.
7. Campbell AM, Paradise CJ. Animal Physiology. New York: Momentum Press; 2016.
8. Carere C, Maestripieri D, editors. Animal personalities: Behavior, Physiology, and Evolution. Chicago: University of Chicago Press; 2016.
9. Carlson NR, Birkett MA. Physiology of behavior. 12th edition. London: Pearson; 2017.
10. Cunningham JG, Klein BG. Cunningham's textbook of veterinary physiology. 5th ed. St. Louis: Elsevier Saunders; 2013.
11. Elliott WH, Elliott DC. Biochemistry and Molecular Biology. 3rd ed. Oxford University Press; 2005.
12. Frandson RD, Wilke WL, Fails AD. Anatomy and Physiology of Farm Animals. 7th ed. Wiley-Blackwell; 2009.
13. Hill RW, Wyse GA, Anderson AM. Animal Physiology 3rd ed. Sunderland, Massachusetts: Sinauer Associates, Inc; 2012.
14. Hill RW, Wyse GA, Anderson M. Animal Physiology. 4th ed. Oxford University Press; 2017.
15. Koeppen BM, Stanton BA. Renal Physiology. 5th ed. Mosby Elsevier; 2012.
16. Lawson R. Anatomy and Physiology of Animals. WikiBooks; 2015.
17. Mazurkevich AY, Karpovsky VI, Kambur MD, Trokoz VO, Bublyk VM, Golovach PI, Hryban VG, et al. Animal physiology. 2nd ed. Vinnytsia: New book; 2012. (Ukrainian).
18. Scanes CG, Brant G, Ensminger ME. Poultry Science. 4th ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2004.
19. Singh B. Evolve Resources for Dyce, Sack and Wensing's Textbook of Veterinary Anatomy. 5th ed. Philadelphia: Saunders; 2016.

ACh	acetylcholine
ACTH	adrenocorticotropic hormone
ADH	antidiuretic hormone
AMP	adenosine monophosphate
ADP	adenosine diphosphate
ANS	autonomic nervous system
AP	action potential
ATP	adenosine triphosphate
A-V	atrioventricular
B_1	vitamin b1(thiamine)
B_2	vitamin b2(riboflavin)
B_6	vitamin b6(pyridoxine)
B_{12}	vitamin b12(cyanocobalamin)
BMR	basal metabolic rate
Ca	calcium
Ca^{2+}	calcium ion
cAMP	cyclic amp
CCK	cholecystokinin
Cl	chlorine
GFR	glomerular filtration rate
CNS	central nervous system
CO	carbon monoxide
CO_2	carbon dioxide
Cu	copper
D	vitamin d (antirachitic vitamin)
DNA	deoxyribonucleic acid
ECF	extracellular fluid
Fe	iron
Fe^{2+}	ferrous iron (low valence)
Fe^{3+}	ferric iron (high valence)
FSH	follicle-stimulating hormone
GABA	γ-aminobutyric acid
GALT	gut-associated lymphatic tissue
GH	growth hormone
GIP	gastric inhibitory peptide
H^+	hydrogen ion
Hb	hemoglobin
HbO_2	oxyhemoglobin
HCl	hydrochloric acid
HCO_3-	bicarbonate ion
HDL's	high density lipoproteins
H_2CO_3	carbonic acid

H_2O	water (hoh)
H_2O_2	hydrogen peroxide
HPO_4	monobasic phosphate ion
H_3PO_4	phosphoric acid
I	iodine
Ig	immunoglobulin
IGF-1	insulin-like growth factor 1
IGF-2	insulin-like growth factor 2
JG	juxtaglomerular or granular cells
K^+	potassium
LH	luteinizing hormone
LDL's	low density lipoproteins
MP	membrane potential
N	nitrogen
Na^+	sodium
NADH	reduced nicotinamide adenine dinucleotide
$NaHCO_3$	sodium bicarbonate
NaOH	sodium hydroxide
NH_3	ammonia
NSAIDs	nonsteroidal anti-inflammatory drugs
O_2	oxygen
OH^-	hydroxyl ion
P	phosphorus
PCO_2	partial pressure of carbon dioxide
PRL	prolactin
RBC	red blood cells
RNA	ribonucleic acid
RP	resting potential
SA	sinoatrial
STH	growth (somatotropic) hormone
T_3	triiodothyronine
T_4	thyroxine (tetraiodothyronine)
TCT	thyrocalcitonin
TSH	thyroid-stimulating hormone
WBC	white blood cells
VFAs	volatile fatty acids
VIP	vasoactive intestinal peptide
VLDLs	very low density lipoproteins

ANIMAL PHYSIOLOGY. MANUAL.

Animal Physiology. Manual: manual / comp. I.A. Kolomiiets, I.I. Kovalchuk, ed. I.A. Kolomiiets, M.V. Podoliak; LNUVM named after S.Z. Gzhytskyi. – Lviv, 2022.– 190 p. – a – il.

Recomended by Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies Lviv Manual «Animal Physiology. Manual» (comp. I.A. Kolomiiets, I.I. Kovalchuk, ed. I.A. Kolomiiets, M.V. Podoliak) for students of the speciality 211 «Veterinary medicine» of second educational level (Order №317 as of 24th December, 2021)

Editor:
Iryna Kolomiiets
English language editor:
Mykhailo Podoliak

Reviewers:
Oleksii Danchuk
Dmytro Masiuk
Mykola Zhyla

Авторська редакція
Комп'ютерна верстка: Корпан Борис

Підписано до друку 01.02.2022. Формат 60x84/16
Гарн. Times New Roman. Папір офсетний. Ум. друк. арк. 10,58.
Наклад 100 прим. Зам. № 01/02.

Друк ФОП Корпан Б.І.
Львівська обл., Пустомитівський р-н., с Давидів, вул. Чорновола 18
Ел. пошта: bkorpan@ukr.net, тел. (093) 480-6141
Код ІНДРФО 1948318017, Свідоцтво фізичної особи-підприємця:
В02 № 635667 від 13.09.2007