CLINICAL & FORENSIC

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Khat

Should a Drug With Centuries of Legal Use and Cultural Heritage Be Banned?

By Samir Aleryani, PhD, FACB, MT(ASCP), CLS(NCA)

Khat (*Catha edulis forsk*) is a plant that is chewed as a stimulant in several cultures. It is widely cultivated in four primary countries: Kenya, Ethiopia, Somalia, and Yemen. The first three of these are in the Horn of Africa, and the last is on the tip of the Arabian Peninsula. The people of these countries have chewed leaves from khat shrubs for many centuries, and this use is deeply rooted in their cultures.

Khat is chewed like loose tobacco during what is known as a "khat session" or "chewing session." In a khat session, people meet in the afternoon to chew the plant. Male chewing sessions are generally at the home of a friend and attended by all ages. Female sessions may be held at the same time, but the sexes gather separately. Children as young as eight years old may accompany their parents and sometimes chew khat, too.

Khat sessions are held for a variety of reasons, including celebrating a wedding, extending funeral condolences, discussing politics, resolving social issues facing a community, attending a soccer game, or holding a poetry contest. Khat users may discuss ideas; celebrate the arrival of a baby; and resolve conflicts between tribes, families, and friends and thus bypass court proceedings. Most sessions begin after lunch in the early afternoon and continue for several hours. Most sessions end by 6 p.m. At times, a meeting can start as early as 10 a.m. and last until midnight. Morning khat use is very rare, and khat is not allowed at workplaces.

Khat chewers buy their plants from local markets around noon, when khat starts arriving from farms. Purchasers wash it with water, dry it, and wrap it in a plastic bag to keep it fresh but not wet. The small young leaves, tender shoots, and red stems are rich with juicy fluid and thus believed to contain more of the active ingredients, the stimulants cathinone and cathine (Figures 1 and 2). Chewed khat mixes with saliva and is swallowed. The fluid generally tastes sweet, but can be bitter, depending on the place of origin and type.

Cathinone is absorbed slowly, with plasma concentrations peaking in 2 hours (127 ng/mL). Cathine and norephederine levels peak at 3 hours (89 ng/mL and 110 ng/mL, respectively) (1). Users try not to swallow the leaves, keeping a wad in the cheek, where the mouth's mucous membranes absorb the cathinone and cathine and get them into the blood stream quickly.

The price of khat ranges from $5 to $100 for 200–300 g of leaves, depending on factors such as freshness, softness, and place of origin. Fresh, softer leaves are more expensive than harder leaves, which contain less juice. There are hundreds of kinds of khat, usually named for the region or village where each is grown. Good quality khat is associated with these names.

Why Chew Khat?

Cathinone and cathine lead to symptoms including a feeling of euphoria, increased energy, increased self-esteem, and mood swings. Khat chewers' moods can vary from happiness to sadness, depending on the khat's country of origin, potency, and freshness. Most symptoms level off as soon as a user removes the leaves from the mouth. Some symp-

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toms, including energy level, dry mouth, depressed mood, irritability, and loss of appetite begin immediately and can continue for an extended time, even into the next day for most users. Some users even experience them for a few days.

As mentioned earlier, khat use is widespread and not limited to any gender or group. In Yemen, for example, students from middle to graduate school chew khat frequently during exam preparations. In Ethiopia and Kenya, many students chew khat or make it into tea. Students use khat to stay awake, alert, and focused. No studies prove the effectiveness of khat in improving short-term memory, but students report feeling memory and performance improvements. Some 4.8 million U.S. children take Adderall, which is a combination of amphetamine and dextroamphetamine, to treat attention deficit hyperactivity disorder. Khat may appeal to students because cathinone resembles amphetamine in its structure and symptomology (2).

Chemical Structures and Composition

The phenylalkylamines (cathinone, cathine, and norephedrine) and the cathedulins are the major alkaloids present in khat (Figure 2). In addition, khat contains a large number of other compounds, including tanins such as glycosides, quercetin, and myricetin, as well as fatty acids, amino acids, minerals, vitamins, and ascorbic acid (3). Sugar alcohols account for the sweet taste.

Studies vary widely in their findings about khat's potency. One study found that 100 g of leaves contain 78–343 mg of cathinone and cathine (4). Another study reported much lower concentrations, with average concentrations of 9.5 mg of cathinone, 5.4 mg of cathine, and 5.4 mg of norephedrine in 100 g of fresh leaves. This variability could be attributed to the diversity of khat brands and the freshness of the leaves. Ethiopian khat has a reputation as being the strongest.

Khat and "Bath Salts"

Cathinone is a mild stimulant with fewer effects than amphetamine, but it can become harmful when chemically modified, as it is to be used in "bath salts." Labeled "not for human consumption" to try to skirt the law, bath salts are sold in convenience stores and online under a wide range of names like Ivory Wave, Cloud Nine, Bliss, and Vanilla Sky. They are also marketed as bath crystals, plant food, and herbal incense. Designed to be snorted or eaten, they have methamphetamine-like effects. They are now prohibited in almost all of the U.S. Two of the most common active ingredients in bath salts available in the U.S. are methylenedioxypyrovalerone (MDPV) and mephedrone (4-methylmethcathinone) (5) (Figure 3). Bath salt manufacturers do not use khat as a source of cathinone because it is much easier to synthesize than to extract from a plant.

Figure 1. Khat leaves. The tender, soft, red leaves and stems contain the most stimulants.
Photo courtesy of the author

A Harmful Drug?

A recent article ranked 20 drugs according to their danger in terms of their potential harm to an individual user, their tendency to induce dependence, and their effects on families and the general community (6). Khat ranked lowest in its harmfulness score. Heroin ranked first, cocaine second, and alcohol fifth. Khat also had the lowest healthcare cost.

Legal Issues

Khat's legal status varies from country to country because of controversy over its chemical make-up

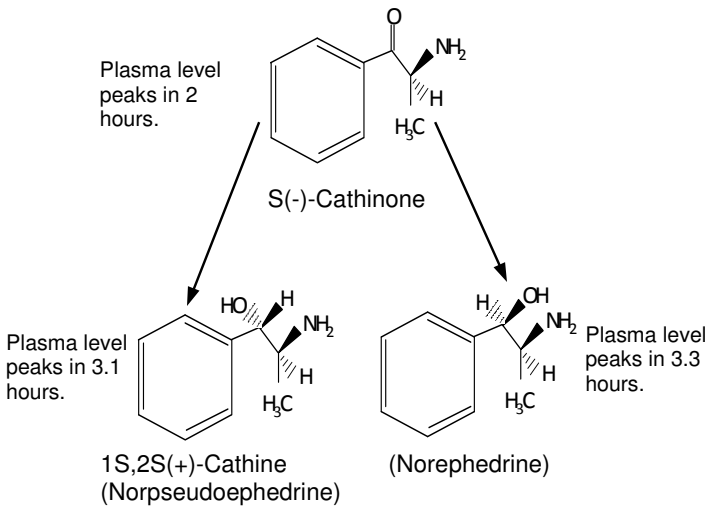
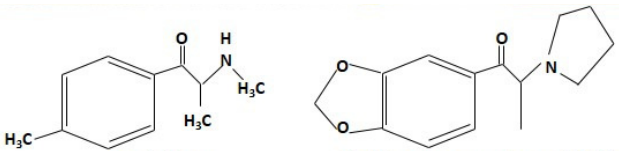


Figure 2. Chemical structures of khat's main active ingredient and its major metabolites. Cathine and norephedrine are also found in the leaves. Their half-lives are more than 10 hours.
Figure courtesy of the author



Mephedrone
4-methylmethcathinone

Methylenedioxypyrovalerone
(MDPV)

Figure 3. Chemical structures of "bath salts."
Figure courtesy of the author

and potency. A labile alkaloid, cathinone is often referred to as a natural amphetamine, even though it has many fewer effects. When leaves are dried and stored, an enzymatic reduction degrades cathinone into a less active alkaloid, cathine (7). Some government reports lump together cathinone with amphetamine, a controlled substance. Other reports consider cathinone a short-lived compound that transforms quickly into less potent cathine. This dichotomy leads to different treatment in different countries.

United States and Canada

Khat has been prohibited in the U.S. since 1993, when the Drug Enforcement Agency prohibited its transportation, sale, distribution, and possession because of the presence of cathinone (8). Recently, the U.S. stepped up its efforts to confiscate illegal khat shipments, most of which arrive from African nations like Kenya and Somalia via the U.K. The U.S. vigorously prosecutes khat smugglers not only because of its amphetamine-like activity, but also out of fear that money generated from its sale could fund terrorists (9). U.S. law enforcement agencies seized more than 89,600 kg of khat in 2010 (10).

Canada also bans khat. In 2009, Canadian authorities seized more than 19,000 kg, second only to marijuana. In 2008, they confiscated 22,000 kg, with half of it being shipped by regular mail. Air shipment is the most common method for khat imports to Canada. Khat users are mainly immigrants from the cultivating countries of Somalia, Yemen, Ethiopia, and Kenya. They are challenging the seizures in court.

Rest of the World

Earlier this year, the U.K.'s Advisory Council on the Misuse of Drugs declined to list khat as a controlled drug under the Misuse of Drugs Act 1971. This ruling would have legalized its use and distribution (11). The council based its decision on the lack of studies showing substantial health harm, although it cited a need for more scientific evidence on its health effects. However, after many Somali immigrants objected to the ruling, in July the government overturned the decision and banned khat imports out of fear that the U.K. could be a hub for khat trafficking. The ruling classified khat as class "C," the least harmful designation under the drugs act, so possession is subject to lenient punishment (12).

This decision ended decades of debate on khat's legal status, and is consistent with the policies of neighboring countries. Khat use is illegal in at least 15 European countries.

In Israel, khat leaves are traditionally used fresh or dried. However, recently, Israeli convenience stores began selling khat juice mixed with illegal recreational drugs under the name Green Energy. As a result, Israeli authorities added cathinone and cathine to the list of dangerous drugs except when they are contained in leaves, so khat can still be planted and sold legally (14). Israeli authorities seized 15,000 bottles of Green Energy in Jerusalem alone and shut down a factory with a khat farm (15).

Egypt and Tanzania are the only African countries that prohibit khat importation or consumption. Ethiopia, Somalia, and Kenya are the main African exporters.

Discussion and Conclusions

The World Health Organization Expert Committee on Drug Dependence recently reviewed the published data on khat and concluded that its potential for addiction and abuse is low (16). The committee found that khat does not threaten public health nor require an international ban and control.

Despite its relatively safe risk profile, law enforcement officials and others worry that khat could become a global problem by crossing over from its indigenous user population to a wider general public. Khat smuggling, transportation, and consumption continue to concern many countries around the globe. The potential adverse effects vary from country to country. For instance, in Yemen, where khat use is endemic, the major concern is the danger of losing natural underground water resources to khat agriculture. The capital of Yemen is at risk of running out of water in the next 10 to 15 years, according to some estimates (17).

In Ethiopia, taxes on khat exports provide the government a source of revenue. In the U.S., authorities fear that revenues from khat could fund other illegal activities.

Globally, the question of whether khat is a drug of abuse is still being debated. Many khat users argue that khat is not addictive and they can quit when they choose, whereas alcohol is legal but some users find it difficult to abstain and can develop dependency, with withdrawal symptoms.

The many cathinone-derived drugs now appearing present another challenge to law enforcement officials. However, international manufacturers do not use khat to extract cathinone because it is difficult to

obtain fresh leaves and extraction is time-consuming. Instead, illegal labs synthesize these drugs as pure compounds to create bath salts.

To develop informed policy, more research is needed on the health effects of khat, particularly comorbidity issues that it may exacerbate. The extent to which khat use leads to mental health problems and substance abuse needs to be better understood. Some evidence suggests that khat promotes the use of other, more lethal, substances, such as tobacco (18). It may also lead to early sexual initiation (19).

Any efforts to control or reduce khat use should take into account the need to help countries find alternative income for millions of farmers who depend on it as a source of income. Without alternative economic development in Yemen, Kenya, and Ethiopia, khat farmers will continue to suffer the consequences of khat prohibition. Countries around the world should also push for massive health education campaigns as they strive to develop sound international policy for the regulation of khat.

References

1. Widler P, Mathys K, Brenneisen R, et al. Pharmacodynamics and pharmacokinetics of khat: a controlled study. Clin Pharmacol Ther 1994;55:556–62.
2. Diller L. The United States of Adderall. The Huffington Post (2011). http://www.huffingtonpost.com/larry-diller/overuse-of-prescription-drugs_b_950802.html (Accessed November 2013).
3. Szendrei K. The chemistry of khat. Bull Narc 1980;32:5–36.
4. Ramadan MA, Tash FM, Qirbi AA, et al. Evaluation of cathine and cathinone in khat all over different areas of Yemen and factors affecting it. Paper presented at UNESCO Arab Chemical Research in Tunisia. In: Khat Research. Dept. of Biochemistry, Sana'a University, Sana'a, Yemen 1981 (Mimeographed).
5. Heltsley R, Shelby M, Crouch D, et al. Prevalence of synthetic cannabinoids in U.S. athletes: initial findings. J Anal Toxicol 2012;36:588–93.
6. Nutt D, King LA, Saulsbury W, et al. Development of a rational scale to assess the harm of drugs of potential misuse. Lancet 2007;369:1047–53.
7. Kelly JP. Cathinone derivatives: a review of their chemistry, pharmacology and toxicology. Drug Test Anal 2011;3:439–53.
8. Gebissa E. Khat: is it more like coffee or cocaine? Criminalizing a commodity, targeting a community. Sociology Mind 2012;2:204–12.
9. Hartley A. This is khat: the natural high available on British streets and suspected of funding terrorism. The Daily Mail Newspaper (2012). http://www.dailymail.co.uk/home/moslive/article-2159321/Khat-The-natural-high-available-British-streets--suspected-funding-terrorism.html (Accessed November 2013).
10. Bear ME. Financing of terrorist activities. In: Encyclopedia of transnational crime and justice. California: SAGE Publications 2012:412.
11. Advisory Council on the Misuse of Drugs. Khat (qat): assessment of risk to the individual and communities in the UK. http://www.homeoffice.gov.uk/publications/agencies-public-bodies/acmd1/khat-report-2005/Khat_Report_.pdf?view=Binary (Accessed November 2013).
12. Travis A. Theresa May ignores experts and bans use of qat. The Guardian (2013). http://www.theguardian.com/politics/2013/jul/03/theresa-may-bans-qat (Accessed November 2013).
13. European Monitoring Center for Drugs and Drug Addiction. Khat use in Europe: implications for European policy. Drugs in Focus 2011;1:1–4. http://www.emcdda.europa.eu/publications/drugs-in-focus/khat (Accessed November 2013).
14. Will Israel outlaw khat juice? The Harraetz, June 3, 2012. http://www.haaretz.com/news/national/will-israel-outlaw-khat-juice.premium-1.434148 (Accessed November 2013).
15. Lidman M. J'lem: Six nabbed for peddling strange 'energy drink.' The Jerusalem Post Newspaper, Aug. 21, 2012. http://www.jpost.com/National-News/Jlem-6-nabbed-for-peddling-strange-energy-drink (Accessed November 2013).
16. World Health Organization. WHO Expert Committee on Drug Dependence, Thirty-fourth Report, 2007. WHO Technical Report Series #942. http://www.who.int/substance_abuse/right_committee/en/ (Accessed November 2013).
17. Time running out for solution to Yemen's water crisis.The Guardian Newspaper, Aug. 27, 2012. http://www.theguardian.com/global-development/2012/aug/27/solution-yemen-water-crisis (Accessed November 2013).
18. al'Absi M, Grabowski J. Concurrent use of tobacco and khat: added burden on chronic disease epidemic. Addiction 2012;107:451–2.
19. Malaju MT, Asale GA. Association of khat and alcohol use with HIV infection and age at first sexual initiation among youths visiting HIV testing and counseling centers in Gamo-Gofa zone, south west Ethiopia. BMC Int Health Hum Rights 2013;13:10.

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Caffeine's Safety

It Is Not Easy to Overdose on This Drug of Global Appeal

By Dwain Fuller, D-FTCB, TC-NRCC

Caffeine is a ubiquitous drug, consumed by all ages in almost all cultures. Caffeine's ubiquity became apparent to the author several years ago during a research project investigating caffeine concentrations in human serum. No internal standards and controls were commercially available, and our attempts to create our own were stymied because finding caffeine-free human serum was essentially impossible.

Caffeine has become even more in vogue in recent years with the rising popularity of coffee shops, energy drinks, caffeine-containing energy "shots," and even caffeine-laced candy and chewing gum for endurance sports. Recently, however, media reports have raised concerns that consumption of these products can have potentially life-threatening consequences. Thus, a closer look at the toxicology of caffeine is warranted.

Pharmacodynamics

Caffeine is structurally similar to adenosine, an inhibitory neurotransmitter, and, not surprisingly, is an adenosine receptor antagonist. One hypothesis proposes that the accumulation of adenosine through the day causes increasing sleepiness. Caffeine also inhibits acetylcholinesterase, thereby increasing activity of the neurotransmitter acetylcholine. The combined effects of these actions are to increase acetylcholine, epinephrine, dopamine, serotonin, norepinephrine, and glutamate, resulting in overall stimulation and wakefulness.

Pharmacokinetics

Caffeine has a bioavailability of 99% and a volume of distribution of 0.4–0.6 L/kg. It reaches a peak concentration in approximately 1–1.5 hours. Its half-life of about 5 hours is influenced by gender, age, use of oral contraceptives, pregnancy, and smoking. Caffeine's half-life in newborns ranges from 50 to 100 hours, but approaches that of an adult by 6 months of age. Its half-life is 20–30% shorter in females than in males and about twice as long in females using oral contraceptives than in ovulatory females. During pregnancy, the half-life increases steadily from four hours during the first trimester to 18 hours during the third trimester. Cigarette smoking is associated with about a twofold increase in caffeine's elimination rate.

Caffeine is metabolized in the liver by CYP1A2 enzymes to paraxanthine, theophylline, and theobromine, with only a small percentage excreted unchanged in the urine. It has a pKa of 0.8, thus it is significantly protonated only at a very low pH (1,2).

Potential Beneficial Effects

Caffeine's stimulatory effects are well-documented. Although more study is needed, several positive effects are being reported: lower risk of cardiovascular disease and diabetes, minimization of age-related cognitive decline, reduced risk of cancer, reduced risk of Parkinson's disease, and a positive effect on driving performance during monotonous conditions (3).

Toxicity

The many studies performed to explore caffeine's adverse effects have been fairly consistent in determining that moderate doses of 400–450 mg/day or less have little to no effect on cardiovascular health, bone and calcium balance, mutagenicity, genotoxicity, and carcinogenicity. Studies suggest that intake of more than 300 mg/day may adversely affect female fertility and fetal development, as well as increase the risk of miscarriage. Thus, women who are pregnant or are planning to become pregnant would be prudent to limit their consumption to less than 300 mg/day (2).

Recent Reports of Problems

Despite these findings of safety, the Drug Abuse Warning Network (DAWN) reported a tenfold increase in emergency room visits due to the use of caffeine-containing energy drinks between 2005 and 2009 (4). Additionally, there are documented cases of caffeine overdose resulting in death. The acute lethal dose of caffeine is estimated to be 10 g. However, some patients have died from ingesting as little as 5.3 g, whereas others have survived 24 g.

Baselt reports 14 deaths caused by oral ingestion of 5.3 to 50 g of caffeine, with postmortem whole blood concentrations ranging from 79–344 mg/L (mean = 183 mg/L) (1). Kerrigan and Lindsey report a case with a postmortem femoral blood concentration of 567 mg/L (5). Dietrich and Mortensen report the survival of a child who ingested 2–3 g and had a peak plasma concentration of 385 mg/L (6). Toxic and fatal concentrations appear to overlap signifi-

cantly, with medical intervention perhaps providing the deciding factor.

DAWN points out (4): "Energy drink consumption by itself can result in negative health events serious enough to require emergency care." However, a purely pharmacological fatal caffeine overdose (one not exacerbated by an underlying medical condition) is quite rare because of the extremely large amount of caffeine required. Typically, a fatal event requires the ingestion of relatively pure caffeine in the form of powder or tablets. A literature search by the author failed to locate any well-documented fatal overdoses attributable to caffeine alone, in which the source of the caffeine was coffee, tea, any other beverage, or food sold as a consumer product.

Caffeine's safety profile appears to be quite good. It is nearly impossible for a healthy individual to ingest the large amount needed to incur a fatal overdose by partaking of coffee, tea, sodas, chocolate, or even energy drinks. However, adverse effects are possible in those who are particularly sensitive when high intake is combined with other drugs or alcohol.

References

1. Caffeine. In: Baselt DR, ed. Disposition of toxic drugs in chemicals and man.7th Ed. Foster City, Calif.: Biomedical Publications 2004:157–9.
2. Nawrot P, Jordan S, Eastwood J, et al. Effects of caffeine on human health. Food Add Contam 2003;20:1–30.
3. Mets M, Baas D, van Boven I, et al. Effects of coffee on driving performance during prolonged simulated highway driving. Psychopharmacology (Berl) 2012:222;337–40.
4. Subtance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. The DAWN report: emergency department visits involving energy drinks. Rockville, Md. 2011. http://www.samhsa.gov/data/2k11/WEB_DAWN_089/WEB_DAWN_089.htm (Accessed November 2013).
5. Kerrigan S, Lindsay T. Fatal caffeine overdose: two case reports. Forensic Sci Intl 2005;153: 67–9.
6. Dietrich A, Mortensen M. Presentation and management of an acute caffeine overdose. Pediatr Emerg Care 1990;6:296–8.

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Childhood Blood Lead Levels

CDC Advisory Committee Finds No Amount of Lead in Blood Is Safe

By Robert A. Middleberg, PhD, DABFT, DABCC(TC)

Because lead in the body can lead to developmental and other health problems in children, various government agencies have promulgated recommendations and requirements to protect their health (1–3). Individual states and the U.S. Centers for Disease Control and Prevention (CDC) have established criteria for acceptable blood lead levels (BLLs) and testing.

In recent years, various government entities have re-examined their recommendations in the light of new research. To this end, in January 2012, the CDC's Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) issued a report, "Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention" (4).

Zero Tolerance for Lead

This report found that there is no amount of lead in a child's blood that should be considered safe and recommended remedial steps be taken at lower levels than previously considered. Prior to this report, the CDC termed a BLL of 10 µg/dL to be a "blood level of concern" and recommended various stages of remedial steps be taken based on the BLL (5). Because many studies have demonstrated that BLLs below 10 µg/dL can be harmful to children, the committee recommended that the term "blood level of concern" be abandoned.

Data from the National Health and Nutrition Examination Survey (NHANES) demonstrated that a more useful measure of risk is a reference value based on the 97.5 percentile of BLL distribution among U.S. children aged 1–5 years. Current data sets this reference value at 5 µg/dL (4).

A reference value approach has the advantage of characterizing individual results as elevated or not elevated compared with the population average. The ACCLPP concluded that "a BLL without deleterious effects cannot be identified at present." The adverse effects of lead are now recognized to extend beyond cognitive skills to include potential effects on cardiovascular, immunological, and endocrine systems. As a result, the CDC program to eradicate blood lead issues in children now focuses on prevention.

Highlighted Recommendations

The ACCLPP report promulgated 13 recommendations. The CDC responded to the recommendations

with statements that either "concurred" or "concurred in principle" with all of them (6). The phrase "concurred in principle" means that the CDC agrees with a recommendation but lacks the resources, such as funding or staff, to implement it.

Laboratorians affected by the CDC's changes will find it useful to read all 13 recommendations and the CDC's response (see references). The implications of the recommendations most relevant to laboratories performing BLL testing are described below.

As mentioned previously, the term "level of concern" should be replaced in future CDC policies, guidance documents, and publications with a "reference value" based on the 97.5 percentile of BLLs in children that is currently set at 5 µg/dL. The committee noted that this reference value will help identify children and environments associated with lead exposure hazards. It recommended that the CDC update this value every 4 years based on the most recent population-based surveys among children.

This change puts an added burden on laboratories to ensure that their techniques are accurate and precise at this lower BLL. Laboratories performing blood lead testing should be able to routinely measure at 1 µg/dL using techniques such as inductively coupled plasma mass spectrometry and graphite furnace atomic absorption spectrometry. The reference value is likely to be lowered in the future, so to accommodate this eventuality, laboratories that don't currently measure to 1 µg/dL should probably develop methods to do so.

Assisting Clinicians

The committee made recommendations on the role of clinicians that laboratorians should be aware of. The report said that clinicians should take the primary role in educating families about preventing lead exposure, monitoring the health and BLLs of children with a level greater than 5 µg/dL, and ensuring that children with these BLLs are reported to local and state health officials and housing departments.

Laboratorians should be prepared to assist clinicians in implementing these steps, including potential educational opportunities and direct notification of agencies per state public health requirements. As a result of these recommendations, laboratories are likely to experience increases in blood lead testing volume with the need for longitudinal reporting capabilities.

Proficiency and Confirmatory Testing

The ACCLPP recommended that the Centers for Medicare and Medicaid Services revise regulations for allowable laboratory error for blood lead proficiency testing programs from ±4 µg/dL to ±2 µg/dL for BLLs ≤20 µg/dL. Additional adjustments may be necessary at BLLs <10 µg/dL. This quality improvement will be challenging for many laboratories, especially those using point-of-care devices.

The ACCLPP also recommended that confirmatory testing be based on the uncertainty of individual blood lead test results. Many preanalytical and analytical issues can affect the accuracy of results, but the main concern is contamination of puncture sites for capillary blood sampling.

With respect to confirmatory testing, the committee recommended that all capillary and venous BLL results ≥5 µg/dL be confirmed within 1 to 3 months. Confirmatory testing should be performed immediately in children with BLLs ≥45 µg/dL or with symptoms of lead poisoning.

Response actions should be initiated only after an elevated BLL is confirmed.

The ACCLPP provided no technical details on how to perform confirmatory testing, but the current best practice is to analyze a newly collected specimen using a highly specific, sensitive method with defined error such as ±2 µg/dL. Capillary blood measurements should be confirmed using a venous sample.

The ACCLPP recommended research priorities ranging from improvements in the use of data from screening programs to development of next generation point-of-care analyzers. Current point-of-care devices are limited in their sensitivity, accuracy, and precision.

Conclusions

Research data on blood lead concentrations and their effects continues to grow. Regulatory bodies seek to protect all people from the perils of lead tox-

Revised Lead Testing Guideline

The Clinical and Laboratory Standards Institute has published a new version of *C40-A2: Measurement Procedures for the Determination of Lead Concentrations in Blood and Urine; Approved Guideline—Second Edition*.

Written in light of the Centers for Disease Control and Prevention recommendation of a new reference value approach, the guideline provides direction for specimen collection as well as measurement by graphite furnace atomic absorption spectrometry, anodic stripping voltammetry, and inductively coupled plasma mass spectrometry. It includes information on quality assurance and quality control, proficiency testing programs, and laboratory certification.

For more information, visit www.clsi.org.

icity, but tend to focus on the young, who are more susceptible than adults to lead toxicity because of higher gastrointestinal absorption and their developing central nervous systems (7).

As a result of increasing knowledge, regulatory bodies can be expected to continue to modify their approaches to blood lead. The most significant of the CDC ACCLPP's recent recommendations is the development of a blood lead reference value to replace the "level of concern" approach. Some ACCLPP recommendations directly affect laboratories in terms of preanalytical, analytical, and postanalytical phases of blood lead testing. Laboratories have a responsibility to stay abreast of such changes, and given the rapid accumulation of information regarding BLLs, laboratories can be expected to be pushed to the brink of testing capabilities in the future.

References

1. California Department of Health, Childhood Lead Poisoning Prevention Branch. http://www.cdph.ca.gov/programs/CLPPB/Pages/AboutCLPPB.aspx (Accessed November 2013).
2. New York State Department of Health, New York State Public Health Laws and Regulations for Lead Poisoning. http://www.health.ny.gov/environmental/lead/laws_and_regulations/ (Accessed November 2013).
3. Pennsylvania Department of Health, Lead Poisoning Prevention and Control. http://www.portal.state.pa.us/portal/server.pt/community/lead_poisoning_prevention___control/14175 (Accessed November 2013).
4. Advisory Committee on Childhood Lead Poisoning Prevention of the Centers for Disease Control and Prevention. Low level lead exposure harms children: a renewed call for primary prevention. Jan. 4, 2012. http://www.cdc.gov/nceh/lead/ACCLPP/Final_Document_030712.pdf (Accessed November 2013).
5. Preventing Lead Poisoning in Young Children. A statement by the Centers for Disease Control and Prevention, August 2005. http://www.cdc.gov/nceh/lead/publications/prevleadpoisoning.pdf (Accessed November 2013).
6. CDC Response to Advisory Committee on Childhood Lead Poisoning Prevention. Recommendations in "Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention." June 7, 2012. http://www.cdc.gov/nceh/lead/ACCLPP/CDC_Response_Lead_Exposure_Recs.pdf (Accessed November 2013).
7. Middleberg RA. Lead and other toxic metals. In: Magnani BJ, Bissell MG, Kwong TC, Wu AHB, eds. Clinical toxicology testing: a guide for laboratory professionals. Northfield, Ill.: CAP Press: 2012:196–207.

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CAP Surveys Update

New Toxicology Proficiency Surveys to Be Offered in 2014

By Glynnis Ingall, MD, PhD

Beginning in 2014, the College of American Pathologists (CAP) will offer two new proficiency testing surveys: Synthetic Cannabinoid/Designer Drugs (SCDD) and Vitreous Fluid, Postmortem (VF). These surveys are designed for labs that perform forensic or esoteric (reference) toxicology testing.

Synthetic Cannabinoid/Designer Drugs

Synthetic cannabinoids and cathinones are of clinical and forensic toxicology interest because they are implicated in growing numbers of overdoses and emergency room visits. CAP is currently the only provider of proficiency testing surveys for synthetic cannabinoids and the newer designer drugs.

This survey provides two shipments per year with each shipment consisting of three 10-mL urine specimens. It includes the following target drugs and metabolites:

- Alpha-pyrrolidinopentiophenone (Alpha-PVP)
- AM-2201 N-(4-hydroxypentyl) metabolite
- JWH-018 N-(4-hydroxypentyl) metabolite
- JWH-018 N-(5-hydroxypentyl) metabolite
- JWH-018 N-pentanoic acid
- JWH-073 N-(3-hydroxybutyl) metabolite
- JWH-073 N-(4-hydroxybutyl) metabolite
- JWH-073 N-butanoic acid
- JWH-122 N-(4-hydroxypentyl) metabolite
- JWH-122 N-(5-hydroxypentyl) metabolite
- Mephedrone
- Methylenedioxypyrovalerone (MDPV)
- Methylone
- UR-144 N-(4-hydroxypentyl) metabolite
- UR-144 N-(5-hydroxypentyl) metabolite
- UR-144 N-pentanoic acid metabolite

Vitreous Fluid, Postmortem

CAP has developed the first survey to provide proficiency testing material and expert educational

guidance for analysis of postmortem vitreous fluid specimens. It is designed for laboratories that perform this analysis for medico-legal purposes.

The program provides two shipments per year, with each shipment consisting of three 5-mL synthetic vitreous fluid specimens. Each challenge includes the relevant clinical history.

The survey includes the following analytes: chloride, creatinine, ethanol, glucose, potassium, sodium, and vitreous urea nitrogen.

Proficiency Survey Grading Changes

These two new surveys will not be formally graded during the first year.

Beginning in 2014, the Urine Adulterant/Integrity Testing, Oral Fluid for Drugs of Abuse, Therapeutic Drug Monitoring Extended, and Trace Metals Urine surveys will be graded. For the Drug Monitoring for Pain Management Survey, the wet lab challenges will also be evaluated for the first time in 2014, but the dry lab interpretive challenges will remain educational and will not be graded.

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