Endocrinology

University College Maastricht Course SCI3007 2017

Organization:

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Objectives

Specific physiological objectives

- Homeostasis
- Integration of the endocrine and nervous system
- Function and location of endocrine glands and organs
- Intracellular signal transduction of the hormones subject of study
- The autonomic nervous system
- Synthesis, structure, function, mode of action and regulation of the hormones subject of study such as:

Catecholamine's, erythropoietin, melatonin, thyroid hormones, human growth hormone, prolactin, oxytocin, glucocorticoids, androgens, estrogens, progestin's, anti-diuretic hormone, mineralocorticoids, atrial natriuretic peptide, parathyroid hormone, vitamin D, insulin, glucagon, somatostatin, gastrin, motilin, cholecystokinin, and secretin.

- Axis hypothalamus-pituitary-target gland/tissue
- · Common disorders affecting steroid hormone homeostasis
- Contraception
- Endocrine and autonomic control of digestion
- Digestion and absorption of macronutrients
- Absorption and function of micronutrients and minerals
- Hunger and satiety control
- Common disorders affecting digestion
- Kidney function
- Hypo- and hypernatremia
- Endocrine control of water and salt homeostasis
- Bone composition, buildup, and breakdown
- Endocrine control of calcium and phosphate homeostasis
- Hypo-and hypercalcemia
- Common bone disorders: (osteoporosis, rickets, and osteomalacia)

Personal development and attitude

- Collaboration in order to produce team presentations
- Oral presentations on course assignments
- Active participation during group meetings

Introduction

This second, advanced Physiology course is intended to increase your knowledge on disturbances of (*endocrine*) homeostasis in the human body. The course is constructed as such that you will be stimulated to perform both individual and collaborative work using a PBL-variant called Team-based Learning.

Literature suggestions

Accessmedicine via UM library databases: (http://library.maastrichtuniversity.nl/databases/)

Specific endocrinology e-books available via UM library.

https://maastrichtuniversity.on.worldcat.org/atoztitles/ebooks?searchType=matchAll&btitle=e

ndocrinology

Texbook of Medical Physiology; Hall&Guyton 12th edition or higher

Medical Physiology; Boron&Boulpaep

Pathologic Basis of Disease; Kumar et al.

Essentials of Anatomic Pathology 3rd, Cheng and Bostwick (Via UB- maastrichtuniversity e-books)

Evaluation

We will evaluate your progress in this course in three ways:

- by oral presentations throughout the course (duration 15 minutes + 5 minutes discussion)

on pathophysiology topics as indicated in the manual. Some research will be needed to

find the necessary and relevant literature. Help will be provided if necessary. This group

work will result in PowerPoint presentations that will be presented each week and graded

(30%, group grade).

- by a written examination at the end of the course. This examination will consist of a limited

number of essay guestions and MCQ's. Time required: maximum 2 hours (70%, individual

grade).

- by attendance, participation and professional conduct during the course (during plenary

meetings and in teams). (Pass/Fail).

A possible resit will be a written exam.

This course is subject to UCM rules and regulations.

Because of the group effort in the course the presence of all students during course

meetings is compulsory. Students who have not met this attendance/participation

requirement, but who have not missed more than 30% of the group meetings (with

notification), will be given a provisional overall grade, but will not receive credits for the

course until they have successfully completed an additional assignment.

We wish you success in finishing this course and hope you will enjoy it.

Andries Gilde, course coordinator

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Course layout

Higher organisms like humans have a large number of vegetative (autonomic) functions in their body aiming at the maintenance of the homeostasis of the "milieu interieur". Disturbances in the body homeostasis can lead to serious pathophysiological changes and in certain conditions, to life-threatening diseases. The maintenance of the "milieu interieur" demands the presence of a large number of *physiological regulatory mechanisms* involving various organs. Signaling between and within these organs depends to a large extent on circulating and locally produced mediators like hormones and neurotransmitters.

