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Chicago, IL

DECEMBER 5-7, 2025
Future Leaders Conference
Chicago, IL

EDITOR'S MESSAGE

Cultivating Connection to Combat Isolation and Burnout

Paula Gregory, DO, MBA, FACOFP

Physicians in all areas may face isolation and loneliness, with many showing signs of burnout and emotional exhaustion. We are connected to the physician and insurance networks by our computers and often work late hours, perhaps rushing home to an event for our families.

Meetings with peers and other staff meetings at hospitals have dwindled. In the past, these meetings tied us to managing issues of concern at hospitals and within our professional organizations. Other social constructs in the form of professional development and committee meetings also allow us to stay connected professionally to our peers. As we move towards making connections as a student, resident, or practicing physician, the ability to be a part of the conversations within our organizations, hospitals, and communities matters. It is difficult to designate time to meet on the outside after a busy day or to spend time on a meeting taking away from home duties.

ACOFP can help by linking us with others in our profession and allowing us to discuss issues that are becoming more evident over the country. Community and professional volunteering can help us form new associations with people and gives our voices weight as we discuss health and other issues.

Related to this is our general community distance from others. This has been called an epidemic of loneliness and social isolation, noted by the Surgeon General. Developing stronger social connections with our communities, in our organization, and with our peers can alleviate the loneliness and burnout that we may experience with long work hours. One of the contributing factors to burnout can be feeling that our voices are not impactful. Joining conversations during meetings and with leadership from our organizations and hospitals can give us a voice to help ourselves, our patients, and our peers.

A few tips to avoid burnout, social isolation, and loneliness include attending a meeting with peers, joining a volunteer group or activity, and finding time to reconnect socially so that our voices can be heard. These activities are valuable in preventing depression and loss of autonomy.

Many of our patients could use similar advice from us. Adolescents can benefit from volunteering and working on community projects to help them stay connected and avoid social isolation. Elderly patients have so much to give when joining community projects.

As physician leaders in our communities, joining peers in committee work or attending a conference can help us stay connected and learn how our opinions matter. I look forward to hearing your ideas and stories of how you stay connected!

FROM THE PRESIDENT'S DESK

Preparing for the Challenges and Opportunities Ahead

Brian A. Kessler, DO, DHA, FACOFP *dist.*

Dear Members,

As we approach the close of another year, it is important to reflect on the challenges and progress we have made in our profession. The year's final months often prompt us to think about personal and professional renewal and how we can better serve our patients, colleagues, and communities in the year to come. This time also encourages us to evaluate the values that define our osteopathic profession: holistic care, compassion, and a focus on the person as a whole.

The evolving healthcare landscape continuously presents new obstacles, but as osteopathic family physicians, we are uniquely positioned to face these challenges head-on. Our role as primary care physicians allows us to be the first point of contact for patients, building relationships beyond episodic care. We serve as stewards of our patients' well-being across a lifetime, embodying the principles of prevention and early intervention.

This issue of *Osteopathic Family Physician* offers a collection of timely and critical topics that reflect the multifaceted nature of family medicine. From addressing the management of chronic pain to understanding the growing concerns around binge eating disorder and the complexities of ADHD in the family medicine setting, these articles provide us with essential insights to improve patient care and refine our clinical approaches.

For instance, the narrative review of opioid use in elderly patients underscores the importance of safer alternatives like buprenorphine, especially as we continue to confront the opioid epidemic. Managing opioid use remains a cornerstone of ethical and effective patient care, particularly for vulnerable populations.

Moreover, this issue delves into other significant areas of patient care, including strategies for treating trigger finger and managing acute kidney injury due to medications like clindamycin. These practical discussions directly impact our patients' day-to-day lives, reminding us of the importance of continuous education and staying current with clinical best practices.

In the article discussing vitamin C, topical retinoids, and sunscreen, we are reminded of preventive care's role in dermatology—an area often overlooked in primary care but critical to long-term health outcomes. In all its forms, preventive care remains at the heart of our practice as osteopathic family physicians, empowering our patients to maintain wellness before illnesses manifest.

We must also remember our role as advocates for those who cannot advocate for themselves. The article on abuse of older adults serves as a poignant reminder of the vigilance required in our profession to safeguard the dignity, safety, and well-being of this often-overlooked population. Our responsibility is to remain attuned to the physical, emotional, and financial vulnerabilities that older adults may face and intervene where necessary to protect them.

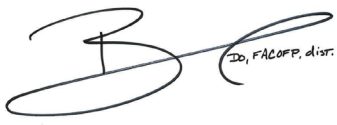
As we reflect on the passing year, I am particularly excited to invite you to the upcoming **ACOFP 62nd Annual Convention and Scientific Seminars in Palm Springs, California, April 2-6, 2025**. This event will be extra special as we celebrate the 75th Anniversary of our professional family with enthusiasm and energy. The ACOFP '25 convention promises to be a monumental occasion, highlighting the unity, strength, and evolution of osteopathic family medicine over the past seven and a half decades.

ACOFP '25 will feature extensive educational sessions, workshops, and networking opportunities to enhance our skills and foster connections across the profession. Whether you are a seasoned practitioner or early in your career, this event offers invaluable opportunities to grow and engage with our professional community. Registration is now open, and I encourage you to explore our preliminary schedule online and begin planning your participation. More details will follow soon, and we are excited to share this significant milestone with all of you!

As we move toward the end of this year and prepare for the opportunities and challenges of 2025, I encourage each of us to continue seeking knowledge, remain compassionate in our care, and stay engaged with the osteopathic principles that guide our work. The path forward may not always be easy, but together, we can meet these challenges and ensure we continue to provide the highest quality care to our patients, communities, and profession.

Wishing you all a restful and reflective end to the year, and I look forward to seeing you in Palm Springs next April as we celebrate this remarkable occasion together.

Warm regards,



Brian A. Kessler, DO, DHA, FACOFP *dist*.
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REVIEW ARTICLE

Opioid Use in the Elderly: A Narrative Review of Buprenorphine Use for Chronic Noncancer Pain

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KEYWORDS

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ABSTRACT

Chronic noncancer pain presents a significant challenge worldwide, particularly among the elderly population, where concerns of polypharmacy and additional morbidity and mortality risks exist. When nonopioid treatment approaches are deemed ineffective, the decision to use opioids requires a careful risk-benefit analysis. Our objective was to review recent literature in the use of opioid analgesics and opioid alternatives to analyze treatment protocol recommendations when prescribing pain medication for elderly patients. Databases such as PubMed, CDC, Embase, JAMA, and SCOPUS were used as primary sources for literature. Following a review of the literature, benefits and consequences of opioid use in the elderly were reviewed. Opioid use in the elderly continues to be a debated topic due to the systemic effects of the medication, risk of polypharmacy, and risk of opioid dependency. However, the use of buprenorphine may help with minimizing risk and maximizing relief of pain in the elderly, positioning it as a strong contender if not a replacement for first-line treatment for chronic noncancer pain in the elderly. Future research should focus on further analysis of drug combinations to provide optimal pain relief for elderly care with the goals of improving quality of life without risking patient health.

INTRODUCTION

Chronic pain is a pervasive and debilitating health condition that affects millions of people worldwide, significantly impacting their quality of life and well-being. Defined as persistent or recurrent pain that lasts for more than 3 months, chronic pain represents a multifaceted challenge, particularly in the elderly population.[1] With the aging of societies globally, the prevalence of chronic pain among older adults has surged, posing considerable burdens on healthcare systems and underscoring the urgency for effective management strategies tailored to this unique demographic. The utilization of opioids as a primary pharmacologic approach to managing chronic pain in the elderly has seen a notable rise, yet it remains a topic of extensive debate and concern.[2]

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Prevalence and Epidemiology

Various studies have reported differing rates of chronic pain in older adults, highlighting the complexity of accurately assessing its prevalence. Nevertheless, a consistent pattern emerges, indicating that the prevalence of chronic pain increases with age, reaching its peak in the oldest age groups. As older adults often experience age-related conditions like osteoarthritis, arthritis, fibromyalgia, musculoskeletal disorders, neuropathy, and neurodegenerative diseases,[3] the likelihood of experiencing chronic pain is significantly elevated. The presence of comorbidities and the interaction of chronic pain with other health issues further exacerbate the complexity of pain management in the elderly.[4]

Chronic noncancer pain has far-reaching health implications. Chronic pain in the elderly is associated with depression, Alzheimer's and other types of dementia, increased suicide risk, and substance use and misuse.[5] Chronic pain has been shown to have a direct effect on increasing risk of falls and an indirect effect on mediating disordered sleep.[6] The existing burden of increasing morbidity associated with increasing age is compounded by the presence of chronic pain. Likewise, the increasing use of opioids in elderly patients has raised concerns about their safety, efficacy, and potential for misuse and addiction.[7]

Challenges With Opioid Use in the Elderly

The use of opioids in elderly patients presents unique challenges and risks that demand cautious consideration. Advanced age is associated with physiologic changes that affect drug metabolism and clearance, leading to an increased susceptibility to adverse drug reactions and drug interactions. As a result, elderly patients are at higher risk of experiencing opioid-related side effects such as sedation, respiratory depression, constipation, and cognitive impairment. Such adverse events can have severe consequences for the elderly, impacting their functional independence and overall health. Furthermore, the potential for opioid misuse and the development of tolerance pose significant concerns in this population. The growing opioid epidemic has shed light on the need for judicious opioid prescribing to mitigate the risks of addiction and abuse, particularly in vulnerable populations like the elderly.[2] Ultimately, by updating and refining current management practices, we can pave the way for improved pain management strategies, ultimately enhancing the quality of life for elderly individuals living with chronic pain.[8]

METHODS

By critically examining the prevalence, epidemiology, and medications used in managing chronic pain, with a particular focus on opioids, this paper seeks to contribute to a deeper understanding of the complexities surrounding pain management in the elderly. Furthermore, it aims to highlight the potential risks associated with opioid therapy, as well as the need for evidence-based tailored approaches that prioritize the safety and well-being of older adults. To accomplish this, a narrative review was employed. Databases such as PubMed, Cochrane, Google Scholar, and others were used for primary literature.

RESULTS

Long-Acting Opioids

Long-acting opioids, also referred to as extended-release opioids, are formulated to provide a sustained analgesic effect over an extended period, reducing the need for frequent dosing. These opioids are typically prescribed for chronic pain management, as they offer more consistent pain relief and can improve patient compliance with treatment regimens. Common examples of long-acting opioids include controlled-release morphine, methadone, oxycodone, and fentanyl patches.

While long-acting opioids may be advantageous for managing chronic pain, their use in elderly patients demands careful consideration. Due to age-related changes in drug metabolism and sensitivity, older adults may experience prolonged drug effects, heightening the risk of side effects and adverse events. Furthermore, long-acting opioids may have a delayed onset of action, making it essential to monitor patients closely during initial treatment and dosage adjustments.[10]

Buprenorphine Overview

Buprenorphine, a unique opioid, has gained recognition for its role in opioid agonist therapy and pain management. Unlike traditional opioids, buprenorphine is a partial agonist at opioid receptors, meaning it has a ceiling effect on respiratory depression and a lower potential for overdose compared to full agonists like morphine or oxycodone. Buprenorphine is used in the treatment of opioid use disorder (OUD) and has been found effective in reducing opioid cravings and withdrawal symptoms.

Additionally, buprenorphine is utilized for pain management, especially in situations where other opioids may not be suitable due to the risk of adverse effects or drug interactions. The unique pharmacologic profile of buprenorphine may make it a safer alternative for elderly patients with chronic pain, particularly those with a history of substance abuse or a higher risk of opioid-related adverse events.

This review aims to provide an in-depth update and narrative expansion upon the previous systematic review conducted by Guerriero[11] on the use of opioids in the elderly with chronic pain, incorporating newer clinical data released since their review in 2017, to gain further insight into the potential benefits and risks of this treatment modality.

General Adverse Side Effect Summary

The pharmacologic class that are opioids have their benefits but are not without their own unique challenges. While they are utilized for their ability to produce analgesia, there are also many side effects associated with opioid usage. Due to the relatively high concentration of opioid receptors in the enteric nervous system, opioid usage commonly causes gastrointestinal (GI) symptoms, such as nausea, vomiting, and constipation. Nausea and vomiting also occur through stimulation of the brain's chemoreceptor activating zone, sometimes called the brain's vomiting center. Fatigue and sedation are potentially concerning adverse side effects in the elderly that can increase the risk of falls. The sedation effect occurs primarily through acetylcholine inhibition in the medial pontine reticular formation, among other mechanisms.[12]

Dizziness is another potentially dangerous adverse side effect that can contribute to fall risk and increases morbidity associated with opioid use. Dizziness and nausea occur by altering neuronal excitability within the vestibular apparatus.[13]

Other common adverse side effects include sweating, pruritus, and hot flashes. These and the above-mentioned side effects have all been shown to be significantly associated with medium- and long-term opioid use.[14] A 2023 Cochrane review found no studies that met inclusion criteria in evaluating the efficacy and safety of high-dose opioids for chronic noncancer pain.[15]

Additional common adverse side effects include opioid-induced hyperalgesia from toxic metabolites, urinary retention from anticholinergic effects, dysphoria or euphoria, impaired host immunity,[16] and, most notably, respiratory depression,

which is the target for naloxone in opioid overdoses. All adverse side effects that are not life-threatening should be managed by either: dosage reduction, symptomatic treatment, rotating medication choice, and/or changing administration method.[17]

Regarding delirium, in an analysis of critically ill patients with an average age of 60.9 years, use of any opiate was associated with a significant risk of delirium the next day if that patient was awake.[18] Whereas an observational study of emergency department (ED) patients ≥65 years found that pain was significantly associated with development of delirium and not opiate consumption.[19] These conflicting data bring into question the causes of delirium, suggesting pain and opioid usage may both contribute.

