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Patient Access to Lab Results Via Electronic Health Records

Patient Portals Can Raise Questions About Drug and Toxicology Testing

By Matthew D. Krasowski, MD, PhD

Electronic health records (EHRs), also known as electronic medical records, are common in many industrialized countries (1,2). EHRs store patient health information, allowing authorized users to access this information securely and efficiently. Recently, applications have been developed that allow patients to access their health information from the EHR via online "patient portals" (3–5).

In the U.S., legislative and regulatory initiatives such as the Health Information Technology for Economic and Clinical Health Act promote the use of patient portals to encourage patient involvement in healthcare decisions (6). The act also includes financial incentives and penalties that have driven adoption of EHRs by physician practices, approximately 90% of which now use EHRs. Two of the most widely used patient portals in the U.S. are My HealtheVet (Department of Veterans Affairs) (7) and MyChart (Epic, Inc.) (8).

EHR patient portals are one mechanism by which patients or their delegates can access protected health information that traditionally was available only through hard copies provided by the healthcare team or through formal medical record requests.

Portals Popular

The portals are popular among patients, leading healthcare institutions to work to increase portal use and functionality (5,9,10). In theory, patient portals can streamline otherwise time-consuming tasks such as appointment scheduling and cancellation, prescription refill requests, phone calls for nonurgent issues, and mailing hard copies of test results or referral letters. Patients can download health information such as clinic notes, inpatient discharge summaries, medication lists, immunization records, and growth charts. Patient portal use has been shown to improve healthcare coordination and communication between patients and their healthcare teams (11–13).

Institutions that offer patient portals typically establish a process for patients to activate their accounts, with security safeguards to limit access to unauthorized information (11–13). Depending on local statutes and institutional policy, parents and legal guardians can obtain "proxy" portal access to health information of their dependents.

Appointment scheduling, prescription refills, laboratory results, radiology imaging reports, and direct messaging with the healthcare team are some of the most popular features of patient portals.

In the U.S. and Europe, multiple studies have shown that the most frequent users of patient portals tend to be Caucasian, female, and adults aged 25 to 50 years (7,8,10,14). Factors that impact use of patient portals include fluency with the language used in the EHR, comfort and familiarity with using the Internet, broadband Internet access, healthcare literacy, support and assistance from family and friends, and encouragement by the healthcare team. Although the functions of patient portals apply most commonly in the ambulatory/outpatient setting, recent efforts have focused on developing applications for the inpatient setting (for example, ordering meals and sending nonurgent questions to the clinical team) (15–17).

Issues with Releasing Lab Results

Most patient portals release diagnostic test results (laboratory results and radiology imaging reports), although institutions vary in their practices for doing so (2,8,18–20). No government regulations delineate overall policies on the release of test re-

Continued on page 2

Inside...

Patient Portals

Continued from page 1

sults through patient portals, but some local statutes apply to specific tests. For example, in some states statutes mandate that patient counseling must occur before positive human immunodeficiency virus (HIV) results may be released. These laws preclude unrestricted release of HIV results through a patient portal (19).

The release of diagnostic test results can involve ethical and safety implications, particularly with those that are abnormal, challenging to interpret, or convey unfavorable news (19). Examples include laboratory results that indicate diagnosis or recurrence of cancer or the presence of a life-threatening chronic disease such as HIV. On the other hand, a delay in releasing results may increase patient angst caused by waiting.

There are many approaches to releasing laboratory test results to the patient portal once the result is finalized in the EHR (19,20). The simplest is to release the result immediately after it appears in the EHR (unrestricted release). Based on the author's experience, this approach is not common, at least as a global policy for laboratory tests. However, some institutions have moved toward rapid release for common tests such as electrolytes, liver enzymes, and pregnancy tests.

Restricting Release

Most institutions restrict the release of results, and there are many possible approaches to doing so (19,20). One approach is to release results after an authorized healthcare provider has reviewed them in the EHR. This release can be done by clicking a button for a result or set of results. This "manual release" potentially allows results to be released quickly after becoming available in the EHR. The healthcare provider may add some comments or annotations such as a brief interpretation with reassurance of a normal result or the need for follow-up.

An alternative approach is to automatically release results at a specified time after finalized results appear in the EHR (auto-release) (19,20). At institutions that allow for manual release of test results to the patient portal, auto-release can occur if a provider does not release the results within a specified time range.

Depending on functionality of the patient portal, multiple categories of auto-release can be created for different types of laboratory tests. For example, routine laboratory tests (such as electrolytes, urinalysis, blood glucose, complete blood count, and prothrombin time) may be in a faster auto-release category than more sensitive tests, such as tumor markers, surgical pathology reports, and genetic tests.

Routine tests may be released on the same day, next business day, or after one business day, whereas more sensitive tests may have an auto-release window of four or seven business days to allow more thorough review by the healthcare provider. Finally, some tests may be designated as "do not release" and never appear in the patient portal. These may include HIV testing (as discussed above) and genetic or biochemical tests that require face-to-face counseling due to the serious implications of the diagnosis, such as Huntington's disease gene testing.

Auto-Release Challenges

There are challenges regardless of the auto-release strategy adopted. Rapid auto-release practices can lead to patients viewing their results before busy providers have had a chance to review and discuss them with the patient in person or by phone. This may present no problems for test results that are normal, were expected, or discussed as possibilities. At my own institution (an academic medical center in Iowa), we documented rare cases where patients were distressed by seeing concerning results, such as recurrence of cancer, in the patient portal prior to communication with the clinical team. These cases occurred with both auto-release and manual release when information was inadvertently released earlier than intended. The cases led to safety alerts and educational efforts. Slower auto-release can increase patient angst for what may ultimately be a normal and reassuring result.

More complex strategies for auto-release include releasing "normal" results, such as a negative screen or a value within the reference range, earlier than abnormal results. This strategy has appeal for tests like sexually transmitted disease testing or tumor markers. One potential challenge is that patients who do not see a result appear quickly may infer that the result is abnormal, even if final interpretation of a positive result is pending confirmatory testing.

Iowa Studies on Portals

Even though laboratory test access is a popular feature of patient portals, there is relatively little literature on institutional experience with this practice. The author and colleagues have published several studies analyzing patient access to laboratory results at the University of Iowa Hospitals and Clinics, an 811-bed academic medical center in Iowa City (18–20). Several trends are evident.

First, the patterns of access to laboratory test results parallel the broader trends in EHR usage, with higher viewing by Caucasians, females, and patients aged 18–50. Viewing of laboratory tests is also high among patients under the age of 11, where the access is by proxy by the parent or legal guardian.

Second, patients view laboratory tests in the portal far more frequently when the tests are ordered in the outpatient setting than in inpatient and emergency department settings. This is likely influenced in part by institutions advertising their portals to out-

patients. The large numbers of tests ordered in some inpatient encounters may also impact viewing. Outpatients who have activated their accounts view tests at rates of 60–70%. When all patients, including those who never activate their accounts, are included, viewing rates are around 30–40%. In contrast, viewing rates of inpatient and emergency department tests are below 10% overall.

Third, the most frequently viewed laboratory tests are those for sexually transmitted disease, pregnancy, thyroid function, glucose metabolism, and hematology.

Implications for Toxicology and Drug Testing

At the University of Iowa, patient portal view rates for drugs of abuse/toxicology testing and therapeutic drug levels tended to be near the median view rates for laboratory tests ordered in similar settings (outpatient, inpatient, and emergency department). However, these test results triggered a disproportionately high rate of patient phone calls to the laboratory director. These calls increased after the introduction of the patient portal, and a high percentage of patients indicated they accessed the results in the portal. Their questions to the laboratory director fell into several broad categories.

The first category related to drugs of abuse screening and confirmatory testing, with the patient often challenging or disputing positive screening results. Some were prompted by automobile insurance or workplace injury claims affected by positive drug results. Interestingly, many patients indicated that the opportunity to view these results prompted them to activate their portals.

The second category involved questions related to interpretation of quantitative values and units. The most common question in this category related to concentrations of ethanol for serum/plasma (mg/dL) compared with blood-alcohol testing in percent v/v. Another interesting example was that many patients misinterpreted osmolal gaps that were negative numbers, confusing -18 for +18. These patients thought the negative sign was a dash and wondered why the value did not flag as abnormal as it appeared to be above the abnormal limit. Our laboratory staff had never encountered this question from healthcare professionals.

The last category involved confusion between interpretive comments and the actual result. In the author's experience, this confusion was more common when results were viewed online rather than on a hard copy, and resulted from formatting inconsistencies between the electronic and paper results. In the toxicology realm, this issue occurred most frequently with the institutional panel for workup of possible toxic alcohols and glycols, which included tests needed for osmolal gap calculation (osmolality, sodium, blood urea nitrogen, glucose) along with a plasma ethanol level and a calculated osmolal gap that accounted for the estimated contribution of ethanol (21). This panel included a detailed interpretive comment intended for healthcare providers that was appended to the result component for the osmolal gap, explaining its calculation and interpretation. The comment would be visible to healthcare providers viewing the EHR only after they double-clicked on the result component. In the patient portal, the result and comment appeared together without any additional clicks. Patients were confused by the comment, mistaking it as part of the laboratory result.

This issue was seen with some other laboratory tests as well. For example, after the institution changed the testing algorithm for syphilis testing, some patients read a comment explaining the change in testing protocol and erroneously concluded that their test results were positive when in fact they were negative. These phone calls led us to adjust the portal for the toxic alcohol/glycol panel and syphilis tests to display the interpretive comment only for positive results to limit patient confusion.

Summary

EHR patient portals are an increasingly popular tool for patients to access their protected health information, including laboratory test results. There is significant inter-institutional variability in laboratory test release strategies and little consensus on best practices. Clinical laboratory professionals should be aware of patient portal policies and provide input into procedures. As illustrated by the examples above, patients viewing their toxicology and drug testing results through patient portals can lead to confrontational questions for the clinical laboratory director.

Learning Objectives

After reading this article, the reader will be able to describe the basic features of electronic health record patient portals, including access to laboratory test results, and identify potential challenges with manual as well as auto-release of laboratory test results.

References

1. Adler-Milstein J, DesRoches CM, Kralovec P, et al. Electronic health record adoption in US hospitals: progress continues, but challenges persist. Health Aff (Millwood) 2015;34:2174–80.
2. Kern LM, Edwards A, Kaushal R, et al. The meaningful use of electronic health records and health care utilization. Am J Med Qual 2016;31:301–7.
3. Fix GM, Hogan TP, Amante DJ, et al. Encouraging patient portal use in the patient-centered medical home: three stakeholder perspectives. J Med Internet Res 2016;18:e308.
4. Gheorghiu B, Hagens S. Use and maturity of electronic patient portals. Stud Health Technol Inform 2017;234:136–41.
5. Griffin A, Skinner A, Thornhill J, et al. Patient portals: Who uses them? What features do they use? And do they reduce hospital readmissions? Appl Clin Inform

2016;7:489–501.
6. Mennemeyer ST, Menachemi N, Rahurkar S, et al. Impact of the HITECH Act on physicians' adoption of electronic health records. J Am Med Inform Assoc 2016;23:375–9.
7. Nazi KM, Woods SS. MyHealtheVet PHR: a description of users and patient portal use. AMIA Annu Symp Proc 2008:1182.
8. Redelmeier DA, Kraus NC. Patterns in patient access and utilization of online medical records: analysis of MyChart. J Med Internet Res 2018;20:e43.
9. Curtis J, Cheng S, Rose K, et al. Promoting adoption, usability, and research for personal health records in Canada: the MyChart experience. Healthc Manage Forum 2011;24:149–54.
10. Irizarry T, Shoemake J, Nilsen ML, et al. Patient portals as a tool for health care engagement: a mixed-method study of older adults with varying levels of health literacy and prior patient portal use. J Med Internet Res 2017;19:e99.
11. Kruse CS, Bolton K, Freriks G. The effect of patient portals on quality outcomes and its implications to meaningful use: a systematic review. J Med Internet Res 2015;17:e44.
12. North F, Crane SJ, Chaudhry R, et al. Impact of patient portal secure messages and electronic visits on adult primary care office visits. Telemed J E Health 2014;20:192–8.
13. Pillemer F, Price RA, Paone S, et al. Direct release of test results to patients increases patient engagement and utilization of care. PLoS One 2016;11:e0154743.
14. Gerber DE, Laccetti AL, Chen B, et al. Predictors and intensity of online access to electronic medical records among patients with cancer. J Oncol Pract 2014;10:e307–12.
15. Walker DM, Menser T, Yen PY, et al. Optimizing the user experience: identifying opportunities to improve use of an inpatient portal. Appl Clin Inform 2018;9:105–13.
16. Winstanley EL, Burtchin M, Zhang Y, et al. Inpatient experiences with MyChart bedside. Telemed J E Health 2017.
17. Yen PY, Walker DM, Smith JMG, et al. Usability evaluation of a commercial inpatient portal. Int J Med Inform 2018;110:10–8.
18. Foster B, Krasowski MD. The use of an electronic health record patient portal to access diagnostic test results by emergency patients at an academic medical center: retrospective study. J Med Internet Res 2019;21:e13791.
19. Krasowski MD, Grieme CV, Cassady B, et al. Variation in results release and patient portal access to diagnostic test results at an academic medical center. J Pathol Inform 2017;8:45.
20. Oest SER, Hightower M, Krasowski MD. Activation and utilization of an electronic health record patient portal at an academic medical center—impact of patient demographics and geographic location. Acad Pathol 2018;5:2374289518797573.
21. Krasowski MD, Wilcoxon RM, Miron J. A retrospective analysis of glycol and toxic alcohol ingestion: utility of anion and osmolal gaps. BMC Clin Pathol 2012;12:1.

Matthew D. Krasowski, MD, PhD, is a clinical professor and vice chair of clinical pathology and laboratory services in the department of pathology at the University of Iowa Hospitals and Clinics in Iowa City. He chairs the editorial advisory board of Clinical & Forensic Toxicology News*. E-mail: mkrasows@healthcare.uiowa.edu.*

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MSACL Conference Covers a Variety of Toxicology Subjects

By Bridgit O. Crews, PhD

The annual Mass Spectrometry: Applications to the Clinical Lab (MSACL) Conference and Exhibits took place in Palm Springs, CA, from April 2 to 4. More than 800 attendees from 27 different countries participated, with over 135 attendees receiving educational grants to attend or present their work.

On the first day, a state-of-the-science address included updates in data science, tissue imaging, proteomics, and small molecule analysis. The opening plenary provided an overview of exosomes and efforts to isolate and quantify changes in the exosomal proteome of patients being treated for locally advanced cancer (1).

The second day was packed with six scientific tracks and several keynote presentations. The keynotes included a talk on the applications of matrix-assisted laser desorption ionization imaging mass spectrometry for the evaluation of drug distribution and molecular changes in tissues, and the impact the technique is having on understanding pharmacology and disease pathogenesis. A second keynote elucidated machine learning as it is being applied to data analysis and quality assessment (2,3).

Toxicology Sessions

Toxicology-focused sessions covered noninvasive matrices (oral fluid and breath) for analysis of cannabinoids as well as for comprehensive pain management testing. The afternoon offered practical training in the interpretation of urine drug testing for pain management and discussion of several cases demonstrating utility of quantitative analysis (4–6). Environmental contaminant exposure was the focus of another track, with presentations on urinary markers of volatile organic compounds and environmental exposure to antibiotics during pregnancy (7,8).

A session on new analytical approaches evaluated multi-point internal calibration for rapid quantitation of methotrexate in a single injection and remote monitoring of immunosuppressant levels for pediatric renal transplant patients (9,10). A special session covered nonspecific binding issues in liquid chromatography-tandem mass spectrometry (LC-MS/MS)

and an overview of methods for evaluation of non-specific binding and tips for dealing with it (11).

A highlight of Wednesday was an award lecture that described several recent scientific breakthroughs in cancer immunotherapy, including use of mass spectrometry to characterize proteins and peptides related to cancer immunotherapy (12).

The third day continued with a focus on toxicology applications and practical training. There were several presentations on applications of mass spectrometry for emergency toxicology screening, therapeutic drug monitoring, and paired maternal and neonatal urine drug screens (13). A session covering automation of mass spectrometry data review, results entry, and quality monitoring rounded out the day (14,15).

Industry-Sponsored Sessions

Other highlights of the conference included industry-sponsored sessions focused on topics such as the art of LC-MS/MS data review and advances in cloud-based, automated LC-MS/MS data-review platforms. Guided poster walks offered attendees an opportunity to interact with the presenters in group discussions, and there were structured opportunities to connect with experts in various fields of clinical mass spectrometry during "meet-a-mentor" roundtable sessions.

The meeting offered an abundance of practical training that covered many topics related to clinical mass spectrometry. This synopsis summarizes only a few toxicology highlights, as there were more than 100 oral presentations and 180 posters presented on quantitative protein analysis, metabolomics, and informatics, in addition to over 40 vendor exhibits.

MSACL also offered training workshops in the days leading up to the meeting. This year's topics included method development and validation, practical liquid chromatography-mass spectrometry troubleshooting, and an introduction to R statistical programming. A two-day workshop on forensic toxicology was well-attended, which is a testament to the toxicology community's commitment to continuing education.

References

Abstracts Presented at MSACL Meeting

1. Lubman D. Analysis of exosomes from patient serum samples: proteomic, metabolomics, and lipidomic analyses.
2. Castellino S. MALDI imaging MS: transforming drug discovery and development through molecular images of biological systems.
3. Eshghi S. Toward automated quality assessment and analysis of targeted mass spectrometry data using machine learning.
4. Hubbard J. Cannabinoid concentrations in whole blood, oral fluid, and breath after recent use.
5. Badea A. A high resolution mass spectrometry method for detecting a comprehensive pain-management drug panel in oral fluid.
6. Saitman A. Interpretation of urine drug testing results for pain management (including contributions from French D, Strathmann F, and Pesce A).
7. De Jesus V. Analysis of urinary biomarkers of exposure to volatile organic compounds from the population assessment of tobacco and health (PATH) study (wave1).
8. Cao Z. Environmental antibiotic exposure in pregnancy.
9. Hoffman M. Multi-point internal calibration: IntrinsiX LC-MS/MS analysis of methotrexate.
10. Dickerson J. The impact of remote monitoring in pediatric renal transplant patients: multiplexed quantification of immunosuppressants and creatinine by LC-MS/MS.
11. Henion J. Resolving non-specific binding in qLC-MS/MS.
12. Hunt D. Immunotherapy of cancer and the role of mass spectrometry: an overview and new results.
13. Roper S. Concordance of paired maternal and newborn urine drug screens using low cutoffs for positivity.
14. Beppler B. No typing allowed: reflections and advice one year after automating all mass spectrometry results entry at a regional clinical reference laboratory.
15. Haymond S. Monitoring clinical mass spectrometry system performance.

Bridgit O. Crews, PhD, DABCC, TC, is an assistant clinical professor of pathology and laboratory medicine and director of clinical chemistry and toxicology at the University of California Irvine Medical Center in Orange as well as a member of the Clinical & Forensic Toxicology News *board of editors. Email: crewsb@uci.edu.*

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Kratom's Opioids Can Lead to Neonatal Abstinence Syndrome

Increasing Number of Case Reports Are Appearing in the Literature

By Sarah Shugarts, PhD

Chronic pain, defined as pain lasting longer than three months, was estimated to affect 20% of Americans in 2016 (1,2). Although the efficacy of treating chronic pain with opioids is debatable, as many as one in five people receive prescription opioids long-term for non-cancer pain in primary-care settings (3). A recent poll by the American Psychiatric Association found that about one third of Americans say they know someone who is or has been addicted to opioids or prescription pain killers (4). Data from the Centers for Disease Control and Prevention show that opioid overdose deaths have risen steadily in the U.S., increasing from about 8000 in 1999 to just under

48,000 in 2017 (5).

As awareness spreads about the dangers of opioid use, some people are turning to legal alternatives to self-treat pain, anxiety, and opioid withdrawal symptoms. The users perceive these alternatives as safer, and they are easy to obtain.

Kratom

Kratom, a natural product derived from the *Mitragyna speciosa* tree endemic to southeast Asia, is such an alternative. Estimates of the prevalence of its use in the U.S. vary widely, ranging from several hundred thousand to 4 to 5 million users (6). Although the Drug Enforcement Administration and Food and Drug Administration have discussed changing its classification to a Class I substance, kratom is still legal in the U.S., except where local jurisdictions have banned it, as in Alabama, Arkansas, District of Columbia, Indiana, Rhode Island, Tennessee, Vermont, and Wisconsin (6,7,8). Kratom can be obtained without a prescription over the Internet and in smoke shops in a variety of formulations, including powders, capsules, tablets, dried leaves, and concentrated extracts.

Opioid Activity

Kratom has gained attention because of its opiate-like activity, which is caused by two compounds—the indole alkaloids mitragynine and 7-hydroxymitragynine. Both compounds have mu and kappa opioid receptor as well as $\alpha 2$ adrenergic receptor agonist activity (9). Mitragynine is present in kratom leaves in much higher amounts than 7-hydroxymitragynine, but 7-hydroxymitragynine is reported to be 46 times more potent. It is 17 times more potent than morphine, making it comparable to acetylfentanyl and furanylfentanyl (10). At low doses, kratom produces stimulant effects. High doses lead to sedative-narcotic effects.

With the increased use of kratom, reports of adverse events are increasing. The American Poison Control Centers reported nearly 2,000 kratom exposures from 2011 to 2017, with more than half occurring in the last two years (11). Commonly reported adverse effects include nausea and constipation, sleep disturbance, itching, sweating, and temporary erectile dysfunction. Long-term use has been reported to cause hyperpigmentation, tremor, anorexia, and weight loss. As one would expect based on its interaction with opioid receptors, cessation of kratom use is reported to lead to withdrawal symptoms, including muscle aches and jerking, irritability, mood disturbance, diarrhea, and rhinorrhea.

Neonatal Abstinence Syndrome

The reports of neonatal abstinence syndrome (NAS) in babies whose mothers used kratom during pregnancy are particularly disturbing. NAS is a constellation of symptoms including central nervous system, metabolic, vasomotor, respiratory, and gastrointestinal disturbances (12).

Treatment for NAS varies among institutions, with some using pharmacologic treatment in neonatal intensive care units and others using a nonpharmacologic approach focusing on low-stimulation environments and bonding with the mother. Whatever treatment is provided, babies with NAS require longer hospital stays (median 19 days) than babies without NAS and no other health problems (2–3 days) (13). The National Institute on Drug Abuse reports that hospital costs for treatment of NAS increased from $90.9 million in 2004 to $563 million in 2014 (14).

Case Reports

Murthy and Clark from the University of Calgary in Alberta were some of the first to publish a case of NAS suspected to be due to kratom ingestion. After a healthy cesarean delivery, the infant displayed symptoms of opiate withdrawal (irritability, excessive sucking, and sleep disturbance) at 12 hours post-birth. Providers often assess the severity of NAS using the Finnegan Neonatal Abstinence Scoring System, which assigns points based on presence and severity of withdrawal symptoms. Three continuous scores ≥ 8 or two continuous scores ≥ 12 are the cutoffs to identify infants who may need pharmacological treatment for withdrawal (15).

The infant had a modified Finnegan score of 18, so was admitted to the neonatal intensive care unit at 22 hours post-birth (16). Further investigation revealed that the mother had used kratom tea three to four times daily during pregnancy to alleviate symptoms of anxiety and restless leg syndrome. She had no other history of opiate use. The mother rapidly detoxified from kratom over seven days, but the baby continued morphine treatment for a little over two months.

Eldridge et al. reported a case of NAS in an infant born to a mother who had successfully completed rehab for oxycodone dependence and had not used opiates in the two years prior to delivery. She tested negative on opioid immunoassay screening on admittance for delivery, but at 33 hours the infant displayed symptoms of opiate withdrawal with modified Finnegan scores ranging from 9 to 14. Upon further interview, the father revealed that the mother had used kratom tea daily during pregnancy to help with sleep and withdrawal symptoms. The baby was treated with clonidine and discharged on day 8 (17).

Mackay et al. describe a case in which a mother consumed 50 to 60 g of powered kratom daily during pregnancy to treat chronic back pain and anxiety two years after going through detoxification for oxycodone abuse. Her infant was treated with morphine. The mother also received morphine treatment after the birth to wean her off kratom prior to discharge (18).

Davidson et al. describe a case of a mother who

took 5 to 15 g of kratom daily during pregnancy as an over-the-counter herbal supplement in a tablet formulation. The mother had chronic low back pain, fibromyalgia, and anxiety for which she was taking prescribed gabapentin and clonazepam. The infant began to exhibit withdrawal symptoms 24 hours after birth with modified Finnegan scores of 10 and above. The infant received morphine treatment for NAS and was discharged 14 days after birth (19).

Smid et al. reported two cases of treating kratom withdrawal in pregnant women. Both women presented to their care providers with the desire to wean themselves off kratom to decrease risk to their fetuses. Both women had attempted to self-wean but experienced withdrawal symptoms. One woman was successfully treated with buprenorphine, and her baby exhibited no symptoms of NAS. The other woman was treated with buprenorphine-naloxone, and her baby received treatment with morphine for NAS symptoms (20).

The recent cases in the U.S. and Canada were all published in 2018–9, with no previously published reports. This timing indicates that NAS due to kratom use is a relatively new phenomenon in North America. The cases reviewed in this article illustrate the importance of raising awareness among OB-GYNs so they can counsel their patients about the dangers of using kratom during pregnancy, identify patients with unmanaged pain so appropriate treatment can be provided, and identify patients who would benefit from supervised opiate replacement therapy.

Learning Objectives

After reading this article, the reader will be able to summarize risks of using kratom during pregnancy and list the active compounds in kratom responsible for its opiate-like effects.

References

1. National Institutes of Health. Medline Plus. Chronic pain: symptoms, diagnosis, and treatment. Spring 2011. https://medlineplus.gov/magazine/issues/spring11/articles/spring11pg5-6.html (Accessed June 2019).
2. National Institutes of Health. National Center for Complementary and Integrative Health. Defining the prevalence of chronic pain in the United States. Sept. 14, 2018. https://nccih.nih.gov/research/results/spotlight/Prevalence-of-Chronic-Pain (Accessed June 2019).
3. American Physical Therapy Association. 7 staggering statistics about America's opioid epidemic. https://www.moveforwardpt.com/resources/detail/7-staggering-statistics-about-america-s-opioid-epi (Accessed June 2019).
4. American Psychiatric Association. Nearly one in three people know someone addicted to opioids; more than half of millennials believe it is easy to get illegal opioids. May 7, 2018. https://www.psychiatry.org/newsroom/news-releases/nearly-one-in-three-people-know-someone-addicted-to-opioids-more-than-half-of-millennials-believe-it-is-easy-to-get-illegal-opioids (Accessed June 2019).
5. National Institute on Drug Abuse. Overdose death rates. January 2019. https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates (Accessed June 2019).
6. White CM. Pharmacologic and clinical assessment of kratom. Am J Health Syst Pharm 2018;75:261–7.
7. Henningfield JE, Fant RV, Wang DW. The abuse potential of kratom according the 8 factors of the controlled substances act: implications for regulation and research. Psychopharmacology (Berl) 2017;235:573–89.
8. Wallace F. American Kratom Association. Is it illegal to fly with kratom within the United States? Dec. 24, 2018. http://speciosa.org/is-it-illegal-to-fly-with-kratom-within-the-united-states/ (Accessed June 2019).
9. Cinosi E, Martinotti G, Simonato P, et al.. Following "the roots" of kratom (*Mitragyna speciosa*): the evolution of an enhancer from a traditional use to increase work and productivity in southeast Asia to a recreational psychoactive drug in western countries. Biomed Res Int 2015;2015:1–11.
10. Horie S, Koyama F, Takayama H, et al. Indole alkaloids of a Thai medicinal herb, *Mitragyna speciosa*, that has opioid agonistic effect in guinea-pig ileum. Planta Med 2005;71:231–6.
11. Post S, Spiller HA, Chounthirath T, et al. Kratom exposures reported to United States poison control centers: 2011–2017. Clin Toxicol (Phila) 2019 Feb 20:1–8. doi: 10.1080/15563650.2019.1569236
12. D'Apolito K. March of Dimes Foundation. Assessment of neonatal abstinence. https://www.marchofdimes.org/nursing/modnemedia/othermedia/slidemodules/sm04_neonatal_abstinence_TEXT.pdf (Accessed June 2019).
13. Tolia VN, Patrick SW, Bennett MM, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N Engl J Med 2015 372: 2118–26.
14. National Institute on Drug Abuse. Dramatic increases in maternal opioid use and neonatal abstinence syndrome. January 2019. https://www.drugabuse.gov/related-topics/trends-statistics/infographics/dramatic-increases-in-maternal-opioid-use-neonatal-abstinence-syndrome (Accessed June 2019).
15. Gomez-Pomar E, Finnegan LP. The epidemic of neonatal abstinence syndrome, historical references of its origins, assessment, and management. Front Pediatr 2018 Feb 22;6(33), doi: 10.3389/fped.2018.00033
16. Murthy P, Clark D.. An unusual cause for neonatal abstinence syndrome. Paediatr Child Health 2018;24:12–4.
17. Eldridge WB, Foster C, Wyble L. Neonatal abstinence syndrome due to maternal kratom use. Pediatrics 2018;142(6), doi: 10.1542/peds.2018-1839
18. Mackay L, Abrahams R. Novel case of maternal and neonatal kratom dependence and withdrawal. Can Fam Physician 2018;64:121–2.
19. Davidson L, Rawat M, Stojanovski S, et al. Natural drugs, not so natural effects: neonatal abstinence syn-

drome secondary to 'kratom.' J Neonatal Perinatal Med 2019;12:109–12.
20. Smid MC, Charles JE, Gordon AJ, et al. Use of kratom, an opioid-like traditional herb, in pregnancy. Obstet Gynecol 2018;132:926–8.

Sarah Shugarts, PhD, DABCC, TC, is technical director of toxicology at Kaiser Permanente Regional Laboratory in Richmond, CA. Email: sarah.b.shugarts@kp.org.

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- American Society for Clinical Laboratory Science
- American Society for Clinical Pathology
- American Medical Technologists
- Association of Clinical Scientists
- International Federation of Clinical Chemistry
- National Registry in Clinical Chemistry
- States of California, Florida, Louisiana, Montana, Nevada, North Dakota, Rhode Island, and West Virginia

Learning Objectives

Learning objectives vary by article, but in general, after completing *Clinical & Forensic Toxicology News*, the reader will be able to:

- Describe emerging and changing trends in drug abuse, including new designer drugs, usage patterns, and contaminants/adulterants.
- Identify potential analytes (drugs, metabolites, biomarkers) of clinical and/or forensic significance.
- Evaluate methodologies for their utility and limitations relative to the needs of toxicology labs.
- Discuss relevant regulations, such as analytical performance requirements, or the legality of new drugs of abuse.
- Explain the analytical and regulatory issues unique to specific applications, including postmortem toxicology, workplace drug testing, and drug screening.
- Describe the medical implications of drug abuse, toxicity associated with therapeutic agents, and exposure to other toxicants.

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