In order to understand the role of these regulatory mechanisms, we need to study the role of hormone-producing organs (endocrine system), like hypothalamus, pituitary gland, thyroid gland, adrenal gland, gastro-intestinal wall and pancreas, but also of the autonomic nervous system, being the major source of electrical signals in our body. Because it will be impossible to discuss all aspects of the hormonal and nervous system in the 6 weeks period, we will make a selection of potentially interesting subjects. As such the following **week** schedule is proposed:

1) Basic principles of endocrine regulatory mechanisms

This week we will recapitulate the basic principles of the physiological regulatory mechanisms. What is the essence of physiological regulatory mechanisms and of the milieu interieur, which processes need to be regulated, what are hormones, how do they work, what are target organs and target cells?

2) Steroid hormones and the regulation of homeostasis

In this week, we will concentrate upon a large class of hormones, i.e. the steroid hormones. For the production of these hormones, we have to turn our attention to the function of hypothalamus/pituitary - gonadal, and adrenal - axis.

3) Gastrointestinal system and digestion of food

Also in the gastrointestinal system, digestion of food is under the control of hormones, which are produced by a variety of organs. These same organs are involved as well in the fine-tuning of the various processes which are essential in providing the body cells of adequate amounts of energy and substrates.

4) Hormonal regulation of energy- and protein balance

Since our body is an open system, with a lot of spillage of energy as warmth, our energy and protein balance has to be kept as functional as possible. Both storage and recruitment of carbohydrates, fat, and protein are under the guidance of hormones, as well as the transport between the various organs in need of energy. Finally, how will the energy be liberated in the form of ATP?

5) Water- and salt regulatory mechanisms

For all organs and cells it is of the utmost importance that their water and electrolyte (salt) content is delicately fine-tuned. We will study in large detail the function of the kidney as well as the hormones which are important for the regulation of water and salt content.

6) Calcium- and phosphate homeostasis

In this week we will concentrate especially on the formation and degradation of bone tissue. For this the parathyroid gland is very important, therefore this gland in particular will be subject of our attention.

7) Written exam in week 7 date and time via UM personal calendar.

Organization of the course

This course is divided in 6 modules of one week each. The instructional format is Team-Based Learning. In each week there is a plenary lecture, followed by team-presentations (except in week one) and a few days later a tutorial meeting (See MyUM calendar for schedule). During the plenary lecture, an introduction will be given on the module. This lecture is intended to refresh and reactivate the existing knowledge and to enhance your understanding of the subject. At the end of this lecture a number of assignments will be distributed to the student teams. Each team will consist of at least of 2 students. During the remainder of the week, the students will elaborate on their case and prepare a Powerpoint presentation. For background information the students can use the suggested literature, but also other reliable (peer-reviewed, see form last page of manual) scientific sources should be consulted. At the end of each week there will be a tutorial meeting, during pre-described learning goals are discussed and progress on the team-presentations will be monitored.

Guidelines for preparation of the PowerPoint presentation

Each presentation should start with a title-slide including the academic year and the names of the participating students. The next slide should give a content structure of the presentation. Subsequently, a short introduction and explanation of the assignment should be provided, followed by detailed description of the subject. Finally, a slide with a short summary/conclusion with ONE MCQ covering the main message and a final slide with a list of scientific resources should be given.

Presentation time is 15 minutes. On average: count 1 minute to explain 1 slide.

The presentations will be graded with formative and summative grading using the list at page 22.

Week 1: Basic principles of physiological regulatory mechanisms

This week we will recapitulate the basic principles of the physiological regulatory mechanisms. What is the essence of physiological regulatory mechanisms and of the milieu interieur, which processes need to be regulated, what are hormones, how do they work, what are target organs and target cells?

Claude Bernard (France 1813-1878) was the first scientific investigator who concluded that there is a remarkable resemblance between the composition of seawater and of the interstitial fluids in our bodies. Besides, the composition of the interstitial fluid seems to be similar all through our body. In order to describe the nature and general characteristics of this interstitial fluid, Bernard introduced the term 'milieu interieur'. He compared this interstitial fluid with that surrounding the human body (this can be liquid as well as humidified atmosphere) and named the latter one the 'milieu exterieur'. Bernard developed the remarkable thesis that an organism in fact does not live in the milieu exterieur. This thesis was based upon the observation that cells only can live, grow and exert their specialized function if the characteristics of their immediate neighborhood (i.e. the milieu interieur) such as pH, concentrations of gasses and ions, temperature and substrates were and remained very constant. In other words, he concluded that only the quality of the milieu interieur is of any importance for the optimal functioning of body cells.