A lesser-known consequence of chronic opioid use is opioid-related endocrinopathy, which can manifest as OPIAD (opiate-induced androgen deficiency).[20] Morphine use can inhibit the secretion of gonadotropin-releasing hormone at the level of the hypothalamus and can induce peripheral androgen catabolism.[21] Chronic opioid use is associated with a higher risk of diagnosis of and treatment for hypogonadism compared to short-term use.[22] Additionally, there is an apparent dose-dependent relationship between higher opioid doses and increased odds of developing OPIAD.[23] This is significant in light of the knowledge that the aging male is likely to have decreased levels of testosterone over his lifetime.[24]

Opioid withdrawal syndrome is of particular concern in chronic pain patients and the elderly. An observational study found that individuals who are older, have more severe substance use, are female, have chronic pain, and have more severe withdrawal symptoms at intake and across different timepoints.[25] Onset of withdrawal symptoms depends on the duration of effect of the opioid used. Withdrawal from opiates is subjectively severe but can cause death, primarily by way of dehydration or hypernatremia.[26]

While prevalence is not well understood, sensorineural hearing loss can occur with any opioid. Much of the data are scant and exist as case reports. A 20-year retrospective study in New Jersey found that most cases occurred with heroin. There were also multiple cases that occurred with hydrocodone, oxycodone, tramadol, fentanyl, and methadone.[27]

It is also worth noting that OUD is on the rise in the elderly population. OUD is associated with comorbid major depressive disorder, anxiety, and posttraumatic stress disorder (PTSD) in the elderly.[28]

General Opioid Usage

For chronic pain patients, it is currently recommended that patients be trialed first on short-acting opioids while long-acting opioids only be reserved for severe and intractable pain or once initial interventions have failed. A low dose is considered up to 40 MME (milligram morphine equivalents), a medium dose ranges from 41 to 90 MME, and a high dose is considered >90 MME per day.[29] CDC guidelines agree with these numbers.

In 2009, the American Geriatrics Society (AGS) formulated treatment guidelines for persistent pain in the elderly that does not rank the utility of specific opioids.[30] In 2017, the American Society of Interventional Pain Physicians (ASIPP) constructed recommendations for specific opioid usage in chronic noncancer pain, although it is worth noting that these guidelines are for the public and not specifically for elderly individuals.

Chronic kidney disease (CKD) is a common concern in the elderly. Transdermal buprenorphine and fentanyl do not require dose adjustments in nondialysis CKD patients. Oral immediate-release (IR) hydromorphone seems to be more tolerable than morphine in nondialysis CKD patients. Tramadol, codeine, and morphine are cautioned against in nondialysis CKD patients.[31]

With regard to liver failure of any etiology, it is recommended that the lowest starting dose be used, or less, if opioids are deemed as the most appropriate therapy for analgesia. Generally, IR formulations with lengthy dosing intervals are preferable over alternatives in this population. A high degree of caution should be used when prescribing opioids in patients with liver failure, and frequent monitoring for side effects and further decompensation with appropriate dosage adjustment is necessary.[32,33]

Lastly, it is worth noting, there seems to be little clinical benefit in alleviating pain with usage of high-dose opioid regimens, though it is understudied.[34] Additionally, the pharmacokinetics of different opioids and how they interact with an individual's unique pharmacogenetics is not well understood but plays a significant role in how different opioids affect people differently.

Buprenorphine

Buprenorphine has promising benefits in treating pain and limiting adverse side effects, though it is considered third-line treatment for severe pain by the ASIPP. Buprenorphine is most often given in the sublingual and transdermal form for chronic pain. Sublingual administration is preferred for its superior bioavailability. No dose reduction is required in renal impairment as the drug is metabolized extensively by the liver and is primarily excreted in the biliary system and in the feces. While hepatic impairment will prolong the half-life, the other metabolites have little activity.[35] Safety studies of buprenorphine use in patients with hepatic impairment are still lacking. Buprenorphine has also demonstrated clinically insignificant effects on the QTc interval when used at usual doses (0.006-0.03 mg/kg), but this may not be true at high or atypical doses, suggesting a safe cardiac profile.[36] A thorough overview of the unique pharmacologic profile was performed by Gudin and Fudin.[37]

According to 2022 CDC guidelines, buprenorphine is not considered in calculating daily MME. This is because it is primarily viewed as a treatment for opioid dependence; meanwhile, its unique partial agonist profile confers a ceiling on its potency and limits the extent to which respiratory

depression can occur.[29] A retrospective, postmortem, toxicology study of overdose deaths in Rhode Island between 2016 and 2018 concluded that the small percentage of individuals who were found to have buprenorphine or its metabolites upon toxicology testing were not recently exposed and thus buprenorphine did not likely contribute to that decedent's death.[38] This shows promise in the context of the opioid epidemic and rising rate of overdose deaths.

Buprenorphine has exhibited benefits in various situations. In a single-blinded study of 60 elderly patients with severe pain from osteoarthritis, there was significant relief when treated with transdermal buprenorphine, while the lower doses of 8.5 and 17.5 mcg/h resulted in fewer side effects than a starting dose of 35 mcg/h. Seven of the eight patients who did not complete the study were in the high-dose buprenorphine group, and the most reported side effect was confusion.[39] This suggests that starting with a low dose and titrating up as needed should be safe and efficacious in the elderly where delirium is highly concerning. Low-dose transdermal buprenorphine has been shown to cause no central nervous system side effects when combined with low-dose oxycodone in elderly patients. Transdermal buprenorphine has also shown lower rates of constipation.[40] A 2021 article described the effectiveness of buprenorphine in managing musculoskeletal pain and promising effects in managing diabetic neuropathy.[41]

Only one Cochrane review in 2015 has been performed evaluating buprenorphine in the use of noncancer patients and only included one article in the final analysis.[42] This highlights the paucity of high-quality evidence surrounding buprenorphine for chronic noncancer pain. A systematic review of sublingual buprenorphine in 2014 resulted in qualitative analysis due to wide-spread methodologic weakness of the studies. This team cited literature that buprenorphine shows safety in the elderly and the renally impaired, shows less immunosuppression, exhibits an antidepressant effect, and shows less development of tolerance and less hyperalgesia while on sublingual buprenorphine.[43]

Buprenorphine is used in a tapering fashion for management of opioid withdrawal syndrome. Since it is a partial agonist but is highly potent, it can precipitate withdrawals if an individual has been using opiates regularly.[44] In treating OUD, it is advised to wait until withdrawal symptoms emerge to administer buprenorphine. This also raises concern if cross-tapering from any other opioid with agonist action to buprenorphine. Buprenorphine formulated with naloxone (Subutex, Suboxone) is FDA approved for treating OUD. It is occasionally used off label for chronic pain management in high-risk OUD patients.

Transitioning from other opioids to buprenorphine has been investigated. A retrospective study to evaluate transitioning from high-dose therapy to buccal buprenorphine found nearly 90% of patients were stabilized on buccal buprenorphine. A higher average dose was utilized among those who were directly converted to buprenorphine compared to those who were titrated to a lower MME before switching. These results favor an aggressive titration schedule that results in lower MMEs than manufacturer recommendations (reducing to ≤30 MMEs). There were also patients safely using other full opioid agonists for breakthrough pain while still using the buccal buprenorphine without reports of withdrawal.[45]

DISCUSSION

As with any study, there were limitations inherent to this present design. As this was not a systematic review, this is not an exhaustive review of the literature. We also chose to exclude animal studies and as such could have excluded valuable data. This review did not include all opioids currently on the market.

In the process of this review, there were potential areas for future research uncovered. There is some evidence that intraoperative methadone may be superior to morphine for pain relief, but further controlled trials are needed.[46] There is further research needed regarding the safe rotation to and from methadone. There is also a lack of high-quality controlled studies evaluating and describing high-dose opioid use and its efficacy. There is a need for controlled studies to examine the use of buprenorphine for the management of chronic pain of different etiologies. There is also further work needed in formulating guidelines for opioid prescribing in elderly patients with CKD or impaired hepatic function.

CONCLUSION

Pain management in the elderly is complicated by the presence of comorbid conditions that increase mortality and provide contraindications for certain treatment regimes. In the elderly, who already have a high burden of disease, with chronic pain, the investigation of safe and effective pain management methods for aging and associated disease states is crucial for the effective and judicious use of opioid pain medications. In our review of the literature, we found evidence that while there are risks associated with its use, buprenorphine appears no more hazardous and is likely safer and more efficacious than other opioids for chronic noncancer pain management in the elderly. There is a sincere lack of high-quality randomized controlled trials investigating long-term use of buprenorphine for chronic pain management that likely accounts for its relatively lower standing in clinical guidelines. We urge clinicians and medical societies alike to consider buprenorphine as a potential first-line agent in opioid-centered chronic pain management.

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REVIEW ARTICLE

Abuse of Older People

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KEYWORDS

Abuse

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ABSTRACT

Abuse of older people, also known as elder abuse, occurs when there is harm or distress to older adults from an action or lack of action by an individual expected to be trusted. Abuse of older people comes in different forms including physical abuse, psychological or emotional abuse, sexual abuse, financial abuse, and neglect. Abuse of older people is often underreported, and with the aging population, will increase as a public health concern. It is imperative that healthcare providers recognize signs of abuse of older people and how to assess and evaluate the situation. Cases of abuse of older people should be evaluated for safety risks to the individual to determine a plan of care. In cases of suspected abuse of older people, it is important to understand the reporting requirements to Adult Protective Services. When abuse of older people is suspected, it can be helpful to work with interprofessional team members to identify services that may be available to the individual and caregivers.

INTRODUCTION

Abuse of older people, also known as elder abuse or elder mistreatment, is defined by the World Health Organization, as "a single or repeated act or lack of appropriate action occurring with any relationship in which there is an expectation of trust that causes harm or distress to an older person (aged 60 years and older)."[1] Based on a national survey of cognitively intact community dwelling individuals over the age of 60 years, abuse of older people in the United States is estimated to occur in 1 out of 10 older adults each year.[2] This is likely an underestimate as cases of abuse of older people are underreported. Prevalence rates vary among studies based on population and research methods. One study of community-dwelling older adults ages 57 to 85 years asked individuals about their experience with verbal, financial, and physical mistreatment. Nine percent of respondents reported verbal mistreatment, 3.5% financial mistreatment, and 0.2% physical mistreatment by a family member.[3] Another study in the United States of individuals over 60 years old found that the 1-year prevalence for emotional abuse was 4.6%, physical abuse 1.6%, sexual abuse 0.6%, potential neglect 5.1%, and financial abuse 5.2%.[2] Abuse of older people may occur in the home or institutional setting and may be caused by adult caregivers, family members, or other individuals. In the long-term care setting, abuse may result not only from caregivers but also from interactions with other residents of the facility.

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There are five types of abuse of older people.[4,5] Physical abuse takes place when there is intentional action that causes pain or injury. Examples may include hitting, kicking, or inappropriate use of restraints. Sexual abuse happens when there is sexual contact that is not consensual or if it occurs with someone who is not able to give consent. This may occur with unwanted touching, sexual advances, or exposure. Neglect occurs when there is failure to take care of the needs of an older adult that may result in harm. Examples of neglect include withholding food, clothing, medications, or not ensuring that a person has their personal hygiene maintained or physical aides available. Older adults may also experience emotional/psychological abuse, which happens when there are verbal or nonverbal acts that cause pain or distress. Cases of this type of abuse include verbal harassment, threats of punishment, treating an older adult like an infant, or isolating an older adult from others. Another type of abuse is financial abuse. This occurs when there is an improper use of the older adult's property or money and may include stealing, forging a signature, or pressuring an older adult to sign documents or change a will. Financial abuse may also include making financial decisions that are not in the best interest of the individual.

Patients may also experience self-neglect. This happens when an older adult does not perform or refuses assistance with essential self-care tasks. Self-neglect may include not eating, not taking medications, not performing personal hygiene, or not maintaining a safe home environment. Individuals may have limited contact with others outside of the home.

There are several different risk factors for abuse of older people as highlighted in Table 1.[6,7] Functional dependence on another person and cognitive impairment are significant risk factors for abuse of older people.[8] Individuals may have caregivers who are not trained or equipped to provide the care that the older adult needs. There are several risk factors

for perpetrators of abuse of older people such as caregiver burden or stress, psychiatric illness, and substance misuse.[7,8] Relationship risk factors, such as family disharmony or relationships in conflict, may also lead to abuse of older people.[8]

TABLE 1:

Risk factors for abuse of older people

RISK FACTORS IN OLDER ADULTS
Cognitive impairment/dementia
Poor physical health
Functional dependence
Low socioeconomic status
Substance abuse
Social isolation/poor social support
RISK FACTORS IN PERPETRATORS OF ABUSE
Mental illness
Substance abuse
Abuser dependency on the older adult, e.g., for housing or financial assistance

Abuse of older people can produce several repercussions and may result in physical or psychological consequences for the older adult. There may be increased rates of depression and anxiety among older people subjected to abuse.[9] Older people who experience abuse are more likely to be hospitalized. A study of community-dwelling individuals over the age of 65 years who were reported to Adult Protective Services for concerns of abuse of older people found that after adjusting for comorbidities, socioeconomic variables, and cognitive and physical function, there was a higher rate of hospitalization among those with reported abuse of older people (rate ratio, 2.00 [95% confidence interval, 1.45-2.75]).[10] Individuals who are referred to Adult Protective Services with concerns for abuse of older people are more likely to be admitted to a nursing facility.[11] Older people who experience abuse also have a higher rate of disability and a higher mortality rate than those who do not undergo abuse of older people.[12,13] A study of community-dwelling individuals over the age of 65 years who were referred to Adult Protective Services examined mortality rates over at least a 9-year follow-up period associated with abuse of older people. The study found a shorter survival for individuals who had experienced abuse of older people (9%) than those who were found to have self-neglect (17%) and compared to other members of the study who did not have contact with Adult Protective Services (40%).[13]

EVALUATION FOR ABUSE OF OLDER PEOPLE

Screening

There is no uniform consensus on screening for abuse of older people by all organizations. The US Preventative Services Task Force notes there is insufficient evidence to recommend screening all older adults for abuse of older people.[14] On the other hand, the American Academy of Neurology and American College of Obstetricians and Gynecologists do recommend screening for abuse of older people.[15,16] The American Medical Association recommends inquiry about family violence, which includes abuse of older people.[17] A number of screening tools for abuse of older people have been developed.[18] One such screening tool is the Elder Abuse Suspicion Index (EASI), which can be used for cognitively intact individuals in the primary care setting. This instrument includes five questions that the patient answers, plus one question that the physician answers. At least one "yes" answer on questions 2 through 6 indicates a need for further assessment. The EASI generally takes less than 2 minutes to perform and has an estimated sensitivity of 0.47 and specificity of 0.75.[19]

History and Exam

Evaluation for abuse of older people involves looking holistically at the patient and caregiver. Osteopathic family physicians are trained to evaluate and treat the whole person, including mind, body, and spirit. Utilizing the whole-person and social situation evaluation can be helpful in identifying older adults at risk for or undergoing abuse.

During medical visits, healthcare providers can observe the interactions between the caregiver and older adult. When possible, older adults should be interviewed individually so they can speak freely. The interview should begin with open-ended questions and then move to more specific questions based on answers. It may be particularly challenging to get an accurate history and evaluation if the older adult has cognitive impairment. It is also important to understand the older adult's functional status and who is responsible for helping to care for them if there are functional deficits. It may be helpful to better understand the skill level of the caregiver in order to see if their skill set matches with the older adult's needs. It is also important to identify caregiver stress.

During a medical exam, a healthcare provider can look for unexplained injuries or injuries that do not match the patient's history. In abuse of older people, there may be a delay between the injury or onset of medical illness and seeking medical treatment. An older adult experiencing abuse may visit multiple clinicians or emergency departments for similar injuries. A healthcare provider should consider whether abuse may be playing a role if there is inconsistent compliance with medications, appointments, or following instructions. A complete physical exam for abuse of older people includes a skin and musculoskeletal exam. Signs of abuse of older people are noted in Table 2.[20-23]

Chronic medical conditions may mimic abuse of older people. For example, fractures may occur from osteoporosis or metabolic bone disease, or an individual may have a skin manifestation due to chronic disease or medications, such as anticoagulants.[20] Dehydration may be caused by medications or uncontrolled medical conditions. A gastrointestinal disease process, malabsorption, or malignancy may cause an individual to lose weight and appear malnourished.

TABLE 2:

Signs of abuse of older people

PHYSICAL ABUSE
Bruising in atypical locations, eg, lateral arms, back, face, ears, or neck
Burns
Injuries suggestive of the shape of belts, fingers, or another object
Wrist or ankle lesions suggestive of restraints
Multiple fractures or bruises at different states
SEXUAL ABUSE
Genital, rectal, or oral trauma
Evidence of sexually transmitted infection
NEGLECT
Malnutrition
Dehydration
Pressure injuries
Poor hygiene or soiled incontinence products
Dirty clothing
Poor oral hygiene

Psychological assessment is also beneficial in the evaluation for suspected abuse of older people. The healthcare provider may identify signs of increased anxiety, fear, or anger that can suggest a need for further assessment. Cognitive assessment is also helpful to determine if the older adult has the capacity to make decisions and advocate for themselves.

If there are concerns about financial abuse, a healthcare provider may see signs of a disparity between assets and the individual's living situation or appearance. For example, financial abuse might be suspected if a caregiver is suddenly able to acquire items when they appear to have limited financial assets. Another example may be if a caregiver is unwilling to allow access to the home of an older adult. If an older adult has a progressive cognitive impartment, they will ultimately have difficulty with managing their finances. Healthcare providers can assist these patients by proactively discussing options for financial management with the patient and caregivers.

Laboratory and Imaging Studies

Laboratory findings may be beneficial in some evaluations for abuse of older people. For example, findings of dehydration or malnutrition may suggest neglect if another medical reason is not apparent. Laboratory evaluation of prescription medications or illicit drugs may help to determine if patients are receiving medications they should not be receiving or if some medications are being withheld. Imaging studies may be valuable if there is concern for fractures or injury.

If a healthcare provider performs a home visit for a patient undergoing abuse or self-neglect, they may note that there is not enough food in the refrigerator, excessive clutter, or insect infestation.

INTERVENTIONS FOR SUSPECTED ABUSE OF OLDER PEOPLE

It is important to understand the reporting regulations for abuse of older people in each individual state. Healthcare providers are often required to report to Adult Protective Services or state agencies associated with aging. Healthcare providers can find more information about the specific state requirements at the U.S. Department of Justice website (https://www.justice.gov/elderjustice/elder-justice-statutes-0).[24] The National Center on Elder Abuse (https://ncea.acl.gov) provides useful information about signs of abuse of older people and what to do if abuse is suspected, including how to report concerns of abuse.[25]

If abuse of older people is suspected, the healthcare provider should consider whether there is an immediate risk to the individual and if they are able to safely return to their current living environment.[5] Determination of a safety plan is important. If a patient is not safe to return home, they may require hospitalization until a safe alternative is determined.

When abuse of older people is suspected, osteopathic family physicians may find it particularly beneficial to work with interprofessional team members to provide a holistic management plan. Social workers and case managers may be valuable in determining if there are additional resources that may be available to the individual and caregiver. Setting the individual up for support services such as Meals on Wheels, transportation, or extra services in the home may be helpful. Healthcare providers may access information about local resources and services at eldercare.gov.[26] The osteopathic family physician and team members may also work with an individual on managing depression and anxiety that may accompany the abuse. Healthcare providers may also need to determine the individual's capacity to make decisions and, in particular, identify if the individual has the ability to refuse services and care.

In cases of suspected abuse of older people, documentation should occur as accurately and completely as possible. Using the patient's own words within the medical documentation can be helpful. Detailed documentation of injuries, including size, location, and stage of healing, should be performed.

CONCLUSION

Abuse of older people is often underreported. Clinicians have the opportunity to recognize and intervene in abuse of older people. Resources may be provided by working with interprofessional team members and community agencies such as Adult Protective Services.

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REVIEW ARTICLE

VITAMIN C, TOPICAL RETINOIDS, AND SUNSCREEN IN CLINICAL PRACTICE: ESSENTIALS FOR FAMILY PHYSICIANS

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ABSTRACT

The field of skincare has been rapidly evolving, making it harder to navigate the plethora of products and trends. Vitamin C, topical retinoids, and sunscreen effectively prevent and combat the effects of photoaging with sunscreen being the most crucial product for daily use. Daily application of a broad-spectrum mineral sunscreen 15 minutes prior to sun exposure demonstrates the greatest protection from ultraviolet (UV)-induced skin damage. Vitamin C and retinol prevent the breakdown of collagen and stimulate its growth, which prevents and repairs photodamaged skin. Application of vitamin C prior to sunscreen in the morning is most advantageous, whereas retinol use at night is preferred to avoid photosensitivity. The most effective vitamin C formulations contain 15% L-ascorbic acid, 1% vitamin E, and 0.5% ferulic acid, while strengths ranging from 5% to 20% are safe. Tretinoin, only available via prescription, is the gold-standard retinol for photoaging with a strength of 0.05% being most utilized. Overall, these three products are safe to use together and when used correctly can effectively prevent and treat signs of photoaging with sunscreen providing the additional benefit of protection from skin cancer. The purpose of this paper is to review popular skincare products currently circulating on the internet, focusing on vitamin C, retinol, and sunscreen, by examining their ingredients, benefits, and different formulations based on the available literature on these products. This will better equip family physicians in navigating the ever-evolving landscape of skincare while enabling them to make informed recommendations to their patients.

INTRODUCTION

Attaining flawless skin has been a rising desire for many patients; however, due to the variety of opinions and vast range of cosmeceutical products available, many remain uncertain on how to attain unblemished skin safely and effectively. “Cosmeceuticals,” a term coined in 1984 by Dr. Kligman, refers to widely available products in retail stores across the United States and are defined as hybrid products that have active ingredients providing therapeutic effects that supersede simple cosmetic enhancement but do not qualify as a pharmaceutical drug. This article will concentrate on three commonly used products in daily skincare routines: vitamin C, retinol, and sunscreen. The review will provide a comprehensive overview explaining the benefits, ingredients, and different formulations of the products, allowing family physicians to make appropriate and safe recommendations to their patients.

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VITAMIN C

Vitamin C, also known as ascorbic acid, has been widely used in the cosmetology industry for its photoprotective, antipigmentary, and antiaging properties.[1,2] The reduced form of vitamin C, L-ascorbic acid, is the biologically active form, which acts as a cofactor for various enzymes, aids in the synthesis of collagen, and helps maintain the integrity of the skin.[2] Due to the inherent functions of this hydrophilic vitamin, it has been widely used in the skincare industry as a product that protects against sun-induced skin damage, lessens hyperpigmentation, and reverses signs of aging.[3]

One of the most important environmental factors that cause cancer and photoaging is exposure to ultraviolet (UV) radiation.[4] UV radiation damages the skin by creating reactive oxygen species (ROS), which upregulate certain factors, such as activator protein 1 (AP-1) and nuclear factor-B.[4] Collectively, the factors increase the production of metalloproteinases (MMPs), which break down collagen and inhibit the production of new fibers, resulting in skin manifestations such as photoaging, pigmentation and wrinkles.[4] Vitamin C neutralizes free radicals with its antioxidant characteristics and has been shown to inhibit the UV-induced upregulation of AP-1, leading to an overall decrease in the production of matrix MMP and subsequent collagen breakdown.[2]

Vitamin C is involved in various stages in the synthesis of collagen and the molecule stimulates the transcription of procollagen

I and procollagen III genes, which provides antiaging properties.[5] Collagen is essential for the preservation of skin firmness and elasticity while also smoothing out wrinkles.[6] Additionally, the molecule acts as a cofactor for the proline and lysine hydroxylases, which play a vital role in stabilizing the tertiary structure of collagen.[3]

Additionally, hyperpigmentation is associated with certain areas of the skin appearing darker in color, which may be a result of increased melanin deposition in keratinocytes.[5] L-ascorbic acid inhibits the enzyme tyrosinase, which is the rate-limiting step in melanogenesis, making the compound potentially useful in treating certain causes of hyperpigmentation.[3,5]

Vitamin C Formulations

A barrier to the topical application of L-ascorbic acid is its high reactivity and lipophobicity; therefore, even if the molecule resists oxidation before application, it may not be able to penetrate the skin due to the lipophilic stratum corneum.[3] The absorption and stability of vitamin C can be increased by applying a derivative of L-ascorbic acid instead of the pure compound or by generating an environment with a pH that is less than 3.5.[2]

The most stable derivative of vitamin C is magnesium ascorbyl phosphate (MAP), a hydrophilic compound that is stable at a neutral pH.[2] The phosphate group adds protection against oxidation, which is also seen in another derivative: sodium L-ascorbyl-2-phosphate (SAP).

Formulations of SAP contain various strengths, ranging from 0.3% to 5%.[7] Effects of skin brightening are observed in SAP concentrations of 3% or above, while antiaging properties are noticed in formulations containing 5% SAP.[8] Additionally, application of topical formulations with 5% SAP has been shown to reduce inflammatory and noninflammatory lesions induced by acne vulgaris, due to its antimicrobial activity against *Propionibacterium acnes*, the major bacterium responsible for the development of acne vulgaris.[8] Compared to other vitamin C derivatives, SAP has shown superior penetration into human skin as well as a higher rate of bioconversion into the biologically active form of the vitamin.[8] This vitamin C derivative has shown minimal irritation, making it a popular option for patients with acne-prone skin or those who experience irritation from conventional acne treatments.[9] In patients with acne vulgaris, formulations containing SAP may be especially beneficial; however, patients using benzoyl peroxide should be educated to use vitamin C products on alternate days or at different times of the day since benzoyl peroxide oxidizes and, therefore, inactivates vitamin C.[10]

A more novel derivative of vitamin C is 3-O-ethyl ascorbic acid (EAA), which is a water-soluble molecule that displays minimal skin irritation while aiding in skin brightening and reversing signs of aging.[10,11] Moreover, a combination of 30% EAA with 1% lactic acid has been shown to lessen manifestations of hyperpigmentation by reducing melanin content.[11] These effects allow EAA to be recommended for patients with hyperpigmented or sensitive skin.

The stability of L-ascorbic acid in product formulations can be increased by adding ferulic acid, a ubiquitous plant antioxidant. Ferulic acid acts as an antioxidant by scavenging free radicals, inhibiting reactions that form ROS, and providing stability to other antioxidants' damage.[12] Additionally, ferulic acid has demonstrated prevention of photoaging by protecting against UV-induced skin damage.[12] The addition of a ferulic acid formulation with a pH of less than 3.5 reduces the reactivity of vitamin C and adds synergistic photoprotection.[2,13] The acidity of ferulic acid–containing formulations may cause skin irritation and, therefore, should not be recommended to patients with sensitive skin. In patients with normal resilient skin, formulations containing pure L-ascorbic acid may be used, while patients with sensitive skin or acne may experience better results with a vitamin C derivative, such as SAP or EAA, since they are stable at a higher pH and, therefore, have a decreased risk of skin irritation.[10]

Vitamin E—another vitamin that functions as an antioxidant—has been shown to protect the skin's lipid structure via its oxidative properties.[13] When used in combination with vitamin E, the actions of vitamin C are potentiated fourfold.[13] Moreover, studies have shown that adding 0.5% ferulic acid to a combination of 1% vitamin E and 15% vitamin C increases the efficacy of vitamin C eightfold.[13]

Overall, further investigation is required to determine the efficacy of topical vitamin C derivatives; however, usage of these products is safe and has not been associated with adverse effects. Vitamin C may be used with other topical antiaging products, such as sunscreen and tretinoin, without causing adverse effects.[13]

Recommendations

Vitamin C products are easily accessible since they are sold over the counter at most stores and may be purchased online. A formulation containing pure vitamin C in the form of L-ascorbic acid may be purchased from SkinCeuticals. The formulation sold by SkinCeuticals is a patented formula containing 15% L-ascorbic acid, 1% vitamin E, and 0.5% ferulic acid. Despite extensive research on the efficacy of this product, its price of $182 for 30 mL may not make it a viable recommendation for all patients. Alternatively, other companies, such as CeraVe, Olay, and VERSED, may be more budget-friendly recommendations, with the cost of vitamin C products starting around $20. Even though the optimal concentration of vitamin C depends on the formulation, a safe recommendation in order to attain the biologic benefits provided by vitamin C is a strength of 5% to 20%.[2] Formulations containing 20% or more vitamin C have not demonstrated increased efficacy and may cause skin irritation.[2]

Patients with a history of sensitive skin should be advised to begin with a formulation that contains a lower concentration of vitamin C to prevent unwanted skin irritation.[10] Patients complaining of signs of skin irritation, such as erythema or stinging, should be informed that applying moisturizer to the affected area should resolve the irritation. Studies have shown that the appearance of wrinkles on the face improved when using a vitamin C formulation for at least 3 months; therefore, patients should be educated that the benefits are not immediate and that application of the product once or twice per day is required to attain optimal saturation levels of the vitamin and experience its subsequent benefits.[3,13]

TABLE 1:

Products containing different vitamin C formulations[14]

PRODUCTS CONTAINING L-ASCORBIC ACID			
Product	**Ingredients**	**Approximate Price***	**Properties**
SkinCeuticals - C E Ferulic	L-ascorbic acid (15%), ferulic acid (0.5%, alpha tocopherol (1%)	~$182/30 mL	**Antioxidant:** L-ascorbic acid (15%), alpha tocopherol (1%), ferulic acid (0.5%) **Skin brightening:** L-ascorbic acid (15%)
La Roche-Posay - Pure Vitamin C Face Serum	L-ascorbic acid (10%), tocopherol, salicylic acid, glycerin	~$44.99/30 mL	**Antiacne:** salicylic acid **Antioxidant:** L-ascorbic acid, tocopherol **Skin brightening:** L-ascorbic acid
CeraVe - Skin Renewing Vitamin C Serum	L-ascorbic acid (10%), glycerin, tocopheryl acetate, ceramides, phytosphingosine	~$29.99/30 mL	**Antiacne:** phytosphingosine **Antioxidant:** L-ascorbic acid (10%), tocopheryl acetate **Skin brightening:** L-ascorbic acid (10%)
Olay - Age Defying Anti-Wrinkle Night Cream	L-ascorbic acid, niacinamide, glycerin, tocopheryl acetate, retinyl propionate, benzyl alcohol	~$16.49/60 mL	**Antiacne:** niacinamide **Antioxidant:** ascorbic acid, tocopheryl acetate **Skin brightening:** L-ascorbic acid, niacinamide
PRODUCTS CONTAINING SODIUM ASCORBYL PHOSPHATE (SAP)			
Product	**Ingredients**	**Approximate Price***	**Properties**
Olay Regenerist – Brightening Vitamin C Serum	SAP, niacinamide, glycerin, panthenol	~$29.99/~40 mL	**Antiacne:** SAP, niacinamide **Antioxidant:** SAP **Skin brightening:** niacinamide
Paula's Choice – Resist Anti-Aging Clear Skin Hydrator	SAP, glycerin, niacinamide, dimethicone, adenosine	~$39.00/50 mL	**Antiacne:** SAP, niacinamide **Antioxidant:** SAP, adenosine **Skin brightening:** niacinamide
BLISS – Bright & Radiant Whipped Mask	SAP, zinc pca, L-ascorbic acid, glycerin, tocopheryl acetate, ascorbyl glucoside	~$15.00/50 mL	**Antiacne:** SAP, zinc pca **Antioxidant:** SAP, tocopheryl acetate, ascorbyl glucoside, L-ascorbic acid **Skin-brightening:** L-ascorbic acid, ascorbyl glucoside
PRODUCTS CONTAINING MAGNESIUM ASCORBYL PHOSPHATE (MAP)			
Product	**Ingredients**	**Approximate Price***	**Properties**
Paula's Choice – Skin Recovery Replenishing Moisturizer	MAP, tocopherol acetate, glycerin, ceramides, squalene, ethylhexyl stearate, seed oil	~$35.00/60 mL	**Antioxidant:** MAP, tocopherol acetate, SAP **Antiacne:** SAP **Skin brightening:** MAP
The Ordinary – Magnesium Ascorbyl Phosphate 10%	MAP (10%), tocopherol, glycerin	~$11.70/30 mL	**Antioxidant:** MAP, tocopherol acetate **Skin brightening:** magnesium ascorbyl phosphate
PRODUCTS CONTAINING ETHYL ASCORBIC ACID (EAA)			
Product	**Ingredients**	**Approximate Price***	**Properties**
The Ordinary – Ethylated Ascorbic Acid 15% Solution	EAA 15%	~$20.00/30 mL	**Antioxidant:** EAA **Skin brightening:** EAA
Paula's Choice – 5% Vitamin C Sheer Moisturizer SPF 50w	EAA, ascorbyl glucoside, tetrahexyldecyl ascorbate, tocopherol, glycerin, ethylhexyl methoxycinnamate, butyl methoxycinnamate, titanium oxide	~$45.00/60 mL	**Antioxidant:** EAA, ascorbyl glucoside, tetrahexyldecyl ascorbate, tocopherol **Skin brightening:** EAA, ascorbyl glucoside, tetrahexyldecyl ascorbate **Sunscreen:** glycerin, ethylhexyl methoxycinnamate, butyl methoxycinnamate, titanium oxide

**These price averages can differ based on where purchased.*

The instability of vitamin C may cause the formula to undergo oxidative changes, resulting in yellow discoloration of the skin.[13] Patients should be educated that even though this side effect is harmless, it indicates that the antioxidant properties were lost and subsequently will not produce the desired benefits. Vitamin C products should be stored in cool and dark environments to minimize compound oxidation and subsequent skin discoloration.

Vitamin C serums can be applied in the morning or at night, following use of a thorough cleanser. For added protection against UV-induced damage, sunscreen may be applied after the vitamin C serum has completely dried. Additionally, due to their ability to improve vitamin C stability and absorption, formulations containing L-ascorbic acid, vitamin E, and ferulic acid can be recommended, keeping individual skin sensitivity in mind.

Table 1 provides a summary of various vitamin C formulations from different companies to give physicians an overview of the ingredients in different products. While this list includes commonly used commercial products, it is not exhaustive. The ingredients and their properties are detailed for each product. It is important to be cautious when recommending these products since cosmeceutical products in the United States do not require FDA approval before being sold since the FDA does not formally recognize cosmeceutical products.[1] As seen in Table 1, some brands list the concentration of vitamin C within their product, whereas others do not. The only product with specific research on its patented formulation is SkinCeuticals. The other listed products contain ingredients backed by research supporting their efficacy. Physicians should exercise caution when advising patients to use a specific brand. To avoid a severe reaction upon first-time use to any product, physicians may advise their patients to consider testing on a small area of the skin prior to using on the entirety of the face.

RETINOIDS

Topical retinoids are utilized to treat acne and signs of photoaging (fine lines, wrinkles, hyperpigmentation).[15] In the epidermis, aging is attributed to the loss of proliferation and turnover of its most abundant cell—the keratinocyte, which provides support to the outermost layer of skin—its loss resulting in thin, fragile skin.[16] Meanwhile, in the dermis, collagen fibrils are tightly woven to provide strength and durability; the breakdown of these collagen fibers by MMPs is attributed to aging.[15] Retinoids treat photoaging through keratinocyte proliferation, epidermal and dermal thickening, fibroblast growth, formation of new blood vessels within the dermis, and TGF-β/CTGF (transforming growth factor beta/connective tissue growth factor) pathway activation (resulting in mature collagen growth).[15,17] Additionally, the use of topical retinoids has been shown to decrease the production of MMPs, resulting in an additional collagen-enhancing effect.[15,17,18]

Retinoids are comprised of vitamin A (retinol) and its natural derivatives, retinoic acid, retinaldehyde, and retinyl esters, in addition to other synthetic derivatives.[15] Topical retinoids are FDA approved to treat photoaging, acne vulgaris, psoriasis, cutaneous T-cell lymphoma, and Kaposi sarcoma.[17] This article will focus on topical retinoids indicated specifically for photoaging.

There are four generations (Table 2) of retinoids that exist in both oral and topical formulations. The FDA-approved topical retinoids to treat photoaging are tretinoin and tazarotene, and adapalene is used off label (Table 3). Within the first generation, there are retinol, retinaldehyde, and retinyl esters (precursors to retinoic acid) that are not FDA approved but are available over the counter (OTC) in cosmeceutical products marketed to combat photoaging (Table 3).

The potency of topical retinoids plays a large role in the product's efficacy. The difference between FDA-approved products available via prescription vs OTC is that OTC products are less potent.[15] Retinoic acid, also known as tretinoin, is the biologically active component and therefore more potent and effective. Retinyl esters (least potent) are converted to retinoic acid through these steps:

Retinyl esters → Retinol → Retinaldehyde → Retinoic Acid [20]

The forms that take the least number of steps to convert to retinoic acid such as retinaldehyde (only requiring one conversion) will be more potent and effective.[19] Keeping this in mind can help discern which forms of topical retinoids are best for patients for improving skin texture, fine lines, and dyspigmentation. It is important to be aware that since tretinoin is the most potent, its use topically has an increased risk of side effects such as retinoid dermatitis.[19]

Topical tretinoin is the gold-standard treatment for photoaging and the most studied retinoid to date. Its 0.05% emollient is most commonly prescribed due to strong research backing its efficacy, although 0.025% is considered therapeutically beneficial and generally safe.[20] A 2-year long placebo controlled clinical trial with 204 subjects concluded that 0.05% tretinoin emollient used once a day was safe and effective.[20] Alternatively, a study revealed that tazarotene has comparable effectiveness to tretinoin, however, the product is less budget friendly.[19,20]

Adapalene has been shown to be less irritating and maintain similar efficacy to tretinoin; therefore, it may be recommended to patients with sensitive skin, although further research is warranted.[17,20,26] Additionally, in comparison to tretinoin and tazarotene, which are photolabile, adapalene is more stable and therefore, will not undergo molecular photodegradation, which allows daytime use.[26]

Moreover, retinol, retinaldehyde, and retinyl palmitate, none of which are FDA approved, are the most common agents in cosmeceuticals.[20] While these are widely used in cosmetic products, their concentrations and stability vary since they are not regulated.[20] Meanwhile, multiple studies have compared different concentrations of these retinoids and shown successful treatment of photodamage in addition to decreased adverse effects.[19,20] Retinaldehyde has been deemed the most effective, although retinol is the most studied with substantiated improvements to photodamage through epidermal thickening and collagen synthesis.[19,20] Additionally, retinol is less irritating than tretinoin but is

TABLE 2:

Retinoid generations[15,17,19]

Generation	Generic Names	Available Topically?	Formulation Type and % Available
1st Generation *(naturally occurring retinoids)*	Tretinoin (all-trans-retinoic acid)	Yes	Gel, cream 0.1%, 0.08%, 0.06%, 0.05%, 0.04%, 0.025%, 0.02%, 0.01%
	Isotretinoin (13-cis retinoic acid)		Gel 0.05%
	Alitretinoin (9-cis retinoic acid)		Gel 0.1%
	Retinol (all-*trans*-retinol, vitamin A)		Cosmeceutical products 0.15%-0.3%
	Retinal (retinaldehyde)		Cosmeceutical products 0.05%-0.1%
	Retinyl esters (retinyl palmitate, retinyl propionate, retinyl acetate, retinyl retinoate, and retinyl N-formyl aspartame (retinyl aspartate)		Cosmeceutical products Various/unknown %
2nd Generation	Acitretin	No	--
	Etretinate		--
3rd Generation	Adapalene	Yes	Gel, cream, lotion 0.1%, 0.3% *0.1% available OTC
	Tazarotene		Gel, cream, lotion, foam 0.045%, 0.05%, 0.1%
	Bexarotene		Gel 1%
4th Generation	Trifarotene	Yes	Gel, cream, lotion 0.1%, 0.3% *0.1% available OTC
	Seletinoid G	No	--
	Tamibarotene		--

TABLE 3:

Topical retinoids to treat photoaging[15,17,19-25]

	Generic	Brand Name/Formulations	Notes/Extra
FDA-approved topical retinoids for photoaging	Tretinoin	Retin-A (cream, 0.02%, 0.05%)	• Apply once topically at bedtime • 0.05% is the most studied strength • 0.025% is considered therapeutically beneficial and generally safe
	Tazarotene	Avage (cream, 0.1%)	Apply pea-sized amount topically at bedtime
	Adapalene (off label)	Differin (gel, 0.3% or OTC gel, 0.1%)	• Most studied • 0.3% is recommended for best efficacy and outcomes • 10 times less potent than tretinoin but more tolerable
OTC cosmeceutical products used to treat photoaging (not FDA approved)	Retinol	--	• Most studied • 0.3% is recommended for best efficacy and outcomes • 10 times less potent than tretinoin but more tolerable
	Retinaldehyde	--	Most effective for photoaging
	Retinyl esters (retinyl palmitate, retinal acetate, retinol propionate, retinyl aspartate)	--	• Further research is needed

tenfold less potent.[20] Although the latter is better tolerated than tretinoin, the potency and efficacy of these products cannot be validated due to the lack of regulation.[20] For example, there are brands available in retail stores that advertise their product as retinol based but include additional ingredients (hyaluronic acid, ceramides, etc) and may not include the percentage of retinol within the product. These products may combat fine lines and wrinkles, but it is difficult to isolate which ingredients are responsible for any antiaging benefits.

Ultimately, one should exercise caution when recommending OTC cosmetic products due to the lack of regulations over those containing retinol, retinaldehyde, or retinyl esters.

RECOMMENDATIONS

Educating patients on the side effects and expectations regarding the outcomes of topical retinoid use is important. The major side effect of topical retinoids is retinoid dermatitis, which manifests as erythema, peeling, scaling, dryness, burning, pruritus, and photosensitivity.[17] Other uncommon side effects that can occur are hypo- or hyperpigmentation, allergic contact dermatitis, or sticky skin.[17]

Recommendations regarding topical retinoid application include the application of a pea-sized amount to clean dry skin at bedtime (30 minutes after face washing). This decreases absorption through the dermis, which may decrease skin irritation.[19] Moreover, to combat dryness, use of a moisturizer should be applied to create a hydration barrier.[19] To allow for proper retinol penetration, moisturizers should be applied 30 minutes after retinol application.[19] Individuals with sensitive skin and those prone to acne and/or hyperpigmentation should use moisturizers that do not contain pore-clogging ingredients (cocoa butter, coconut oil, mineral oil etc).[27] Patients can look for moisturizers labeled "noncomedogenic," indicating that the product does not block pores. Cetaphil Moisturizing Cream, La Roche-Posay Double Repair Facial Moisturizer with SPF, and Vanicream Daily Facial Moisturizer are available to the public and are known for their noncomedogenic properties. Retinol application to the eyelids and perioral areas should be limited or avoided due to increased sensitivity and peeling.[17,26] As retinoids are lipophilic, it is advised that patients use non-oil–based or noncomedogenic makeup, sunscreens, and other skin care products in addition to nonalkaline synthetic detergent cleansing products (gentle cleansers).[26]

When first using a topical retinoid, patients should start at a low concentration (0.025% for tretinoin specifically) and slowly incorporate this product into their skincare regimen.[19] Patients can begin using the product three times a week and gradually increase the frequency of use based on tolerance.[19] Moreover, short-contact application (washing the medicine off after an hour) may prevent adverse effects.[17] The irritative effects of topical retinoid use may cause hyperpigmentation in patients with darker skin colors; therefore, starting at a low concentration and providing counseling on preventative measures are important.[27]

To improve adherence to medication regimens, patients should be advised that the benefits of using retinol are more noticeable over time. When used for the treatment of photoaging, results can take from 3 to 6 months of daily application to become apparent.[17,19] Despite the lack of conclusive research, patients should understand that the proven teratogenic effects of oral retinoids discourage topical retinoids during pregnancy.[20] Lastly, topical use of retinoids is considered a long-term treatment since its benefits cease with discontinuation.[20]

SUNSCREEN

Sunscreen is recommended for everyone by the American Academy of Dermatology (AAD) for baseline skin protection.[28] Its use is encouraged over exposed skin regardless of if the sun is visible or not. Prolonged exposure to the sun can lead to loss of skin elasticity, cancers, and other discoloration issues. One in five Americans will develop skin cancer regardless of age, gender, and skin type.[28] The AAD currently recommends the use of sunscreen with an SPF of at least 30, broad spectrum protection against UVA and UVB rays, and water-resistant properties.[29] SPF is defined as the sun protective factor, or the measure of how much UV radiation is necessary to produce sunburn on protected skin vs on unprotected skin.[30] The higher the SPF, the more protection against UV radiation.[30] The most important outcomes of sunscreen include antiphotoaging and cancer protection.[31]

The sun emits UVA, UVB, and UVC rays.[32] Ultraviolet radiation can directly damage DNA, and the accumulation of this DNA damage leads to cancer development.[33] The combined effects of UV damage can potentially lead to photoaging and the development of melanoma and nonmelanoma skin cancers.[28]

Sunscreen products are categorized as mineral or chemical compounds that include inorganic and organic ingredients respectively.[32] Chemical sunscreens absorb UVA and UVB rays and then deactivate them, whereas physical or mineral sunscreens use inorganic ingredients to act as a barrier and shield the skin by reflecting and scattering the UV rays.[32] Mineral sunscreens are recommended over chemical sunscreens for those with sensitive skin due to their nonirritant and noncomedogenic properties.[29] The white chalky cast that appears when using mineral sunscreens can be an undesirable cosmetic result for people, however, this can be minimized with different formulations.[34]

The two main inorganic ingredients in mineral sunscreens are zinc oxide (ZnO) and titanium dioxide (TiO2).[33] These ingredients are integrated as nanoparticles and are used in nearly every sunscreen because of their effectiveness in protecting against UVA and UVB rays.[30] Together they create a broad-spectrum filter that blocks UV rays, with zinc oxide primarily blocking UVA rays and titanium dioxide reflecting UVB rays.[30] ZnO and TiO2 are the only two ingredients that are FDA approved as generally recognized and safe and effective for people over 6 months of age or those with sensitive skin.[35-37] For cosmetic reasons, the addition of inorganic substances is more favorable when creating

a desirable sunscreen formulation as they do not cause skin irritation, comedogenic acne, or discoloration.[32]

There are several organic, soluble filters that make up chemical sunscreens such as avobenzone, octinoxate, homosalate, octisalate, and octocrylene.[36] Avobenzone is an oil soluble ingredient in sunscreen that filters UVA rays while octinoxate, homosalate, octisalate, and octocrylene cater to UVB rays, and oxybenzone does both (Table 4).[31] Organic sunscreens function by absorbing the harmful UV rays and deactivating them through a reaction that releases them as heat.[36] This reaction has been linked to worsening preexisting skin conditions such as melasma or rosacea.[38] According to the National Eczema Association, organic ingredients such as oxybenzone, avobenzone, and benzophenone-4, along with high alcohol concentrations, can exacerbate eczema as well.[39] Organic ingredients tend to be comedogenic, compared to mineral sunscreens.[40] However, a chemical (organic) sunscreen that has comedogenic properties can still help prevent skin cancer, hyperpigmentation, and erythema.[39] Patients can discuss their personal considerations with their physician when deciding between mineral or chemical sunscreen utilization.

Mineral sunscreens are generally preferred due to their noncomedogenic and hypoallergenic properties; however, because the sunscreen is not absorbed into the skin and has reflective properties, more frequent reapplication is needed. It is beneficial to recommend purchasing mineral sunscreens labeled "water resistant" or "waterproof" to maximize their efficiency. Chemical sunscreens are indicated when the skin is exposed to water or sweat. Chemical sunscreens are absorbed into the skin, allowing for a longer-lasting sun protective factor that can be beneficial with prolonged water/sweat exposure with UVA/B rays.[42]

UV radiation can also be physically blocked by wearing hats, sunglasses, and tightly woven clothes. The ultraviolet protective factor (UPF) measures the amount of UV radiation that can penetrate clothing and reach the underlying skin.[42] Clothing with polyester or cotton blends typically have a UPF value of 50 (Table 5).[42]

Avoiding the sun between the hours of 10 am and 4 pm and using an SPF of 30 or higher that has a broad spectrum will also provide significant protection.[32,42] To ensure optimal protection, adults should apply 1 to 2 ounces of sunscreen to all exposed areas 15 minutes before sun exposure. Reapplication of sunscreen every 2 hours, if exposed to water and/or sweat, is also important to obtain sustainable sun protection.[32]

CONCLUSION

Sunscreen, vitamin C, and retinol may be used in combination to combat the effects of UV-induced skin damage, as they each exert photoprotective properties via different mechanisms. The following order allows for the most effective absorption of the products: vitamin C or retinol, followed by moisturizer, followed by sunscreen. Educating patients on the correct application and ways to avoid irritation is crucial for adherence to skincare regimens involving these products in addition to ensuring each product's efficacy. In this ever-changing arena of products, it is important for family physicians to stay up to date and to make informed recommendations on these, while considering specific benefits and precautions with certain product formulations.

LITERATURE SEARCH AND DATA SOURCES

This literature review was synthesized using a variety of sources from PubMed and WorldCat Discovery databases. Additional sources were the American Academy of Dermatology, the Cleveland Clinic, and other government-regulated dermatology institutions. Peer-reviewed journal articles and studies were searched using specific parameters to ensure accurate and recent information. Keywords used to search for articles were vitamin C, L-ascorbic acid, photoaging, hyperpigmentation, retinoids, topical retinoids, retinol, sunscreen, organic sunscreens, inorganic sunscreens, skin cancer, melanoma, nonmelanoma skin cancer, photoaging, sun protective factors, sunburn, antiaging, mineral sunscreen, chemical sunscreen.

TABLE 4:

Active ingredients in sunscreens[36,41]

Active Ingredient	Type	Method of Protection Against UV Rays	FDA Recommendation of Maximum Concentration
Avobenzone	Chemical	Absorbs UVA	3%
Octinoxate	Chemical	Absorbs UVB	7.5%
Homosalate	Chemical	Absorbs UVB	15%
Octisalate	Chemical	Absorbs UVB	5%
Octocrylene	Chemical	Absorbs UVB	10%
Oxybenzone	Chemical	Absorbs UVA and UVB	6%
Zinc oxide	Mineral	Absorbs UVB	25%
Titanium dioxide	Mineral	Absorbs UVB	25%

TABLE 5:

SPF ratings[43]

SPF	% of UV Radiation Blocked	UPF	% of UV Radiation Blocked
15	93%	15	93.3%
30	97%	30	96.7%
50	98%	50+	98%
100	99%		

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REVIEW ARTICLE

ADHD IN THE FAMILY MEDICINE SETTING: ETIOLOGY, PRESENTATION, AND DIAGNOSIS

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KEYWORDS

ADHD

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ABSTRACT

Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental phenomenon commonly presented to the primary care physician for diagnosis and treatment. The primary care physician has the capability to diagnose ADHD and should remain well-informed in the current body of literature regarding ADHD. The diagnosis of ADHD is complicated because it presents with significant heterogeneity throughout development and among individuals. Understanding the neurodevelopmental etiology associated with ADHD helps to contextualize the behavioral, emotional, and cognitive deficits with which these patients struggle. Through a more in-depth understanding of ADHD, the primary care physician is more informed and better able to care for patients. As presented in this article, a literature review on the underlying etiology, clinical presentation, and clinical diagnosis of ADHD, this article helps the primary care physician stay up to date on ADHD.

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) has been known under various names since 1775.[1] It is a neurodevelopmental syndrome caused by the cumulative effects of various genetic and environmental risk factors.[1] ADHD manifests as lifelong patterns of inattentiveness, hyperactivity, and impulsivity that are severe enough to impair daily functioning.[1] People with ADHD have been found to be at an increased risk for behavioral health issues such as substance use disorders, unemployment, educational underachievement, delinquency, gambling, depression, relationship difficulties, and teenage pregnancy.[1-4] Correlation with a significantly heightened risk of unnatural causes of death resulting from suicide, unintentional injury, and fatal accidents, such as motor vehicle accidents, has also been identified.[1] There is an upward trend of patients seeking ADHD diagnosis and treatment in the primary care setting.[5] Sixty-five to eighty-five percent of ADHD patients are diagnosed in the primary care setting, and an even larger proportion will seek prescriptions from primary care providers for management of this condition.[6-9] Therefore, it is essential for the primary care provider to be comfortable recognizing, assessing, and treating ADHD to prevent unnatural causes of death and decreased quality of life in these patients.[1-4]

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ETIOLOGY

The etiology of ADHD is a complex interaction of genetic, social, and environmental factors. There is evidence that the genes responsible for ADHD development work through a complex polygenic mechanism. Despite this, ADHD has a 74% heritability from parent to offspring.[1]

In addition to genetics, prenatal factors appear to determine the development of ADHD. The greater the number of prenatal risk factors appears to correlate with an increasing severity of symptoms that develop later in life.[10] Children born preterm are diagnosed with ADHD twice as often as full-term children.[1] Maternal smoking and hypertension also correlate with ADHD development.[1] Early pregnancy vitamin D levels have been inversely correlated with the manifestation of ADHD.[11] This is explained by vitamin D playing a critical neuroprotective and neurodevelopmental role in the embryo during early brain development.[11] Maternal penicillin use also appears to correlate with ADHD development, but it is unclear whether this association exists as a result of the drug or because of the presence of an infection.[12] For example, maternal inflammation, measured by C-reactive protein level, is also associated with ADHD symptom load.[13]

The core etiology of ADHD is impaired neurodevelopment resulting in arousal dysregulation in the brain.[14,15] Recent data show that ADHD correlates with biomarkers on electroencephalogram (EEG), functional magnetic resonance imaging (fMRI), hemodynamics, and genetics.[16] Biomarkers typically show significant differences in the anatomy and physiology of cerebral structures such as the

prefrontal cortex and amygdala.[16] Future research is working to develop strategies to utilize biologic correlates for diagnosis in the clinical setting.

The major symptoms of ADHD: inattention, hyperactivity, and impulsivity are primarily attributed to abnormalities of the prefrontal cortex principally involving the neurotransmitters dopamine and norepinephrine.[18]

ADHD is associated with different etiologies and variable changes in brain development, leading to a spectrum of symptomatology.[18] Dopamine and norepinephrine neurotransmission play key roles in the underpinnings of this disorder.[18] Medical literature typically describes ADHD through the lens of the "dopamine hypothesis," which attributes symptoms to dysregulation of dopaminergic pathways.[18] To understand the complete spectrum of ADHD symptoms, it is important to recognize the role of norepinephrine, too. Further evidence from genetic studies suggests that variation in genes that are responsible for norepinephrine production can disrupt the prefrontal cortex and disrupt the regulation of attention and behavior. It is likely that a combination of both dopaminergic and noradrenergic disruptions explains the heterogeneity of ADHD among different individuals.[18] Alpha-2 adrenergic agonists are effective pharmacotherapies for ADHD and are believed to modulate both dopaminergic and noradrenergic neurotransmission to alleviate ADHD symptoms.[18]

PRESENTATION

Childhood Presentation

The average age of ADHD diagnosis is 7 years.[4] The child shows a pattern of inattentiveness, hyperactivity, and/or impulsivity, which is detrimental to his or her daily functioning and school participation.[4] Hyperactive children with ADHD may run and climb excessively or have difficulty playing quietly.[20] Girls may have fewer externalizing problems than boys and are more likely to present with fatigue and inattention.[20] Boys may present as more hyperactive or aggressive and as a result are more likely to draw the attention of parents and teachers.[20]

Adolescent Presentation

Identifying ADHD is more difficult in undiagnosed adolescents and adults. This age bracket will often display less hyperactivity.[4] Despite this, the underlying etiology of ADHD persists, and affected adults will often display similar pitfalls as younger people with untreated ADHD.[4] As children grow older, their impulsive behaviors conform less to typical social norms, possibly resulting in adolescents with ADHD being rejected by their peers.[22] Other individuals with ADHD make conscious efforts to mask their symptoms around their peers. This can result in an adolescent who presents with drastically different levels of hyperactivity with peers than at home with family.[22]

Adult Presentation

Approximately one-third of children in the United States diagnosed with ADHD will continue to struggle with symptoms into adulthood.[6] However, these symptoms do not present the same in adulthood as they did in childhood.[4,6] Adults with ADHD are more likely to experience hyperactivity in the form of restless energy, an inability to relax, persistent talkativeness, and difficulty engaging in sedentary activities.[20] Hyperactivity in adults may also be expressed as excessive fidgeting, the inability to sit still, or being "on the go" all the time.[6,20] Inattentive ADHD symptoms tend to predominate over hyperactive symptoms in adults.[6] Inattentiveness manifests as a difficulty sustaining attention, disdain towards tasks involving sustained attention, and distractibility.[2,4,6] Inattentiveness can also manifest in the form of disorganization, tardiness, boredom, indecisiveness, and carelessness, which are detrimental to employment and productivity.[20] Emotional dysregulation may present in adulthood as irritability, emotional lability, and emotional reactivity.[6] Adult patients may also report developmentally attenuated emotional symptoms such as mood swings and various difficulties with social, family, and romantic relationships.[2] Adults with ADHD often experience lifetime mood lability with frequent highs and lows, and short-fuse temper outbursts.[20] ADHD partners add strain to their romantic relationships by being inattentive to the needs of their partner or operating on a "short fuse."20 Impulsivity may be expressed as persistent impatience, acting carelessly, spending irresponsibly, rapidly moving between jobs and relationships, and sensation-seeking behaviors.[20]

DIAGNOSTIC CRITERIA

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* determines the ADHD diagnostic criteria in the United States. The *DSM-5* characterizes ADHD as a detrimental pattern of inattention and hyperactivity that has persisted since childhood. Symptoms must be robust across different environments, scenarios, and settings. An adult ADHD diagnosis requires at least five inattention symptoms or five hyperactive/impulsive symptoms since childhood. A childhood diagnosis requires six or more for either inattention or hyperactive/impulsive symptoms impairing quality of life. Symptoms must be severe, present before 12 years of age, and inappropriate for the patient's current age and developmental level.[21] *DSM-5* ADHD symptoms are listed in Table 1.

ADHD is exclusively a clinical diagnosis.[23] But other diagnostic tools such as neuroimaging and EEG have been used in the diagnosis of ADHD. The Neuropsychiatric EEG-Based Assessment Aid (NEBA) is FDA approved but should only be used as a complementary tool.[24] Rating scales are available to help the physician determine that the *DSM-5* criteria have been met. Most ADHD rating scales are accessible via computer and are practical enough to be completed within a few minutes in the office. A nonexhaustive list of validated ADHD rating scales available to the primary care physician is listed in Table 2.[8,25]

While specialists are valuable in diagnosing ADHD patients through neuropsychiatric batteries, primary care physicians can diagnose and treat ADHD. Since the primary care physician can diagnose ADHD in the clinic, it may be more cost-effective and practical to do so rather than referring patients to a specialist for diagnosis. The physician should determine that the *DSM-5* criteria have been met, through acquiring documentation of symptoms occurring in more than one setting and from at least two credible

TABLE 1:

DSM-5 ADHD symptoms

Inattentive Symptoms	Hyperactive Symptoms	Impulsive Symptoms
Poor listening skills	Squirms or fidgets	Difficulty waiting turn
Loses or misplaces items	Marked restlessness that is difficult to control	Interrupts or intrudes into conversations and activities of others
Sidetracked by external or unimportant stimuli	Appears to be driven by "a motor" or is often "on the go"	Impulsively blurts out answers before questions are completed
Forgets daily activities	Lacks ability to engage in leisure activities in a quiet manner	
Diminished attention span	Incapable of staying seated in class	
Lacks ability to complete work or to follow instructions	Overly talkative	
Aversion to tasks requiring concentration		
Fails to focus on details and/or makes thoughtless mistakes		

sources, including but not limited to impairment in school from a teacher and documentation of symptoms at home from parents.[4]

To make a diagnosis in preschool-aged children, clinicians should conduct a clinical interview with parents, examine the child, and also ask parents and teachers to complete standardized ADHD rating scales.[4] The physician should be reminded that since boys are typically more hyperactive in their symptom presentations, girls are less likely to receive treatment than boys for their ADHD because they primarily experience inattentive symptoms.[20]

Obtaining teacher and parent accounts for adolescents is often more challenging than for younger children. Adolescents are less likely to exhibit overt hyperactive behavior, and self-reports of their own symptoms often differ from other observers.[26] Despite this challenge, physicians should obtain information from at least two adults who interact with the adolescent regularly. Reliable informants include parents, teachers, and youths themselves. No single informant in a single setting is a gold-standard for diagnosis.[26] Additionally, the adolescent patient must actively participate in the evaluation for it to be reliable.[4,26]

TABLE 2:

ADHD rating scales available to the primary care physician

Age Range	Narrowband/ADHD Specific Scales	Broadband/Global Behavioral Scales
All ages	Brown attention/ executive function scale function scales	
Pediatrics	Comprehensive Executive Function Inventory (CEFI)	Behavior Assessment System for Children (BASC-3)
	Behavior Rating Inventory of Executive Function 2 (BRIEF-2)	Child Behavior Checklist (CBCL)
		Connors Comprehensive Behavior Scale (CBRS)
Adults	Barkley Adult ADHD Rating Scale-IV (BAARS-IV)	
	Conners Adult ADHD Rating Scales (Conners-3, CAARS)	
	Wender Utah Rating Scale	

Diagnosis of ADHD in adults is also made clinically, after excluding other possible causes of inattention, hyperactivity, and impulsivity.[8] In addition to the clinical evaluation in adults is the reliance on self-report assessments rather than informant accounts by parents and teachers. Structured self-report rating scales and instruments are available to assist physicians in the diagnosis of ADHD.[8] The instruments take less than 20 minutes to complete and assess the diagnostic criteria for ADHD. While there is still limited data estimating the sensitivity and specificity for all scales, they are still the most practical method to quantify ADHD symptoms in the clinic.[8]

There are two important criteria to assess adults. First, that the symptoms of adult ADHD have persisted since childhood. Second, the symptoms impair their quality of life.[9] The reliability of self-reported assessments depends on the accurate recall of the patients for their childhood symptoms. However, adults with ADHD frequently struggle to accurately recall the onset and severity of their symptoms. While a diagnosis based only on self-report is possible, further corroborating information from a family member or parent is recommended.[20] Self-reporting of symptoms may be less reliable to objective reports from outside observers.[9] Adults with higher IQ may also have more effective compensatory strategies to mask their symptoms from others, which further complicates the ability to obtain an accurate diagnosis.[20] Future research aims to develop biologic correlates to diagnose ADHD in the clinical setting through EEG, fMRI, hemodynamics, or genetics.[16] For now, standardized reports from the patients and observers are the mainstay of diagnosis in the primary care setting.[8,9]

Differential Diagnoses

Some neuropsychiatric conditions are commonly misdiagnosed as ADHD including but not limited to learning disorders, sleep disorders, oppositional defiant disorder, anxiety disorder, intellectual disability, language disorder, mood disorders, tic disorders, conduct disorder, and autism spectrum disorder.[27] Oppositional defiant disorder can be mistaken for hyperactivity or impulsive reactivity.[27] Generalized anxiety disorder and major depressive disorder may be mistaken for inattentive presentation, and bipolar disorder may mimic the emotional lability of ADHD.[27] However, daily mood changes in ADHD represent a poorly regulated but normal range of moods, rather than the more severe extremes associated with bipolar disorder.[20] Social disinhibition, resulting from adjustment disorders and posttraumatic stress disorder (PTSD), may resemble the impulsivity and social isolation seen in ADHD.[27] However, many children with ADHD can make initial social overtures but have difficulty maintaining long-term relationships.[27] Children who function at extremes of cognitive development may be disconnected, inattentive, or disruptive in class if the content is perceived as too easy or too difficult.[27] The movements associated with autism spectrum disorders and other neurodevelopmental disorders may be mistaken for hyperactivity. Social deficits and lack of social engagement can help identify autism spectrum disorder, and movement qualities help identify tic disorders.[27] Personality disorders, psychosis, and substance abuse disorders should be considered when assessing adolescents and adults, as these conditions may present as inattention, impulsivity, and academic problems.[27] In the ADHD patient, impulsivity and anger are usually short-lived and thoughtless, rather than intentionally theatrical or manipulative as seen in personality disorders.[20]

Medical conditions can mimic the inattentive signs of ADHD including conditions causing fatigue, pain, sensory impairments, and neurologic conditions that affect attention and arousal.[27] Common somatic diseases that contribute to inattention include obstructive sleep apnea, inflammatory bowel disease, epilepsy, and postconcussion status.[27] The primary care physician needs to recognize the utility of acquiring thorough medical and family histories and physical examination to effectively diagnose ADHD and rule out mimics of the disorder.[27] Laboratory tests, such as thyroid studies, liver function tests, and lead levels, may be helpful for ruling out pathologies mimicking ADHD.[8] Of particular note, adults presenting with new-onset symptoms are not likely to have ADHD.[9] False positive late-onset ADHD cases are common without careful assessment, and clinicians should screen for impairment, psychiatric history, and substance use.[9]

Challenges to Diagnosis

There is an upward trend of ADHD diagnoses and treatments in recent years, especially in the primary care setting.[5,28,29] Evidence suggests an overdiagnosis of ADHD in youth.[29,30] In 1994 and 2013, the *DSM-4* and *DSM-5* expanded the criteria for ADHD diagnosis, and the prevalence of the diagnosed individuals naturally increased in the United States.[29] The current *DSM-5* guidelines have expanded the diagnostic criteria to include more mild ADHD symptoms, which correlates with the rising proportion of people treated for ADHD in recent years.[29]

CONCLUSION

Naturally, primary care physicians will be presented with opportunities and challenges of diagnosing ADHD within their patient population. As this disorder presents significant heterogeneity throughout development and among individuals, the physician should equip himself or herself with the tools to properly diagnose these individuals. Understanding the neurodevelopmental etiology associated with ADHD will help to contextualize the behavioral, emotional, and cognitive deficits with which these patients struggle. Accurately recognizing ADHD and its diverse spectrum of presentations is the first step in providing sufficient care to patients affected with the disorder. While there is debate that ADHD is overdiagnosed in patients with milder symptoms, the family physician is in the first-line position to prevent milder ADHD symptoms from becoming overtreated with pharmacotherapies as well. Therefore, with continued study and analysis of new developments and up-to-date treatments, the physician can more fully, completely, and accurately treat patients.

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BRIEF REPORT

MANAGEMENT OF BINGE EATING DISORDER

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KEYWORDS

Eating disorder

Binge eating disorder

Behavioral health

Nutrition

Obesity

ABSTRACT

Binge eating disorder (BED) is a mental health condition characterized by recurrent episodes of consuming large amounts of food, in the absence of the compensatory behaviors seen in bulimia nervosa. Patients with BED often first present to primary care physicians (PCPs), who play a pivotal role in diagnosing and managing BED. BED is a complex condition that may require an interdisciplinary team for effective management. The first-line treatment with the most evidence is eating disorder–informed cognitive behavioral therapy. However, pharmacotherapy with an antidepressant (like a selective-serotonin reuptake inhibitor) or lisdexamfetamine (the only FDA-approved medications for BED) is a reasonable alternative for patients who prefer medications or have barriers to psychotherapy. PCPs must be equipped to address the comorbidities and consequences associated with BED with a comprehensive and evidence-informed approach.

