3-23-19

Science 2019 Feb 22; 363:880

Sleep and Tau Are Connected

Sleep deprivation is associated with increased levels of tau in animals and humans.

Disrupted sleep is associated with dementia and might increase β-amyloid (Aβ) and tau deposition. Tau aggregation is seen in Alzheimer disease, chronic traumatic encephalopathy, progressive supranuclear palsy, and other diseases. Because tau levels are higher during wakefulness than sleep, investigators explored the relationship of sleep deprivation to levels of Aβ and tau in interstitial fluid (ISF) and cerebrospinal fluid (CSF) in animals and humans.

Mouse ISF tau increased almost 90% during normal wakefulness and doubled during sleep deprivation when compared with levels in normal sleep. This increase is greater than the investigators previously found with Aβ. Six humans (age range, 30–60) had lumbar catheters placed for 1 night of normal sleep and 1 night of sleep deprivation. CSF tau increased

by more than 50% during sleep deprivation, whereas Aβ showed increases of 30%; synuclein (but not neurofilament light chain and astrocytic glial fibrillary acidic protein) also increased. In other animal experiments, sleep deprivation increased the spread of tau pathology through the brain.

COMMENT: In this series of studies, sleep deprivation influenced the pathologic processes believed to regulate tau pathology. Causal relationships are difficult to prove because tauopathies are also associated with disrupted sleep. Other questions arise: Is sleep deprivation a risk factor for chronic traumatic encephalopathy and other tauopathies? Does the need for less sleep (such as in hypomania) also increase risk? Does sleep disruption explain the observed link between bipolar disorder and dementia? Disrupted circadian rhythm and sleep deprivation could be useful targets for treatment of conditions such as dementia, traumatic brain injury, and mood disorders.

CITATION(S): Holth JK et al. The sleep-wake cycle regulates brain interstitial fluid tau in mice and CSF tau in humans. Science 2019 Feb 22; 363:880. (https://doi.org/10.1126/science.aav2546)

Noble W and Spires-Jones TL. Sleep well to slow Alzheimer's progression? Science 2019 Feb 22; 363:813. (https://doi.org/10.1126/science.aaw5583)

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BMJ 2019 Mar 6; 364:l665

Does Menopausal Hormone Therapy Raise Risk for Alzheimer Disease?

In a Finnish national observational study, modest elevations in AD risk do not imply causation by HT use.

Although sex hormones may influence the etiology of Alzheimer disease (AD) in women, studies addressing the effects of menopausal hormone therapy (HT) on AD risk have yielded conflicting data. Using national records, investigators in Finland identified 84,739 women with diagnoses of AD between 1999 and 2013, then matched them with the same number of control women (those without AD) during that period; HT use was also ascertained.

Women with AD diagnoses were more likely to have been former or current users of systemic HT than controls (18.6% vs. 17.0%, $P<0.001$). Increased risk for AD was modest and did not differ significantly among users of estradiol only (odds ratio, 1.09; 95% confidence interval, 1.05–1.14) and estrogen-progestin HT (OR, 1.17; 95% CI, 1.13–1.21). Initiation of HT before age 60 was less common among cases than controls ($P=0.006$). Use of vaginal estrogen was not associated with excess risk for AD.

COMMENT: AD is more prevalent in women than men (and women are more likely to be caregivers for individuals with AD), making this disease particularly concerning for midlife and older women. Current guidelines from the North American Menopause Society (NEJM JW Womens Health Aug 2017 and *Menopause* Jul 2017; 24:728) and other organizations do not recommend use of systemic HT to prevent AD. As the authors and editorialists note, the modest increases in AD risk with HT use seen in this observational study are subject to bias. The editorialists also point out that a conclusive, large randomized trial assessing HT's impact on AD is unlikely to be performed. I agree that these findings should not change current practice, and I will continue to counsel recently menopausal women with bothersome vasomotor symptoms and no contraindications that initiating systemic HT is appropriate.

CITATION(S): Savolainen-Peltonen H et al. Use of postmenopausal hormone therapy and risk of Alzheimer's disease in Finland: Nationwide case-control study. BMJ 2019 Mar 6; 364:l665. (https://doi.org/10.1136/bmj.l665)

Maki PM et al. Menopausal hormone therapy and cognition. BMJ 2019 Mar 6; 364:l877. (https://doi.org/10.1136/bmj.l877)

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Neurology 2019 Feb 21

Midlife Cognitive and Physical Activity and Dementia Risk in Women

Jennifer Rose V. Molano, MD reviewing Najar J et al. Neurology 2019 Feb 21

A 44-year longitudinal study shows that midlife cognitive and physical activity decreased dementia risk in Swedish women.

Midlife factors may contribute to dementia risk, but many studies have had a high mean age at baseline and short follow-up times. Researchers have now analyzed whether midlife cognitive and physical activity at baseline (1968–1969) were associated with dementia risk in 800 Swedish women during a 44-year follow-up period. Levels of cognitive activity (intellectual, artistic, manual, club, and religious) were assessed by semistructured interviews, and the frequency of each cognitive activity was rated from 0 (no/low) to 2 (high), with a sum score of 0 to 10. Levels of physical activity were determined by a validated scale. Dementia diagnoses were determined by established criteria using neuropsychological testing, informant interviews, and national registry data.

At baseline, the mean age was 47 years, about 40% had a cognitive activity sum score of 2 or 3, and 70% had regular physical activity for at least 4 hours per week. During follow-up, 194 women developed dementia (52.6% Alzheimer disease [AD], 13.9% vascular dementia, 21.1% mixed dementia, and 7.2% other dementias). After adjustment for age, education, socioeconomic status, smoking, body–mass index, and medical/psychiatric comorbidities, cognitive activity reduced the risk for total dementia by 34% and AD by 46%; physical activity reduced the risk for total dementia and vascular dementia by 28%, mixed dementia by 57%, and dementia with cerebrovascular disease by 53%. Higher levels of cognitive activity correlated with a greater risk reduction for AD and total dementia, and higher levels of physical activity correlated with a greater risk reduction for mixed dementia.

COMMENT: These results suggest that midlife cognitive and physical activity decrease dementia risk in women. Although this study included only Swedish women and activity levels were assessed only at baseline, clinicians should continue to encourage engagement in cognitive and physical activities to promote brain health in both women and men.

CITATION(S): Najar J et al. Cognitive and physical activity and dementia: A 44-year longitudinal population study of women. Neurology 2019 Feb 21; [e-pub]. (https://doi.org/10.1212/WNL.0000000000007021)

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JAMA Netw Open 2019 Mar 1; 2:e190185

New Evidence of Lower Risk for Lung Cancer with Low-Dose Aspirin

Using low-dose aspirin for 5 to 9 years was associated with modestly reduced relative risk.

Inhibition of cyclooxygenase by aspirin is a plausible explanation for how aspirin could lower risk for lung cancer. Some randomized trials have shown a benefit for long-term, low-dose aspirin use, but epidemiological and cohort studies, especially in women, have shown no benefit. In this Korean study, researchers used a national database to identify nearly 13,000,000 patients for whom information on aspirin use and lung cancer diagnoses was available. Low-dose aspirin use was defined as doses of ≤100 mg daily, at least 2 days per week.

During mean 5-year follow-up, about 63,000 cases of lung cancer were diagnosed. Analyses were adjusted for demographic variables and clinical risk factors. Compared with no aspirin use, long-term, low-dose aspirin use was associated with significantly lower risk for lung cancer; risk reductions were 4%, 6%, and 11% after aspirin use for 5 to 6 years, 7 to 8 years, and 9 years, respectively. In subgroup analyses, similar benefits were reported for older patients (age, ≥65). Relative risk reductions for those younger than 65 were small and not statistically significant.

COMMENT: Although the results of this observational study could reflect confounding, the correlation between longer use of low-dose aspirin and lower risk for lung cancer strengthens the findings. However, the magnitude of benefit is small and needs to be factored into a more comprehensive assessment.