Therefore Claude Bernard writes in 1787: '... The stability of the milieu interieur is the primary condition for freedom and independence of existence...' and '... the necessary conditions for the life of elements which must be brought together and kept up constantly in the milieu interieur if freedom and independence of existence are to be maintained, are already known to us: water, oxygen, heat, and reserve substances...'. With this last statement Bernard indicates the importance of a number of organs like heart, lungs and kidneys. Claude Bernard was also convinced that the brain played a crucial role in the control of the optimal quality of the milieu interieur. He wrote '... In the perfect animal whose existence is independent, the nervous system is called upon to regulate the harmony which exists between all these conditions...'. With this thesis Bernard indicates that control systems must exist that govern the quality of the milieu interieur and that regulate and harmonize the functions of the various organs in the body.

In highly evolved organisms like humans very complicated systems are needed to guarantee the quality of the milieu interieur in very deep tissues. For this regulatory mechanisms were developed so that signals from deep in the tissues can be recognized and interpreted. Thus, for this not only sensors are needed but also signaling systems. We recognize several signaling systems in the human body: direct neurotransmission, hormonal signal transmission via the blood (endocrine), signaling between cells within tissues (autocrine/paracrine) and intracellular signal transmission. To this end our body developed molecules which can be recognized by their specific receptors, the activation of which can lead to further actions of the cells or the genetic apparatus. It is known that the excretion of hormones and neurotransmitters are under the direct guidance and control of so-called regulatory circuits.

Learning goals

- knowledge and insight in the actions of hypothalamus/pituitary axis
- what is a hormone and what types can be distinguished?
- how do hormones work and where do they act upon?
- intracellular signal transduction pathways are known which are steered by hormones
- adrenaline noradrenalin, growth hormone, thyroid hormone, EPO, melatonin, prolactin, and oxytocin.
- Circadian rhythms, central and peripheral clocks.

Assignment:

- 1A. Discuss pheochromocytoma. Try to explain the characteristics of this condition based upon the working mechanisms of (nor) adrenaline. Where are these molecules secreted, where do they attach, and how are they inactivated. Make no indefinitely long list of organs and the effects of both substances on them, but stick to the highlights.
- 1B. Discuss the acromegaly and gigantism. What are the causes and consequences? What is the role of the pituitary in these deviations? Discuss also the secondary effects on glucose- and fatty acids metabolism.
- 1C. It is known that the pregnant female body increases the production (in the liver) of the protein that binds in the blood plasma to the thyroid hormone. Through this binding there is a feedback driven increase of the plasma concentration of the thyroid hormone. However, hyperthyroidism does not occur. Explain this phenomenon and use the regulatory circuits which are important for the functions of the thyroid gland.

- 1D. The hormone erythropoietin (EPO) is a well-known hormone in circles of top athletes. Discuss the physiological role of this hormone. Where is it produced and how is the production and secretion of this protein regulated? Discuss also why abuse of EPO can lead to serious cardiac complaints such as ischemic heart disease.
- 1E. Frequent trans meridian air travels, shift-workers and students experience problems related to extended sleep. Describe the circadian regulation of sleep and the involvement of melatonin. Also pay attention to the mammalian circadian clock and "Seitgebers".
- 1F. Breast feeding is next to a histological and anatomical complex mechanism also a neuro-hormonal wonder. Describe the neuro-hormonal regulation of breastfeeding. Also pay attention to the production and ejection of milk.

Week 2: Steroid hormones

This week, we will concentrate upon a large class of hormones, i.e. steroid hormones. For the production of these hormones, we have to turn our attention to the function of hypothalamus/pituitary axis, the gonads, and the adrenal glands.

Steroid hormones are crucial for the procreation of humans: No steroids, no babies! However, not only for reproduction these hormones are crucial, but also for the general homeostasis and growth.

The precursor for the production of steroid hormones is cholesterol. Cholesterol is partly absorbed by our body from food, but is also produced partly in the liver. A number of organs (or even better said a number of special cells within organs) are capable to transform cholesterol into specific steroids. These organs are the ovaries, testes and adrenal cortex. Steroids are metabolized by other organs resulting in new (secondary) active steroid hormones. In this metabolic process also inactive metabolites are produced.

