**Making HIV Transmission a ‘Rare Event’**

Approximately 80% of new human immunodeficiency virus (HIV) transmissions are from people who don’t realize they have HIV or who are not receiving regular care, according to a Centers for Disease Control and Prevention (CDC) report. This makes improvements in early detection and “rapid entry into care” key to ending the HIV epidemic within 10 years—the current goal of the Department of Health and Human Services (HHS).

Recent studies have shown that viral suppression prevents sexual transmission of HIV, say the researchers. The studies found no HIV transmissions attributable to sex between HIV-discordant couples when the infected partner was maintaining viral suppression through treatment—even when the HIV-negative partner was not using pre-exposure prophylaxis. Those findings mean that HIV transmission could become a “rare event,” according to the researchers.

Today’s treatments are a far cry from the pile of pills a patient used to have to take; sometimes, a patient needs only a single-tablet regimen. Most people, say the CDC, can achieve viral suppression within six months of starting treatment.

But many of the 1.1 million people living with HIV infection don’t receive effective treatment. In 2015, 14.5% of people did not have a diagnosis and 37.2% were not receiving care (having one or more CD4 tests in a measurement year). Nearly half of people with HIV were not virally suppressed. Lack of effective treatment, which results in worse outcomes and higher rates of transmission, was associated with 38,700 new infections in 2016.

The researchers used a model to estimate transmission rates in 2016 along the HIV continuum of care. Overall, the rate was 3.5 per 100 person-years. Among 9,600 people who were acutely infected and unaware of their infection, the rate was 16.1 per 100 person-years. Among 154,400 people who were non-acutely infected and unaware, the rate was 8.4 per 100 person-years.

Of approximately 250,000 people who were aware of infection but not receiving care, 16,500 transmissions were generated (6.6/100 person-years). Among the 125,300 who were receiving care but not virally suppressed, 7,700 transmissions were generated (6.1/100 person-years).

The transmission rate was zero for virally suppressed patients. The researchers note that 100% efficacy was assumed based on trial results for sexual transmission; no data are available on the efficacy of viral suppression in reducing HIV transmission from injection-drug use.

Better detection and linkage to treatment will address most of the problem, but what about patients who don’t maintain viral suppression? Among patients in clinical care, close to 80% were virally suppressed at their most recent visit but approximately one-third of them did not sustain suppression over a year. For those patients, a tailored approach aimed at the barriers most relevant for a particular patient is critical for improving adherence.

The CDC recommends the routine screening of all Americans aged 13 to 64 years at least once in their lifetime and at minimum, annual testing for those who are at high risk. In addition, continue the researchers, it’s important to spread the word that maintaining viral suppression prevents sexual transmission. Sharing this knowledge more generally might reduce the stigma associated with HIV and help engage patients in consistent care.

Source: Centers for Disease Control and Prevention, March 18, 2019

**Trial to Study New Drug for Opioid Cravings**

How to curb the cravings that can plague people with opioid dependence and block their road to sobriety? Hoping to find the answer, researchers are starting a new trial at the National Institutes of Health (NIH) Clinical Center.

Habitual use of opioids “rewires” the brain’s reward system. In this study, researchers will be testing ANS-6637 (Amygdala Neurosciences), a drug that may inhibit the dopamine surge from opioid use without affecting the dopamine levels required for normal brain function.

The phase 1, 10-day trial will enroll up to 50 healthy adults aged 18 through 65 years. On day 1, participants will receive a single dose of midazolam, chosen to act as a template for liver metabolism. After a drug-free day 2, on days 3 through 7 they will receive 600 mg/day of ANS-6637. On day 8, participants will be given the two drugs together to determine how the investigational drug affects midazolam levels, which will also help the researchers understand how ANS-6637 is processed in the body. The participants will then return for a final outpatient visit after one week.

At present, few pharmacological interventions target opioid-related cravings, says Henry Masur, MD, chief of the Clinical Center’s Critical Care Medicine Department. If proven effective, ANS-6637 could be part of a comprehensive package of services, including harm reduction, opioid-agonist therapy, and behavioral interventions.

The study is being funded through NIH’s Helping to End Addiction Long-Term (HEAL) Initiative, an “aggressive, trans-agency effort to speed scientific solutions” to the opioid crisis.

Source: National Institutes of Health, March 21, 2019

**Do Collaborative Models Work for Mental Health Patients in a General Clinical Setting?**

Collaborative chronic care models (CCMs) are effective in serious mental illnesses—this has been demonstrated in extensive randomized clinical trials. Much of the effectiveness comes from their emphasis on flexibility; they are implemented according to local needs, capabilities, and priorities. The models also provide support for redesigned work roles promoting “anticipatory” continuous care; for self-management; and for
clinical decision-making at a local level.

In 2013, the Veterans Administration (VA) Office of Mental Health and Suicide Prevention (OMHSP) began an initiative to enhance care coordination in general mental-health clinics among mixed-diagnosis populations. It established interdisciplinary teams in each VA medical center throughout the U.S. Although OMHSP provided centrally developed guidance, it gave facilities “broad latitude” to develop their own team processes. In 2015, OMHSP adopted the CCM.

However, most of the data on how well CCMs work for mental health conditions come from depression treatment in primary care—and the effects seem to be inconsistent. Thus, researchers from the VA Boston Healthcare System and others partnered with OMHSP to find out whether the CCM model would be effective in a general clinical setting.

They recruited nine VA facilities for a two-year study conducted in three waves. The implementation strategy was based on the premise that “health care is a complex adaptive system rather than a highly controlled machine.” In other words, that the system would work best when local solutions for local challenges are developed according to evidence-based guidance. The multifaceted approach included an external facilitator who provided guidance and quality-improvement expertise and an on-site internal facilitator to direct the implementation.

In the study, 5,596 veterans treated by outpatient general mental-health teams were included in hospitalization analyses. A randomly selected sample of 1,050 veterans (including 210 women) was identified for health status interviews. The researchers found a “robust” and sustained reduction in mental health hospitalization. However, the effects on self-reported health outcomes were “limited.” The mental component score (the primary intervention outcome), and other interview measures, had no statistically significant change with implementation support in adjusted or unadjusted models.

The researchers say they saw no difference in the manner in which veterans were treated between higher- and lower-implementing teams.

In post hoc analyses, however, it became clear that patients with more complex problems—defined as receiving treatment for three or more mental health diagnoses in the previous year—did show statistically significant improvements in the facilitation year (by a magnitude of 0.31 standard deviation [SD]). By contrast, patients with two or fewer diagnoses declined non-significantly during the same time. The researchers note that other studies have found that CCM-based teams in patient-centered medical homes have also shown more benefit among higher-morbidity patients.

Overall, the model was shown to be effectively implemented with “practical, scalable support” for clinicians. Another benefit was that teams performed better. The researchers assessed team function at baseline and during the second six months on measures including communication, cohesion, role clarity, and team primacy (prioritizing team over individual goals). The subscales showed high ratings for cohesion and communication at baseline, which did not change with implementation support. However, role clarity and team primacy improved significantly. The researchers concluded that under typical practice conditions, CCMs can help clinicians to help the sickest patients.

Source: Department of Veterans Affairs, April 1, 2019

Promising New Approach for Treating Chronic Infections in Cystic Fibrosis

A long-time antifungal standard, amphotericin, may hold the key to reducing or even preventing the chronic infections that bedevil patients with cystic fibrosis (CF).

In cystic fibrosis, a defective gene makes a defective protein that produces acidic and sticky mucus; this clogs the lungs and puts patients at risk for bacterial infections. Because different people have different protein mutations, and 10% of patients with CF make no protein at all, treatments are limited. But amphotericin has the potential to work regardless of mutation, even when the protein is missing. The researchers liken the drug to a “molecular prosthetic,” because it restores function in much the same way that a prosthetic device replaces a limb.

In the study, supported in part by the National Heart, Lung, and Blood Institute, researchers used lung tissue from patients with CF, as well as animal models. Rather than trying to correct the protein or perform gene therapy (which the researchers say is not yet effective in the lung), they used a small-molecule protein that can perform the channel function of the missing or defective protein.

They found that amphotericin restored pH levels, improved viscosity, and increased antibacterial activity. Amphotericin also can be delivered directly to the lungs to avoid common side effects.

Although more studies are needed, according to the NIH, “experts are hopeful.”

Source: National Heart, Lung, and Blood Institute, March 13, 2019

Study Delivers Insight Into Alcohol’s Effects on The Brain

“Brain power” takes on new meaning with results from a study funded by the National Institute on Alcohol Abuse and Alcoholism. The findings could lead the way to understanding the brain’s intake and output of energy in good health and bad, and what part alcohol plays.

In previous studies, the researchers showed that alcohol significantly affects brain-glucose metabolism—a measure of energy use—as well as regional brain activity, which is assessed through changes in blood oxygenation. But regional differences in glucose metabolism are hard to interpret, say the researchers. In a study with healthy volunteers, they used brain imaging techniques to help quantify “match and mismatch” in

Source: National Heart, Lung, and Blood Institute, March 13, 2019
energy consumption and expenditure across the brain—which they termed “power and cost.”

The researchers assessed power by observing to what extent brain regions are active and use energy, and assessed cost by observing how they expend energy. They found that different brain regions that serve distinct functions have “notably different power and different cost.”

Next, they tested a group of light drinkers and heavy drinkers and found that both acute and chronic alcohol exposure affected power and cost. In heavy drinkers, there was less regional power, for example, in the thalamus, sensory gateway, and frontal cortex. The researchers interpreted the power decreases as reflecting the toxic effects of long-term alcohol exposure on brain cells.

They also found that power dropped in the visual regions during acute alcohol exposure, which was related to the disruption of visual processing. Visual regions also had the most significant drops in cost of activity during intoxication, which is consistent with the reliance of those regions on alternative energy sources, such as acetate (a by-product of alcohol metabolism).

Their approach for characterizing energetic patterns related to alcohol consumption could be useful in other ways. “Studying energetic signatures of brain regions in different neuropsychiatric diseases is an important future direction,” said co-lead investigator Dr. Ehsan Shokri-Kojori. “The measures of power and cost may provide new multimodal biomarkers.”

Source: National Institute on Alcohol Abuse and Alcoholism, March 4, 2019

**During Flu Season, Risk of Heart Failure Rises**

A study of more than 450,000 adults has “confirmed the long-held notion” that influenza and heart failure are connected. The Atherosclerosis Risk in Communities (ARIC) study found that influenza significantly increased the risk of hospitalization for heart failure.

Every flu season, approximately 36,000 people die, and more than 200,000 are hospitalized, which is known to be associated with a higher risk of cardiovascular events. Several mechanisms likely contribute to this; some form of immunocompromise is thought to be a crucial link. But few studies, the researchers note, have explored the temporal association between influenza activity and hospitalizations, particularly those caused by heart failure.

In ARIC, the researchers analyzed hospitalization data from 2010 to 2014 for adults aged 35 to 84 years in geographically diverse communities in Mississippi, Minnesota, North Carolina, and Maryland. They correlated those data with reports of influenza activity from the CDC Surveillance Network.

A 5% monthly increase in influenza activity was associated with a 24% relative increase in heart-failure hospitalization rates. Myocardial infarction hospitalizations did not rise significantly. The greatest number of deaths associated with pneumonia and influenza occurred during the 2012–2013 season, when influenza-like illness (ILI) activity was highest, and the fewest deaths occurred during the 2011–2012 season, when ILI activity was lowest. The ARIC model suggests that in a month with high influenza activity, approximately 19% of hospitalizations could be attributable to the illness.

Source: MDedge, April 18, 2019

**Gout Drug May Help in Metabolic Syndrome**

Colchicine, used to suppress or prevent inflammation in patients with gout and pericarditis, may have a role in treating metabolic syndrome, according to an NIH pilot study.

Colchicine inhibits the formation of the Nod-like Receptor Family Pyrin Domain Containing 3 (NLRP3) inflammasome, a key component in the obesity-associated inflammatory cascade. In a retrospective study, long-term colchicine treatment had glyceric benefit in patients with gout. Other research suggested that suppressing NLRP3 could improve peripheral insulin resistance as well as beta-cell insulin production. However, no randomized controlled trial had investigated colchicine’s long-term effects on glucose metabolism in adults with obesity and metabolic equivalents (METS).

The researchers enrolled 40 adults to receive either colchicine or placebo, 37 of whom completed the three-month study. Adherence was high in both groups.

Colchicine significantly reduced multiple markers of obesity-associated inflammation, including high-sensitivity C-reactive protein and erythrocyte sedimentation rate. The colchicine group also had moderate but statistically significant reductions in white blood-cell count, monocytes, neutrophils, and platelets, without significant effects on lymphocyte count.

Although colchicine’s effects on the primary outcome—insulin sensitivity—were not significant, some of the secondary outcomes related to glucose homeostasis, such as insulin resistance and fasting insulin, suggest that colchicine might improve hepatic insulin sensitivity. Moreover, say the researchers, a trend toward improvement in disposition index suggests that the drug might delay the onset of diabetes in people at risk.

Although some small, short-term studies suggested that colchicine could actually worsen metabolic variables by inhibiting insulin secretion, other recent retrospective studies have found that long-term colchicine use did not negatively affect insulin secretion or glycemic control. Similarly, in the Atherosclerosis Risk in Communities (ARIC) study, chronic colchicine use did not impair first-phase insulin response or insulin sensitivity, and other markers of metabolic health, such as HbA1c and cholesterol, were not significantly changed. However, the researchers acknowledge that their study might have been too small to confirm those differences and that larger studies are warranted.

Source: National Institutes of Health, April 2, 2019