REQUIREMENTS

Semmelweis University, Faculty of Medicine
Name of the managing institute (and any contributing institutes):
Gestor Institute: Department of Physiology

Name of the subject: Szívelektrofiziológia

in English: Cardiac electrophysiology

in German: Herz-Elektrophysiologie

Credit value: 2

Number of lessons per week: 2 **lecture: practical course: seminar: 2**

Subject type: compulsory course elective course optional course

Academic year: 2022/2023

Subject code: AOVELT856_1A

Name of the course leader: András TÓTH, DSc.

His/her workplace, phone number: Semmelweis University, Department of Physiology; phone: +36-1-459-1500/60436

Position: External lecturer

Date and registration number of their habilitation: 18/2009 (SZTE, ÁOK).

Objectives of the subject, its place in the medical curriculum:

The course is intended to provide up-to-date and extended knowledge based on the latest literature for practically all medical students, especially those planning to be cardiologists or internists in order to meet a predictable future requirement of a strongly established knowledge related to the electrophysiological background and ion channel dependent pathomechanisms of severe, often lethal heart diseases and to facilitate their better understanding of the corresponding scientific literature. Their expected competent knowledge on cardiac electrophysiological mechanisms will significantly help young MDs to introduce novel, highly effective cardiopharmacological agents and/or to select optimal clinical therapeutic strategies. Via providing a detailed introspection into molecular and cellular basis of the electric activity of the heart the course is willing to offer the students an opportunity to collect an important section of these competences during their student years. During the course the motivated students may collect a comprehensive knowledge on:

- the biophysical basis of cardiac electrophysiology; the principles of operation and regulation of major cardiac ion channels
- the kinetic properties and regulation of ion currents generating cardiac action potentials; the significance of the repolarization reserve; the molecular background of substantial differences between atrial and ventricular and among various ventricular action potentials; and the basic pathomechanisms of arrhythmogenesis
- the principles of intracellular Ca^{2+} homeostasis in cardiomyocytes; the major mechanisms of excitation/contraction coupling; functional adaptation of the Ca^{2+}-cycle; pathomechanisms of Ca^{2+}-dependent and Ca^{2+}-facilitated heart diseases and several therapeutic strategies
- common genetic disturbances leading to malfunction of cardiac ion channels
- most important experimental techniques and animal models applied in experimental cardiac electrophysiology and the human/clinical relevance of the collected data

Finally a practical demonstration (13-th week) based on the material of the seminars is organized in order to help realistic, problem-oriented application of the theoretical knowledge via jointly processing experimental data derived from a few running scientific projects

Place where the subject is taught (address of the auditorium, seminar room, etc.):

Semmelweis University; EOK; H-1094 Budapest, Tűzoltó u. 37-47

Successful completion of the subject results in the acquisition of the following competencies:
Understanding of the human physiology which is foundation of medical practice.

Course prerequisites:
Medical Physiology 1 (the course is suggested for 2-4 year students)

Minimum and maximum number of students registering for the course: Minimum 5 and maximum 80 students
Student selection method in case of oversubscription: chronology of registration in the NEPTUN system.

How to apply for the course:
Registration must be recorded through the NEPTUN system.