The production of steroid hormones on itself is under the control of other hormones. Specific protein hormones that are produced in the pituitary are crucial in this regulation. In turn these protein hormones are produced under the control of the hypothalamus. Therefore, one often speaks of the hypothalamus-pituitary-gonadal/adrenal axis.

Steroids affect many processes in the human body. This depends on the chemical structure and concentration of the steroid hormone but also on the steroid receptors in the target organs. Such processes as growth, ovarian cycle, maturation of reproductive cells, energy metabolism, water- and salt homeostasis are all regulated by steroid hormones.

Learning goals

- hypothalamus pituitary gonadal axis
- hypothalamus pituitary adrenal cortex axis
- synthesis of steroids in testis, ovaries, adrenal cortex and peripheral tissues
- nuclear receptors and there classes.
- most occurring disturbances in steroid hormone homeostasis:
 - mismatch on production (too much, too little)
 - enzymatic deficiencies
 - Cushing syndrome
 - Addison's disease
 - hirsutism
 - contraceptive pills

Assignment

- 2A Mister A.K. regularly visits a fitness center to remain in good condition and to 'reconstruct' his body shape to the fashioned male ideal. Because his muscle mass does not increase fast enough, he decides to use anabolic androgenic steroids.
 - what are AAS, how do they work, what are the negative effects?
 - where are endogenous androgens produced and how is synthesis controlled?
 - which metabolic conversions are necessary to convert cholesterol into androgens?
 - which hormones regulate the production of androgens?
 - what is the biological activity of endogenous androgens?
 - what are their target organs and cells
- 2B . Miss T.Z. (18 years old) decides to take the pill. Her GP prescribes a second generation pill. Ten years later, when T.Z. and her partner decide to start a family, she stops taking the pill. About six months later she becomes pregnant and 9 months later she gives birth to a healthy Babyboy.
 - what are the active substances in the oral anti-conception pill? Explain their biological activity
 - how and where were the endogenous steroid hormones of T.Z. produced before she took the pill? How was this production regulated?
 - which metabolic conversions, in which cells, lead to the production of female sex hormones?
 - what is the biological activity of female steroid hormones? What are the target organs and cells? Which biological processes do they activate?
 - which changes in steroid hormone production do occur during the first 3 months of T.Z.'s pregnancy? What were the consequences of these changes?
 - What are the essential differences between the 1st, 2nd, and 3rd generation anti-conceptive pills?
- 2C . Misses W.T. is 34 years old and visits an internist for the following complaints: increasing hair growth, amenorrhea since 4-5 months, and increase in muscle mass. The internist takes some blood and asks the department of clinical chemistry to determine the content of various steroids. It seems that the content of 17-ketosteroids is significantly increased. Also the ACTH content seems to be increased. The internist decides to treat misses W.T. with prednisone

- explain the complaints of W.T. How can disturbances in the steroid metabolism explain these phenomena?
- which role does the adrenal cortex play in healthy individuals? How are steroids produced in this compartment of the adrenal gland? Which metabolic conversions are important? Think also of differences between glucocorticoids and mineralocorticoids. How is the production if these steroid hormones regulated by other hormones?
- what are the biological effects of these steroid hormones? What are the target organs and cells?
- explain based upon what is known about the regulation of steroid hormone production – why prednisone is the indicated therapy in this case
- 2D The Addison's disease is characterized by an almost complete function loss of the adrenal cortex.
 - describe the possible causes and consequences of this disease. Add to this
 the disturbances in the synthesis of steroids and their biological action
 - describe why the so-called crisis of Addison is a feared complication of Addison's disease, often with fatal ending
 - which therapeutic interventions are possible, how do they work?
 - describe the differences between the Addison's disease and a secondary adrenal cortex insufficiency
- 2E Patients who suffer from the Cushing syndrome show particular body characteristics.
 - explain the steroid hormone production in the adrenal cortex in these patients, and the causes of disturbances in this production, the relation between the enhanced cortisol production and the phenomena occurring in the body
 - describe the similarities and differences between the Cushing syndrome and Cushing's disease
 - describe the therapeutic treatment, its working mechanism and possible complications
- 2F . Hypogonadism in the male population has multiple causes.
- describe the disease and elaborate on the shortage of male sex hormones
- describe where the androgen synthesis occurs, what the metabolic pathway of these hormones is, how they are regulated in the healthy fetus, and in the growing male teenager.
- elaborate on the biological activity of androgens and the possible therapies in hypogonadism

