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FOR FLORIDA
DENTAL PROFESSIONALS
2024

Published by NetCE,
a TRC Healthcare Company
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Medical Error Prevention and Root Cause Analysis

This course fulfills the Florida requirement for 2 hours of education on the Prevention of Medical Errors.

Audience
This course is designed for all licensed dental professionals.

Course Objective
The purpose of this course is to satisfy the requirement of the Florida law and provide all licensed dental professionals with information regarding the root cause process, error reduction and prevention, and patient safety.

Learning Objectives
Upon completion of this course, you should be able to:

1. Describe how the Institute of Medicine defines "medical error."
2. Describe the types of sentinel events the Joint Commission has identified.
3. Discuss what factors must be included in a root cause analysis in order for the Joint Commission to consider it "thorough" and "credible."
4. Identify what types of adverse incidents must be reported to the Florida Agency for Healthcare Administration.
5. Identify the most common sentinel events reported to the Joint Commission.
6. Evaluate the most common misdiagnoses, as recognized by the Florida Board of Medicine, and outline the safety needs of special populations, including non-English-proficient patients.

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Marjorie Conner Allen, BSN, JD, received her Bachelor of Science in Nursing degree from the University of Florida, Gainesville, in 1984. She began her nursing career at Shands Teaching Hospital and Clinics at the University of Florida, Gainesville. While practicing nursing at Shands, she gave continuing education seminars regarding the nursing implications for dealing with adolescents with terminal illness. In 1988, Ms. Allen moved to Atlanta, Georgia where she worked at Egleston Children's Hospital at Emory University in the bone marrow transplant unit. In the fall of 1989, she began law school at Florida State University. After graduating from law school in 1992, Ms. Allen took a two-year job as law clerk to the Honorable William Terrell Hodges, United States District Judge for the Middle District of Florida. After completing her clerkship, Ms. Allen began her employment with the law firm of Smith, Hulsey & Busey in Jacksonville, Florida where she has worked in the litigation department defending hospitals and nurses in medical malpractice actions. Ms. Allen resides in Jacksonville and is currently in-house counsel to the Mayo Clinic Jacksonville.

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Special Approvals
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INTRODUCTION

The Institute of Medicine's (IOM) 1999 publication *To Err is Human: Building a Safer Health System*, illuminated the unfortunate reality of medical errors in the healthcare industry. The report reviewed the prevalence of medical errors in the United States and highlighted measures that should be taken to prevent them. Specifically, the authors of the report noted that at least 44,000 and perhaps as many as 98,000 Americans were dying in hospitals each year as a result of medical errors and many more were being seriously injured [1]. They further noted that, even when using the lower estimate of 44,000, deaths in hospitals due to medical errors exceeded the annual deaths attributable to motor vehicle accidents (43,458), breast cancer (42,297), or AIDS (16,516) [1]. A 2016 report stated that the average number of annual in-hospital deaths attributable to medical error might actually be much higher, at around 400,000 [2]. This report places medical errors as the third leading cause of death in the United States. Certainly, these numbers must be balanced against the millions of admissions to hospitals in the United States, which is in excess of 33 million annually [1; 3].

It does appear that some progress has been made in the past decade. The Agency for Healthcare Research and Quality found a 17% decline in hospital-acquired conditions between 2014 and 2017, or 910,000 fewer conditions and 20,500 fewer deaths than if the 2014 rate had remained steady [4]. Though the precise mechanism(s) responsible for this decline is not clear, it occurred following a concerted effort by federal agencies, organizations, and individual providers to curtail medical errors. However, the statistics indicate that medical errors continue to be an issue. Healthcare professionals should commit to continuing to pay greater attention to evaluating approaches for reducing errors and to building new systems to reduce the incidence of medical errors.

Spurred by a commitment to reducing medical error incidents, the Florida Legislature mandates that all healthcare professionals in Florida complete a two-hour course on the topic of prevention of medical errors [5]. This continuing education course is designed to satisfy the requirements of the Florida law and provide all licensed healthcare professionals with information regarding the root cause analysis process, error reduction and prevention, and patient safety, as well as information regarding the five most misdiagnosed conditions as determined by the Florida Board of Medicine.

DEFINING "MEDICAL ERROR"

The IOM Committee on Quality of Healthcare in America defines error as "the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim" [1]. It is important to note that medical errors are not defined as intentional acts of wrongdoing and that not all medical errors rise to the level of medical malpractice or negligence. Errors depend on two kinds of failures: either the correct action does not proceed as intended, which is described as an "error of execution," or the original intended action is not correct, which is described as an "error of planning" [1]. A medical error can occur at any stage in the process of providing patient care, from diagnosis to treatment, and even while providing preventative care. Not all errors will result in harm to the patient. Medical errors that do result in injury are sometimes called preventable adverse events or sentinel events—sentinel because they signal the need for immediate investigation and response [6].

Preventable adverse events or sentinel events are defined as those events that cause an injury to a patient as a result of medical intervention or inaction on the part of the healthcare provider whereby the injury cannot reasonably be said to be related to the patient's underlying medical condition. Thus, for example, if a patient has a surgical procedure and dies postoperatively from pneumonia, the patient has suffered an adverse event. But was that adverse event preventable; was it caused by medical intervention or inaction? The specific facts of this case must be analyzed to determine whether the patient acquired the pneumonia as a result of poor handwashing techniques of the medical staff (i.e., an error of execution), which would indicate a preventable adverse event, or whether the patient acquired the pneumonia because of age and comorbidities, which would indicate a nonpreventable adverse event.

Healthcare professionals can learn much by closely scrutinizing and evaluating adverse events that lead to serious injury or death. The evaluation of such events would also enable healthcare professionals to improve the delivery of health care and reduce future mistakes. In addition, healthcare professionals should have a process in place to evaluate those instances in which a medical error occurred and did not cause harm to the patient. By reviewing these processes, healthcare professionals are afforded the unique opportunity to identify system improvements that have the potential to prevent future adverse events. The Joint Commission, recognizing the importance of analyzing both preventable adverse events and near-misses, has established guidelines for recognizing these events and requires healthcare facilities to conduct a root cause analysis to determine the underlying cause of the event [7].

ROOT CAUSE ANALYSIS PROCESS

The Joint Commission is a national organization with a mission to improve the quality of care provided at healthcare institutions in the United States. It accomplishes this mission by providing accredited status to healthcare facilities. Accreditors play an important role in encouraging and supporting actions within healthcare organizations by holding them accountable for ensuring a safe environment for patients. Healthcare organizations should actively engage in a cooperative relationship with the Joint Commission through this accreditation process and participate in the process to reduce risk and facilitate desired outcomes of care.

Root cause analysis, as defined by the Joint Commission, is "a process for identifying the basic or causal factors that underlie variation in performance, including the occurrence or possible occurrence of a sentinel event" [6]. In the 2022 update, the Joint Commission defines a sentinel event as a "patient safety event (not primarily related to the natural course of the illness or underlying condition) that reaches a patient and results in death, severe harm (regardless of duration of harm), or permanent harm (regardless of severity of harm)" [6; 10]. Furthermore, the Joint Commission revision clarified the terms "severe" and "permanent" harm with regard to sentinel events. "Severe harm" is an event or condition that reaches the individual, resulting in life-threatening bodily injury (including pain or disfigurement) that interferes with or results in loss of functional ability or quality of life that requires continuous physiologic monitoring or a surgery, invasive procedure, or treatment to resolve the condition [6; 10]."Permanent harm" is an event or condition that reaches the individual, resulting in any level of harm that permanently alters and/or affects an individual's baseline [6; 10].

The following subsets of sentinel events are subject to review by the Joint Commission [6; 11]:

- The event has resulted in an unanticipated death or major permanent loss of function, not related to the natural course of the patient's illness or underlying condition

or

- The event is one of the following (even if the outcome was not death or major permanent loss of function unrelated to the natural course of the patient's illness or underlying condition):
  - Suicide of any patient receiving care, treatment, and services in a staffed around-the-clock care setting or within 72 hours of discharge
  - Unanticipated death of a full-term infant
  - Abduction of any patient receiving care, treatment, and services
  - Any elopement (i.e., unauthorized departure) of a patient from a staffed around the-clock care setting (including the emergency department), leading to death, permanent harm, or severe temporary harm to the patient
  - Discharge of an infant to the wrong family
  - Rape, assault (leading to death or permanent loss of function), or homicide of any patient receiving care, treatment, and services
  - Rape, assault (leading to death or permanent loss of function), or homicide of a staff member, licensed independent practitioner, visitor, or vendor while on site at the healthcare organization
  - Hemolytic transfusion reaction involving administration of blood or blood products having major blood group incompatibilities (e.g., ABO, Rh, other blood groups)
  - Invasive procedure, including surgery, on the wrong patient or wrong site
  - Unintended retention of a foreign object in a patient after surgery or other invasive procedures
  - Severe neonatal hyperbilirubinemia (bilirubin >30 mg/dL)
  - Fluoroscopy resulting in permanent tissue injury when clinical and technical optimization were not implemented and/or recognized practice parameters were not followed
  - Fire, flame, or unanticipated smoke, heat, or flashes occurring during an episode of patient care
  - Any intrapartum (related to the birth process) maternal death
  - Severe maternal morbidity
  - Fall resulting in: any fracture; surgery, casting, or traction; required consult/management or comfort care for a neurological or internal injury; a patient with coagulopathy who receives blood products as a result of the fall; or death or permanent harm as a result of injuries sustained from the fall (not from physiologic events causing the fall)

Alternatively, the following examples are events that are NOT considered reviewable under the Joint Commission's sentinel event policy [6]:

- Any close call ("near miss")
- Full or expected return of limb or bodily function to the same level as prior to the adverse event by discharge or within two weeks of the initial loss of said function, whichever is the longer period

- Any sentinel event that has not affected a recipient of care (e.g., patient, individual, resident)
- Medication errors that do not result in death or major permanent loss of function
- Suicide other than in an around-the-clock care setting or following elopement from such a setting
- A death or loss of function following a discharge against medical advice
- Unsuccessful suicide attempts unless resulting in major permanent loss of function
- Minor degrees of hemolysis not caused by a major blood group incompatibility and with no clinical sequelae

For further definition of terms, please refer to the Joint Commission's Sentinel Event Policy and Procedures at https://www.jointcommission.org/resources/patient-safety-topics/sentinel-event/sentinel-event-policy-and-procedures.

As part of the accreditation requirement, the Joint Commission requires that healthcare organizations have a process in place to recognize these sentinel events, conduct thorough and credible root cause analyses that focus on process and system factors, and document a risk-reduction strategy and internal corrective action plan that includes measurement of the effectiveness of process and system improvements to reduce risk [6]. This process must be completed within 45 business days of the organization having become aware of the sentinel event.

The Joint Commission will consider a root cause analysis acceptable for accreditation purposes if it focuses primarily on systems and processes, not individual performance [6]. In other words, the healthcare organization should minimize the individual blame or retribution for involvement in a medical error. In addition, the root cause analysis should progress from special causes in clinical processes to common causes in organizational processes, and the analysis should repeatedly dig deeper by asking why, then, when answered, why again, and so on. The analysis should also identify changes that can be made in systems and processes, either through redesign or development of new systems or processes, which would reduce the risk of such events occurring in the future. The Joint Commission requires that the analysis be thorough and credible. To be considered thorough, the root cause analysis must include [6]:

- A determination of the human and other factors most directly associated with the sentinel event and the process(es) and systems related to its occurrence
- Analysis of the underlying systems and processes through a series of "why" questions to determine where redesign might reduce risk
- Inquiry into all areas appropriate to the specific type of event
- Identification of risk points and their potential contributions to this type of event
- A determination of potential improvement in processes or systems that would tend to decrease the likelihood of such events in the future, or a determination, after analysis, that no such improvement opportunities exist

To be considered credible, the root cause analysis must meet the following standards [6]:

- The organization's leadership and the individuals most closely involved in the process and systems under review must participate in the analysis.
- The analysis must be internally consistent; that is, it must not contradict itself or leave obvious questions unanswered.
- The analysis must provide an explanation for all findings of "not applicable" or "no problem."
- The analysis must include consideration of any relevant literature.

Finally, as previously discussed, after conducting this root cause analysis, the organization must prepare an internal corrective action plan. The Joint Commission will accept this action plan if it identifies changes that can be implemented to reduce risk or formulate a rationale for not undertaking such changes, and if, where improvement actions are planned, it identifies who is responsible for implementation, when the action will be implemented, and how the effectiveness of the actions will be evaluated [6].

FLORIDA LAW

Healthcare professionals have an obligation to report adverse events to leadership and ensure that organizations have processes in place to satisfy the Joint Commission requirement. In Florida, certain serious adverse incidents must also be reported to Florida's Agency for Health Care Administration (AHCA). Florida law requires that licensed facilities, such as hospitals, establish an internal risk management program. As part of that program, licensed facilities must develop and implement an incident reporting system, which requires the development of appropriate measures to minimize the risk of adverse incidents to patients, as well as imposes an affirmative duty on all healthcare providers and employees of the facility to report adverse incidents to the risk manager or to his or her designee. The risk manager must receive these incident reports within 3 business days of the incident, and depending on the type of incident, the risk manager may have to report the incident to AHCA within 15 days of receipt of the report.

Florida Statute 395.0197 specifically defines an adverse incident as [8]:

For purposes of reporting to the agency pursuant to this section, the term "adverse incident" means an event over which health care personnel could exercise control and which is associated in whole or in part with medical intervention, rather than the condition for which such intervention occurred, and which:

a) Results in one of the following injuries:
   1. Death;
   2. Brain or spinal damage;
   3. Permanent disfigurement;
   4. Fracture or dislocation of bones or joints;
   5. A resulting limitation of neurological, physical, or sensory function which continues after discharge from the facility;
   6. Any condition that required specialized medical attention or surgical interven-tion resulting from nonemergency medical intervention, other than an emergency medical condition, to which the patient has not given his or her informed consent; or
   7. Any condition that required the transfer of the patient, within or outside the facility, to a unit providing a more acute level of care due to the adverse incident, rather than the patient's condition prior to the adverse incident

b) Was the performance of a surgical procedure on the wrong patient, a wrong surgical procedure, a wrong-site surgical procedure, or a surgical procedure otherwise unrelated to the patient's diagnosis or medical condition;

c) Required the surgical repair of damage resulting to a patient from a planned surgical procedure, where the damage was not a recognized specific risk, as disclosed to the patient and documented through informed-consent process; or

d) Was a procedure to remove unplanned foreign objects remaining from a surgical procedure.

In 2021, the Florida AHCA reported that a total of 184 deaths occurred as a result of hospital error, 21.4% of 859 adverse incidents reported for the year. The next most common incidents during this period were transfer of the patient to a unit providing a more acute level of care due to the adverse incident (18.7%), fracture or dislocation of bones or joints (17.0%), surgical procedures unrelated to the patient's diagnosis or medical needs (10.4%), surgical procedure to remove foreign object from a previous surgical procedure (10.2%), brain or spinal damage (5.0%), and surgical procedure performed on wrong site (4.3%) [9]. The following adverse incidents must be reported to the AHCA within 15 calendar days after their occurrence [8]:

- The death of a patient
- Brain or spinal damage to a patient
- The performance of a surgical procedure on the wrong patient
- The performance of a wrong-site surgical procedure
- The performance of a wrong surgical procedure
- The performance of a surgical procedure that is medically unnecessary or otherwise unrelated to the patient's diagnosis or medical condition
- The surgical repair of damage resulting to a patient from a planned surgical procedure, where the damage is not a recognized specific risk, as disclosed to the patient and documented through the informed-consent process
- The performance of procedures to remove unplanned foreign objects remaining from a surgical procedure

Each incident will be reviewed by the AHCA, who will then determine the penalty to be imposed upon the responsible party [8]. All Florida healthcare professionals who practice in licensed facilities should familiarize themselves with these requirements and ensure that the facility in which they practice has processes in place to ensure compliance.

Unlike Florida's mandatory reporting of serious adverse incidents, the Joint Commission recommends that healthcare organizations voluntarily report sentinel events, and it encourages the facilities to communicate the results of their root cause analyses and their corrective action plans. As a result of the sentinel events that have been reported, the Joint Commission has compiled Sentinel Event Alerts. These alerts are intended to provide healthcare organizations with important information regarding reported trends and, by doing so, highlight areas of potential concern so an organization may review its own internal processes to maximize error reduction and prevention with regard to a particular issue [7].

ERROR REDUCTION AND PREVENTION

Between 2005 and 2021, the Joint Commission reviewed 14,731 sentinel events [11]. Some events, such as fire, impacted multiple patients. Sentinel event reviews during this time period were frequently conducted for patient fall; delay in treatment; unintended retention of a foreign body; wrong-patient, wrong-site, wrong-procedure surgery; patient suicide; operative and postoperative complications; and medication error [11].

PATIENT FALLS

In 2021, the Joint Commission introduced a separate sentinel event line item for patient falls, making it the most frequently reported sentinel event that year. Patients who are at highest risk include the elderly, those who have an altered mental status due to chronic mental illness or acute intoxication, and those who have a history of prior falls. Additionally, the Joint Commission calls for an increased awareness to an under-recognized population at risk for falls. Newborns and infants are at risk for falls and/or drops, often due to maternal risk factors such as cesarean birth, use of pain medication within four hours, second or third postpartum night (specifically around midnight to early morning hours), and drowsiness associated with breastfeeding. It is obvious from these factors that a thorough and complete patient history may be the key to identifying those at risk.

The root causes of patient falls that healthcare facilities identified as sentinel events and reported to the Joint Commission included inadequate assessment; communication failures; lack of adherence to protocols and safety practices; inadequate staff orientation, supervision, staffing levels, or skill mix; deficiencies in the physical environment; and lack of leadership [19]. Risk reduction strategies to these root causes are fairly straightforward, although in practice, preventing falls is difficult. The most important are the use of a standardized assessment tool to identify fall and injury risk factors, assessing an individual patient's risks that may not have been captured through the tool, and interventions tailored to an individual patient's identified risks [19].

Because patient falls often result in morbidity, mortality, immobility, and early nursing home placement for patients, it is imperative that healthcare facilities initiate adequate fall prevention programs, which will ultimately reduce injuries. Failure to do so will result in a spiraling increase in the number of falls in healthcare facilities, particularly among the elderly who are at highest risk. As more Americans live beyond 65 years of age, the need to develop mobility protocols and programs to reduce the risk of falls and injuries for the older adult grows more urgent.

DELAYS IN TREATMENT

According to the Joint Commission, more than half of all reported delay in treatment sentinel events in 2010–2014 resulted in patient death [16]. It is important to keep in mind that delays in treatment can occur in any healthcare setting. The most common reason for a delay in treatment is misdiagnosis; however, delays can also result from delayed test results, lack of physician availability, delayed administration of ordered care, incomplete treatment, and even inability to get an initial appointment or follow-up appointment in a timely manner [16]. The main root causes contributing to delays in treatment are inadequate assessments, poor planning, communication failures, and human factors. Additionally, 48% of patients self-reported a delay in accessing healthcare during the COVID-19 pandemic. One study suggests that delays in treatment are likely due to widespread public health messages to avoid unnecessary visits, triage uncertainty, lack of providers, and lack of resources [36]. Recommendations from the Joint Commission include avoiding cognitive shortcuts, improving health information technology, incorporating diagnostic checklists into the electronic record, promoting provider-to-provider communication, engaging leadership in developing solutions, focusing organization attention on the scheduling process and on ordering tests and reporting test results, improving access to care, implementing a standardized communications method, maintaining adequate staffing levels, and increasing patient and family engagement/activation [16].

UNINTENDED RETENTION OF A FOREIGN BODY

In 2021, unintended retained foreign objects were the third most frequently reported sentinel event reported to the Joint Commission [11]. The prevalence of these events has remained relatively stable since 2009, indicating that preventing these errors remains difficult for practitioners and facilities. The most commonly retained items are sponges, followed by catheter guidewires and other (a broad category encompassing a wide variety of items) [11].

In addition to harming patients and contributing to distrust in the medical system, the unintended retention of foreign objects significantly contributes to patient care costs [13]. The average total cost of care related to unintended retained foreign objects is $166,000 to $200,000 [13].

According to the sentinel event data, the most common root causes of unintended retained foreign objects reported to the Joint Commission are [13]:

- The absence of policies and procedures
- Failure to comply with existing policies and procedures
- Problems with hierarchy and intimidation
- Failure in communication with physicians
- Failure of staff to communicate relevant patient information
- Inadequate or incomplete education of staff

WRONG-SITE SURGERY

Operating on the wrong part of a patient's body is an obvious sign that there is a problem in the operating room system. Interestingly, wrong-site surgery occurred more commonly in orthopedic procedures than in all other surgical specialties combined. The American Academy of Orthopaedic Surgeons takes this issue seriously, and it has taken special steps to eliminate the problem. For example, it recommends that a surgeon sign their initials at the correct site of surgery with an indelible pen. Unless the initials are visible, the surgeon

should not make an incision [12]. Writing "NO" in large black letters on the side not to be operated on was suggested in the past, but this is discouraged due to possible confusion with the surgeon's initials. In spinal surgery, the Academy recommends that an intraoperative radiograph and radiopaque marker be used to determine the exact vertebral level of spinal surgery [12]. Whatever the mechanism used to prevent and reduce the incidence of this error, it is clear that this is not just the surgeon's problem. All operating room personnel, including physicians, nurses, technicians, anesthesiologists, and other preoperative allied health personnel, should monitor procedures to ensure verification procedures are followed, especially for high-risk procedures.

Due to the prevalence of wrong-site, wrong-procedure, and wrong-person surgeries, the Joint Commission, along with more than 50 professional healthcare organizations, convened two summits to help reduce the occurrence of these errors. The first summit, convened in 2003, developed a Universal Protocol that consisted of the following: a preprocedure verification process; marking the operative/procedure site with an indelible marker; taking a "time-out" with all team members immediately before starting the procedure; and adaptation of the requirements to all procedure settings, including bedside procedures. However, the incidence of wrong-site surgeries continued to increase, and in 2007 and 2010, additional summits were organized to pinpoint barriers in compliance and discover new strategies to eliminate these errors [14]. As of 2019, the Universal Protocol has been incorporated into the National Patient Safety Goal chapter of the Joint Commission accreditation manual [15].

PATIENT SUICIDE

It is estimated that between 48 and 65 hospital inpatient suicides occur per year in the United States. Most of these cases (31 to 52) occur in psychiatric units or involve psychiatric inpatients. The most common method is hanging [50]. Times of care transition are particularly risky, with a 200% increase in risk in the week after discharge from a psychiatric facility; the elevated risk continues for four years [18]. Other risk factors include previous suicide attempt or self-injury, mental or emotional disorders, history of trauma or loss, serious illness or chronic pain, substance use disorder, social isolation, and access to lethal means.

The most common root cause documented for patient suicide reported between 2010 and 2014 was shortcomings in assessment, most commonly psychiatric assessment [18]. In addition, nearly 25% of behavioral health facilities accredited by the Joint Commission were found noncompliant with the requirement to conduct an adequate suicide risk assessment in 2014.

The Joint Commission has recommended a number of suicide risk reduction strategies, including [18]:

- Review each patient's personal and family medical history for suicide risk factors.
- Screen all patients for suicide ideation, using a brief, standardized, evidence-based screening tool.
- Review screening questionnaires before the patient leaves the appointment or is discharged.
- Establish a collaborative, ongoing, and systematic assessment and treatment process with the patient involving the patient's other providers, family, and friends, as appropriate.
- To improve outcomes for at-risk patients, develop treatment and discharge plans that directly target suicidality.
- Educate all staff in patient care settings about how to identify and respond to patients with suicide ideation.
- Document decisions regarding the care and referral of patients with suicide risk.

A simple review of these measures demonstrates that healthcare providers can avoid the devastating impact of an inpatient suicide by implementing routine preventative strategies, such as removing harmful items and careful screening through the admission and discharge processes.

OPERATIVE AND POSTOPERATIVE COMPLICATIONS

Many of the sentinel events reported to the Joint Commission regarding operative and postoperative complications occurred in relation to nonemergent procedures, such as interventional imaging and/or endoscopy, tube or catheter insertion, open abdominal surgery, head and neck surgery, orthopedic surgery, and thoracic surgery [17]. The majority of the reporting healthcare facilities cited miscommunication as the primary root cause. Other identified causes include failure to follow established procedures, incomplete preoperative assessment, inconsistent postoperative monitoring procedures, and failure to question inappropriate orders. In order to reduce the risk, reporting facilities have identified a number of strategies, including improving staff orientation and training, increasing educational opportunities for physicians, clearly defining expected channels of communication, and monitoring consistency of compliance with procedures. Healthcare facilities should review postoperative patient monitoring procedures to ensure an adequate level appropriate to the needs of the patient, regardless of the setting (e.g., operating room, endoscopy suite, radiology department) [17]. Based upon these findings, it is clear that direct communication among healthcare providers is key to preventing operative and postoperative complications. Healthcare facilities should provide more staff education regarding preventative measures, and healthcare providers can do their part by engaging in a healthy and mutual respect for all of the members of the healthcare team [17].

MEDICATION ERRORS

Unquestionably, medication errors are one of the most common causes of avoidable harm to patients. These errors may occur at any of these critical points: when ordered or prescribed by a physician; during documentation; while transcribing; when dispensed by a pharmacist; when administered by a nurse; or during monitoring.

The National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as [20]:

> Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing: order communication; product labeling; packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

It has been estimated that up to 50% of medication errors are caused by a provider writing the wrong medication, the wrong route or dose, or the wrong frequency, and nearly 75% of medication errors have been attributed to distraction of the care provider [24]. In addition, a number of medication errors can be linked to the prescriber who continually uses potentially dangerous abbreviations and dose expressions. Despite repeated warnings by the Institute for Safe Medication Practices about the dangers associated with using certain abbreviations when prescribing medications, this practice continues. To eliminate this factor, there are fairly simple steps that can eliminate much confusion. Prescribers should [21]:

- Avoid the use of the symbol "U" or "u" but rather spell "units" when ordering drugs, such as insulin.
- Spell out medication names completely rather than using abbreviations and acronyms.
- Avoid using abbreviations for "daily" (QD), "every other day" (QOD), or "four times daily" (QID), which are easily confused.
- Use leading zeros before a decimal point (e.g., 0.2 mg instead of .2 mg), and do not use trailing zeros (e.g., 2 mg instead of 2.0 mg).
- Write out "morphine sulfate" and "magnesium sulfate" instead of using the abbreviations (MS, MSO_4, $MgSO_4$).

The Institute for Safe Medication Practices publishes a list of error-prone abbreviations, symbols, and dose designations online at https://www.ismp.org/recommendations/error-prone-abbreviations-list.

Other factors contributing to prescriber errors are illegible or confusing handwriting and, a frequently cited cause of many adverse and sentinel events, the failure of healthcare providers to assess risk and prevent errors. Addressing illegibility may include developing appropriate policies and procedures, tracking and trending patterns, and evaluating results through peer review committees. Improving communication might include developing protocols for the use of verbal orders to assure that those from an onsite practitioner would be limited to an emergency situation only. No verbal orders should be taken for certain medications, such as for chemotherapy, and all verbal orders should be repeated for clarification and, whenever possible, reiterated to a third person. Another method of improving communication might involve reviewing the hospital formulary in collaboration with the Pharmacy and Therapeutics Committee of the medical staff to limit, where appropriate, the number of therapeutically and generically equivalent products [22].

It has been estimated that between 0.2% and 10% of prescriptions are dispensed incorrectly [23]. The three most common dispensing errors are: dispensing an incorrect medication, dosage strength, or dosage form; miscalculating a dose; and failing to identify drug interactions or contraindications [24]. Safe medication dispensing practices may include a number of risk reduction strategies to reduce the incidence of errors that may cause harm to patients [22; 25; 54; 61]:

- Ensure that appropriate and current drug reference texts and/or online resources are immediately available to pharmacy personnel.
- Ensure that essential patient information, such as allergies, age, weight, current diagnoses, pertinent lab values, and current medication regimen, is available to the pharmacist prior to the dispensing of a new medication order.
- Require clarification of any order that is incomplete, illegible, or otherwise questionable using an established process for resolving questions.
- Whenever possible, dispense dosage units in a ready-to-administer form.
- Dispense single-dose vials and ampoules rather than multidose vials.
- Select oral rather than injectable routes, when possible.
- Require that a pharmacist double-check all mathematical calculations for neonatal and pediatric dilutions, parenteral nutrition solutions, and other compounded pharmaceutical products.
- Create an environment for the dispensing area that minimizes distractions and interruptions, provides appropriate lighting, air conditioning, and air flow, safe noise levels, and includes ergonomic consideration of equipment, fixtures, and technology.

- Require that a second pharmacist double-check the accuracy of order entry and dose calculations for all orders involving antineoplastic agents and other high-risk drugs dispensed by the pharmacy.
- Enhance the awareness of look-alike and sound-alike medications, and use warning signs to help differentiate medications from one another, especially when confusion exists between or among strengths, similar looking labels, or similar sounding names.
- Separate look-alike and sound-alike medications in pharmacy dispensing areas or consider repackaging or using different vendors.
- Follow-up and periodically evaluate the need for continued drug therapy for individual patients.

Once again, communication is likely the key to avoiding dispensing errors. Pharmacists should work closely with their staff to ensure that proper protocols are followed, and most importantly, when questions arise regarding a prescription, the pharmacist should take the time to contact the prescriber directly to obtain clarification.

The healthcare provider who has the responsibility to administer a medication has the final opportunity to avoid a mistake. In most cases, particularly in inpatient settings, this responsibility falls to the nurse. Nurses are often taught in nursing school to review the five "rights" prior to administering any medication: the right patient is given the right drug in the right dose by the right route at the right time [26]. Medication errors generally fall into four categories, which mimic these five "rights." The first is the failure to follow procedural safeguards, such as ensuring that essential patient information, including allergies, age, weight, and current medication regimen, is available. The second is unfamiliarity with a drug. In one case, a jury determined that a nurse was negligent for giving a drug without having reviewed the literature, which stated that the necessary precautions for the administration of the drug required the specialized skill of an anesthesiologist. The third category of drug administration is failure to use the correct mode of administration. A nurse in Delaware was held liable for administering a medication by injection after an order had been written to change the route to oral. The final category involves failure to obtain clarification if an order is incomplete, illegible, or otherwise questionable. In a case tried in Louisiana, a nurse was held liable for administering a medication that a physician ordered, notwithstanding that the dose was excessive. The nurse's administration of the drug led to the patient's death [27].

In addition, healthcare facilities should implement appropriate guidelines, policies, and procedures to ensure safe medication administration practice. These policies should require that staff members who administer medications [24; 25; 54; 61]:

- Are knowledgeable about the drug's uses, precautions, contraindications, potential adverse reactions, interactions, and proper method of administration
- Resolve questions prior to medication administration
- Only administer medications that have been properly labeled with medication name, dose to be administered, dosage form, route, and expiration date
- Utilize a standard medication administration time schedule and receive education on how and when to incorporate newly started medication orders safely into the standardized schedule
- Have a second person verify a dosage calculation if a mathematical calculation of a dose is necessary
- Receive adequate education on the operation and use of devices and equipment used for medication administration (for example, patient-controlled anesthesia pumps and other types of infusion pumps)
- Have another person double-check infusion pump settings when critical, high-risk drugs are infused
- Document all medications immediately after administration

Finally, healthcare facilities should have proper quality assurance measures in place to monitor medication administration practices. Included among these would be protocols and guidelines for use with critical and problem-prone medications to help optimize therapies and minimize the possibility of adverse events and to integrate "triggers" to indicate the need for additional clinical monitoring [25].

It is important to note that the pediatric population is especially vulnerable to medication errors. When children are prescribed adult medications, care must be taken to adjust dosage according to weight, requiring the physician to use pediatric-specific calculations. Also, many healthcare settings are not trained to care for the pediatric patient. Intolerance due to physiologic immaturity is also a factor in adverse response to medications, and in many cases, this population cannot communicate their discomfort due to adverse reactions. Risk reduction strategies include standardizing and effectively identifying medications and processes for drug administration, ensuring pharmacy oversight, and using technology, such as medication dispensing programs, infusion pumps, and bar-coding, judiciously [28].

COMMON MISDIAGNOSES

As Florida healthcare professionals, it is important to be aware that in addition to wrong-site/wrong-procedure surgery, several medical conditions also continue to be misdiagnosed. As of 2022, the Florida Board of Medicine has determined the five most misdiagnosed conditions to be [29]:

- Cancer-related conditions
- Gastroenterology-related issues
- Cardiology-related issues
- Neurologic conditions
- Missed spinal cord compression

It is important to be aware of the possibility of misdiagnosis and incorporate this knowledge into practice.

Cancer

The early detection and diagnosis of cancers is crucial for selecting the appropriate treatment approach and to ensure an optimum outcome. However, an estimated 12% of cancer patients are initially misdiagnosed, and the missed or delayed diagnosis of cancers remains a significant cause of medical malpractice claims [30; 31]. The causes of missed diagnoses vary widely among cancers in different parts of the body. In many cases, patients who do not fit the typical profile for a specific cancer (e.g., young age) may be underdiagnosed, and it is important that cancer is considered as part of the differential diagnosis in ambiguous cases [31; 32; 33]. In order to prevent missed or delayed cancer diagnosis, practitioners may take steps to ensure adherence to clinical guidelines for screening and diagnosis, use tools to facilitate communication, and engage strategies to ensure appropriate follow-up [55].

Gastroenterology-Related Conditions

Gasteroenterologic conditions may present with nonspecific complaints (e.g., abdominal pain, nausea) common to a variety of illnesses, complicating and delaying diagnosis. In one study of patients with pancreatic cancer, more than 30% were initially misdiagnosed, most commonly with gall bladder disease [58]. Diagnosis and screening for gastrointestinal disorders may be complicated by a lack of definitive test (e.g., irritable bowel syndrome) or by limits on screening recommendations (e.g., colorectal cancer). However, delayed diagnosis can lead to worsening conditions and poorer prognosis.

In general, gastrointestinal syndromes/symptoms may be classified into three general diagnostic categories: organic, motility, or functional disorders [59; 60]. Functional GI disorders are idiopathic disorders of gut-brain interaction and, unlike organic and motility disorders, diagnosis involves identification of symptom clusters. As such, misdiagnosis is more common. Another important consideration is GI symptom-specific anxiety, an important perpetuating factor that describes threatening interpretation and out-of-proportion behavioral response to GI sensations. This anxiety to real GI symptoms and the frequency of psychiatric comorbidity can lead to functional GI syndromes being dismissed as psychological or psychosomatic in nature.

Cardiology-Related Issues

The clinical presentation of chest pain has many possible etiologies, ranging from benign (e.g., panic/anxiety, pneumonia, peptic ulcer, gastroesophageal reflux disease, and pericarditis) to life-threatening (e.g., pulmonary embolism, acute coronary syndrome [ACS], aortic dissection, and pneumothorax). In many cases, it is best to rule out the more urgently threatening possibilities before testing for other causes.

Of the potentially life-threatening causes of chest pain, ACS is the most prevalent. Although a large percentage of individuals with suspected ACS will be seen initially in emergency departments, patients in any healthcare setting, regardless of other diagnoses, may abruptly develop chest pain suspicious for ACS. When a patient presents with clinical signs suspicious for myocardial infarction, immediate medical intervention is directed at confirming a diagnosis and stratifying the person's risk for adverse events such as cardiac arrest and severe/significant damage to the myocardium [41]. It is important to note that while some patients will present with classic ACS-related chest pain (tightness, sensation of pressure, heaviness, crushing, vise-like, aching pain in the substernal or upper left chest), many patients, particularly women and older patients, will present with "atypical" ACS-related chest pain [45; 46]. Words commonly used to describe "atypical" chest pain associated with ACS include numbness, tingling, burning, stabbing, or pricking. Atypical chest pain location includes any area other than substernal or left sided, such as the back, area between shoulder blades, upper abdomen, shoulders, elbows, axillae, and ears [43; 44; 45; 46]. Aside from atypical clinical presentation, other possible causes of missed ACS diagnosis include failure of interpretation of the history, failure to correctly interpret the electrocardiogram, failure to perform an electrocardiogram when necessary, and lack of proper use of cardiac enzyme test [47].

Neurologic/Spinal Cord-Related Conditions

Delayed or missed diagnoses of neurologic conditions may result in serious morbidity and mortality. Headaches are a common presenting condition in acute and primary care, and an estimated 5% of all patients admitted to emergency departments have neurologic symptoms [34]. Acute headache with neurologic symptoms may be misdiagnosed as stroke [35; 64]. In addition, missed spinal fracture diagnoses are one of the leading causes of malpractice claims against radiologists [48].

One of the most common neurologic conditions is headache; however, it has been estimated that 50% of migraine patients remain undiagnosed or misdiagnosed, and only a small number (8% to 10%) of individuals with migraine take migraine-specific medications such as triptans or ergotamines [65; 66]. Patients suffering from daily migraines may be misdiagnosed with chronic sinusitis or rhinitis and repeatedly and unsuccessfully treated with broad-spectrum antibiotics [62; 63]. The diagnosis of migraine is based solely on a constellation of signs and symptoms, and a comprehensive medical and neurological examination is required to exclude secondary headache [56]. Useful evidence-based clinical guidelines for migraine screening have been developed and are summarized in the mnemonic POUND: pulsatile headache; one-day duration (4 to 72 hours); unilateral location; nausea or vomiting; and disabling intensity [57]. Competence of the clinician and effective communication with the patient play a crucial role in the diagnosis of migraine.

Missed Spinal Cord Compression

Epidural compression syndrome is an umbrella term that encompasses spinal cord compression, cauda equina syndrome, and conus medullaris syndrome. While these conditions differ in the level of neurologic deficit at presentation, they are otherwise similar in symptoms, evaluation, and management. Massive herniation of a midline disk, typically at the L4 to L5 disk level, is the most common cause of epidural compression syndrome. Tumor, epidural abscess, spinal canal hematoma, or lumbar spine spondylosis represent other causes [37].

Spinal cord compression is often secondary to herniated disk, vertebral fracture, or space-occupying lesion. Missing this diagnosis, typically by attributing the associated pain to muscle or nerve causes, will miss potentially catastrophic conditions [38; 39; 40; 41]. In a study of 3,786 individuals, the estimated prevalence of asymptomatic spinal cord compression in a healthy population was 24.2%, with a significantly higher prevalence in older populations compared with younger populations and American/European populations compared with Asian populations [42].

In patients with spinal cord compression, neurologic status at diagnosis is the greatest predictor of ultimate neurologic outcome and underscores the importance of early accurate diagnosis. The dominant symptom is back pain with accelerating pain severity. Pain from epidural spinal cord compression is made worse with recumbent positioning, and unilateral or bilateral radiculopathy may develop over time. For many patients, leg pain or neurologic symptoms are more dominant than back pain. Also common at diagnosis is symmetrical lower extremity weakness that may have progressed to gait disturbance or paralysis. Decreased lower extremity reflexes are associated with cauda equina syndrome [37].

OTHER CONSIDERATIONS FOR PATIENT SAFETY

The most important issue to improving patient safety is being aware of the particular safety hazards that may exist for various patient populations and on particular specialty units. In addition, education of the patient and the family should be a priority.

Infants and young children are not developmentally or cognitively able to participate in care and decision making, thus putting them at higher risk, especially for medication errors. In addition, when a medication error occurs in this population, infants and young children are at higher risk because of their physical immaturity and increased sensitivity to the effects of drugs. The family or guardian of a pediatric patient should be encouraged to ask questions, especially if something seems wrong. In addition, a meta-analysis found that computerized provider order entry with clinical decision support reduced pediatric medication errors by 36% to 87% [51]. As such, the adoption of electronic support systems may help to reduce or eliminate these errors.

An estimated 30% of individuals 65 years of age or older who are living in the community fall each year [52]. Older patients may have poor vision, as a result of cataracts, glaucoma, and/or macular degeneration, and cardiovascular problems, which might result in syncope or postural hypotension. These conditions may affect patients' balance and stability. Bladder dysfunction, such as nocturia, may cause an elderly patient to have to ambulate more during the night in an unfamiliar environment, thereby increasing the risk of a fall. Lower extremity dysfunctions, such as arthritis, muscle weakness, or peripheral neuropathy, may make it more difficult to ambulate at any time. In addition to being at greater risk for falls, the elderly are also more prone to medication errors as their ability to understand instructions or to recognize an unfamiliar medication may be affected by dementia or other cognitive disorders. Interventions that can help prevent falls in the elderly include exercise programs, tai chi, vision improvement (e.g., first cataract surgery), and multifactorial assessment and intervention [52].

There are also unique factors that increase the risk of medical errors on specialty units. For instance, in critical care units, patients may be suffering from environmental psychosis, which could inhibit participation in their care. This is also true of lethargic and comatose patients. These patients are at particular risk because they cannot participate in the identification process. On psychiatric wards, patients may be suicidal or depressed, which may cause them to act out or attempt to harm themselves or others. Patients may also experience orthostatic side effects due to certain psychiatric medications, which may increase the incidence of falls. Obstetric patients are at higher risk for falls because they may have decreased sensation and mobility due to administration of epidural anesthesia, and they may also suffer from excessive blood loss, which could lead to postural hypotension [49]. Again, the key is identifying the unique needs of the particular population.

With regard to education, a number of organizations have developed guidelines to facilitate the role of patients as their own safety advocates. These guidelines are not intended to shift the burden of monitoring medical error to patients. Rather, they encourage patients to share responsibility for their own safety. As healthcare professionals, we should ensure that all of our patients are familiar with these guidelines. The Agency for Healthcare Research and Quality has developed a "Patient Fact Sheet" that outlines 20 tips for patients to help prevent medical errors [53]. Although some of these suggestions may seem extreme, many patients now desire to have a more active role in their care. Some of these items have become routine or are currently required, such as consultations by pharmacists when a patient picks up a prescribed medication.

USE OF AN INTERPRETER

As a result of the evolving racial and immigration demographics in the United States, interaction with patients for whom English is not a native language is inevitable. Because patient education is such a vital aspect of preventing medical errors, it is each practitioner's responsibility to ensure that information and instructions are explained in such a way that allows for patient understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required.

Interpreters are more than passive agents who translate and transmit information back and forth from party to party. They should be professionally trained in ethics, accuracy, completeness, and impartiality. Furthermore, it is the interpreter's role to negotiate cultural differences and promote culturally responsive communication and practice. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter. In any case in which information regarding diagnostic procedures, treatment options, or medication/treatment measures is being provided, the use of an interpreter should be considered.

CONCLUSION

Although the United States has one of the top healthcare systems in the world, it is apparent that the numbers of medical errors are at unacceptably high levels. The consequences of medical errors are often more severe than the consequences of mistakes in other industries. They may lead to death or to serious and long-term disability, which underscores the need for aggressive action in this area. As a starting point, we should become an active part of the solution. This will only happen if all healthcare professionals voice their concerns when they identify problems in a system or process. In addition, we should actively participate in the root cause analysis process, understanding that the goal is not to assign blame, but rather to identify how we can improve the process to provide the best quality care to our patients. Medical errors are costly, not only because patients may lose their lives or livelihoods, but also because patients lose trust in the system and colleagues lose faith in each other. To preserve the integrity of our system, we must correct this problem, and the solution begins with each of us.

Customer Information/Answer Sheet/Evaluation insert located between pages 60–61.

COURSE TEST - #51334 MEDICAL ERROR PREVENTION AND ROOT CAUSE ANALYSIS

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 CE Credit Hour activity must be completed by August 31, 2025.

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1. **The Institute of Medicine's (IOM) Committee on Quality of Healthcare in America defines error as the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim.**
   A) True
   B) False

2. **Patient rape is an example of a sentinel event subject to review by the Joint Commission.**
   A) True
   B) False

3. **A "thorough" root cause analysis is one in which the participants identify risk points and their potential contributions to this type of event.**
   A) True
   B) False

4. **A credible root cause analysis must be based upon a survey of everyone employed at the healthcare institution.**
   A) True
   B) False

5. **A wrong-site surgical procedure that did not result in the death of the patient must be reported to the risk manager within three business days according to Florida law.**
   A) True
   B) False

6. **The Joint Commission prepares and distributes Sentinel Event Alerts in order to recommend ways in which the healthcare facility can terminate employees whose actions result in a sentinel event.**
   A) True
   B) False

7. **Infant abduction is among the most common sentinel events reported to the Joint Commission.**
   A) *True*
   B) *False*

8. **The most common root cause documented for patient suicide was shortcomings in assessment, most commonly psychiatric assessment.**
   A) *True*
   B) *False*

9. **A medication error may occur when ordered by a physician, administered by a nurse, or dispensed by a pharmacist.**
   A) *True*
   B) *False*

10. **Approximately 32% of patients with cancer are initially misdiagnosed.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet located on the envelope insert.
DO NOT send these test pages to NetCE. Retain them for your records.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Domestic Violence: The Florida Requirement

This course fulfills the Florida requirement for 2 hours of education on Domestic Violence.

Audience
This course is designed for all Florida dental professionals required to complete domestic violence education.

Course Objective
The purpose of this course is to enable dental professionals in all practice settings to define domestic violence and identify those who are affected by domestic violence in the United States. This course describes how a victim can be accurately diagnosed and identifies the community resources available in the state of Florida for domestic violence victims.

Learning Objectives
Upon completion of this course, you should be able to:

1. Define domestic violence and its impact on health care.
2. Cite the general prevalence of domestic violence on a national and state level and identify state laws pertaining to the issue.
3. Describe how to screen and assess individuals who may be victims or perpetrators of domestic violence, including the importance of conducting a culturally sensitive assessment.
4. Identify community resources presently available for domestic violence victims and their perpetrators throughout Florida concerning legal aid, shelter, victim and batterer counseling, and child protection services.

Faculty
Marjorie Conner Allen, BSN, JD, received her Bachelor of Science in Nursing degree from the University of Florida, Gainesville, in 1984. She began her nursing career at Shands Teaching Hospital and Clinics at the University of Florida, Gainesville. While practicing nursing at Shands, she gave continuing education seminars regarding the nursing implications for dealing with adolescents with terminal illness. In 1988, Ms. Allen moved to Atlanta, Georgia where she worked at Egleston Children's Hospital at Emory University in the bone marrow transplant unit. (A complete biography appears at the end of this course.)

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families. (A complete biography appears at the end of this course.)

Faculty Disclosure
Contributing faculty, Marjorie Conner Allen, BSN, JD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Alice Yick Flanagan, PhD, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Mark J. Szarejko, DDS, FAGD

Senior Director of Development and Academic Affairs
Sarah Campbell

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Designations of Credit
NetCE designates this activity for 2 continuing education credits.

AGD Subject Code 156.

Special Approvals
This course fulfills the Florida requirement for 2 hours of Domestic Violence education every third renewal period.

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EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the study questions and course material for better application to your daily practice.

INTRODUCTION

Domestic violence continues to be a prevalent problem in the United States today. Because of the number of individuals affected, it is likely that most healthcare professionals will encounter patients in their practice who are victims. Accordingly, it is essential that healthcare professionals are taught to recognize and accurately interpret behaviors associated with domestic violence. It is incumbent upon the healthcare professional to establish and implement protocols for early identification of domestic violence victims and their abusers. In order to prevent domestic violence and promote the well-being of their patients, healthcare professionals in all settings should take the initiative to properly assess all women for abuse during each visit and, for those women who are or may be victims, to offer education, counseling, and referral information.

Victims of domestic violence suffer emotional, psychologic, and physical abuse, all of which can result in both acute and chronic signs and symptoms of physical and mental disease, illness, and injury. Frequently, the injuries sustained require abused victims to seek care from healthcare professionals immediately after their victimization. Subsequently, physicians and nurses are often the first healthcare providers that victims encounter and are in a critical position to identify domestic violence victims in a variety of clinical practice settings where victims receive care. Accordingly, each healthcare professional should educate himself or herself to enhance awareness of the presence of abuse victims in his or her particular practice or clinical setting.

Specifically, healthcare professionals should be aware of the signs and symptoms associated with domestic violence. In addition, when family violence cases are identified, there should be a plan of action that includes providing information on, and referral to, local community resources related to legal aid, sheltering, victim counseling, batterer counseling, advocacy groups, and child protection.

DEFINING DOMESTIC VIOLENCE

Domestic violence, which is sometimes also referred to as spousal abuse, battering, or intimate partner violence (IPV), refers to the victimization of an individual with whom the abuser has or has had an intimate or romantic relationship. Researchers in the field of domestic violence have not agreed on a uniform definition of what constitutes violence or an abusive relationship. The Centers for Disease Control and Prevention (CDC) defines IPV as, "violence or aggression that occurs in a romantic relationship" [1]. According to the Florida Department of Children and Families, domestic violence is "a pattern of abusive behaviors that adults use to maintain power and control over their intimate partners or former partners. People who abuse their partners use a variety of tactics to coerce, intimidate, threaten, and frighten their victims" [2]. Domestic violence may include physical violence, sexual violence, emotional abuse, economic abuse, isolation, pet abuse, threats relating to children, and a variety of other behaviors meant to increase fear, intimidation, and power over the victim [2]. Florida law defines domestic violence as "any assault, aggravated assault, battery, aggravated battery, sexual assault, sexual battery, stalking, aggravated stalking, kidnapping, false imprisonment, or any criminal offense resulting in physical injury or death of one family or household member by another family or household member" [3]. Family or household members, according to Florida definition, must "be currently residing or have in the past resided together in the same single dwelling unit" [3]. Domestic violence knows no boundaries. It occurs in intimate relationships regardless of race, religion, culture, or socioeconomic status [2].

Whatever the definition, it is important for healthcare professionals to understand that domestic violence, in the form of emotional and psychologic abuse, sexual abuse, and physical violence, is prevalent in our society. Because of the similar nature of the definitions, this course will use the terms "domestic violence" and "IPV" interchangeably.

NATIONAL AND STATE STATISTICS AND LEGISLATION

Domestic violence is one of the most serious public health problems in the United States [4]. More than 36.4% of women and 33.6% of men have a lifetime history of IPV [4]. In Florida, the weighted lifetime prevalence of IPV (including rape, physical violence, and/or stalking) is 37.4% among women and 29.3% among men [5]. Although many of these incidents are relatively minor and consist of pushing, grabbing, shoving, slapping, and hitting, IPV resulted in approximately 1,500 deaths in the United States in 2019, with 214 of those deaths occurring in Florida in the same year. Statistics indicate a slightly higher rate in 2020, with 217 deaths in Florida in 2020 [7; 8]. One of the difficulties in addressing the problem is that abuse is prevalent in all demographics, regardless of age, ethnicity, race, religious denomination, education, or socioeconomic status [2].

Victims of abuse often suffer severe physical injuries and will likely seek care at a hospital or clinic. The health and economic consequences of domestic violence are significant. Statistics vary from report to report, and due to the lack of studies on the national cost of domestic violence, the U.S. Congress funded the CDC to conduct a study to determine the cost of domestic violence on the healthcare system [9]. The 2003 CDC report, which relied on data from the National Violence Against Women Survey conducted in 1995, estimated the costs of IPV by measuring how many female victims were nonfatally injured; how many women used medical and mental healthcare services; and how many women lost time from paid work and household chores. The estimated total annual cost of IPV against women in the 1995 survey was more than $5.8 billion [9]. When updated to 2017 dollars, the amount was more than $9.3 billion annually. The costs associated with IPV at this time would be considerably more, but no further studies have been conducted [10]. It should be noted that the costs of any one victimization may continue for years; therefore, these statistics most likely underestimate the actual cost of IPV [9].

The national rate of nonfatal domestic violence against women declined 72% between 1993 and 2011 [11]. The rate of overall violent crime fell by nearly 60% in this same time period [11]. Studies reveal that several factors may have contributed to the reduction in violence, including a decline in the marriage rate and decrease of domesticity, better access to federally funded domestic violence shelters, improvements in women's economic status, and demographic trends, such as the aging of the population [13; 14]. Of note, declines in the economy and stress associated with financial hardship and unemployment are significant contributors to IPV in the United States. Following the economic downturn in late 2008, there was a significant increase in the use of the National Domestic Violence Hotline in 2009, with more than half of victims reporting a change in household financial situation in the last year [15].

This trend continued with the COVID-19 pandemic, with stressors from lockdown orders, unemployment, financial insecurity, childcare and homeschool responsibilities, and poor coping strategies (e.g., substance abuse) increasing the rate of domestic violence. Reports showed a 9.7% increase in domestic violence calls for service in the first two months state-mandated lockdowns were imposed; furthermore, the National Commission on COVID-19 and Criminal Justice reported an increase of 8.1% in domestic violence incidents within the first months of mandated stay-at-home orders [6].

FLORIDA

In response to troubling domestic violence statistics, Governor Lawton Chiles appointed a Task Force on Domestic Violence on September 28, 1993, to investigate the problems associated with domestic violence in Florida and to compile recommendations as to how the problems should be approached and ultimately resolved. On January 31, 1994, the Task Force issued its first report on domestic violence. This report recommended standards to accurately measure the extent of domestic violence and strategies for increasing public awareness and education. It identified programs and resources that are available to victims in Florida, made legislative and budgetary suggestions for needed changes, provided a methodology for implementing these changes, and identified areas of domestic violence that require further study.

As a result of this report, Florida enacted legislation during the 1995 session implementing various suggestions of the Task Force. Specifically, the Legislature amended Section 455.222 of the Florida Statutes to require that all physicians, osteopaths, nurses, dentists, dental hygienists, midwives, psychologists, and psychotherapists obtain, as part of their biennial continuing education requirements, a one-hour continuing education course on domestic violence [17]. In June of 2006, Governor Jeb Bush signed into law House Bill 699. The bill, which went into effect July 1, 2006, changed the domestic violence continuing education requirement from one hour every renewal period to two hours every third renewal period.

In 1997, at the request of the Governor's Task Force, a workgroup was established by the Florida Department of Law Enforcement (FDLE) to evaluate the feasibility of tracking incidents of domestic violence in the state [18]. This resulted in the creation of the Domestic Violence Data Resource Center (DVDRC). The original mission of the DVDRC was to collect information related to domestic violence and to report and maintain the information in a statewide tracking system [19]. Domestic Violence Fatality Review Teams were established to examine those cases of domestic violence that resulted in a fatality and identify potential changes in policy or procedure that might prevent future deaths. The teams were comprised of representatives from law enforcement, the courts, social services, state attorneys, domestic violence centers, and others who may come into contact with domestic violence victims and perpetrators [20]. In 2000, the creation of Florida Statute 741.316 required the FDLE to annually publish a report based on the data gathered by the Fatality Review Teams [19]. Due to budgetary constraints, responsibility of compiling this data transferred to the Department of Children and Families in 2008 [21].

As part of Governor Jeb Bush's initiative, the "Family Protection Act" was signed into law in 2001. The act requires a 5-day mandatory jail term for any crime of domestic battery in which the perpetrator deliberately injures the victim. The law also makes a second battery crime a felony offense, treating offenders as serious criminals. Additional legislation, signed into law in 2002, includes Senate Bills 716 and 1974. Senate Bill 716 protects domestic violence victims by including dating relationships of six months in the definition of domestic violence laws. Senate Bill 1974 requires judges to inform victims of their rights, including the right to appear, be notified, seek restitution, and make a victim-impact statement. Governor Bush also created the Violence Free Florida campaign to increase public awareness of domestic violence issues [22].

In 2003, Governor Bush signed House Bill 1099, which transferred funding authority of the Florida Domestic Violence Trust Fund from the Department of Children and Families to the Florida Coalition Against Domestic Violence. According to the Domestic Violence in Florida 2010–2011 Annual Report to the Legislature, this has strengthened domestic violence services provided by streamlining the process of allocating funds [23].

In 2007, the Domestic Violence Leave Act was signed into law by Governor Charlie Crist [21]. This law requires employers with 50 or more employees to provide guaranteed leave for domestic violence issues.

In 2020, the FDLE reported 106,736 domestic violence offenses [8]. In general, domestic violence rates have been declining since 1998. An estimated 19.5% of domestic violence incidents involved spouses and 27.8% involved cohabitants; 11.6% of the victims were parents of the offenders. Domestic violence offenses resulted in the death of 217 victims in Florida in 2020, a number that has been decreasing since 2014 [8]. Domestic violence accounted for 16.9% of the state's murders in 2020 [8].

In their 2019 Annual Report, Fatality Review Teams summarized 31 cases of domestic violence fatalities and near fatalities [49]. The most significant findings included the following observations [49]:

- The perpetrators were predominantly male (94%) with female victims (90%) and had prior criminal histories, non-domestic-violence-related (67%) and for domestic violence specifically (69%).
- In 31% of fatalities, the perpetrators had a known "do not contact" order filed against them, and 13% of perpetrators had a known permanent injunction for protection against them filed by someone other than the victim.

- Substance abuse histories by the perpetrator was identified in 77% of the cases and diagnosed mental health disorders in 45%.
- In most cases, neither the decedent nor perpetrator sought help from the various intervention programs available to them.

To obtain a copy of the most current Florida Statewide Domestic Violence Fatality Review report, please visit https://www.myflfamilies.com/service-programs/domestic-violence/publications.shtml.

IDENTIFYING GROUPS AT RISK FOR DOMESTIC VIOLENCE

Healthcare professionals are in a critical position to identify domestic violence victims in a variety of clinical practice settings. Nurses are often the first healthcare provider a victim of domestic violence will encounter in a healthcare setting and should therefore be prepared to provide care and support for these victims. Although women are most often the victims, domestic violence extends to others in the household as well. For example, domestic violence includes abused men, children abused by their parents or parents abused by their children, elder abuse, and abuse among siblings [3].

Many victims of abuse sustain injuries that lead them to present to hospital emergency departments. Research has found that 49.6% of women seen in emergency departments reported a history of abuse and 44% of women who were ultimately killed by their abuser had sought help in an emergency department in the two years prior to their death [25; 50]. Another study of 993 police-identified female victims of IPV found that only 28% of the women were identified in the emergency department as being victims of IPV [26]. These alarming statistics demonstrate that healthcare professionals who work in acute care, such as hospital emergency rooms, should maintain a high index of suspicion for battering of the patients that they see. Healthcare professionals who work in these settings should work with hospital administrators to establish and institute assessment mechanisms to accurately detect these victims.

For every victim of abuse, there is also a perpetrator. Like their victims, perpetrators of domestic violence come from all socioeconomic backgrounds, races, religions, and walks of life [1; 4]. Accordingly, healthcare professionals should likewise be aware that seemingly supportive family members may, in fact, be abusers.

PREGNANT WOMEN

Because a gynecologist or obstetrician is frequently a woman's primary care physician, the American College of Obstetricians and Gynecologists (ACOG) recommends that all women be routinely assessed for signs of IPV (i.e., physical and psychologic abuse, reproductive coercion, and progressive isolation), including during prenatal visits, and providers should offer support and referral information for those being abused [25]. According to the ACOG, IPV affects as many as 324,000 pregnant women each year [25]. A meta-analysis of 92 independent studies found that the average reported prevalence of emotional abuse during pregnancy was 28.4%, physical abuse was 13.8%, and sexual abuse was 8% [51]. As with all domestic violence statistics, these estimates are presumed to be lower than the actual incidence as a result of under-reporting and lack of data on women whose pregnancies ended in fetal or maternal death. This makes IPV more prevalent among pregnant women than some of the health conditions included in prenatal screenings, including pre-eclampsia and gestational diabetes [25]. Because 96% of pregnant women receive prenatal care, this is an optimal time to assess for domestic violence and develop trusting relationships with the women. Possible factors that may predispose pregnant women to IPV include being unmarried, lower socioeconomic status, young maternal age, unintended pregnancy, delayed prenatal care, lack of social support, and use of tobacco, alcohol, or illegal drugs [25; 51].

The overarching problem of violence against pregnant women cannot be ignored, especially as both mother and fetus are at risk. At this particularly vulnerable time in a woman's life, an organized clinical construct leading to immediate diagnosis and medical intervention will ensure that therapeutic opportunities are available to the pregnant woman and will reduce the potential negative outcomes [29]. Healthcare professionals should also be aware of the possible psychologic consequences of abuse during pregnancy. There is a higher risk of stress, depression, and addiction to alcohol and drugs in abused women. These conditions may result in damage to the fetus from tobacco, drugs, and alcohol and a loss of interest on the part of the mother in her or her baby's health [16; 30]. Possible direct injuries to the fetus may result from maternal trauma [25].

Control of reproductive or sexual health is also a recognized trend in IPV. This type of abuse includes trying to impregnate or become pregnant against a partner's wishes, refusal to use birth control (e.g., condoms, oral contraceptives), or stopping a partner from using birth control [4].

CHILDREN

Children exposed to family violence are at high risk for abuse and for emotional damage that may affect them as they grow older. The Department of Justice estimates that of the 76 million children in the United States, 46 million will be exposed to some type of violence during their childhood [52]. Results of the National Survey of Children's Exposure to Violence indicated that 11% of children were exposed to IPV at home within the last year, and as many as 26% of children were exposed to at least one form of family violence during their lifetimes [31]. Of those children exposed to IPV, 90% were direct eyewitnesses of the violence; the remaining children were exposed by either hearing the violence or seeing or being told

about injuries [31]. Of note, according to Florida criminal law, witnessing domestic violence is defined as "violence in the presence of a child if an offender is convicted of a primary offense of domestic violence, and that offense was committed in the presence of a child under age 16 who is a family or household member with the victim or perpetrator" [32].

A number of studies indicate that child witnesses are at increased risk for post-traumatic stress disorder, impaired development, aggressive behavior, anxiety, difficulties with peers, substance abuse, and academic problems than the average child [33; 54; 55]. Children exposed to violence may also be more prone to dating violence (as a perpetrator or a victim), and the ability to effectively cope with partnerships and parenting later in life may be affected, continuing the cycle of violence into the next generation [34; 56].

In addition to witnessing violence, various studies have shown that these children may also become direct victims of violence, and children who both witness and experience violence are at the greatest risk for adverse psychosocial outcomes [53]. Research indicates that between 30% and 65% of husbands who batter their wives also batter their children [27; 35]. Moreover, victims of abuse will often turn on their children; statistics demonstrate that 85% of domestic violence victims abuse or neglect their children. The 2020 Crime in Florida report found that more than 13% of domestic homicide victims were children killed by a parent [8]. Teenage children are also victimized. According to the U.S. Department of Justice, between 1980 and 2008, 17.5% of all homicides against female adolescents 12 to 17 years of age were committed by an intimate partner [36]. Among young women (18 to 24 years of age), the rate is estimated to be 43% in the United States and 8% to 57% globally. Abused teens often do not report the abuse. Individuals 12 to 19 years of age report only 35.7% of crimes against them, compared with 54% in older age groups [28; 37]. Accordingly, healthcare professionals who see young children and adolescents in their practice (e.g., pediatricians, family physicians, school nurses, pediatric nurse practitioners, community health nurses) should have the tools necessary to detect these "silent victims" of domestic violence and to intervene quickly to protect young children and adolescents from further abuse. Without such critical intervention, the cycle of violence will never end.

ELDERLY

Abused and neglected elders, who may be mistreated by their spouses, partners, children, or other relatives, are among the most isolated of all victims of family violence. In a national study conducted by the National Institute of Justice in 2010, 4.6% of participants (community dwelling adults 60 years of age or older) were victims of emotional abuse in the past year, 1.6% physical abuse, 0.6% sexual abuse, 5.1% potential neglect, and 5.2% current financial abuse by a family member [38]. A 2017 study found a self-reported incidence of 11.6% psychological abuse, 2.6% physical abuse, 6.8% financial abuse, 4.2% neglect, and 0.9% sexual abuse [59]. The estimated annual incidence of all elder abuse types is 2% to 10%, but it is believed to be severely under-measured. According to one study, only 1 in 24 cases of elder abuse are reported to the authorities [39].

The prevalence rate of elder abuse in institutional settings is not clear. However, in a 2019 review of nine studies, 64% of elder care facility staff disclosed to having perpetrated abuse against an elderly resident in the past year [40]. In a random sample survey, 24.3% of respondents reported at least one incident of elder physical abuse perpetrated by a nursing home staff member [57].

As healthcare professionals in Florida, which leads the nation in percentage of older residents, it is important to understand that the needs of older Floridians will increase as will the numbers of elder victims of domestic violence. Because elder abuse can occur in family homes, nursing homes, board and care facilities, and even medical facilities, healthcare professionals should remain keenly aware of the potential for abuse. When abuse occurs between elder partners, it is primarily manifested in one of two ways: either as a long-standing pattern of marital violence or as abuse originating in old age. In the latter case, abuse may be precipitated by issues related to advanced age, including the stress that accompanies disability and changing family relationships [39].

It is important to understand that the domestic violence dynamic involves not only a victim but a perpetrator as well. For example, an adult son or daughter who lives in the parents' home and depends on the parents for financial support may be in a position to inflict abuse. This abuse may not always manifest itself as violence but can lead to an environment in which the elder parent is controlled and isolated. The elder may be hesitant to seek help because the abuser's absence from the home may leave the elder without a caregiver [39]. Because these elderly victims are often isolated, dependent, infirm, or mentally impaired, it is easy for the abuse to remain undetected. Healthcare professionals in all settings should remain aware of the potential for abuse and keep a watchful eye on this particularly vulnerable group.

The U.S. Preventive Services Task Force concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for abuse and neglect in all older or vulnerable adults.

(https://jamanetwork.com/journals/jama/fullarticle/2708121. Last accessed July 26, 2022.)

Strength of Recommendation: I (Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.)