Detailed curriculum (presented & discussed by prof. András TÓTH)**:**

1. week: **Introduction**
   - the role and importance of cellular level cardiac electrophysiology in medical practice
   - historical background
2. week: **Basic contexts of electrophysiology; propagation of stimulus in cardiac muscle**
   - biophysical principles of transcellular ion movements, Nernst equation, Donnan equilibrium, equilibrium potential
   - generation and maintenance of the resting potential
   - generation and propagation of the action potential (AP)
3. week**: Ion channels**
4. week: **Action potentials in the heart; major contributing ion channels/ion currents**
   - generation of the cardiac action potentials, fast and slow AP
   - atrial-ventricular and ventricular regional differences in action potentials and distribution of ion channels
   - Na^+ and Ca^{2+} specific ion channels and -currents
   - properties of various of K^+ currents (early/late, ultrarapid/rapid/slow, ATP-dependent, inward rectifying, etc.) and their role in the AP
5. week: **Developmental mechanisms of cardiac arrhythmias**
   - significance of the repolarization reserve, consequences of its decrease
   - mechanisms of generation of afterpotentials; extrasystole
   - ventricular arrhythmias: torsade de point (TdP), ventricular fibrillation
   - atrial fibrillation
6. week: **Experimental techniques in cardiac electrophysiology 1. – Microelectrode based measurements**
   - action potential measurements with conventional microelectrodes
   - ion current determinations using the „patch clamp" technique
7. week: **Ca^{2+} homeostasis in cardiac cells**
   - intracellular Ca^{2+} compartments
   - ion transport mechanisms involved in the Ca^{2+} cycle
   - cardiac Ca^{2+} transporters, their major characteristics and principles of function
   - the relationship between intracellular Ca^{2+} movements and AP repolarization
8. week: **The electromechanical coupling (ECc) and its regulation in cardiac cells**
   - regulation of the Ca^{2+} transport and -homeostasis
   - conditions for steady state activity of the heart
   - mechanisms of functional adaptation of the heart
9. week: **Perturbations of Ca^{2+} homeostasis and their role in development and progress of a number of heart diseases**
   - Pathomechanisms leading to cellular Ca^{2+} overload or Ca^{2+} deficit
   - Ca^{2+}-dependent and Ca^{2+}-facilitated heart diseases
   - afterpotentials and arrhythmogenesis; atrial fibrillation
   - ischemia/reperfusion injury
   - malignant hypertrophy and heart failure
10. week: **Experimental techniques in cardiac electrophysiology 2. Optical techniques**
    - basic principles of the application of fluorescent „tracer" molecules
    - „single" and „multichannel" measurements in isolated cardiomyocytes, isolated heart
    - novel, complex imaging (mapping) experimental techniques
11. week: **Experimental (animal) models and their clinical relevance**
    - the importance of experimental (animal) models in cardiology
    - small animal (mouse, rat, guinea pig) models
    - large animal (dog, rabbit, goat, etc.) models

- human relevance of data and information derived from animal models
- significance of human models and samples

12. week: **Genetic background of malfunction of cardiac ion channels**
    - „QT" syndromes and their genetic background
    - consequences of genetics originated disturbances of Ca^{2+} transporters
    - transgenic animal models
13. week: **Antiarrhythmic drug classes + a few examples from arrhythmia research**
    - Classification of antiarrhythmic drugs provided by Vaughan Williams
    - Principles of the „Sicilian Gambit"
    - Modernized scheme of antiarrhythmic drug classes
    - A few examples from experimental arrhythmia research
14. week: **Consultation**

Other subjects concerning the border issues of the given subject (both compulsory and optional courses!). Possible overlaps of themes:
Minimal overlap with Medical Physiology 1 and Cardiology

Special study work required to successfully complete the course:
None.

Requirements for participation in classes and the possibility to make up for absences:
It is required to attend at least 75% of the seminars (21 of 28 h of seminars).
Missing attendance may be partially compensated at a consultation offered during the semester

Methods to assess knowledge acquisition during term time:
(E.g. homework, reports, mid-term test, end-term test, etc., the possibility of replacement and improvement of test results)
Understanding of the material of the previous seminars will be verified by two „multiple choice" tests (10-10 questions) + interactive during the seminars

Requirements for signature:
It is required to attend at least 75% of the seminars (10 seminars).
Missing attendance may be partially compensated at a consultation offered during the semester

Type of examination:
Colloquium. Oral exam. Theoretical exam.