Week 3: Gastrointestinal system and digestion of food

Also in the gastrointestinal system, digestion of food is under the control of hormones, the production of which resides in a variety of organs. These same organs are involved as well in the fine-tuning of the various processes which are essential in providing the body cells of adequate amounts of energy and substrates.

An adequate supply of building materials is essential for the maintenance of body homeostasis. For this process the digestive system plays a crucial role. After digestion of the food in the intestines, molecules are absorbed through the intestinal wall and transported to the organs via blood or lymph. Our food contains not only carbohydrates, proteins and fats, but also minerals, vitamins, water and other essential compounds. In this week we will concentrate upon carbohydrates, fats and proteins. The digestive system consists of a variety of organs (mouth, oesophagus, stomach, small intestine, colon) in which the functions have to be adapted to each other. Aside from these organs, the pancreas and the liver/gallbladder are crucial. The concerted action of all these organs is regulated both by the nervous system and by hormones. The following processes can be distinguished: intestinal motility (propulsion and mixing), digestion (degradation of proteins, fat and carbohydrates), excretion of digestive fluids with hydrolytic enzymes, excretion and reabsorption of biliary salts, absorption of digestive products through the intestinal wall and resorption of water. Disturbances in these processes and their regulation lead to pathophysiological changes and diseases like constipation, dehydration, diarrhoea, malnutrition, etc.

Learning goals

- Structure and function of the digestive tract
- Hormonal and nervous regulation of digestive processes
- Digestion and absorption macro-and micronutrients
- Production and secretion of digestive fluids, hydrolytic enzymes and bile
- Entero-hepatic circulation
- Pathophysiology of a number of frequently occurring diseases of the digestive tract
- APUD concept of endocrine tumors

Assignments

- 3A . Mrs. P.T. has a long standing problem with biliary stones. She visits her GP with the complaint that she has yellow colored feces over the last week. The GP thinks his patient has steatorrhea.
 - indicate which disturbance has occurred in the digestive tract of Mrs. P.T.
 - Pay attention to the following aspects:
 - which liquid color is absent in the feces of P.T. Where does this come from?
 - it can be assumed that the entero-hepatic circuit is disturbed in the gastrointestinal tract of P.T. Which molecules are involved in this circuit?
 - where are these molecules synthesized and stocked?
 - which hormones play a role in the synthesis and secretion of these molecules?
 - what is the working mechanism of these molecules in the digestion and absorption of fat?
 - Investigate the role of these molecules in activating FXR receptors.
- 3B As a doctor you are consulted by a woman with a rear endocrine disorder called VIPoma. Patients with VIPoma exhibit watery diarrhea, hypokalemia, and achlorhydria.
 - Explain the symptoms of the patients in relationship to uncontrolled expression of VIP.
 - Explain the normal control of VIP and its physiological role. Pay attention to receptors and second messenger systems.
- 3C Taste is important in survival of the species. Ageusia, hypogeusia, and dysgeusia are related to taste.
 - Discus the concept of taste sensation. Pay attention to receptors, neurotransmission and the reward center of the brain.
 - Try to explain why some people have a soft spot for sweet, sour or fatty foods.
- 3D .Ulcers at the duodenum are frequently observed in patients with the syndrome of Zollinger-Ellison.
 - describe to possible causes of this disease
 - describe in detail the HCl production in the parietal cells in the stomach wall and its humoral and nervous regulation.
 - discuss the biological importance of HCI production in the stomach and the pathophysiological consequences.
 - which therapeutic interventions are possible for the treatment of Zollinger-Ellison, how do these drugs work?