MEN

Statistics confirm that domestic violence is predominantly perpetrated by men against women; however, there is evidence that women also exhibit violent behavior against their male partners [4]. Studies demonstrate approximately 5% of homicides against men are perpetrated by intimate partners [36]. It is persuasively argued that the impact on the health of female victims of domestic violence is generally much more severe than the impact on the health of male victims [42]. Approximately 512,770 women were raped and/or physically assaulted by an intimate partner in 2008, compared to 101,050 men [58]. In addition, 1 in 4 women has been physically assaulted, raped, and/or stalked by an intimate partner, compared with 1 out of every 10 men [1]. Rape, non-contact unwanted sexual experiences, and stalking against men are primarily perpetrated by other men, while other forms of violence against men were perpetrated mostly by women [5]. Male victims of IPV experienced 3 victimizations per 1,000 boys and men 12 years of age or older in 1994, and this rate decreased by 64%, to 1.1 per 1,000, in 2010 [11]. Of all homicides committed against men between 1980 and 2008, 7.1% were committed by an intimate partner [36]. Although women are more often victims of IPV, healthcare professionals should always keep in mind that men can also be victimized and assess accordingly.

LESBIAN, GAY, BISEXUAL, TRANSGENDER, AND QUEER/QUESTIONIONG VICTIMS

Domestic violence exists in lesbian, gay, bisexual, transgender, and queer/questioning (LGBTQ+) communities, and the rates are thought to mirror those of heterosexual women—approximately 25% [43]. However, women living with female intimate partners experience less IPV than women living with men [8]. Conversely, men living with male intimate partners experience more IPV than do men who live with female intimate partners [8]. In addition, 78% of IPV homicide victims reported in 2017 were transgender women or cisgender men [24]. This supports other statistics indicating that IPV is perpetrated primarily by men. A form of abuse specific to the gay community is for an abuser to threaten or to proceed with "outing" a partner to others [41; 43].

Transgender individuals appear to be at particular risk for violence. According to a large national report, transgender victims of IPV were 1.9 times more likely to experience physical violence and 3.9 times more likely to experience discrimination than other members of the LGBTQ+ community [24].

In 2017, an annual national report recorded 52 incidences of hate violence-related homicides of LGBTQ+ people, the highest incident number recorded in its 20-year history [24]. This increasing prevalence of anti-LGBTQ+ violence can exacerbate IPV in LGBTQ+ communities. For example, a person who loses their job because of anti-trans bias may be more financially reliant on an unhealthy relationship. An abusive partner may also use the violence that an LGBTQ+ person experiences from their family as a way of isolating that person further [24].

Because of the stigma of being LGBTQ+, victims may be reticent to report abuse and afraid that their sexual orientation or biologic sex will be revealed. In one study, the three major barriers to seeking help were a limited understanding of the problem of LGBTQ+ IPV, stigma, and systemic inequities [41]. Many in this community feel that support services (e.g., shelters, support groups, crisis hotlines) are not available to them due to homophobia of the service providers. Unfortunately, this results in the victim feeling isolated and unsupported. Healthcare professionals should strive to be sensitive and supportive when working with homosexual patients.

CHARACTERISTICS OF PERPETRATORS OF DOMESTIC VIOLENCE

Abuser characteristics have been studied far less frequently than victim characteristics. Some studies suggest a correlation between the occurrence of abuse and the consumption of alcohol. A man who abuses alcohol is also likely to abuse his mate, although the abuser may not necessarily be inebriated at the time the abuse is inflicted [44]. Domestic violence assessment questionnaires should include questions that explore social drinking habits of both victims and their mates.

Other studies demonstrate that abusive mates are generally possessive and jealous. Another characteristic related to the abuser's dependency and jealousy is extreme suspiciousness. This characteristic may be so extreme as to border on paranoia [12]. Domestic violence victims frequently report that abusers are extremely controlling of the everyday activities of the family. This domination is generally all encompassing and often includes maintaining complete control of finances and activities of the victim (e.g., work, school, social interactions) [12].

In addition, abusers often suffer from low self-esteem and their sense of self and identity is directly connected to their partner [12]. Extreme dependence is common in both abusers and those being abused. Due to low self-esteem and self-worth, emotional dependence often occurs in both partners, but even more so in the abuser. Emotional dependence in the victim stems from both physical and psychologic abuse, which results in a negative self-image and lack of self-worth. Financial dependence is also very common, as the abuser often withholds or controls financial resources to maintain power over the victim [1; 4].

SCREENING FOR DOMESTIC VIOLENCE AND ABUSE

There is no universal guideline for identifying and responding to domestic violence, but it is universally accepted that a plan for screening, assessing, and referring patients of suspected abuse should be in place at every healthcare facility. Guidelines should review appropriate interview techniques for a given setting and should also include the utilization of assessment tools. Furthermore, protocols within each facility or healthcare setting should include referral, documentation, and follow-up. This section relies heavily on the guidelines outlined in the Family Violence Prevention Fund's *National Consensus Guidelines on Identifying and Responding to Domestic Violence Victimization in Health Care Settings*; however, protocols should be customized based on individual practice settings and resources available [35]. The CDC has provided a compilation of assessment tools for healthcare workers to assist in recognizing and accurately interpreting behaviors associated with domestic violence and abuse, which may be accessed at https://www.cdc.gov/violenceprevention/pdf/ipv/ipvandsvscreening.pdf [45].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The U.S. Preventive Services Task Force recommends that that clinicians screen for intimate partner violence (IPV) in women of reproductive age and provide or refer women who screen positive to ongoing support services.

(https://jamanetwork.com/journals/jama/fullarticle/2708121. Last accessed July 26, 2022.)

Strength of Recommendation: B (There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.)

Several barriers to screening for domestic violence have been noted, including a lack of knowledge and training, time constraints, lack of privacy for asking appropriate questions, and the sensitive nature of the subject [35]. Although awareness and assessment for IPV has increased among healthcare providers, many are still hesitant to inquire about abuse [46]. At a minimum, those exhibiting signs of domestic violence should be screened. Although victims of IPV may not display typical signs and symptoms when they present to healthcare providers, there are certain cues that may be attributed to abuse. The obvious cues are physical. Injuries range from bruises, cuts, black eyes, concussions, broken bones, and miscarriages to permanent injuries such as damage to joints, partial loss of hearing or vision, and scars from burns, bites, or knife wounds. Typical injury patterns include contusions or minor lacerations to the head, face, neck, breast, or abdomen and musculoskeletal injuries. These are often distinguishable from accidental injuries, which are more likely to involve the extremities of the body. Abuse victims are also more likely to have multiple injuries than accident victims. When this pattern of injuries is seen, particularly in combination with evidence of old injury, physical abuse should be suspected [44].

In addition to physical signs and symptoms, domestic violence victims also exhibit psychologic cues that resemble an agitated depression. As a result of prolonged stress, various psychosomatic symptoms that generally lack an organic basis often manifest. For example, complaints of backaches, headaches, and digestive problems are common. Often, there are reports of fatigue, restlessness, insomnia, or loss of appetite. Great amounts of anxiety, guilt, and depression or dysphoria are also typical. Women who experienced IPV are also more likely to report asthma, irritable bowel syndrome, and diabetes [4]. Healthcare professionals should look beyond the typical symptoms of a domestic violence victim and work within their respective practice settings to develop appropriate assessment mechanisms to detect victims who exhibit less obvious symptoms.

The unique relationship dynamics of the abuser and abused are not easily detected under the best of circumstances. They may be especially difficult to uncover in circumstances in which the parties are suspicious and frightened, as might be expected when a victim presents to the emergency department. The key to detection, however, is to establish a proper assessment tool that can be utilized in the particular setting and to maintain a keen awareness for the cues described in this course. Screening for IPV should be carried out at the entry points of contact between victims and medical care (e.g., primary care, emergency services, obstetric and gynecologic services, psychiatric services, and pediatric care) [35].

The key to an initial assessment is to obtain an adequate history. Establishing that a patient's injuries are secondary to abuse is the first task. Clearly, there will be times when a victim is injured so severely that treatment of these injuries becomes the first priority. After such treatment is rendered, however, it is important that healthcare professionals not ignore the reasons that brought the victim to the emergency department [35].

ASSESSING DOMESTIC VIOLENCE AND ABUSE

Healthcare providers have reported that even if routine screening and inquiry results in a positive identification of IPV, the next steps of assessing and referring are often difficult, and many feel that they are not adequately prepared [46]. According to the Family Violence Prevention Fund, the goals of the assessment are to create a supportive environment, gather information about health problems associated with the abuse, and assess the immediate and long-term health and safety needs for the patient to develop an intervention [35].

ASSESSMENT OF IMMEDIATE SAFETY FOR DOMESTIC VIOLENCE VICTIMS
Are you in immediate danger?
Is your partner at the health facility now?
Do you want to (or have to) go home with your partner?
Do you have somewhere safe to go?
Have there been threats or direct abuse of the child(ren) (if applicable)?
Are you afraid your life may be in danger?
Has the violence gotten worse or is it getting scarier? Is it happening more often?
Has your partner used weapons, alcohol, or drugs?
Has your partner ever held you or your child(ren) against your will?
Does your partner ever watch you closely, follow you or stalk you?
Has your partner ever threatened to kill you, him/herself or your child(ren)?
Source: [35] *Table 1*

Assessment of domestic violence victims should occur immediately after disclosure of abuse and at any follow-up appointments. Assessing immediate safety is priority. Having a list of questions readily available and well-practiced can help alleviate the uncertainty of how to begin the assessment (***Table 1***). If the patient is in immediate danger, referral to an advocate, support system, hotline, or shelter is indicated [35].

If the patient is not in immediate danger, the assessment may continue with a focus on the impact of IPV on the patient's mental and physical health and the pattern of history and current abuse [35]. These responses will help formulate an appropriate intervention.

CULTURALLY SENSITIVE ASSESSMENT

During the assessment process, a practitioner should be open and sensitive to the patient's worldview, cultural belief systems and how he/she views the illness [47]. This may reduce the tendency to over-pathologize or minimize health concerns of ethnic minority patients.

Pachter proposed a dynamic model that involves several tiers and transactions [48]. The first component of Pachter's model calls for the practitioner to take responsibility for cultural awareness and knowledge. The professional should be willing to acknowledge that he/she does not possess enough or adequate knowledge in health beliefs and practices among the different ethnic and cultural groups he/she comes in contact with. Reading and becoming familiar with medical anthropology is a good first step.

The second component emphasizes the need for specifically tailored assessment [48]. Pachter advocates the notion that there is tremendous diversity within groups. For example, one cannot automatically assume that a Cuban immigrant adheres to traditional beliefs. Often, there are many variables, such as level of acculturation, age at immigration, educational level, and socioeconomic status, that influence health ideologies. Finally, the third component involves a negotiation process between the patient and the professional [48]. The negotiation consists of a dialogue that involves a genuine respect of beliefs. It is important to remember that these beliefs may affect symptoms or appropriate interventions in the case of domestic violence.

Culturally sensitive assessment involves a dynamic framework whereby the practitioner engages in a continual process of questioning. By incorporating cultural sensitivity into the assessment of individuals with a history of being victims or perpetrators of domestic violence, it may be possible to intervene and offer treatment more effectively.

INTERVENTIONS FOR DOMESTIC VIOLENCE AND ABUSE

After the assessment is complete, the patient may or may not want immediate assistance or referral. It is important for healthcare providers to assure patients in a nonjudgmental manner that the decision of what they would like in terms of assistance is their choice and that the provider will help regardless of the decisions they are currently ready to make [35].

If the patient would like to immediately implement a plan of action, information for referral to a local domestic violence shelter to assist the victim and the victim's family should be readily available. The acute situation should be referred immediately to local law enforcement officials. Other resources in an acute situation include crisis hotlines and rape relief centers. After a victim is introduced into the system, counseling and follow-up are generally available by individual counselors who specialize in the care of battered women and their spouses and children. These may include social workers, psychologists, psychiatrists, other mental health workers, and community

mental health services. The goals are to make the resources accessible and safe and to enhance support for those who are unsure of their options [35].

In Florida, a 24-hour domestic violence hotline is available for toll-free counseling and information. The number is 800-500-1119. The counselors answering the toll-free line may refer the victim to her or his local domestic violence center. A list of Florida certified domestic violence centers organized by county may also be found on the Florida Department of Children and Families website at https://www.myflfamilies.com/service-programs/domestic-violence. Florida's domestic violence centers provide information and referral services, counseling and case management services, a 24-hour hotline, temporary emergency shelter for more than 24 hours, educational services for community awareness relative to domestic violence, assessment and appropriate referral of resident children, and training for law enforcement personnel.

DOCUMENTATION AND FOLLOW-UP

It is imperative that healthcare professionals document all findings and recommendations regarding domestic violence in the victim's medical record, including a patient's denial of abuse, if applicable. If domestic violence is disclosed, documentation should include relevant history, results of the physical examination, findings of laboratory and other diagnostic procedures, and results of the assessment, intervention, and referral. The medical record can be an invaluable document in establishing the credibility of the victim's story when seeking legal aid [35].

Healthcare professionals should offer a follow-up appointment if disclosure of past or current abuse is present. Reassurance that assistance is available to the patient at any time is critical in helping to break the cycle of abuse [35].

FACULTY BIOGRAPHIES

Marjorie Conner Allen, BSN, JD, received her Bachelor of Science in Nursing degree from the University of Florida, Gainesville, in 1984. She began her nursing career at Shands Teaching Hospital and Clinics at the University of Florida, Gainesville. While practicing nursing at Shands, she gave continuing education seminars regarding the nursing implications for dealing with adolescents with terminal illness. In 1988, Ms. Allen moved to Atlanta, Georgia where she worked at Egleston Children's Hospital at Emory University in the bone marrow transplant unit. In the fall of 1989, she began law school at Florida State University. After graduating from law school in 1992, Ms. Allen took a two-year job as law clerk to the Honorable William Terrell Hodges, United States District Judge for the Middle District of Florida. After completing her clerkship, Ms. Allen began her employment with the law firm of Smith, Hulsey & Busey in Jacksonville, Florida where she has worked in the litigation department defending hospitals and nurses in medical malpractice actions. Ms. Allen resides in Jacksonville and is currently in-house counsel to the Mayo Clinic Jacksonville.

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families.

Previously acting as a faculty member at Capella University and Northcentral University, Dr. Yick Flanagan is currently a contributing faculty member at Walden University, School of Social Work, and a dissertation chair at Grand Canyon University, College of Doctoral Studies, working with Industrial Organizational Psychology doctoral students. She also serves as a consultant/subject matter expert for the New York City Board of Education and publishing companies for online curriculum development, developing practice MCAT questions in the area of psychology and sociology. Her research focus is on the area of culture and mental health in ethnic minority communities.

Customer Information/Answer Sheet/Evaluation insert located between pages 60–61.

COURSE TEST - #57923 DOMESTIC VIOLENCE: THE FLORIDA REQUIREMENT

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 CE Credit Hour activity must be completed by July 31, 2025.

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10/1/2021 to 9/30/2027
Provider ID #217994.

DESIGNATIONS OF CREDIT: NetCE DESIGNATES THIS ACTIVITY FOR 2 CONTINUING EDUCATION CREDITS.
AGD SUBJECT CODE: 156.

1. **Most healthcare professionals will encounter patients in their practice who are victims of domestic violence.**
   A) *True*
   B) *False*

2. **The Florida Department of Children and Families' definition of domestic violence may include pet abuse, physical abuse, and/or emotional abuse.**
   A) *True*
   B) *False*

3. **Florida law defines domestic violence exclusively as spouse abuse or battering.**
   A) *True*
   B) *False*

4. **House Bill 1099 strengthened domestic violence services by streamlining the process of allocating funds.**
   A) *True*
   B) *False*

5. **Domestic violence resulted in 217 deaths in Florida in 2020.**
   A) *True*
   B) *False*

6. **The majority of children exposed to intimate partner violence are direct eyewitnesses.**
   A) *True*
   B) *False*

7. **Domestic violence injury patterns are more likely than accidental injuries to involve the extremities of the body.**
   A) *True*
   B) *False*

8. **In addition to physical signs and symptoms, domestic violence victims may also exhibit psychologic cues that resemble an agitated depression.**
   A) *True*
   B) *False*

9. **Assessment of domestic violence victims should occur immediately after disclosure of abuse and at any follow-up appointments.**
   A) *True*
   B) *False*

10. **Florida does not presently have a toll-free domestic violence hotline, although this was a recommendation of the Governor's Task Force on Domestic Violence.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet located on the envelope insert.
DO NOT send these test pages to NetCE. Retain them for your records.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Strategies for Appropriate Opioid Prescribing: The Florida Requirement

This course is board approved to fulfill the Florida requirement for 2 hours of Controlled Substance education for dentists.

Dental hygienists, you may complete this course for general hours or skip this course and still receive 22 hours of CE.

Audience

This course is designed for all dental professionals who may alter prescribing practices or intervene to prevent drug diversion and inappropriate opioid use.

Course Objective

The purpose of this course is to provide dental professionals who prescribe or distribute opioids with an appreciation for the complexities of opioid prescribing and the dual risks of litigation due to inadequate pain control and drug diversion or misuse in order to provide the best possible patient care and to prevent a growing social problem.

Learning Objectives

Upon completion of this course, you should be able to:

1. Define opioid prescribing and opioid misuse.
2. Apply epidemiologic trends in opioid use and misuse to current practice so at-risk patient populations can be more easily identified, assessed, and treated.
3. Create comprehensive treatment plans for patients with chronic pain that address patient needs as well as drug diversion prevention.
4. Identify state and federal laws governing the proper prescription and monitoring of controlled substances.
5. Evaluate behaviors that may indicate drug seeking or diverting as well as approaches for patients suspected of misusing opioids.

Faculty

Mark Rose, BS, MA, LP, is a licensed psychologist in the State of Minnesota with a private consulting practice and a medical research analyst with a biomedical communications firm. Earlier healthcare technology assessment work led to medical device and pharmaceutical sector experience in new product development involving cancer ablative devices and pain therapeutics. Along with substantial experience in addiction research, Mr. Rose has contributed to the authorship of numerous papers on CNS, oncology, and other medical disorders. He is the lead author of papers published in peer-reviewed addiction, psychiatry, and pain medicine journals and has written books on prescription opioids and alcoholism published by the Hazelden Foundation. He also serves as an Expert Advisor and Expert Witness to law firms that represent disability claimants or criminal defendants on cases related to chronic pain, psychiatric/substance use disorders, and acute pharmacologic/toxicologic effects. Mr. Rose is on the Board of Directors of the Minneapolis-based International Institute of Anti-Aging Medicine and is a member of several professional organizations.

Faculty Disclosure

Contributing faculty, Mark Rose, BS, MA, LP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner

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Division Planner/Director Disclosure

The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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NetCE is approved as a provider of continuing education by the Florida Board of Dentistry, Provider #50-2405.

Designations of Credit

NetCE designates this activity for 2 continuing education credits.

AGD Subject Code 200.

Special Approvals

This course is approved by the Florida Board of Dentistry to fulfill the Florida requirement for 2 hours on the safe and effective prescribing of controlled substance medications.

About the Sponsor

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Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the study questions and course material for better application to your daily practice.

INTRODUCTION

Pain is the leading reason for seeking medical care, and pain management is a large part of many healthcare professionals' practice. Opioid analgesics are approved by the U.S. Food and Drug Administration (FDA) for moderate and severe pain and are broadly accepted in acute pain, cancer pain, and end-of-life care, but are controversial in chronic noncancer pain. In response to the long-standing neglect of severe pain, indications for opioid analgesic prescribing were expanded in the 1990s, followed by inappropriate prescribing and increasing abuse, addiction, diversion, and overdose through the 2000s. In tandem with the continued under-treatment of pain, these practice patterns led to needless suffering from uncontrolled pain, opioid analgesic addiction, and overdose. Opioid analgesic prescribing and associated overdose peaked in 2011 with both now in multi-year decline, but information on these important trends is largely absent in the medical literature and media reporting.

Patients show substantial opioid response variations in analgesia and tolerability and may exhibit a range of psychologic, emotional, and behavioral responses that reflect inadequate pain control, an emerging opioid use problem, or both. Clinician delivery of best possible care to patients with pain requires appreciation of the complexities of opioid prescribing and the dual risks of inadequate pain control and inappropriate use, drug diversion, or overdose. A foundation for appropriate opioid prescribing is the understanding of factual data that clarify the prevalence, causality, and prevention of serious safety concerns with opioid prescribing.

DEFINITIONS

Definitions and use of terms describing opioid analgesic misuse, abuse, and addiction have changed over time, and their current correct use is inconsistent not only among healthcare providers, but also by federal agencies reporting epidemiologic data, such as prevalence of opioid analgesic misuse, abuse, or addiction. Misuse and misunderstanding of these concepts and their correct definitions have resulted in misinformation and represent an impediment to proper patient care.

Inappropriate opioid analgesic prescribing for pain is defined as the non-prescribing, inadequate prescribing, excessive prescribing, or continued prescribing despite evidence of ineffectiveness of opioids [1]. Appropriate opioid prescribing is essential to achieve pain control; to minimize patient risk of abuse, addiction, and fatal toxicity; and to minimize societal harms from diversion. The foundation of appropriate opioid prescribing is thorough patient assessment, treatment planning, and follow-up and monitoring. Essential for proper patient assessment and treatment planning is comprehension of the clinical concepts of opioid abuse and addiction, their behavioral manifestations in patients with pain, and how these potentially problematic behavioral responses to opioids both resemble and differ from physical dependence and pseudo-addiction. Prescriber knowledge deficit has been identified as a key obstacle to appropriate opioid prescribing and, along with gaps in policy, treatment, attitudes, and research, contributes to widespread inadequate treatment of pain [2]. For example, a 2013 survey measuring 200 primary care physicians' understanding of opioids and addiction found that [3]:

- 35% admitted knowing little about opioid addiction.
- 66% and 57% viewed low levels of education and income, respectively, as causal or highly contributory to opioid addiction.
- 30% believed opioid addiction "is more of a psychologic problem," akin to poor lifestyle choices rather than a chronic illness or disease.
- 92% associated prescription analgesics with opioid addiction, but only 69% associated heroin with opioid addiction.
- 43% regarded opioid dependence and addiction as synonymous.

This last point is very important because confusion and conflation of the clinical concepts of dependence and addiction has led to accusations of many non-addicted patients with chronic pain of misusing or abusing their prescribed opioid and in the failure to detect treatment-emergent opioid problems [4]. Knowledge gaps concerning opioid analgesics, addiction, and pain are related to attitude gaps, and negative attitudes may interfere with appropriate prescribing of opioid analgesics. For example, when 248 primary care physicians were asked of their prescribing approach in patients with headache pain with either a past or current history of substance abuse, 16% and 42%, respectively, would not prescribe opioids under any circumstance [5]. Possibly contributing to healthcare professionals' knowledge deficit in pain treatment is the extent of educational exposure in school. A 2011 study found that U.S. medical school students received a median seven hours of pain education and Canadian medical students a median 14 hours, in contrast to the median 75 hours received by veterinarian school students in the United States [6].

The terms related to addiction are often inconsistent, inaccurate, and confusing, partially reflecting the diverse perspectives of those working in the related fields of health care, law enforcement, regulatory agencies, and reimbursement/payer organizations. Changes over time in the fundamental understanding of addiction have also contributed to the persistent misuse of obsolete terminology [7]. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM), published by the American Psychiatric Association, is the standard reference for the diagnosis of addiction and all other psychiatric disorders. Prior to the 2013 release of the DSM-5, versions of the DSM eschewed the term "addiction" in favor of "substance dependence," with a separate diagnostic entity of "substance abuse" representing a less severe version of dependence [8]. Also in earlier DSM versions, physiologic dependence, manifesting as substance tolerance and withdrawal, was considered a diagnostic criterion of substance dependence. The result was the perpetuation of patient and healthcare professional confusion between physical and substance dependence and the belief that tolerance and withdrawal meant addiction. This confusion also enhanced provider and patient fears over addiction developing from opioid analgesics and contributed to the undertreatment of pain [9]. The DSM-5 has eliminated substance dependence and substance abuse by combining them into the single diagnostic entity of substance use disorder. The disorder is measured on a continuum from mild to severe [8].

In 2011, the American Society of Addiction Medicine (ASAM) published their latest revision in defining the disease of addiction. In 2018, ASAM's board recognized the need for an updated definition of addiction that would be more accessible to its stakeholder groups, including patients, the media, and policymakers. Accordingly, the Board appointed a Task Force that revised the definition of addiction for use in ASAM's policy statements. The revised definition states that [10]:

> Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

EPIDEMIOLOGY OF CHRONIC PAIN AND OPIOID MISUSE

Chronic pain affects about 100 million American adults—more than the total affected by heart disease, cancer, and diabetes combined [2]. It also costs the nation up to $635 billion each year in medical treatment and lost productivity and is the leading reason for receiving disability insurance [3; 11]. The lifetime prevalence of chronic pain ranges from 54% to 80%, and among adults 21 years of age and older, 14% report pain lasting 3 to 12 months and 42% report pain that persists longer than one year [2]. While 5 to 8 million Americans receive long-term opioids for the management of chronic pain, an estimated 41% of patients with chronic pain report their pain is uncontrolled, and 10% of all adults with pain suffer from severe, disabling chronic pain [11].

The increasing prevalence of chronic pain is the result of multiple factors, including the aging population; rising rates of obesity and obesity-related pain conditions, such as joint deterioration; advances in life-saving trauma interventions; poorly managed post-surgical pain; and greater public awareness of pain as a condition warranting medical attention [2]. In addition, many armed forces veterans have been returning from military action in Afghanistan and Iraq with traumatic injuries and chronic pain, and veterans' care clinicians have been reporting the perception that long-term pain management is lacking support in the veteran healthcare infrastructure [12].

There is a widespread misperception that opioid analgesic prescribing and overdose continues to grow, fueling an opioid epidemic [13; 14; 15; 16; 17]. This is refuted by the following data showing that national opioid analgesic prescribing and overdose peaked in 2011 and are in multiyear decline.

According to a 2019 report from the National Forensic Laboratory Information System (NFLIS), prescription reports for hydrocodone increased dramatically from 2001 to 2010, but then steadily decreased through 2019. Oxycodone reports increased steadily from 2001 to 2004, and again from 2006 to 2010, and then steadily declined through 2019 [18]. Methadone prescribing data were not captured in the report.

Opioid analgesic-associated overdose fatalities have also decreased since 2011, despite published Centers for Disease Control and Prevention (CDC) data reporting a sharp rise in opioid analgesic fatalities in 2014 [19]. This increase was the result of the CDC adding clandestine fentanyl fatalities to figures for prescription opioids in 2014, a difference of more than 4,000 fatalities [20]. The CDC acknowledged this and presented revised 2014 figures with clandestine fentanyl overdoses removed, which supports the belief that opioid analgesic-associated overdose fatalities peaked in 2011 [21; 22; 23]:

- 2011: 16,917 fatalities
- 2013: 16,235 fatalities
- 2014: 14,000 fatalities

In addition, some heroin overdose fatalities are misclassified as morphine fatalities. The metabolite unique to heroin, 6-monoacetylmorphine (6-MAM), quickly breaks down into morphine, and medical examiners may be reluctant to label a death heroin-related without 6-MAM present [24]. In 2014, fatal heroin overdoses increased 26% from 2013, and heroin deaths mistakenly attributed to morphine may also have increased during this period [19].

Opioid analgesic prescribing in the United States has declined from the 2011 peak but remains substantially higher than 1990. Before 1990, physicians seldom prescribed opioids for chronic noncancer pain. By the mid-2000s, 1 of 25 adults was prescribed an opioid for chronic pain, and annual opioid analgesic sales totaled more than $9 billion [25]. There is nearly universal agreement that opioid analgesics were injudiciously overprescribed during the 2000s. Interpretation of the broader trend of increased prescribing from 1990 might be viewed by public health professionals as entirely problematic and by pain medicine professionals as necessary in part, given the past neglect of patients in pain. This reflects the polarized nature of pain care and opioid analgesic prescribing in particular. Efforts to reduce opioid analgesic overprescribing and associated overdose have been successful but have come at a cost to patients who have faced increasing barriers to access, including stigma and abuse in a healthcare system, tapering of opioids without consideration for pain or functional improvements, and difficulty finding a physician [14; 26].

Worldwide consumption of opioid analgesics has increased dramatically in the past few decades, driven primarily by U.S. consumption. For example, the global consumption of oxycodone was 3 tons (2,722 kg) in 1990 and 77 tons (69,853 kg) in 2009, with 62 tons (81%) consumed in the United States [25]. In 2010, the United States had 4.5% of the world population but consumed 80% of global opioid supplies and 99% of hydrocodone supplies [27]. This is partially because access to opioid analgesics is virtually or entirely non-existent for 5.8 billion people worldwide (80%) and highly restricted for 4.1% of the world population [28]. Other countries with adequate opioid access prefer dihydrocodeine or low-dose morphine over hydrocodone for use in moderate or moderately severe pain [29].

Many prescribed opioid analgesic fatalities result from the co-ingestion central nervous system (CNS)/respiratory depressants (especially benzodiazepines) or prescribed methadone. According to the National Institute on Drug Abuse (NIDA), deaths involving benzodiazepines rose from 1,135 in 1999 to 11,537 in 2017. In 2019, 16% of persons who died of an opioid overdose also tested positive for benzodiazepines [30;

31]. A Canadian study evaluated 607,156 adults prescribed opioids for noncancer pain, and of those whose deaths were related to opioids, co-prescribed benzodiazepines were detected in 84.5% [32]. In another study of 2,182,374 North Carolina residents receiving one or more opioid analgesics in 2010, benzodiazepines were present in 61.4% who fatally overdosed [33]. This is significant considering that dispensed benzodiazepine prescriptions increased 226% between 2009 and 2014 [34]. Additionally, many users obtain benzodiazepines by getting prescriptions from more than one doctor, forging prescriptions, or buying the drugs illicitly. Alprazolam and clonazepam are the two most frequently encountered benzodiazepines on the illicit market [18].

OPIOID MISUSE IN FLORIDA

In Florida, misuse of prescription opioids became a serious problem in the 1990s and 2000s, but efforts to stem the problem appear to be working. The rate of drug overdose deaths increased 58.9% during 2003–2010, and in 2009, one in eight deaths in Florida was attributable to drug overdose [35; 36]. On average, from 2017 to 2019, opioids accounted for 79.4% of fatal drug overdoses [35]. In 2015, Florida experienced an increase in oxycodone-caused deaths, the first in six years [35]. These trends resulted in the enactment of several measures to address prescribing that was inconsistent with best practices, and partnership with the U.S. Drug Enforcement Administration (DEA) to close and prevent "pill mills" from introducing millions of opioid dose units into illicit markets [37; 38]. In May 2017, Governor Rick Scott signed an executive order declaring the opioid epidemic a public health emergency, providing additional funding and empowering state health professions to take steps to address this pressing issue [38]. As part of this order, the State Health Officer has issued a standing order for opioid antagonists to ensure emergency responders have access [38]. The order has been extended several times and, as of August 2021, it is still in place.

Drug overdose fatalities in Florida have continued rising from increased use of heroin, synthetic cannabinoids, and novel psychoactive substances such as alpha-PVP ("flakka"). An influx of clandestine fentanyl into Florida in early 2014, and several fentanyl analogs and other novel non-pharmaceutical opioids more recently, has largely driven the increases in opioid overdose fatalities. Analyses of data from 2013–2015 indicate sharp increases in overdose fatalities in Florida linked to counterfeit alprazolam, oxycodone, and hydrocodone tablets that contained fentanyl [39]. The decrease in prescription opioid fatalities, offset by increasing overdose fatalities from other opioid and non-opioid agents, reflects the intervention focus on the supply side ("pill mill laws") and neglect of treatment funding that would address the demand side of problematic drug use [40].

In Florida, fatalities with benzodiazepines present peaked in 2010 with 6,188, falling to 2,182 in 2020 (38% were alprazolam) [41]. Other primary contributors to opioid analgesic-related fatalities include alcohol and prescribed methadone [30; 42].

In addition to the executive order issued in 2017, several new state laws were passed in 2018 to impose additional legal requirements on controlled substance prescribers [43]. These laws will be discussed in detail later in this course.

INITIATION AND MANAGEMENT OF THE PATIENT WITH PAIN

In 2016, the CDC issued updated opioid prescribing guidelines for chronic pain that address when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use [44]. In addition, the CDC further updated guidance against the misapplication of this guideline in 2019, noting that some policies and practices attributed to the guideline were inconsistent with the recommendations [45]. Some of the recommendations are standard risk mitigation approaches, but others have been criticized by pain medicine physicians and patient advocates. A common criticism is the sole focus on curtailing prescribing and patient access [46; 47; 48; 49].

It can be difficult to balance the benefits and harms of prescription opioids. This is exacerbated by inadequate education and by opioid prescribing guidelines based on expert opinion instead of scientific evidence. This has resulted in wide variation in clinical practice, inconsistent prescriber guidance, and clinician confusion [50]. For instance, the CDC and other opioid guidelines state that opioids should be considered only after non-opioid therapy fails. However, when pain is severe and patients require powerful analgesic control, there is little choice because no other pain medications are as effective as opioids with lower addiction risk [51].

However, many guidelines do share common recommendations. These represent the current "conventional wisdom" in opioid analgesic prescribing and can inform healthcare professionals of the best clinical practices in opioid prescribing that include approaches to the assessment of pain and function and pain management modalities. Pharmacologic and nonpharmacologic approaches should be used on the basis of current evidence or best clinical practice. Patients with moderate-to-severe chronic pain without adequate pain relief from non-opioid or nonpharmacologic therapy can be considered for a trial of opioid therapy [44; 52]. Initial treatment should always be considered individually determined and as a trial of therapy, not a definitive course of treatment [53].

ACUTE PAIN

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids in a quantity no greater than that needed for the expected duration of severe pain. In most cases, three days or less will be sufficient; more than seven days will rarely be needed [44]. Florida law dictates that, for the treatment of acute pain, a prescription for an opioid drug may not exceed a three-day supply; an exception may be made for a seven-day supply if [54]:

- The prescriber, in his or her professional judgment, believes that more than a three-day supply of such an opioid is medically necessary to treat the patient's pain as an acute medical condition.
- The prescriber indicates "ACUTE PAIN EXCEPTION" on the prescription. (For the treatment of pain other than acute pain, a practitioner must indicate "NON-ACUTE PAIN" on a prescription.)
- The prescriber adequately documents in the patient's medical records the acute medical condition and lack of alternative treatment options that justify deviation from the three-day supply limit.

With postoperative, acute, or intermittent pain, analgesia often requires frequent titration, and the two- to four-hour analgesic duration with short-acting hydrocodone, morphine, and oxycodone is more effective than extended-release formulations. Short-acting opioids are also recommended in patients who are medically unstable or with highly variable pain intensity [55; 56; 57].

As part of House Bill 21, passed in 2018, the Florida Board of Medicine and the Board of Osteopathic Medicine are required to establish guidelines for prescribing controlled substances for acute pain; these guidelines are forthcoming [54].

PATIENT EVALUATION AND ASSESSMENT OF ADDICTION RISK

Information obtained by patient history, physical examination, and interview, from family members, a spouse, or state prescription drug monitoring program (PDMP), and from the use of screening and assessment tools can help the clinician to stratify the patient according to level of risk for developing problematic opioid behavioral responses (***Table 1***). Low-risk patients receive the standard level of monitoring, vigilance, and care. Moderate-risk patients should be considered for an additional level of monitoring and provider contact, and high-risk patients are likely to require intensive and structured monitoring and follow-up contact, additional consultation with psychiatric and addiction medicine specialists, and limited supplies of short-acting opioid formulations [44; 58].

Anxiety disorders, major depressive disorder, and intense emotional distress alter pain perception and response. Intensity and perception of reported pain is also influenced by factors such as mood, cultural background, social supports, and financial resources. A biopsychosocial model is required to inform pain assessment in order to address the biologic basis of pain and presence of social and psychologic contributors [51].

Before deciding to prescribe an opioid analgesic, clinicians should perform and document a detailed patient assessment that includes [1]:

- Pain indications for opioid therapy
- Nature and intensity of pain
- Past and current pain treatments and patient response
- Comorbid conditions
- Pain impact on physical and psychologic function
- Social support, housing, and employment
- Home environment (i.e., stressful or supportive)
- Pain impact on sleep, mood, work, relationships, leisure, and substance use
- Patient history of physical, emotional, or sexual abuse

Depression is perhaps the single most important comorbidity in patients with chronic pain and is vastly underdiagnosed and untreated. Patients with unrecognized and untreated depression are unlikely to respond to opioids and other pain therapies, but successful treatment of depression can promote analgesia [62].

If substance abuse is active, in remission, or in the patient's history, consult an addiction specialist before starting opioids [1]. In active substance abuse, do not prescribe opioids until the patient is engaged in a treatment/recovery program or other arrangements made, such as addiction professional co-management and additional monitoring. When considering an opioid analgesic (particularly those that are extended-release or long-acting), one must always weigh the benefits against the risks of overdose, abuse, addiction, physical dependence and tolerance, adverse drug interactions, and accidental exposure by children [44; 63].

Screening and assessment tools can help guide patient stratification according to risk level and inform the appropriate degree of structure and monitoring in the treatment plan. It should be noted that despite widespread endorsement of screening tool use to help determine patient risk level, most tools have not been extensively evaluated, validated, or compared to each other, and evidence of their reliability is poor [64].

RISK STRATIFICATION FOR PATIENTS PRESCRIBED OPIOIDS
Low Risk
No or well-defined and controlled personal or family history of alcohol/substance use disorder No or minimal co-occurring psychiatric disorders or medical comorbidities Age 45 years or older High levels of pain acceptance and active coping strategies High motivation and willingness to participate in multimodal therapy, attempting to function at normal levels
Medium Risk
Moderate concomitant psychiatric disorders, well controlled by therapy Moderate coexisting medical disorders well-controlled by medical therapy and not affected by chronic opioid therapy (e.g., central sleep apnea) History of personal or family alcoholism/substance abuse/addiction Willing to participate in multimodal therapy, attempting to function in normal daily life Pain involving more than three regions of the body
High Risk
Widespread pain without objective signs and symptoms Pain involving more than three regions of the body Aberrant drug-related behavior History of alcoholism or drug misuse, abuse, addiction, diversion, dependency, tolerance, or hyperalgesia Major psychologic disorders Age younger than 45 years Unwilling to participate in multimodal therapy, not functioning close to a near normal lifestyle
Source: [1; 59; 60; 61] — *Table 1*

Despite limited evidence for reliability and accuracy, screening for opioid use is recommended by the American Society of Interventional Pain Physicians, as it will identify opioid abusers and reduce opioid abuse.

(https://painphysicianjournal.com/2012/july/2012;%2015;S67-S116.pdf. Last accessed August 19, 2021.)

Level of Evidence: Limited (Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.)

Opioid Risk Tool (ORT)

The Opioid Risk Tool (ORT) is a five-item assessment to help predict aberrant drug-related behavior. The ORT is also used to establish patient risk level through categorization into low, medium, or high levels of risk for aberrant drug-related behaviors based on responses to questions of previous alcohol/drug abuse, psychologic disorders, and other risk factors [65; 66].

Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)

The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) is a patient-administered, 24-item screen with questions addressing history of alcohol/substance use, psychologic status, mood, cravings, and stress. Like the ORT, the SOAPP-R helps assess risk level of aberrant drug-related behaviors and the appropriate extent of monitoring [67; 68].

Screening Instrument or Substance Abuse Potential (SISAP)

The Screening Instrument or Substance Abuse Potential (SISAP) tool is a self-administered, five-item questionnaire addressing history developed to predict the risk of opioid misuse. The SISAP is used to identify patients with a history of alcohol/substance abuse and improve pain management by facilitating focus on the appropriate use of opioid analgesics and therapeutic outcomes in the majority of patients who are not at risk of opioid abuse, while carefully monitoring those who may be at greater risk [69].

CAGE and CAGE-AID

The original CAGE (Cut down, Annoyed, Guilty, and Eye-opener) Questionnaire consisted of four questions designed to help clinicians determine the likelihood that a patient was misusing or abusing alcohol. These same four questions were modified to create the CAGE-AID (adapted to include drugs), revised to assess the likelihood of current substance abuse [70].

Diagnosis, Intractability, Risk, and Efficacy (DIRE) Tool

The Diagnosis, Intractability, Risk, and Efficacy (DIRE) risk assessment tool is a clinician-rated questionnaire that is used to predict patient compliance with long-term opioid therapy [71]. Patients scoring lower on the DIRE tool are poor candidates for long-term opioid analgesia.

Mental Health Screening Tool

The Mental Health Screening Tool is a five-item screen that asks about a patient's feelings of happiness, calmness, peacefulness, nervousness, and depression in the past month [72]. A lower score on this tool is an indicator that the patient should be referred to a specialist for pain management.

CREATING A TREATMENT PLAN

Opioid therapy should be presented as a trial for a pre-defined period (e.g., ≤30 days). The goals of treatment should be established with all patients prior to the initiation of opioid therapy, including reasonable improvements in pain, function, depression, anxiety, and avoidance of unnecessary or excessive medication use [1; 44]. The treatment plan should describe therapy selection, measures of progress, and other diagnostic evaluations, consultations, referrals, and therapies. All patients prescribed an opioid for pain related to a traumatic injury (severity score ≥9) should be concurrently prescribed an antagonist (e.g., naloxone) [54].

In opioid-naïve patients, start at the lowest possible dose and titrate to effect. Dosages for opioid-tolerant patients should always be individualized and titrated by efficacy and tolerability [1]. The need for frequent progress and benefit/risk assessments during the trial should be included in patient education. Patients should also have full knowledge of the warning signs and symptoms of respiratory depression.

Prescribers should be knowledgeable of federal and state opioid prescribing regulations. Issues of equianalgesic dosing, close patient monitoring during all dose changes, and incomplete cross-tolerance with opioid conversion should be considered. If necessary, treatment may be augmented, with preference for nonopioid and immediate-release opioids over long-acting/extended-release opioids. Taper opioid dose when no longer needed [63].

Non-Opioid Pain Management Options

Nonpharmacologic Approaches

Several nonpharmacologic approaches are therapeutic complements to pain-relieving medication, lessening the need for higher doses and perhaps minimizing side effects. These interventions can help decrease pain or distress that may be contributing to the pain sensation. Approaches include palliative radiotherapy, complementary/alternative methods, manipulative and body-based methods, and cognitive/behavioral techniques. The choice of a specific nonpharmacologic intervention is based on the patient's preference, which, in turn, is usually based on a successful experience in the past.

Methods to provide distraction from pain come in a wide variety of methods, including reciting poetry, meditating with a calm phrase, watching television or movies, playing cards, visiting with friends, or participating in crafts. Music therapy and art therapy are also becoming more widely used as nonpharmacologic options for pain management.

Non-Opioid Analgesics

Nonopioid analgesics, such as aspirin, acetaminophen (Tylenol), and nonsteroidal anti-inflammatory drugs (NSAIDs), are primarily used for mild pain and may also be helpful as coanalgesics for moderate and severe pain. Acetaminophen is among the safest of analgesic agents, but it has essentially no anti-inflammatory effect. Toxicity is a concern at high doses, and the maximum recommended dose is 3–4 g per day [73]. Acetaminophen should be avoided or given at lower doses in people with a history of alcohol abuse or renal or hepatic insufficiency [73].

NSAIDs are most effective for pain associated with inflammation. Among the commonly used NSAIDs are ibuprofen (Motrin, Advil), naproxen (Aleve, Naprosyn), and indomethacin (Indocin). There are several classes of NSAIDs, and the response differs among patients; trials of drugs for an individual patient may be necessary to determine which drug is most effective [74]. NSAIDs inhibit platelet aggregation, increasing the risk of bleeding, and also can damage the mucosal lining of the stomach, leading to gastrointestinal bleeding. There is a ceiling effect to the nonopioid analgesics; that is, there is a dose beyond which there is no further analgesic effect. In addition, many side effects of nonopioids can be severe and may limit their use or dosing.