INTRODUCTION

Binge eating disorder (BED) is a psychiatric condition that involves episodes of binge eating, defined as eating a larger amount of food than most people would eat within 2 hours, at least once a week on average for 3 months. These episodes involve a lack of control and distress related to eating behavior. To meet *Diagnostic and Statistical Manual of Mental Disorders. 5th ed. (DSM-5)* criteria, episodes must involve at least three of the following features: binge eating when not hungry, eating more rapidly than normal, eating until feeling uncomfortably full, eating alone or feeling embarrassed about eating, and feeling disgusted or guilty after a binge. To differentiate between BED and bulimia nervosa, it is essential to ask about compensatory behavior, including purging, using laxatives or diuretics, fasting, misusing prescription medication (eg, insulin, thyroid replacement), or exercising excessively. BED usually involves a long-term remitting and relapsing course.[1]

The goals of treatment for a patient with BED should be distinct from the treatment goals for obesity. While many patients meet the criteria for both, a patient with BED may have goals surrounding reducing the frequency or intensity of binge eating episodes in addition to losing weight. Some patients with BED may have a body mass index (BMI) in the healthy range and may want to prevent weight gain or not focus on their weight at all.[2]

A patient who meets the criteria for BED should be comprehensively assessed before establishing a treatment plan. In addition to asking about how often binge eating episodes occur and with what associated symptoms, history taking should gather information about the patient's weight and dieting history and the current pattern of eating outside of binge eating episodes. Common comorbidities should be assessed by collecting psychiatric history and measuring height and weight (to calculate BMI), waist circumference, blood pressure, fasting blood glucose, and cholesterol levels. It is appropriate to manage a patient with BED in the outpatient setting unless they have psychiatric comorbidities that require a higher level of care.

Psychotherapy alone has been shown to be more effective in the treatment of BED than pharmacotherapy alone. The first-line treatment for BED is eating disorder–focused cognitive-behavioral therapy (CBT), a 1C recommendation by the American Psychiatric Association.[3] A meta-analysis in 2010 found a large clinical effect in reducing binge eating behavior in patients receiving CBT or dialectical behavior therapy.[4] Interpersonal therapy has shown similar efficacy.[5] Self-help CBT that specifically addresses binge eating has been demonstrated as superior to controls and is a good option, especially to bridge care while waiting for alternative interventions with a higher level of evidence.[6-8] Family therapy has limited data but is a reasonable option, especially for pediatric patients. Behavioral weight loss therapy does not target binge eating but may be helpful for patients who are overweight or

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obese and may be used in combination with CBT. Other emerging options include emotion-focused therapy and physical exercise plus dietary therapy.[9,10]

Using medication for BED is a second-line option but may be a reasonable first-line option in patients who prefer pharmacotherapy (eg, less time commitment, lower costs, limited access to psychotherapy). Medications that have been studied for BED include antidepressants like selective-serotonin reuptake inhibitors (SSRIs), lisdexamfetamine, antiepileptics (eg, topiramate, zonisamide), methylphenidate, atomoxetine, and modafinil.[10] Using an antidepressant or lisdexamfetamine for patients who did not respond to psychotherapy or in patients who prefer medication is a 2C suggestion by the American Psychiatric Association.[3] SSRIs have shown a small clinically significant effect in a meta-analysis of randomized controlled trials.[12] SSRIs can be prescribed for BED with similar doses as what is prescribed for major depressive disorder and are typically preferred over other agents, which are associated with more side effects.[2]

Lisdexamfetamine is the first FDA-approved treatment of BED in adults.[13] Though there have not been any investigations directly comparing efficacy to SSRIs, lisdexamfetamine has shown modest short-term effects in BED. Sold under the brand name Vyvanse, this stimulant acts as a dopamine and norepinephrine reuptake inhibitor and releaser. It reverses the theoretical shift occurring in BED when reward-related feedback from impulsive eating becomes a compulsive habit. It is also indicated for attention-deficit hyperactivity disorder (ADHD) and used off label for treatment-resistant depression. The starting dose of lisdexamfetamine for BED is 30 mg/day, which can be increased by 20 mg per week to a target dose of 50 to 70 mg/day. Patients may see immediate effects following the first dose, but a full effect may not be seen until several weeks later. Potential side effects include tremors, nausea, insomnia, headache, and irritability. Dangerous adverse effects include psychosis, seizures, tachycardia, and hypertension. Lisdexamfetamine should not be used in patients with preexisting hypertension and could cause sudden death in patients with preexisting cardiac structural abnormalities. If side effects occur, consider adjusting the dose, switching to another agent, changing the timing of the dose, or adding an augmenting agent like a beta-blocker (for tachycardia or hypertension). As a schedule II drug, patients may develop dependence or start to misuse lisdexamfetamine.[14]

One randomized placebo-controlled crossover trial showed the efficacy of phentermine/topiramate, but topiramate is known to cause significant side effects, like cognitive dysfunction, even at low doses.[15] Glucagon-like peptide-1 (GLP-1) receptor agonists, medications used to treat diabetes mellitus, activate the GLP-1 receptor to reduce food intake, lower body weight, and stimulate insulin secretion. Observational studies have shown the benefit of decreasing episodes of binge eating, but there have not been any randomized controlled trials to demonstrate safety or efficacy in treating BED.[16-18] In a randomized trial, treatment with naltrexone/bupropion after acute treatment of BED has been shown to lead to higher rates of remission, but the results were not statistically significant.[19] There is also growing evidence showing the benefits of neuromodulation in patients with BED.[20]

The treatment team may involve a PCP, therapist (for psychotherapy), psychiatrist (for management of severe psychiatric comorbidity or referral for medication management if needed), and registered dietician (for behavioral weight loss therapy). In the United States, only about half of patients with BED seek treatment, partly due to stigma, shame, and a lack of awareness about BED.[21,22] PCPs hold a vital role in making the diagnosis of BED, assessing for comorbidities, prescribing medication, coordinating referrals (if applicable), and managing the medical consequences of BED.

LITERATURE SEARCH AND DATA SOURCES

Sources were found by searching "binge eating disorder" on PubMed, Cochrane Library, ACESSSS, ECRI Guidelines, and Up to Date in May-July, 2024, using a filter for publications in the last 5 years (2019-2024).

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BRIEF REPORT

ATYPICAL CASE OF ACUTE KIDNEY INJURY DUE TO CLINDAMYCIN USE IN A CHILD

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KEYWORDS

Urology

Injury

Cellulitis

Side Effects

ABSTRACT

Acute kidney injury (AKI) is commonly caused by medications including, but not limited to, aminoglycosides, cephalosporins, penicillins, trimethoprim-sulfamethoxazole, and amphotericin. Among pediatric patients, clindamycin has been widely used to treat skin and soft-tissue infections, abscesses, osteomyelitis, and aspiration pneumonia.[1,2] Clindamycin is well-known to cause diarrhea, *Clostridioides difficile* (C. diff) infection, hypersensitivity reactions, and gastrointestinal upset.[3] However, AKI is not a commonly associated side effect of clindamycin, despite its widespread use among pediatric patients.[3,4] A review of the literature reveals no previous reports of AKI caused by clindamycin in children. This case report presents a case of a 14-year-old female with extensive cellulitis who developed AKI most likely from clindamycin.

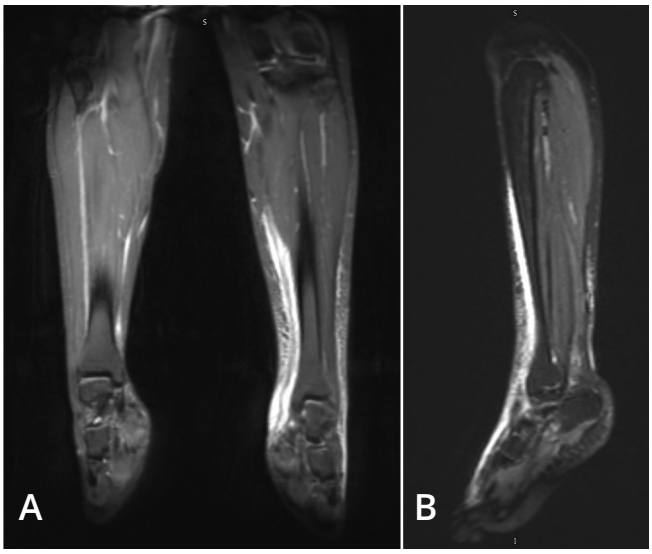
CASE PRESENTATION

A 14-year-old previously healthy female was admitted to our institution with extensive left foot and ankle cellulitis. She had a history of tinea pedis and multiple skin breakdowns. The patient visited a beach where she walked barefoot. Before admission, she had a 5-day history of scaling and pustules between her toes, which continued to worsen despite treatment with cephalexin and clotrimazole cream. Three days before admission, she developed fever, limping, and worsening erythema and swelling of her left foot and ankle.

Physical examination revealed an ill-appearing and diaphoretic teenage female with swelling in her left foot and ankle. Her temperature was 37.1°C, with a maximum of 38.5°C. Her blood pressure was 94/52 mmHg, heart rate was 112 beats/min, respiratory rate was 16 breaths/min, and oxygen saturation was 98% on room air. Her weight was 53.6 kg at admission. She had good perfusion with a capillary refill time of less than 2 seconds. On musculoskeletal and skin examination, she had erythematous swelling of the dorsal and plantar aspects of her left foot, with swelling of the left ankle and pain on flexion and rotation. Point tenderness on palpation was noted on the medial malleolus. Interdigital skin breakdowns with an erythematous base without pustules or drainage were also noted.

Laboratory testing revealed a complete blood count (CBC) with a white blood cell count of 18,500 cells/μL (90% neutrophils, 4.5% lymphocytes, 4.4% monocytes, 1% eosinophils), hemoglobin of 10.9 g/dL, and a platelet count of 247,000 cells/μL. C-reactive protein (CRP) was 7.6 mg/dL, and procalcitonin was 0.24 ng/mL. The basic metabolic panel (BMP) showed sodium 138 mmol/L, potassium 3.3 mmol/L, chloride 108 mmol/L, bicarbonates 20 mmol/L, blood urea nitrogen (BUN) 8.0 mg/dL, creatinine 0.46 mg/dL, glucose 107 mg/dL, and calcium 8.9 mg/dL. Blood culture was negative. Magnetic resonance imaging (MRI) of the left tibia, foot, and ankle was ordered with concerns of osteomyelitis, septic joint,

FIGURE 1: MRI of left tibia, foot, and ankle with contrast.



(A) Coronal view and (B) sagittal view MRI images showing edema adjacent to the fascial structures of the anterior and posterior compartments of the left lower extremity, extending onto the dorsum of the foot.

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TABLE 1:

Laboratory trends of BMP, CRP, and CBC

Length of Stay (Days)	1	3	4	5	6	7	12	36
BUN (mg/dL)	8.0	14.0 / 17.0	23.0	26.0	26.0	22.0	13.0	11.0
Creatinine (mg/dL)	0.46	2.02 / 3.29	4.60	5.38	4.54	3.48	0.92	0.51
C-reactive protein (mg/dL)	7.6	16.0	10.0	8.3				
White blood cell (10^3/µL)	18.5	20.3		17.1				
Absolute neutrophil count (10^3/µL)	16.6	17.9		13.8				

and necrotizing fasciitis, and showed edema up to the midmedial gastrocnemius level adjacent to fascial structures of the anterior and posterior compartments of the left lower extremity, extending onto the dorsum of the foot (Figure 1).

Upon admission, the patient received one dose of piperacillin-tazobactam 3 g (of piperacillin) intravenously (IV) and two doses of vancomycin 1000 mg IV for possible necrotizing fasciitis, as well as one dose of ibuprofen 400 mg. Once the MRI of the left foot and ankle ruled out septic joint, osteomyelitis, and necrotizing fasciitis, antibiotics were switched to clindamycin 720 mg (40 mg/kg/day divided every 8 hours) to treat extensive cellulitis including methicillin-resistant *Staphylococcus aureus* (MRSA) shortly after admission. On day 3 of hospitalization, the patient reported dark urine. The basic metabolic profile showed BUN 17.0 mg/dL and creatinine 2.02 mg/dL (Table 1). Urinalysis showed protein of 30 mg/dL and moderate blood with red blood cells of 85/µL, with negative pyuria, negative leukocyte esterase, and negative nitrites. While on monotherapy with clindamycin, without nephrotoxic medications such as ibuprofen, renal function continued to worsen with BUN 26.0 mg/dL and creatinine 5.38 mg/dL by day 5 of hospitalization. BUN and creatinine trending are described in Table 1. Inflammatory markers started showing an improvement on day 4. The patient also required amlodipine for hypertension associated with acute kidney injury (AKI). Due to concern for AKI from clindamycin, the antibiotic was switched to linezolid 600 mg IV every 12 hours. Over the next 2 days, BUN and creatinine improved to 22.0 mg/dL and 3.48 mg/dL, respectively. The patient was discharged home with a total 14-day course of linezolid. She was followed by nephrology as an outpatient. BUN and creatinine normalized at 1-month follow-up.

DISCUSSION

Clindamycin remains one of the commonly used antibiotics for treating skin and soft-tissue infections (SSTIs), particularly in light of the 25-fold increase in hospital admissions of children with MRSA infections in the 1990s.5 Despite a 52% decline in hospital admissions due to MRSA, the infection continues to pose a significant threat to pediatric populations.[6] Clindamycin has good penetration into bone and joint tissues, as well as high bioavailability with oral administration, which contributes to its widespread use in both outpatient and inpatient settings.[7]

Nephrotoxicity is a common side effect of many medications, but it is rarely caused by clindamycin. We expound the limited clinical evidence for AKI with clindamycin, highlighting that while documented cases in adults exist, pediatric instances remain exceptionally rare, thus underscoring the significance of our case report.

