INTRODUCTION

Training an individual to become a physician requires the acquisition of a foundation of knowledge, the understanding of how systems work normally and in pathological states, and the lifelong gaining of experience in diagnosing and treating patients. The standards for accrediting medical education programs are described in the document entitled "Functions and Structure of a Medical School" from the LCME. In that document there are several educational objectives that apply to teaching pathology. In particular, ED-11 states "the curriculum of a medical education program must include content from the biomedical sciences that supports students' mastery of the contemporary scientific knowledge, concepts, and methods fundamental to acquiring and applying science to the health of individuals and populations and to the contemporary practice of medicine."

Pathology is specifically named among the subobjectives of scientific disciplines to which this standard relates. Thus, medical students must learn the basic mechanisms of disease, their manifestations in major organ systems and how to apply that knowledge to clinical practice for diagnosis and management of patients. Another educational objective ED-33 refers to a curriculum committee and states "There must be integrated institutional responsibility in a medical education program for the overall design, management, and evaluation of a coherent and coordinated curriculum." With the advent of integrated curricula, Pathology must be appropriately represented in the curriculum committee to insure that there is full integration for teaching pathologic processes from basic mechanisms to organ system pathology to laboratory diagnosis.

The first educational objective ED-1 states "The faculty of an institution that offers a medical education program must define the objectives of its program. The objectives must serve as guides for establishing curriculum content and provide the basis for evaluating the effectiveness of the program." The following web-based competencies for Pathology are proposed as a national standard identifying the content for teaching pathology in three basic competencies: disease mechanisms, integration of disease mechanisms into organ system pathology, and application of pathology to diagnostic medicine. Each competency will include learning goals, objectives, and examples to assess the acquisition, integration and application of knowledge to demonstrate the development of competency.

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NOTE: These are "living" competencies, subject to regular review and updating by the APC UME Committee and UMEDS Section Council. To submit a recommendation for change or a new example, please email your suggestion to ume@apcprods.org.
COMPETENCY 3
Diagnostic Medicine and Therapeutic Pathology

Diagnosis and patient management require the student to learn how to apply their knowledge of disease mechanisms and processes to achieve efficient and effective use of clinical laboratory tests. The student should learn the proper use of clinical laboratory tests and blood/blood products to enable diagnosis and optimal treatment selection for the guidance of optimal patient care.

OVERVIEW
There are 11 topics within this competency area. Each topic includes general learning goals and specific objectives that medical students should be able to meet upon graduation from medical school. The table below lists the topic areas and show the number of goals and objectives for each.

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GENERAL PRINCIPLES

Physicians should have an appreciation for the pre-analytical, analytical and post-analytical phases of laboratory testing. In addition, physicians need an appreciation of the statistical treatment of data that underlies test utilization. This includes but is not limited to the ability to choose the correct test to make a diagnosis enabling treatment selection and to employ the appropriate testing paradigm to monitor patients with chronic diseases enabling optimal clinical management.

Learning Goal 1: Apply knowledge of clinical medicine, pathology and statistics to determine the utility of a laboratory test in making a diagnosis and in monitoring chronic disease management. Explain the interpretation and limitations of clinical laboratory assays.

OBJECTIVE(S):

GP1.1 Give examples of common sources of pre-analytical and post-analytical errors and categorize errors when the following procedures are not properly followed: pairing patient/specimen identification with the requisition form; using correct specimen containers/tubes for specific tests; and timing of collection, transport, and storage.

Examples: Explain why it is not a good idea for the clinician to pressure the lab to release results when errors have occurred.

GP1.2 Evaluate the quality of an assay in differentiating disease versus non-disease states, including graphically presenting and interpreting the data. Determine the relationship between sensitivity and specificity for this assay.

Example: CBC Utilization. A member of the hospital urology practice orders daily CBCs on all patients admitted for the evaluation of a possible neoplastic process. Describe the appropriate laboratory utilization for CBC testing.

Example: Urinalysis. A 28 year-old female presents for her annual physical examination. The physician orders a routine urinalysis. Under what circumstances would a physician order urine culture for this patient?

Example: Screening tests. A basic metabolic panel is a useful test under what circumstances? Discuss how frequently the test should be done in each circumstance including both inpatient and outpatient testing.
GP1.3 Determine the value of an assay by evaluating the impact of differing pre-test probabilities such as prevalence on the positive and negative predictive value of the test. Give examples of the laboratory tests used to evaluate clinical disorders where predictive values are used to develop screening, diagnostic, prognostic and patient management protocols.

Examples: HIV screening, influenza diagnosis

Example: strep throat diagnosis- antigen screening for Group A strep in a patient with pharyngitis as compared to culture for prevention of sequelae of S.pyogenes infections. Also discuss the value of serology in post-streptococcal syndromes.

Example: Explain how the measurement of a myocardial protein (e.g. use of troponin T or I vs. CK-MB) in serum could and should be used in the diagnosis of myocardial infarction.

GP1.4 Describe the methods used to establish reference intervals and how the following conditions apply: the effect of demographics, treatments, or disease states on reference intervals variability; the difference between reference ranges and therapeutic ranges and why 5% of laboratory test results fall outside a reference range; analytical vs. clinical sensitivity; and mixing test results in the clinical information system from different laboratories that use different methodologies.

GP1.5 Explain the difference between technical variability and biologic variability including how physical and chemical parameters, such as sample size, hemolysis and lipemia, can affect test results. Define analytical uncertainty, precision, accuracy and coefficient of variation, and describe factors that contribute to each.

Example: Coagulation profiling. A surgeon is ordering Protein S testing and notices an “epidemic” of low Protein S results. Describe the circumstances contributing to this result.

GP1.6 Compare and contrast appropriate uses of “stat” and “routine” test priorities with discussion of critical values and the elements of “turn-around-time.” Predict which elements affect turn-around-time the most.

Example: A hospital clinical laboratory is designing a protocol for rapid reporting of critical values. Suggest a list of laboratory tests and their abnormal ranges that should be included in this protocol.

Example: Discuss the difference between a treating physician’s definition of TAT and the laboratory definition of TAT.
GP1.7 Explain the broad differences between FDA-approved tests and laboratory-developed tests, including CLIA waived and non-waived tests, and discuss the regulatory issues involved in physician-office laboratories, home testing, and provider-performed microscopy.

GP1.8 Explain how “Point of Care” (POC) testing in the physician office, multispecialty clinic and hospital can enable better patient and population management of acute and chronic disease and why values generated using POC methods could differ from values generated in a high throughput laboratory.

*Example: Explain how a low or high hematocrit can affect point of care results.*

GP1.9 Create a clinical scenario that begins with a patient diagnosis and monitors a chronic disease for years, taking into account the following aspects: a laboratory testing decision tree to make the diagnosis; a protocol for monitoring the patient; the use of test panels and individual tests; the impact on healthcare cost for over utilization of laboratory testing; and the potential impact on cost for underutilization both at the diagnostic stage and in the management of chronic disease.

**TRANFFUSION MEDICINE**

**Learning Goal 1:** Apply knowledge of pathology, hematopoietic cell physiology and immunology to explain concepts of blood component transfusion and the therapeutic interventions in transfusion medicine.

**OBJECTIVE(S):**

TM1.1 Define the blood components and blood component substitutes available for clinical use; the evidence-based indications and dosing for transfusion of these components; and how the efficacy of transfusion may be monitored.

*Example: Cryoprecipitate transfusion. Describe the indications for the transfusion of cryoprecipitate.*

*Example: Platelet Transfusion. A 35 year-old male patient is receiving chemotherapy for lung cancer. He has a platelet count of 35,000/mcL. Describe a change in circumstances that would require platelet transfusion. What should be ruled out before a platelet transfusion is considered?*
TM1.2 Compare and contrast the pathophysiology, presentations, prophylaxis, and acute management of the different types of transfusion reactions.

TM1.3 Define infectious disease risks of transfusion.

TM1.4 Explain the HLA system and its role in both transfusion and transplantation.

TM1.5 Explain the clinical role of therapeutic apheresis in the management of the following disorders: sickle cell anemia, thrombotic thrombocytopenia, acute and chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, anti-glomerular basement membrane disease, organ transplantation, plasma cell dyscrasias, leukemia and lymphoma.

HEMATOLOGY

Hematology: Coagulation

**Learning Goal 1:** Apply knowledge of biochemistry, pharmacology and pathology to describe the basic cellular and molecular events associated with blood coagulation.

**OBJECTIVE(S):**

HC1.1 Describe the process whereby platelets are activated and aggregate after blood vessel injury.

HC1.2 Explain the action and the clinical use of common platelet function inhibitor drugs including, but not limited to, aspirin and clopidogrel.

HC1.3 Describe the process of fibrin formation in terms of the initiation of coagulation reactions by the exposure of tissue factor and/or “contact activation” and the subsequent proteolytic interactions that involve coagulation factor proteins.

HC1.4 Explain the action and clinical use of commonly used anticoagulants including warfarin, the heparins, and the new oral direct inhibitors of thrombin and of factor Xa.

**Learning Goal 2:** Apply knowledge of biochemistry, pharmacology and pathology to describe the use of specific laboratory tests to diagnose and manage coagulation disorders.

**OBJECTIVE(S):**
HC2.1 Explain selection of appropriate tests for identifying the cause(s) of bleeding and to monitor therapeutic anticoagulation.

HC2.2 Explain platelet function testing.

HC2.3 Identify the likely deficiency of clotting factor(s) using the prothrombin time and the partial thromboplastin time coagulation tests.

HC2.4 Compare and contrast the roles of the following in evaluating coagulopathies: clinical history, prothrombin time test, partial thromboplastin time test, D-dimer assay, platelet count, and platelet function tests.

HC2.5 Describe how to evaluate a bleeding patient with a hemorrhagic disorder, and explain how the history influences testing; include the uses and limitations of screening PT, PTT, and platelet counts.

HC2.6 Explain how bleeding occurs in patients with disseminated intravascular coagulation and in patients with severe liver disease.

HC2.7 Describe the major hereditary and acquired risk factors for thrombosis.

Example: Report on the major heritable thrombotic states, specifically noting the relatively high frequency in patients having European ancestries of the factor V Leiden mutation and the prothrombin 20210 mutation.

Example: Describe how commonly acquired risk factors for thrombosis, such as immobilization for prolonged periods, alcoholism and the use of oral contraceptives or estrogen supplements, potentiate heritable hypercoagulable states and lead to thrombosis.

Hematology: Anemia

**Learning Goal 1:** Apply knowledge of Red Blood Cell (RBC) structure / function and nutrient metabolism, the mechanisms of anemia, and the clinical and pathological features of common causes of anemia, to develop an appropriate differential diagnosis.

**OBJECTIVE(S):**

HA1.1 Summarize the key cellular structures and functions of the RBC, including: surface membrane, hemoglobin molecules, and cytoplasmic enzymes.

HA1.2 Discuss the requirements for specific nutrients including iron and vitamins to erythropoiesis.
**Learning Goal 2:** Apply knowledge of Red Blood Cell (RBC) structure / function and nutrient metabolism, the mechanisms of anemia, and the clinical and pathological features of common causes of anemia, to develop a diagnostic decision tree and recommend appropriate intervention for a patient with anemia.

**OBJECTIVES:**

HA2.1 Describe the primary causes of anemia, compare and contrast the clinical features and mechanisms of each, and discuss the different testing strategies for normocytic, macrocytic and microcytic anemia.

*Examples: iron or vitamin repletion, erythropoietin administration, avoidance of certain drugs, genetic counseling*

*Examples: reticulocyte count, Hgb electrophoresis or HPLC, direct antiglobulin test, testing for hereditary spherocytosis, B12/folate levels*

HA2.2 Use the Complete Blood Count (CBC) with the red and white blood cell morphology on a peripheral smear to develop a differential diagnosis for a patient with anemia.

*Example: Anemia Testing. A 78 year-old male presents to the EMC with a hemoglobin result of 8.0 g/dL. Describe the test utilization scenarios for laboratory testing for anemia.*

HA2.3 Correlate the genetic, pathological, and clinical features in patients with common inherited anemias.

*Examples: including sickle cell anemia, thalassemia, G6PD deficiency, and Hereditary Spherocytosis.*

HA2.4 Discuss when specific interventions should and should not be used for patients with specific types of anemia.

**MICROBIOLOGY**

**Learning Goal 1:** Apply knowledge of infectious organisms to explain the pathogenesis of disease and clinical syndromes, appropriate collection of patient samples, organism identification and classification, antibiotic choice, and selection of medical/surgical
OBJECTIVE(S):

M1.1 Explain the types of pre-analytical variables that affect diagnostic accuracy and discuss factors that affect length of turnaround time for microbiological work-ups.

*Example: Blood Culture Utilization.* A 32 year-old man is seen in the EMC post-chemotherapy for a sarcoma of the left arm, with an absolute neutrophil count of 150/mcL, fever and an unstable blood pressure. Describe the appropriate testing and test collection protocols for this patient including the number of samples and the collection sites (venipuncture vs. line draw).

M1.2 Compare and contrast the interpretations of gram stains for rapid diagnosis of causative bacterial agents from sterile and contaminated sites and discuss the clinical settings where recognition of bacteria is most meaningful.

M1.3 Give examples of the types of testing, and their optimal usage, performed in microbiology to identify an infectious disease.

*Example: Infectious disease testing.* A 53 year-old female is admitted to the hospital with fever after traveling to India and South Africa. Describe appropriate utilization of the following laboratory tests: blood smears, blood culture, stool culture, stool for ova and parasites.

*Example: Epstein-Barr virus infection.* When would EBV-VCA IgM antibody testing be appropriate?

M1.4 Explain how a process that coordinates identification of the infectious organism, antibiotic sensitivity susceptibility testing, and reporting to the pharmacy antibiotic steward team and treating physician will optimize patient care and reduce healthcare costs.

Learning Goal 2: Integrate knowledge of antimicrobial agents with bacterial culture and susceptibility testing results to guide treatment of infectious diseases.

OBJECTIVE(S):
M2.1 Associate mechanisms of action with antimicrobial agents including the following: disruption of cell wall synthesis; inhibition of protein synthesis; inhibition of DNA synthesis; antimetabolites.

*Examples: β-lactams, vancomycin; macrolides, tetracyclines, aminoglycosides; quinolones, metronidazole; trimethoprim, sulfonamides*

M2.2 State the spectrum of activity for common antimicrobial agents.

M2.3 Describe mechanisms of resistance found in common pathogens including the following: Penicillinase and mecA in Staphylococcus spp.; vanA and vanB in Enterococcus spp.; Extended spectrum β-lactamases and carbapenemases in Enterobacteriaceae.

M2.4 Describe the standardized techniques used in antimicrobial susceptibility testing; why standardization is important; and the differences between a qualitative and quantitative result including disk diffusion, broth microdilution, and automated antimicrobial susceptibility testing systems.

*Example: Bacterial culture and susceptibility testing. A 36 year-old male patient with HIV presents with a rash he acquired two weeks ago, possibly from his gym. Describe the appropriate microbiological work-up for this condition. What considerations need to be made in determining relevant antibiotic susceptibility testing for a Gram positive coccus on smears made from the skin lesions? Explain how Gram positive cocci appearing in clusters vs. pairs or chains will affect your clinical decision.*

M2.5 Name the genetic element detected by Extrapolate cefoxitin and oxacillin susceptibility tests and describe how the results for Staphylococcus sp. are used to predict activity of other β-lactam antibiotics.

M2.6 Describe how the microbiology laboratory determines if an isolate from a blood culture is susceptible or resistant. If the organism is susceptible with an MIC of 1.0ug/mL, describe how the pharmacokinetic (PK)/pharmacodynamic (PD) models may influence a clinician’s choice of antibiotics.

M2.7 Outline the principles that guide an institution’s reporting cascade for the following: organism including efficacy, FDA indication, CLSI guidance; site of infection; formulary; antimicrobial stewardship.

M2.8 Use the institutional antibiogram to prescribe therapy before susceptibility test results are available.
M2.9 List examples of molecular tests that are commonly used in clinical microbiology and explain how they have had an important impact on clinical care.

M2.10 Explain how the application of Matrix- Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) mass spectrometry in the clinical microbiology laboratory can impact patient care.

M2.11 Explain the role of urine studies, including culture, in selecting anti-microbial therapy for infectious cystitis.

M2.12 Describe a testing strategy for a typical uncomplicated community acquired urinary tract infection (UTI) versus a nosocomial UTI in a patient with a foley catheter and list the key microbiological tests in diagnosis of UTI.

M2.13 Explain the role of VDRL/RPR and treponema specific tests in the diagnosis and management of syphilis.

Learning Goal 3: Integrate concepts of virology with diagnostic techniques including culture, molecular and antigen diagnostics to identify viral infections and guide treatment.

OBJECTIVE(S):

M3.1 Describe the laboratory findings that diagnose hepatitis and correlate with the different possible clinical outcomes for each of the major hepatotropic viruses.

M3.2 Explain the diagnosis of influenza in terms of diagnostic tests used, major antigens, and the implications of a major shift in these antigens.

M3.3 Describe the role of serology, PCR and culture in the diagnosis of viral infections and name which viruses are most rapidly identified by each.

M3.4 Explain the testing strategy used to diagnosis HIV and the role of viral load and CD4 count in monitoring HIV infection.

M3.5 Name the tests available to examine the response of an HIV virus to therapeutic agents and explain how each test works.

Examples: phenotyping, genotyping, integrase testing, CxCR4 /CXCR5receptor, and HLA B*5701
Learning Goal 4: Integrate concepts of mycobacteriology with diagnostic techniques including culture, molecular and antigen diagnostics to identify mycobacterial infections and guide treatment.

OBJECTIVE(S):

M4.1 Describe the diagnostic tests available for the identification of mycobacteria including culture methods and new molecular tests.

M4.2 Compare and contrast the methods, culture and molecular, used to identify mycobacteria drug susceptibility and the time required for results by each method.

Learning Goal 5: Integrate concepts of mycology with diagnostic techniques including culture, molecular and antigen diagnostics to identify fungal infections and guide treatment.

OBJECTIVE(S):

M5.1 Differentiate among filamentous fungi, dimorphic fungi and yeast, and describe the diagnostic approaches for each type.

M5.2 Define sensitivity testing and describe how it is performed and used in the management of yeast infections.

M5.3 Explain the basis for the galactomannan and β-glucan tests and how they are utilized to detect fungi and Pneumocystis.

Learning Goal 6: Integrate concepts of parasitology with diagnostic techniques including culture, molecular and antigen diagnostics to identify parasitic infections and guide treatment.

OBJECTIVE(S):

M6.1 Compare and contrast metazoan and protozoan parasites and the diagnostic approaches to each.

M6.2 Explain the role of stool samples, including number examined, role of microscopy, and coproantigen detection in the diagnosis of parasitic disease.

M6.3 Summarize the role of serology and serological tests to diagnose toxoplasmosis and assess the risk of transmission during pregnancy.
M6.4 Contrast P. falciparum with other malaria species on a blood smear and explain the role of thick and thin smears in the diagnosis and management of malaria.

M6.5 Name the rapid tests that do not require blood smears to identify malaria and explain how these tests work.

**CHEMISTRY**

**Learning Goal 1:** Apply knowledge of biochemistry, pharmacology and pathology to describe the basic cellular and molecular events associated with diseases of specific tissues and organ systems and the use of laboratory tests to diagnose and manage these diseases.

**OBJECTIVE(S):**

CHEM1.1 Discuss the clinical presentation and the pathophysiologic bases of thyroid diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: hypothyroidism*
*Example: hyperthyroidism*
*Example: Thyroid disease. Describe the indications for testing for free T3?*

CHEM1.2 Discuss the clinical presentation and the pathophysiologic bases of cardiac diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: myocardial infarction*
*Example: heart failure*

CHEM1.3 Discuss the clinical presentation and the pathophysiologic bases of endocrine diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: Pre-Diabetes Testing. A 65 year-old female outpatient has a family history of diabetes. She currently is being treated for high cholesterol and has a bilateral peripheral neuropathy. The physician wishes to evaluate the patient for a pre-diabetic state. Describe the utilization of appropriate tests and testing protocols, including follow-up testing.*
CHEM1.4 Discuss the clinical presentation and the pathophysiologic bases of liver and gastrointestinal diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: Inflammatory Bowel Disease. A pediatric neurologist orders multiple highly specialized tests in his evaluation of pediatric patients with chronic gastrointestinal symptoms. Discuss the appropriate testing required for these patients and the use of any specialized referral tests for diagnosis.*

*Example: hepatitis*

*Example: cirrhosis*

CHEM1.5 Discuss the clinical presentation and the pathophysiologic bases of renal diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: glomerulonephritis*

*Example: acute tubular necrosis*

CHEM1.6 Discuss the clinical presentation and the pathophysiologic bases of lung diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: emphysema*

*Example: asthma*

CHEM1.7 Determine the value of testing for drugs and toxins accounting for the routes of administration; distribution and metabolism of the agent of interest, including the specimen source; the analytes to be detected given the medical questions; and the timing constraints for specimen collection.

*Example: contrast drugs of abuse testing for emergency room patients versus abuse clinics versus a forensic laboratory.*

*Example: Toxicology. An 18 year-old male is brought to the EMC comatose after an automobile accident. Preliminary evaluation does not indicate cerebral trauma. What other conditions should be considered and which tests would be most useful?*
CHEM1.8 Select and interpret appropriate tests for specific cancer diagnostics, including tumor markers and serum monoclonal protein analysis.

*Example: Neuroblastoma testing. What urine metabolites are useful in the evaluation for neuroblastoma?*

*Example: prostate cancer*
*Example: colon cancer*

**Immunology**

**Learning Goal 1:** Apply knowledge of immunology, biochemistry, and pathology to describe the basic cellular and molecular events associated with immune system diseases of specific tissues and organ systems and the use of laboratory tests to diagnose and manage these diseases.

**OBJECTIVE(S):**

IMM1.1 Compare and contrast markers of inflammation in terms of the pathophysiologic basis and stages of the inflammatory response.

IMM1.2 Select and interpret appropriate tests for workup and interpretation of autoimmune disease, immunodeficiencies, and allergy testing.

IMM1.3 Discuss, with examples, the application of serological testing in infectious diseases to establish immune status and diagnose infection.

IMM1.4 Discuss the clinical presentation and pathophysiologic bases of autoimmune diseases including the efficient use of laboratory tests to make a definitive diagnosis and manage the disease.

*Example: rheumatoid arthritis*
*Example: systemic lupus erythematosus*

**Genomics**
Learning Goal 1: Apply knowledge of genetics including the structure and organization of the human genome and regulation of gene expression, genetic variation and inheritance patterns to basic disease processes.

OBJECTIVES

GE1.1 Describe the characteristic features and mechanisms of Mendelian inheritance including autosomal dominant, autosomal recessive, X-linked; non-Mendelian inheritance including mitochondrial and imprinting; unstable repeat expansions; and cytogenetic translocations.

GE1.2 Demonstrate how to take a three-generation family history and draw a pedigree. Distinguish between a non-pathogenic polymorphism and a pathogenic mutation, and describe the mechanisms that produce different types of mutations.

GE1.3 Compare single-gene disorders to diseases with complex inheritance patterns and include the role of rare, high-risk variants and common, low-risk variants.

GE1.4 Outline the principles that underlie genetic linkage analysis and association studies and how they are used to identify genes associated with diseases.

GE1.5 Define the concepts “founder effect” and “genetic drift” and explain how genetic variants are distributed within populations.

GE1.6 Explain how genetic risk is determined by carrier status and carrier frequency of a condition and determine carrier frequencies and incidence of recessive conditions using Hardy-Weinberg Laws.

GE1.7 Distinguish dominant and recessive phenotypes and alleles and describe how incomplete penetrance, variable expressivity, and pleiotropy affect the phenotypic expression of diseases.

GE1.8 Describe the concept of a modifier gene and its contribution to phenotypic variability.

GE1.9 Define the following cytogenetic terms and nomenclature: karyotype, euploidy, aneuploidy, monosomy, trisomy, deletion, ring chromosome, inversion, isochromosome, translocation, balanced reciprocal translocation, robertsonian translocation.

GE1.10 Define mosaicism and explain how it affects the phenotype of a chromosomal disorder.
Learning Goal 2: Apply knowledge of genetics to explain the molecular basis of single gene and non-neoplastic chromosomal disorders.

OBJECTIVES

GE2.1 Describe the genetic and epigenetic causes, pathophysiology and clinical manifestations, and optimal laboratory test used to diagnose specific genetic disorders.

GE2.1a Mendelian, autosomal dominant disorders

Examples: Neurofibromatosis, polycystic kidney disease, von Willebrand disease, Marfan syndrome, osteogenesis imperfecta, achondroplasia, familial hypercholesterolemia

GE2.1b Mendelian, autosomal recessive disorders

Examples: Cystic fibrosis, phenylketonuria, α1-antitrypsin deficiency, Wilson disease, hemochromotosis, glycogen storage disease, sickle cell anemia and thalassemias, alkaptonuria, Friedreich ataxia

GE2.1c X-linked disorders

Examples: Duchenne muscular dystrophy, hemophilia A and B, agammaglobulinemia, Fragile-X syndrome

GE2.1d Chromosomal disorders

Examples: Trisomy 21 (Down syndrome), chromosome 22q11.2 deletion syndrome, Klinefelter syndrome, Turner syndrome

GE2.1e Disorders of non-classic inheritance

Examples: Trinucleotide repeat mutations (Fragile-X syndrome), mutations in mitochondrial genes (Leber’s hereditary optic neuropathy), genomic imprinting (Prader-Willi syndrome)

Learning Goal 3: Apply knowledge of genetics to explain the genetic basis for neoplasia; and the role of genetic testing in diagnosis and treatment of diseases.

OBJECTIVES

GE3.1 Describe three mechanisms by which genes predispose to neoplasia: oncogenes, tumor suppressor genes, DNA repair genes.
GE3.2 Describe the molecular genetic mechanisms that underlie cancers: germline mutations; somatic mutations including point mutations, deletions, amplifications and translocations; epigenetic changes.

GE3.3 Explain the application of molecular testing for diagnosis, prognostication, and therapeutic follow-up of oncologic diseases.

**Learning Goal 4:** Apply knowledge of genetics to explain the role of reproductive genetics and population screening.

**OBJECTIVES**

GE4.1 Describe the role of preconception and prenatal carrier testing for genetic disorders depending upon family history and ethnic background.

GE4.2 Describe the rationale for newborn screening for genetic diseases and explain the difference between screening and diagnostic testing.

**Learning Goal 5:** Apply knowledge of genetics to explain the role of genetic testing in diagnosis and treatment of diseases and in counseling of patients and families.

**OBJECTIVES**

GE5.1 Explain the mechanisms involved in the treatment of genetic diseases: organ transplantation, manipulating metabolic pathways, correction of defective structural proteins or enzymes, modulation of RNA expression, alteration of DNA sequence, and alteration of gene expression.

GE5.2 Describe how genetic variation can predict response to medications, dosing, and risk for adverse effects.

GE5.3 Describe how modification of non-genetic factors can prevent or mitigate disease in genetically-predisposed individuals.

GE5.4 Describe the role of genetic counselors in patient care and when to make appropriate referrals for genetics evaluations.
Anatomic Pathology

This topic is based on the morphologic analysis of tissue performed in surgical pathology, cytopathology and autopsy pathology.

AUTOPSY

Learning Goal 1: Apply knowledge of clinical medicine and quality management to discuss the value of the autopsy and procedures for obtaining permission for post-mortem examination.

OBJECTIVE(S):

AU1.1 Provide examples demonstrating the value of the autopsy towards improvement in clinical diagnosis and management, quality control, medical education, research, and elucidation of “new” diseases.

AU1.2 Identify the legal next-of-kin or individual authorized to consent when obtaining consent for an autopsy.

AU1.3 Describe how to approach a family to request consent for an autopsy, including a discussion of the autopsy procedure in language that the patient’s family can understand.

AU1.4 Write a narrative of the psycho-social-emotional aspects of the “autopsy experience,” including its role in closure, and the importance of communication and professionalism among the healthcare team.

Learning Goal 2: Apply knowledge of quality management to discuss the utility of death certificates and proper approaches for completing them.

OBJECTIVE(S):

AU2.1 Describe the importance of death certificates for tracking and analysis of public health trends.

AU2.2 Discuss the key components of the death certificate; differences among immediate, intermediate and underlying (proximate) cause of death based on disease process; and the role of mechanisms of death on a death certificate.

AU2.3 Explain how under- or over-utilization of medical care, and incorrect diagnoses, therapeutics, or informed consent can lead to medical errors; and give examples of how an autopsy can identify errors thereby improving health care and decision making.
Learning Goal 3: Apply knowledge of clinical medicine and postmortem examination to discuss the indications for medical examiner referral and special procedures in the forensic postmortem examination.

OBJECTIVE(S):

AU3.1 Define the role of a medical examiner in terms of public health and protection of legal rights.

AU3.2 Identify circumstances of death that need to be reported to the medical examiner/coroner.

*Examples: new epidemics/infections & illness that can impact legal space, medical error, gunshot wounds & illegal drug injuries.*

SURIGAL PATHOLOGY

Learning Goal 1: Apply knowledge of clinical medicine and pathology to describe the roles cytology and surgical pathology play in diagnosis and treatment of cancer. Use specific examples from the most common forms of cancer.

OBJECTIVE(S):

SP1.1 Describe the procedures for obtaining a biopsy of a tissue mass in different sites, including superficial and deep soft tissues, solid organs, and tubular organs; associate each procedure and specimen type to either cytology or surgical pathology and give examples of possible reasons and follow-up for false negative biopsies.

*Example: A 45 year old woman with a suspicious breast ultrasound has a negative biopsy. Describe the appropriate next steps.*

SP1.2 List the major differential diagnoses for each type of cytology or surgical pathology specimen derived from a mass and describe appropriate further studies, both special stains and immunohistochemistry.

*Example: Breast masses, lung masses, GI neoplasms (benign and malignant). Undifferentiated large and small cell malignancies, tumors of unknown origin, and non-small cell lung cancers.*
SP1.3 After looking at slides of a tissue mass, the pathologist makes a diagnosis of malignancy. List options for surgical and non-surgical treatment and describe prognostic and therapy-guiding tests that may be performed on the tissue.

*Examples: Pulmonary adenocarcinomas, colonic adenocarcinomas, breast carcinomas*

SP1.4 Describe the information that the pathologist obtains from a resected tissue specimen, how this information is reported, how it is combined with clinical information to stage the tumor, and how staging information is used to guide treatment.

*Examples: Use of TNM staging systems and grading.*

**Learning Goal 2:** Apply knowledge of clinical medicine and pathology to describe the roles cytology and surgical pathology play in diagnosis and treatment of inflammatory disease, in particular those with immune or infectious etiologies.

**OBJECTIVE(S):**

SP2.1 Give examples of specific sites and diseases in which specific pathologic diagnoses of inflammatory and/or infectious conditions are critical to treatment and prognosis.

*Examples: Interstitial lung diseases (ex., UIP, NSIP, COP, etc), GERD with and without Barrett esophagus, inflammatory bowel disease*

*Examples: Tuberculosis (tissue diagnosis and culture), fungal disease (same), celiac disease (histology versus laboratory workup), helicobacter infections, Hashimoto thyroiditis (histology versus antibodies).*

**Learning Goal 3:** Apply knowledge of clinical medicine and pathology to describe hereditary/malformative disorders, in terms of clinically useful information that anatomic pathology diagnosis can provide.

**OBJECTIVE(S):**

SP3.1 Define general terminology for pathologic features that are associated with hereditary/malformative disorders.

**Learning Goal 4:** Apply knowledge of clinical medicine and communication skills to interpret pathology reports and communicate the results to patients in the context of risk assessment.
and patient prognosis. Determine appropriate action including additional testing and clinical evaluation.

OBJECTIVE(S):

SP4.1 Explain the results of a pathology report to a patient in language the patient can understand.

*Example:* Explain the significance of abnormal pap test results and such as high grade squamous intraepithelial lesion (High grade SIL). Identify appropriate additional clinical evaluation

*Example:* Explain the risk of colonic cancer in a patient with a pathologic diagnosis of tubular adenoma. Identify appropriate clinical evaluation.

*Example:* Explain the risk of invasive breast cancer in a patient with a biopsy diagnosis of ductal carcinoma in situ. Identify the appropriate additional clinical evaluation

Learning Goal 5: Apply knowledge of pathology and the application of diagnostic decision trees to discuss the classification systems of leukemias and lymphomas, and describe the relative roles of ancillary laboratory studies in classification.

OBJECTIVE(S):

SP5.1 Describe the roles of immunohistochemistry, flow cytometry, cytogenetics, and molecular diagnostics in the diagnosis and classification of lymphoma, and explain how, with examples, different techniques are most appropriate in diagnosis, staging and management of disease.

*Examples:* flow cytometry for CLL or acute leukemia; cytogenetics/FISH or molecular studies for CML; immunohistochemistry for Hodgkin lymphoma

SP5.2 Explain how immunohistochemical, flow cytometric, cytogenetic and molecular studies in the context of routine morphology from various tissues are used for diagnosis, staging and treatment planning in leukemia and lymphoma.

SP5.3 Discuss how a pathologist can use a diagnostic decision tree to make a diagnosis efficiently, minimize the time to report results to the oncologist, and optimize treatment decisions.
Cytopathology focuses on the individual cellular components of disease. Cytopathological examination is an essential tool for its wide-ranging reach in screening, diagnostics, prognostics and prevention of advanced disease states. Furthermore the minimally and non-invasive nature of ascertaining most cytological specimens allows for immediate access to viable cellular material for advanced testing, molecular and biochemical analyses.

**Learning Goal 1:** Apply knowledge of general and systems pathology to understand the meaning and context of cytologic diagnoses.

**OBJECTIVE(S):**

CYP1.1 Compare and contrast the three basic methods to obtain cytologic material for diagnosis, describe the settings in which these can be used to diagnose benign and malignant conditions, and discuss the limitations of each.

*Examples: FNA, body cavity fluid aspiration, exfoliative*

CYP1.2 Compare and contrast the degree of diagnostic certainty applied to general categorization in cytologic diagnosis.

*Examples: Negative, atypical (and comparable terminology in various sites), suspicious, positive, non-diagnostic.*

CYP1.3 Describe the uses and limitations of cytology, with examples, in identifying common infectious diseases.

*EXAMPLES: Human Papilloma Virus (HPV), Herpes Simplex Virus, Human Polyomavirus*

**Learning Goal 2:** Apply knowledge of clinical medicine, pathology and healthcare delivery to describe the advantages cytopathologic examination offers over conventional pathologic tissue examination.

**OBJECTIVE(S):**

CYP2.1 Describe the principles of an effective screening test and the uses and limitations of cytology.

*EXAMPLE: Identify how the Pap test fulfills criteria for effective screening test.*
EXAMPLE: Describe how fine needle aspiration of thyroid cytopathology can prevent unnecessary surgical intervention.

CYP2.2. Describe how adjunct testing is used in conjunction with cytology examination.

Example: HPV testing in Pap tests.

CYP2.3 Describe how to find and utilize current algorithms for management of cervical screening.

Examples: Bethesda terminology, ASCCP guidelines.