

BIOPATHOLOGY AND INTRODUCTION TO MEDICAL THERAPY 1 (ML0363)

1. language

English.

2. course contents

Coordinator: Prof. GIOVAMBATTISTA PANI

Anno di corso/Year Course: 3

Semestre/Semester: Annual

CFU/UFC: 23

Moduli e docenti incaricati /Modules and lecturers:

- MEDICAL GENETICS (ML0382) - 0.9 cfu - ssd MED/03

Prof. Francesco Danilo Tiziano

- MEDICAL GENETICS PRACTICALS (ML0383) - 0.1 cfu - ssd MED/03

Prof. Francesco Danilo Tiziano

- MEDICAL MICROBIOLOGY (ML0380) - 4.8 cfu - ssd MED/07

Prof. Ivana Palucci, Elena De Carolis, Giovanni Delogu, Rosaria Santangelo

- MEDICAL MICROBIOLOGY PRACTICALS (ML0381) - 0.2 cfu - ssd MED/07

Prof. Rosaria Santangelo

- MOLECULAR PATHOLOGY, IMMUNOLOGY AND PATHOPHYSIOLOGY (ML0378) - 16.3 cfu - ssd MED/04

Prof. Simona Serini, Tobias Longin Haas, Francesco Ria, Ruggero De Maria Marchiano,

Giovambattista Pani, Gabriella Calviello, Carlo Provenzano, Mariapaola Marino

- MOLECULAR PATHOLOGY, IMMUNOLOGY AND PATHOPHYSIOLOGY PRACTICALS (ML0379) - 0.7 cfu - ssd MED/04

Prof. Donatella Lucchetti, Carlo Provenzano, Mariapaola Marino, Simona Serini, Antonella Sistigu

3. BIBLIOGRAPHY

BANASIK-COPSTEAD-: Pathophysiology. 6th Edition. Saunders-Elsevier 2018

ROBBINS & COTRAN: Pathologic Basis of Disease. 10th Edition, 2020

Harrison - Jameson - Loscalzo - Fauci - Kasper - Hauser - Longo , Harrison' s principles of internal medicine - 20th Edition. Mcgraw-hill 2018 (limited to chapters: 36, "Hypoxia and cyanosis"; 37, "Edema"; 49, Fluid and Electrolyte Disturbances, 50, Hypercalcemia and Hypocalcemia; 51, Acidosis and Alkalosis; 59, "Anemia/Polycythemia", 61, "Bleeding and Thrombosis"; 279, "Disturbances of respiratory Function"; 309, Cell biology and Physiology of the Kidney; 311, Chronic Kidney Disease (Note that this material and updates are available on the Access Medicine platform through the UCSC Roma Library website)

Sherris Medical Microbiology 6th Edition. McGraw Hill (8th Edition available through Access Medicine)

AK Abbas-HH Lichtman-S Pillai' Cellular and Molecular Immunology' Elsevier. 9th or 10th Edition

Strachan-Read. Human Molecular Genetics.Garland Science. 5th edition, 2019.

Robert A. Weinberg The Biology of Cancer (Edition 2), ISBN 9780429258794

4. LEARNING OBJECTIVES

The course of *Biopathology and Introduction to Medical Therapy 1* focuses on the causes of molecular and cellular damage (etiology) and on the biological processes (pathogenesis) whereby cell/tissue injury, and the ensuing body reaction, lead to organ and system dysfunction and eventually to illness.

The course, placed at the transition point between basic science studies and early exposure to clinical disciplines and practice, aims at reorganizing student's knowledge of human body structure and functions into logic scaffolds, that mechanistically connect aberrant cell and tissue responses (Molecular Pathology) with signs, symptoms and laboratory evidence of disease (Pathophysiology). In doing so, *Biopathology and Introduction to Medical Therapy 1* lays the groundwork for medical reasoning.

Within this framework, special attention is paid, on the one side, to the mechanisms and consequences of host-microbe interactions (Medical Microbiology); on the other side, to the biochemical pathways linking gene defects with tissue morphologic changes and functional derangement in the context of genetically determined disorders (Medical Genetics).

Learning objectives according to Dublin's descriptors.

Conoscenza e capacità di comprensione - Knowledge and understanding (Dublino 1)

Core information conveyed by the course covers the primary causes of cell and tissue damage (physical, chemical, biological/infectious and genetic) as well as the molecular circuitries and signaling networks whereby those agents impact cell morphology and function. A fundamental message the students will get is that the endless potential etiologies converge onto a few major routes to dysfunction and disease, i.e. Inflammation, malignancy, and degeneration/senescence. Of these processes, students will recognize the relevant biomolecular and cellular players (capitalizing on their previous knowledge of basic sciences), and understand how they interact with each other and which macro and microscopic pathologic changes they induce in tissues and organs. Students will also become familiar with the mechanisms of the innate and adaptive immune response to danger and infection, with the consequences of the host-microbe interaction on health, and with the cascades whereby derangement of immune mechanisms can link to diseases in the context of either reduced or exaggerated activity. Also, students will learn the pathomechanism of genetic defects, their modeling and potential therapeutic approaches, mostly of clinical relevance.

Conoscenza e capacità di comprensione applicate – Applying knowledge and understanding (Dublino 2)

In practical, "hands-on" sessions, students will learn how to recognize basic pathologic processes in microscopic tissue sections, read a complete cell blood count, perform and interpret diagnostic microbiological tests, and identify and interpret genetic variants in genomic sequences. Moreover, in the second part of the course, students will build on their knowledge of causes and general mechanisms of tissue damage to understand how and why disease occurs in specific organs and systems. This is the domain of Pathophysiology, a higher-order integrative knowledge pivotal to acquiring medical reasoning.

Autonomia di giudizio - Making judgements (Dublino 3)

Students will be involved in problem-solving sessions and presented small clinical vignettes that integrate information on laboratory data, clinical signs/symptoms and morphologic tissue changes, so as to encourage diagnostic hypotheses on organ/system dysfunction and individual evaluations on disease likelihood and severity. Moreover, students will be introduced to genetic counseling as a model assessment that combines reflection on relevant scientific, social and ethical issues.

Abilità comunicative – Communication skills (Dublino 4)

The course will promote

students' ability to communicate knowledge and personal judgments by adjusting the language and the conceptual complexity to either specialist (teachers, other students) or non-specialist audiences. Students must demonstrate the capacity to elaborate information from multiple sources, express synthetically and logically complex concepts, and catch their audience with clear and visually attractive presentations.

Capacità di apprendere – Learning skills (Dublino 5) By the end of the course, students will have developed better study skills and strategies aimed at multi-source, self-directed and ongoing learning. In particular, they'll become able to deepen and update their knowledge by capitalizing on bibliographic searches and web-based electronic databases.

5. prerequisites

Essential course prerequisites include knowledge of a) the fundamentals of cell biology (cell structure, organelle organization and function, principles of bioenergetics and cellular metabolism, principal pathways of signal transduction, basic biochemistry, chemistry of reactive oxygen and nitrogen species), and b) the normal physiology of organs and systems, body fluids compartments and electrolytes, oxygen transport and acid-base balance regulation. Students must also be familiar with c) the general structure and biology of procaryotes and viruses and d) the basic concepts of human and bacterial genetics (concepts of gene, allele, locus, genetic inheritance, etc.). The knowledge of human genetics fundamentals is also required, alongside (e) the appropriate scientific English terminology covering all the above subjects.

6. TEACHING METHODS

Core course content will be taught through *interactive frontal lessons* and more student-centered strategies (i.e. "reverse classrooms", with materials being provided in advance for students' homework in the form of slide presentations, book chapters and links to web-based multimedia, and presented in the classroom from students to students under teachers guidance). Integration among different subjects/teachers of the course will be actively pursued through calendar optimization and the organization of multidisciplinary lectures on overlapping topics.

The course includes *hands-on practical sessions* at the microscope (Molecular Pathology) or in the Microbiology and Genetics laboratories.

7. OTHER INFORMATIONS

Optional course-related learning opportunities will be provided in the form of

a) ad hoc seminars in the "**Cellular and Molecular Basis of Disease**" series (Vertical Domain), to be announced time by time. Attendance to all the workshops (6 or 7) is requested to earn 1CFU.

b) semestral internship in research laboratories. Interns (1 or 2 per laboratory) are introduced by PhD students and young researchers to the most common cellular and molecular biology techniques and are actively involved in experiment design and data interpretation. Semestral attendance (minimum 25 hours), certified by the supervisor, grants 1 CFU.

ML000132 Internship In General Pathology

(MED/04) open to years III, IV, V, and VI

5 students/semester (total 10)

Continuous feedback will be provided to students during classes and at the end of each lesson. In addition, teachers are available for consultation by email or in person, at preset office hours, or upon appointment.

Students failing the exam may request remedial tutoring at the Course coordinator's discretion upon consultation with the teaching staff.

8. METHODS FOR VERIFYING LEARNING AND FOR EVALUATION

Methods for verifying learning include:

- a) Ongoing: Interactive frontal teaching with class involvement (open questions, multiple choice questions, app-based surveys, and written self-evaluation tests).
- b) Intermediate: Written multiple-choice evaluation test at the end of Semester1 and in any of the subsequent exam sessions. Taking the test is optional at students' discretion, and failing the intermediate test does not affect the final evaluation (see below).
- c) Final: Written multiple-choice evaluation test at the end of the course, covering the entire course content (including Practicals) or just the content of Semester 2 (for those students who have successfully passed the intermediate test).

Written tests will be administered in person through the Blackboard platform from within the Campus, in a PC-equipped room under the direct supervision of the teaching staff.

Tests are representative of the different disciplines of the integrated course, with numbers of question items proportionate to the respective UFC. Part of the question items (5 options, one best answer) are presented in the form of short clinical vignettes that aim to assess student's capacity not only to retrieve knowledge, but also to utilize information in a realistic situation, and to demonstrate critical evaluation and judgment ability.

In each test evaluation, the percentage of correct answers is translated into marks in an 18 (pass mark)- to -31 (maximum mark with *laude*) scale using a linear scale alignment, with 95% correct answers set as 31 and **60%** as 18 (pass mark). A table for % points-to-mark conversion is provided to students at the beginning of the course.

The final score is the arithmetic average of marks obtained in the Intermediate (if applicable) and final test. If the exam is taken all at once, students will receive one single questionnaire (no division by topic) covering the entire course (normally 120 question items). To pass their test, students must respond correctly to at least half of the test items of each discipline, irrespective of the overall number of correct answers provided. In this calculation, sub-chapters of the same domain (i.e. Microbiology) will be counted as a whole even if taught by different teachers. Exceptionally, partial credits may be granted to students reaching proficiency in single topics, at the teachers' discretion. In case of failure in the final exam, a positive outcome in the intermediate test can be retained for the later sittings within the same academic year.

During exams, any portable electronic device, including mobile phones, must be switched off. Violations will be referred to the Disciplinary Committee.

For privacy, exam results are communicated to students by individual email messages; students are requested to accept/refuse the assigned mark (by replying to the course secretariat within the indicated timeframe) before exam final registration in the system.

9. program

Molecular pathology, immunology and pathophysiology.

Cellular Pathology. Concepts of health and disease, etiology and pathogenesis. Mechanisms of cellular adaptations, injury and death. Free radicals and reactive oxygen species. Degenerative diseases: intracellular and extracellular accumulations. Biological bases of cellular aging. Molecular mechanisms of diseases.

Genetic and environmental pathology. Physical agents as causes of diseases. Chemical agents as causes of diseases. Smoking-related diseases. Diseases related to ethanol abuse. Multifactorial diseases. Epigenetics and Non-communicable diseases.

Inflammation and repair. Etiology, classification, mediators and consequences of acute Inflammation. Chronic Inflammation. Pathogenesis of tuberculosis. Systemic effects of Inflammation (fever, acute phase proteins, leukocytosis). Mechanisms of resolution and repair, clinical examples of repair (wound healing, fibrosis).

Innate and adaptive immunity. Vaccination. Cells and tissues of the Immune system. Leukocyte circulation and migration in tissues. Innate immunity. Antigens and antibodies. The MHC/HLA system, antigen presentation. T and B cell receptors. Diversity of immune receptors and lymphocyte development. T cell functions, CD4, CD8, T cell polarization. T/B cross-talk. Signal transduction in the immune cells. Effector mechanisms of humoral

immunity. Immunologic memory. Immunologic tolerance. Hypersensitivity and allergy. Tumor-related immunity. Transplants and rejection. Immunity and pregnancy. Introduction to Autoimmunity. Introduction to congenital and acquired immunodeficiencies.

Neoplastic diseases. Introduction, definitions and classifications. Benign and malignant tumors. Cancer epidemiology. The neoplastic phenotype. Morphological characteristics of tumors. Carcinogenesis as a process. Cancer as a genetic disease. Oncogenes and tumor suppressor genes. Hallmarks of cancer. Tumor-host relationships: microenvironment, angiogenesis and the metastatic process. Cell differentiation in cancer and hematological malignancies. Therapeutic implications of oncogenes and tumor suppressor genes. Genetic predisposition. Preneoplastic lesions. Paraneoplastic syndromes. Tumor immunology.

Pathophysiology.

- o Blood cells: anemias and bleeding disorders.
- o Cardiovascular system: edema, thrombosis and embolism. Infarction. Atherosclerosis and arteriosclerosis. Shock and hypertension. Heart Failure.
- o Respiratory system: obstructive and restrictive lung diseases. Respiratory failure. Hypoxemia. Hypoxia and Cyanosis.
- o Kidney: mechanisms of kidney damage: glomerular, tubular, tubular-interstitial; nephrotic and nephritic syndromes, kidney failure.
- o The acid-base and hydro-saline balance and their alterations.
- o Liver and biliary tract: hepatitis, jaundice, cirrhosis and liver failure.
- o Endocrine system: The hypothalamus-pituitary axis: hyper and hypopituitarisms; hyper- and hypothyroidism; adrenal pathophysiology.
- o Pathophysiology of Metabolism: Inborn errors of Metabolism. Obesity and Metabolic Syndrome. Diabetes mellitus. Eating and nutritional disorders.
- o Pathophysiology of thermoregulation: Non-febrile hyperthermias. Malignant hyperthermia.

Molecular pathology, immunology and pathophysiology practicals.

- o *Acute Inflammation:* At the microscope: recognition of the basic morphological signs of different types of inflammation in microscopic sections of diseased tissues
- o *Chronic Inflammation:* tissues
- o *Neoplasia:* At the microscope: recognition and analysis of the morphological features of benign and malignant tumor specimens in microscopic tissue sections.
- o *Blood 1.* Preparation of a peripheral blood smear, staining with May-Grunwald Giemsa and recognition of the different corpuscular elements at the microscope, with particular regard to white blood cells (WBC differential count).

- o *Blood 2*: Reading and interpretation of normal and pathologic Complete Blood Count (CBC) tests.
- o *Blood 3*: Blood group typing (principal systems) and transfusion rules

Students will be divided in two groups; each hands-on session will be scheduled in the afternoon, lasting 3-4 hours. The white coat is required for Blood 1 and Blood 3.

Medical Genetics.

Population genetics. Multifactorial disorders and association studies. Disease modeling. Cure and care of genetic disorders. Therapeutic approaches to genetic defects.

Medical Genetics practicals: Exercises of population genetics in classroom

Medical Microbiology.

Microbes and humans (commensalism, colonization, infection and disease); microbial biodiversity, host-pathogen interactions in health and disease.

Bacteriology: bacterial pathogenesis: adhesion, toxins, secretion systems, intracellular bacteria; antibacterial agents and mechanisms of drug resistance in bacteria; *Staphylococcus* spp, *Streptococcus* spp, *Clostridium* spp., *Bacillus anthracis*, *Vibrio* spp, *Helicobacter* and *Campylobacter* spp., *Salmonella* spp, *Escherichia coli*, *Klebsiella* spp, *Yersinia* spp, *Pseudomonas* spp, *Haemophilus influenzae*, *Neisseria*. spp, *Bordetella pertussis*, *Legionella* spp, *Mycobacterium* spp, *Rickettsia* spp, *Chlamydia* spp, *Treponema*, *Borrelia*. *Mycoplasma*.

Special focus on: *Streptococcus pneumoniae*, *Clostridium difficile*, *Vibrio cholerae*, *Helicobacter pylori*, *Yersinia pestis*, *Mycobacterium tuberculosis*, *Escherichia coli*;

Virology: mechanisms of viral pathogenesis; antiviral agents and mechanism of resistance to antiviral drugs; Papillomavirus and Poliovirus, Adenovirus, Herpesvirus, Poxvirus, Parvovirus, Picornavirus, Coronavirus e Norovirus, Paramyxovirus, Orthomyxovirus , Rhabdovirus, Filovirus, Bornaviurs, Reovirus, Togavirus, Flavivirus, Retrovirus

Special focus on HPV, Poliovirus, measles, HIV, Influenza, Coronavirus, Ebola.

Mycology: fungal pathogenesis: immunological aspects, virulence factors; antifungal agents and mechanisms of resistance in fungi; superficial, subcutaneous, systemic and opportunistic fungal infections; Aspergillosis, Candidiasis, Zgomycosis, Cryptococcosis, Scedosporiosis, Fusariosis, Dermatophytosis.

Special focus on: Candidemia, *Aspergillus fumigatus*, *Cryptococcus neoformans*.

Parasitology: parasitic classification, structure and replication; pathogenesis of parasitic diseases; intestinal and urogenital protozoa; blood and tissue protozoa; nematodes, trematodes, cestodes, arthropods.

Special focus on: *Plasmodium* spp and malaria; *Toxoplasma*.

Medical Microbiology practicals: Laboratory presentation, clinical sample management, traditional vs molecular microbiological tests preparation and results interpretation. Students will be divided in groups (10 for each group). Practical will take place in the Laboratory of Microbiology; the white coat is required.

A synopsis of the Program, broken down by teacher and topic, follows in **Table 1**.

COURSE	MOLECULAR PATHOLOGY, IMMUNOLOGY AND
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	PATHOPHYSIOLOGY	
<i>Teacher</i>	<i>Semester 1 (October-January)</i>	<i>Semester 2 (March-June)</i>
Calviello Gabriella		Pathophysiology of Metabolism: Inborn errors of Metabolism. Obesity and Metabolic Syndrome. Diabetes mellitus. Atherosclerosis and arteriosclerosis. Pathophysiology of Liver and Bile tract: Jaundice, Hepatitis, Cirrhosis, Portal Hypertension, Liver failure Eating and nutritional disorders. Smoking-related diseases. Diseases related to ethanol abuse. Epigenetics and Non-communicable diseases.
De Maria Marchiano Ruggero	Neoplastic diseases: Molecular bases of cancer therapies Tumor immunology & Immunotherapy	
Haas Tobias Longin	<u>Acute Inflammation</u> : morphologic patterns of inflammation; exudate; inflammation mediators; vascular changes; leukocyte migration, phagocytosis. <u>Immunology</u> : Innate and adaptive immunity. Vaccination. Cells and tissues of the Immune system. Leukocyte circulation and migration in tissues. Innate immunity. Antigens and antibodies. The MHC/HLA system, antigen presentation. T and B cell receptors. Diversity of immune receptors and lymphocyte development. T cell functions, CD4, CD8, T cell polarization. T/B cross-talk. Signal transduction in the immune cells. Effector mechanisms of humoral immunity. Immunologic memory. Immunologic tolerance. <u>Neoplastic diseases</u> : Introduction, definitions and classifications. The Hallmark of Cancer Oncogenes and tumor suppressor genes Genetic predisposition to cancer Tumor-host relationships: microenvironment, angiogenesis and the metastatic process <u>Hematological Malignancies</u>	
Lucchetti Donatella	PRACTICALS: Acute Inflammation	