Requirements of the examination:
Before the exam the examinee should suggest at least six topics he/she knows best from at least six seminars. From the suggested topics the examiner will pick two to be orally presented.
The most important requirement is the best possible understanding of the selected seminars.
Seminar 1:

Seminar 2:

Seminar 3:
1. Basic features and classification of ion channels
2. Characterization and principles of regulation of voltage-gated ion channels
3. Characterization and principles of regulation of ligand-gated ion channels

Seminar 4:
1. Heterogeneity of action potentials and depolarizing ion currents in the heart
2. Repolarizing ion currents in the heart – the principle of repolarization reserve
3. Atrium specific, nonselective and anion currents in the heart

Seminar 5:
1. Principal mechanisms of arrhythmogenesis

2. Atrial fibrillation
3. Ventricular arrhythmias
Seminar 6:
1. Cardiomyocyte isolation techniques; patch-clamp measurement
2. Multicellular heart preparations; action potential measurements
Seminar 7:
1. Major Ca2+ compartments in cardiomyocytes
2. Trans-sarcolemmal Ca2+ transport in cardiomyocytes
3. Ca2+ transport in the sarcoplamic reticulum and in mitochondria
Seminar 8:
1. Principal mechanisms of the EC-coupling – the local control theory
2. Contol of Ca2+ release and Ca2+ content of the sarcoplasmic reticulum
– principle of flux balance
3. Mechanisms of functional adaptation of the heart
Seminar 9:
1. Afterpotentials and arrhythmogenesis
2. Intracellular Ca2+ overload and ischemia/reperfusion injury
3. Cardiac hypertrophy and heart failure
Seminar 10:
Basic properties of Ca2+-sensitive dyes; Ca2+ measurements in isolated single cardiomyocytes and in isolated intact heart; subcellular Ca2+ measurements
Optical mapping of membrane potential; principles of using genetically encoded Ca2+ indicators;
Seminar 11:
1. QT syndromes and their genetic background; consequences of genetic disorders of Ca2+ transporters
2. Transgenic animal models in cardiac electrophysiology – principles and perspectives of human gene transfer
Seminar 12:
1. Advantages and limitations of small and large animal models;
human relevance of data and information derived from animal models
2. Animal models of arrhythmogenesis, ischemic heart disease and heart failure
human relevance of data and information derived from animal models
Seminar 13:

Method and type of evaluation:

Two simple topics from the corresponding topic list will be picked randomly by the examinee. The overall grade of the exam is the mean of two partial grades:

Excellent (5):	4.51 - 5.00
Good (4):	3.51 - 4.50
Satisfactory (3):	2.51 - 3.50
Pass (2):	2.00 - 2.50
Fail (1):	below 2.00

How to register for the examination?:

Registration for the exam must be recorded through the NEPTUN system.

Possibilities for exam retake:

According to The Study and Examination Policy

Printed, electronic and online notes, textbooks, guides and literature (URL address for online

material) to aid the acquisition of the material:

Obligatory:

- The material presented during the classroom seminars and made also available on-line.

Suggested:

- Ion channels for communication between and within cells; Erwin Neher Nobel Lecture, 1991
- Heart Rate and Rhythm Ed. O.N Tripathi, U. Ravens and M.C. Sanguinetti; Springer, 2011
- Excitation-Contraction Coupling and Cardiac Contractile Force D. Bers; Springer, 2001
- Basis and Treatment of Cardiac Arrhythmias Ed.: R.S. Kass, C.E. Clancy; Springer, 2006
- Electrical Diseases of the Heart Ed. I. Gussak, C. Antzelevitch; Springer, 2008
- Handbook of Cardiac Electrophysiology Ed. A. Natale; Informa UK, 2007

Klinikai szív-elektrofiziológia és aritmológia Sz. Fazekas T., Merkely B., Papp Gy., Tenczer J.; Akadémiai Kiadó 2009

Signature of the habilitated instructor (course leader) who announced the subject:
Prof. András TÓTH, DSc.

Signature of the Director of the Managing Institute:
Prof. Attila MÓCSAI, DSc

Hand-in date:
07/06/2022

Opinion of the competent committee(s):

Comments of the Dean's Office:

Dean's signature: