Although sexual desire and pleasure have been difficult to define objectively, they have behavioral, attentional, and learned components that reliably reflect an individual’s trajectory. Low levels of sexual desire and sexual pleasure appear to shorten telomere length. Chronic or childhood psychological adversity can initiate telomere shortening, and telomeres prematurely. Life History Theory may help explain the links between early sexual function as a means of placing modern interventions in perspective. Likewise, the presentation will describe the elements of the history of pharmacologic manipulation of the opioid, endocannabinoid, and serotonin systems are activated during periods of sexual activity, which special emphasis on women’s reproductive health factors. Converging research suggests sex and hormone effects on telomere length. Telomeres are longer in women, starting from birth. Telomere length appears to be associated with certain reproductive factors related to higher exposure to estrogen, although not all findings are consistent across studies and require further examination. Longer telomeres are associated with a longer reproductive period, later menopause, and later childbirth. Experimental studies suggest estrogen exposure increases telomerase activity throughout the body, the enzyme that can protect and elongate telomeres. Countering the protective effects of sex hormones, stress mediators such as glucocorticoids, oxidative stress, and inflammation appear to shorten telomere length. Chronic or childhood psychological adversity shorten telomeres prematurely. Life History Theory may help explain the links between early sexual function and increased risk of cancer recurrence (impacted by stage, grade, presence of invasive disease). Hormone receptor status, use of endocrine therapy, time since diagnosis) with the severity of symptoms and impact on QOL. Based on consensus in the absence of definitive data, women with lower risk of recurrence vs higher risk; hormone receptor negative disease vs hormone receptor positive disease; use of tamoxifen vs AI who are using risk-reducing strategies such as aromatase inhibitors (AI) or risk-reducing bilateral salpingo-oophorectomy about genitourinary symptoms, including vulvovaginal dryness, burning, or irritation; dyspareunia; and urinary symptoms of urgency, dysuria, or recurrent urinary tract infection. The lack of data regarding safety of vaginal hormone treatments for GSM in women with or at high risk for breast cancer specifically has led to avoidance of treatment, potentially adversely affecting quality of life (QOL) and partner relationships. Decision making regarding the type of treatment for GSM includes balancing risk of cancer recurrence (impacted by stage, grade, presence of invasive disease, hormone receptor status, use of endocrine therapy, time since diagnosis) with the severity of symptoms and impact on QOL. Based on consensus in the absence of definitive data, women with lower risk of recurrence vs higher risk; hormone receptor negative disease vs hormone receptor positive disease; use of tamoxifen vs AI who are experiencing severe symptoms, impairment of QOL, and have failed nonhormone options, may be more attractive candidates for vaginal hormone therapy. Counseling women who at high risk for breast cancer about management options for GSM includes a shared decision-making approach and, when hormone-based treatments are considered, consultation with the woman’s oncology team. Nonpharmacologic treatments, including vaginal moisturizers for maintenance of vaginal moisture and vaginal lubricants for comfort, ease of sexual activity, are generally considered safe and effective. Although efficacy data are limited. Dilator therapy, vibratory stimulation, and pelvic floor physical therapy may help reduce pain with vaginal penetration. Although randomized controlled clinical trial data regarding the risk of breast cancer or ovarian cancer with the use of vaginal lubricants are lacking, the relative safety of local estrogen. Intravaginal dehydroepiandrosterone (DHEA) approved for use in menopausal women with low estrogen who are symptomatic.
by the FDA has not been studied in survivors of breast cancer, nor have there been studies directly comparing it to vaginal estrogen in terms of efficacy or hormone levels. As such, no recommendation can be made that DHEA is a safer option than vaginal estrogen for women with or at high risk for breast cancer. Despite its antiestrogenic effects on the breast in preclinical trials, the selective estrogen receptor modulator ospemifene has not been studied in women with or at high risk for breast cancer and is not FDA approved for use in these populations. Ospemifene is a nonhormone pharmacologic option that has been shown to relieve insertional dyspareunia in survivors of breast cancer. Preliminary data suggest vaginal lasers have the potential to alleviate GSM symptoms without the use of hormones, although longer-term, sham- or placebo-controlled, randomized studies are needed to confirm their efficacy. Hormones are recommended for women who are address and include women at high risk for breast cancer; women with estrogen receptor positive breast cancer; women with triple negative breast cancer; and women with metastatic disease. Treatment should be individualized, taking into account recurrence risk, severity of symptoms and impact on QOL, and personal preferences, with nonhormone options offered as first line therapies for symptom management. Consensus-based recommendations offer clinicians caring for this population of women some guidance regarding therapeutic decision making in the absence of clinical trial data. Additional research evaluating the safety and efficacy of existing therapies, including vaginal estrogen, DHEA, ospemifene, and laser therapies is needed.

PLENARY SYMPOSIUM #3
Perimenopause as a Neurological Transition State: Emergence of Vulnerabilities to Neurodegenerative Disease
Robert A. Brinton, PhD. Center for Innovation in Brain Science, University of Arizona, Tucson, AZ
Women >85 million women are 40-60 years of age during which the endocrine transitions of perimenopause, menopause, and postmenopause will occur. Alzheimer’s disease (AD) prevalence is greatest in postmenopausal women and is proceeded by 10-20 year preclinical/prodromal period. The ~20-year separation between average of menopause and first symptoms diagnosis is a critical period for identifying mechanisms of AD and therapeutic targets to prevent, delay, and reverse AD prodromal endophenotype. To identify key drivers of Alzheimer’s in women, we conducted preclinical and clinical analyses. Transcriptomic, metabolomic, electrophysiological, in vivo PET- and T-MRI analyses were conducted in rodent models of human endocrine and chronological aging. Bioinformatic pathway analyses was followed by hierarchical clustering to identify activated gene networks and interactions between enriched pathways. Mechanistic discovery outcomes served as the framework for clinical analyses in pre, peri, and postmenopausal women. For comparison, men were matched in age. Women and men, 40-60 years of age, underwent volumetric MRI, in vivo PET- and PIB-PET (b Estradiol (Ab) deposition) brain imaging. Cytochrome c oxidase activity (COX) was determined in platelet derived mitochondria. Two distinct aging programs emerged: chronological and endocrine. Early endocrine aging transition was characterized by decline in bioenergetic gene expression which was confirmed by down-regulation of mitochondrial function, and long-term potentiation. Bioinformatic analysis predicted insulin/insulin like growth factor-1 and AMPK/PGC1a signaling pathways as upstream regulators. Later endocrine aging transition was accompanied by rise in genes required for fatty acid metabolism, inflammation, and mitochondrial function. An increase in fatty acids and fatty acid metabolites was coincident with rise in gene ketone bodies linking bioenergetic deficits early in aging with later development of Alzheimer’s disease. Bioinformatic analyses indicated up-regulation of key genes of bioenergetic pathway decline with rise in genes involved in AD. Mechanistic outcomes were paralleled in human brain imaging analyses indicating that compared to premenopausal, perimenopausal and menopausal women across endocrine aging and to age-matched control women, endocrine aging, respectively, of women postmenopausal endophenotype, including hypometabolism, increased Ab deposition, and reduced gray and white matter volumes in AD vulnerable regions. AD biomarker abnormalities were greatest in menopausal women, intermediate in perimenopausal women, and lowest in control women and men. Ab deposition was exacerbated in APOE4 positive menopausal women. Collectively, these findings indicate that endocrine and chronological aging transitions are critical periods for women during which vulnerability for later life risk of Alzheimer’s and other age-associated neurological disease can emerge. Research supported by National Institute on Aging P01-AG026572; R37AG035389 and The Women’s Alzheimer’s Movement