Marino Mariapaola	<p>LECTURES Mechanisms of cell injury, free radicals and reactive oxygen species. Biological bases of cellular aging. Molecular mechanisms of accumulations. Concepts of environmental pathology. Physical agents as causes of diseases. Chemical agents as causes of diseases. Mechanisms of tissue repair Clinical examples of tissue repair (cutaneous scar, peptic ulcera, muscle fibers, myocardium)</p> <p>PRACTICALS Blood 1 (blood smear)</p>	<p>LECTURES Cardiovascular system: thrombosis and embolism. Infarction. Endocrine system: hypothalamic-pituitary axis, hyper and hypopituitarisms Endocrine system: adrenal glands (hyper- and hypo-) Endocrine system: thyroid (hyper- and hypo-)</p>
Pani Giovambattista	Introduction to the course	<p>Acid-base and hydro-saline imbalances. Edema. Hypovolemia Cardiovascular system: Shock and Heart Failure. Hypertension. Respiratory system: obstructive and restrictive lung diseases; respiratory failure; hypoxemia. Hypoxia and Cyanosis. Kidney: mechanisms of kidney damage: glomerular, tubular, tubular-interstitial; nephrotic and nephritic syndromes, kidney failure (acute and chronic).</p>
Provenzano Carlo		<p>PRACTICALS Blood 2: Reading and interpretation of normal and pathologic Complete Blood Count (CBC) tests. Blood 3: Blood group typing (principal systems) and transfusion rules</p>
Ria Francesco	<p>Immunopathology:</p> <ul style="list-style-type: none"> • Vaccine • Hypersensitivity and allergy • Tolerance and Autoimmunity • Immunodeficiency • Transplant and Transplant rejection • Immunology and immunopathology of pregnancy 	
Serini Simona	<p>Cellular Pathology. Concepts of health and disease, etiology and pathogenesis. Mechanisms of cellular adaptations, injury and death. Chronic Inflammation; Systemic effects of inflammation PRACTICALS: Tumors 1 and 2</p>	<p>Blood cells: Hemopoiesis and Hemocatheresis Blood cells: Anemias Blood cells: Bleeding Disorders.</p>
Sistigu Antonella	PRACTICALS: Chronic Inflammation	
COURSE	MEDICAL MICROBIOLOGY	

Teacher	Semester 1 (October-January)	Semester 2 (March-June)
De Carolis Elena	<p>Mycology: fungal pathogenesis: immunological aspects, virulence factors; antifungal agents and mechanisms of resistance in fungi; superficial, subcutaneous, systemic and opportunistic fungal infections; Aspergillosis, Candidiasis, Zgomycosis, Cryptococcosis, Scedosporiosis, Fusariosis, Dermatophytosis. Special focus on: Candidemia, Aspergillus fumigatus, Cryptococcus neoformans. Parasitology: blood and tissue protozoa; nematodes, trematodes, cestodes.</p>	
Delogu Giovanni	<p>Microbes and humans (commensalism, colonization, infection and disease); microbial biodiversity, host-pathogen interactions in health and disease. Bacteriology: bacterial pathogenesis: adhesion, toxins, secretion systems, intracellular bacteria; antibacterial agents and mechanisms of drug resistance in bacteria; Bacillus anthracis, Vibrio spp, Helicobacter and Campylobacter spp., Salmonella spp, Yersinia spp, Legionella spp, Mycobacterium spp, Rickettsia spp, Chlamydia spp, Treponema, Borrelia. Mycoplasma. Special focus on: Vibrio cholerae, Helicobacter pylori, Yersinia pestis, Mycobacterium tuberculosis; Parasitology: parasitic classification, structure and replication; pathogenesis of parasitic diseases; intestinal and urogenital protozoa; blood and tissue protozoa; Special focus on: Plasmodium spp and malaria; Toxoplasma</p>	
Palucci Ivana	<p>Bacteriology: Staphylococcus spp, Streptococcus spp, Clostridium spp., Bordetella, Haemophilus, Legionella, Neisseria, Enterobacteria, Pseudomonas spp. Special focus on: <i>Streptococcus pneumoniae</i>, <i>Clostridium difficile</i>, <i>Escherichia coli</i>, <i>Bordetella pertussis</i>;</p>	

Santangelo Rosaria	<p>LECTURES Virology: mechanisms of viral pathogenesis; antiviral agents and mechanism of resistance to antiviral drugs; Papillomavirus and Poliomasvirus, Adenovirus, Herpesvirus, Poxvirus, Parvovirus, Picornavirus, Coronavirus e Norovirus, Paramyxovirus, Orthomyxovirus , Rhabdovirus, Filovirus, Bornaviurs, Reovirus, Togavirus, Flavivirus, Retrovirus Special focus on HPV, Poliovirus, measles, HIV, Influenza, Coronavirus, Ebola.</p> <p>PRACTICALS Laboratory presentation, clinical sample management, traditional vs molecular microbiological tests preparation and results interpretation.</p>	
COURSE	MEDICAL GENETICS	
<i>Teacher</i>	<i>Semester 1 (October-January)</i>	<i>Module 2 (March-June)</i>
Tiziano Francesco Danilo	<p>LECTURES Population genetics. Multifactorial disorders and association studies. Disease modeling. Cure and care of genetic disorders. Therapeutic approaches to genetic defects.</p> <p>PRACTICALS Exercises of population genetics in classroom</p>	