CITATION(S): Ye S et al. Association of long-term use of low-dose aspirin as chemoprevention with risk of lung cancer. JAMA Netw Open 2019 Mar 1; 2:e190185. (https://doi.org/10.1001/jamanetworkopen.2019.0185)

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Endoscopy 2019 Feb 20;

Choosing Between Aggressive Treatments for Difficult Bile Duct Stones

Laser lithotripsy was superior to mechanical lithotripsy in a small randomized study.

Although most bile duct stones are easily removed via biliary sphincterotomy and balloon extraction, about 10% require more-aggressive treatments, including endoscopic balloon dilation of the bile duct, mechanical lithotripsy, laser lithotripsy, and electrohydraulic shock wave lithotripsy (used alone or in combination). To date, few studies have compared these advanced modalities.

Now, investigators have conducted a randomized study to compare the effectiveness of cholangioscopy-guided laser lithotripsy versus mechanical lithotripsy to remove large bile duct stones in 32 patients with who had failed treatment with endoscopic balloon dilation of the bile duct. Patients assigned to either modality could cross over to the other study arm in the event of treatment failure.

The success rate for stone clearance with a single procedure was higher with laser lithotripsy than with mechanical lithotripsy (100% vs. 63%; $P<0.01$). Six patients in the mechanical lithotripsy arm crossed over to the laser arm of the study after 120 minutes of procedure time; of these, three achieved stone clearance. Procedure times were similar in the two study arms, although mechanical lithotripsy required significantly more fluoroscopy time. There were no differences in adverse events or stone recurrence between the two arms.

COMMENT: This is the first randomized study to date that compares two different lithotripsy techniques in patients with difficult common bile duct stones. Although the data presented strongly favor laser lithotripsy, I have some concerns about the study. First, the sample size was quite small, with only 16 patients in each study arm. Small changes in patient outcomes in a study of this size could markedly affect the overall results. Second, whereas all practitioners of endoscopic retrograde cholangiopancreatography should have access to mechanical lithotripters, few have access to a laser, and the laser lithotripter requires the use of a cholangioscope, further adding to the cost and complexity of the procedure. I have seen a much higher rate of success with mechanical lithotripsy than these authors found, raising questions about the generalizability of the data. I would like to see a larger, multicenter study that compares these techniques before making a judgement on which one is superior.

CITATION(S): Angsuwatcharakon P et al. Digital cholangioscopy-guided laser versus mechanical lithotripsy for large bile duct stone removal after failed papillary large-balloon dilation: A randomized study. Endoscopy 2019 Feb 20; [e-pub]. (https://doi.org/10.1055/a-0848-8373)

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Am J Gastroenterol 2019 Mar; 114:384

Management of Ulcerative Colitis

The extent and severity of disease drive decisions regarding induction and maintenance regimens.

Sponsoring Organization: American College of Gastroenterology

Background and Objective: The management of ulcerative colitis (UC) has changed since the last guideline was published in 2010. The recommendations in the current update are based on the quality of evidence using GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology.

What's Changed: New tests, including those based on serum drug levels and fecal calprotectin, as well as newer FDA-approved therapies, including budesonide, vedolizumab, and tofacitinib

Key Recommendations

- Screen patients with UC for coexisting anxiety and depressive disorders, and when identified, provide patients with resources to address these conditions.
- Treat patients with UC to achieve mucosal healing, increase the likelihood of sustained steroid-free remission, and prevent hospitalizations and surgery.
- Use fecal calprotectin as a surrogate for endoscopy to assess for mucosal healing when endoscopy is not feasible or available.
- In patients with moderately active UC, use nonsystemic corticosteroids, such as budesonide MMX, before systemic therapy.
- In patients with moderately to severely active UC, use vedolizumab to induce remission.
- In patients with moderately to severely active UC, use tofacitinib (10 mg orally twice daily for 8 weeks) to induce remission.
- Do not defer colectomy because of exposure to infliximab and cyclosporine, as these agents do not increase the risk for postoperative complications.
- In patients with acute severe UC and concomitant *Clostridium difficile* infection, use vancomycin instead of metronidazole.
- Perform surveillance colonoscopies in patients with UC at 1- to 3-year intervals, based on the combined risk factors for colorectal cancer in UC and the findings on previous colonoscopy.

COMMENT: These updated guidelines discuss important extraintestinal issues of UC patients, including psychological and psychiatric conditions that can affect disease outcomes. Also highlighted is the importance of testing and using the optimal treatment for *C. difficile* infection as a concurrent condition. Recommendations about the use of newer therapies, including vedolizumab and tofacitinib, are given for both anti–tumor necrosis factor–exposed and naive patients. The new recommendations for cancer surveillance are more individualized, and patients with no other risk factors may now be scoped at intervals as long as every 3 years, instead of yearly.

CITATION(S): Rubin DT et al. ACG clinical guideline: Ulcerative colitis in adults. Am J Gastroenterol 2019 Mar; 114:384. (https://doi.org/10.14309/ajg.0000000000000152)

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JAMA Pediatr 2019 Feb 25

Eating Breakfast in the Classroom Increased Obesity in Schoolchildren

School Breakfast Program participation also increased, possibly mitigating food insecurity.

The federal School Breakfast Program is offered to children of low-income families in U.S. public schools to help improve academic achievement and food security. Offering breakfast in the classroom, rather than before school, is an innovative way to address relatively low program usage, but its effects have not been studied.

Researchers randomized 16 Philadelphia public schools (kindergarten–8th grade) to offer either the standard School Breakfast Program (control; breakfast offered in cafeteria before the school day started, standard nutrition education given) or the intervention, where breakfast was offered in the classroom and special nutrition education activities were carried out in the school and in the surrounding community. Study participants were students in 4th through 6th grade at baseline who were followed for 2.5 years. Outcomes included incidence and prevalence of overweight and obesity and program participation.

Students in intervention schools had similar incidence and prevalence of combined overweight and obesity, but higher incidence (11.6% vs. 4.4%; odds ratio, 2.4) and prevalence (28.0% vs. 21.2%; OR 1.5) of obesity alone. Although students' breakfast program participation was similar between intervention and control schools at baseline (32.1% and 29.7% of days, respectively), by study's end it was much higher in intervention schools (53.8% vs. 24.9% of days).

COMMENT: Despite the widely held belief that increased breakfast consumption leads to decreased risk for childhood obesity, the intervention studied here had the opposite effect. While policymakers and school breakfast program leaders will want to proceed with caution, clinicians can check with families about their children's breakfast habits. In particular, it is important to understand if children are eating two breakfasts, one at home and one at school, as well as exactly what is being served and consumed.

CITATION(S): Polonsky HM et al. Effect of a breakfast in the classroom initiative on obesity in urban school-aged children: A cluster randomized clinical trial. JAMA Pediatr 2019 Feb 25; [e-pub]. (https://doi.org/10.1001/jamapediatrics.2018.5531)

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Lancet 2019 Feb 28

Stillbirth Needn't Preclude a Next Pregnancy Within a Year

Large cohort study found no evidence that interpregnancy interval after stillbirth affected subsequent birth outcomes.

The WHO recommends that women wait ≥2 years after a livebirth and ≥6 months after a miscarriage or induced abortion before conceiving another child, but guidelines for optimal interpregnancy interval after stillbirth are lacking. Thus, researchers conducted a population-based study from a database of 1,700,000 births spanning 37 years in Finland, Norway, and Western Australia to investigate the effects on the next pregnancy of spacing following a stillbirth at ≥22 weeks' gestation.

The study cohort included almost 14,500 singleton births after previous singleton stillbirth. Median interpregnancy interval was 9 months, and 63% of women had conceived again within 12 months of the stillbirth. Among these pregnancies, 228 (2%) resulted in another stillbirth, 2532 (18%) in preterm birth, and 1284 (9%) in small-for-gestational-age birth. Pooled adjusted analysis showed that, compared with an interpregnancy interval of 24 to 59 months (reference group), intervals of <6 months (odds ratio, 1.09) and 6 to 11 months (OR, 0.91) had no association with risk for subsequent stillbirth. When stratified by gestational duration of the previous stillbirth, length of interpregnancy interval did not affect birth outcomes.

COMMENT: Although these findings must be confirmed and may not apply to women from developing countries, the authors suggest that the data may help in counseling women who want to attempt another pregnancy shortly after a stillbirth. An editorialist more rationally suggests that clinical guidance should take several maternal factors into consideration, including current health status, age, preferences regarding child spacing and ultimate family size, and emotional readiness to become pregnant again.

CITATION(S): Regan AK et al. Association between interpregnancy interval and adverse birth outcomes in women with a previous stillbirth: An international cohort study. Lancet 2019 Feb 28; [e-pub]. (https://doi.org/10.1016/S0140-6736(18)32266-9)

Klebanoff MA. Interpregnancy interval after stillbirth: Modifiable, but does it matter? Lancet 2019 Feb 28; [e-pub]. (https://doi.org/10.1016/S0140-6736(18)32430-9)

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Pediatrics 2019 Mar 4

How Does Social Media Influence Children's Choice of Foods?

Instagram marketing of unhealthy foods increased intake, but Instagram marketing of healthy foods had no effect.

Broadcast marketing and product placement of unhealthy foods high in saturated fat, salt, and sugar have been solidly linked to the global childhood obesity epidemic.

Now, to determine the impact of social media marketing of food to children, investigators in the U.K. conducted a randomized trial of 178 youths (age, 9 to 11 years) randomized to one of three groups: Participants were exposed to mock Instagram images of unhealthy foods, healthy foods, or nonfood items (e.g., sneakers) held by a 23-year-old male and a 26-year-old female YouTube video blogger (vlogger), who were among the 10 most popular vloggers in the U.K. (4 and 12 million Instagram subscribers, respectively). Most of the children (71%) had a healthy weight, 18% were overweight, and 10% were obese. The children completed a validated hunger rating tool, were exposed to the Instagram images, and then were offered a known amount of snack foods (measured in kcals) for 10 minutes.

Children exposed to the unhealthy food images consumed 15% more kcals overall than those exposed to healthy food images (P=0.05) and 26% more kcals than those exposed to nonfood images (P=0.01); the amount of kcals consumed was similar between those exposed to healthy food images or nonfood images. Moreover, children exposed to unhealthy food images consumed 20% more kcals from unhealthy foods than those exposed to healthy food images (P=0.03) and 32% more kcals from unhealthy foods than those exposed to nonfood images (P=0.001).

COMMENT: Instagram media exposure to unhealthy food increased immediate caloric intake of unhealthy food and of food overall, whereas the equivalent exposure to healthy foods had no effect. It is discouraging that the social media personalities were not able to influence the eating of healthy foods. But I'm not surprised, since food preferences that lead to healthy food choices most likely begin early in the preschool-aged years.

CITATION(S): Coates AE et al. Social media influencer marketing and children's food intake: A randomized trial. Pediatrics 2019 Mar 4; [e-pub]. (https://doi.org/10.1542/peds.2018-2554)

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JAMA Psychiatry 2019 Feb 13

Teenagers' Cannabis Use: Public Health Implications Are Not Trivial

The links from cannabis use to later depression and suicidality are strong, in a new meta-analysis and systematic review.

Whether use of marijuana in adolescence leads to psychiatric problems in early adulthood has not been definitively answered. These researchers examined the question in a meta-analysis and systematic review.

The meta-analysis involved 11 longitudinal, prospective cohort studies of cannabis use at age 18 or younger and later depression, anxiety, and suicidality at ages 18 through 32. All studies controlled for baseline depression. In pooled analyses, cannabis use in adolescence significantly increased the risks in early adulthood for depression by 37%, suicidal ideation by 50%, and suicide attempts in adolescence or young adulthood by 346%.

Another 24 studies that reported data differently from the pooled studies could not be included in the meta-analysis. Most of these studies also demonstrated a correlation between adolescent cannabis use and later depression; the risk increased most with more-chronic use and with use by girls.

COMMENT: The authors note that 21% of U.S. adolescents report monthly cannabis use and 7% of high-school seniors admit to daily or almost-daily use and that more than 400,000 adolescents might thus be at risk for depression attributable to cannabis use.

Adolescents at risk for becoming depressed might also be more prone to substance use, which often involves marijuana, increasingly the substance used most frequently by adolescents. Conversely, exposure of the developing brain to cannabis is known to alter the structure of limbic regions with high cannabinoid receptor-1 density and to alter elements of neurotransmission implicated in mood and anxiety disorders. Even if the risk to any given adolescent is relatively low, the population risk is substantial enough to warrant efforts to dampen the high rate of cannabis use that is now being encouraged by legalization of the substance.

CITATION(S): Gobbi G et al. Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: A systematic review and meta-analysis. JAMA Psychiatry 2019 Feb 13; [e-pub]. (http://dx.doi.org/10.1001/jamapsychiatry.2018.4500)

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JAMA Intern Med 2019 Mar 4

Some Patients on Warfarin Also Take Aspirin Without Clear Indications

Researchers found higher rates of bleeding complications when patients took aspirin with warfarin than warfarin alone.

Patients with atrial fibrillation (AF) or venous thromboembolism (VTE) who receive prescriptions for warfarin also might take aspirin for reasons that do not conform to recommended indications. This dual therapy might expose them to unnecessary bleeding risks. Researchers identified 6500 patients in six Michigan anticoagulation clinics who were receiving warfarin for AF or VTE for at least 3 months; patients had no heart valve replacements or myocardial infarctions in the previous 6 months.

More than one third of patients were taking aspirin, mostly low dose (i.e., ≤100 mg/day). At 1-year follow-up, after adjustment for comorbidities, other medications, and history of bleeding or thrombosis, patients taking both aspirin and warfarin, compared with those taking warfarin alone, had significantly higher rates of overall bleeding events (26.0% vs. 20.3%) and major bleeding events (5.7% vs. 3.3%). Cumulative differences in bleeding complications between the two groups continued through 3 years and then narrowed by 6 to 7 years. Rates of thrombosis and death were similar in the two groups throughout follow-up.

COMMENT: These results highlight the need to counsel patients who start warfarin about the dangers of taking concomitant aspirin. Whether the potential benefits of dual treatment will outweigh the potential harms will depend on the reasons the patient is taking each of the two drugs. The number of patients needed to harm (NNH) for overall bleeding events was about 18, and the NNH for major bleeding events was about 42. We need studies that lead to more precise calculations of risks and benefits in specific populations.

CITATION(S): Schaefer JK et al. Association of adding aspirin to warfarin therapy without an apparent indication with bleeding and other adverse events. JAMA Intern Med 2019 Mar 4; [e-pub]. (https://doi.org/10.1001/jamainternmed.2018.7816)

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N Engl J Med 2019 Feb 18

No Benefit to Adding Pneumatic Compression to Pharmacologic Prophylaxis for Preventing Venous Thromboembolism

In critically ill patients, dual therapy was not more effective than drug therapy alone.

In many intensive care units (ICUs), patients commonly receive "dual therapy" for preventing venous thromboembolism (VTE): pharmacologic prophylaxis (subcutaneous unfractionated heparin or low-molecular-weight heparin) plus pneumatic compression devices. Critically ill patients clearly are at risk for VTE, but does combining two forms of prophylaxis confer benefit?

About 2000 patients at ICUs in Saudi Arabia, Canada, Australia, and India were randomized to receive pharmacologic prophylaxis alone or in combination with intermittent pneumatic compression. Most pneumatic compression was accomplished with lower limb, knee-length sleeves. Compression was applied for a median 22 hours daily and for a median 7 days. Most participants were medical patients; one half were admitted from emergency departments. Lower-extremity ultrasound assessment for deep venous thrombosis (DVT) was performed twice weekly, and clinical care continued throughout the trial.

New cases of DVT and pulmonary embolism were rare (4% and 1%, respectively), and incidences were similar in both intervention and control groups. The incidences of pressure ulcers and skin injury were similar in both groups. Subgroup analyses yielded consistent findings. The percentage of trauma patients was low, and no data were reported for high-risk patients, such as those with malignancy.

COMMENT: Compression devices tether patients to bed, and they are noisy and often uncomfortable. Although pneumatic compression likely is useful if a patient has a contraindication to pharmacologic prophylaxis, routine dual VTE prophylaxis use warrants reconsideration. I would consider adding compression devices for particularly high-risk patients, but, for most patients, heparin or low-molecular-weight heparin alone should suffice.

CITATION(S): Arabi YM et al. Adjunctive intermittent pneumatic compression for venous thromboprophylaxis. N Engl J Med 2019 Feb 18; [e-pub]. (https://doi.org/10.1056/NEJMoa1816150)

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Obstet Gynecol 2019 Mar; 133:477

Accessing Abortion in the U.S.

In a nationally representative survey, only 24% of OB/GYNs reported providing abortion care during the past year.

Although undesired pregnancy remains common in the U.S., access to abortion services is increasingly restricted. To estimate the percentage of U.S. obstetrician-gynecologists (OB/GYNs) who provide abortion services, researchers surveyed a national sample of American College of Obstetrics and Gynecology members.

Among 597 respondents, 72% reported having a patient who requested abortion services within the past year. However, only 24% of practicing OB/GYNs reported providing abortion care during the past year. Of those who provided any

abortion services, only half offered the option of medication abortion. Even more concerning, of those who offered medication abortion, only 58% offered mifepristone **(RU-486)**.

COMMENT: While I'm pleased that the proportion of OB/GYNs providing abortion services appears to have risen since similar recent surveys (NEJM JW Womens Health Oct 2011 and *Obstet Gynecol* 2011; 118:609; NEJM JW Womens Health May 2018 and *Contraception* 2018; 97:297), the present study highlights the need for continuing medical education about best practices for managing undesired pregnancy. Given mifepristone's impressive safety and efficacy profile, it's unfortunate that so few clinics currently stock this medication. Although FDA labeling precludes pharmacy dispensing, licensed physicians or advanced practice clinicians can provide mifepristone in most states. Patients should not have to travel miles to swallow a pill.

CITATION(S): Grossman D et al. Induced abortion provision among a national sample of obstetrician–gynecologists. Obstet Gynecol 2019 Mar; 133:477. (https://doi.org/10.1097/AOG.0000000000003110)

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J Neurol Neurosurg Psychiatry 2019 Mar; 90:333

Combined Therapy for PTSD and TBI

A hybrid psychotherapeutic approach was effective for military veterans who have both diagnoses.

Veterans with a history of a traumatic brain injury (TBI) during service frequently have post-traumatic stress disorder (PTSD) as well (NEJM JW Psychiatry Apr 2019 and *JAMA Psychiatry* 2019 Jan 30; [e-pub]). But do patients with PTSD respond to cognitive therapy for TBI, and would those with TBI be responsive to PTSD-targeted therapy? In a controlled, randomized study, researchers examined the response of 100 veterans with PTSD and mild-to-moderate TBI (mild TBI, 94%) to cognitive processing therapy (CPT) for PTSD or to a hybrid of CPT and compensatory cognitive-training elements of cognitive symptom management and rehabilitation therapy (for TBI symptoms). Each therapy is effective for the individual conditions.

Diagnosis of PTSD was made by chart review or a semistructured interview. History of TBI was based on chart review and confirmed by a structured assessment. Therapies were delivered individually for 12 weeks (session length, 60–75 minutes). At end of treatment and 3 months later, both study arms showed improvements in postconcussive symptoms, PTSD symptoms, and quality of life. Combined therapy was additionally associated with neuropsychological improvements in multiple domains (attention, novel problem solving, and verbal learning/memory).

COMMENT: In this possibly practice-changing study, veterans with TBI and PTSD demonstrated significant improvements with CPT. The addition of compensatory cognitive strategies did not diminish from this efficacy but resulted in further improvement in cognitive domains. Both TBI and PTSD can result in cognitive problems, and this study could not assess the etiology. The challenge now is to generalize these findings to other patient populations and to train providers, including those at brain injury centers, to use this modality.

CITATION(S): Jak AJ et al. SMART-CPT for veterans with comorbid post-traumatic stress disorder and history of traumatic brain injury: A randomised controlled trial. J Neurol Neurosurg Psychiatry 2019 Mar; 90:333. (https://doi.org/10.1136/jnnp-2018-319315)

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