A Scientific Update on Alzheimer Disease: Etiology, Diagnosis, and Treatment
Mark W. Bondi, PhD, ABPP-CN. School of Medicine, University of California San Diego, San Diego, CA
We will sumarilly review recently published criteria for the diagnosis of dementia due to Alzheimer’s disease (AD) (McKhann et al, 2011, Alzheimer’s & Dementia), mild cognitive impairment due to AD (Albert et al, 2011, Alzheimer’s & Dementia), and Preclinical AD (Sperling et al, 2011, Alzheimer’s & Dementia). Pivotal to these criteria we will discuss the role of biomarkers in the diagnostic process to compare the relative value of biomarkers alongside cognition in predicting progression to dementia, and discuss when and whether biomarkers are helpful in this process. In 2010, the National Institute on Aging and Alzheimer’s Association convened workgroups to revise the three-decade-old criteria for the diagnosis of AD (McKhann et al 1984). The new criteria added two additional workgroups: on establishing diagnostic criteria for MCI as well as research criteria for the diagnosis of preclinical Alzheimer’s disease. With the publication of these recent work groups’ recommendations, it is clear we have entered an era increasingly focused on the role of biomarkers in disease detection, diagnosis, and monitoring. The current review will review the value of non-invasive markers added to these criteria and an actuarial neuropsychological method we have developed. Results from these studies suggest that the conventional method is susceptible to diagnostic errors, whereas actuarial neuropsychological criteria yields dissociable cognitive subtypes (eg, amnestic, dysexecutive, significant) AD biomarker associations, more complete with stable and dynamic measures, and greater performance is needed. Specific performance indices for MCI diagnostic criteria. Findings support refining MCI diagnoses by incorporating more comprehensive neuropsychological methods, with resulting gains in characterization of specific cognitive subtypes, biomarker associations, diagnostic stability and prediction performance. Additional developments have called into question the specific uses of the biomarker strategies identified in these criteria, and we may be in the midst of a paradigm shift in our understanding of the development of AD. For the prior decade or more the amyloid cascade hypothesis (see Musiek & Holtzman 2015) has predominated research, drug discovery, clinical trials, and provided the framework underlying the revisions to diagnostic criteria. However, many biomarker studies do not conform to its temporal sequence, in which amyloid accumulation is presumed to occur first, then tangle-based neurodegenerative changes, and finally cognitive and functional declines. In addition, the prior decade of clinical trials, many of which have centered on clearance of amyloid, have summarily failed. Another long-standing theory that neurofibriillary tangle (NFT) pathology proceeds along well-defined predilection sites beginning in the temporal lobe (Brandt et al, 1991) has been re-examined. The current review is the framework that the pathogenic process instead commences with the formation of tangle material in the lower brainstem (Braak et al 2011) and spreads upward to cortex. Importantly, the time course of these initial pathological accumulations in brainstem and its projections to cortex appear to occur in a temporal sequence, the first stage of which occurs in the lower brainstem. The evidence reviewed in this seminar concludes that a multi-faceted approach that integrates biomarker and neuropsychological assessments will likely be needed to characterize the preclinical phase of AD and ends with the suggestion that neuropsychological assessment provides a central role in and non-interchangeable role in the diagnosis of the elderly, older and that cognitive measures are among the best predictors of the initial symptomatic stages of an evolving dementia.

