

Chromatography, mass spectrometry and metabolic lab resident rotation

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Overview: The Metabolic and Toxicology Laboratories use chromatography and mass spectrometry for quantitation of a variety of compounds. The low volumes, limited automation for these tests and panels with large numbers of compounds provide unique challenges to providing accurate test results quickly. This rotation allows residents to expand their knowledge of chromatography and mass spectrometry, using webinars, independent reading, case studies and review of clinical test procedures and results. The rotation also helps residents develop an understanding of the processes necessary for the development, validation and implementation of manual (non-automated) lab-developed testing.

Educational goals of the rotation: The goals and depth of learning depend on the rotation duration and residents' year in training when they begin this rotation. At the beginning of the rotation, residents should meet with the attending to decide on specific goals to achieve by the end of the rotation.

Medical knowledge:

- Develop a basic understanding of the separation principles of common types of chromatography, including gas chromatography and various types of liquid chromatography.
- Identify the uses of different types of mass spectrometers in a clinical lab, as well as the characteristics of instrumentation that make it appropriate for various tests.
- Develop an understanding of the analytical principles used in testing. This is done by reading procedure manuals for each test and observing specimen processing, from receipt to results. Residents should be able to describe the analytical principles and clinical relevance of the testing upon request.
- Understand how pathophysiology of various conditions affects the results of testing. This is done by reviewing textbooks, articles or casebooks, as well as discussion during bench-time or sign-out.

Patient care:

- Interpret straightforward results, integrating with clinical data as necessary.
- Review the results of any abnormal newborn screens, create a differential diagnosis and determine the most appropriate testing. Interpret the results of diagnostic testing in light of the newborn screening results

Practice-based learning:

- Identify at least one appropriate review article related to the testing techniques or interpretation of test results. The article will be added to a bibliography of suggested reading that is to be maintained by the residents.
- Review quality management (QM) data and identify steps in troubleshooting any QM issues. Residents should be able to recall criteria for acceptable results and the statistics necessary to determine acceptability.
- Review proficiency testing instrument data from the most recent proficiency test. For quantitative results, review lab performance and determine potential reasons for any results outside of acceptable range. For tests with interpretations, write an interpretation and compare it to the submitted results.
- Demonstrate understanding of quality management by participating in quality improvement projects in each lab, including data collection and analysis. For projects with inadequate improvement, identify possible barriers to improvement, in addition to possible ways to remove those barriers.
- Understand the requirements related to competency assessment by preparing a competency assessment process for one test or instrument.

Interpersonal communication:

- Demonstrate effective communication by presenting a case study or review of an inherited metabolic disorder.
- Demonstrate adequate written communication skills by writing and editing interpretations of results.

Professionalism: Demonstrate professional behavior at all times by dressing appropriately, practicing punctuality in attendance and with laboratory responsibilities, and by engaging in meaningful interactions with others.

Systems-based practice:

- Determine the most appropriate CPT code and CMS reimbursement for each test.
- Review one test protocol and determine if it provides all of the necessary information delineated in the College of American Pathologists checklists. Suggestions should be made on how to bring the document into compliance and on what data or testing is necessary to achieve this.
- Understand the parameters that contribute to cost-effective practice by selecting one send-out test and determining the volume necessary to make in-house testing cost-effective.

Learning resources

Chromatography

- **Principles of chromatography:** <https://www.khanacademy.org/test-prep/mcat/chemical-processes/separations-purifications/a/principles-of-chromatography>
- **Gas chromatography:** <https://www.khanacademy.org/test-prep/mcat/chemical-processes/separations-purifications/v/gas-chromatography>
- **LC primer:** http://www.waters.com/waters/en_US/HPLC---High-Performance-Liquid-Chromatography-Explained/nav.htm?locale=en_US&cid=10048919
- **HPLC basics:** http://polymer.ustc.edu.cn/xwxx_20/xw/201109/P020110906263097048536.pdf
- **Size exclusion chromatography:** http://www.waters.com/waters/en_US/Size-exclusion-chromatography-%28SEC%29-Gel-Permeation-Chromatography-%28GPC%29-Guide/nav.htm?locale=en_US&cid=10167568
- **Solid phase extraction:** http://www.waters.com/waters/en_US/Solid-Phase-Extraction-SPE-Guide/nav.htm?locale=en_US&cid=134721476
- **Chromacademy.com:** <http://chromacademy.com/index.html> Sign up with .edu email and get access to webcasts and tutorials on various types of chromatography including GC, HPLC
- **Missing peaks:** <https://www.aacc.org/publications/cln/articles/2017/february/the-center-did-not-hold-missing-peaks-in-the-middle-of-the-liquid-chromatography-run>
- **HPLC self-test:** <http://studyhplc.com/hplcselftest.php>

Mass spectrometry

- **Virtual mass spectrometry lab:** <http://svmsl.chem.cmu.edu/vmsl/default.htm>
- **Chromacademy MS module:** <http://chromacademy.com/mass-spec-training.html>, <http://www.ecs.umass.edu/eve/background/methods/chemical/Openlit/Chromacademy%20LCMS%20Intro.pdf>
- **What's mass got to do with it?:** <http://www.ccmr.cornell.edu/wp-content/uploads/sites/2/2015/11/WhatsMassGottoDoWithIt.pdf>
- **Mass spectrometry primer:** http://www.waters.com/waters/en_US/MS---Mass-Spectrometry-%28MS%29-Beginner%27s-Guide/nav.htm?locale=en_US&cid=10073244

- **Intro to MS:**
[https://chem.libretexts.org/LibreTexts/Purdue/Purdue%3A Chem 26200%3A Organic Chemistry II \(Wenthold\)/Chapter 11%3A IR and Mass Spectrometry/11.06%3A Introduction to Mass Spectrometry](https://chem.libretexts.org/LibreTexts/Purdue/Purdue%3A%20Chem%2026200%3A%20Organic%20Chemistry%20II%20(Wenthold)/Chapter%2011%3A%20IR%20and%20Mass%20Spectrometry/11.06%3A%20Introduction%20to%20Mass%20Spectrometry)
- **Mass spectrometry basics, including high resolution:**
<https://www2.chemistry.msu.edu/faculty/reusch/virttxtjml/Spectrpy/MassSpec/masspec1.htm#ms5>
- **Clinical MS:** <http://clinchem.aaccjnls.org/content/62/1/92>
- **MALDI:** <http://clinchem.aaccjnls.org/content/62/1/134>
- **Sequencing via MS:** <https://getpocket.com/a/read/1451197005>
- **MS for protein analysis:** <https://www.thermofisher.com/us/en/home/life-science/protein-biology/protein-biology-learning-center/protein-biology-resource-library/pierce-protein-methods/overview-mass-spectrometry.html.html>
- **Ambient ionization:** <http://clinchem.aaccjnls.org/content/62/1/111>
- **MS for microbiology:** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4125470/>
- **Quality management:** <http://www.sciencedirect.com/science/article/pii/S0009912016301370>
- **LC-MS in clinical biochemistry:** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2643089/>
- **LC-MS method validation:** https://sisu.ut.ee/lcms_method_validation/course-introduction
- **Drug screening:** <http://clinchem.aaccjnls.org/content/63/5/958>
- **Thyroglobulin immunoassay vs. LC-MS/MS:** <http://clinchem.aaccjnls.org/content/60/11/1452>
- **Thiopurine TDM:** <http://www.arup.utah.edu/education/tpmt.php>
- **Pain management lab support:** <http://www.arup.utah.edu/education/PainManageLT.php>

Metabolic

- **Overview of biochemical genetics:**
<http://onlinelibrary.wiley.com/doi/10.1002/0471142905.hg1701s89/abstract>
- **IEM review:** <http://pedsinreview.aappublications.org/content/pedsinreview/37/1/3.full.pdf>
- **Metbio.net introductory training modules:** <http://metbio.net/metbioTrainingDocuments.asp?s=1>
- **Metbio.net presentations, techniques and disorders:** <http://metbio.net/metbioTrainingPresentations.asp>
- **Amino acids:** <http://www.arup.utah.edu/education/IEM.php>
- **Newborn screening:** <https://cdn.intechopen.com/pdfs-wm/29024.pdf>
- **NBS and confirmatory testing:** <https://www.degruyter.com/downloadpdf/j/cclm.2013.51.issue-1/cclm-2012-0472/cclm-2012-0472.pdf>
- **MS/MS vs. fluorescence for newborn screening lysosomal enzyme assay:**
<http://clinchem.aaccjnls.org/content/61/11/1363>
- **Biochemical findings in IEMs:** <http://onlinelibrary.wiley.com/doi/10.1002/ajmg.c.30086/abstract>

Case studies

- **Metabolic lab casebook**
- **MMA/Homocysteine:** https://www.aacc.org/~media/files/ccj/case-studies/2017/ccs_june_2017.pdf?la=en
- **C3 acylcarnitine:** <http://clinchem.aaccjnls.org/content/62/10/1410>
- **Milky serum:** <http://clinchem.aaccjnls.org/content/61/12/1441>

- **Abnormal newborn screen:** <http://clinchem.aaccjnls.org/content/57/6/927.full>
- **Seizures and discrepant tryptophan concentrations:** <http://clinchem.aaccjnls.org/content/57/4/545.full>
- **Unidentified plasma amino acid peak:** <http://clinchem.aaccjnls.org/content/62/5/781>
- **Hypercholesterolemia and xanthomas:** <http://clinchem.aaccjnls.org/content/62/6/899>
- **Dystonia and seizures in 14-year-old:** <http://clinchem.aaccjnls.org/content/62/8/1159>
- **Increased C5-OH acylcarnitine:** <http://clinchem.aaccjnls.org/content/62/9/1278>
- **Liver dysfunction in neonate:** <http://clinchem.aaccjnls.org/content/62/11/1539>
- **Dilated cardiomyopathy:** <http://clinchem.aaccjnls.org/content/63/1/433>
- **Dark urine:** <http://clinchem.aaccjnls.org/content/63/3/786>
- **Newborn with acidosis and hypoglycemia:** <http://clinchem.aaccjnls.org/content/63/2/613>
- **Acid lipase deficiency:** <http://www.arup.utah.edu/education/lysosomalALipase.php>