The Brown University Child and Adolescent Behavior Letter

CABL

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Highlights…

Our page 1 stories this month look at the need for trauma-informed health care, and whether lab tests for suitability of medications for specific people are ready for prime time.

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Commentary

✦ ✦ ✦

Free Parent Handout…

You think you're confused? Even clinicians say drug names are misleading

Trauma

Making universal trauma-informed health care a reality: A pilot initiative to train future providers

By Meghna Nandi; Sravanthi Puranam; Margaret Paccione-Dyszlewski, Ph.D.; Harry VanDusen; and Sadie Elisseou, M.D.

The medical field traditionally classifies "trauma" as acute physical injury, requiring immediate medical attention. Psychological trauma is a separate entity, traditionally viewed as under the purview of behavioral health. Although mental health providers have expertise in treating the consequences of psychological trauma, medical providers can also play a distinct role in addressing the impact of such trauma on patients' health. Medical providers often work in settings where patients with anxiety, depression, chronic pain, or other pathologies related to underlying trauma may first interact with the health care sector, such as a primary care clinic or an emergency room.

By working at the frontlines of health care, medical providers are well-positioned to identify trauma, connect patients to appropriate resources, and establish patients' long-term engagement with services. Pediatricians, for example, are uniquely poised to address trauma during childhood and adolescence, when events can have especially profound effects on development. Furthermore, traumatic experiences during this period are highly prevalent; every year, an estimated 60.8% of children in the United States are directly exposed to violence, crime, or abuse. Pediatricians also have a clearer view of their patients' social environments

*See **Trauma**, page 5…*

Pharmacogenetics

Pharmacogenetic testing: Is a lab test able to replace clinical acumen and thoughtful medication management?

By Sibel Algon, M.D.

In short, most often the answer to the question posed in this article's headline is "Not yet." Pharmacogenetics is a field of research looking for predictable correlations between genetic variations (polymorphisms) and clinical responses to medications. At present, there are over 20 such tests available at high cost. None are regulated by the Food and Drug Administration (FDA), and most lack double-blind randomly controlled trials.

Pharmacogenetic tests are looking for genetic variants in pharmacokinetic genes and/or candidate genes that may impact serum drug levels and/or drug efficacy. Pharmacokinetic genes are cytochrome P450 (CYP 450) hepatic (liver) enzymes involved in the metabolism of many psychotropic medications. CYP 450 polymorphisms may be used to determine an individual's metabolizer status: extensive metabolizers (metabolize drugs at predictable rates), intermediate metabolizers (people at risk for increased drug levels and adverse effects due to reduced drug metabolism), poor metabolizers (people at risk for very high drug levels and adverse effects due to significant reductions in drug metabolism), and ultra-rapid metabolizers (people at risk for low drug levels due to increased drug metabolism). Candidate

*See **Pharmacogenetics**, page 7…*

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Keep your eye on…

…free articles on ACEs from *JAACAP*

The American Academy of Child and Adolescent Psychiatry (AACAP) has been upfront in its opposition to separating families, as has been happening in the United States under harsh immigration policies. Recently, its flagship journal released an open-access collection of articles on family separation, focusing on the problems caused by adverse childhood experiences (ACEs) and toxic stress. More than 2,300 children have been separated from their parents at the Mexican border; most are still being detained and have not been reunited. More than 13,000 children — many of whom came to the United States on their own, hoping to be connected with family or friends — are still being detained, many in tent cities or prison-like facilities (see story, p. 4). "When children experience sudden separation from one or both parents, especially under frightening, unpredictable, and/or chaotic circumstances, they are at heightened risk for developing posttraumatic stress disorder (PTSD), anxiety, depression, and other trauma-related reactions that may last for the rest of their lives," the AACAP stated. As the leading publication for pediatric mental health, the *Journal of the American Academy of Child and Adolescent Psychiatry* (*JAACAP*) has published many articles over the past 20 years showing the damaging effects of early childhood trauma, the role of parental stress in transmitting psychiatric and other problems to children, and the positive role of parents in promoting child and adolescent mental health. Therefore, *JAACAP* announced that it joins colleagues at *Pediatrics* in opposing the practice of separating immigrant children from their families, and has created an open-access collection of articles it has published since 2008 on the effects of separation, early-life trauma, and related topics. *JAACAP* will maintain and update this site until family separations stop. "We hope that this will encourage policymakers and the public to recognize the potentially life altering effects that these and similar policies have on children, adolescents, and their families," the editors announced. For access to the articles, go to *https://jaacap.org/toxicstress*.

…the need for pediatric readiness in the ED

Last month, the American Academy of Pediatrics issued a revision of its previous joint policy statement, along with the American College of Emergency Physicians and Emergency Nurses Association, entitled "Guidelines for Care of Children in the Emergency Department." Most sick and injured children who end up in a community hospital emergency department (ED) are there because it's the closest facility. But not all EDs have the appropriate resources and staff to provide effective emergency care for children, so in this policy statement, the necessary resources are listed, including medications, equipment, policies, and education. Children have special needs, separate from adults, so it is essential for all ED staff, administrators, and medical directors to meet or exceed these recommendations. For more information, go to *http://pediatrics.aappublications.org/content/142/5/e20182459*.

…the high level of daily marijuana use in young adults

The latest Monitoring the Future (MTF) survey results on teens transitioning to adulthood show that more than 13% who are not in college are using marijuana on a daily basis. Conducted for the National Institute on Drug Abuse (NIDA), MTF is a national survey released in December every year, with a specialized focus on 19- to 22-year-olds released in the following September. This fall, the focus compared full-time college students to their noncollege peers.

Highlights:

- Thirteen percent of young adults not in college use marijuana daily, at three times the rate of college students.
- Past-month vaping of marijuana is higher among noncollege young adults (7.8%) compared to college students (5.2%).
- Past-month alcohol use is higher in college students (62%) than noncollege peers (56.4%).

For more on young adults from NIDA, go to *https://www.drugabuse.gov/related-topics/collegeage-young-adults*.

Teen cannabis vaping and edible use increased in high-density dispensary states

By Alison Knopf

Legalizing cannabis has resulted in an increased use of vaping and edibles, which may be particularly appealing to young people. Whether these alternative methods of consumption magnify or mitigate the developmental harms of cannabis use is not known. Researchers wanted to find out whether legal cannabis laws, such as dispensary regulations, affect the way youth consume cannabis.

Young people are particularly vulnerable to the adverse effects of cannabis: chronic cannabis use during adolescence has been linked to impaired brain development, educational achievement, and psychosocial functioning. No cannabis laws allow recreational use by those under 21, of any type of product.

There are two basic types of cannabis laws: medical and recreational. Legalizing either form promotes alternative products such as edibles and vaping devices. Edible products, such as baked goods, drinks, and candy, while increasingly popular, "are often inaccurately labeled and deliver variable doses of cannabis' primary psychoactive constituent, tetrahydrocannabinol (THC)," the researchers write in background, introductory language to their study. Most edible cannabis products lack safety standards and packaging regulations, and products are marketed in ways that appeal to youth, they add.

In response to sharp increases in edible cannabis overdoses among youth, some states have taken steps to limit the appeal of edibles to youth.

It is known that e-cigarettes and other vaping devices — also technically banned among youth — are on the rise among middle and high school youth. The devices allow the user to inhale nicotine or THC, for example. Vaping can, according to research, reduce the carcinogens consumed when inhaling combustible smoke — either from cannabis or tobacco — and youth perceive e-cigarettes as "healthier" than traditional cigarettes.

In fact, among e-cigarette users, high schoolers are more likely than adults to vape cannabis, researchers have found. In addition, adolescents who vape cannabis are more likely to use high-potency preparations. "How the use of these high-potency products impacts neurodevelopment is unknown, but of pressing concern as it may place youth at risk for psychosis," as well as cannabis use disorders, some researchers have suggested. Vaping also can contribute to increased rates of consumption of cannabis, lower age of cannabis-use onset, and increased public cannabis use.

Despite these potential risks, there is little data on the use of cannabis vaping or edibles among youth.

Some states allow only medical cannabis, while others allow both medical and recreational use. Within these two sets of regulations, there is broad variation of access and distribution mechanisms. Some states allow for-profit dispensaries, some allow home cultivation, and some do not. Limits on personal possession amounts vary and are ambiguous. In some states, cannabis products are only available in vaped or edible form, not smoked.

The literature has produced equivocal results on the effects of cannabis legalization on public health.

In a previous study, the researchers used Facebook sampling to show strong cross-sectional relations between cannabis medical legalization and increased vaping and edible use by adults. In particular, adults living in areas with a higher number of cannabis dispensaries per person, and longer durations of legalized cannabis, were significantly more likely to have tried vaped and edible cannabis products.

In this study, they used the same sampling method to examine the associations in a youth sample, adding two provisions — home cultivation and recreational legalization. The researchers hypothesized that, as with adults, having a longer period of legalization and a greater number of dispensaries would be associated with a higher likelihood of lifetime use of vaped and edible products. They also hypothesized that these variables would be associated with a younger age of onset, and that a home cultivation provision and recreational legal marijuana would also be associated with increased use of edible and vaped products, and a younger age of onset.

Study details

Using an online survey distributed via Facebook, researchers collected data from 2,630 cannabis-using youth ages 14 to 18. They tested associations among lifetime use and age of onset of cannabis vaping and edibles, and the legal cannabis laws locally.

The survey was hosted by Qualtrics and collected information on demographics, including state of residence, and cannabis use. The study was approved by the Dartmouth Committee for the Protection of Human Subjects.

