

**DEPARTMENT OF PATHOLOGY & LABORATORY MEDICINE
CLINICAL CHEMISTRY**

Residency Training Program Outline

The structure and function of a clinical chemistry laboratory encompass four basic responsibilities:

1. Service to patients.
2. Consultation and education.
3. Research and development and instrument evaluation
4. Management - this includes the collection and processing of samples, the accumulation and utilization of data, overall responsibility for laboratory services, equipment and personnel.

Our training program incorporates all these facets so that residents will have the knowledge and skills necessary for administering the affairs of a clinical chemistry laboratory. Training in our laboratory consists of a three month rotation and is divided into several units (segments). The staff will work closely with the resident during each segment and progress will be reviewed on a weekly basis.

LEARNING OBJECTIVES

At the end of the rotation through the Clinical Chemistry Laboratory, the resident should be able to:

1. Demonstrate understanding of the operation and underlying physical or chemical principles of laboratory instrumentation.
2. Understand patient preparation and specimen collection as well as processing and storage requirements for tests performed in the chemistry laboratories.
3. Demonstrate comprehension of the basic principles, precision levels, common interferences, approximate reference ranges, automation feasibility, and relative merits of analytical procedures offered by the Routine Chemistry, Special Chemistry, Pediatrics, Immunochemistry, Toxicology, and Therapeutic Drug Monitoring
4. Understand the basis and limitations of quantitative measurements of analytes in biological matrices by performing selected procedures offered by these laboratories.
5. Demonstrate the ability to use data reduction techniques (e.g., interpret standard curves and perform necessary calculations to obtain test results).
6. Demonstrate the ability to use basic statistical theory to monitor quality control, evaluate analytical errors, and design experiments.
7. Demonstrate familiarity with methods for evaluating and introducing a new procedure or instrument into the laboratory.
8. Demonstrate the ability to determine reference values.
9. Demonstrate the ability to evaluate clinical effectiveness of new laboratory methods.
10. Demonstrate familiarity with the varieties of clinical decisions that are based on laboratory test results.
11. Demonstrate the ability to function as a consultant to other physicians in use and interpretation of laboratory tests.
12. Monitor current literature in clinical chemistry and related subject areas and demonstrate ability to critically evaluate journal articles concerning laboratory tests and their interpretation.

13. Demonstrate the ability to comprehend and conduct quantitative approaches to cost benefit and cost effectiveness analysis.
14. Demonstrate understanding of fundamentals of business methods and management, and the processes involved in evaluating and purchasing laboratory equipment.
15. Understand the operation and role of commercial laboratories.
16. Demonstrate familiarity with requirements for inspection and accreditation.
17. Demonstrate the ability to organize and contribute to in-service education of medical and laboratory staff.

Obviously, none of these objectives are mutually exclusive of one another, nor is the training program intended to be a dogmatic scheme through which one will emerge as an "expert clinical chemist." Rather, the intention is to design a program that allows the resident to grow while gaining knowledge and experience - a process that will hopefully continue long after the resident has finished rotation on this service.

Each resident is asked to provide a written notice to Dr. Pappas two (2) weeks prior to any scheduled absence. Unscheduled absences due to illness, etc., should be phoned to the director's office.

At the start of the rotation, the resident will meet with Dr. Pappas to go over the rotation and respective units. These units outline specific learning objectives, teaching exercises, and suggested reading assignments. It is suggested that the resident keep a notebook divided into sections corresponding to the major subject topics of the rotation outline. In this way, the resident can systematically compile references, supplements and textual materials.

The resident is expected to complete all assignments satisfactorily. Dr. Pappas will meet with the resident to assess progress, knowledge, and ability to react to unusual situations. As a part of the rotation, each resident will be asked to review results of specific laboratory tests and provide oral or written professional interpretations (e.g., immunofixation and protein electrophoretic patterns, lipid profiles, metabolic screens). The resident will then be expected to review his interpretations with a chemistry faculty member, follow up selected abnormal results (e.g., by reviewing charts, consulting with attending physicians, etc.), and present unusual findings to the chemistry staff.

At the conclusion of the rotation, chemistry staff members evaluate the resident's proficiency. The se evaluations are then forwarded to the department chair. The resident will in turn be asked to provide his own observations and suggestions for the training program.

References:

1. Burtis CA and Ashwood E (Eds.). Tietz Textbook of Clinical Chemistry. 3rd Edition, WB Saunders, Philadelphia PA (1994). 1999.
2. Tietz NW, Conn RB, and Pruden EL (Eds.) Applied Laboratory Medicine. WB Saunders, Philadelphia PA (1992).
3. Tietz NW (d.). Clinical Guide to Laboratory Tests. 3rd Edition. WB Saunders, Philadelphia PA (1995).
4. Kaplan LA and Pesce AJ (Eds.). Clinical Chemistry: Theory, Analysis, and Correlation. 2nd Edition. Mosby, St. Louis, MO (1989).
5. Henry JB (Ed.). Clinical Diagnosis and Management by Laboratory Methods. 19th Edition. WB Saunders, Philadelphia, PA (1991).

6. Williams Textbook of Endocrinology. 9th Edition. WB Saunders, Philadelphia PA. (1992).
7. Barnett RN: Clinical Laboratory Statistics. Little-Brown, Boston MA (1979).
8. Bakerman S. Clinical Chemistry Reviews (1986).
9. Bakerman S. ABC's of Interpretive Laboratory Data. 3rd Edition. (1994).

Journals:

Clinical Chemistry
Clinical Chimica Acta
American Journal of Clinical Pathology
Clinical Biochemistry
Journal of Clinical Chemistry and Clinical Biochemistry
Scandinavian Journal of Clinical and Laboratory Investigation
Annals of Clinical Biochemistry
Annals of Clinical and Laboratory Science

Internet Sites:

Search Engines:

Google.com - Metasearch
Pubmed.com - Medline search
Ovid

Learning Sites:

UNIT A: INTRODUCTION TO THE CLINICAL CHEMISTRY ROTATION

1. Receive outlines, reading materials, and meet with Dr. Pappas to discuss rotation and unit assignment.
2. Review of daily activities and sign-out.
3. Tour lab.

UNIT B: SPECIMEN COLLECTION, PROCESSING, STABILITY, PRE-ANALYTICAL VARIABLES

1. What is considered part of the preanalytical process.
2. What does the term serum index refer to and how are serum indices determined?
3. What is the most practical way to minimize interference from highly lipemic samples?

4. What are potential problems associated with the use of serum separator tubes?
5. What is the major difference(s) between blood drawn in a lavender tube and a plain red top tube?
6. Describe the different blood collection tubes and what additives are present in each tube.
7. Describe physiologic factors that affect laboratory results.
8. What tests are affected by posture?
9. What tests can be affected if the tourniquet is left on the arm for a prolonged period before drawing the blood sample?
10. What tests exhibit diurnal variation?
11. What tests are routinely collected after fasting? How long should the fast be?
12. What tests are affected by hemolysis? Does hemolysis only influence tests results at the analytical stage?
13. What effect does lipemic and icteric samples have on laboratory results?
14. How would you distinguish between in vivo and in vitro red cell hemolysis?
15. What tests require blood samples to be kept on ice prior to analysis?
16. What tests require blood to be kept warm prior to analysis?
17. What tests have special collection requirements such as minimal nervous stasis, special collection tubes, etc.?
18. Do all blood samples require separation of the serum/plasma from the red cells upon receipt?
19. How are samples stored after testing? Are there any special handling concerns?
20. How long would you save samples after analysis? Is it the same for all tests? Defend your answer.

UNIT C: REPORTING OF LAB RESULTS; STATISTICS, QC, LAB EVALUATION

1. Understand calculations for standard deviation and coefficient of variation; interpret data.
2. Distinguish between the within-run versus day-to-day imprecision; describe percentage of people or observations that fall within + or - SD, or + or -2SD, and + or -3SD.
3. Explain the clinical usefulness of quality control and quality assurance programs.
4. Understand and calculate diagnostic sensitivity, specificity, predictive value (positive and negative result) (Ref: Galen and Gambino: Beyond Normality).
5. Familiarize yourself with use and interpretation of ROC (receiver operator characteristic) curves; find relevant examples in the literature for discussion.
6. Normal Values/Reference Ranges:
 - a. Describe parametric and nonparametric techniques and the inherent statistical bias and

- problems.
- b. Review normal range book in chemistry; understand how we calculate normal ranges using parametric and nonparametric methods. Prepare to discuss how ranges were accepted.
 - c. Describe conditions that affect the normal values.
7. Read Chapter 9 in Gradwohl's on Non-analytical Sources of Variation.
 8. Be familiar with SI units.
 9. Discuss throughout rotation the rationale of offering "panel" tests vs. "individual" test ordering. Review BC/BS and American College of Physicians guidelines. Understanding HCFA guidelines for panels and the need for documenting medical necessity.
 10. Review how new assay evaluation protocol is performed: precision, linearity, patient crossover, recovery, interferences, etc.
 11. Be familiar with chemistry specimen processing, data handling, record keeping, telephone answering, and STAT procedure system.
 12. Be familiar with the reporting units (SI and conventional) and enzymatic units.
 13. Know what the following terms mean and how to establish them in your laboratory:
 - Invalid ("Absurd") Results.
 - Delta Checks
 - Panic Values
 - Abnormal Results
 14. Understand electrophoresis profiles, immunoelectrophoretic patterns, and immunofixation patterns as they relate to polyclonal, monoclonal, and oligoclonal gammopathies and Bence Jones proteins.
 15. Understand the genetic variation of alpha-1 -antitrypsin and its clinical significance.
 16. Understand the physiologic role of albumin; cause and clinical significance of hypoalbuminemia, bisalbuminemia, and analbuminemia
 17. Understand IgG subclass analysis and clinical significance.
 18. Understand the advantages and disadvantages of specific methods (RIA, EIA, RID, and nephelometry).
 19. Know more common serum protein electrophoresis patterns (e.g., acute phase reaction, liver disease, renal disease, monoclonal gammopathies, etc.) and their significance to a degree needed to sign-out the daily serum protein electrophoresis and immunofixation gels.

UNIT D: INSTRUMENTATION & METHODS OF ANALYSIS - CHEMISTRY & IMMUNOCHEMISTRY

1. Define the classes of methods used to measure analytes in chemistry.
2. What is spectrophotometry?
3. How is the concentration of an analyte related to light absorption?
4. What are potential limitations of spectrophotometry?

5. What is commonly measured as an endpoint in spectrophotometric assays?
6. How are spectrophotometric interferences overcome?
7. How does reflectance spectrophotometry and densitometry work?
8. What is the principle behind flame photometry and how does it work?
9. What is the principle behind atomic absorption and how does it work?
10. How do turbidimetric and nephelometric assays differ? What is the advantage of each method?
11. What types of spectrophotometric assays are used here?
12. What analytes are measured by turbidimetric and nephelometric assays?
13. Discuss principles of immunoassay techniques. What are the different formats?
14. What factors influence immunoassay reactions?
15. What is the difference between a heterogeneous and homogeneous immunoassay. What are the advantages of each type? Give examples of each type.
16. Discuss different detection systems used for immunoassays.
17. What is FPIA, EMIT, MPEIA. Discuss how these assays work.
18. What are heterophile antibodies?
19. What is high-dose hook effect (prozone) and how is it overcome?
20. What types of immunoassays are used at UCLA? Provide samples with specific analytes.
21. Describe functions of the principle components of and major differences between the following instruments using a block diagram:
 - a. A simple single-beam spectrophotometer
 - d. Several major automated instruments
22. Describe Beer's Law, stray light, bandwidth, and Allen's correction.
23. Know the importance of a spectrophotometer bandwidth.
24. Describe the main clinical use of fluorescence polarization Why is it useful?
25. Describe the principles of flame emission and atomic absorption spectroscopy and the clinical uses of each.

UNIT E: ELECTROLYTE/ACID-BASE BALANCE

1. Understand the general operation of the following:
 - Flame Photometer
 - Atomic Absorption

- Blood Gas and pH Instruments
 - Osmometer
 - Oncometer
 - Lithium Analyzer
 - Ionized Calcium Analyzer
2. Understand the theoretical basis and applications of ion-selective electrodes; understand the analytical difference between direct and indirect potentiometry, ion-specific electrodes on different instruments.
 3. Know the flame emission methods for Na^+ and K^+ , the atomic absorption methods for Cardiopulmonary $^{++}$, and Mg^{++} , the major methods for Cardiopulmonary $^{++}$, phosphorus, Cl^- , CO_2 , and HCO_3^- , the flame, atomic absorption and electrode methods for lithium.
 4. Understand the analytical principles and the quality control for blood gas measurements.
 5. Understand the pathophysiology of water regulation, extracellular fluid, sodium content, ventilation, and oxygenation.
 6. Understand the pathophysiology of hyponatremia, hypernatremia hypokalemia, hyperkalemia, hypercalcemia, hypophosphatemia, hypomagnesemia.
 7. Understand the pathophysiology of acid-base disturbances. Be familiar with the tables and nomograms for acute and chronic disorders.
 8. Know the causes of hypoxemia; learn to calculate the arterial/alveolar P_{O_2} difference.
 9. Become familiar with the kinetics and affects of CO on oxygen saturation of hemoglobin. Know the principles of measuring saturated hemoglobin and methemoglobin by CO oximeter.

UNIT F. RENAL FUNCTION

1. Know the major methods for BUN and creatinine measurements.
2. Know the relationship between BUN and creatinine in pre-renal and renal azotemia.
3. Know the relationship between serum creatinine and creatinine clearance and how methods (Jaffe vs. enzymatic creatinine) will affect these results.
4. Know uric acid metabolism.
5. Know the usual causes of hyperuricemia and their management.
6. Discuss the ways of distinguishing pre-renal, renal, and post-renal failure.
7. Know how to evaluated polyuria.

UNIT G: PROTEINS

1. Understand the principles of electrophoresis, immunoelectrophoresis, and nephelometry.
2. Perform a serum protein electrophoresis and immunofixation.

3. Become proficient at interpreting serum and urine protein electrophoresis and immunofixation patterns.
4. Draw a normal SPEP and identify the subcomponents of each region. Know the various disease states associated with each fraction. Know the effects of fibrinogen and/or hemolysis.
5. Diagnosis and monitoring of monoclonal gammopathies:
 - a. List disorders where a monoclonal protein can be present.
 - b. What is multiple myeloma?
 - c. How common is the disease and who and at what age group does it effect?
 - d. How do patients with multiple myeloma present clinically?
 - e. How is a diagnosis of multiple myeloma made?
 - f. What forms of treatment are available for multiple myeloma?
 - g. What lab tests are useful for either diagnosis or monitoring of disease?
 - h. What tests have prognostic value in multiple myeloma?
 - i. What other lab tests are elevated and decreased in this disease?
 - j. Describe the different varieties of the disease.
 - k. Which carries the best and worse prognosis and why?
 - l. Describe and explain patterns of electrophoresis that would be encountered in treated and untreated multiple myeloma patients.
 - m. Describe criteria for making a call of a monoclonal protein and a protein electrophoresis gel?
6.
 - a. What type of specimen is used for electrophoresis and why?
 - b. What criteria are used for sample rejection?
7.
 - a. What is cryoglobulin and how is it measured?
 - b. List the different types of cryoglobulin and diseases associated with each.
 - c. What is amyloid and how is it detected?

UNIT H: SERUM LIPID TESTING

1. Describe the methods used in quantifying serum total cholesterol, triglycerides.
2. Describe the methods used to fractionate and quantitate the following: HDL-C, LDL-C, VLDL-C. Understand utility of calculated LDL-C. Illustrate (draw) the electrophoretic migration of lipoproteins.

What, if any, is the utility of this test?

3. Describe the clinical utility of total cholesterol, HDL-C, LDL-C, and VLDL-C, and trigs. Become familiar with the NIH National Cholesterol Education guidelines and recommendations.
4. Understand the methods and utilization and apolipoproteins for clinical diagnosis of lipid disorders; specifically A₁, G₁₀₀, and Lpa - and their use as tumor markers for coronary artery disease.
5. Review the pathophysiology, clinical significance, and role for measuring homocysteine as a marker for CAD. Review technologies available for measurement.

UNIT I: The Role of the Laboratory in Acute Coronary Syndrome

1.
 - a. What is acute coronary syndrome (ACS), myocardial infarction, and unstable angina?
 - b. Describe the pathophysiology of ASC.
 - c. List risk factors for acute myocardial infarction (AMI) - primary and secondary.
 - d. How is a diagnosis if AMI made?
 - e. What biochemical markers are available for diagnosis of AMI?
 - f. How is each biochemical marker used in the diagnosis of AMI?
 - g. What is the sensitivity and specificity of each marker?
 - h. Are any of the markers used to assess reperfusion?
 - i. Can any of these markers be used in a risk stratification? Provide samples.
2.
 - a. Is there any role for lactate dehydrogenase isoenzymes in diagnosis of AMI? Defend your answer.
 - b. Know the fractions of LDH isoenzymes (LD1 to LD6) and clinical correlates. Draw the patterns.
3.
 - a. What about CK-MB. In what situations (if any) does CK-MB play a role in AMI?
 - b. Know the isoenzymes of CK and associated diseases. Draw the patterns.
4. What is the difference between troponin I and T?
5. How is C-reactive protein used? Do we measure it here?
6. Why is homocysteine testing performed?

UNIT J: BASIC ENZYMOLOGY, LIVER DISEASE, & GI DISEASE

1. Residents should have a knowledge of the following basics:
 - a. The Michaelis-Menten equation.
 - b. Zero-order and first-order kinetic portions of this equation.
 - c. Principles used in the measurement of an organic molecule's concentration using an enzymatic method.
2. Know the factors involved in clinical interpretation of enzyme tests:
 - a. Tissue distribution, intracellular location, isozymic forms of the commonly measured serum enzymes.
 - b. Mechanisms of release and duration of release from damaged cells and tissues.
 - c. How rates of enzymes clearance from plasma effect serum enzyme concentrations.
 - d. Which enzymes rise primarily because of induced enzyme synthesis rather than release from damaged cells.
3. Be familiar with the analytical methods used in determination of enzyme activity, enzyme mass, and isoenzymes:
 - a. Electrophoretic.
 - b. Spectrophotometric.
4. Know the normal anatomy, physiology, and biochemistry of the liver:
 - a. Micro and macroanatomy of the liver and biliary tract.
 - b. Metabolism of carbohydrates, lipids, and proteins in the liver.
 - c. Hormonal influences in the liver (e.g. insulin, glucagon).
 - d. Synthesis of specific plasma proteins.
 - e. Bile acid synthesis and excretion.
 - f. Urea synthesis and excretion.
 - g. Drug metabolism in the liver.
 - h. Metabolism and excretion of bilirubin.
5. Understand the etiology and diagnosis of the major types of jaundice:
 - a. Pre-hepatic (hemolysis, ineffective
 - b. Hepatic (pre-microsomal, microsomal, post-microsomal, intrahepatic obstruction).
 - c. Post-hepatic (gallstones, stricture, carcinoma of the pancreas or tree).
6. Be familiar with the basic liver function tests:

- a. Hepatocellular serum enzyme indicators (serum AST, ALT).
 - b. Obstructive jaundice indicators (serum conjugated bilirubin, alkaline phosphatase, 5'-nucleotidase, gamma-glutamyltransferase).
7. Know the macro and microanatomy of the upper and lower gastrointestinal tract and the specialized functions of each region.
 8. Understand the pathogenesis, diagnosis, and management of acute and chronic pancreatitis.
 9. Know the difference between malabsorption and maldigestion and how the laboratory is used to distinguish them.
 10. Understand the pathogenesis of diarrhea, the techniques for evaluation and the interpretation of stool testing.
 11. Specific Objectives - Liver
 - a. Describe basic functions of the liver.
 - b. List tests that can be used to evaluate each of these functions.
 - c. What are the 3 major forms of bilirubin? What is the predominant form in healthy individuals?
 - d. List disorders resulting in unconjugated hyperbilirubinemia (>80% of the total). Where is the defect in each disorder?
 - e. List disorders resulting in conjugated hyperbilirubinemia (>50% of the total). Where is the disorder in each effect?
 - f. What biochemical tests are used to detect hepatocellular necrosis?
 - g. What biochemical tests are used to detect cholestasis?
 - h. What are the most important enzymes in evaluation of liver disease?
 - i. Which organs contain high concentrations of each of these enzymes?
 - j. What laboratory tests are used to distinguish between viral and alcoholic hepatitis?
 - k. What laboratory tests are used in distinguishing hepatitis from obstruction?
 - l. What liver function tests do we offer here?
 - m. Are there any liver function tests not offered here that are useful clinically?
 - n. What test is often used as a screening test for alcoholic abuse? Why it is useful?
 - o. How would you distinguish biochemically between chronic hepatitis and cirrhosis?
 - p. What laboratory tests may be useful in diagnosis of patients with liver tumors?

UNIT K: FETAL & NEONATAL

1. Understand the protocol and technology used for screening for fetal lung maturity (FLM).

2. Beware of other amniotic fluids tests: foam stability.
3. Understand amniotic fluid and maternal serum alpha4etoprotein (MSAFP), beta hCG, and unconjugated estriol monitoring (triple test) and the protocols followed. Determine effects of race, diabetes, and weight on MoM.
4. Know what the Delta OD-450 test is and how to interpret.
5. Blood Gases-Peds Lab
6. Know the various screening tests performed on neonates and the rationale for each test.

UNIT L: TUMOR MARKERS AND FETAL TESTING

1. Review methods, pathophysiology, and clinical use of the following tumor markers:
 - a. PSA (Total and Free)
 - b. CEA
 - c. Beta hCG
 - d. AFP
 - e. CA19-9
 - f. CA-125
 - g. LD
 - h. Others

UNIT M. Therapeutic Drug Monitoring (TDM) -Kinetics

1. What are the indications for performing TDM? How do you choose drugs to monitor?
2. Know the definition and clinical utility of the following pharmacokinetic terms:
 - a. Volume of Distribution
 - b. Half-Life
 - c. Clearance
 - d. Loading Dose
 - e. Steady State
 - f. Bioavailability
 - g. Therapeutic Concentration
 - h. Peak
 - i. Trough
3. Review the pharmacokinetics of the following drugs through case review and problems:
 - a. Theophylline
 - b. Vancomycin
4. Know the principles (describe in words or with diagrams) that are involved in the measurement of therapeutic drugs by?
 - a. Fluorescent Polarization Immunoassays (FPIA)
 - b. Enzyme Multiplied Immunoassays (EMIT)
 - c. Cloned Enzyme Donor Immunoassay (CEDIA)
 - d. Kinetic Interaction of Microparticles in Solution (KIMS)

- e. High Performance Liquid Chromatography (HPLC)
 - f. Gas Chromatography (GC)
5. Know the advantages and disadvantages of measuring drug levels by immunoassay techniques compared to those that use HPLC or GC.
 6. Know the circumstances wherein determinations of serum free drug levels are necessary.
 7. Describe the mechanism of toxicity, relevant serum drug concentrations, and treatment for the overdose of salicylate and acetaminophen. Know how to interpret the respective nomograms.
 8. Do we routinely measure drug metabolites? If so, when and why?
 9. Are the TDM assays relatively specific or are there a lot of cross-reactivity and interferences? Provide samples.
 10. What is the most common cause of an elevated therapeutic drug level?
 11. What types of samples are used for TDM and why?
 12. How are aminoglycosides administered and when are samples collected for drug levels.
 13. How is methotrexate used and when is it measured?
 14. Is it necessary to monitor salicylate and acetaminophen blood levels for therapeutic purposes? Defend your answer.
 15. What factors influence the half-life of drugs?
 16. What cardiac drugs do we monitor?
 17. What anticonvulsants do we monitor?
 18. How often do we routinely measure drug levels? Give examples.
 19. Do we measure immunosuppressive agents? How and why? What is the specimen of choice and why?

UNIT O: CLINICAL TOXICOLOGY

1. Toxicology, Drug Analysis (Always be familiar with where, how, and when assay/test is performed. Also be familiar with back-up procedures; assay down policies, etc.)
 - a. Describe the operation, utility, and components of a gas spectrometer (CG-MS), HPLC.
 - b. Describe screening and quantitative methods for the following:
 1. Volatiles: Ethanol, Methanol, Isopropanol, Acetone
 2. Pentobarbital
 3. Phenytoin (Total/Free)
 4. CO
 5. Lithium
 6. Thiocyanate, cyanide
 7. Tricyclic antidepressants
 8. Chloramphenicol

9. Arsenic
10. Caffeine
11. Digoxin
12. Drugs of Abuses, Including:
 - a. Amphetamines
 - b. Methadone
 - c. Cocaine
 - d. Cannabinoids
 - e. Morphine
 - f. LSH
 - g. Benzodiazepines
 - h. PCP
 - i. Opiates

2. Describe the mechanism of toxicity, relevant to serum concentrations, and treatment for salicylate and acetaminophen overdose.
3. Explain the pathophysiology of alcohol (ethanol) with respect to:
 - a. Absorption, metabolism, elimination
 - b. Blood, urine, breath analyses
 - c. Forensic use of vitreous humor
 - d. Review calculations in dram shop ethanol case (forensic)
4. Know pathways of iron metabolisms; Iron OD-chronic vs. acute.
5. Review specimen handling/screening/quantitation in forensic cases.
6. Become familiar with NIDA and CAP-TOX guidelines for drugs of abuse screening and confirmation; and what quality control procedures must be maintained.
7. Review the mechanism for lead intoxication. Describe the methods used to measure lead. Understand problems involved with collections
8. What is the difference between a screening test and a confirmatory test?
9. What criteria dictate whether a test is a screen or a confirmatory test?
10. What are the limitations of a screening test?
11. How do we confirm results here at UAMS? Briefly describe methods.
12. What drug class causes the highest number of deaths from poisoning in the US. What is the age group involved?
13. Of the two drugs, salicylate and amphetamine, would you recommend monitoring either or both of these drugs to assess the degree of overdose? Defend your answer.
14. What DOA would you recommend performing on STAT basis (in <1 hr) and why?
15. When would you want quantitative testing versus qualitative testing?
16. What low-molecular weight volatiles are involved in poisonings?
17. What is the osmolar gap and how it is used?
18. How would you distinguish between ethanol, methanol, isopropanol, and ethylene glycol intoxication

without specific assays?

19. Do we always measure the parent drug when testing for DOA? Defend your answer with examples.
20. What can cause a positive opiate screen?
21. Can we screen for DOA without knowing what to look for? How does this testing differ from testing for specific drugs?

UNIT P: Hematologic Chemistry

1. Know the basic physiology of the erythrocytes, including hemoglobin synthesis, iron, folate, and B-12 metabolism.
2. Know how to interpret the various anemias using iron, TIBC, TIBC %, Ferritin, and Erythropoietin. Correlate with CBC.
3. Understand the pathophysiology and diagnosis of the common disorders of hemoglobin synthesis and metabolism.
4. Know the biochemical, genetic, and physiologic abnormalities of the six major types of porphyria.
5. Know the etiology of porphyrinuria caused by lead poisoning and how to use the laboratory to identify lead poisoning.
6. Draw the common hemoglobinopathies using an acid and alkaline gel.
7. Know the elution times used on our HPLC system at UAMS.
8. Know how to interpret electrophoretograms (HPLC results) for the common hemoglobinopathies and thalassemias. Correlate with CBC and morphology.

UNIT Q: Lab Management

1. Review CAP - QA data as it arrives with Dr. Pappas.
2. Know the laboratory organization hierarchy and laboratory design.
3. Understand the following personnel matters (discuss with Chem Managers):
 - a. Registration, certification, licensure of various levels of laboratory personnel (CLA, MLT, MT, clinical chemists, pathologists) and agencies involved (ASCP, ISCLT, NCA, ABCC, ABP).
 - b. Position descriptions, performance evaluations.
 - c. Ways of handling personnel problems with employees.
 - d. Productivity measurements (work units).
4. Understand principles of:
 - a. Method selection - analytical, economic, and other considerations.
 - b. Instrument selection - financing (lease, purchase, reagent rental), routine vs. STAT, sample size,

- random access.
- c. Instrument maintenance - in-house availability or vendor service, service contracts.
 - d. Reagent selection - kits, price, delivery, vendor QC.
 - e. Review the bid process - use example, i.e., GC MS, Immunoassay Analyzer.
 - f. Purchasing.
5. Understand the importance of good communications. Meet with lab administrator, lab manager, laboratory staff, and other parts of the hospital (medical and nursing staff, hospital administration, medical records, etc.).
 6. Be visible and always work on good communications.
 7. Obtain a CAP Laboratory Inspection and Accreditation Checklist and some time within the first month of the rotation inspect the Chemistry, Immunology, and Pediatrics Lab.

Clinical Chemistry CP Resident Rotation and Goals

Objectives:

1. Become familiar with fundamental general chemistry assays that are performed in the laboratory.
2. Obtain a thorough understanding of basic test methodologies, potential interferences (both pre-analytical and analytical) and limitations, availability of various tests, proper specimen collection, QC charts, and clinical interpretations.
3. Become familiar with all instruments used to perform chemistry testing such as:
 - a. Beckman CX3: Electrolytes, Glucose, BUN, Creatinine, and Calcium Malyzer
 - b. Beckman Synchron CX3ICX7: General Chemistry Malyzers
 - c. Abbott AxSym: Special Chemistry Malyzer
 - d. Freezing Point Osmometer
 - e. Nova 8: Ionized Calcium Malyzer
 - f. Scanning Spectrophotometer for plasma free hemoglobin and delta OD 450 (fetal bilirubin).
 - g. Cliniscan: Scanning Densitometer for L/S Ratio
 - h. HPLC System: HgbAl c and Hgb S
 - i. DPC Immunlite Analyzer Fertility Testing
 - j. Kodak 750: Special Chemistry Malyzer
4. Gain experience as a physician/lab consultant by being readily available to the technical and medical staff Responsibilities include answering questions, dealing with problems, following-up on difficult diagnoses, as well as being a general liaison between the lab and medical staff.
5. Review and discuss QC charts periodically to detect bias, shifts, and trends.
6. Review on a daily basis shift sign-off sheets including abnormal results, invalid results, and daily comparisons. Follow-up all abnormal results to determine whether the change is consistent with the patient's condition or due to an improperly collected specimen.
7. Become familiar with how to perform a CAP inspection and the necessary requirements that are needed to pass such an inspection.

8. Review the appropriate CLIA 88 Regulatory Requirements in regards to the regulated analytes in the area, required proficiency, and quality assurance.

General Methods To Achieve Objectives:

1. There will be a 2 month, planned program of activities to include daily and weekly responsibilities. This program is integrated with other areas of the laboratory such as Immunochemistry (Endocrinology) and Immunology. Although the resident will cover all three (3) sections throughout the rotation, it is recommended that the resident focus on various aspects of the General Chemistry section the first month and Immunochemistry/Immunology during the second month.
2. Three notebooks (2 labeled Chemistry and 1 labeled Immunology) will be distributed in July (that can be kept by the Resident) containing material that should be read during the 2 month rotation. Material from these notebooks will be discussed during the rotation with the Director.
3. Several additional reference books/articles will also be available in various areas of the laboratory and/or the Director's office,
4. Briefly touch bases daily with the Section Supervisor and Director to relay information, discuss problems, follow-up, and review laboratory results as they relate to various disease states.
5. Meet at least once a week with the Director to discuss the weeks activities and reading materials, testing methodologies, pre-analytical, and analytical interferences, new test menus, etc.
6. Attend morning report regularly and present interesting patient dilemmas, unusual laboratory findings, unusual STAT requests, etc.
7. Sign-out interpretive reports such as L'S ratios and OD 450 scans and discuss results with the Director.
8. Review quality control data and sign-off on daily comparisons and discuss any abnormalities with the Director.
9. Learn how procedure manuals are organized and updated and write and/or re-write a procedure according to NCCLS Guidelines.

Specific Schedule to Complete Objectives:

Week 1

- a) Learn the various sections of the lab and meet the people.
- b) Become familiar with basic chemistry instrumentation that we use and what tests are generally performed by each instrument.
- c) Review Westgard QC rules and begin reviewing QC results. what is considered an acceptable chemistry run? When and how often are controls run? what is done when a control is out of range?
- d) Questions to think about when reviewing the above tests:
 - Do we measure TIBC and LDL? If not: how do we calculate them?
 - Can TIBC and LDL be directly measured? If so, what should we do to measure it?
 - What is delta bilirubin? Do we measure it? Should we?
 - What tests would you order to rule-out liver disease? Why?
 - How are alkaline phosphatase isoenzymes measured? Do we measure them? If not: why?
 - Do we really measure elemental phosphorus? What forms of phosphorus are present in the body? How do we report out phosphorus?

- What are the general methods to measure the above analytes?
- e) Schedule time (with the Supervisor) to visit the Pediatrics Lab and learn what tests they perform and how the testing differs from the main lab (see Pediatrics Lab Rotation handout for specific objectives). In addition to the specific scheduled described above, the resident is expected to deal with the problems as they arise for all three sections of the laboratory. In addition, the resident is expected to attend morning report regularly and present interesting cases (see Presentation of Calls... at Morning Report) as well as perform daily responsibilities (see Daily Responsibilities document) throughout the 2 month rotation.

Names and Numbers:

Manager: Sidney Skinner, BSMT (ASCP)
Ext. 68009
Pager: 688-2193

Director: Alex Pappas: M.D.
Ext. 65786
Pager: 688-6490

**Clinical Immunochemistry CP Resident
Rotation and Goals**

Objectives:

The objectives are to become familiar with fundamentals of radioimmuno-assays and other ligand assays, therapeutic drug monitoring, and gain experience in consulting with physicians on these matters. Areas to be covered during the rotation include:

1. Proper specimen collection for various endocrine tests and therapeutic drug monitoring.
2. Methodologies for various techniques such as competitive and noncompetitive radioimmunoassays, enzyme immunoassays, and fluorescence immunoassays.
3. A basic understanding of data reduction such as log-logit, semilog, linear, reciprocal, ratio and linear regression.
4. Familiarization with Immunochemistry instrumentation such as gamma counters, TDX, FLX, IMX, AxSym, HPLC, and plate readers.
5. A basic understanding of the quality control program in Immunochemistry.
6. Obtain a basic understanding and discuss how to use HPLC to measure specific analytes.
7. Review Immunochemistry delta checks and follow-up consistent results.
8. Understand the methods used to measure tumor markers and how the results can aid in the diagnosis and monitoring of disease.
9. Understand and discuss how to evaluate new tests, perform method comparisons, and establish reference intervals.
10. Become familiar with CLIA '88 Regulatory Requirements, CAP Requirements, and Proficiency Testing associated with this area.

General Methods to Achieve Goals:

The overall objectives (i.e., review of techniques, experiences in problem solving, and experience in laboratory-physician liaison) will be achieved in the following manner:

1. The resident will primarily focus on Immunochemistry and immunology by following a one month planned program of activities during the second month of the rotation through Chemistry/Immunochemistry/Immunology.
2. Material contained in two (2) notebooks labeled Chemistry (that were distributed in July) pertaining to the Immunochemistry section of the lab is to be read and discussed with the Director throughout the rotation. Additional supplemental material is also available in various areas of the laboratory and/or Director's Office.
3. The resident will consult with clinicians as required to resolve problems, interpret unusual test results, help select appropriate tests, and to determine whether STAT requests should be performed based on the clinical picture.
4. Briefly touch base with the Section Supervisor and Director at the beginning and end of the day to relay information, discuss problems, and follow-up unusual patient results.
5. Meet at least once a week with the Director to discuss the weeks activities and reading materials, testing methodologies, pre-analytical and analytical interferences, bringing new tests in-house, method comparisons, etc.
6. Attend morning report regularly and present interesting patient dilemmas, unusual laboratory findings, unusual STAT requests, etc.
7. Become familiar with how method comparisons are performed and reference intervals are established for a specific analyte. The resident also has the opportunity to assist in the direction of a method comparison test evaluation (these are continually ongoing in the lab) and present the results at a national meeting.
8. Learn how the procedure manuals are organized and updated in Immunochemistry and how to write a procedure according to NCCLS Guidelines.

Specific Schedule to Complete Objectives:

Week 1:

- a. Introduce yourself to the Immunochemistry staff and become familiar with instrumentation in the section (where it is and what it is used for).
- b. Understand and be able to discuss tests that are available to screen and confirm thyroid disease. How are they performed (basic methodology)? What is a free thyroxine index and how is it used? How would you differentiate hyperthyroidism from euthyroid sick syndrome? How would you confirm Graves' Disease?
- c. Understand how we measure B12/folate (both serum and RBC folate) and ferritin. How are these results interpreted? What other tests are helpful in diagnosing anemia?
- d. Understand the principle behind how a competitive RIA is performed. Use the gastrin assay as an example. How is the standard curve generated? What is expressed on the x and y-axis and why? How are patient results calculated? Understand the various data reduction approaches routinely used and why one method is favored over another.

Week 2:

- a. Understand and discuss how we measure therapeutic drugs. What drugs do we test for?
- b. Understand basic principles of pharmacokinetics such as volume of distribution, clearance, steady state, half life, zero/first order kinetics, and how they relate to therapeutic drug monitoring.
- c. What criteria is used to determine which therapeutic drugs are monitored? Should free or total drug levels be measured? What antidotes or treatments exist for toxic drug levels?
- d. When should specimens be collected to measure drug levels? For what drugs are trough and peak level desirable, and why?
- e. Understand and discuss the following tests:
 - Erythropoietin
 - IL-6
 - Hemoglobin A1c & Hgb S
 - LD Isoenzymes

Questions to consider when discussing the above tests:

- Why measure serum levels of IL-6?
- What are glycohemoglobins and why A1c is measured?
- What other glycoproteins might be useful for monitoring diabetics?
- Should LD isoenzymes be fractionated? Why not measure only LDI?

Week 3

- a. Understand and discuss available tests for fertility?
- b. What tests are used to evaluate pituitary hyper and hypofunction? How are the results interpreted?
- c. How is Cushing's Disease differentiated from other causes of Cushing's Syndrome?
- d. What is the differential diagnosis for hyperaldosteronism? How is renin levels used to aid in the diagnosis? What is specimen types are submitted for renin studies and why?

Week 4:

- a. What are tumor markers and what are their potential uses?
- b. Understand and discuss the following tumor marker tests:
 - Alpha Fetoprotein
 - Beta 2 Microglobulin
 - Carcinoembryonic Antigen
 - Prostate Specific Antigen
 - CA125
 - Human Chorionic Gonadotropin
- c. What is the differential diagnosis for hyperparathyroidism? How do the various PTH assays differ and in what clinical settings would one assay be preferred over another?
- d. In what clinical settings are gastrin determinations useful? How do we measure it?
- e. What tests are available for diagnosing bone disorders?

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Weekday Daily Resident Responsibilities For Chemistry & Immunology

1. Briefly touch bases with the Director and Supervisors of Chemistry and Immunology each morning for

relay of information and to discuss problems.

2. Attend morning report regularly and present consultative calls, interesting patient results, and clinical dilemmas.
3. Review and sign-off on the following chemistry logs:
 - a. shift check-off list & daily comparisons
 - b. invalid results
 - c. abnormal results
 - d. canceled test log

Follow-up on any results from the above logs (such as invalid and abnormal results log) as warranted and present unusual findings at morning report).

4. Follow-up on chemistry and immunochemistry delta checks as they arise.
5. Investigate any osmolar discrepancies in suspected alcohol intoxications.
6. Sign-out serum/urine protein electrophoresis and immunofixation gels (around 8:00am, 11:30am, & 4:00pm).
7. Check-out at the end of the day with the Director to discuss the days activities and relay pertinent information.
8. Review peripheral smears on hemoglobin electrophoresis specimens and sign-out hemoglobin HPLC results.
9. Call the VA Hospital on Tuesday afternoon each week (ext. 2270) to find out when the protein electrophoresis and immunofixation gels will be available for your review. Review gels as well as any ANA results.

**Weekend/Holiday Daily Resident Responsibilities for
Chemistry/Immunochemistry/Immunology**

1. Briefly meet with the Chemistry Supervisor each morning for relay of information and to discuss problems.
2. Review and sign-off on the following chemistry logs:
 - a. shift check-off list & daily comparisons
 - b. invalid results
 - c. abnormal results
 - d. canceled test log

Follow-up on any results from the above logs (such as invalid and abnormal results log) as warranted and present unusual findings at morning report).

3. Review morning lab results printout (this is printed out around 8:30am each day and can be found at the 6A headed microscope). Separate the following:
 - a. tests pending since 5:00am (routine tests performed 24 hours a day).
 - b. corrected reports.
 - c. invalid results.

Tests pending and corrected reports are given to the appropriate Supervisors. Invalid results are investigated by the Resident.

4. Review L'S ratio results and OD 450 scans whenever performed.
5. Alcohol and delta-osmolality: Investigate any osmolar discrepancies.

CLINICAL MICROBIOLOGY RESIDENT ROTATION

M. A. Scott, M.D. Rotation Director

GOALS and OBJECTIVES:

The core rotation in clinical microbiology at UAMS for pathology residents is an initial rotation of two months with an additional third month scheduled towards the end of the residency program. Basic goals of the rotation are:

1. Gain a basic understanding of the clinically important pathogens in the areas of bacteriology, mycobacteriology, mycology and parasitology.
2. Gain sufficient technical and clinical background to direct microbiology technologists as a Laboratory Medical Director in the private practice setting.
3. Acquire education information and resources needed to pass the general Clinical Pathology Boards section for Microbiology.
4. Provide necessary background and training which would prepare those who wish to seek advanced training in Clinical Microbiology.
5. Observe and perform, as possible, the procedures and techniques outlined below in the clinical microbiology checklist.

TEACHING METHODS:

1. Reading assignments: Koneman et al. Color Atlas and Textbook of Diagnostic Microbiology, Fifth Edition, Lippincott, 1997.
2. One-on-one didactic sessions with rotation director (usually one hour each day)
3. Observe technologist benchwork (participation encouraged)
4. Literature searches related to interesting clinical laboratory cases
5. Consultation with clinician and infectious disease fellow concerning current interesting cases.

ROTATION SCHEDULE:

Week #1:

There are introductory meetings with the rotation director to cover basic principles of clinical microbiology and infectious disease pathology. Didactic sessions during this time to cover Chapters 1-3 of required textbook. This phase will be completed or near completion prior to the resident initiating laboratory bench rounds and/or bench work.

Week #2 and forward:

The resident will attend morning report each week-day morning and participate in microbiology/infectious disease journal reviews and interesting case reports. Following morning report the resident will report to the Clinical Microbiology laboratory to work with the medical technologists. At noon each day the resident will attend departmental noon conferences. During the academic school year, the microbiology resident will attend the Infectious Diseases Current Case Report Conference held on Mondays from 12:00 noon to 1:00pm in the Shorey ID Conference room. In the afternoons the resident will meet with the rotation director to:

1. discuss interesting cases seen in the laboratory that morning
2. discuss procedures observed and/or performed in the laboratory
3. review the assigned reading chapter in Koneman's text
4. plan literature searches or patient follow-up steps on current cases

VIROLOGY FOCUS WEEK:

This week will take place during the second month of the clinical microbiology core rotation. The resident will report each morning to the Arkansas Children's Hospital Laboratory and work with the virology technologists at the bench to gain a baseline level of understanding and introductory experience in virology laboratory techniques. The virology supervisory (Rebecca Nelson), Dr. Paula North and Dr. David Parham will coordinate the daily activities during this week long rotation. At the end of the week long rotation, the resident will give a short interesting case report at the following Tuesday Clinical Pathology Morning Report.

CLINICAL MICROBIOLOGY RESIDENT ROTATION CHECKLIST

Upon completion of the Clinical Microbiology rotation, the resident will be able to perform and explain the principle of the tasks listed below.

Set-Up Station

- A. For the solid and broth media used for isolation, state
 1. Purpose & type of media (Enrichment, selective, differential, etc)
 2. Clinical application
- B. For each type of Specimen state the appropriate culture method.
- C. Explain the purpose and properties of a good transport medium.
- D. Gram Stains: Know the principle and expected reaction of the procedure. Be able to interpret gram stain smears with respect to expected bacterial morphology (cocci, bacilli, yeast, etc.)
- E. List specimens for which gram stains should be performed.
- F. List criteria for unacceptable specimens.
- G. Know appropriate processing techniques.

Blood Culture Station

- A. State the principle of blood culture collection and the automated blood culture' system.
- B. Observe processing and work-up of positive and negative blood cultures
- C. Compare and contrast aerobic and anaerobic blood cultures
- D. Given a smear result, determine the appropriate "next step" in working up positive blood cultures.
- E. Discuss the clinical relevance of commonly isolated organisms.

Workbench Stations

- A. Observe and understand the proper streaking methods
- B. Know how to optimize colony isolation
- C. On the basis of morphology be able to recognize:
 - Mixed flora in upper respiratory cultures
 - Mixed flora in urine cultures
 - Normal flora in stool cultures
 - Normal flora in genital cultures
 - Common Enterobacteriaceae (E. coli, Klebsiella, Proteus)
 - Pseudomonas
 - Streptococci
 - Staphylococci
 - Yeast
- D. Know the initial biochemical identification steps for Staphylococci, Streptococci, Enterobacteriaceae, Enterococci, Common nonenterobacteriaceae
- E. Be familiar with the Vitek and API identification systems
- F. Observe anaerobic culture set-up and read-outs
- G. Explain the principles of antibiotic sensitivity testing (Disk diffusion; MIC and Estrips)
- H. Explain the concept of antibiotic synergy

Mycobacteriology

- A. Discuss safety precautions appropriate for the TB lab

- B. Observe specimen processing and testing procedures
- C. Interpret Ziehi-Neelson and Fluorescent stains for AFB
- D. Observe conventional (U) and BacTec media work-ups
- E. Observe Mycobacteriology sensitivity testing

Mycology

- A. Discuss safety precautions appropriate for the mycology lab
- B. Observe specimen processing and testing procedures
- C. Observe and interpret KOH preps and fungal stains (i.e. Lactophenol cotton blue stain)
- D. Observe workup and identification

Virology

- A. Read and understand safety precautions and sterile techniques as they pertain to the Virology laboratory.
- B. Observe Specimen Set-up
- C. Be familiar with appropriate cell lines and types used for the more common viral pathogens including, but not limited to: Human Cytomegalovirus, Herpes simplex, RSV, Influenza & Parainfluenza, and Adenovirus.
- D. Be familiar with specific and non-specific cytopathic effect (CPE)
- E. Be familiar with immunofluorescent staining techniques for direct stains and culture confirmations
- F. Be familiar with the CMV antigenemia assay
- G. Be familiar with viral serology/immunology techniques
- H. Describe the suitability of the various diagnostic techniques for the common viral pathogens noted above.

Parasitology

- A. Describe methods used to collect appropriate stool specimens
- B. Be familiar with concentration and floatation ID methods
- C. Describe methods to diagnose:
 - Pinworm infection
 - Nematode infections
 - Filariform infections
 - Protozoan infections
- D. Identify common parasites based on morphology:
 - Entamoeba coli vs E. histolytica
 - Iodamoeba butschlii
 - Giardia lamblia
 - Trichomonas
 - Balantidium coli
 - Plasmodium species
 - Babesia
 - Leishmania
 - Trypanosomes
 - Toxoplasma
 - Hookworms
 - Ascaris
 - Strongyloides
 - Common arthropods

Acting Laboratory Director, Little Rock VA

Name: Rotation: Laboratory Director
 Site: 2E-148, Little Rock VA Hospital
 Length: One month

Faculty in Charge: Margaret Scott, MD and VA Staff

Goals and Objectives:

1. Become familiar with QA, QC monitors, governmental regulators and regulations.
2. Learn to deal with implementation of new tests.
3. Learn how to become a useful laboratory consultant.
4. Learn to solve problems₁ including technical and personnel problems.

Duties and Responsibilities:

1. Make rounds and investigate problem cases or unusual cases. Check clinical correlations.
2. Attend management and clinical conferences with staff.
3. Become familiar with the QA and QC programs and monitors. Prepare and analyze a QA problem.
4. Become familiar with the preparations for a laboratory inspection.
5. Learn how to institute a new test methodology, including the statistical analysis of the test and the generation of reference ranges.

Suggested Reading List and References:

Henry, JB, 1996. Clinical Diagnosis and Management by Laboratory Methods. 19th Edition W.B. Saunders Company. Part I, Chapters 1,2,4, and 6.

Kaplan, I-A and Pesce, AJ, 1996. Clinical Chemistry: Theory, Analysis, and Correlation. 3rd Edition. Mosby. Section One, Chapters 1, Part I and II, Chapter 2 and 3.

Ashwood, ER and Burtis, CA, Editors 1994 Tietz Textbook of Clinical Chemistry. 2nd Edition. W.B. Saunders Company Section 1V₃ Chapters 16 and 17.

Name: Resident Rotation in Molecular Pathology
Site: Little Rock VA Hospital, PLMS 2E129
Arkansas Children's Hospital, Pathology, 5257

Faculty in Charge: Steven Schichman, M.D., Ph.D (VAMC).; Marjorie Scott, M.D. (VAMC).; Paula North, M.D., Ph.D (ACH).; Bin Chen, M.D., Ph.D (ACH).

Goals and Objectives:

1. Learn the biochemical principals of nucleic acid structure, purification, amplification and detection.
2. Understand the principals of operation of instrumentation used in the Molecular Diagnostics laboratory.
3. Learn the diagnostic applications of Molecular Pathology. These include the following areas:
 - a. infectious disease
 - b. genetic (inherited) disease
 - c. neoplasia
 - d. human identification
4. Learn how basic techniques in nucleic acid biochemistry are applied to different types of molecular diagnostic tests.

5. Learn how to interpret different types of molecular test results.
6. Learn how to organize and run an academic Molecular Diagnostics laboratory.

Description of VAMC Rotation (2 weeks):

The two week rotation in Molecular Pathology at the VAMC consists of five didactic lectures, observation of test procedures, hands-on participation, and instruction in test interpretation. In addition, the resident will correlate clinical information and other pertinent laboratory data with molecular test results.

1. Didactics (1 hr each)
 - a. Nucleic acid biochemistry (Dr. Schichman)
 - b. Basic techniques in molecular diagnostics (Dr. Schichman)
 - c. HIV viral load testing (Dr. Schichman)
 - d. Quantitative bone marrow engraftment testing (Dr. Schichman)
 - e. Molecular diagnosis of Mycobacteria (Dr. Scott)
2. Observation of test procedures
 - a. HIV viral load
 - b. HCV qualitative testing
 - c. HCV viral load
 - d. HCV genotyping
 - e. Prothrombin 20210
 - f. Methylenetetrahydrofolate reductase
 - g. Hereditary hemochromatosis
 - h. Quantitative bone marrow
3. Hands-on participation
 - a. DNA purification (the resident will purify genomic DNA from his/her on peripheral blood).
 - b. Factor V Leiden RFLP test (includes PCR, restriction enzyme digest, and agarose gel electrophoresis).
 - c. Mycobacteria PCR (nucleic acid purification, primer labeling, PCR, polyacrylamide gel electrophoresis).
4. Instruction in test interpretation and report generation
 - a. all tests listed in #2 and #3 above.
5. Organization, work-flow, and quality control in a Molecular Pathology Laboratory

Description of ACH Rotation (2 weeks):

The two week rotation in Molecular Pathology at ACH provides an exposure to molecular testing particularly suited for in the pediatric setting, and for cancer-related research. It consists of informal didactic sessions, observation of procedures used in detection of infectious and inherited disease and in analysis of tumor loss of heterozygosity, consideration of alternative testing methodologies, and discussion of test interpretation and quality control issues. The resident will also participate in routine correlation of molecular testing results with clinical presentation of the patient and with other testing modalities (serology, muscle biopsy, etc.).

1. Didactics (1 hr each)
 - a. Chlamydia trachomatis PCR using an FDA-approved kit (Roche Amplicor) (Dr. North)
 - b. Qualitative detection of Ehrlichia chaffeensis, HSV, and Mycoplasma pneumoniae DNA using home-brewed PCR methodologies (Dr. North)
 - c. Detection of enteroviral RNA in cerebrospinal fluid by RT-PCR (Dr. North)

- d. Detection of inherited disease (Fragile X syndrome and Duchenne muscular dystrophy) by PCR and Southern Blot analysis (Dr. Chen).
 - e. Determination of tumor allelic loss (loss of heterozygosity) by microsatellite PCR (Dr. North).
2. Observation of test procedures
- a. Chlamydia PCR
 - b. Ehrlichia chaaffeensis PCR (gel electrophoresis)
 - c. HSV PCR (microplate-immobilized probe analysis).
 - d. Enteroviral RT-PCR
 - e. DMD PCR
 - f. Southern blot analysis
 - g. Loss of heterozygosity analysis
3. Hands-on participation
- a. DNA purification
 - b. RNA purification
 - c. Microsatellite allelic analysis, comparing resident's own DNA to that of another person.
 - d. Ehrlichia chaaffeensis PCR (nucleic acid purification, PCR, polyacrylamide gel electrophoresis, fluorescent laser detection)
4. Instruction in test interpretation and report generation
5. Instruction in quality control and assurance, and specifically in control of contamination in a Molecular Pathology Laboratory (comparison of control measures used at VAMC and ACH)

Suggested Reading and References:

Farkas, DH, Editor, 1993. Molecular Biology and Pathology, Academic Press Inc., San Diego

Ellis, R, Editor, 1996. Molecular Diagnosis of Genetic Diseases, Humana Press.

Coleman WB and Tsongalis GJ, Editors, 1997. Molecular Diagnostics for the Clinical Laboratorian, Humana Press.

Reference Guide for Diagnostic Molecular Pathology/How Cytometry: Fascicle VII. Prepared by: The Patient Preparation and Specimen Handling Editorial Board. College of American Pathology.

Lo YMD (1998) Clinical Applications of PCR, Humana Press

Wiedbrauk DL and Farkas DH (1995) Molecular Methods for Virus Detection, Academic Press