

1 Principles of leadership, laboratory organization, and management

1.1 Be able to discuss and describe the following topics related to laboratory organization, regulatory compliance, leadership and management

- General aspects of laboratory facilities and design: centralized versus POC/near patient testing, workflow analysis, temperature monitoring, water purity monitoring, waste management
- Laboratory health and safety issues:
 - Fire, chemical, electrical, biological sample disposal regulations, blood and body fluid precautions, infection control, interpretation of Material Safety Data Sheets (MSDS), OSHA requirements
- Laboratory test ordering and reporting systems: general aspects of electronic health records, hospital information systems, laboratory information systems
- Medico-legal requirements, chain of custody
- Health Insurance Portability and Accountability Act (HIPAA)
- Institutional review board (IRB)
- Accreditation requirements and regulatory agencies (CMS, CLIA, CAP, Joint Commission, COLA, etc)
- Strategies for selecting appropriate instrumentation: Total lab automation, automated, centralized instrumentation, POC, standalone instrument
- General aspects of financial management of laboratory: cost-analysis, financial justification for capital equipment purchase or reagent rental, depreciation, direct and indirect costs, billing and reimbursement concepts (CPT codes, hospital billing, reimbursement)
- Understand and calculate the following:
 - Return on investment (ROI)
 - Cost per reportable result
 - FTE calculations (salary, benefits) in determining testing costs
- Preparation and maintenance of policies and standard operating procedures (SOPs)
- Quality management concepts: control of pre-analytical, analytical, post-analytical variables, development and monitoring of quality indicators, quality assurance, quality improvement, quality control standards and practices, external quality assessment and proficiency testing programs, accreditation requirements.
- Overview of Lean and Six Sigma
- Requirements for non-waived and waived testing, mock inspection, checklists, individualized quality control plan (IQCP)
- Regulatory requirements for method evaluation (CLIA requirements, FDA-cleared versus lab developed test (LDT)). Validating and implementing laboratory developed tests (LDTs)
- Analyte specific reagents (ASRs)
- General understanding of reference methods, reference materials, NIST standards, traceability, primary and secondary standards, harmonization
- Evaluating the diagnostic and clinical utility of laboratory test(s)
- Critical values

2 Basic Statistics and Common Mathematical Concepts Used in Laboratory Medicine

2.1 Be able to describe, apply and/or calculate common equations used in laboratory medicine

- Anion Gap
- Albumin-adjusted calcium (corrected calcium)
- Base excess
- Bicarbonate
- BUN to urea ratio (and interpretation)
- Converting between mass and molar units
- Corrected sodium
- Estimated glomerular filtration rate (eGFR) – equations, strengths, weaknesses
- Globulins
- International normalized ratio (INR)
- Calculated LDL-cholesterol (Friedewald equation or others)
- Osmolar Gap (including calculated osmolarity)
- % Transferrin saturation (including origin of TIBC)
- Normalization of urine drug concentrations using creatinine
- Calculating clearance (e.g. creatinine)
- Volume of distribution
- Maintenance dose
- Time to steady-state based on half-life
- Half-life calculations

2.2 Be able to define and calculate basic statistical concepts routinely used in the laboratory

- Mean, median, mode
- Standard deviation (SD)
- Coefficient of variation (CV)
- Standard Deviation Index (SDI)
- Confidence limits
- Statistical principles of quality control
 - Levey-Jennings charts
 - Determining QC target values and ranges
 - Application of Westgard rules
- Multiples of the Median (MOM)
- Patient Moving Averages

2.3 Be able to distinguish the appropriate statistical tests to employ based on the distribution of the data

- Interpretation and appropriate use of comparative statistics: t-test, F-test, analysis of variance, Chi-square,
- Linear and other regression analyses (e.g. Deming, Passing-Bablok)
- Evaluation of differences between populations
- Concepts of parametric and non-parametric statistics used in determining reference intervals

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2.4 Be able to define and apply the following analytical/mathematical concepts in laboratory medicine:

- Addition dilution
- Serial dilutions
- Bias
- Allowable Total Error (TEa)
- Recovery
- Sigma metric (TEa-Bias)/CV
- Receiver operator characteristic (ROC) curve
- Delta check
- Relative change value (RCV)
- Biologic variation
- S.I. and conventional units and unit conversions
- Concentrations, molarity, buffer solutions (concentrations, %, vol/vol etc)
- RPM to relative centrifugal force (g)
- Ideal gas law
- Beer's law
- Henderson Hasselbach
- Henry's law (calculating tCO₂ from PCO₂)
- pH from H⁺ concentration

2.5 Be able to define, calculate and/or analyze the following concepts related to analytical and clinical evaluation of laboratory methods

- Comparisons of methods and instruments
- Bland-Altman chart and bias plot (constant and proportional bias)
- Calibration verification
- Analytical measurement range (AMR)
- Clinical Reportable Range (CRR)
- Accuracy
- Linearity
- Precision (Intra-assay, Inter-assay, Simple, Complex, Total Imprecision)
- Recovery
- Principles of calibration
- Variability due to reagent lot and instrument calibration
- Analytical sensitivity
- Analytical specificity
- Clinical sensitivity
- Clinical specificity
- Diagnostic accuracy
- Limit of blank (LOB)
- Limit of detection (LOD)
- Limit of quantitation (LOQ)
- Functional sensitivity
- Determining acceptable bias
- Allowable Total Error
- Analytical interferences: hemolysis, icterus, lipemia, heterophile/anti-animal antibodies, spectral, structural, hook effect

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- Carryover
- Analyte stability
- Establishing and verifying reference intervals, reference populations
- Medical decision limits
- Therapeutic and toxic concentrations of drugs
- Pre- and post-test predictive value
- Positive predictive value
- Negative predictive value
- Odds ratio, hazard ratios, and likelihood ratio

3 Specimen Collection and Processing

3.1 Be able to describe appropriate specimen collection and processing steps and their importance

- Patient preparation for tests
 - Dietary, collection requirements, exercise, time of day
- Specimen collection
 - Phlebotomy, body position (supine, sitting), arterial, venous, capillary
- Anticoagulants, preservatives/additives and gel-separator tubes used for specimen collection
- Order of draw
- Specimen identification requirements
- Specimen transportation considerations
- Regulations and precautions related to collection, transportation and processing of biological specimens
- Pre-analytic considerations for specimens other than blood
 - Urine, body fluids, CSF, saliva, meconium

4 Analytical Techniques Used in Clinical Chemistry

4.1 Be able to discuss the basic principle of use of generic laboratory equipment

- Balances
- Centrifuges
- Microscopes
- pH meters
- Water baths

4.2 Be able to discuss the basic techniques/concepts below applied to laboratory medicine

- Buffer selection and preparation
- Partition coefficient
- Dialysis
- Concentration
- Desalting
- Preparation of derivatives
- Blanking
- Extractions (liquid-liquid, solid phase)
- Filtration
- Freeze-drying
- Pipetting

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- Ultrafiltration
- Volumetric measurement
- Weighing
- Centrifugation (ultracentrifugation, airfuge, etc.)
- Water purification and types of water

4.3 Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in a Core Laboratory

- Absorption, nephelometry and turbidimetry
- Acid-base measurement
- Blood gas measurement and co-oximeters
- Immunoassay techniques and detection systems (e.g. chemiluminescence, electroluminescence)
- Ion-selective electrode
- Total laboratory automation
- Random access vs batch analyzers
- Osmometry

4.4 Be able to discuss the method principle/concepts and potential advantages and limitations of instruments and analytical techniques commonly used in Clinical Specialty Laboratories

- Atomic absorption
- Cell counters
- Chromatography
 - Principles of chromatography
 - Affinity chromatography
 - Column chromatography
 - Planar chromatography
 - Direct and reverse-phase liquid chromatography
 - Gas chromatography
 - High-performance liquid chromatography
 - Ion-exchange chromatography
 - High-pressure liquid chromatography (HPLC)
- Electrophoresis
 - 2-dimensional
 - Agarose
 - Capillary zone
 - Cellulose acetate
 - Isoelectric focusing (IEF)
 - Immunofixation
 - Immunosubtraction
 - Polyacrylamide
 - Partition techniques
 - Size exclusion techniques
- Emerging technologies
 - Nuclear magnetic resonance (NMR) spectroscopy
 - Sensors
- Enzymology

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- Enzyme kinetics (Michaelis-Menten, K_m , V_{max})
- Enzymes as reagents, coupled enzymatic reactions, zero-order (enzyme) assays, first-order (substrate) assays
- Flame emission photometry
- Flow cytometry
- Fluorescence polarization
- Immunofluorescence
- Isotopic techniques
- Luminescence and fluorescence
- Multiplex flow immunoassay
- Spectrophotometry

4.5 Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in Molecular Diagnostics

- Principles and methods of DNA and RNA isolation, purification
- Polymerase chain reaction (PCR)
- DNA probes
- Hybridization
- Restriction fragment length polymorphism (RFLP)
- Blotting techniques
- DNA chips/microarrays
- Sequencing
- Real Time PCR
- fluorescent in situ Hybridization (FISH)
- Other methods of genomic analysis

4.6 Be able to outline the components of a mass spectrometer, including ionization sources (electron impact, chemical ionization, electrospray ionization), mass filters (quadrupole, magnetic), detectors

4.7 Be able to describe the basic principles of mass spectrometry (MS) and explain the mass to charge ratio and mass spectra

- Mass spectrometry
 - Chromatographic separation (see above)
 - Gas Chromatography-MS (GC-MS)
 - Inductively Coupled Plasma MS (ICP-MS)
 - Liquid Chromatography MS (LC-MS)
 - LC-MS-MS
 - Matrix Assisted Laser Desorption/ Ionization – Time of Flight (MALDI-TOF)

4.8 Be able to describe the relationship of the clinical laboratory to medical practice by applying and/or defining the following concepts

- Roles (screening, diagnosis, monitoring) and limitations for laboratory testing in clinical practice
- Structure, use and limitations of the electronic medical record
- Extracting and interpreting laboratory and medical information from information systems
- Assess the design and performance of clinical outcome studies

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- Design studies and appropriately analyze and interpret data related to determination of diagnostic performance
- Economic evaluation of diagnostic testing and application of principles of evidence-based laboratory medicine
- Principles and application of evidence-based laboratory medicine in test implementation and patient evaluation
- Implementation of appropriate test utilization practices

4.9 Be able to describes concepts related to interpretation of laboratory test results

- Understand the establishment and appropriate use of reference intervals, medical decision limits and critical values
- Understand the sources and effects of analytic variables on laboratory tests
- Understand the sources and effects of physiological variables (diurnal and individual variations, rest, exercise, age, gender, fasting and the pharmacologic effects) on test results
- Understand the effects of disease on test results and recognize typical disease patterns
- Recognize the use and limitations of current disease-related testing strategies/algorithms, e.g., use of cardiac markers for AMI and ACS, lipid screening, for CHD, diabetes screening, PSA screening, etc.
- Understand the principles of screening, confirmatory and reflex testing

5 Clinical Pathology and Laboratory Evaluation of Disease with a Focus on Clinical Cases

For each disease state, achieve the following core competencies:

- A. Be able to understand the causes and clinical signs and symptoms of the disease state or disorder.
- B. Be able to understand the pathophysiology and biochemical changes of the disease or disorder.
- C. Be able to describe the laboratory tests that are relevant for detection, diagnosis and management, or monitoring of the disease or disorder.
- D. Be able to select laboratory tests and interpret the analytical results in light of the clinical signs and symptoms in the individual patient
- E. Be familiar with the analytical methods available for laboratory tests.

5.1 Cardiovascular Disorders and Hypertension

5.1.1 Be able to describe the causes and manifestations of cardiovascular disease and the assessment of individual risk for

- Acute coronary syndrome
- Cardiac risk assessment
- Myocardial infarct

5.1.2 Be able to describe which laboratory investigations are important in the detection, diagnosis and management of

- Atherosclerosis
- Cardiac amyloid
- Congestive heart failure
- Hypertension
- Myocardial infarction
- Stable angina

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- Unstable angina

5.1.3 Be able to appropriately select and interpret results of the following laboratory tests and recognize the analytical methods available

- High-sensitivity CRP
- Natriuretic peptides
- Serum and urine electrophoresis and immunoglobulins
- Troponin and high-sensitivity troponin

5.2 Endocrinology

5.2.1 Be able to describe all aspects of hormone action, including feedback inhibition and other regulatory mechanisms for hormone release and to acquire a detailed knowledge of the major endocrine organs and systems

Hypothalamic-pituitary axis

- Anterior pituitary hormones
- Communication between pituitary and hypothalamus – anterior vs. posterior
- Hirsutism and virilization
- Hypothalamic hormones
- Inhibitory hormones
- Posterior pituitary hormones
- Primary vs. secondary causes
- Renin-angiotensin-aldosterone pathway
- Steroid biosynthesis pathway
- Stimulation tests
- Suppression tests

5.2.2 Be able to describe the causes, clinical signs and symptoms of the following endocrine disorders

5.2.3 Be able to describe which laboratory investigations are important in the detection, diagnosis and management of each endocrine disorder

- Acromegaly/gigantism
- Addison's syndrome
- Adrenal insufficiency
- Congenital adrenal hyperplasia
- Cushing's syndrome and Cushing's disease
- Diabetes insipidus
- Female infertility
- Growth hormone deficiency
- Hyperaldosteronism
- Hyperprolactinemia
- Hyperthyroidism
- Hypothyroidism
- Non-thyroidal illness
- Male infertility
- Pheochromocytoma

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- Polycystic ovarian syndrome
- Premature ovarian failure
- Sheehan's syndrome
- SIADH
- Thyroid cancer

5.2.4 Be able to explain the following specific laboratory investigations and their importance in the study of endocrine disorders

5.2.5 Be able to recognize the analytical methods available for their measurement

5.2.6 Be able to select laboratory investigations and interpret the analytical results in context of the clinical signs and symptoms in the patient

- 17-hydroxyprogesterone
- Adrenocorticotrophic hormone (ACTH)
- Anti-diuretic hormone (ADH) or Arginine vasopression
- Aldosterone, renin and ratio
- Androstenedione
- Angiotensin converting enzyme (ACE)
- Autoantibodies to the relevant endocrine organ
- Catecholamines (plasma and urine)
- Cortisol – serum, urine, salivary
- Dexamethasone suppression test
- Dehydroepiandrosterone sulfate (DHEAS)
- Estradiol
- Follicle stimulating hormone (FSH)
- Growth hormone (GH)
- Growth hormone suppression test (OGTT)
- Insulin-like growth factor 1 (IGF-1)
- Lutenizing hormone (LH)
- Metanephrines (plasma and urine)
- Progesterone
- Prolactin and macroprolactin
- Sex hormone binding globulin (SHBG)
- Testosterone – total, free, bioavailable
- Thyroglobulin (TG), ant Thyroid stimulating hormone (TSH), Free T3, free T4 Total T3, Total T4
- TSH receptor antibodies
- Thyroperoxidase (TPO) antibodies

5.3 Gastrointestinal and Pancreatic Disease

5.3.1 Be able to provide general overview and describe functions of the gastrointestinal and pancreatic systems

- Intestinal absorption of proteins, fats and carbohydrates
- Endocrine and exocrine functions of the pancreas
- Vitamin B12 absorption

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5.3.2 Be able to describe diseases of gastrointestinal and pancreatic function

- Acute and chronic pancreatitis
- Autoimmune bowel disease
- Causes of gastric ulceration
- Inflammatory bowel disease
- Neuroendocrine tumors

5.3.3 Be able to recognize the causes, clinical signs and symptoms of the following disorders relating to gastrointestinal and pancreatic function

5.3.4 Be able to describe which laboratory investigations are important in detection, diagnosis and management of gastrointestinal and pancreatic diseases

- Acute and chronic pancreatitis
- Carcinoid syndrome
- Celiac Disease
- Crohn's Disease
- Food allergy
- H. pylori infection
- Intestinal malabsorption, including vitamins, (see also trace elements and vitamins)
- Neuroendocrine tumors
- Pancreatic Exocrine Insufficiency
- Pyloric stenosis (see also acid base regulation and pulmonary function)
- Pernicious anemia
- Zollinger-Ellison syndrome

5.3.5 Be able to describe the following specific laboratory investigations important to the study of disorders of gastrointestinal and pancreatic function

5.3.6 Be able to describe analytical methods available for their measurement

5.3.7 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- $^{14}\text{CO}_2$ urea breath test for H. pylori
- Amylase and macroamylase
- CA 19-9
- Carcinoembryonic antigen (CEA)
- Chromogranin A
- Elastase
- Endomysial autoantibodies
- Fecal calprotectin
- Fecal occult blood
- Colon cancer screening methods
- Hydrogen breath test for lactose intolerance
- IgE and specific IgE
- Intrinsic factor antibodies
- Lipase

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- Serotonin and 5 HIAA
- Transglutaminase autoantibodies
- Vitamin B12 and folate
- Xylose absorption test
- Stimulation/suppression tests

5.4 Inborn Errors of Metabolism

5.4.1 Be able to describe the rationale for screening and the process

- Challenges with newborn screening
- Diseases appropriate for newborn screening – characteristics
- Newborn screening process

5.4.2 Be able to recognize the causes, clinical signs and symptoms of the following inherited conditions

5.4.3 Be able to describe which laboratory investigations are important in the detection, diagnosis and management of the following inherited conditions

- Congenital hypothyroidism
- Cystic fibrosis
- Enzyme deficiencies: biotinidase, galactokinase
- Fatty acid oxidation disorders: short, medium, long and very long chain
- Hemoglobinopathies
- Homocystinuria
- Lysosomal disease, glycogen storage diseases: lipidoses, hexosaminidases, Fabry's disease
- Maple syrup urine disease
- Phenylketonuria
- Tyrosinemia

5.4.4 Be able to describe the following specific laboratory investigations important to the study of inherited metabolic diseases

5.4.5 Be able to recognize analytical methods available for their measurement

5.4.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Acylcarnitines
- Alpha-1-antitrypsin genotyping
- Amino acids
- Hemoglobin electrophoresis
- Immunoreactive trypsinogen
- Organic acids
- Specific enzyme testing (e.g., biotinidase, galactokinase)
- Sweat chloride and conductivity

5.5 Iron and Hemoglobin Disorders, including porphyrias

- 5.5.1 Be able to describe the control and metabolism of iron and heme, the mechanisms which lead to iron overload and deficiency, and the implications of these states**
- 5.5.2 Be able to recognize the enzymatic defects of heme synthesis which lead to the porphyrias**
- Heme biosynthesis
 - Heme metabolism
 - Iron absorption, transport and storage
 - Iron deficiency
 - Iron overload
- 5.5.3 Be able to describe the causes, clinical signs and symptoms and manifestations of disorders of iron and heme metabolism**
- 5.5.4 Be able to describe which laboratory investigations are important in their detection, diagnosis and management**
- Acute and chronic porphyrias and their differential diagnosis
 - Anemia secondary to malignancy
 - Glucose-6-phosphate dehydrogenase (G6PD) deficiency
 - Hemochromatosis
 - Hemoglobinopathies
 - Intravascular hemolysis
 - Iron deficiency anemia
 - Thalassemia
- 5.5.5 Be able to describe the following specific laboratory investigations important to the study of iron and heme metabolism and the porphyrias**
- 5.5.6 Be able to recognize the analytical methods available for their measurement**
- 5.5.7 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms**
- Delta-aminolevulinic acid (ALA)
 - Ferritin
 - Complete blood count (CBC)
 - G6PD
 - Haptoglobin
 - Hemoglobin
 - Hemoglobin variants and thalassemias
 - Hemopexin
 - Iron
 - Porphobilinogen (PBG)
 - Porphyrins
 - Soluble transferrin receptor
 - Total iron binding capacity

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- Transferrin
- Transferrin saturation

5.6 Infectious Diseases

5.6.1 Be able to describe the role of the laboratory and serology testing in diagnosis and monitoring of the following infectious disease

5.6.2 Be able to recommend and interpret laboratory tests for diagnosis and management of (per CDC and/or local guidelines)

- HIV
- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis E
- Herpes Simplex Virus 1/2
- EBV
- CMV
- M. Tuberculosis
- SARS-CoV-2
- Syphilis
- Lyme

5.7 Hepatobiliary Disease

5.7.1 Be able to describe the metabolic functions of the liver and the following aspects of hepatobiliary disease

- Autoimmune disease
- Cholestasis
- Drugs – acute and chronic
- Genetic – e.g. A1AT deficiency (*see also acid-base regulation and pulmonary function*)
- Inflammatory and infective liver disease (hepatitis)
- Liver autoantibodies
- Liver cirrhosis
- Liver function – synthesis, conjugation, detoxification
- Liver transplantation
- Liver tumors – primary or secondary
- Origin, metabolism and transport of bilirubin

5.7.2 Be able to describe the causes, clinical signs and symptoms of the following disorders relating to hepatobiliary function

5.7.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Acute hepatitis
- Alcoholic liver disease
- Allograft rejection

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- Biliary damage and dysfunction
- Chronic hepatitis
- Cirrhosis (Including primary biliary cirrhosis)
- Elevated bilirubin levels: conjugated, unconjugated and total
- Elevated neonatal bilirubin levels
- Inherited disorders of bilirubin metabolism
- Infectious hepatitis
- Acetaminophen overdose/toxicity
- Wilson's disease

5.7.4 Be able to describe the following specific laboratory investigations important to the study of disorders of hepatobiliary function

5.7.5 Be able to recognize analytical methods available for their measurement

5.7.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Albumin (blood and ascites)
- Alpha-1 antitrypsin concentration and phenotype/genotype
- Alpha-fetoprotein (AFP)
- Ammonia
- Bile acids
- Bilirubin – conjugated, unconjugated, total,
- Transcutaneous bilirubin measurement
- Ceruloplasmin
- Ethanol
- Ferritin
- Hepatitis serology
- Iron
- Liver enzymes: ALT, AST, ALP, GGT
- Measurement of immunosuppressant drugs (cyclosporine, tacrolimus, sirolimus, everolimus)
- Acetaminophen
- PT-INR
- Autoantibodies: Liver Kidney Microsomal Ab, smooth muscle antibody, etc.

5.8 Immunology

5.8.1 Be able to describe the principles, components and control of the immune system

5.8.2 Components of the immune system (Cells, Lymphoid tissue, Soluble components and mediators)

- Immunoglobulin production, structure and function
 - Acute phase response
 - Adaptive immune system

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- Principles of cellular immunity, humoral immunity and inflammatory reactions
- Complement
 - Alternative pathway
 - Classical pathway
 - Mannose-binding lectin (MBL) pathway
- Cytokines
 - Colony stimulating factors and hematopoietic
 - Interferons
 - Interleukins
 - Tumor necrosis factors
- Hypersensitivity reactions
 - Types I – IV (or V)
- Immunoglobulins
 - Function
 - Gene rearrangement
 - Structure
- Innate Immune system
- Lymphocytes
 - B lymphocytes
 - T lymphocytes

5.8.3 Be able to describe the causes, clinical signs and symptoms of disorders relating to the immune system

5.8.4 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Allergy and anaphylaxis
- Autoimmune diseases
 - Endocrine
 - Gastro intestinal (GI) tract
 - Liver
 - Renal
 - Rheumatic and articular
 - Skin
- Lymphoid malignancy
 - B cell
 - T cell
- Primary immune deficiency
- Secondary immune deficiency
- Immunoglobulin overproduction (e.g. monoclonal gammopathies, cryoglobulinemia)
- Immunologic impact of transplantation

5.8.5 Be able to describe the following specific laboratory investigations important to the study of disorders of the immune system

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5.8.6 Be able to recognize analytical methods available for their measurement

5.8.7 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Autoantibodies to
 - Skin basement membrane, intercellular cement, Nuclear (ANA), smooth muscle, mitochondrial
 - Neutrophil cytoplasmic (ANCA), glomerular basement membrane, ANA
 - Rheumatoid factor, cyclic citrullinated peptides, nuclear, double stranded DNA, extractable nuclear antigens
 - Thyroid, pancreas, adrenal, ovary, testis
 - Tissue transglutaminase, endomysial, intrinsic factor
- Complete blood count
- HLA typing
- Immunoglobulin quantification and IgG subclasses
- Lymphocyte subsets (CD3, 4, 8, 16/56, 19)
- Monoclonal protein identification and quantification in serum, CSF and urine
 - Interpretive skills for evaluation of electrophoretic and immunofixation results in serum, urine and CSF for monoclonal and/or oligoclonal gammopathies
- Total and specific IgE
- Tryptase

5.9 Disorders of Kidney and Urinary Tract

5.9.1 Be able to describe the principles and control of renal function and the urinary tract and clinical interventions that supplement/replace declining renal function

- Normal renal function
- Endocrine functions of the kidney
- Hemodialysis
- Peritoneal dialysis
- Renal transplant biochemistry

5.9.2 Be able to describe the causes, clinical signs and symptoms of the following features of disorders relating to renal function, the urinary tract and uric acid metabolism

5.9.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Acute kidney injury
- Chronic kidney disease (CKD)
- Amyloid
- Antineutrophil cytoplasmic antibodies (ANCA) associated-vasculitis
- Cryoglobulin-associated renal damage
- Drug-induced renal damage
- Glomerular dysfunction/Glomerulonephritis
- Goodpasture's syndrome
- Gout

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- Hyperuricemia
- Myeloma-associated renal damage
- Proteinuria; glomerular permeability, tubular proteinuria
- Nephritic syndrome
- Nephrotic syndrome
- Diabetic nephropathy
- Renal tubular disease (*see also acid-base regulation and pulmonary function*)
- Diseases of renal endocrine dysfunction
- Systemic lupus erythematosus (SLE)
- Urinary tract infection (UTI)
- Renal stone formation
- Uremia
- Vasculitis (ANCA associated)

5.9.4 Be able to describe the following specific laboratory investigations important to the study of renal function, the urinary tract and uric acid metabolism

5.9.5 Be able to recognize the analytical methods available for their measurement

5.9.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Clearance (creatinine, cystatin C, inulin)
- Creatinine (serum and urine) and creatinine standardization
- Cystatin C
- Estimated glomerular filtration rate (eGFR) calculations
- Measured GFR
- Anti-nuclear antibodies (ANA)
- ANCA
- Beta-2-microglobulin
- Complement C3 and C4
- Cryoglobulins
- Erythropoietin
- Examination and identification of renal calculi
- Measurement of immunosuppressant drugs (cyclosporine, tacrolimus, sirolimus)
- Phosphate, calcium and magnesium
- Renal calculi analysis
- Serum and urine electrophoresis and immunoglobulins
- Urea and urea kinetics
- Uric acid
- Urine albumin
- Urine dip stick analysis
- Urine microscopic analysis
- Urine oxalate

5.10 Diabetes Mellitus

5.10.1 Be able to describe the pathogenesis of diabetic states and the following aspects of the study of diabetes mellitus

- Regulation of glucose homeostasis
- Etiology of Type I, Type 2 and gestational diabetes
- Complications of diabetes (microvascular, macrovascular)
- Diabetic ketoacidosis
- HbA1c standardization
- Guidelines for the screening, diagnosis and monitoring of diabetes
- Non-ketotic hyperosmolar coma
- Self-monitoring of blood glucose

5.10.2 Be able to describe the causes, clinical signs and symptoms of the following aspects of diabetes mellitus

5.10.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Diabetic ketoacidosis
- Gestational diabetes
- Hypoglycemia
- Metabolic syndrome
- Non-ketotic hyperosmolar coma
- Pre-diabetes/Impaired glucose tolerance
- Type I diabetes
- Type 2 diabetes

5.10.4 Be able to describe the following specific laboratory investigations important to the study of diabetes mellitus

5.10.5 Be able to recognize analytical methods available for their measurement

5.10.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Anti-glutamic acid decarboxylase (GAD) antibodies
- Anti-insulin antibodies
- Blood gas and hydrogen ion measurements
- C-peptide
- Fructosamine and other glycated proteins
- Glucagon
- Glucose
- Glucose tolerance tests
- HbA1c
- Insulin
- Insulinoma antigen 2 (IA-2)
- Ketones (β -hydroxy butyrate)

- Microalbumin
- Zinc Transporter 8 (ZnT8)

5.11 Lipids and Disorders of Lipoprotein Metabolism

5.11.1 Be able to describe the principles and control of lipid metabolism and the following aspects of the study of lipid and lipoprotein disorders

- Apolipoproteins: functions, receptors (e.g. LDL-R)
- Cardiovascular disease risk calculation and evaluation, and cost-effectiveness of lipid screening strategies
- Fatty acid transport and oxidation
- Lipid absorption, transport and metabolism
- Lipoprotein metabolism: endogenous and exogenous pathways

5.11.2 Be able to describe the causes, clinical signs and symptoms of the following features of disorders relating to lipid and lipoprotein disorders

5.11.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Atherosclerosis
- Hypercholesterolemia
- Hyperlipidemia
 - Inherited disorders
 - Non-inherited disorders
- Hypolipidemia
- Metabolic syndrome

5.11.4 Be able to describe the following specific laboratory investigations important to the study of disorders of lipid and lipoprotein metabolism

5.11.5 Be able to recognize analytical methods available for their measurement

5.11.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Total cholesterol
- Triglycerides
- Apolipoprotein A and B
- Genotyping of ApoE, LDL receptor and LPL
- HDL cholesterol
- High-sensitivity CRP
- LDL cholesterol – direct and calculated methods (Friedewald Equation)
- Lipoprotein electrophoresis
- Lipoprotein ultracentrifugation
- Lp(a)
- Non-HDL cholesterol (calculated)

5.12 Calcium, Magnesium, Parathyroid, Bone Disorders

5.12.1 Be able to describe the control of calcium and phosphate homeostasis including the following specific aspects of the process

- Circulating forms of calcium
- Metabolism of vitamin D
- Markers of bone resorption and bone formation
- Primary versus secondary hyper/hypocalcemia
- Regulation of calcium and phosphate concentrations

5.12.2 Be able to describe the causes, clinical signs and symptoms of the following disorders and manifestations of calcium and phosphate metabolism and bone disease

5.12.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Hypercalcemia
- Hypermagnesemia
- Hyperparathyroidism
- Hyperphosphatemia
- Hypocalcaemia
- Hypomagnesemia
- Hypoparathyroidism
- Hypophosphatemia
- Hypophosphatasia
- Pseudohypoparathyroidism
- Osteogenesis imperfecta
- Osteoporosis
- Paget's disease
- Hypercalcemia of malignancy

5.12.4 Be able to describe the following specific laboratory investigations important to the study of calcium and phosphate metabolism and bone disease

5.12.5 Be able to recognize the analytical methods available for their measurement

5.12.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- 1,25 di-hydroxy vitamin D
- 25 hydroxy vitamin D
- C- and N-telopeptides
- Calcium – total and ionized
- Magnesium
- Osteocalcin
- Phosphate
- PTH
- PTHrp

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- Pyridinolines
- Total and bone-specific ALP

5.13 Vitamins and Trace Elements

5.13.1 Be able to describe importance of trace elements and vitamins to metabolic processes and wellbeing, the mechanisms of their actions and the consequences of deficiency and overload states

- Essential and non-essential metals
- Fat soluble vitamins; A and carotene, D, E and K
- Folate metabolism and function
- Genetic disorders of copper metabolism
- Genetic disorders of iron metabolism
- Potential vitamin toxicity
- Toxic and non-toxic metals
- Vitamin B12 absorption, metabolism and function
- Water soluble vitamins; B group vitamins and C

5.13.2 Be able to describe the causes, clinical signs and symptoms of the following aspects of disorders of trace element and vitamin metabolism

5.13.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Arsenic poisoning
- Cadmium poisoning
- Copper deficiency/excess
- Folate deficiency
- Iron overload
- Lead poisoning
- Mercury poisoning
- Vitamin B12 deficiency

5.13.4 Be able to describe the following specific laboratory investigations important to the study of trace elements and vitamins

5.13.5 Be able to recognize analytical methods available for their measurement

5.13.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Arsenic in blood and urine
- Cadmium in blood and urine
- Ceruloplasmin
- Delta amino levulinic acid (ALA)
- Ferritin
- Folate
- Homocysteine

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- Intrinsic factor antibody
- Laboratory assessment of specific B vitamin status
- Lead in blood and urine
- Mercury in blood and urine
- Methylmalonic Acid (MMA)
- Serum and urinary iron
- Serum and urinary copper
- Transferrin
- Vitamin B12
- Vitamin D

5.14 Pregnancy and Prenatal Diagnosis

5.14.1 Be able to describe the following concepts in relation to laboratory medicine support during pregnancy and related to the health of the mother and fetus

- Biochemical, hematological and endocrine changes during pregnancy
- Changes in analyte concentrations throughout pregnancy
 - Multiples of the median
- Fetal lung maturity
- hCG doubling time
- hCG forms/variants
- Maternal serum screening – purpose, limitations, screen vs. definitive testing
 - First trimester screening
 - Integrated screening
 - Second trimester screening
 - Non-invasive prenatal testing/cell free DNA testing
- Premature rupture of membranes and pre-term labor
- Preterm birth prediction
- Rh isoimmunization

5.14.2 Be able to describe the causes, clinical signs and symptoms of the following complications of pregnancy and fetal development

5.14.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Choriocarcinoma
- Ectopic pregnancy
- Gestational diabetes
- Molar pregnancy
- Obstetric cholestasis
- Open neural tube defects
- Pre-eclampsia, HELLP syndrome
- Rh isoimmunisation
- Trisomy 21, 18 and 13
- Trophoblastic disease

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- 5.14.4 Be able to describe the following specific laboratory investigations important to the study of pregnancy and fetal development**
- 5.14.5 Be able to recognize the analytical methods available for their measurement**
- 5.14.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms**
- AFP
 - hCG
 - Inhibin A
 - PAPP-A
 - Plasma nucleic acids
 - Serum bile acids
 - Unconjugated estriol
- 5.14.7 Be able to discuss the clinical rationale for tests using amniotic fluid**
- Acetylcholinesterase
 - AFP
 - Karyotype

5.15 Therapeutic Drug Monitoring and Toxicology

- 5.15.1 Be able to describe the following key concepts of pharmacology and the key factors relevant to drug action and measurement**
- 5.15.2 Be able to describe the mode of action and clinical uses of drugs in the categories listed**
- Pharmacokinetics (PK)***
- Absorption
 - Bioavailability
 - Compliance
 - Distribution
 - Excretion
 - Metabolism
 - Peak vs. trough drug levels
 - Steady state
 - Immediate vs extended release PK
- Pharmacodynamics (PD) and Pharmacogenetics (PG)***
- Antibiotics
 - Anticonvulsants/antiepileptics
 - Antidepressants
 - Anti-infectives
 - Anticoagulants
 - Immunosuppressants/Chemotherapeutics

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5.15.3 Be able to describe the following specific laboratory investigations and concepts important to therapeutic drug monitoring and toxicology

5.15.4 Be able to recognize the analytical methods available for their measurement

5.15.5 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Peak vs trough
- Major classes of drugs where TDM is employed
- Rationale for therapeutic drug monitoring
- Free vs total drug
- Interpretive guidelines, cutoffs and therapeutic ranges
- Investigation of suspected poisoning or toxic ingestion
- Toxic concentrations
- Drug of abuse testing
- Pain and addiction management
- Chain of custody
- Work place testing
- Common antidotes

5.16 Fluid and Electrolyte Disorders

5.16.1 Be able to describe the principles and control of fluid and electrolyte balance

- Clinical assessment of extracellular fluid (ECF) volume
- Extracellular and intracellular fluid volumes
- Hormonal control of fluid and electrolyte balance (renin, angiotensin, aldosterone, ADH)
- Principles of correcting fluid and electrolyte losses

5.16.2 Be able to discuss the causes, clinical signs and symptoms of the following disorders relating to fluid and electrolyte metabolism

5.16.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Dehydration
- Diabetes insipidus
- Extracellular fluid (ECF) volume loss
- Hyponatremia
- Hyperkalemia and pseudohyperkalemia
- Hypokalemia
- Hyponatremia and pseudo hyponatraemia
- Shock
- Syndrome of inappropriate antidiuretic hormone (SIADH)
- Oncotic disorders (e.g. edema, ascites)

5.16.4 Be able to describe the following specific laboratory investigations important to the study of fluid and electrolyte disorders

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5.16.5 Be able to recognize analytical methods available for their measurement

5.16.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms

- Aldosterone
- Electrolytes (sodium, potassium, chloride)
- Serum and urine osmolality
- Renin-angiotensin axis (RTA) assessment
- Urine and fecal electrolytes

5.17 Acid-Base Regulation and Pulmonary Function

5.17.1 Be able to describe the principles and control of acid – base balance and pulmonary function

- Anion gap
- Compensation for acidosis and alkalosis
- Control of respiration
- Henderson-Hasselbach equation
- Hemoglobin dissociation curves and limitations of calculated oxygen saturation
- Osmolar gap
- Systematic approach to investigating acid-base disturbances

5.17.2 Be able to discuss the causes, clinical signs and symptoms of the following disorders relating to acid-base balance and pulmonary function

5.17.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Alpha 1 antitrypsin (A1AT) deficiency (see also hepatobiliary disease)
- Carbon monoxide poisoning
- Metabolic acidosis
- Metabolic alkalosis
- Pyloric stenosis
- Renal tubular acidosis (see also disorders of kidney and urinary tract)
- Respiratory acidosis
- Respiratory alkalosis

5.17.4 Be able to describe the following specific laboratory investigations important to the study of acid-base balance and pulmonary function

5.17.5 Be able to recognize the analytical methods available for their measurement

5.17.6 Be able to select laboratory investigations and interpret the analytical results in the context of the clinical signs and symptoms

- Alcohols (ethanol, methanol, ethylene glycol, isopropanol)
- Anion gap
- Blood gas and hydrogen ion measurements
- Co-oximetry (carboxyhemoglobin and methemoglobin)
- Calculated blood gas parameters and their limitations

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- Ketones (urine and serum)
- Lactate
- Osmolality
- Osmolar gap
- Salicylate

5.18 General Pediatric Clinical Chemistry

- 5.18.1 Be able to discuss the following special considerations in relation to the provision of a general pediatric clinical laboratory service**
- How to collect heel stick samples
 - Issues with capillary specimens
 - Pediatric reference intervals – dynamic changes with growth, development and puberty
 - Sample volume and collection issues, including sweat collection
- 5.18.2 Be able to discuss the causes, clinical signs and symptoms of the conditions which may present to a general pediatric laboratory**
- 5.18.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management**
- Congenital thyroid disease
 - Cystic fibrosis
 - Delayed puberty
 - Diabetes mellitus type 1
 - Disorders of sex development, including congenital adrenal hyperplasia
 - Growth retardation and growth hormone deficiency
 - Hypocalcemia
 - Inborn errors of metabolism
 - Neonatal hypoglycemia
 - Neonatal jaundice
 - Neuroblastoma
 - Precocious puberty
 - Respiratory distress
- 5.18.4 Be able to discuss the following specific laboratory investigations for the evaluation of disorders presenting in the neonate and in childhood**
- 5.18.5 Be able to recognize the analytical methods available for their measurement**
- 5.18.6 Be able to select laboratory investigations and interpret the analytical results in the context of clinical signs and symptoms**
- 5.18.7 Be able to recognize the importance of blood volume limitations in method selection**
- Acid base / blood gases
 - Calcium
 - Glucose
 - Hormone measurement (*see also Endocrinology*)

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- Anterior hypothalamic hormones
- Cortisol
- Neuropeptides
- Ovarian hormones
- Testicular Hormones
- Thyroid function
- Other adrenal hormones
- HVA, dopamine
- Performance of the sweat test
- Plasma catecholamines
- Total and direct bilirubin

5.18.8 Be able to recognize that the population-based reference intervals for many chemistry tests change throughout childhood

5.18.9 Be able to discuss the importance of and challenges associated with determining pediatric reference intervals

5.19 Neurological and Psychiatric Disorders

5.19.1 Be able to describe the following key concepts relating to neurological disorders

- Blood brain barrier
- Paraneoplastic syndromes

5.19.2 Be able to discuss the causes, clinical signs and symptoms of the following disorders, some of which are primary neurological disorders and some of which have neurological manifestations

5.19.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Acute porphyrias
- Alzheimer's disease
- Meningitis
- Multiple sclerosis
- Myasthenia gravis
- Paraneoplastic syndrome

5.19.4 Be able to discuss the following specific laboratory investigations related to the study of neurological disorders

5.19.5 Be able to recognize the analytical methods available for their measurement

5.19.6 Be able to select laboratory investigations and interpret the analytical results in the context of the clinical signs and symptoms

- Aminolaevulinic acid (ALA)
- Anti-acetylcholine receptor antibodies
- Anti-Hu, Anti-Yo antibodies
- CSF beta-2-transferrin in rhinorrhea and otorrhea (fistula)

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- CSF glucose
- CSF protein
- Examination of synovial fluid
- Oligoclonal banding (isoelectric focusing)
- Paraneoplastic antibodies
- Porphobilinogen (PBG)
- Porphyrins (urine, feces, serum)

5.20 Biochemical Aspects of Monitoring Malignant Disease

5.20.1 Be able to describe the following key concepts relating to the choice, use and measurement of biomarkers of malignancy

- Characteristics of ideal tumor/cancer biomarkers
- Uses and limitations of current biomarkers of cancer
- Uses of biomarkers of cancer: prognosis, monitoring, recurrence

5.20.2 Be able to describe the following specific laboratory investigations in the management of malignant diseases

5.20.3 Be able to recognize analytical methods available for their measurement

5.20.4 Be able to select laboratory investigations and interpret the analytical results in the context of the clinical signs and symptoms

- AFP
- ALP isoenzymes
- CA 15-3
- CA 19-9
- CA 125
- CA 27-29
- Calcitonin
- CEA
- HE4
- hCG
- HER2/Neu
- LDH isoenzymes
- Mammary specific antigen
- PSA (total and free)
- PTHrp
- Protein electrophoresis
- Thyroglobulin, anti-thyroglobulin antibodies
- Other emerging biomarkers

5.21 Musculoskeletal Diseases

5.21.1 Be able to discuss muscle function and the use and limitations of autoimmune testing in diagnosis

- Autoimmune disorders
- Muscle function

5.21.2 Be able to discuss the causes, clinical signs and symptoms of the following musculoskeletal disorders

5.21.3 Be able to describe which laboratory investigations are important in their detection, diagnosis and management

- Duchenne / Becker dystrophy
- Osteoarthritis
- Rhabdomyolysis
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Vasculitis

5.21.4 Be able to describe the following specific laboratory investigations used in the management of musculoskeletal diseases

5.21.5 Be able to recognize the analytical methods available for their measurement

5.21.6 Be able to select laboratory investigations and interpret the analytical results in the context of the clinical signs and symptoms

- Anti-CCP antibodies
- Anti-ds DNA
- Anti-neutrophilic cytoplasmic antibodies (ANCA)
- Anti-nuclear antibodies (ANA and specific antibodies SSA, SSB, Sm, RNP)
- Rheumatoid factor
- Serum creatine kinase