Several mechanisms of medication-induced nephrotoxicity have been identified: alteration of glomerular filtration rate, tubular cell toxicity, interstitial nephritis, and crystal nephropathy.[8] Based on biopsy case series, acute interstitial nephritis and acute tubular necrosis were discovered among patients with clindamycin-induced AKI.[9] One retrospective analysis of adult patients reported that reversible clindamycin-induced kidney disease occurred on average 1.5 days after the first dose, with patients receiving 1.0 to 2.0 g of clindamycin per day.[10] Common manifestations include proteinuria, gross hematuria, oliguria, edema, nausea, vomiting, abdominal pain, and diarrhea.

In this case, the patient initially received nephrotoxic medications including piperacillin-tazobactam, vancomycin, and ibuprofen briefly. Lexicomp reported increased cases of AKI when vancomycin was concurrently used with either ibuprofen or piperacillin. Although one dose of piperacillin-tazobactam and ibuprofen, and two doses of vancomycin, may have contributed to nephrotoxicity in this case, the persistently worsening AKI while on monotherapy with clindamycin for 4 days raises concerns about the nephrotoxic nature of clindamycin. According to Lexicomp, clindamycin did not have any drug interactions with these three medications. After clindamycin was switched to linezolid, serial basic metabolic profiles showed persistent improvement.

CONCLUSION

Our case underscores the importance of considering AKI as a rare but potential side effect of clindamycin among pediatric patients, as clindamycin is commonly prescribed in both outpatient and inpatient pediatrics. This case highlights that a high level of clinical suspicion can help clinicians facilitate appropriate evaluation and treatment for reversible clindamycin-induced AKI.

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PATIENT EDUCATION HANDOUT

Osteoporosis

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WHAT IS OSTEOPOROSIS?

Osteoporosis is a condition in which bones become thinner, weaker, and are more likely to break. Osteoporosis is called a "silent" disease because there are typically no symptoms until a bone is broken. In the absence of broken bones, osteoporosis is typically diagnosed with a DEXA scan, which is a measure of bone density. DEXA scans are recommended for women older than 65 years and men older than 75 years.

Some individuals are at greater risk for developing osteoporosis than others. Risk factors include the following:

- **Age:** As you age, bone loss happens more quickly
- **Sex:** Females have a greater risk than males; however, men are still at risk, especially over the age of 70 years
- **Race:** White and Asian females are at a greater risk, and White males are at a greater risk
- **Lifestyle:** Low physical activity, excessive alcohol consumption, smoking, and diet low in calcium and vitamin D all increase the risk of osteoporosis
- **Changes to hormones:** Females with decreased estrogen and males with decreased testosterone have an increased risk
- **Medications:** Steroids, reflux medications, selective-serotonin reuptake inhibitors (SSRIs), thiazolidinediones, seizure medications, aromatase inhibitors, and chemotherapy

CAN OSTEOPOROSIS BE PREVENTED?

There are ways to prevent or slow down the progression of osteoporosis including:

- Staying physically active with weight-bearing exercises such as walking
- Drink alcohol in moderation
- Smoking cessation
- Eat a nutritious diet with calcium and vitamin D to maintain bone health

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HOW CAN OSTEOPOROSIS BE TREATED?

There are ways to prevent or slow down the progression of osteoporosis including:

- **Exercise**: Weight-bearing exercises are ideal and include walking, climbing stairs (with use of a handrail for stability), yoga or tai chi (to improve balance and decrease risk of falls), and several other options that get you on your feet
- **Lifestyle modifications**: Smoking cessation, limiting alcohol intake to one glass a day for women or two for men, increasing calcium intake with low-fat dairy, fortified cereals or other fortified foods, and dark leafy green vegetables like collard greens and turnips
- **Osteopathic treatment**: Functional joint mobility techniques and soft-tissue techniques can be used by your osteopathic physician to help improve the ability of your body to adapt to movement and possibly decrease pain and functional limitations while improving self-sufficiency and independence

There are medications your doctor can prescribe for you if you meet certain guidelines. These medications help slow the progression of bone loss but do not replace bone you have already lost. It is important to talk to your doctor and start early with lifestyle modifications to decrease your likelihood of developing osteoporosis.

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Human Papillomavirus

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Human papillomavirus (HPV) refers to a single virus with numerous subtypes that can be spread between sexual partners through skin-to-skin contact, sexual activity (including vaginal, anal, and oral) or through the use of shared toys or other objects. The subtypes of HPV can be considered either **low** or **high risk**.

- **Low-risk** HPVs have the potential to cause no disease, but some can cause warts on or around the mouth, throat, anus, or genitals. HPV6 and HPV11 are the most common of the low-risk subtypes, but there are numerous subtypes in this category

- **High-risk** HPVs can cause several types of cancer. There are 15 high-risk subtypes with HPV16 and HPV18 that are responsible for most related cancers. These can include cervical cancer, oropharyngeal cancer, anal cancer, penile cancer, vaginal cancer, or vulvar cancer. High-risk HPVs in the United States cause 3% of all cancers in women and 2% of all cancers in men.

WHO IS AT RISK?
Anyone who is sexually active can be infected regardless of sex, gender, or sexual orientation. Most sexually active people are already infected with HPV.

SYMPTOMS
Most infections do not cause cancer because your immune system can control the infection to not cause cancer. Certain high-risk infections cannot be controlled and can persist for many years.

Infection with high-risk strains usually **does not** cause any symptoms. If the infection develops into cancer, there can be symptoms such as bleeding, pain, or swollen glands.

SCREENING
Cervical cancer is currently the only HPV-related cancer that can be screened for The screening test is an HPV test, Pap test, and the HPV/Pap co-test for both high-risk HPV and cervical cell changes. Women and anyone assigned female at birth should schedule a Pap smear with their primary care provider **once they turn 21 years of age**. Even if a patient is sexually active before 21 years, their immune system typically clears the infection, therefore not warranting a Pap smear before 21 years old. HPV testing continues until the patient is **65 years old** or if the patient has had a hysterectomy and cervix removed. After the test, your provider will notify you of your results and your next steps.

TREATMENT OPTIONS
The HPV infection itself cannot be treated. Precancerous changes seen on Pap smears can be treated with a procedure to remove the tissue. Genital and anal warts or lesions can generally be treated in the office unless they develop into full-blown cancers. HPV-related cancers are usually treated the same as other cancers in that body region.

WHY DO DOCTORS RECOMMEND THE HPV VACCINE IN TEENS?
The HPV vaccine protects your child from certain cancers later in life. Early protection works the best because it protects your child before they ever even come in contact with the virus.

85% of people will get an HPV infection at some point in their life. Infections with HPV types that can cause cancer or warts have dropped **88%** among teenage girls. HPV is estimated to cause about **36,500** cases each year. **33,700** of these cancers can be prevented by preventing the infection that causes them.

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VACCINATION RECOMMENDATIONS

Both males and females can get the HPV vaccine. The HPV vaccine series (*Gardasil 9*) is recommended at age 11 or 12 years, but it can be received as early as 9 years old. The vaccine is recommended for everyone up to age 26 years. For those 27 to 45 years, your doctor can talk with you about whether they recommend the vaccination series for you.

- If you start the series **before your 15th birthday**, you will receive **two doses**. The second dose should be received 6 to 12 months after the first dose
- If you start the series **after your 15th birthday**, you will receive **three doses**. The second dose is received 1 to 2 months after the first dose, and the third dose is received after 6 months
- Anyone who is considered immunocompromised should receive the three-dose series

PRECAUTIONS AND CONTRAINDICATIONS TO THE VACCINE

People with a history of an allergic reaction to yeast and those who are currently moderately or severely ill are cautioned against receiving the vaccine. The vaccine is not recommended during pregnancy.

Some adverse reactions can include pain or redness at the injection site, fever, dizziness, fainting, nausea, headache, muscle, or joint pain. These are usually mild and short term.

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Nephrolithiasis, or Kidney Stones

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Kidney stones, medically known as nephrolithiasis, are characterized by the formation of hard mineral deposits in the kidneys or urinary tract1 (Figure 1). These stones can range in size from a tiny grain of sand to a larger stone that can cause significant pain.

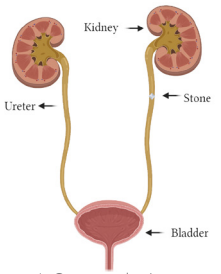

Figure 1: Cartooned urinary tract system with ureteral stone

COMMON RISK FACTORS[2]

- Inadequate consumption of fluids
- Diet high in salt and animal protein
- Family history of kidney stones
- Gout
- Inflammatory bowel disease
- Hyperparathyroidism
- Previous history of gastric bypass surgery

SYMPTOMS

The symptoms of kidney stones can vary depending on the size and location of the stone. Small stones may not cause noticeable symptoms and can pass through the urinary tract without causing any pain. However, larger stones can cause severe pain from the back to the lower abdomen, nausea, vomiting, and blood in the urine. In some cases, a stone can become lodged in the urinary tract, leading to a urinary tract infection, kidney obstruction leading to impaired function, or even kidney failure.

DIAGNOSIS

Diagnosis of kidney stones usually involves a medical history, comprehensive examination and imaging studies such as an X-ray, ultrasound, or computed tomography (CT) scan.[1,2] Urine tests may also be conducted to check for the presence of blood, infection, or other abnormalities. 24-hour urine study and stone analysis can determine the type of stones.

TREATMENT

Treatment for kidney stones is determined based on the size and location of the stone and the severity of symptoms.[1] Small stones may pass on their own with the help of increased oral fluid intake, pain medication, and/or prescription medication to relax the ureters. Larger stones greater than 6 mm may require surgical intervention, such as ureteroscopy and stent placement, or a stent placed within the ureter, extracorporeal shock wave lithotripsy (ESWL), or soundwaves that break up the stone, or percutaneous nephrolithotomy (PCNL), which includes catheter placement within the kidney from the flank.[3]

PREVENTION

Prevention of kidney stones requires following a low-salt diet and drinking plenty of fluids, especially water to maintain a urine output greater than 2 L/day.[3] In addition, depending on the type of the kidney stone, certain lifestyle modifications are recommended. For example, avoiding food high in oxalate, such as spinach, rhubarb, and rice bran will decrease the chances of developing calcium oxalate stones, which is the most common type of kidney stones. Increasing the intake of citrus fruits such as lemon, lime, oranges, and grapefruit also prevents certain types of kidney stones. Individuals predisposed to kidney stones due to underlying medical conditions may be prescribed medication to reduce these risks.

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What is Sjögren's Syndrome?

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Sjögren's syndrome is an autoimmune disease in which your body's immune system mistakenly attacks healthy glands of the eyes and mouth. This syndrome can occur independently, or with other autoimmune conditions. Sjögren's syndrome typically affects females in the age range of 30-50 with a female to male predominance.[1]

The hallmark of disease symptoms include fatigue, joint pain, and oral and eye dryness.

COMMON SIGNS AND SYMPTOMS

- Dry eyes
- Dry mouth
- Dental caries
- Problems swallowing
- Joint pain
- Morning stiffness
- Fatigue

Not everyone will experience the same symptoms, and symptoms can highly vary from person to person. Figure 1 outlines common organ system symptoms. Furthermore, the syndrome will affect everyone to different degrees, from mild to severe. Although some symptoms can be tolerated, it is important to start therapy as soon as possible to prevent organ damage.[2]

It is important to get regular eye exams with your ophthalmologist as well as to follow up with your dentist to prevent and treat cavity formation and tooth decay.

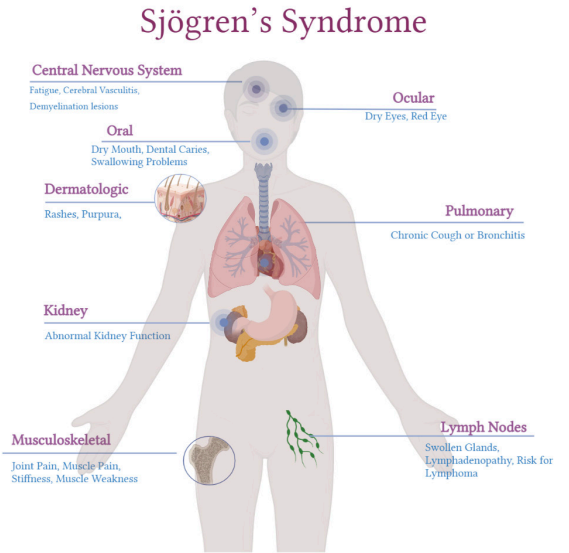

Figure 1: Organ systems and symptoms of Sjögren's Syndrome

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HOW IS SJÖGREN'S SYNDROME DIAGNOSED?

- **Symptoms**[3]
  - Dry mouth
  - Dental caries
  - Problems swallowing
  - Joint pain
  - Morning stiffness
  - Fatigue
- **Testing**[3]
  - Blood tests to evaluate for specific antibodies (ANA and anti-SSA/SSB)
  - Eye lubrication testing or Schirmer's test
  - Saliva gland biopsy

HOW IS SJÖGREN'S SYNDROME DIAGNOSED?

Unfortunately, there is no cure for the disease. Treatment is focused on easing the severity of symptoms and preventing complications.

- For dry eyes, you can use artificial eye drops, or take medication to increase lubricating tear production.
- For dry mouth, patients have found sucking lozenges, chewing gum, and increasing fluid intake to be helpful.
- Sometimes, patient symptoms can be widespread, requiring steroids and immune-suppressing drugs such as methotrexate and azathioprine.[3]

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