To target cannabis-using youth, advertisements with cannabis-related imagery were sent to the screens of youth ages 14–18 who had endorsed cannabis-related interests on their Facebook profile. Examples of these interests included cannabis-related organizations (e.g., Marijuana Policy Project), magazines (e.g., *High Times*), music (e.g., Pink Floyd), and notable individuals (e.g., Tommy Chong). Advertisements were shown to 126,945 individuals. Of these individuals, 5,480 (4.3%) clicked the advertisement and were redirected to the survey's informed consent/assent page; among those, 33 (0.6%) did not consent, and 210 (3.8%) were not within the targeted age. Of those who started the survey, 3,035 (58.0%) completed it and passed data quality checks. Of these, 405 (13.3%) had never used cannabis and were excluded from the present analyses, resulting in a final sample size of 2,630. Included in the consent was an explanation that the researchers were not encouraging cannabis use, and youth should consider first discussing the survey with a parent before taking it.

Results

The longer the duration of legalization, and the higher the density of dispensaries, the greater the likelihood that the young people would have tried cannabis vaping and edibles. Laws permitting home cultivation were also related to a greater likelihood of vaping and edibles among young people, and also to a younger age of onset of edibles.

The mean age of the sample was 16 years, about 46% were male, 3% African-American, and 14% Hispanic. About 84% were between eighth and 12th grade.

Participants from states that had legal marijuana differed significantly from those from states that did not have legal marijuana in terms of current education level, lifetime days of cannabis use, and age of cannabis use onset. Compared to a sample of lifetime cannabis-using youth (ages 14–18) from

Continued ***on next page...***

the 2014 National Survey on Drug Use and Health, this sample had a higher proportion of past-month users (12.4% vs. 83.1%) who had, on average, used more frequently in the past month (11.2 days vs. 16.7 days).

Lifetime prevalence of cannabis vaping and edible use was about 15 percentage points greater among youth in states where marijuana was legal than in states where it wasn't. The prevalence of lifetime vaping and edible use ranged from 35.6% to 56.5% in states that had shorter durations of legalization, compared to 52.0% to 77.7% in states with longer durations. The prevalence of lifetime vaping and edible use ranges from 35.6% to 54.4% in low-density dispensary states, compared to 52.0% to 74.8% in high-density dispensary states.

The age of onset of vaping did not differ across any variables in states that had legalized marijuana. For edibles, age of onset was earlier for longer-duration legalization states, and higher dispensary density categories.

Youth in states with legal marijuana were more than twice as likely to have tried vaping and edibles as youth in states that had not legalized marijuana.

Implications

Specific cannabis law provisions affect the likelihood that young people will use vaping or edible forms of cannabis administration, as well as the age at which they start. Because vaping and edibles may have different risks for initiation and escalation of use, it's important to understand associations between laws and use as authorities work on effective regulatory strategies.

The longer cannabis had been legal, and the higher the dispensary density, the higher the likelihood of vaping and edible use by teens. This had been shown with adults as well. This study extended the data by showing that recreational cannabis provisions and home cultivation were also related to a higher lifetime likelihood of vaping and edible use. Living in a high-dispensary-density state doubled the likelihood of trying vaping and tripled the likelihood of trying edibles.

This is not about adults — this is about teens. In fact, the higher dispensary density was also associated with a younger age of onset of vaping.

Youths are particularly vulnerable to changes in cannabis norms that accompany legalization, the researchers wrote. They noted that small differences — two to five months — in the age of onset of vaping and edibles translated into statistically significant differences because of the large sample size, but that "the functional importance of this magnitude of difference is unclear."

One theory for the observed relationship between home cultivation and earlier and more probable initiation of use of edible (but not vaping) products is that adults may condense the low-THC "leftover" parts of the plants they grow, to extract enough THC to make edible products, which may make edible products more available, increasing the risk of diversion to youth.

Limitations of the study include the sample — a self-selected convenience sample of social media users. Cannabis-using youth recruited by other methods may have had different responses. Second, the sample identified respondents based on their online endorsement of specific products related to "cannabis culture," which may not generalize to light cannabis users or heavy users who are not affiliated with online cannabis culture.

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The study was funded by the National Institute on Drug Abuse.

The authors have no conflicts of interest to declare.

Borodovsky JT, Lee DC, Crosier BS, et al. U.S. cannabis legalization and use of vaping and edible products among youth. *Drug Alcohol Depend* 2017 Aug 1; 177:299–306. doi: 10.1016/j.drugalcdep.2017.02.017. Epub 2017 Jun 9. Email: jacob.borodovsky@gmail.com.

What's happening in the Texas 'tent city' for immigrant children

By Alison Knopf

In October, the Department of Health and Human Services (HHS) went to Tornillo, Texas, to visit the temporary shelter it established for "unaccompanied alien children" (UAC) at the U.S. Customs and Border Protection (CBP) land port of entry (LPOE). The press referred to this shelter as a "tent city."

Here are some facts from the HHS agency, the Administration for Children and Families (ACF), that is responsible for providing care and services to the children, issuing grants and contracts to do so.

The temporary shelter established at Tornillo has 3,800 beds for UAC; 1,400 of those beds are on reserve status. Why is this operation continuing? Because HHS is required to provide appropriate care for these children while identifying a suitable sponsor, according to the ACF.

In the meantime, Border Control, which is not part of HHS, has to "continue its vital national security mission to prevent illegal migration [and] trafficking, and protect the borders of the United States" according to the ACF — and not be in charge of the children.

The need for the temporary shelter at Tornillo is not related to the family separations caused by the Trump administration's "zero tolerance policy," which ended June 20, according to the ACF. No children that were part of the family separations are at the Tornillo facility. Rather, these children need to be housed in this temporary shelter because they are part of the large number of children who crossed the border alone, without a parent or guardian.

HHS operates a network of just over 100 shelters in 17 states. As of October, the average length of care for UAC in the program is approximately 59 days. The overwhelming majority of UAC are released to suitable sponsors who are family members within the United States to await immigration hearings.

The task of assigning each child to the most appropriate shelter is complex, according to ACF. As of October, there were about 1,500 children residing at the Tornillo shelter, all ages 13 to 17 years. About 80% are male. Most were about to be released to a sponsor.

Minors in the program receive educational services from teachers under the oversight of an experienced senior public school administrator using textbooks and workbooks, according to the ACF.

The children residing in HHS shelters do not integrate into the local community or attend local schools, and they remain under the supervision of shelter staff at all times. The General Services Administration is providing HHS temporary use of the Tornillo site under a lease agreement.

While using space at the Tornillo LPOE site to temporarily shelter UAC, HHS assumes full security responsibility for the UAC. HHS has on-site security 24 hours per day, seven days per week. The children have, on average, a supervision ratio of no more than one adult for every eight children, 24 hours per day. This ratio does not include the additional security, medical, case management, education, recreation and operations personnel hired by HHS grantees/contractors to work with the UAC.

Accreditation

COA, founded in 1977 by the Child Welfare League of America and Family Service

America (now the Alliance for Strong Families and Communities), is working with some of the agencies which are responsible for the "unaccompanied alien children" who have come to the United States, some without their parents, some with their parents but separated from them during the now-discontinued zero-tolerance program of this spring.

"Unaccompanied alien children who come here largely from Central America and have no legal status in the United States are housed – and that's a polite word for it – in centers across America," said COA CEO Richard Klarberg. "These centers have been established for many years, going back to the Obama administration – this is not something new," he said. Unfortunately, the children do not have to be housed in an accredited facility, because the government has its own system of quality review. "But obviously, we believe that the centers that are accredited are meeting a higher standard," said Klarberg. The decision to separate children from their parents – now discontinued – was "a terrible" one, he said. "What we're interested in accrediting are the facilities that house the unaccompanied alien children," he said. "Hopefully they will be placed into foster care or aligned with family members. We take care of a number of these kids."

About unaccompanied alien children

By law, HHS has custody of and must provide care for each unaccompanied alien child referred to its care, defined as a child who has no lawful immigration status in the United States; has not attained 18 years of age; and with respect to whom there is no parent or legal guardian in the United States, or no parent or legal guardian in the United States available to provide care and physical custody. HHS plays no role in the apprehension or initial detention of UAC prior to their referral to HHS custody.

UAC are referred to the Office of Refugee Resettlement (ORR), also an HHS agency, by another federal agency, usually the Department of Homeland Security. Most children are placed into ORR care because they were apprehended by immigration authorities while trying to cross the border, according to the ACF; others are referred after coming to the attention of immigration authorities at some point after crossing the border. UAC are transferred to the care and custody of HHS until they are released to a suitable sponsor, usually a relative, while their immigration cases are adjudicated. The children come primarily from Guatemala, Honduras, and El Salvador.

You can find resources and contacts in your state at *https://www.acf.hhs.gov/orr/state-programs-annual-overview*.

Trauma

From page 1

through familial interactions, allowing them to better assess potential sources of trauma in their patients' lives. These aspects of pediatrics provide special opportunities to facilitate early identification and intervention for patients who have experienced trauma.

In spite of the significant impact of trauma on health, most undergraduate and graduate medical programs lack formal training in trauma-informed care, an established approach from behavioral health fields for providing care to trauma survivors. To truly make trauma-informed care a mainstay of both pediatrics and medicine, these principles must be integrated during medical school, when students first begin forming clinical habits. While there are a handful of studies evaluating trauma-informed trainings for medical providers, even fewer initiatives have focused on undergraduate medical education. In order to further address this gap, we designed and implemented a preclinical elective course for medical students titled "A Trauma-Informed Approach to Patient-Centered Medical Care."

Course description

The course met for 10 two-hour sessions over a semester during the 2017–18 academic year and involved first-year medical students at the Warren Alpert Medical School of Brown University. The class began with an overview of what experiences define trauma and the prevalence of trauma in the United States. The class then delved into the biopsychosocial impact of trauma on both neurodevelopment and medical illness. With this foundation, students learned the key principles of trauma-informed care: implementing universal trauma precautions, including enhancing patients' sense of safety, autonomy, and trust during a clinical encounter. The course also underscored vicarious trauma and the need to foster resiliency for both patients and providers themselves.

Once students felt comfortable with the key tenets of trauma-informed care, the class used a mixed didactic-interactive model to delve deeper into different forms of trauma, including adverse childhood experiences, intimate partner violence, racism, sexual assault, and military conflict. Interactive components included clinical, case-based discussions and a final, simulated clinical experience involving standardized patients that allowed students to both apply and practice trauma-informed principles. Two sessions were devoted to the impact of trauma-informed care, vicarious trauma, and resiliency on clinical practice. Students completed the course understanding how trauma-informed care can be applied as a universal approach to working in a mutually therapeutic way with all patients in the clinical setting and beyond.

One hallmark of the course was a series of sessions that focused on childhood and adolescent trauma. Clinical psychologists and triple board residents from Emma Pendleton Bradley Hospital in East Providence, Rhode Island, led these sessions.

Through case studies, students learned how trauma can stunt the maturity of executive function and dysregulate the hypothalamic-pituitary-adrenal axis. The resulting chemical imbalances and epigenetic effects create a perpetual state of emotional "survival" leading to deficits in attachment, emotional regulation, and cognitive processing. As children move into adolescence and adulthood, these once-effective survival tactics become perceived as disruptive and remain difficult to change. Without proper support focused on rehabilitating the effects of trauma, the long-term consequences include societal isolation, substance use, rapid cellular aging, immune dysfunction, and cardiovascular disease.

Additionally, the clinical cases demonstrated how trauma manifests differently across ages. The perception and impact of trauma are affected both by the genetic loading of a child (sex, innate resiliency, and familial risk factors) and by environmental factors like age of onset, duration, cultural background, and type(s) of trauma experienced. In particular, the pediatric-focused sessions touched upon the following topics: foster care, parental incarceration, human

trafficking, sexual assault, neglect, and evolving perceptions of racial, sexual, and gender identity. Each of these topics was introduced to students using a case-based model, encouraging students to identify different types of trauma and opportunities for multidisciplinary medical and psychosocial interventions to better support patients.

Finally, the pediatric sessions closed with an overview of what a trauma-informed health system could look like, beginning with a discussion of the establishment and continuing evolution of Bradley Hospital. During this session, the class also reflected on how medical institutions perpetuate individual and systemic trauma, as well as techniques students can use to identify trauma as the fuel for what we in medicine often label as a "dysfunctional" patient.

Lessons learned

At the end of the course, the 11 participating first-year medical students completed a survey assessing course satisfaction, knowledge, and attitudes using five-point Likert scales. On average, students had high levels of satisfaction with the course (mean = 4.73, SD = 0.47). Students also agreed that vicarious trauma would be a part of their future careers (mean = 4.64, SD = 0.50) and reported moderate to high confidence in their ability to manage the impact of vicarious trauma on their own well-being (mean = 4.00, SD = 0.63). When asked if elements of this course should be required for all medical students, every student who completed the course answered "yes." Students overall valued trauma-informed care as important to patient care (mean = 4.91, SD = 0.30).

In their qualitative feedback, students reported that the approach taught in the course informed and improved their patient experiences during medical school. One student noted that the course "has been very helpful in creating my foundational clinical interview and counseling skills from the bottom up with a trauma-informed perspective." Another student reflected, "It has given me a new lens with which I can analyze behavior and think about clinical scenarios."

Students also highlighted a number of course strengths. Many students valued the breadth of multidisciplinary perspectives offered during the course. Students also liked the emphasis on practical skills; one student reflected, "This course presents incredibly important content in a way that is engaging and provides tangible strategies that can be integrated early on in our careers as med students." A few students also commented on the community and safe space the class created. Of note, multiple students identified the sessions on pediatric and adolescent trauma as a few of the most powerful sessions in the course.

For areas of improvement, students reflected that the interactive, case-based sessions were the most helpful, suggesting more time be dedicated to practicing trauma-informed skills through clinical scenarios and discussion. Additionally, students mentioned the course would benefit from improving the way the course guides discussions processing vicarious trauma.

Students' high satisfaction and consensus that this course has improved their clinical experiences demonstrate that a combination of lectures, case-based learning, and simulated clinical experiences can successfully introduce first-year medical students to trauma-informed care as a universal approach to practicing medicine. We have incorporated student feedback to improve the second iteration of the course being held over the fall 2018 semester. To make the course more interactive, we restructured the sessions to increase the proportion of each class devoted to clinical scenarios, discussion, and time to practice concrete trauma-informed skills. Furthermore, we hope to be more intentional about the community and space we create in order to process vicarious trauma. Finally, in order to better understand the impact of this course, we will include more direct and indirect assessment of students' knowledge and use of trauma-informed principles.

Conclusion

This pilot trauma-informed care elective for first-year medical students was an initial step to establish a series of tools future clinicians can use to help support the healing of patients who have experienced trauma. No matter the clinical setting, trauma-informed care is relevant. Every patient arrives with their own unique set of experiences, and no population is immune to trauma. Therefore, our goal is that every future physician is able to apply the foundational principles of trauma-informed care wherever they ultimately practice.

This article is a call to action for each of us to recognize how our own clinical practices contribute to systemic and individual trauma. The time is now to advocate for trauma-informed training within standard medical and clinical education. We must do our part to ensure the next generation of providers recognizes trauma-informed care as integral to their clinical practice.

For Further Reading

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Pharmacogenetics

From page 1

genes are genes selected due to their suspected influence on drug efficacy, such as the serotonin transporter gene for selective serotonin reuptake inhibitors.

Metabolites

A major concern in relying on such reports to guide clinical practice is that drug efficacy and metabolism aren't predicted entirely by hepatic metabolism and genetic variation. The gastrointestinal tract, volume of distribution (amount of drug in fatty tissue versus body water), developmental stage, and renal (kidney) system are a few factors known to impact drug metabolism, absorption, excretion, or concentration. Many conditions, such as inflammation, seizures, or infections, may weaken the blood brain barrier, exposing the brain to higher concentrations of drugs regardless of pharmacogenetics. Nonadherence, missed doses, presence or absence of food, and inconsistent dosing times may also influence drug efficacy. Another situation is that of medications with active metabolites. One may be able to metabolize a psychotropic normally as an extensive metabolizer at the primary CYP 450 at which it's a substrate and be a poor metabolizer at a CYP 450 involved in metabolism of its active metabolite, leading to unanticipated drug levels or adverse effects. In practice, CYP 450 metabolizer status hasn't reliably predicted treatment response to psychotropic substrates even in those found to have related CYP 450 polymorphisms.

Genomewide association studies (GWASs) are available that analyze our entire genome rather than individual candidate genes. These studies have found that numerous genes have small associations with treatment response. Available pharmacogenetics tests analyze at most a small percentage of these genes. Promising candidate genes have been found to predict antidepressant response. For example, polymorphisms in introns (areas between DNA regions coding for genes) or in genes coding for the serotonin transporter, specific serotonin receptors, or proteins involved in adult neurogenesis.

Replication problem

Although these findings are fascinating, they haven't yet been reliably replicated, either due to inconsistent findings in subsequent trials or a lack of replication trials. Often the industry-funded studies that were either randomized and/or blinded have significant methodological biases that influence outcome data. For instance, diagrams may show only the active treatment condition receiving colorful test results that influence placebo response or having treatment conditions blinded to patients and not to researchers.

The pace of all aspects of human life seems to be increasing exponentially over time. Consider fast food of countless varieties, home-cooked meals delivered to doorsteps in boxes with ingredients inside pre-portioned and prepped, social media permitting instant connections without mail or time zone concerns, EZ-Pass systems replacing toll booths on highways, or the increasing amount of pharmaceutical knowledge being crammed into all stages of medical education and training over a fixed number of years. It follows that many have come to expect instant gratification across all domains of life, including in medical treatment. However, at this juncture it isn't likely that obtaining pharmacogenetic testing will reliably reduce the time required to find a patient's optimized psychotropic regimen for most mental health disorders.

No single candidate gene is reliably predictive of psychotropic treatment response, reducing the utility of the majority of pharmacogenetic tests that include candidate gene data in their recommendations. Similarly, information on the CYP 450 function wouldn't appreciably change most prescribers' first drug trial given most prescribers follow the classic adage "Start low and go slow."

Low-dose risperidone

Most pediatric prescribers would initiate risperidone, a CYP 450 3A4 substrate, at a low dose. In a CYP 450 3A4 poor metabolizer, we may find either treatment effects or adverse effects at low doses, and most prescribers would then continue low-dose treatment or discontinue the drug as indicated. Conversely, if risperidone were initiated in a CYP 450 3A4 ultra-rapid metabolizer, the dose would likely be titrated over time prior to observation of efficacy or side effects and then the dose would either be held at the higher dosing range or the drug discontinued.

At the rate we're forging ahead, I expect a day will come when validated candidate gene algorithms devised from GWAS data will be run against our personal genomic test data. These results may be able to suggest a "best first drug" to trial within a class for treatment of a specific condition. Presently, there are times when testing the hepatic CYP 450(s) function may be useful. Knowledge of psychotropic hepatic drug metabolisms or access to CYP 450 tables allows psychiatrists to make educated hypotheses about a patient's CYP 450 function based on their clinical response to specific medications. Confirming hypotheses may be useful with a lab test for the involved CYP 450(s). CYP 450 testing may also be considered in patients requiring dosing at the extremes for numerous psychotropic trials, frequently experiencing unusual adverse effects, taking a drug(s) that has an FDA pharmacogenetic warning on its label, or remaining treatment refractory despite numerous therapeutic trials of evidence-based psychotropics. Given high lab testing costs, potential for misinterpreting results, difficulty replacing clinical acumen, and little utility in improving treatment, pharmacogenetic testing is not indicated at this time.

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Correction

"Case presentation: Mental health stigma and the effect on children in Kenya" from the November issue of *CABL* listed only one author, in error. There should have been three. The three authors are Caley Arzamarski, Ph.D.; Yohanis Anglero-Diaz, M.D.; and Alison Duncan, M.D. Arzamarski is an outpatient child and family psychologist at Bradley Hospital who works within the crisis clinic and also facilitates the iFriend social skills group; she is also clinical assistant professor of psychiatry and human behavior at the Warren Alpert Medical School of Brown University. Anglero-Diaz is a graduate of the Brown Child and Adolescent Psychiatry fellowship program and is currently an attending in the Boston Children's Hospital inpatient medical and psychiatric unit and an instructor in psychiatry at Harvard Medical School. Duncan earned her M.D. in the charter class of the Geisinger Commonwealth School of Medicine; she trained in general psychiatry at the University of New Mexico and in child and adolescent psychiatry at Brown University and is the associate director for psychiatric emergency services at Boston Medical Center and an instructor in the Boston University School of Medicine. We regret the error.

Guest Commentary

Trauma-informed health care: Its time is now

Margaret Paccione-Dyszlewski, Ph.D.

Those of us who work in health care are intimately familiar with trauma. Medical trauma routinely appears on our doorstep as the fractured pelvis, serious burn, or brain injury. But what of the other trauma — the one that is less visible, excruciatingly painful, and always present in health care settings: psychological trauma. There is hardly a patient or visitor who crosses the threshold of a health care facility who does not carry a reservoir of worry, fear, stress, or trauma.

In brief, psychological trauma can be defined as any adverse experience that affects a person's ability to function. Having individuals in our health care system who have experienced trauma has always been true. What has changed, however, is that we now know the consequence of prolonged exposure to stress is universal and impacts all major domains of human development and functioning. As documented by the landmark Adverse Childhood Experiences study (Felitti et al., 1998) and other subsequent research, childhood exposure to abuse, neglect, family mental illness, discrimination, parental incarceration, violence, and other adverse experiences increase an individual's lifelong potential for serious health problems and engaging in health-risk behaviors.

Attitude toward medical care

As many traumatic events erode the dignity and safety of the individual, such events may also influence a survivor's attitude toward medical care and the provider of that care. Many health care procedures, especially those that involve a patient to be alone with a provider, placed in a physically vulnerable position, or touched in intimate areas, may be retriggering for traumatized patients. Depending on the nature of their trauma, many individuals may be reluctant to trust providers with critical information or may avoid the health care system altogether.

A concept termed trauma-informed care (TIC) has invited evolutionary change in a variety of settings, including schools, prisons, and social service agencies. This shift in culture has resulted in improved care to individuals who have histories of traumatic life events or toxic stress. The time has come for pediatric health care providers to implement ambitious initiatives toward becoming trauma-informed. According to the Substance Abuse and Mental Health Services Administration, a program, organization, or system that is trauma-informed:

- realizes the universal impact of trauma;
- recognizes the signs and symptoms of trauma in individuals involved with the system;
- integrates knowledge about trauma into policies, procedures and practice; and
- seeks to actively resist retraumatization.

Although the concept of trauma-informed care can take many forms as it is applied to health care, studies suggest that TIC in our delivery system consists of two major domains: universal trauma precautions and trauma-specific care.

Employing universal trauma precautions assumes that every individual receiving services in that system has a history of trauma. With this foundational culture shift in place, the stage is set for the provider to establish trust and rapport with survivors of traumatic life events, encourage patients with undisclosed trauma histories to reveal their vulnerabilities, and create a more therapeutic environment for the small percentage of individuals who have escaped life trauma.

Awareness is the first step. If a patient presents with challenging behaviors, an enlightened provider views the behavior through the lens of trauma. Brain science informs that dysregulated behaviors, emotional dyscontrol, and cognitive interruptions are hallmark trauma reactions. In a trauma-sensitive culture, trauma would be considered as a root cause of a behavior such as a patient raising her voice, a parent forgetting their child's birthdate, or a visitor pushing past a provider. Trauma research provides the back story behind many patient behaviors that challenge our health care system. Armed with nuanced knowledge and interpersonal skills, especially de-escalation skills, health care providers can vastly improve the patient experience for all populations.

Tools to help

Once the patient has revealed a history of trauma or toxic stress, specific strategies can be utilized to support the needs of the patient. These techniques may involve targeted screening to determine the health effects of the trauma, interdisciplinary collaboration, and provider education concerning the risks and prevention for vicarious traumatization.

According to author and trauma survivor Danielle Bernock: "Trauma is personal. It does not disappear if it is not validated. When it is ignored or invalidated, the silent screams continue internally heard only by the one held captive. When someone enters the pain and hears the screams, healing can begin."

A shift in culture to become more trauma-informed will set the stage for maximum healing to take place. If health care environments recoil from validating damaging trauma experiences, the toxicity of trauma may corrode the very potential for healing. For additional information, go to http://www.samhsa.gov and https://www.chcs.org.

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You think you're confused? Even clinicians say drug names are misleading

By Alison Knopf

Clinicians are used to the names of psychotropic medications — so used to them that they may forget how odd they sound to patients and parents. In an article in the October issue of the *Journal of the American Academy of Child and Adolescent Psychopharmacology*, top researchers in the field write that the medication names are actually unclear and misleading, and propose a new nomenclature.

Parents may think serotonin reuptake inhibitors are for depression only, even though they help with pediatric anxiety disorders. "Stimulant" medications could be easily misunderstood by parents of children with attention-deficit/hyperactivity disorder, who wonder why their rambunctious child needs stimulation. And antipsychotics, which may be prescribed — on label — to children with mania, bipolar depression, tics, or irritability in autism, could be upsetting to parents who don't think of their child as "psychotic."

Parents and patients sometimes, instead of asking questions, just don't come back. They think you don't understand their child, the authors wrote.

Outdated and inaccurate

Where did these names come from? Mainly the 1960s and 1970s, when "stimulants" promoted wakefulness, "antidepressants" improved mood, and "major tranquilizers" became "antipsychotics." Benzodiazepines and tricyclic antidepressants got their names from their chemical structure.

But none of these terms are scientifically accurate based on contemporary knowledge. "Antidepressants" don't bind to "depression receptors," but rather block monoamine transporters. Noradrenergic "antidepressants" are effective only in treating depression, but serotonergic reuptake inhibitor "antidepressants" are effective for depression and obsessive compulsive disorder. And selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors (SNRIs), despite being called antidepressants, can treat more than that.

It's not only that the current psychotropic medications are out of date — they adversely affect patient care by conflating diagnoses and treatment targets, and contributing to stigma.

The problem isn't restricted to pediatric psychotropics. "Blockers" are often considered antihypertension medications, but they have other indications as well, including arrhythmias, migraine prophylaxis, and even anxiety. But in psychiatry, misnomers are more troublesome, especially for children. They think they are "depressed" if prescribed an "antidepressant," and well-meaning parents may try to explain, just muddying the waters.

"Legacy naming" is a problem as well. For example, bupropion, mirtazapine, duloxetine, and fluoxetine are all "antidepressants," but they have extremely differing mechanisms of action, side effects, and indications. In addition, patients don't understand why they should try a different "antidepressant" when the first hasn't worked.

NbN app

What's the solution? A group of international organizations has created a Nomenclature Taskforce to develop a neuroscience-based approach, classifying psychiatric medications by pharmacology rather than chemical structure or disease. For example, instead of medicines under the nonspecific title of "antidepressants," they would be named based on pharmacology and mode of action.

This change would be useful to both clinicians and patients, and would also help reduce stigma, the authors wrote. "Instead of 'antidepressants' for enuresis, clinicians can talk about 'recruiting brain systems to change the depth of your sleep.' Instead of giving 'antipsychotics,' clinicians can discuss 'targeting the dopamine system to help you with your tics,'" they wrote.

The Neuroscience-based Nomenclature (NbN) system includes more than 130 psychotropic medications. It expands and replaces terminology into 11 pharmacological domains, such as norepinephrine, dopamine,

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glutamate, and serotonin. Ten modes of action are identified, ranging from effects at receptors and transporters to impacts on ion channels and enzymes. "These pharmacological domains and modes of action are cornerstones for a nuanced description of psychotropic medications," the authors concluded.

Challenges

However, there are many challenges to adopting this new system. One is the inertia among clinicians themselves, who are used to the legal nomenclature, with all its flaws. But overcoming that inertia would have benefits. "For example, when providing psychoeducation about attention-deficit/hyperactivity disorder (ADHD), explaining the etiology of ADHD in the context of the dopamine and norepinephrine systems logically flows into a discussion of medication treatment — methylphenidate and amphetamine salts as dopamine and norepinephrine reuptake inhibitors and releasers," the researchers wrote. "Dropping the term 'stimulant' and talking about the mechanism of action creates a more insightful, coherent, and less misleading explanation."

Another challenge is that the knowledge of medication mechanisms and pharmacology is incomplete, as is best exemplified by lithium. This medication has its own category in the NbN. But despite this challenge, it's better than "lumping lithium with valproic acid and lamotrigine as 'mood stabilizers,' as if their pharmacology had anything in common," the researchers wrote.

The ultimate goal is for NbN to be accessible for free via an app that would be available on mobile devices, including full descriptions of psychotropic medications, their former terminology, pharmacology targets, modes of action, approved indications, efficacy (off-label use), side effects, practical notes, and neurobiology. A separate child psychiatry–specific app (NbN-ca) has also been developed. It includes child-based dosing information as part of the practical notes. The NbN would be updated and improved as new information becomes available.

The authors reported multiple possible conflicts of interest in relationships with pharmaceutical companies and publishers.

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