- discuss also patients who suffer from achlorhydria. How do they differ from the Zollinger-Ellison patients?
- what learns achlorhydria about the importance of HCl production in the stomach?
- 3E . Both in acute and chronic pancreatitis the digestion of food is disturbed
 - discuss the causes of both forms of pancreatitis, as well as the pathophysiological mechanism of both diseases
 - explain why initially mostly the exocrine pancreas is diseased. How are digestive enzymes produced in the pancreas and excreted and how is this excretion regulated?
 - which relation exists between these enzymes and the occurrence of pancreatitis?
 - discuss the function of the excretion products of the exocrine pancreas in the healthy body.
 - which therapeutic possibilities exist in acute and chronic pancreatitis? Explain how they work.
- 3F One of the possible explanations for the success of the Atkins diet is that the satisfaction center in the brain is activated earlier in a fat-rich diet than in a carbohydrate-rich diet
 - Investigate how the intestines and certain centers in the brain communicate (via hormones or nerve impulses). Which hormones can play a role?
 - Are there other explanations and possibilities for the fact that the Atkins diet provokes weight loss? Are there any disadvantages when using this diet?

Week 4: Hormonal regulation of energy- and protein balance

During this week, we will try to gain understanding of the regulation of energy metabolism. Dependening on the composition and quantity of the food we eat daily and on the physical exercise, our metabolism adapts to provide sufficient energy to all body cells. Both in organs, tissues and cells we find a very integrated network of enzymatic reactions which have to be adapted to each other. This concerted action is regulated – among others - by hormones. Sometimes this regulation is disturbed when certain metabolites accumulate or when shortage of substrates develops. This can have serious consequences for the good function of the various organs.

Learning goals

- Integrated regulation (neuro-endocrine) of energy metabolism in feeding and starvation (see cases)
- Metabolic, endocrine and neuronal control of the endocrine pancreas
- Involvement of the liver
- Involvement of adipose tissue
- Involvement of muscle

Assignments

- 4A. Wim Hof, a.k.a. the Iceman, is famous for controlling his ANS in withstanding prolonged exposure to cold.
 - Describe the control of human thermoregulation
 - Identify and integrate the different tissues involved in thermoregulation
- 4B. Obesity (BMI>30kg/m2) is a risk factor for the development of Type 2 Diabetes Mellitus
 - Insulin signaling
 - describe common theories of insulin resistance
 - role of corticosteroids
 - leptin
 - hypothyroidism

- 4C. Metabolic changes as a result of a low carbohydrate diet.
 - Compare and contrast: low-carb diet with low-caloric diet in reducing and losing weight.
 - Hormonal changes involved.
- 4D.Between 1944 and 1945 the Minnesota Starvation Experiment was conducted under supervision of Dr. Ancel Keys.
 - · metabolic changes during fasting, starvation, and refeeding
 - hormonal control
 - ketone bodies
- 4E. Sprinting or marathon running
 - metabolic differences
 - muscle fiber types involved
 - hormonal regulation
 - energy substrate utilization
 - acidification
 - respiration

Week 5: Water- and salt regulatory mechanisms

The human body is very variable in it uptake and loss of water. Of course, it is a typical open system. But, at the same time, it is of utmost importance that the body water and its solutes are kept constant. Together the kidney and the thirst-regulatory center in the brain are the main regulatory organs and within the kidney the regulatory action of ADH (anti-diuretic hormone) is quantitatively the most important. The most occurring examples of fast water loss are transpiration and diarrhea. Also excessive use of diuretics causes disturbances in volume regulation. Aside from that there are some peculiar diseases which cause excessive water loss (diabetes insipidus). On itself, disturbances in volume regulation interfere negatively with certain syndromes like heart failure.

Learning goals

- mechanisms of water retention and excretion
- mechanisms of sodium retention and excretion
- kidney function in relation to water homeostasis and sodium, potassium and chloride (re)absorption
- causes and consequences of hypo- and hypernatremia

Assignments

- 5A. A woman of 50 years old has been subject to a pituitary infarction after heavy postpartum blood loss. During a heavy influenza she becomes very ill, gets diarrhea, vomits, and feels disoriented. On the first aid she seems to have a very low blood pressure, high heart frequency and low blood sugar, low sodium and high potassium content in the blood.
 - what is your diagnosis?
 - explain the disturbances in the electrolytes content
 - how should this woman be treated, immediately and after her recovery?
 - this is an acute and potentially fatal situation. If occurring, what could be the cause of the woman's death?
- 5B. While watching the movie 127 hours you realize you do know little about severe dehydration.
 - Describe the main sequence of events that happen during the onset of severe dehydration resulting in death. Pay attention: to the time course of 127 hours as in the movie and hormonal control.