PLENARY SYMPOSIUM #4
KNDy Neurons, Neurokinin 3 Receptor Signaling and the Etiology of HotFlushes
Naomi E. Rance, MD, PhD. Department of Pathology, University of Arizona College of Medicine, Tucson, AZ
Estrogen withdrawal in postmenopausal women leads to a rise in LH secretion from the anterior pituitary gland and dramatic cellular changes in the human hypothalamus. In postmenopausal women, there is hypertrophy and increased gene expression of a subpopulation of neurons that express estrogen receptor alpha. These neurons are co-localized with expression of kisspeptin and neurokinin B (KNDy) and dynorphin. The importance of KNDy neurons in reproduction is underscored by the discovery that patients with mutations in the genes encoding NBK or kisspeptin are infertile and do not go through puberty. A consensus is emerging that KNDy neurons play an important role in regulating pulsatile secretion of GnRH. Because KNDy neurons hypothyrope in postmenopausal women in response to estrogen withdrawal, we hypothesized that they could play a role in the generation of hot flushes. Hot flushes are characterized by the activation of the physiological effectors that dissipate heat, including skin vasodilation, sweating, and cold-seeking behavior. Therefore, understanding the relationship between KNDy neurons and the neural circuits that regulate heat defense could provide clues to the mechanism of flushes. Our experiments in rodents provided evidence that KNDy neurons modulate cutaneous vasodilation (flushing) via projections to NK3 receptor-expressing neurons in the preoptic hypothalamus. A dual function for KNDy neurons in modulating LH pulses and thermoregulatory vasodilation explains why in humans, LH pulses are timed with hot flushes. Recent clinical trials have shown that NK3 receptor antagonists effectively reduce the number and severity of hot flushes, thus providing strong support for our hypothesis. Notably, NK3 receptors are located both on KNDy neurons and in the preoptic area providing two CNS sites for NK3 receptor antagonists to influence thermoregulation. These studies illustrate how basic research on the mechanisms of flushing could lead to the development of targeted therapeutics. References 1. Rance NE, Young WS, III. Hypoestrogen and gene expression of neurons containing neurokinin-B and substance-P messenger ribonucleic acids in the hypotalamic of postmenopausal women. Endocrinology 128:2239-2247, 1991. 2. Takato A, Krajewska-Schulz J, Nakamura ML, Rance NE. Kisspeptin gene expression in the hypotalamic infundibular nucleus of postmenopausal women and ovarietomized monkeys. J Clin Endocrinol Metab 92:2744-2750, 2007. 3. Mittelman-Smith MA, Williams H, Krajewska-Hall SJ, McMullen NT, Rance NE. A new mechanism for the secretion of LH: Role for kisspeptin neurokinin B/dynorphin (KNDy) neurons in the modulation of body temperature. Proc Natl Acad Sci USA 109:19846- 19851, 2012. 4. Rance NE, Dacks PA, Mittelman-Smith MA, Romanovsky AA,
Recent Advances in the Treatment of Vasomotor Symptoms: KNDy May Be the New Sweet Spot

Susan D. Reed, MD, MPH. Women’s Health Research Program, Department of Obstetrics and Gynecology, University of Washington School of Medicine, Seattle, WA

Pulsatile GnRH secretion is governed by a network of estrogen-sensitive neurons, in the hypothalamus, which express Kisspeptin (Kiss1), Neurokinin B (NK2), and Dynorphin (Dy). These KNDy neurons project to and are immediately adjacent to the thermoregulatory center. KNDy neurons express the key isoform of the estrogen receptor, ERα, and are the primary targets for estrogen-dependent GnRH regulation. They drive the pulsatile secretion of GnRH and LH — as evidenced by the fact that blockade of kisspeptin signaling in the brain inhibits GnRH pulses. To date, there are no Federal Drug Administration (FDA) approved products for menopause directed toward the KNDy neuron complex, but drugs first developed for pain control and for mood disorders acting on these receptors have shown promise. During this session, we will review the evidence for efficacy of these new novel drugs and their long term potential as nonhormonal therapies for menopause symptoms.

HYPOTHALAMUS

Vaginal Estrogen Safety and Labeling: State of the Science
Carolyn J. Crandall, MD, MS, NCMP. David Geffen School of Medicine at University of California, Los Angeles, CA

There are numerous preparations of vaginal estrogen that are available by prescription. Given the high prevalence of the genitourinary syndrome of menopause (GSM), and the substantial adverse impact of GSM on sexual function and quality of life, it is clinically relevant to assess the safety and efficacy of local vaginal estrogen use. In this presentation, we will review the timeline of availability of preparations of vaginal estrogen and vaginal dehydrospiandrosterone, their class labeling, and the evidence regarding their long-term safety. The class labeling is based on extrapolations of data from clinical trials of systemic hormone therapy which involved substantially higher levels of systemic exposure; it was not based on evidence from clinical trials of vaginal estrogen. Clinical trials regarding the long-term safety of vaginal estrogens have not been performed. However, in a recent study from the Women’s Health Initiative Observational Study, we evaluated data from 32,433 postmenopausal women without a hysterectomy and 14,133 postmenopausal women with previous hysterectomy (Crandall, et al, Menopause 2017). In this large prospective cohort study, compared to nonusers of vaginal estrogen, postmenopausal women who used vaginal estrogen had similar risks of invasive breast cancer, stroke, colorectal cancer, endometrial cancer, and venous thromboembolism. We did not find evidence for elevated risk of coronary heart disease or death in vaginal estrogen users compared with non-users. These findings should provide reassurance to women and their health providers regarding the safety of vaginal estrogen and help to inform menopausal hormone therapy clinical decision-making.

PLENARY SYMPOSIUM #5

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PLENARY SYMPOSIUM #6

Goal-directed Management of Osteoporosis
Steven R. Cummings, MD, FACP. Department of Medicine, University of California, San Francisco, San Francisco, CA

Standard current treatment of all patients to prevent fractures starts with prescription of “1st line” drug, usually alendronate. If a patient’s treatment is monitored during follow-up, a BMD test may be repeated at 1 or 2 years and the patient reports fractures that have occurred. If her BMD has increased, even a little, and she has had no fracture, then the patient has “responded.” What’s wrong with this approach? Goal-directed treatment proposes that treatment should aim to achieve goals, such as BMD “T-score” that is at least higher than -2.5 (indicating osteoporosis) and freedom from fracture. For patients who start with a BMD T-score below -3, treatment with an oral bisphosphonate such as alendronate has a very low probability of reaching that BMD goal. Thus, patients with more severe osteoporosis and high risk of fracture, the best initial choice is a stronger agent that is more likely to improve BMD above the goal. In goal-directed treatment, follow-up focuses on progress toward achieving the goal with measurement of BMD and history of fracture – not “response” to treatment. However, response is less important than progress toward the goal. A patient may “respond” with a 2% increase in BMD but remain very far from a goal. In that case, for example, it would be warranted to switch to a more potent treatment despite the biological “response.” The presentation will set out a systematic approach to initial assessment and follow-up based on treatment goals.

Bone Turnover Markers in Clinical Practice
Douglas Bauer, MD. Department of Medicine, University of California, San Francisco, San Francisco, CA

Biochemical markers of bone turnover (BTMs) are serum and urine measurements that represent an integrated picture of skeletal remodeling (the linked process of bone resorption and formation). Rates of bone turnover are elevated in some conditions, such as postmenopausal osteoporosis, and reduced in other conditions, such as hypothyroidism. In some, but not all studies, higher bone turnover is independently associated with increased fracture risk in older women, but the optimal level of bone turnover is unknown. Treatment of osteoporotic individuals with effective antiresorptive agents results in rapid and large reductions in bone turnover. A recently completed Foundation for NIH meta-analysis of patient-level data from 13 antiresorptive clinical trials with over 50,000 participants suggest that greater short-term reductions in bone turnover are associated with, on average, greater reductions in spine and non-spine fracture risk. Conversely, anabolic treatments initially increase bone turnover. There is also some evidence that BTMs may be useful to select specific treatments and to identify secondary causes of fragility. An International Federation of Clinical Chemistry and International Osteoporosis Foundation (FCC-IOF) working group recently endorsed procollagen type I N-propeptide (PINP) and C-terminal telopeptide of type I collagen (SCTX) as the preferred serum formation and resorption markers, respectively, for clinical use. However, both individual biologic and laboratory variability complicate the clinical use of BTMs. Collectively, current data suggest that BTMs may be used in certain clinical situations but several ongoing concerns continue to limit their use in routine clinical practice.

Advances in Osteoporosis in the Last 40 Years
J C Gallagher, MD. Creighton University School of Medicine, Omaha, NE

When I started osteoporosis research in 1970, there were no drugs under study for osteoporosis. Estrogen was used but there was little known about the correct dose for preventing bone loss. In retrospect, we were using doses 5 times too high. At that time, fractures were not recognized as a disease but regarded as part of normal aging. From 1970 to 2018 there have been huge advances in the osteoporosis field ranging from epidemiology of fractures to the remarkable invention of precise bone mineral density measurements. There have been major advances in therapeutic options available for patients for prevention and treatment of osteoporosis. In parallel, the advances in the laboratory helped us understand the process of bone remodeling, not only at the macroscopic level but also at the cellular level. This has led to rapid advances in translational research from cellular biology to new therapies exemplified by the development of monoclonal antibodies for treatment of osteoporosis. Further understanding will lead in the future to new small molecules for treatment and perhaps less adverse events. University-based research all over the world has been a leader in most of these advances and pharma support for phase 1-4 studies helped bring these discoveries to the patients. In the osteoporosis field alone, one sees the tremendous value of grant support for university research by national funding agencies such as the National Institutes of Health in the United States and similar agency in other countries. Advances in osteoporosis represents the innovative work of many dedicated and creative scientists during this era. There are less intellectual but formidable challenges that have to be managed. Long-term adherence and persistence with medication if we want to reduce fracture incidence long-term and the fact that following a hip fracture, which represents metabolic bone disease, less than 15 percent of patients are started on appropriate treatment. This issue cuts right across the interface between hospital surgery and primary care. Surely, we can do much better!

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Update on Heart Failure: Ixabradine andSacubitril-Valsartan
Michelle M. Kittleson, MD, PhD. Heart Failure Research, Smidt Heart Institute at Cedars-Sinai, Los Angeles, CA

Current guideline-directed medical therapy for heart failure is a triumph of translation medicine where an understanding of neurohumoral activation, translated into medication, has worked to ameliorate systolic dysfunction and culminated in improved quality of life and survival for patients with heart failure. The most effective drug therapies for chronic systolic heart failure are those that inhibit the activity of the sympathetic nervous system (SNS) and renin angiotensin aldosterone system (RAAS). These agents include the beta-blockers to inhibit SNS activity and the angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II type 1 receptor blockers (ARBs), and mineralocorticoid receptor antagonists (MRA) to act on the RAAS pathway. Two new heart failure medications have recently been approved and represent a deepened understanding of neurohumoral mechanisms in heart failure. The first is ivabradine, which inhibits the funny current of the sinoatrial node and lowers heart rate without reducing contractility. In patients already on maximally tolerated beta-blocker dosages, ivabradine reduces the risk of heart failure hospitalization. The second medication is sacubitril combined with valsartan which takes advantage of the natriuretic peptide system and other endogenous vasoactive peptides. Sacubitril, a nephrilysin inhibitor, increases vasoactive peptide levels resulting in beneficial effects in heart failure. The angiotensin receptor-neprilysin inhibitor combination sacubitril-valsartan is superior enalapril in reducing death and heart failure hospitalizations. An increased understanding of the sympathetic nervous system and breakthroughs in capitalizing on the natriuretic peptide system have resulted in two additions to the heart failure armamentarium, ivabradine and sacubitril/valsartan. Moving forward, goal of physicians who treat heart failure patients should be to ensure that all eligible patients receive these important therapies.

Hypertension Guidelines
Martha Gulati, MD, MS, FACC, FAHA, FASPC. Cardiology, University of Arizona College of Medicine-Phoenix, Phoenix, AZ

Hypertension is a leading cause of cardiovascular morbidity and mortality nationally. Based on the most recent NHANES survey from 2011-2014, 85.7 million US adults age ≥20 have hypertension, more than half of whom are women. One in three deaths of women in the US are attributed to cardiovascular disease (CVD). Of the major modifiable CV risk factors, the complete elimination or control of hypertension resulted in the largest impact on CV mortality in women (38% and 7.3% reduction, respectively). Despite the magnitude of its societal impact, awareness, treatment and control of hypertension remain suboptimal in women. The 2017 Guidelines for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults is comprehensive and is highly applicable to women. Both sex and gender differences will regarding hypertension will be discussed in this presentation, for management of one of the most modifiable risk factor in women.

PLENARY SYMPOSIUM #7

EMPOWIR Study Findings
Ruth Freeman, MD. Medicine and Obstetrics and Gynecology, Montefiore Medical Center, Bronx, NY

There are many different causes of obesity, although the ultimate cause is an imbalance between energy intake and energy utilization. Even very minor increases in energy intake over utilization will ultimately cause obesity. Addressing more individualized causes of the underlying problem may help people lose their excessive weight. The adverse effects of being obese is in part due to the area of fat storage. The adverse effects of being obese is in part due to the area of fat storage. The magnitude of the societal impact, awareness, treatment and control of hypertension remain suboptimal in women. The 2017 Guidelines for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults is comprehensive and is highly applicable to women. Both sex and gender differences will regarding hypertension will be discussed in this presentation, for management of one of the most modifiable risk factor in women.

PLENARY SYMPOSIUM #8

Sleep-circadian Rhythms and Aging in Women: A Bidirectional Relationship
Phyllis C. Zee, MD, PhD. Center for Circadian and Sleep Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL

Sleep and circadian timing are fundamental biological imperatives, and are often challenged by changes in the environment, hormone transitions, unhealthy behaviors, and disease, leading to sleep deficiency. In the past decade, advances in the scientific knowledge of sleep and circadian biology, indicate that sleep and circadian disruption have a central role in the expression and development of cardiometabolic, cognitive, and mood disorders. Sleep deficiency is common in the general population, and even more prevalent in women, with only approximately 40% reporting adequate sleep. The sleep-circadian system to this high prevalence of sleep disturbances and lifestyle factors. A study by the National Sleep Foundation demonstrates that insomnia symptoms affect women, especially older women, disproportionately. This disparity grows as men and women reach middle age and older age, particularly at menopause and postmenopausal women. Hot flashes, mood disturbances, other sleep disorders, age-related changes in sleep and circadian rhythm regulation may be a predisposing factor for sleep disturbances. However, with aging there is also increased comorbid medical and psychiatric conditions, which are important contributing factors for sleep disturbance. Symptoms of sleep disturbance should be differentiated from insomnia disorder and circadian rhythm sleep-wake disorders such as advanced and delayed sleep phase disorders and shift work. Insomnia disorder is characterized by difficulty falling and or staying asleep that is accompanied by daytime impairment in functioning for at least 3 months. Circadian rhythm disorders may present with symptoms of insomnia, but are due to changes in the circadian timing system. This lecture will review the foundational science of age-related changes and sex differences and how they contribute to sleep and circadian disturbances. In addition, discuss the causes of sleep disturbances and potential interventions that aim to promote more constructive disagreement between people on all sides of the pressing political issues.
and enhanced with the multimedia capabilities of the Web. Making behavioral/psychosocial/mental health treatment and prevention programs widely available on the Internet has obvious appeal. Delivering care in this way can help overcome many of the traditional barriers to providing care, including inadequate treatment access, limited trained clinicians, poor geographical distribution of knowledgeable professionals, and expense. They clearly have promise as an efficacious, scalable, and cost effective prevention and treatment option with significant public health impact. Furthermore, interventions can be delivered in a standardized manner with fidelity across a variety of settings. Outcome trials of Internet interventions have consistently demonstrated significant changes in behavior and meaningful symptom improvements. One area that has shown particular promise is the delivery of treatment for insomnia via the Internet. Insomnia is the most common sleep complaint, with approximately 6-15% of the general population worldwide meeting diagnostic criteria. Of particular note, sleep difficulties in peri- and postmenopausal women and have been identified as a key symptom of the menopausal transition. Cognitive-behavioral therapy for insomnia (CBT-I) is an extremely effective treatment for insomnia. However, obstacles to accessing this treatment remain.

As a means to overcome these barriers, a number of Internet interventions for insomnia that have inadequate evidence to guide treatment choices for women with insomnia. Despite this high prevalence of genitourinary syndrome of menopause (GSM), evidence based information about its symptoms and treatment may offer an efficacious means to reducing the public health burden of insomnia. However, many programs and applications that are currently available have little scientific basis or empirical validity, and even fewer have been evaluated in rigorous research trials. These issues, including the availability and applicability of current applications, the science behind some of the empirically evaluated programs, and the need for more research, will be discussed.

PLENARY SYMPOSIUM #10

Four Updates on the MsFLASH Postmenopausal Vaginal Health Study: Quality of Life, Sexual Attitudes and Activities, Vaginal Inflammation, and the Vaginal Microbiome

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Background: Bothersome postmenopausal vaginal symptoms are prevalent and adversely affect quality of life and sexual activity. Up to 40% of postmenopausal women have vaginal symptoms presumed to be related to vaginal atrophy. Despite this high prevalence of genitourinary syndrome of menopause (GSM), evidence based information to guide treatment choices is limited. The MsFLASH Vaginal HealthRCT demonstrated no significant difference in improvement in vaginal symptoms between women randomized to 1) estradiol vaginal tablet (Vagifem®) + placebo gel or 2) hydrophilic moisturizing vaginal gel (Replens®) + placebo tablet vs. placebo gel + placebo tablet. To better understand these primary results, we evaluated both impact of treatment on other measures, such as quality of life and sexual activity, and biologic characteristics of the vaginal environment. Methods: The MsFLASH network conducted a multicenter trial comparing popular treatments for bothersome vaginal symptoms and sexual dysfunction, and created a biorepository of specimens for translational, mechanistic research on the etiology of vaginal symptoms. Recruitment was via mass mailing and Facebook advertisements. The primary outcome was change from baseline to 12 weeks in severity of the most bothersome symptom (MBS) - dryness, itching, irritation, soreness and pain with penetration. Secondary outcomes included quality of life (using MENQOL) measured at 0, 4 and 12 weeks during the trial, frequency of sexual activity measures during the trial and baseline attitudes toward sex. Biologic markers included vaginal cytokines measured in cervicovaginal lavage fluid using MesoScale Discovery, and vaginal microbiota characterized by metagenomic sequencing from vaginal swabs. A subset of 144 women (45 estradiol, 48 moisturizer, 51 dual placebo) with complete sample sets were selected for analysis of cytokines at 0, 4 and 12 weeks. From the larger MsFLASH biorepository, 65 White and 44 Black women were selected. Results: Women were randomly assigned to receive Vagifem (N=102), Replens (N=100) or placebo (N=100). Study continuation was high: 293 women provided week 12 data (95% Vagifem, 99% Replens, 97% placebo). No meaningful differences in baseline characteristics were observed between treatment groups. Mean age was 61 (SD 4) years and 88% were white. The mean MBS score was 2.5 (SD 0.6): pain with sexual activity 61%, vaginal dryness 21%, vulvar or vaginal itching 7%, vulvar or vaginal irritation 6%, and vulvar or vaginal pain or soreness 5%. The mean (SD) baseline MENQOL score was 3.3 (3.1) and mean number of days with sexual acts in the first week of the trial was 3.3 (3.1) and mean number of days with sexual acts in the first week of the trial was 3.3 (3.1). The MsFLASH Vaginal Health Trial assessing hormonal and nonhormonal products has provided valuable evidence to guide treatment decisions for women with GSM. Among women with bothersome vaginal symptoms, a better understanding of quality of life, sexual activity and attitudes, vaginal inflammation and the vaginal microbiome will help guide development of future therapies.