Informed Consent and Treatment Agreements

The initial opioid prescription is preceded by a written informed consent or "treatment agreement" [1]. This agreement should address potential side effects, tolerance and/or physical dependence, drug interactions, motor skill impairment, limited evidence of long-term benefit, misuse, dependence, addiction, and overdose. Informed consent documents should include information regarding the risk/benefit profile for the drug(s) being prescribed. The prescribing policies should be clearly delineated, including the number/frequency of refills, early refills, and procedures for lost or stolen medications.

The treatment agreement also outlines joint physician and patient responsibilities. The patient agrees to using medications safely, refraining from "doctor shopping," and consenting to routine urine drug testing (UDT). The prescriber's responsibility is to address unforeseen problems and prescribe scheduled refills. Reasons for opioid therapy change or discontinuation should be listed. Agreements can also include sections related to follow-up visits, monitoring, and safe storage and disposal of unused drugs.

PERIODIC REVIEW AND MONITORING

When implementing a chronic pain treatment plan that involves the use of opioids, the patient should be frequently reassessed for changes in pain origin, health, and function [1]. This can include input from family members and/or the state PDMP. During the initiation phase and during any changes to the dosage or agent used, patient contact should be increased. At every visit, chronic opioid response may be monitored according to the "5 A's" [1; 75]:

- Analgesia
- Activities of daily living
- Adverse or side effects
- Aberrant drug-related behaviors
- Affect (i.e., patient mood)

Signs and symptoms that, if present, may suggest a problematic response to the opioid and interference with the goal of functional improvement include [76]:

- Excessive sleeping or days and nights turned around
- Diminished appetite
- Short attention span or inability to concentrate
- Mood volatility, especially irritability
- Lack of involvement with others
- Impaired functioning due to drug effects
- Use of the opioid to regress instead of re-engaging in life
- Lack of attention to hygiene and appearance

The decision to continue, change, or terminate opioid therapy is based on progress toward treatment objectives and absence of concerning adverse effects and risks of overdose or diversion [1]. Satisfactory therapy is indicated by improvements in pain, function, and quality of life. It is important to remember that for some patients with severe chronic pain, improved function may take longer than pain control or either pain or function (not both) will improve. In some cases, preventing worsening pain/functional impairment is the best achievable outcome. Brief assessment tools to assess pain and function may be useful, as may UDTs. Treatment plans may include periodic pill counts to confirm adherence and minimize diversion.

Involvement of Family

Family members or the partner of the patient can provide the clinician with valuable information that better informs decision making regarding continuing opioid therapy. Family members can observe whether a patient is losing control of his or her life or becoming less functional or more depressed during the course of opioid therapy. They can also provide input regarding positive or negative changes in patient function, attitude, and level of comfort. The following questions can be asked of family members or a spouse to help clarify whether the patient's response to opioid therapy is favorable or unfavorable [76]:

- Is the person's day centered around taking the opioid medication? Response can help clarify long-term risks and benefits of the medication and identify other treatment options.
- Does the person take pain medication only on occasion, perhaps three or four times per week? If yes, the likelihood of addiction is low.
- Have there been any other substance (alcohol or drug) abuse problems in the person's life? An affirmative response should be taken into consideration when prescribing.
- Does the person in pain spend most of the day resting, avoiding activity, or feeling depressed? If so, this suggests the pain medication is failing to promote rehabilitation. Daily activity is essential, and the patient may be considered for enrollment in a graduated exercise program.
- Is the person in pain able to function (e.g., work, do household chores, play) with pain medication in a way that is clearly better than without? If yes, this suggests the pain medication is contributing to wellness.

Assessment Tools

VIGIL

VIGIL is the acronym for a five-step risk management strategy designed to empower clinicians to appropriately prescribe opioids for pain by reducing regulatory concerns and to give pharmacists a framework for resolving ambiguous opioid analgesic prescriptions in a manner that preserves legitimate patient need while potentially deterring diverters. The components of VIGIL are [77]:

- Verification: Is this a responsible opioid user?
- Identification: Is the identity of this patient verifiable?
- Generalization: Do we agree on mutual responsibilities and expectations?
- Interpretation: Do I feel comfortable allowing this person to have controlled substances?
- Legalization: Am I acting legally and responsibly?

The foundation of VIGIL is a collaborative physician/pharmacist relationship [77; 78].

Current Opioid Misuse Measure (COMM)

The Current Opioid Misuse Measure (COMM) is a 17-item patient self-report assessment designed to help clinicians identify misuse or abuse in patients with chronic pain. Unlike the ORT and the SOAPP-R, the COMM identifies aberrant behaviors associated with opioid misuse in patients already receiving long-term opioid therapy [58]. Sample questions include: In the past 30 days, how often have you had to take more of your medication than prescribed? In the past 30 days, how much of your time was spent thinking about opioid medications (e.g., having enough, taking them, dosing schedule)?

PATIENT RISK LEVEL AND FREQUENCY OF MONITORING			
Monitoring Tool	**Patient Risk Level**		
	Low	**Medium**	**High**
Urine drug test	Every one to two years	Every 6 to 12 months	Every three to six months
State prescription drug monitoring program	Twice per year	Three times per year	Four times per year

Source: [81] *Table 2*

Pain Assessment and Documentation Tool (PADT)

Guidelines by the CDC, the Federation of State Medical Boards (FSMB), and the Joint Commission stress the importance of documentation from both a healthcare quality and medicolegal perspective. Research has found widespread deficits in chart notes and progress documentation for patients with chronic pain who are receiving opioid therapy, and the Pain Assessment and Documentation Tool (PADT) was designed to address these shortcomings [79]. The PADT is a clinician-directed interview, with most sections (e.g., analgesia, activities of daily living, adverse events) consisting of questions asked of the patient. However, the potential aberrant drug-related behavior section must be completed by the physician based on his or her observations of the patient [80].

The Brief Intervention Tool

The Brief Intervention Tool is a 26-item, "yes-no," patient-administered questionnaire used to identify early signs of opioid abuse or addiction. The items assess the extent of problems related to drug use in several areas, including drug use-related functional impairment [72].

Urine Drug Tests

UDTs may be used to monitor adherence to the prescribed treatment plan and to detect unsanctioned drug use. They should be used more often in patients receiving addiction therapy, but clinical judgment is the ultimate guide to testing frequency (***Table 2***) [81]. The CDC recommends clinicians should use UDT before starting opioid therapy and consider UDT at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs [44]. However, this recommendation was based on low-quality evidence that indicates little confidence in the effect estimate.

Initially, testing involves the use of class-specific immunoassay drug panels [1]. If necessary, this may be followed with gas chromatography/mass spectrometry for specific drug or metabolite detection. It is important that testing identifies the specific drug rather than the drug class, and the prescribed opioid should be included in the screen. Any abnormalities should be confirmed with a laboratory toxicologist or clinical pathologist. Immunoassay may be used point-of-care for "on-the-spot" therapy changes, but the high error rate prevents its use in major clinical decisions except with liquid chromatography coupled to tandem mass spectrometry confirmation.

Urine test results suggesting opioid misuse should be discussed with the patient using a positive, supportive approach. The test results and the patient discussion should be documented.

CONSULTATION AND REFERRAL

It is important to seek consultation or patient referral when input or care from a pain, psychiatry, addiction, or mental health specialist is necessary. Clinicians who prescribe opioids should become familiar with opioid addiction treatment options (including licensed opioid treatment programs for methadone and office-based opioid treatment for buprenorphine) if referral is needed [1].

Ideally, providers should be able to refer patients with active substance abuse who require pain treatment to an addiction professional or specialized program. In reality, these specialized resources are scarce or non-existent in many areas [1]. Therefore, each provider will need to decide whether the risks of continuing opioid treatment while a patient is using illicit drugs outweigh the benefits to the patient in terms of pain control and improved function [82].

MEDICAL RECORDS

As noted, documentation is a necessary aspect of all patient care, but it is of particular importance when opioid prescribing is involved. All clinicians should maintain accurate, complete, and up-to-date medical records, including all written or telephoned prescription orders for opioid analgesics and other controlled substances, all written instructions to the patient for medication use, and the name, telephone number, and address of the patient's pharmacy [1]. Good medical records demonstrate that a service was provided to the patient and that the service was medically necessary. Regardless of the treatment outcome, thorough medical records protect the prescriber.

PATIENT EDUCATION ON THE USE AND DISPOSAL OF OPIOIDS

Patients and caregivers should be counseled regarding the safe use and disposal of opioids. As part of its mandatory Risk Evaluation and Mitigation Strategy (REMS) for extended-release/long-acting opioids, the (FDA has developed a patient counseling document with information on the patient's specific medications, instructions for emergency situations and incomplete pain control, and warnings not to share medications or take them unprescribed [63]. A copy of this form may be accessed online at https://www.accessdata.fda.gov/drugsatfda_docs/rems/ERLA_opioids_2016-04-26_Patient_Counseling_Document.pdf [83].

When prescribing opioids, clinicians should provide patients with the following information [63]:

- Product-specific information
- Taking the opioid as prescribed
- Importance of dosing regimen adherence, managing missed doses, and prescriber contact if pain is not controlled
- Warning and rationale to never break or chew/crush tablets or cut or tear patches prior to use
- Warning and rationale to avoid other central nervous system depressants, such as sedative-hypnotics, anxiolytics, alcohol, or illicit drugs
- Warning not to abruptly halt or reduce the opioid without physician oversight of safe tapering when discontinuing
- The potential of serious side effects or death
- Risk factors, signs, and symptoms of overdose and opioid-induced respiratory depression, gastrointestinal obstruction, and allergic reactions
- The risks of falls, using heavy machinery, and driving
- Warning and rationale to never share an opioid analgesic
- Rationale for secure opioid storage
- Warning to protect opioids from theft
- Instructions for disposal of unneeded opioids, based on product-specific disposal information

There are no universal recommendations for the proper disposal of unused opioids, and patients are rarely advised of what to do with unused or expired medications [84]. According to the Office of National Drug Control Policy, most medications that are no longer necessary or have expired should be removed from their containers, mixed with undesirable substances (e.g., cat litter, used coffee grounds), and put into an impermeable, nondescript container (e.g., disposable container with a lid or a sealed bag) before throwing in the trash [85]. Any personal information should be obscured or destroyed. The FDA recommends that certain medications, including oxycodone/acetaminophen (Percocet), oxycodone (OxyContin tablets), and transdermal fentanyl (Duragesic Transdermal System), be flushed down the toilet instead of thrown in the trash [85]. The FDA provides a free toolkit of materials (e.g., social media images, fact sheets, posters) to raise awareness of the serious dangers of keeping unused opioid pain medicines in the home and with information about safe disposal of these medicines. The Remove the Risk Outreach toolkit is updated regularly and can be found at https://www.fda.gov/drugs/ensuring-safe-use-medicine/safe-opioid-disposal-remove-risk-outreach-toolkit [86]. Patients should be advised to flush prescription drugs down the toilet only if the label or accompanying patient information specifically instructs doing so and no other disposal method is appropriate.

The American College of Preventive Medicine has established best practices to avoid diversion of unused drugs and educate patients regarding drug disposal [84]:

- Consider writing prescriptions in smaller amounts.
- Educate patients about safe storing and disposal practices.
- Give drug-specific information to patients about the temperature at which they should store their medications. Generally, the bathroom is not the best storage place. It is damp and moist, potentially resulting in potency decrements, and accessible to many people, including children and teens, resulting in potential theft or safety issues.
- Ask patients not to advertise that they are taking these types of medications and to keep their medications secure.
- Refer patients to community "take back" services overseen by law enforcement that collect controlled substances, seal them in plastic bags, and store them in a secure location until they can be incinerated. Contact your state law enforcement agency or visit https://www.dea.gov to determine if a program is available in your area.

DISCONTINUING OPIOID THERAPY

The decision to continue or end opioid prescribing should be based on a physician-patient discussion of the anticipated benefits and risks. An opioid should be discontinued with resolution of the pain condition, intolerable side effects, inadequate analgesia, lack of improvement in quality of life despite dose titration, deteriorating function, or significant aberrant medication use [1; 44].

Clinicians should provide physically dependent patients with a safely structured tapering protocol. Withdrawal is managed by the prescribing physician or referral to an addiction specialist. Patients should be reassured that opioid discontinuation is not the end of treatment; continuation of pain management will be undertaken with other modalities through direct care or referral.

As a side note, cannabis use by patients with chronic pain receiving opioid therapy has traditionally been viewed as a treatment agreement violation that is grounds for termination of opioid therapy. However, some now argue against cannabis use as a rationale for termination or substantial treatment and monitoring changes, especially considering the increasing legalization of medical use at the state level [82].

CONSIDERATIONS FOR NON-ENGLISH-PROFICIENT PATIENTS

For patients who are not proficient in English, it is important that information regarding the risks associated with the use of opioids and available resources be provided in their native language, if possible. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required. Interpreters can be a valuable resource to help bridge the communication and cultural gap between patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers who ultimately enhance the clinical encounter. In any case in which information regarding treatment options and medication/treatment measures are being provided, the use of an interpreter should be considered. Print materials are also available in many languages, and these should be offered whenever necessary.

CRISIS INTERVENTION: MANAGEMENT OF OVERDOSE

Individuals who have first contact with persons suspected of experiencing an opioid-related overdose are in the position to intervene to prevent the potentially devastating consequences. In these cases, care begins with crisis intervention directed at immediate survival by reversing the potentially lethal effects of overdose with an opioid antagonist.

Opioid antagonists have obvious therapeutic value in the treatment of opioid overdose. A 2012 study found that wider distribution of naloxone and training in its administration might have prevented numerous deaths from opioid overdoses in the United States [87]. Since the first community-based opioid overdose prevention program began distributing naloxone in 1996, more than 10,000 overdoses have been reversed [87].

In Florida, licensed healthcare providers may prescribe and pharmacists may dispense opioid antagonists (even as a standing order) for at-risk individuals, these individuals' relatives or other caregivers, and emergency responders to be used in their course of duties [88]. Emergency responders include (but are not limited to) law enforcement officers, paramedics, and emergency medical technicians [88]. As noted, there is a statewide standing order for naloxone for all emergency responders in Florida [38].

OPIOID ANTAGONISTS

Relatively minor changes in the structure of an opioid can convert an agonist drug into one with antagonistic actions at one or more opioid receptor types. Opioid antagonists include naloxone, naltrexone, and nalmefene. Interestingly, naloxone also appears to block the analgesic effects of placebo medications and acupuncture. These agents have no abuse potential [89].

In response to acute overdose, the short-acting opioid antagonist naloxone is considered the gold standard, and it remains the most widely used opioid antagonist for the reversal of overdose and opioid-related respiratory depression. It acts by competing with opioids at receptor sites in the brain stem, reversing desensitization to carbon dioxide, and reversing or preventing respiratory failure and coma. There is no evidence that subcutaneous or intramuscular use is inferior to intravenous naloxone. This has prompted some states to pass laws allowing opioid antagonists to be available to the general public for administration outside the healthcare setting to treat acute opioid overdose [90]. In 2014, the FDA approved naloxone as an autoinjector dosage form for home use by family members or caregivers, and in 2015, the agency approved intranasal naloxone after a fast-track designation and priority review. Intranasal naloxone is indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression [91; 92].

When used for opioid overdose, a dose of 0.4–2 mg of naloxone is administered intravenously, intramuscularly, or subcutaneously [93]. If necessary, the dose may be repeated every two to three minutes for full reversal. For ease of use, naloxone is also available in a pre-filled auto-injection device. It is important that standard Advanced Cardiac Life Support (ACLS) protocols be continued while naloxone is being administered and that medical treatment (at a healthcare facility) be given immediately.

COMPLIANCE WITH STATE AND FEDERAL LAWS

In response to the rising incidence in prescription opioid abuse, addiction, diversion, and overdose in the late 1990s and 2000s, the FDA has mandated opioid-specific REMS to reduce the potential negative patient and societal effects of prescribed opioids. Other elements of opioid risk mitigation include FDA partnering with other governmental agencies, state professional licensing boards, and societies of healthcare professionals to help improve prescriber knowledge of appropriate and safe opioid prescribing and safe home storage and disposal of unused medication [76].

Several regulations and programs at the state level have been enacted in an effort to reduce prescription opioid abuse, diversion, and overdose, including [94]:

- Physical examination required prior to prescribing
- Tamper-resistant prescription forms
- Pain clinic regulatory oversight
- Prescription limits
- Prohibition from obtaining controlled substance prescriptions from multiple providers
- Patient identification required before dispensing
- Immunity from prosecution or mitigation at sentencing for individuals seeking assistance during an overdose

CONTROLLED SUBSTANCES LAWS/RULES

The DEA is responsible for formulating federal standards for the handling of controlled substances. In 2011, the DEA began requiring every state to implement electronic databases that track prescribing habits, referred to as PDMPs. Specific policies regarding controlled substances are administered at the state level [95].

According to the DEA, drugs, substances, and certain chemicals used to make drugs are classified into five distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential [96]. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs are considered the most dangerous class of drugs with a high potential for abuse and potentially severe psychologic and/or physical dependence.

In Florida, the prescribing, dispensing, and consumption of certain controlled substances are governed by Chapter 893 of the Florida Statutes [97]. This law establishes the standards for controlled substance prescribing, including reporting system requirements, for prescribers and pharmacists in Florida. As of 2021, the Florida schedule of controlled substances aligns with the DEA schedule [43].

THE ELECTRONIC FLORIDA ONLINE REPORTING OF CONTROLLED SUBSTANCES EVALUATION PROGRAM

Emerging trends and patterns of prescription opioid abuse, addiction, and overdose are monitored by several industry and government agencies through data collection from a variety of sources. These include health insurance claims; the Automation of Reports and Consolidated Orders System, a DEA-run program that monitors the flow of controlled substances from manufacturing through distribution to retail sale or dispensing; the Treatment Episode Data Set, which monitors treatment admissions; the National Center for Health Statistics state mortality data; and the Researched Abuse, Diversion, and Addiction-Related Surveillance System, which monitors prescription drug abuse, misuse, and diversion [98].

Almost all states, including Florida, have enacted PDMPs to facilitate the collection, analysis, and reporting of information on controlled substances prescribing and dispensing [1]. All prescribers must consult the Electronic Florida Online Reporting of Controlled Substances Evaluation (E-FORCSE) to review a patient's controlled substance dispensing history before prescribing or dispensing a controlled substance to a patient 16 years of age or older [99]. This is mandated even for existing patients and should be done each time a controlled substance is prescribed or dispensed [43]. If the system is nonoperational or cannot be accessed due to a temporary technologic or electrical failure, the prescription may be issued (with documentation of the exception) for up to a maximum three-day supply.

All clinicians who dispense controlled substances are required to report the action to E-FORCSE as soon as possible, but no later than the close of the next business day [99]. This should be repeated each time the substance is dispensed. This reporting requirement is waived in certain circumstances, including for [99]:

- The dispensing of a controlled substance in the healthcare system of the Department of Corrections
- The dispensing of a controlled substance to a person younger than 16 years of age

IDENTIFICATION OF DRUG DIVERSION/SEEKING BEHAVIORS

Research has more closely defined the location of prescribed opioid diversion into illicit use in the supply chain from the manufacturer to the distributor, retailer, and the end user (the patient with pain). This information carries with it substantial public policy and regulatory implications. The 2019 National Survey on Drug Use and Health asked non-medical users of prescription opioids how they obtained their most recently used drugs [100]. Among persons 12 years of age or older, 38.6% obtained their prescription opioids from a friend or relative for free, 34.7% got them through a prescription from one doctor (vs. 17.3% in 2009–2010), 9.5% bought them from a friend or relative, and 3.2% took them from a friend or relative without asking [100]. Less frequent sources included a drug dealer or other stranger (6.5%); multiple doctors (2.0%); and theft from a doctor's office, clinic, hospital, or pharmacy (0.8%) (vs. 0.2% in 2009–2010) [100].

As discussed, UDTs can give insight into patients who are misusing opioids. A random sample of UDT results from 800 patients with pain treated at a Veterans Affairs facility found that 25.2% were negative for the prescribed opioid while 19.5% were positive for an illicit drug/unreported opioid [101]. Negative UDT results for the prescribed opioid do not necessarily indicate diversion, but may indicate the patient halted his/her use due to side effects, lack of efficacy, or pain remission. The concern arises over the increasingly stringent climate surrounding clinical decision-making regarding aberrant UDT results and that a negative result for the prescribed opioid or a positive UDT may serve as the pretense to terminate a patient rather than guide him/her into addiction treatment or an alternative pain management program [102].

In addition to aberrant urine screens, there are certain behaviors that are suggestive of an emerging opioid use disorder. The most suggestive behaviors are [82; 103; 104]:

- Selling medications
- Prescription forgery or alteration
- Injecting medications meant for oral use
- Obtaining medications from nonmedical sources
- Resisting medication change despite worsening function or significant negative effects
- Loss of control over alcohol use
- Using illegal drugs or non-prescribed controlled substances
- Recurrent episodes of:
  - Prescription loss or theft
  - Obtaining opioids from other providers in violation of a treatment agreement
  - Unsanctioned dose escalation
  - Running out of medication and requesting early refills

Behaviors with less association with opioid misuse include [82; 103; 104]:

- Aggressive demands for more drug
- Asking for specific medications
- Stockpiling medications during times when pain is less severe
- Using pain medications to treat other symptoms
- Reluctance to decrease opioid dosing once stable
- In the earlier stages of treatment:
  - Increasing medication dosing without provider permission
  - Obtaining prescriptions from sources other than the pain provider
  - Sharing or borrowing similar medications from friends/family

INTERVENTIONS FOR SUSPECTED OR KNOWN DRUG DIVERSION

There are a number of actions that prescribers and dispensers can take to prevent or intervene in cases of drug diversion. These actions can be generally categorized based on the various mechanisms of drug diversion.

Prevention is the best approach to addressing drug diversion. As noted, the most common source of nonmedical use of prescribed opioids is from a family member or friend, through sharing, buying, or stealing. To avoid drug sharing among patients, healthcare professionals should educate patients on the dangers of sharing opioids and stress that "doing prescription drugs" is the same as "using street drugs" [84]. In addition, patients should be aware of the many options available to treat chronic pain aside from opioids. To prevent theft, patients should be advised to keep medications in a private place and to refrain from telling others about the medications being used.

Communication among providers and pharmacies can help to avoid inappropriate attainment of prescription drugs through "doctor shopping." Prescribers should keep complete and up-to-date records for all controlled substance prescribing. When possible, electronic medical records should be integrated between pharmacies, hospitals, and managed care organizations [84]. It is also best practice to periodically request a report from the E-FORCSE to evaluate the prescribing of opioids to your patients by other providers [84].

When dealing with patients suspected of drug seeking/diversion, first inquire about prescription, over-the-counter, and illicit drug use and perform a thorough examination [84; 105]. Pill counting and/or UDT may be necessary to investigate possible drug misuse. Photo identification or other form of identification and social security number may be required prior to dispensing the drug, with proof of identity documented fully. If a patient is displaying suspicious behaviors, consider prescribing for limited quantities [105].

If a patient is found to be abusing prescribed opioids, this is considered a violation of the treatment agreement and the clinician must make the decision whether or not to continue the therapeutic relationship. If the relationship is terminated, it must be done ethically and legally. The most significant issue is the risk of patient abandonment, which is defined as ending a relationship with a patient without consideration of continuity of care and without providing notice to the patient. The American Medical Association Code of Ethics states, "Physicians have an obligation to support continuity of care for their patients. While physicians have the option of withdrawing from a case, they cannot do so without giving notice to the patient, the relatives, or responsible friends sufficiently long in advance of withdrawal to permit another medical attendant to be secured" [106]. The notice of termination should be sent in writing, should specifically note the causes for the termination, and should give a period of time prior to termination, usually 30 days [107]. Patients may also be given resources and/or recommendations to help them locate a new clinician.

Patients with chronic pain found to have an ongoing substance abuse problem or addiction should be referred to a pain specialist for continued treatment. Theft or loss of controlled substances is reported to the DEA. If drug diversion has occurred, the activity should be documented and a report to law enforcement should be made [108].

CASE STUDY

An unemployed man, 64 years of age, is brought to an emergency department by ambulance, after his wife returned from work to find him lying on the couch, difficult to arouse and incoherent. He has a past history of hypertension, diabetes (non-insulin dependent), mild chronic obstructive pulmonary disease, and chronic back and shoulder pain, for which he has been prescribed hydrocodone/acetaminophen for many years. His wife reports that while he seemed his usual self when she left for work that morning, he had, in recent weeks, been more withdrawn socially, less active, and complained of greater discomfort from the back and shoulder pain. She knows little about his actual medication usage and expresses concern that he may have been taking more than the prescribed amount of "pain medicine."

On evaluation, the patient is somnolent and arouses to stimulation but is non-communicative and unable to follow commands. His blood pressure is normal, he is afebrile, and there are no focal neurologic deficits. Oxygen saturation, serum glucose, and routine laboratory studies (blood counts and metabolic profile) are normal except for mild elevation in blood urea nitrogen (BUN) and creatinine; the urine drug screen is negative except for opioids. Additional history from the family indicates that the patient has been admitted to other hospitals twice in the past three years with a similar presentation and recovered rapidly each time "without anything being found."

Following admission, the patient remains stable-to-improved over the next 12 to 18 hours. By the following day, he is awake and conversant and looks comfortable. On direct questioning, he reports recent symptoms of depression but no suicidal ideation. The patient describes an increased preoccupation with his pain syndrome, difficulty sleeping at night, and little physical activity during the day, in part because of physical discomfort. He is vague about his medication regimen and admits to taking "occasional" extra doses of hydrocodone for pain relief.

The family is instructed to bring in all his pill bottles from home, which they do. In addition to the hydrocodone prescribed by his primary care physician, there is a recent refill of a prescription for the medication given to the patient at the time of his last hospital discharge six months earlier.

ASSESSMENT

A full evaluation, including radiographic studies and consultation with psychiatry and physical therapy, is completed. The working diagnosis for the patient's acute illness is toxic encephalopathy caused by the sedative side effects of opioid medication on the CNS. It is explained that the combination of his advancing age and diabetes likely reduced the efficiency of his kidneys in clearing the medication and its metabolites, making him more susceptible to CNS sedation. It is noted that the patient and his wife have little understanding of the rationale, proper use and safeguards, potential side effects, and limited effectiveness of opioid use for chronic pain.

In addition, the patient is diagnosed with poorly controlled chronic pain syndrome secondary to osteoarthritis and degenerative disc disease; exacerbating factors include deconditioning and reactive depression. The use of an opioid analgesic, at least for the near term, is considered appropriate, if dosed properly, monitored closely, and integrated into a comprehensive, multidisciplinary plan that includes treatment of depression and the use of adjunctive, nonpharmacologic modalities of care. In the setting of possible early diabetic nephropathy, the option of utilizing an NSAID, except for very brief periods of break-through pain, is not considered to be a safe option.

At discharge, and in consultation with his primary care physician, a written treatment and management plan addressing all aspects of the patient's care is presented to the patient and his wife for discussion and consent. Among the key issues addressed are:

- Goals: Improvement in subjective pain experience; improved function of daily living manifested by regular walking exercise and improved social interaction with family and friends; relief of depression; and in the long-term, anticipated withdrawal of opioid medication and resumption of part-time work and/or volunteer community activity

- Outpatient physical therapy and back exercise program to increase core muscular strength, improve flexibility, reduce pain, and increase exercise tolerance
- Patient and family counseling regarding the safe use, dosage regulation, side effects, and proper disposal of opioid medication
- Joint patient-physician responsibilities as regards to regular follow-up, monitoring of goals and treatment effectiveness, avoidance of "doctor-shopping," and assent to single provider for prescription medication

FOLLOW-UP

On follow-up six weeks after discharge, the patient is noticeably improved. He reports that he feels stronger and is sleeping better. His affect is brighter, and he is getting out more. He has maintained his physical therapy and exercise routine and is compliant with his medication. Though he still has pain, it is noticeably less and he is coping better. He and his wife are encouraged by his progress, particularly in regard to his improved functional status.

CONCLUSION

For patients suffering from pain, prescribed opioid analgesics may substantially lessen pain, distress, and impairment. Inappropriate overprescribing and overdose related to opioid analgesics increased dramatically in the 2000s. These trends are in multi-year reversal, but patient safety and risk mitigation remains no less important, and clinical tools, guidelines, and recommendations are available for use when prescribing opioids to patients with pain. By implementing these tools, the clinician can effectively address issues related to the clinical management of opioid prescribing, opioid risk management, regulations surrounding the prescribing of opioids, and problematic opioid use by patients. In doing so, healthcare professionals are more likely to achieve a balance between the benefits and risks of opioid prescribing, optimize patient attainment of therapeutic goals, and avoid the risk to patient outcome, public health, and viability of their own practice imposed by deficits in knowledge.

Customer Information/Answer Sheet/Evaluation insert located between pages 60–61.

COURSE TEST - #55121 STRATEGIES FOR APPROPRIATE OPIOID PRESCRIBING: THE FLORIDA REQUIREMENT

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 CE Credit Hour activity must be completed by August 31, 2024.

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1. Inappropriate opioid analgesic prescribing for pain is defined as
- *A) non-prescribing.*
- *B) inadequate prescribing.*
- *C) continued prescribing despite evidence of ineffectiveness of opioids.*
- *D) All of the above*

2. Data indicate that opioid analgesic prescribing and overdose peaked in
- *A) 2011.*
- *B) 2001.*
- *C) 1990.*
- *D) 1981.*

3. A patient prescribed opioids for chronic pain who has no personal or family history of alcohol or substance abuse is considered at what level of risk for developing problematic opioid behavioral responses?
- *A) Low*
- *B) Medium*
- *C) High*
- *D) Severe*

4. The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)
- *A) consists of five items.*
- *B) is patient administered.*
- *C) diagnoses depression in the past month.*
- *D) assesses the likelihood of current substance abuse.*

5. Which of the following is NOT one of the 5 A's of monitoring chronic opioid response?
- *A) Analgesia*
- *B) Acceptance*
- *C) Affect (i.e., patient mood)*
- *D) Aberrant drug-related behaviors*

6. For patients considered at medium risk for misuse of prescription opioids, urine drug testing should be completed every
- *A) 6 to 12 weeks.*
- *B) three to six months.*
- *C) 6 to 12 months.*
- *D) one to two years.*

Test questions continue on next page ➞

7. **The U.S. Food and Drug Administration recommends that unused OxyContin tablets be disposed of by**
   - A) *burning.*
   - B) *flushing down the toilet.*
   - C) *throwing in the garbage in a sealed container.*
   - D) *sharing with a friend or relative with chronic pain.*

8. **Which government agency is responsible for formulating federal standards for the handling of controlled substances?**
   - A) *Institutes of Medicine*
   - B) *U.S. Drug Enforcement Administration*
   - C) *Office of National Drug Control Policy*
   - D) *U.S. Department of Health and Human Services*

9. **All clinicians who dispense controlled substances are required to report the action to the Electronic Florida Online Reporting of Controlled Substances Evaluation (E-FORCSE) within**
   - A) *2 hours.*
   - B) *one business day.*
   - C) *30 days.*
   - D) *six months.*

10. **Which of the following behaviors is the most suggestive of an emerging opioid use disorder?**
    - A) *Asking for specific medications*
    - B) *Injecting medications meant for oral use*
    - C) *Reluctance to decrease opioid dosing once stable*
    - D) *Stockpiling medications during times when pain is less severe*

Be sure to transfer your answers to the Answer Sheet located on the envelope insert.
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Cultural Competence: An Overview

Audience
This course is designed for dental members of the interprofessional healthcare team.

Course Objective
The purpose of this course is to provide members of the interprofessional healthcare team with the knowledge, skills, and strategies necessary to provide culturally competent and responsive care to all patients.

Learning Objectives
Upon completion of this course, you should be able to:

1. Define cultural competence, implicit bias, and related terminology.
2. Outline social determinants of health and barriers to providing care.
3. Discuss best practices for providing culturally competent care to various patient populations.
4. Discuss key aspects of creating a welcoming and safe environment, including avoidance of discriminatory language and behaviors.

Faculty
Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families. (A complete biography appears at the end of this course.)

Faculty Disclosure
Contributing faculty, Alice Yick Flanagan, PhD, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Mark J. Szarejko, DDS, FAGD

Director of Development and Academic Affairs
Sarah Campbell

Division Planner/Director Disclosure
The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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INTRODUCTION

Culturally competent care has been defined as "care that takes into account issues related to diversity, marginalization, and vulnerability due to culture, race, gender, and sexual orientation" [1]. A culturally competent person is someone who is aware of how being different from the norm can be marginalizing and how this marginalization may affect seeking or receiving health care [1]. To be effective cross-culturally with any diverse group, healthcare professionals must have awareness, sensitivity, and knowledge about the culture involved, enhanced by the use of cross-cultural communication skills [2; 3].

Healthcare professionals are accustomed to working to promote the healthy physical and psychosocial development and well-being of individuals within the context of the greater community. For years, these same professionals have been identifying at-risk populations and developing programs or making referrals to resources to promote the health and safety of at-risk groups. But, because of general assumptions, persistent stereotypes, and implicit and explicit biases, culture-related healthcare disparities persist [2]. In the increasingly diverse landscape of the United States, assessing and addressing culture-related barriers to care are a necessary part of health care. This includes seeking to improve one's cultural competence and identifying blind spots and biases.

DEFINITIONS

CULTURAL COMPETENCE

In healthcare, cultural competence is broadly defined as practitioners' knowledge of and ability to apply cultural information and appreciation of a different group's cultural and belief systems to their work [4]. It is a dynamic process, meaning that there is no endpoint to the journey to becoming culturally aware, sensitive, and competent. Some have argued that cultural curiosity is a vital aspect of this approach.

CULTURAL HUMILITY

Cultural humility refers to an attitude of humbleness, acknowledging one's limitations in the cultural knowledge of groups. Practitioners who apply cultural humility readily concede that they are not experts in others' cultures and that there are aspects of culture and social experiences that they do not know. From this perspective, patients are considered teachers of the cultural norms, beliefs, and value systems of their group, while practitioners are the learners [5]. Cultural humility is a lifelong process involving reflexivity, self-evaluation, and self-critique [6].

DISCRIMINATION

Discrimination has traditionally been viewed as the outcome of prejudice [7]. It encompasses overt or hidden actions, behaviors, or practices of members in a dominant group against members of a subordinate group [8]. Discrimination has also been further categorized as lifetime, which consists of major discreet discriminatory events, or everyday, which is subtle, continual, and part of day-to-day life and can have a cumulate effect on individuals [9].

DIVERSITY

Diversity "encompasses differences in and among societal groups based on race, ethnicity, gender, age, physical/mental abilities, religion, sexual orientation, and other distinguishing characteristics" [10]. Diversity is often incorrectly conceptualized into singular dimensions as opposed to multiple and intersecting diversity factors [11].

INTERSECTIONALITY

Intersectionality is a term to describe the multiple facets of identity, including race, gender, sexual orientation, religion, sex, and age. These facets are not mutually exclusive, and the meanings that are ascribed to these identities are inter-related and interact to create a whole [12]. This term also encompasses the ways that different types and systems of oppression intersect and affect individuals.

PREJUDICE

Prejudice is a generally negative feeling, attitude, or stereotype against members of a group [13]. It is important not to equate prejudice and racism, although the two concepts are related. All humans have prejudices, but not all individuals are racist. The popular definition is that "prejudice plus power equals racism" [13]. Prejudice stems from the process of ascribing every member of a group with the same attributes [14].

RACISM

Racism is the "systematic subordination of members of targeted racial groups who have relatively little social power...by members of the agent racial group who have relatively more social power" [15]. Racism is perpetuated and reinforced by social values, norms, and institutions.

There is some controversy regarding whether unconscious (implicit) racism exists. Experts assert that images embedded in our unconscious are the result of socialization and personal observations, and negative attributes may be unconsciously applied to racial minority groups [16]. These implicit attributes affect individuals' thoughts and behaviors without a conscious awareness.

Structural racism refers to the laws, policies, and institutional norms and ideologies that systematically reinforce inequities, resulting in differential access to services such as health care, education, employment, and housing for racial and ethnic minorities [17; 18].

BIAS: IMPLICIT AND EXPLICIT

In a sociocultural context, biases are generally defined as negative evaluations of a particular social group relative to another group. Explicit biases are conscious, whereby an individual is fully aware of his/her attitudes and there may be intentional behaviors related to these attitudes [19]. For example, an individual may openly endorse a belief that women are weak and men are strong. This bias is fully conscious and is made explicitly known. The individual's ideas may then be reflected in his/her work as a manager.

FitzGerald and Hurst assert that there are cases in which implicit cognitive processes are involved in biases and conscious availability, controllability, and mental resources are not [20]. The term "implicit bias" refers to the unconscious attitudes and evaluations held by individuals. These individuals do not necessarily endorse the bias, but the embedded beliefs/attitudes can negatively affect their behaviors [21; 22; 23; 24]. Some have asserted that the cognitive processes that dictate implicit and explicit biases are separate and independent [24].

Implicit biases can start as early as 3 years of age. As children age, they may begin to become more egalitarian in what they explicitly endorse, but their implicit biases may not necessarily change in accordance to these outward expressions [25]. Because implicit biases occur on the subconscious or unconscious level, particular social attributes (e.g., skin color) can quietly and insidiously affect perceptions and behaviors [26]. According to Georgetown University's National Center on Cultural Competency, social characteristics that can trigger implicit biases include [27]:

- Age
- Disability
- Education
- English language proficiency and fluency
- Ethnicity
- Health status
- Disease/diagnosis (e.g., human immunodeficiency virus [HIV])
- Insurance
- Obesity
- Race
- Socioeconomic status
- Sexual orientation, gender identity, or gender expression
- Skin tone
- Substance use

An alternative way of conceptualizing implicit bias is that an unconscious evaluation is only negative if it has further adverse consequences on a group that is already disadvantaged or produces inequities [20; 28]. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages [28].

When the concept of implicit bias was introduced in the 1990s, it was thought that implicit biases could be directly linked to behavior. Despite the decades of empirical research, many questions, controversies, and debates remain about the dynamics and pathways of implicit biases [21].

Specific conditions or environmental risk factors have been associated with an increased risk for certain implicit biases, including [130; 131]:

- Stressful emotional states (e.g., anger, frustration)
- Uncertainty
- Low-effort cognitive processing
- Time pressure
- Lack of feedback
- Feeling behind with work
- Lack of guidance
- Long hours
- Overcrowding
- High-crises environments
- Mentally taxing tasks
- Juggling competing tasks

ROLE OF INTERPROFESSIONAL COLLABORATION AND PRACTICE

The study of implicit bias is appropriately interdisciplinary, representing social psychology, medicine, health psychology, neuroscience, counseling, mental health, gerontology, gender/sexuality studies, religious studies, and disability studies [28]. Therefore, implicit bias empirical research and curricula training development lends itself well to interprofessional collaboration and practice (ICP).

The main characteristics of IPC allow for implicit and explicit biases to be addressed by the interprofessional team. One of the core features of IPC is sharing—professionals from different disciplines share their philosophies, values, perspectives, data, and strategies for planning of interventions [29]. IPC also involves the sharing of roles, responsibilities, decision making, and power [30]. Everyone on the team employs their expertise, knowledge, and skills, working collectively on a shared, patient-centered goal or outcome [30; 31].

Another feature of IPC is interdependency. Instead of working in an autonomous manner, each team member's contributions are valued and maximized, which ultimately leads to synergy [29]. At the heart of this are two other key features: mutual trust/respect and communication [31]. In order to share responsibilities, the differing roles and expertise are respected.

Experts have recommended that a structural or critical theoretical perspective be integrated into core competencies in healthcare education to teach students about implicit bias, racism, and health disparities [32]. This includes [32]:

- Values/ethics: The ethical duty for health professionals to partner and collaborate to advocate for the elimination of policies that promote the perpetuation of implicit bias, racism, and health disparities among marginalized populations.
- Roles/responsibilities: One of the primary roles and responsibilities of health professionals is to analyze how institutional and organizational factors promote racism and implicit bias and how these factors contribute to health disparities. This analysis should extend to include one's own position in this structure.
- Interprofessional communication: Ongoing discussions of implicit bias, perspective taking, and counter-stereotypical dialogues should be woven into day-to-day practice with colleagues from diverse disciplines.
- Teams/teamwork: Health professionals should develop meaningful contacts with marginalized communities in order to better understand whom they are serving.

Adopting approaches from the fields of education, gender studies, sociology, psychology, and race/ethnic studies can help build curricula that represent a variety of disciplines [33]. Students can learn about and discuss implicit bias and its impact, not simply from a health outcomes perspective but holistically. Skills in problem-solving, communication, leadership, and teamwork should be included [33].

SOCIAL DETERMINANTS OF HEALTH

Social determinants of health are the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks. These circumstances are shaped by the distribution of money, power, and resources at global, national, and local levels. Healthy People 2030 groups social determinants of health into five categories [34]:

- Economic stability
- Education access and quality
- Health care access and quality
- Social and community context
- Neighborhood and built environment

These factors have a major impact on people's health, well-being, and quality of life. Examples of social determinants of health include [34]:

- Safe housing, transportation, and neighborhoods
- Racism, discrimination, and violence
- Education, job opportunities, and income
- Access to nutritious foods and physical activity opportunities
- Polluted air and water
- Language and literacy skills

Social determinants of health also contribute to wide health disparities and inequities. For example, people who lack access to grocery stores with healthy foods are less likely to have good nutrition, which raises the risk of heart disease, diabetes, and obesity and lowers life expectancy compared with those who have easier access to healthy foods [34].

Promoting healthy choices will not eliminate these and other health disparities. Instead, public health organizations and their partners must take action to improve the conditions in people's environments. Healthcare providers play a role by identifying factors affecting the health of their patients, providing resources (when appropriate), and advocating for healthy environments.

BARRIERS TO PROVIDING CARE

Culturally diverse patients experience a variety of barriers when seeking health and mental health care, including:

- Immigration status
- Lower socioeconomic status
- Language barriers
- Cultural differences
- Lack of or poor health insurance coverage
- Fear of or experiences with provider discrimination
- Mistrust of healthcare systems

Such obstacles can interfere with or prevent access to treatment and services, compromise appropriate referrals, affect compliance with recommendations, and result in poor outcomes. Culturally competent providers build and maintain rich referral resources to meet patients' assorted needs.

Encountering discrimination when seeking health or mental health services is a barrier to optimal care and contributor to poorer outcomes in under-represented groups. Some providers will not treat patients because of moral objections, which can affect all groups, but particularly those who are gender and/or sexual minorities, religious minorities, and/or immigrants. In fact, in 2016, Mississippi and Tennessee passed laws allowing health providers to refuse to provide services if doing so would violate their religious beliefs [35]. However, it is important to remember that providers are obligated to act within their profession's code of ethics and to ensure patients receive the best possible care.

BEST PRACTICES FOR CULTURALLY RESPONSIVE CARE

The U.S. Department of Health and Human Services has outlined steps important to incorporate in evaluation and treatment planning processes to ensure culturally competent clinical and programmatic decisions and skills [36].

The first step is to engage patients. In nonemergent situations, it is important to establish rapport before asking a series of assessment questions or delving deeply into history taking. Providers should use simple gestures as culturally appropriate (e.g., handshakes, facial expressions, greetings) to help establish a first impression. The intent is that all patients feel understood and seen following each interaction. Culturally responsive interview behaviors and paperwork should be used at all times [36].

When engaging in any patient teaching, remember that individuals may be new to the specific language or jargon and expectations of the diagnosis and care process. Patients should be encouraged to collaborate in every step of their care. This consists of seeking the patient's input and interpretation and establishing ways they can seek clarification. Patient feedback can then be used to help identify cultural issues and specific needs. If appropriate, collaboration should extend to include family and community members.