- 5C . A man of 55 years old has a malignant tumor which cannot be removed. The tumor is situation at the left main bronchus. Suddenly this disease is complicated by a serious pneumonia. In the hospital an infusion of antibiotics is started and the patient's condition improves. The next day his urine seems to be very concentrated and contains 35 meq sodium. The osmolarity of the blood plasma is 250 mOsm/l (normal range: 280-300).
 - what is the most plausible cause of this concentrated urine?
 - what do you think his ADH level will be?
 - how can this explain the syndrome?
 - describe the pathophysiological background of this phenomenon
- 5D . A 22-year old woman is brought to the ER by ambulance with an epileptic insult. She was picked up from a dance party at which she collapsed. She is has hyperthermia, hypertension, and hyponatremia. After a few hours trying to stabilize her, she dies.
 - Describe the sequence of event resulting in her death.
 - Pay attention to hormonal control
 - Could alcohol intake have been an contributing factor?
- 5E. A man of 65 years old has intermittent claudication (narrowing of the iliac artery with pain in the calf at exercise). He has a blood pressure of 155/120 mmHg. Upon body inspection, a murmur is heard in the abdomen. Upon laboratory investigation of his blood the rennin concentration is increased.
 - what is the most probable diagnosis?
 - what causes the high blood pressure?
 - which parts of the disturbed hormonal system add to the high blood pressure?
 - how should this patient be treated?
- 5F. You have probably experienced the diuretic effect of coffee drinking. It is also generally said that drinking of coffee is bad under circumstances where dehydration can easily occur (summer, transatlantic flights, high altitude, and excercise).
 - Explain the diuretic effect of caffeine
 - do you agree with the thesis that coffee dehydrates? Give arguments for your answer.

Week 6: Calcium- and phosphate homeostasis

Calcium plays an important role in the body homeostasis. The calcium concentration in plasma is one of the best regulated parameters in the human body. In contrast, the phosphate concentration is less well regulated. However, phosphate, like calcium, plays an important role in many physiological processes. By far the highest amount of calcium and phosphate is found in bone, where both minerals play an essential role in bone synthesis and degradation.

The regulation of the calcium and phosphate concentration occurs under the guidance of hormones. We know the parathyroid hormone (PTH) which is produced in the parathyroid glands, calcitonin which is produced in the thyroid glands and vitamin D and its metabolites. Disturbances in the production and/or function of these hormones can lead to deviant calcium- and phosphate concentrations in plasma. This can lead to various pathophysiological phenomena, such as skeletal malformations and changed neuromuscular activity. Besides this, metabolic diseases of bones can occur such as osteoporosis and rickets. In these processes other hormones like steroids can also play a role.

Learning goals

- bone: composition, synthesis and degradation
- hormonal and non-hormonal regulation of the calcium- and phosphate metabolism
- causes and consequences of hypo- and hypercalcemia
- causes and consequences of hypo- and hyperphosphatemia
- diseases with a component of a deviant bone metabolism (osteoporosis, rickets, osteomalacia)

Peer-Assessment in Student Work

(adapted from University of Exeter's Teachers Quality Assurance Manual)

The purpose for using self and peer assessment is for its role in student skill development, in improving learning and in helping students to improve their performance on assessed work.

		F, P, G, E
Content	Is the breadth of the content sufficient? Is the depth of the content sufficient? Is sufficient evidence given to support arguments? Is there evidence of appropriate critical thinking? Are conclusions drawn appropriately? Is the class engaged and is their attention maintained? Is the response to questions and/or comments competent?	
Presentation	Audibility Clarity of articulation Presence Posture, eye contact, etc Management of notes or props Pace Confidence	
Slides	Readability Ratio between text and figures Use of other resources	
Structure	Coherency, appropriateness of structure Identity of beginning (summary), middle and end (conclusion)	
Grade (1-10)		

Specific narrative Feedback: