

The Connection

April 2023

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President's Message



First and foremost, I would like to give a big shout out to our new webmaster Jessica Fry. She has done an awesome job getting the sight redone. Please, if you have not already done so please visit [ASCLS ND](https://www.asclsnd.org) and check it out.

April brought with it the ASCLS ND state meeting which was held April 27-28, 2023 in Minot. While attendance was low, the quality of speakers was large. 23 different talks that covered many subjects. We had speakers from Oklahoma, Wisconsin, Missouri, California, Minnesota, Alabama, South Dakota, North Dakota and Arkansas. Some where in person and some were virtual. Thank you to all the speakers.

The state meeting also brought the voting in of new officers and state awards. These will be highlighted in this newsletter.

I would love to thank all the ND members for your continued membership and participation in our wonderful state society. We could not do it without all of you. Please consider volunteering, we would love to get you involved.

Warmest regards

Sharon Reistad
ASCLS ND president



Meet your 2023-2024 Board (effective July 1, 2023)



Tammy Windish - President



Sharon Reistad - President Elect



Jessica Fry
Secretary/Treasurer



Hannah Hove
Nominations



Elizabeth Jones
Board Member at Large (1yr)



Michelle Steiner
Board Member at Large (2yr)



Luke Huff Towle
Ascending Professional



Samantha Urbanec
Developing Professional

Other Important Members of our Board

Sharon Reistad - Past President

Mary Coleman - PAC Chair & PACE Coordinator

Elaine Ramstead - GAC Chair

Jessica Fry - Web Master

Kyleen Newman and Heather Mayers - Newsletter

Bylaws Chair - Shannon Jongeward

Promotion of the Profession - Alice Hawley

Applications of LC-MS/MS in the Clinical Laboratory

Ethan Phommasy

University of North Dakota

Department of Medical Laboratory Science

INTRODUCTION

Liquid chromatography used in conjunction with tandem mass spectrometry (LC-MS/MS) is becoming increasingly utilized in clinical laboratories. The introduction of LC-MS/MS has allowed for the identification of several analytes simultaneously and the confirmation of positive immunoassays.¹ LC-MS/MS has become the gold standard for the determination of several analytes.¹ However, despite its superiority, clinical labs have been slow at implementing this methodology.² This article highlights the advantages of LC-MS/MS and several uses in a clinical laboratory setting.

DISCUSSION

The determination of low concentration analytes was made possible with the development of immunoassays.³ However, despite its simplicity, problems such as increasing cost, cross-reactivity, and variability have limited their use.³ LC-MS/MS methods have greater sensitivity and specificity and are becoming of greater use in clinical laboratories.³

The use of LC-MS/MS allows laboratories to develop a wide range of potential target analytes with greater sensitivity, specificity, precision, accuracy, and reproducibility.³ This has allowed laboratories to overcome the major limitations of immunoassays.³ Therefore, LC-MS/MS can be implemented in clinical laboratories to replace certain antibody-based methods that lack specificity.³

The detection of small quantities of a compound can pose analytical challenges in clinical laboratories. For example, hormones are generally found in low circulating concentrations in humans. Immunoassays that use antibody-based methods can be sensitive but may lack specificity.³ The accurate determination and quantitation of analytes are important for the diagnosis and treatment of several conditions. The current use of LC-MS/MS is greatly seen in therapeutic drug monitoring (TDM), endocrinology, and toxicology.⁴

Therapeutic Drug Monitoring

TDM is used in combination with pharmacokinetic and pharmacodynamic knowledge of drugs to provide individualized drug therapies.⁵ Optimizing drug therapies improve treatment outcomes, reduce side effects, and decrease the risk for drug resistance.⁵ TDM plays an essential role in the optimal use of critical dose drugs.⁶ Critical dose drugs have a narrow therapeutic window in which concentrations outside this range can have severe consequences.⁶ Therefore, TDM requires accurate and precise drug measurement.⁵

A therapeutic range is an essential requirement to optimize drug therapy.⁵ If the drug level stays within this defined range, therapeutic response and tolerability are assumed.⁵ However, if the measured

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MEET
Mary Dhuyvetter
45 year ASCLS ND member



I graduated from NDSU with a degree in Medical Technology after spending my senior year in an internship at St. Agnes Hospital in Fond du Lac, Wisconsin. I live on a farm southwest of Noonan, ND where my husband Tom farms. We have lived out here our entire married life and raised three sons who are now 40, 38 and 36.

When I chose the laboratory profession I wasn't entirely sure what I was getting into. I just knew I wanted to do something in the medical field but didn't really want to be a nurse. It turned out to be a good choice for me as I have really enjoyed working in the lab all these years.

I was encouraged to join ASCLS as a laboratory student. The organization became more important to me when I started working in a small rural hospital. It was nice to have a resource to keep current in new laboratory developments since the lab I worked in was small with few employees. I especially found the annual meetings in the spring to be a good way to network with others in my profession. When North Dakota became a licensure state, ASCLS was also a good source of CEU's.

I worked my entire career at St. Luke's Hospital in Crosby, ND. I retired June 2022 after 43 years. I had mixed feelings about retirement but so far am enjoying spending more time at home and with my five wonderful grandchildren.

2023 AWARD WINNERS

OMICRON SIGMA AWARD

<u>REGION V</u>	<u>STATE</u>
Christie Massen	Mary Coleman
Sharon Reistad	Elizabeth Jones
Mary Coleman	Jessica Fry
Tammy Windish	
Shannon Jongeward	

KEYS TO THE FUTURE



Allison Waswick
Alissa Volk
Luke Huff Towle



MEMBERSHIP AWARDS

Lauren Bratberg - 5 years
Rebecca Bakke - 5 years
Daniel Gains-Lewis - 5 years
Irene Sorum - 5 years
Mary Dhuyvetter - 45 years



Member of the Year!

For

2023



Alice Hawley

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value is below the therapeutic range, the response to treatment may not be adequate.⁵ If the value is above the range, toxicity may occur with severe consequences.

TDM is performed by the quantification of the drug and its main metabolites. Many therapeutic drugs are currently monitored using immunoassays.⁶ Although immunoassays allow laboratories to automate testing and provide high throughput, some therapeutic drugs lack specificity in immunoassay-based methods. LC-MS/MS allows for the hydrophobic separation of analytes combined with successive mass separations of tandem mass spectrometry.⁶ This makes LC-MS/MS highly sensitive and selective for drug analytes and an excellent method for TDM.⁶

Immunosuppressive Drugs

Immunosuppressive drugs (ISDs) such as cyclosporine A, tacrolimus, sirolimus, and everolimus are used in organ transplantations.⁷ Cyclosporine A and tacrolimus are classified as calcineurin inhibitors and produce cytokines to initiate lymphocyte proliferation.⁷ Sirolimus and everolimus work by blocking interleukin-2 (IL-2) production to inhibit T-cell cycle progression.⁷ These drugs are critical-dose drugs with a narrow therapeutic range.⁷ A low concentration of drugs in blood circulation may lead to organ rejection.⁷ At high blood levels, risk of toxicity including cardiotoxicity and nephrotoxicity may occur.⁷ Also, there is a risk for neurological effects and an increased risk of infections.⁷

The use of TDM of ISDs has become an important laboratory test as circulating drug concentrations can greatly impact clinical outcomes.⁷ The therapeutic range of ISDs can vary on the type of organ transplanted, age of the patient, other medications, and time after transplantation of antifung.⁷ Often these drugs are used in combination because of a similar mechanism of action and their synergistic effects when used together.⁷ Therefore, it is useful for laboratories to determine the concentration of ISDs simultaneously.⁷

The majority concentration of ISDs can be found inside erythrocytes with a small percentage bound to plasma proteins.⁷ Therefore, whole blood is the matrix of choice when determining drug concentration levels.⁷ There have been several analytical methods used to determine the concentration of ISDs such as several types of immunoassays and high-performance liquid chromatography (HPLC).⁷ However, immunoassays are prone to interferences such as heterophile antibodies and lack specificity. HPLC can have time-consuming extraction procedures and can often lack adequate chromatographic separation.⁷

High-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) is considered the gold standard in determining drug concentrations of cyclosporine A, tacrolimus, sirolimus, and everolimus in whole blood.⁷ HPLC-MS/MS shows greater sensitivity and specificity compared to other methods.⁷ This method generally has a simple sample preparation and allows measurement with low sample volumes. In addition, HPLC-MS/MS allows for simultaneous measurements of all four common ISDs.⁷

Antifungal Drugs

Invasive fungal infections are of great concern in high-risk patient populations such as those on immunosuppressive therapy.⁸ Invasive fungal infections are common in immunocompromised individuals and are associated with increased mortality and morbidity among this population.⁸ Triazole antifungals are used for the prevention and treatment of invasive fungal infections.⁸

Triazole antifungals such as voriconazole, posaconazole, and itraconazole inhibit lanosterol 14- α -demethylase, a cytochrome P450 dependent enzyme.⁸ Lanosterol 14- α -demethylase is used in

the conversion of lanosterol to ergosterol, an essential step of the cellular membrane of fungi.⁸ The inhibition of this conversion causes damage to the cell membrane, resulting in cell lysis and death.⁸

TDM of antifungal triazoles is essential as these drugs demonstrate large pharmacokinetic variability and pharmacokinetics.⁸ The use of triazoles has been associated with improved clinical response, decreased infections, and reduced mortality.⁸ However, use over a long period is associated with a high risk of side effects and toxicity. Therefore, TDM of antifungal agents is justified and is essential in the treatment of immunocompromised individuals.⁸

Like ISDs, antifungal concentrations are monitored to ensure efficacy and to avoid toxicity.⁸ However, triazole plasma concentrations have been shown to better correlate with their efficacy and are used to measure drug concentrations.⁸ HPLC-MS/MS can also be used in the measurement of concentrations and allows for greater specificity and sensitivity.⁸ Like ISDs, triazole antifungals can be measured simultaneously, reducing analytical time and cost.⁸

Other methods used in the quantification of triazole antifungals have been utilized. Conventional methods such as HPLC using liquid-liquid extraction (LLE) or solid-phase extraction (SPE) often lack sensitivity and selectivity with longer analysis time resulting in delayed turnaround times needed for TDM.⁸ Although SPE reduces ion suppression effects increasing sensitivity, it is unable to simultaneously measure all compounds.⁸ The rapid sample preparation, short analysis time, sensitivity, and selectivity make LC-MS/MS method suitable for determining triazole antifungal levels in laboratories providing TDM.⁸

Antibiotics

Antibiotics are one of the most widely prescribed drugs and the risk of developing resistance is rising.⁵ Optimizing the use of antibiotics can improve clinical outcomes and reduce the development of antimicrobial resistance.⁵ Also, adequate antibiotic treatment is necessary for patients with severe infections, especially in cases of sepsis.⁵

Classes of antibiotics work in different ways to treat bacterial infections. These drugs also vary in their therapeutic index.⁵ For example, penicillin has a wide therapeutic index, and TDM is not necessary.⁵ However, other classes of drugs such as aminoglycosides can have a narrow therapeutic range and pose the risk for dose-related toxic effects, therefore, TDM is necessary.⁵

TDM of antibiotics is used to achieve therapeutic success, prevent toxicity, and prevent antimicrobial resistance.⁵ Clinicians are increasingly using TDM of various antibiotics to ensure adequate response and to adjust the dosage to optimize patient treatment plans.⁵ Accurate measurements of drug analytes are crucial in TDM and therefore LC-MS/MS methods have been developed for the quantitation of several antibiotic groups.⁵

Anticancer Drugs

It is well known that cancer is one of the leading causes of death worldwide.⁵ New and developing cancer therapies have emerged such as oral targeted anticancer drugs directed against cancer-specific molecules and signaling pathways.⁵ In addition to surgery, chemotherapy, and radiation, cytotoxic drugs are used in the treatment of cancer.⁵

Anticancer drugs are classified into several categories including antimetabolites, molecular-targeting drugs, DNA-interacting agents, and monoclonal antibodies.⁵ These drugs are often dangerous to handle as



[Region V Leadership Academy](#) [Our Mission](#)

The ASCLS Region V Leadership Academy will provide guidance, education, and resources at the regional level to prepare ASCLS members for leadership roles in ASCLS, within the profession and the work place.

Are you looking for an opportunity to help you move into leadership roles both in ASCLS and in your career?

How about a way to network with other committed professionals who are as passionate as you?

Would you like the opportunity to learn from experienced professionals who are leaders in our field?

If any of this sounds appealing to you then the Region V Leadership Academy is for you.

Admission to the Region V Leadership Academy will be through a competitive application process.

The application deadline is August 1st!

Application and Recommendation Forms ([available here](#))

These are downloadable forms in Microsoft Word Format. Click on the appropriate link for each document.

Please complete electronically and submit as indicated.

HERD *the* MOOS?

ASCLS Region V
Symposium



Sept 28-29

Lismore Hotel
Eau Claire, WI



For more information or to register [click here](#),
or visit regionvascls.online

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they can damage normal tissue and are associated with severe side effects.⁵ Bone marrow suppression, hair loss, development of resistance can be caused by non-selectivity, a narrow therapeutic window, and the formation of inactive metabolites.

Anticancer drugs show significant variability following standard dosage regimens and may lead to increased drug concentration or decreased drug concentration.⁵ The use of TDM of anticancer drugs is important for decreasing side effects and establishing a therapeutic dose.⁵ Although LC-MS/MS methods have been developed for the quantification of different anticancer drugs, TDM of anticancer drugs is still rarely used in clinical practice.⁵

Endocrinology

Another use of LC-MS/MS application is clinical endocrinology.⁴ The two most common substance classes identified are endogenous steroids and biogenic amines (catecholamines, metanephrines) used as markers for neuroendocrine and cardiovascular disorders.⁴ Other LC-MS/MS assays include thyroid hormone, 1,25-dihydroxy-vitamin D, and peptide and protein analysis.⁴

LC-MS/MS assays are considered the reference standard for steroid hormone analysis and allow for accurate measurements and the quantification of several steroid hormones simultaneously.² Steroid hormones play an essential role in normal physiological function regulating a range of processes.² The abnormal production or metabolism of steroids can result in a wide range of endocrine conditions.² Therefore,



STATE MEETING A HUGE SUCCESS

The 2023 ND state meeting, which was held in Minot, was a great success and loads of fun. 2 full days of wonderful educational sessions along with a fun vendor social filled with great food, lots of door prizes and visitation with vendors and members. After the vendor session axt throwing was the name of the game. Thank you to the meeting committee for a great time

Sharon Reistad - Committee chair

Jessica Fry - Web master

Elizabeth Jones - Speaker Chair

Mary Coleman - PACE

Make plans to attend the 2024 meeting to be held in Bismarck (dates to be determined)



Attendees enjoying vendor social

Dinah Rauenhorst –Audit speaker & vendor



the accurate quantification of steroid hormones is essential for diagnostic and treatment monitoring.² However, measurements of steroid hormones can be complex due to similar structures of steroid hormones, precursors, and metabolites.²

For example, testosterone is a cholesterol-derived androgen (sex hormone) primarily produced in the Leydig cells in the testes and the theca cells in the ovaries.⁹ Testosterone is crucial in primary sexual development and regulation of secondary male characteristics.⁹ Also, it is necessary for the maintenance of bone density, muscle mass, and erythropoiesis.⁹ The measurement of testosterone is used in the diagnosis and treatment of hypogonadism, hyperandrogenism, as well as a biomarker to monitor supplementation in patients.⁹

However, the measurement of total testosterone with immunoassays can be significantly inaccurate. At low concentrations, testosterone measurement had limited accuracy with most commercially available immunoassays.⁹ Also, different testosterone immunoassays use different approaches, which contributes to the lack of comparison of results between platforms and laboratories.⁹

The implementation of LC-MS/MS of metanephrines and catecholamines in routine clinical settings has dramatically changed the field of pheochromocytoma and paraganglioma diagnosis.⁴ Historically, the detection of biogenic amines has been challenging but the development of an LC-MS/MS assay has allowed for greater sensitivity.⁴

Toxicology

Toxicology is composed of the detection and identification of drugs and other xenobiotics and/or their metabolites in human specimens.¹ Toxicology is often used in treatment decisions of patients or the documentation of the intake of drugs. The number of compounds that an intoxicated person has ingested may be high. This includes prescribed drugs, drugs of abuse, natural toxins (plants, mushrooms), and products such as acids, pesticides, and household chemicals.¹

In clinical laboratories, immunoassays are used as screening assays.¹ Immunoassays have relatively short analytical times and are readily available.¹ However, these assays only cover a small portion of the drugs that may be abused.¹ In addition, immunoassays can have cross-reactivities to compounds not belonging to the intended drug class, which may lead to false-positive results.¹

In larger clinical laboratories, LC-MS/MS methods have been implemented due to their specificity and capability of detecting multiple compounds simultaneously.¹ However, each laboratory needs to develop and validate its analytical method as commercially manufactured kits are not available.¹ Therefore, limiting the number of clinical laboratories offering LC-MS/MS toxicology.¹

LC-MS/MS methods in toxicology can be divided into two groups.¹ The first group is a targeted method for the identification of a limited number of compounds.¹ For example, used for the confirmation of a positive immunoassay.¹ The second group is known as general unknown screening aimed to identify every compound possible.¹

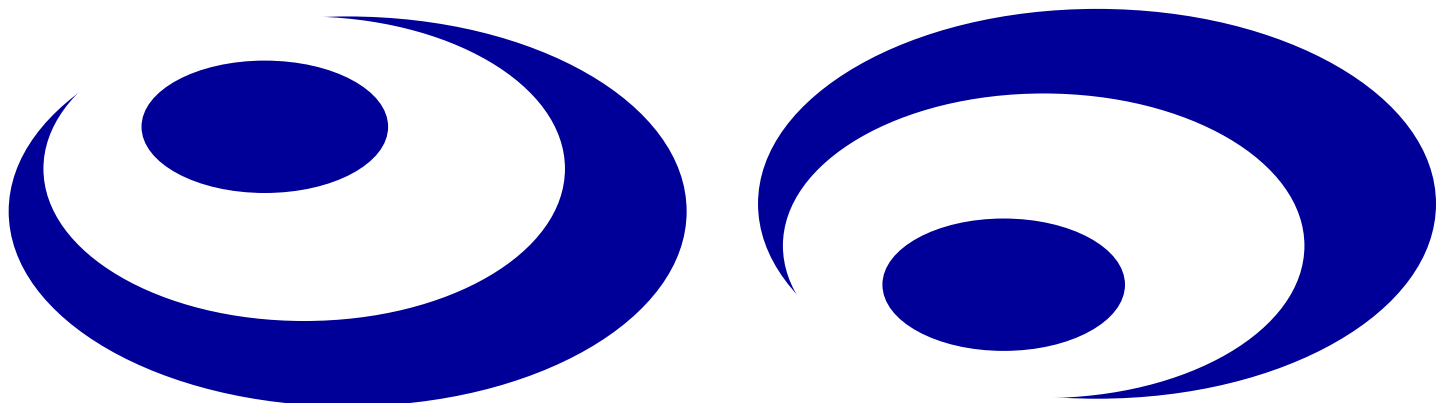
CONCLUSION

Liquid chromatography coupled to mass spectrometry assays is becoming increasingly utilized in clinical laboratories due to their high specificity, sensitivity, and the possibility for simultaneous quantification of different analytes. Routine applications have already been implemented in cases of TDM, endocrinology, and

toxicology. When used appropriately, measurement of analytes may help achieve treatment efficacy and optimize patient outcomes.

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STATE SCIENCE FAIR WINNERS

Each year the ASCLS ND organization donates \$300 to the State Science fair. 6 winners then receive \$50 each, 3 in the senior division and 3 in the junior division for projects related to laboratory medicine.

Below are the 2023 Science Fair Winners

Senior Division:

- Taylor Zenker, Flasher School district, “Synthetic vs Natural”
- James Cessey, Flasher School District, “Is It Worse Than Nicotine”
- Kaitlyn Hauge, Flasher School District, “Mask Efficacy”

Junior Division:

- Carrie LaDuke, Flasher School District, “The Effect Of Disinfectant Wipes On Bacteria”
- Jake Schlothauer, East Fairvier School District, “Sud Studies”
- Gracie Melberg, Tioga School District, “Dandelions & Their Health Benefits”



Congratulations to ASCLS ND Scholarship Recipients.

- Benjamin Pratt
- Jacob O’Toole
- Seneca Vetter

Learn how you can apply to win a scholarship. Visit ASCLS-ND