

## EC4 European Syllabus for Post-Graduate Training in Clinical Chemistry. Version 2 – 1999

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adequate education and specialisation in the field, i.e. by clinical chemists. Clinical laboratory science has developed on a broad front throughout the European Community, resulting in significant differences in what constitutes a national clinical chemistry service in each state. Clinical chemistry is the medical discipline devoted to obtain, explore and employ chemical knowledge and chemical methods of investigation, in order to procure knowledge about normal and abnormal chemical processes in man. These processes are studied on a general level, in order to get insight into human health and disease, and on a patient-specific level for diagnostic or monitoring purposes. The delimitation of clinical chemistry varies from country to country, since there is no sharp boundary to haematology, immunology, molecular biology and microbiology.

One of the main tasks of the clinical chemist is direction and supervision of a laboratory department in a hospital or health service (public or private), where his role involves bridging the gap between rapidly developing laboratory science and technology and the growing knowledge on characteristics of disease. He must possess fundamental biochemical knowledge and have the ability to use this knowledge most appropriately as applied to clinical requirements, i.e. diagnosis of disease and planning and monitoring of therapy. Apart from providing a competent laboratory service, the clinical chemist must be able to function as a consultant to his clinical colleagues and liaise with them in the interpretation of laboratory results. His advice and professional consultation have at least three aspects, i.e. choosing the most appropriate laboratory investigation in a certain case, ensuring that the analyses are performed in the best possible way and correctly reported and, finally, providing information and (most important) interpretation on the significance and consequences of the laboratory data obtained.

As the results of laboratory investigations and the consultation of the clinical chemist have a direct and important influence on the treatment of the patient, it is to the benefit of the public that the profession of the clinical chemist is duly regulated.

### *Clinical chemistry*

#### Definition

Clinical chemistry/Clinical biochemistry is a scientific discipline within medicine. It includes the analysis of body fluids, cells and tissues and interpretation of the results in relation to health and disease.

The discipline encompasses fundamental and applied research into the biochemical and physiological processes of human and animal life, and application of

### **Preamble**

In modern medicine the undeniable value and indispensability of scientific investigations are now universally recognized both for diagnostic purposes and monitoring of disease and in basic epidemiology. The direct treatment of patients is an undeniable task of doctors in medicine. Progress in laboratory science is largely the result of contributions by scientists with an

the resulting knowledge and understanding to the diagnosis, treatment and prevention of disease.

### Syllabus

This Syllabus provides a short description of the profession of clinical chemistry. According to the definitions of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), the name clinical chemist will be used throughout, although it is realised that different names exist in different countries to describe the profession.

The scope of clinical chemistry is not solely confined to laboratory activities as such, but in daily practice is strongly interrelated with patient care and treatment. Moreover, medical laboratory activities apart from being of purely chemical nature, imply to some extent the practice and study of biochemistry and molecular biology, haematology, immunology, microbiology-virology, and parasitology.

This Syllabus leaves undisturbed the different structures of medical laboratories as developed in their national environments. It is meant to describe the minimum scientific contents of the professional knowledge and training, appreciating the national authority and responsibility of each member state to organize laboratory medicine within in its own national health care system.

Although significant differences exist between the development of clinical chemistry throughout the European Community, in all cases there are some core elements (Syllabus, chapters I–XI). In addition to these core elements, knowledge of haematology, microbiology, biochemistry, parasitology, immunology is necessary in the training of clinical chemists (Appendices A, B, C).

Detailed knowledge on the application of chemistry and molecular biology, both in diagnostic medicine, monitoring of therapy and in pathophysiology is indispensable. Although cytology and medical microbiology sometimes are considered as distinct specialities in laboratory medicine, many mutual interfaces in the investigation of biological samples on the level of molecular biology require some general knowledge of infectious diseases and medical microbiology in the practice of clinical chemistry and immunochemistry. This is even more so for haematology and immuno-haematology; laboratory investigations in haematology are rapidly developing towards molecular biology and instrumental analysis which are both based on detailed knowledge of basic chemistry and chemical techniques.

There are important physiological, analytical and technical developments in cellular and molecular biology that demonstrate the importance of scientific investigations in the understanding of disease processes, and consequently in the diagnosis and monitoring of diseases. Obviously techniques and technology will change but basic chemical and scientific principles will not, and research and development at scientific levels are indispensable for good clinical chemistry.

### Quality assurance

Safeguarding and protecting the public against misuse of medical laboratory investigations are important features of good laboratory practice and reliable laboratory diagnostics. Adequate laboratory management and scientifically based quality assurance procedures must be incorporated in the production and management of data in medical laboratories. These elements of good laboratory practice appear to be increasingly important with the growing possibilities of laboratory investigations in clinical chemistry and related medical laboratory sciences.

### The clinical chemist

Training as a clinical chemist must involve dedicated post-graduate study of at least four years, following a complete and appropriate university education of at least four years.

Clinical chemists and specialist medical consultants operate at the same professional level and must dispose their complementary knowledge to the benefit of the patients and institutions they serve. The complexity and wide scope of presently obtainable laboratory information inevitably requires professional interpretation of data obtained.

This interpretation is an essential task of the clinical chemist for which he should be trained appropriately.

The principal subject of the graduate education will usually be either chemistry/biochemistry or medicine or pharmacy, but the specific subjects acceptable in a particular member state will vary across the European Community. The post-graduate study should provide an in depth knowledge of the chemistry of disease and the procedures and analytical techniques used in a medical laboratory. It is important that there should be a commitment to research and development which will often be in association with clinical colleagues. The object being to produce a person competent in laboratory procedures with a sound knowledge relating to the subject and able to interpret and impart laboratory findings and their implication, in consultation with colleagues. The interpretation of obtained data is an essential part of the professional task of the clinical chemist, for which he should be trained adequately. The post-graduate study and training must meet the national requirements, but in formulating the courses consideration should be given as to how such requirements might meet those of the European Community as a whole, in order not to restrict opportunities for their nationals who might wish to practise in other member states.

### European Syllabus

The European Syllabus for post-graduate training in clinical chemistry affords an overview of the fields within the discipline in which the clinical chemist should be able to demonstrate knowledge and experience with regard to scientific, clinical and management aspects of the subject. This programme indicates the

level of requirements in post-graduate training in clinical biochemistry, haematology, immunology, microbiology-virology, and parasitology.

The exact contents of clinical chemistry varies considerably from country to country. Therefore, the training requirements may best be satisfied by a modular system enabling the clinical chemist to adjust his or her competence to the demands of the authorities in the particular country.

The Syllabus is not primarily meant to be a training guide, but on the basis of the given overview, national societies should formulate programmes, indicating where knowledge and experience appropriate to the national service requirements in the different countries is needed.

The scope of work to be found in clinical chemistry across the European Community gives a clear indication that an appropriate description of the field is cellular and molecular clinical chemistry.

This general basis is applicable to the whole of laboratory medicine and helps to unify the scientific and clinical principles on which it is based, and demonstrates the unity of concepts underlying the diversity of practice (which is more apparent than real). Disease is due to metabolic, genetic, infectious or other perturbations of homeostasis. Study, diagnosis and therapy of disease require clinical chemistry, cell and molecular biology to identify such changes. The classical subdivisions of laboratory medicine are becoming blurred by developments in science and technology, and particularly as a result of the rapid advances in biochemical, cellular and molecular biology. It is essential that the European Syllabus for clinical chemistry should not only recognise its current strength but provide a framework within which all constituent states can develop their own approaches towards this model. This should facilitate not only the mutual recognition of national syllabi but also the maintenance and enhancement of standards of practice.

## Syllabus

This Syllabus affords an overview of the fields in which the clinical chemist should be able to demonstrate knowledge and experience with regard to scientific, and clinical, and management and quality assurance aspects of the subject. This programme indicates the level of requirements in post-graduate training in clinical biochemistry. This Syllabus is not meant to be a training guide. On the basis of the given overview, national societies should formulate programmes emphasizing knowledge and experience appropriate to the national service requirements in the different countries.

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I	Basic knowledge
II	Clinical assessment of laboratory analysis

III	Indications for clinical chemistry procedures
IV	Effects of the collection and storage of specimens
V	Analytical principles and techniques
VI	Methodological evaluation of analytical findings
VII	Haematology and immunohaematology
VIII	Case-related medical evaluation of laboratory tests and methods
IX	Clinical training
X	Research and development
XI	Laboratory management and quality assurance

Appendix A Knowledge and experience in accordance with sections I-VIII of the Syllabus in applications in the different fields

Appendix B Extended haematology

Appendix C Medical microbiology-virology  
Medical parasitology

Appendix D Examples of scientific and medical literature

## I Basic Knowledge

1. Basic knowledge in chemistry  
Homogeneous and heterogeneous systems, distribution and absorption with regard to analytical separation methods. Study of atoms and molecules, especially with regard to stoichiometry and chemical aspects of isotopes.  
Knowledge of thermodynamic laws and their application in analysis and biological systems. Reaction kinetics with regard to catalyzed reactions and radioactive decay.
2. Basic knowledge in biochemistry  
Molecular structure of the body; metabolism, enzymes, metabolites, molecular biology aspects of genetics, biological macromolecules, lipids, hormones.
3. Basic knowledge in medicine
  - 3.1 Structure and function of the human body, laws on the distribution of substances in the body
  - 3.2 Human physiology
  - 3.3 Pathobiochemistry, pathophysiology and pathology
  - 3.4 Genetics (basic aspects)
4. Basic knowledge of statistics and biostatistics

## II Clinical Assessment of Laboratory Data

1. Reference intervals and biological variability  
Genetic influences, environmental influences, age, sex, nutrition, season and time of day, influence of therapeutic agents
2. Predictive value of analytical methods, diagnostic sensitivity and specificity

3. Diagnostic strategies and analytical goals in the use of clinical chemistry tests

### III Indications for Clinical Chemistry Procedures

1. In the early detection of disease, and in epidemiology
2. In disease-related diagnosis
3. In organ-related diagnosis
4. In monitoring vital functions
5. In monitoring response to therapy
6. In the field of drug monitoring
7. Indications for subsequent specialist examinations
8. Indications for function tests

### IV Effects of Collection and Storage of Specimens

1. Place and time of sample collection, preservation, influence of nutrition, drugs, posture, etc.
2. Choice and correct use of anticoagulants
3. Care of the specimens, identification, transport, storage, influence of temperature, freezing/thawing

### V Analytical Principles and Techniques

1. Separation techniques including gas and liquid chromatography, electrophoresis and dialysis
2. Standard analytical techniques, such as titrimetry and osmometry
3. Photometric methods: spectrophotometry (UV, visible) atomic reflectometry, turbidimetry, nephelometry, spectrofluorimetry, atomic emission, etc.
4. Spectrometric methods: mass spectrometry, nuclear magnetic resonance, infra-red
5. Electrochemical techniques: potentiometry, amperometry, voltamperometry with stationary diffusion, anodic voltametry
6. Techniques for protein analysis: electrophoresis, chromatography, ultracentrifugation
7. Techniques for nucleic acid analysis: amplification, investigation of mutations and gene expression
8. Immunochemical techniques:  
Immunochemical protein analysis: immunoelectrophoresis, immunofixation, immunonephelometry and turbidimetry  
Immunological and other binding analysis using different labels; homogeneous and non-homogeneous immunoassays
9. Techniques employing radioactive isotopes
10. Enzyme activity and substrate determination methods
11. Cell and particle counting methods
12. Knowledge of analytical instrumentation and evaluation of equipment
13. Knowledge of electronic data processing

### VI Methodological Evaluation of Analytical Findings

1. Precision and accuracy
2. Reference methods and statistical comparison of methods
3. Internal quality assurance and external quality assessment
4. Analytical specificity and analytical sensitivity
5. Interfering factors

### VII Haematology and Immunohaematology

1. General morphology and blood cell counting
  - 1.1 Determination of erythrocytes sedimentation rate; determination of haemoglobin concentration, haematocrite cell counts and knowledge of haematological parameters (MCV, MCH, MCHC, RDW)
  - 1.2 Preparation and staining of blood smears, with microscopical evaluation
  - 1.3 Investigation of haemolysis
  - 1.4 Flow cytometry and leucocyte sub-grouping
2. General haemostasis
  - 2.1 Coagulation tests
  - 2.2 Determination of coagulation factors. Control of anticoagulation factors
  - 2.3 Investigation of fibrinolysis
  - 2.4 Determination of antithrombin III and heparin
3. Immunohaematology
  - 3.1 Blood group typing, ABO and Rh(D); D-variant determination
  - 3.2 Detection of irregular antibodies
  - 3.3 Cross matching of blood samples for transfusion. Indirect antiglobin test, direct antiglobin test
  - 3.4 Rhesus- and ABO-antagonism
4. Haematological biochemistry of erythrocytes
  - 4.1 Detection and measurement of variant and minor (Hb A<sub>2</sub> and HbF) hemoglobins
  - 4.2 Red blood cell enzymes
5. Theoretical and clinical background
  - 5.1 Haemoglobinopathies and thalassemias
  - 5.2 Vitamin B12 and folic acid deficiencies; iron status
  - 5.3 Kinetics of blood cells and platelets
  - 5.4 Enzymology of blood cells and platelets
  - 5.5 Haemato-oncological abnormalities (leukaemias, lymphomas, polycythemias)
  - 5.6 Possible causes and background of anaemias
  - 5.7 Immunological determination of coagulation factors and knowledge of coagulation abnormalities (factor deficiency, increased fibrinolytic activity) and regulation and monitoring of thrombosis and disseminated intravascular coagulation. The use of anticoagulant drugs
  - 5.8 Blood group antigens and other antigen systems as considered in blood transfusion (including genetic)  
Selection criteria of donors for blood transfusion  
Several types of transfusion reactions

- 5.9 Medical applications, clinical relevance and indications for the administration of blood and blood components
- 5.10 Hematopoiesis and hemostasis physiology

### VIII Case-related Medical Evaluation of Laboratory Tests and Methods

The clinical chemist in a consultative role requires a working knowledge of the subject underlying the choice of tests and interpretation of results.

1. Plausibility evaluation (recognition of possible fluctuations in comparison to previous values, plausibility of patterns of evidence, extreme values, etc.)
2. Use of reference values: influences of age, sex, lifestyle, etc. and decision value limits
3. Longitudinal evaluation of disease course and therapy monitoring; critical differences
4. Recognition of combinations of findings typical of diseases
5. Application in the formulation of clinical questions
6. The laboratory report with evaluation of data
7. Independent performance or suggestions for further tests

Note: A more detailed description of the paragraphs I-VIII is given in Appendix A.

### IX Clinical Training

Training in clinical chemistry requires participation in ward rounds as a member of the clinical team and other contact with the users of the laboratory service, for example seminars and case discussions.

Study in the following areas will provide a general basic knowledge of clinical chemistry from which consultative skill can develop.

1. Organ function, anatomy and physiology
2. Metabolism
3. Biochemical exploration and testing
4. Variations in physiology leading to pathological conditions and disease

### X Research and Development

As laboratory medicine is continually and rapidly evolving, research and development of both the laboratory aspects as such and in relation to clinical liaison are indispensable. The clinical chemist must maintain up to date knowledge in all relevant diagnostic procedures. Special attention must be paid to the following:

1. Developments and improvements in methods and techniques; special emphasis on new developments in many areas (e.g. PCR and related techniques)
2. Procedures to test and evaluate the steps of a method or the components of an instrument

3. Evaluation of laboratory-based and clinical research projects
4. Analyses and documentation of results obtained through research and development, with simplification and scientific presentation of data
5. Collaborative planning of clinical research based on the liaison function of the clinical chemist as an indispensable specialist for interpretation of laboratory data
6. Publication of papers reporting new or improved laboratory methods and of clinical research papers

### XI Laboratory Management and Quality Assurance

1. Laboratory organisation and quality management  
Work procedure, work load measurements, emergency laboratory, laboratory planning, selection of equipment and methods, cost-benefit analysis, costing
2. Quality assessment  
Statistical applications in the clinical laboratory: interpretation of statistical laboratory and population data, biological variation, establishment of reference intervals, methods comparison  
Data management: medical informatics, data processing and telecommunication, presentation and communication of results of investigation (choice of units, design and content of request and report form)
3. Education of laboratory personnel and writing and maintaining quality procedures
4. Basic knowledge of clinical epidemiology
5. Laboratory safety  
Handling of potentially infectious samples (HIV and hepatitis), handling of noxious chemicals and isotopes, mechanical and electrical safety, fire precautions, dealing with an accident
6. Legal and ethical regulations  
Laws, guidelines and recommendations on work in clinical laboratories: in particular accident prevention and hygiene regulations, handling of isotopes, calibration law, quality control, education regulations, labour laws and occupational diseases  
Ethical aspects and conventions on production, interpretation, reporting and use of medical laboratory data

### Appendix A Knowledge and Experience in Accordance with Sections I-VIII of the Syllabus in Applications in the Different Fields

1. Carbohydrates
  - 1.1 Glucose metabolism and regulation
  - 1.2 Metabolism and regulation of other carbohydrates (e.g. galactose, lactose, glycogen)
  - 1.3 Type 1 and type 2 diabetes mellitus

- 1.4 Other hereditary and acquired metabolic disorders (e.g. lactose intolerance, galactosaemia, storage diseases)
- 1.5 Ketogenesis
2. Lipids and lipoproteins
  - 2.1 Metabolism
  - 2.2 Hereditary and acquired disorders. Storage diseases. Hypercholesterolaemia. Hypo- and hyperlipoproteinaemia; characterisation by classical methodology; apolipoproteins; lipoprotein lipase
3. Proteins and amino acids
  - 3.1 Metabolism
  - 3.2 Important plasma proteins (albumin, immunoglobulin, haptoglobin, transferrin, C-reactive protein, etc.)
  - 3.3 Dysproteinaemia, monoclonal components
  - 3.4 Tumour-associated proteins
  - 3.5 Hereditary and acquired disorders of amino acid metabolism
4. Nucleic acids and purines
  - 4.1 Metabolism
  - 4.2 Gout
  - 4.3 Other hereditary and acquired disorders of purine metabolism
5. Porphyrins and bile pigments
  - 5.1 Metabolism
  - 5.2 Porphyrins, lead intoxication and hyperbilirubinaemia
6. Biogenic amines
  - 6.1 Metabolism
  - 6.2 Catecholamines, serotonin and their breakdown products
7. Water and electrolytes
  - 7.1 Metabolism
  - 7.2 Sodium, potassium, chloride pathologies
  - 7.3 Edema and ascites
8. Acids, bases, blood gases
  - 8.1 Acid-base balance and disorders; buffer systems (bicarbonate, phosphate, protein); Henderson-Hasselbalch equation; acidosis and alkalosis
  - 8.2 Renal regulatory systems
  - 8.3 Pulmonary gas exchange; oxygen metabolism
9. Blood cells and platelets
  - 9.1 Haemoglobin synthesis and catabolism
  - 9.2 Physiology, morphological cytochemical differentiation of blood cells
  - 9.3 Normal and disturbed functions
  - 9.4 Reactive changes in the blood cell pattern
  - 9.5 Anaemia
  - 9.6 Haemoglobinopathy. Thalassaemia and related disorders; characterisation by DNA analyses
  - 9.7 Haemoblastosis
  - 9.8 Thrombocythaemia/thrombocytopenia
  - 9.9 Mononucleosis
  - 9.10 Leucocytosis
10. Blood clotting and fibrinolysis
  - 10.1 Clotting reactions and fibrinolysis, thrombocyte function
  - 10.2 Hereditary and acquired disorders, bleeding and thrombosis
  - 10.3 Mode of action of anticoagulants, fibrinolytics, and aggregation inhibitors
  - 10.4 Characterisation of normal and disturbed clotting functions with the aid of global tests, phase tests and determinations of individual clotting factors
11. Immune system
  - 11.1 Functions of the humoral and cellular immune systems and their regulation; cytokines; inflammation; acute phase proteins
  - 11.2 Surface antigens
  - 11.3 Hereditary and acquired disorders
  - 11.4 Immunoglobulin deficiency and overproduction, monoclonal and polyclonal immunopathies
  - 11.5 Major histocompatibility complex
  - 11.6 Autoimmune diseases
12. Enzymes
  - 12.1 Induction, synthesis and elimination
  - 12.2 Enzyme patterns in various tissues and body compartments; isoenzymes; diagnostic significance
13. Cerebrospinal fluid (CSF)
  - 13.1 CSF synthesis and circulation
  - 13.2 Composition of CSF in comparison to serum
  - 13.3 CSF cell counting and differentiation
  - 13.4 Hereditary and acquired disorders of CSF homeostasis
14. Digestive tract
  - 14.1 Digestive enzymes in the various sections of the digestive system including the exocrine functions of the liver and pancreas
  - 14.2 Hydrochloric acid, bicarbonate and bile secretion
  - 14.3 Fluid and electrolyte secretion
  - 14.4 Absorption
  - 14.5 Gastrointestinal hormones
  - 14.6 Hereditary and acquired disorders of the digestive system
  - 14.7 Malabsorption including vitamin malabsorption
15. Exocrine functions of the pancreas
  - 15.1 Acute pancreatitis
  - 15.3 Chronic pancreatitis
16. Liver and biliary tract
  - 16.1 Physiology. Normal and disturbed functions of the liver; metabolism; synthesis, biotransformation; excretion
  - 16.2 Enterohepatic circulation; metabolism of bilirubin and bile acids
  - 16.3 Hepatitis, cirrhosis, cholestasis, cytolysis
17. Kidneys and urinary tract
  - 17.1 Physiology. Normal and disturbed renal function
  - 17.2 Excretory substances in the plasma and urine. Glomerular filtration rate and clearance. Activity and effects of diuretics; free water clearance; alkalosis

- 17.3 Proteinuria
- 17.4 Acute and chronic renal insufficiency, nephritis, nephrotic syndrome
- 18. Heart and circulatory system
  - 18.1 Normal and disturbed circulation
  - 18.2 Myocardial infarction and shock; enzyme patterns and marker proteins; fluid balance
  - 18.3 Hypertension
- 19. Skeletal and locomotor system
  - 19.1 Function and metabolism of muscles, bones, cartilage, synovia and connective tissues (fasciae, tendons)
  - 19.2 Hereditary and acquired disorders, especially of calcium and phosphate metabolism, vitamin D, collagen and proteoglycan metabolism
- 20. Endocrine system
  - 20.1 Physiology, biosynthesis and catabolism of hormones
  - 20.2 Hormonal regulation, hormone transport, receptor systems
  - 20.3 Functional disorders of the thyroid gland, the parathyroid glands, the adrenal cortex, the adrenal medulla, the endocrine part of the pancreas, the gonads, the placenta, the pituitary-hypothalamus system
- 21. Pregnancy, perinatal laboratory analysis
  - 21.1 Hormone analyses; *in vitro* fertilisation
  - 21.2 Molecular biology of hereditary disorders
- 22. Drug monitoring
  - 22.1 Pharmokinetics, pharmacodynamics and bioavailability of drugs
  - 22.2 Therapeutic range
  - 22.3 Individual determinations for the most important drugs: digoxin, theophylline, anticonvulsants, etc.
- 23. Poisoning
  - 23.1 Pathomechanisms of the most important types of poisoning
  - 23.2 Knowledge of the preparation and preservation of specimens, regulations for examination, documentation of examinations, chain of custody
  - 23.3 Knowledge of strategies for group recognition of poisons by extraction, isolation and identification
  - 23.4 Individual determinations for the most important types of poisoning, e.g. ethyl alcohol, carbon monoxide, barbiturates, methaemoglobin, methyl alcohol, ethyl eneglycol, benzene, toluene, etc. Cholinesterase in the case of organic phosphate intoxications
  - 23.5 Tests for drugs of abuse
  - 23.6 Radioactive isotope toxicology
  - 23.7 Toxicology: LSD, entactogenic drugs, opiates, cannabis, cocaine
- 24. Molecular biology investigations of non-infectious diseases
  - 24.1 Prenatal diagnosis of inborn errors of metabolism
  - 24.2 Oncogenes

## Appendix B

### Extended Haematology

1. Morphology and haematopoiesis
  - 1.1 Morphological investigation of bone marrow smears including different staining procedures. PAS staining for intracellular glycogen, Sudan black staining for lipids, iron staining, acid phosphatase, esterase and peroxidase staining
  - 1.2 Investigation of cellular characteristics and abnormalities by flow cytometry
  - 1.3 Haemoglobinopathies. Haemoglobin electrophoresis on cellulose acetate, in agar gel. Kleihauer test
  - 1.4 Investigation of anaemias, both congenital and acquired. Ham test and sucrose test
  - 1.5 Detection of abnormal haemoglobin derivatives: spectrophotometric analysis
  - 1.6 Haemato-oncology
  - 1.7 Myelodysplasia
  - 1.8 Ganglion exploration
  - 1.9 Lymphoid system pathology
2. Haemostasis
  - 2.1 Investigation of platelet function. Influence on platelet aggregation by ADP-adrenaline, collagen, ristocetin, ADP, ATP. Determination of serotonin. Spontaneous aggregation. Clot retraction. Platelet factor III determination, glass pearl test
  - 2.2 Use of chromogenic substrates for the determination of coagulation factors
  - 2.3 Detection of circulating inhibitors, thrombo test diluted curve, cephalin dilution curve
  - 2.4 Protein S, protein C
  - 2.5 Theoretical background and clinical background and knowledge of the following subjects: prekallikrein, high molecular kininogen determination, plasminogen, antiplasmin, plasminogen activators
3. Immunohaematology and blood banking
  - 3.1 Typing of irregular (auto)antibodies; determination of antibody titre
  - 3.2 Extended blood group typing (beyond ABO and Rhesus D)
  - 3.3 Investigation of transfusion reactions
  - 3.4 Preparation and application of blood components
  - 3.5 Organisation of blood banking
  - 3.6 Typing of B and T lymphocytes
  - 3.7 Platelet antibodies
  - 3.8 Typing of leucocytes and tissue antigens
  - 3.9 Quantitative determination of immunoglobulins and complement factors
  - 3.10 Recognition of cell markers using monoclonal antibodies
  - 3.11 The application of plasmapheresis in donors and in patients

**Appendix C****Medical Microbiology-Virology**

1. General aspects  
Interdisciplinary interfaces in the investigation of biological samples require some general knowledge of infectious diseases and medical microbiology in the practice of clinical chemistry and immunochemistry
- 1.1 Definition of infection and infectious disease: natural bacteriological ecosystem
- 1.2 Pathogenicity of microbes and viral agents; disinfection
- 1.3 General epidemiology of infection and infectious diseases
2. Diagnostic procedures
- 2.1 Specimen selection and collection (blood, urine, sputum, faeces, others)
- 2.2 Specimen processing: smears, staining, cultures, susceptibility testing
- 2.3 Usual techniques for microbe and virus identification (excluding biochemical characteristics)
- 2.4 Molecular biology techniques for characterisation of microbes and viral agents
- 2.5 Bacteriological and viral serology
3. Bacteria and viruses  
Succinct description of responsible bacteria and viruses in bacteriological and viral syndromes or diseases (excluding biochemical characteristics).
- 3.1 Bacteria: *Neisseria gonorrhoeae* and *N. meningitidis*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *S. agalactiae* and *S. pneumoniae*, *Escherichia coli*, *Salmonella typhi* and *S. typhimurium*, *Shigella spp*, *Vibrio cholerae*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Clostridium perfringens*, *C. tetani*, *Listeria monocytogenes*, *Mycobacterium tuberculosis*, *Treponema pallidum*, *Chlamydia trachomatis* etc.
- 3.2 Viruses: cytomegalovirus and others: influenza, poliomyelitis, hepatitis A, B and C, human immunodeficiency (HIV), herpes etc.
4. Bacteriological and viral diseases and syndromes. Epidemiology, main clinical signs, bases for biological diagnosis, treatment
- 4.1 Meningitis
- 4.2 Septicaemia
- 4.3 Urinary and vaginal infections
- 4.4 Bacterial and viral diarrheas
- 4.5 Respiratory infections
- 4.6 Human acquired immunodeficiency syndrome
- 4.7 Sexually transmitted diseases
- 4.8 Hepatic virus infections
- 4.9 Cytomegalovirus infections
5. Antibiotics
- 5.1 Basic knowledge on antibiotics and antibacterial therapy
- 5.2 Antibiotic sensitivity test
- 5.3 Mechanisms of resistance to antibiotics

**Medical Parasitology**

1. Epidemiology, main clinical signs, basis for biological diagnosis (including a succinct description of parasites and fungi without biochemical characteristics), treatment
- 1.1 Amoebiasis: *Entamoeba histolytica*
- 1.2 Giardiasis, cryptosporidiosis and uro-genital trichomoniasis
- 1.3 Malaria
- 1.4 Toxoplasmosis
- 1.5 Intestinal, hepatic and urinary helminthiasis: strongyloidiasis, ancylostomiasis, enterobiasis, ascariasis, schistosomiasis (*Schistosoma mansoni* and *S. haematobium*) fascioliasis (*Fasciola hepatica*) taeniasis (*Taenia saginata*)
- 1.6 Fungal infections (*Candida albicans*, *Cryptococcus neoformans*)
- 1.7 Aspergillus infections (*Aspergillus fumigatus*)
- 1.8 Dermatophyte infections (*Microsporum canis*, *Epidermophyton floccosum*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*)
- 1.9 Leishmaniasis
- 1.10 Echinococcosis
- 1.11 Pneumocystosis
- 1.12 Filariasis
- 1.13 Pneumocystosis
2. Usual techniques for parasite identification
3. Serological diagnosis of parasitic diseases

**Appendix D****Examples of Scientific and Medical Literature**

1. Textbooks  
Note: As new (editions of) textbooks appear regularly the following list only serves as an example and is certainly not exhaustive; frequent updating is necessary.
- 1.1 Burtis CA, Ashwood ER, editors and Tietz NW. Tietz textbook of clinical chemistry. Philadelphia: WB Saunders Company, 1998.
- 1.2 Greiling H, Gressner AM, editors. Lehrbuch der Klinischen Chemie und Pathobiochemie. 3. Auflage. Stuttgart: FK Schattauer Verlag, 1995.
- 1.3 Thomas L, editor. Clinical laboratory diagnostics. Frankfurt am Main: T-H Books, 1998.
- 1.4 Johnstone A, Thorpe R, editors. Immunochemistry in practice. Oxford: Blackwell Scientific Inc, 1996.
- 1.5 Rose BD, Post T, Narins R. Clinical physiology of acid-base and electrolyte disorders. New York: McGraw-Hill Book Company, 1994.
- 1.6 Greenspan FS, Strewler GJ, editors. Basic & clinical endocrinology. Los Altos: Appleton & Lange Medical Publications, 1997.
- 1.7 Felig P, Baxter JD, Frohman LA, editors. Endocrinology and metabolism. New York: McGraw-Hill Book Company, 1995.
- 1.8 Sackett DL, Haynes RB, Tugwell P, editors. Clinical epidemiology, a basic science for clinical medicine. Boston: Little, Brown and Company, 1991.
- 1.9 Stites DP, Terr AI, Parslow TG, editors. Medical immunology. London: Appleton & Lange, 1997.

- 1.10 Friedman RB, Young DS, editors. Effects of disease on clinical laboratory tests. Washington: AACC Press, 1997.
- 1.11 Young DS, editor. Effects of drugs on clinical laboratory tests. Washington: AACC Press, 1995.
- 1.12 Young DS, editor. Effects of preanalytical variables on clinical laboratory tests. Washington: AACC Press, 1993.
- 1.13 Richard-Lee GL, Foerster J, Lukens J, Wintrobe MM, editors. Wintrobe's clinical haematology. Philadelphia: Lea and Febiger, 1998.
- 1.14 Dacie JV, Lewis SM. Practical haematology. London: Churchill Livingstone, 1995.
- 1.15 Spivak JL, Eichner ER. The fundamentals of clinical hematology. Cambridge: Harper and Row Publishers, 1993.
- 1.16 Bloom AL, Forbes CD, Thomas DD. Haemostasis and thrombosis. London: Churchill Livingstone, 1994.
- 1.17 Engelfriet CP, Contreras M, Mollison PL. Blood transfusion in clinical medicine. Oxford: Blackwell Science Inc, 1997.
- 1.18 Babior BM, Stossel TP. Haematology: "a pathophysiological approach". New York: Churchill Livingstone, 1994.
- 1.19 Hall R, Malia R.G, editors. Medical laboratory haematology. London: Butterworths, 1991.
- 1.20 Colman RW, Hirsh J, Marder VJ, Salzman EW, editors. Hemostasis and thrombosis; basic principles and clinical practice. Philadelphia: JB Lippincott Company, 1994.
- 1.21 Stiene-Martin EA, Lotspeich-Steininger ChA, Koepke JA, editors. Clinical hematology: principles, procedures, correlations. Philadelphia: JB Lippincott Company, 1998.
- 1.22 Harmening DM, editor. Clinical hematology and fundamentals of hemostasis. Philadelphia: FA Davies Company, 1996.
- 1.23 Hoffbrand AV, Petit JE. Essential haematology, Oxford: Blackwell Scientific Publications, 1993.
- 1.24 Adelberg EA, Jawetz E, Melnick JL. Review of medical microbiology. Los Altos: Lange Medical Publications, 1993.
- 1.25 Murray PR, Baron EJ, Pfaller MA, editors. Manual of clinical microbiology. Washington: American Society for Microbiology, 1999.
- 1.26 Bangert SK, Marshall WJ, editors. Clinical biochemistry: metabolic and clinical aspects. London: Churchill Livingstone, 1995.
2. Scientific and medical journals
- 2.1 Annals of Clinical Biochemistry.
- 2.2 British Medical Journal.
- 2.3 Clinical Chemistry.
- 2.4 Clinical Chemistry and Laboratory Medicine.
- 2.5 Clinica Chimica Acta.
- 2.6 Current Advances in Clinical Chemistry.
- 2.7 Current Contents.
- 2.8 Journal of Biological Chemistry.
- 2.9 Journal of Clinical Endocrinology and Metabolism.
- 2.10 Nature.
- 2.11 New England Journal of Medicine.
- 2.12 Scandinavian Journal of Clinical & Laboratory Investigation.
- 2.13 Science.
- 2.14 The Lancet.
3. Primary literature
- It must be stressed that reading so called primary literature (articles, surveys, etc.) is of utmost importance to keep informed on "the state of the art" in clinical chemistry. For this reason students should adopt a system for themselves of keeping constantly informed on developments in the field of laboratory medicine and related subjects.

*Received 27 September 1999; accepted 19 October 1999*

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