Assessment should incorporate culturally relevant themes in order to more fully understand patients and identify their cultural strengths and challenges. Themes include [36]:

- Immigration history
- Cultural identity and acculturation
- Membership in a subculture
- Beliefs about health, healing, and help-seeking
- Trauma and loss

In some cases, it may be appropriate and beneficial to obtain culturally relevant collateral information, with the patient's permission, from sources other than the patient (e.g., family or community members) to better understand beliefs and practices that shape the patient's cultural identity and understanding of the world.

Practitioners should work to identify screening and assessment tools that have been translated into or adapted for other languages and have been validated for their particular population group(s). An instrument's cultural applicability to the population being served should be assessed, keeping in mind that research is limited on the cross-cultural applicability of specific test items or questions, diagnostic criteria, and concepts in evaluative and diagnostic processes [36].

Typically, culturally responsive care establishes holistic treatment goals that include objectives to improve physical health and spiritual strength; utilizes strengths-based strategies that fortify cultural heritage, identity, and resiliency; and recognizes that treatment planning is a dynamic process that evolves along with an understanding of patient history and treatment needs.

In addition to these general approaches, specific considerations may be appropriate for specific populations. While discussion of every possible patient subgroup is outside of the scope of this course, some of the most common factors are outlined in the following sections [36].

RACIAL BACKGROUNDS

Race and color impact the ways in which individuals interact with their environments and are perceived and treated by others. Race is defined as groups of humans divided on the basis of inherited physical and behavioral differences. As part of the cultural competence process and as a reflection of cultural humility, practitioners should strive to learn as much as possible about the specific racial/ethnic populations they serve [37]. However, considerable diversity exists within any specific culture, race, or ethnicity [37]. Cultural beliefs, traditions, and practices change over time, both through generations and within an individual's lifetime. It is also possible for the differences between two members of the same racial/ethnic group to be greater than the differences between two people from different racial/ethnic groups. Within-group variations in how persons interact with their environments and specific social contexts are also often present.

As with all patients, it is vital to actively listen and critically evaluate patient relationships. All practitioners should seek to educate themselves regarding the experiences of patients who are members of a community that differs from their own. Resources and opportunities to collaborate may be available from community organizations and leaders.

Finally, preferred language and immigration/migration status should be considered. Interpreters should be used when appropriate, with adherence to best practices for the use of interpretation services. Stressing confidentiality and privacy is particularly important for undocumented workers or recent immigrants, who may be fearful of deportation.

Black Patients

"Black" or "African American" is a classification that serves as a descriptor; it has sociopolitical and self-identification ramifications. The U.S. Census Bureau defines African Americans or Black Americans as persons "having origins in any of the Black racial groups of Africa" [38].

According to the U.S. Census, African Americans number 46.9 million as of 2020 [39]. By 2060, it is projected they will comprise 17.9% of the U.S. population [40]. This group tends to be young; 30% of the African American population in the United States is younger than 18 years of age. In 2019, the median age for this group was 35 years [41]. In terms of educational attainment, 89.4% of African Americans 25 years of age or older had a high school diploma or completed college in 2020 [39]. Texas has the largest African American population, at 3.9 million [41].

Historical adversity and institutional racism contribute to health disparities in this group. For the Black population, patient assessment and treatment planning should be framed in a context that recognizes the totality of life experiences faced by patients. In many cases, particularly in the provision of mental health care, equality is sought in the provider-patient relationship, with less distance and more disclosing. Practitioners should assess whether their practices connect with core values of Black culture, such as family, kinship, community, and spirituality. Generalized or Eurocentric treatment approaches may not easily align with these components of the Black community [42]. Providers should also consider the impact of racial discrimination on health and mental health among Black patients. Reports indicate that expressions of emotion by Black patients tend to be negatively misunderstood or dismissed; this reflects implicit or explicit biases.

Asian Patients

As of 2019, 22.9 million Americans identified as Asian [43]. Between 2000 and 2019, Asians experienced the greatest growth compared with any other racial group at 81% [44; 45]. The Chinese group represents the largest Asian subgroup in the United States, and it is projected that this population will grow to 35.7 million between 2015 and 2040 [46; 47]. In 2019, Chinese Americans (excluding Taiwanese Americans) numbered at 5.2 million [43]. They also have the highest educational attainment; 54.6% of Asians 25 years of age or older had a bachelor's degree or higher in 2019 [43].

"Asian" is a single term widely used to describe individuals who have kinship and identity ties to Asia, including the Far East, Southeast Asia, and the Indian subcontinent [48]. This encompasses countries such as China, Japan, Korea, Vietnam, Cambodia, Thailand, India, Pakistan, and the Philippines. Pacific Islander is often combined with Asian American in census data. The Pacific Islands include Hawaii, Guam, Samoa, Fiji, and many others [48]. There are more than 25 Asian/Pacific Islander groups, each with a different migration history and widely varying sociopolitical environments in their homelands [49].

Asian American groups have differing levels of acculturation, lengths of residency in the United States, languages, English-speaking proficiency, education attainment, socioeconomic statuses, and religions. For example, there are approximately 32 different languages spoken among Asian Americans, and within each Asian subgroup (e.g., Chinese), multiple dialects may be present [49; 50]. In 2019, California had the largest Asian American population, totaling 5.9 million [44].

Recommended best practices when caring for Asian American patients include:

- Create an advisory committee using representatives from the community.
- Incorporate cultural knowledge and maintain flexible attitudes.
- Provide services in the patients' primary language.
- Develop culturally specific questionnaires for intake to capture information that may be missed by standard questionnaires.
- Emphasize traditional values and incorporate traditional practices (e.g., acupuncture) into treatment plans, when appropriate and desired.
- Explore patient coping mechanisms that draw upon cultural strengths.

Latino/a/x or Hispanic Patients

In 2020, the Hispanic population in the United States numbered 60.6 million [51]. The majority of the Hispanic population in the United States (63.3%) identify themselves as being of Mexican descent [53]. Approximately 27% of the U.S. Hispanic population identify as Puerto Rican, Cuban, Salvadoran, Dominican, Guatemalan, Colombian, Honduran, Ecuadorian, or Peruvian [54].

In 2020, the Hispanic population comprised 18.7% of the U.S. population [51]. As such, they are the largest ethnic minority group in the United States. By 2060, Hispanics are expected to represent 31% of the U.S. population [55]. They are also a young group, with a median age of 29.8 years [51]. In 2019, the three states with the largest Hispanic population growth were Texas (2 million), California (1.5 million), and Florida (1.4 million); these three states have the largest Hispanic populations overall [52].

When involved in the care of Latinx/Hispanic individuals, practitioners should strive to employ *personalismo* (warm, genuine communication) and recognize the importance of *familismo* (the centrality of the family). More flexible scheduling strategies may be more successful with this group, if possible, and some patients may benefit from culturally specific treatment and ethnic and gender matching with providers. Aspects of Latino culture can be assets in treatment: strength, perseverance, flexibility, and an ability to survive.

Native American Patients

The Native American population is extremely diverse. According to the U.S. Census, the terms "Native American," "American Indian," or "Alaskan Native" refer to individuals who identify themselves with tribal attachment to indigenous groups of North and South America [56]. In the United States, there are 574 federally recognized tribal governments and 324 federally recognized reservations [57].

In 2020, it was reported that there were 7.1 million Native Americans in the United States, which is approximately 2% of the U.S. population [57]. By 2060, this number is projected to increase to 10.1 million, or 2.5% of the total population [57].

In general, this group is young, with a median age of 31 years, compared with the general median age of 37.9 years [58]. As of 2018, the states with the greatest number of residents identifying as Native American are Alaska, Oklahoma, New Mexico, South Dakota, and Montana [59]. In 2016, this group had the highest poverty rate (26.2%) of any racial/ethnic group [58].

Listening is an important aspect of rapport building with Native American patients, and practitioners should use active listening and reflective responses. Assessments and histories may include information regarding patients' stories, experiences, dreams, and rituals and their relevance. Interruptions and excessive questioning should be avoided if at all possible. Extended periods of silence may occur, and time should be allowed for patients to adjust and process information. Practitioners should avoid asking about family or personal matters unrelated to presenting issues without first asking permission to inquire about these areas. Native American patients often respond best when they are given suggestions and options rather than directions.

White American Patients

In 2021, 76.3% of the U.S. population identified as White alone [60]. The U.S. Census Bureau defines White race as person having origins in any of the original peoples of Europe, the Middle East, or North Africa [38]. While the proportion of population identifying as White only has decreased between 2010 and 2020, the numbers of persons identifying as White and another race/ethnicity increased significantly. The White population in the United States is diverse in its religious, cultural, and social composition. The greatest proportion of this group reports a German ancestry (17%), followed by Irish (13%), English (10%), and Italian (7%) [61].

Providers can assume that most well-accepted treatment approaches and interventions have been tested and evaluated with White American individuals, particularly men. However, approaches may need modification to suit class, ethnic, religious, and other factors.

Providers should establish not only the patient's ethnic background, but also how strongly the person identifies with that background. It is also important to be sensitive to persons multiracial/multiethnic heritage, if present, and how this might affect their family relationships and social experiences. Assumption of White race should be avoided, as White-passing persons of color have their own unique needs.

RELIGIOUS, CULTURAL, AND ETHNIC BACKGROUNDS

Religion, culture, beliefs, and ethnic customs can influence how patients understand health concepts, how they take care of their health, and how they make decisions related to their health. Without proper training, clinicians may deliver medical advice without understanding how health beliefs and cultural practices influence the way that advice is received. Asking about patients' religions, cultures, and ethnic customs can help clinicians engage patients so that, together, they can devise treatment plans that are consistent with the patients' values [37].

Respectfully ask patients about their health beliefs and customs and note their responses in their medical records. Address patients' cultural values specifically in the context of their health care. For example, one may ask [37]:

- "Is there anything I should know about your culture, beliefs, or religious practices that would help me take better care of you?"
- "Do you have any dietary restrictions that we should consider as we develop a food plan to help you lose weight?"
- "Your condition is very serious. Some people like to know everything that is going on with their illness, whereas others may want to know what is most important but not necessarily all the details. How much do you want to know? Is there anyone else you would like me to talk to about your condition?"
- "What do you call your illness and what do you think caused it?"
- "Do any traditional healers advise you about your health?"

Practitioners should avoid stereotyping based on religious or cultural background. Each person is an individual and may or may not adhere to certain cultural beliefs or practices common in his or her culture. Asking patients about their beliefs and way of life is the best way to be sure you know how their values may impact their care [37].

GENDER

Gender identity is a vital aspect of a person's experience of the world and of themselves. It also impacts the ways in which the world perceives and treats individuals, with a clear effect on the effective provision of health and mental health care. This section will focus on persons presenting as cisgender male or female; special considerations for those who are transgender, non-binary, or gender nonconforming will be explored in the next section.

An increasing amount of research is supporting a relationship between men's risk for disease and death and male gender identity, and the traditional male role has been shown to conflict with the fostering of healthy behaviors [62; 63]. Male gender identity is related to a tendency to take risks, and the predilection for risky behavior begins in boyhood [63; 64; 65]. In addition, boys are taught that they should be self-reliant and independent and should control their emotions, and societal norms for both boys and men dictate that they maintain a strong image by denying pain and weakness [62; 64; 65].

Issues related to male gender identity have several important implications for health. First, risky behavior is associated with increased morbidity and mortality. Second, the concept of masculinity leads to inadequate help- and information-seeking behavior and a reduced likelihood to engage in behavior to promote health [62; 64; 65]. These behaviors appear to be rooted in a decreased likelihood for men to perceive themselves as being ill or at risk for illness, injury, or death [62]. Third, male gender identity, coupled with lower rates of health literacy, creates special challenges for effectively communicating health messages to men [66; 67; 68]. Gender differences in health-related behaviors are consistent across racial/ethnic populations, although specific behaviors vary according to race/ethnicity [63].

Men's beliefs about masculinity and traditional male roles affect health communication, and healthcare practitioners should consider male-specific beliefs and perceptions when communicating with male patients. For example, because men tend to focus on present rather than future health, concepts of fear, wellness, and longevity often do not work well in health messages [69]. Instead, healthcare practitioners should focus more on "masculine" concepts, such as strength, safety, and performance, all of which tie into men's perceptions of their roles as providers and protectors.

Although men are more likely than women to lack a regular healthcare provider and to avoid seeking help or information, women are more likely to have a chronic condition requiring regular monitoring and are more likely to have forgone necessary health care due to the cost [70].

Providing gender-sensitive care to women involves overcoming the limitations imposed by the dominant medical model in women's health. This requires theoretical bases that do not reduce women's health and illness experience into a disease. This philosophy incorporates explanations of health and empowers women to effectively and adequately deal with their situations. The major components incorporated into the development of sensitive care include:

- Gender is a central feature.
- Women's own voices and experiences are reflected.
- Diversities and complexities are incorporated into women's experiences.

- Theorists reflect about underlying androcentric and ethnocentric assumptions.
- Sociopolitical contexts and constraints of women's experiences are considered.
- Guidelines for practice with specific groups of women are provided.

GENDER AND SEXUAL MINORITIES

The gender and sexual minority (GSM) population is a diverse group that can be defined as a subculture. It includes homosexual men, lesbian women, bisexual persons, transgender individuals, and those questioning their sexual identity, among others. The GSM population is diverse, representing all ages and all socioeconomic, ethnic, educational, and religious backgrounds. The population has been described as "hidden and invisible," "marginalized," and "stigmatized." As a result, the unique health and safety needs of the population have often been overlooked or ignored. Clear definitions of the concepts related to sexual identity will be helpful. The following is a glossary of terms used in discussions of this group [71; 72; 73; 74; 75; 76]:

Asexual/aromantic: An individual who does not experience sexual attraction. There is considerable diversity in individuals' desire (or lack thereof) for romantic or other relationships.

Bisexual: An adjective that refers to people who relate sexually and affectionately to both women and men.

Coming-out process: A process by which an individual, in the face of societal stigma, moves from denial to acknowledging his/her sexual orientation. Successful resolution leads to self-acceptance. Coming out is a lifelong process for lesbian, gay, bisexual, and transgender persons and their families and friends as they begin to tell others at work, in school, at church, and in their communities.

Gay: The umbrella term for GSM persons, although it most specifically refers to men who are attracted to and love men. It is equally acceptable and more accurate to refer to gay women as "lesbians."

Gender and sexual minorities (GSM): A term meant to encompass lesbian, gay, bisexual, trans, queer/questioning, intersex/intergender, asexual/ally (LGBTQIA) people as well as less well-recognized groups, including aromantic, two-spirited, and gender-fluid persons.

Heterosexism: An institutional and societal reinforcement of heterosexuality as the privileged and powerful norm.

Heterosexuality: Erotic feelings, attitudes, values, attraction, arousal, and/or physical contact with partners of the opposite gender.

Homophobia: A negative attitude or fear of non-straight sexuality or GSM individuals. This may be internalized in the form of negative feelings toward oneself and self-hatred. Called "internalized homophobia," it may be manifested by fear of discovery, denial, or discomfort with being LGBTQIA, low self-esteem, or aggression against other lesbians and gay men.

Homosexuality: The "persistent sexual and emotional attraction to members of one's own gender" as part of the continuum of sexual expression. Typically not used to describe people.

LGBTQIA: An acronym used to refer to the lesbian, gay, bisexual, transgender/transsexual, queer/questioning, intersex/intergender, asexual/ally community. In some cases, the acronym may be shortened for ease of use or lengthened for inclusivity. Members of this group may also be referred to as gender and sexual minorities (GSM).

Queer: An umbrella term to describe persons with a spectrum of identities and orientations that are outside of the heteronormative standard.

Sexual identity: The inner sense of oneself as a sexual being, including how one identifies in terms of gender and sexual orientation.

Sexual orientation: An enduring emotional, romantic, sexual, and/or affectionate attraction to another person. Individuals may experience this attraction to someone of the same gender, the opposite gender, both genders, or gender nonconforming.

Transgender: An umbrella term describing a number of distinct gender positions and identities including: crossdressing, transsexual, nonbinary, and intersex.

One's intrapersonal acceptance or rejection of societal stereotypes and prejudices, the acceptance of one's self-identity as a sexual minority, and how much one affiliates with other members of the GSM community varies greatly among individuals [77]. Some authors stress the diversity within the GSM community by discussing "GSM populations" [78]. For example, it is understandable that a GSM population living in rural areas of the United States would have little in common with a GSM population living in urban areas or "gay-friendly" neighborhoods. Additionally, mental health experts have suggested that "GSM community" symbolizes a single group of individuals who express their sexuality differently than the majority of heterosexual individuals. However, many distinct communities have been identified, including lesbian, gay, bisexual, and transgender [79]. Each community is different from the other as well as different from the heterosexual community. A culturally competent healthcare provider should keep this diversity in mind so that vital differences among these smaller groups are not lost when thinking of the GSM population in general.

Commonalities exist among the GSM communities as well. For example, many adolescents, whether gay, lesbian, bisexual, transgender, or questioning their sexual identity, lack sexual minority role models to assist with successful psychosocial development [79].

The subtle and pervasive ways that discomfort with GSM individuals may be manifested have been examined and, in some instances, categorized as "cultural heterosexism," which is characterized by the stigmatization in thinking and actions found in our nation's cultural institutions, such as the educational and legal systems [80]. "Cultural heterosexism fosters individual antigay attitudes by providing a ready-made system of values and stereotypical beliefs that justify such prejudice as natural" [81]. Perhaps the paucity of information about the GSM community in basic professional education has been a reflection of cultural heterosexism. Writers, funding sources, and publishers have been exposed to the same cultural institutions for many years.

Individuals generally begin to absorb these institutional attitudes as children and may consequently develop "psychologic heterosexism," which may also manifest as antigay prejudice. Many individuals, as children, have little contact with someone who is openly gay and, as a result, may not be able to associate homosexuality with an actual person. Instead, they may associate it with concepts such as "sin," "sickness," "predator," "outsider," or some other negative characteristic from which the individual wants to maintain distance [81]. Psychologic heterosexism involves (among other factors) considering sexual identity and determining that one does not want to think further about it. The direction of this thinking is undeniably negative, resulting in an environment that allows antigay hostility [81]. The impact of antigay prejudice on the physical and mental health of members of the LGBTQIA community and their families should not be underestimated [82; 83].

Sexual minority individuals also are not immune to societal attitudes and may internalize negative aspects of the antigay prejudice experience. Anxiety, depression, social withdrawal, and other reactions may result [2; 84]. While the study of psychologic heterosexism, both blatant and subtle, is in the early stages of research, it has had a measurable impact on the mental health of the GSM community [85; 86; 87; 88].

Examples of the range of manifestations of heterosexism and/or homophobia in our society are readily available. Without difficulty, each example presented here may be conceptualized as related to the emotional or physical health of a GSM individual or family member:

- A kindergarten student calls another child an LGBTQ+ slur but does not really know what he is saying.
- A teenage girl allows herself to become pregnant, "proving" her heterosexuality to herself, her family, and her friends.
- A parent worries that her 12-year-old daughter is still a "tomboy."
- An office employee decides to place a photo of an old boyfriend in her office rather than a photo of her gender-nonconforming partner of five years.
- A college student buries himself in his studies in an effort to ignore his same-sex feelings and replace feelings of isolation.
- Two teenage girls, thought by peers to be transgender individuals, are assaulted and killed while sitting together in an automobile.
- A female patient is told by a healthcare provider that her haircut makes her look like a lesbian and is examined roughly.
- A gay man chooses not to reveal his sexual identity to his healthcare provider out of fear of a reduction or withdrawal of healthcare services.

The manifestations of heterosexism have inhibited our learning about the LGBTQIA population and its needs [78]. Gay patients have feared open discussion about their health needs because of potential negative reactions to their self-disclosure. Prejudice has impacted research efforts by limiting available funding [77]. All of these factors emphasize that the healthcare education system has failed to educate providers and researchers about the unique aspects of LGBTQIA health [83; 89].

Common Myths

Many myths surround homosexuality; a few are outlined below. The origin of these myths may be better understood after examining the history of homosexuality as well as the attitudes toward human sexuality in general. The history of the development of societal norms related to homosexuality includes misconceptions developed during times when research was not available on which to build a scientific knowledge base [82; 90; 91; 92].

Myth: Sexual orientation is a choice.

Fact: No consensus exists among scientists about the reasons that an individual develops his/her sexual orientation. Some research has shown that the bodies and brains of gay men and women differ subtly in structure and function from their heterosexual counterparts; however, no findings have conclusively shown that sexual orientation is determined by any particular factor or set of factors. Many people confuse sexual orientation with sexual identity. The reader may consider reviewing the definitions of these terms when further considering this myth.

Myth: Gay men and lesbians can be easily identified because they have distinctive characteristics.

Fact: Most gay and lesbian individuals conform to the majority of society in the way they dress and act. Further, a person's appearance is not necessarily an indication of sexual or romantic interests.

Myth: Gay individuals are child molesters.

Fact: This is a very damaging and heterosexist position. According to experts in the field of sexual abuse, the vast majority of those who molest children are heterosexual. The average offender is a White heterosexual man whom the child knows.

Myth: Gay people want to come into our schools and recruit our children to their "lifestyle."

Fact: Efforts to bring issues related to LGBTQIA history and rights into schools are not efforts to "convert," just as education on European history is not an effort to glamorize or "convert" to European identity. The intent has been to teach a more complete history of the world and to prevent children from mistreating LGBTQIA who are often the subjects of harassment and physical attacks. There is no evidence that people could be "recruited" to a gay sexual orientation, even if someone wanted to do this.

AGE

Elderly patients should be routinely screened for health and mental health conditions using tools specifically developed for this population, in spite of some practitioners' discomfort with asking questions about sensitive topics. These population-appropriate assessments may be included in other health screening tools [93].

Wellness and purpose have become important emphases when working with older adults [94]. In the past, aging was associated with disability, loss, decline, and a separation from occupational productivity. Although patient growth and positive change and development are values that practitioners embrace, the unconscious acceptance of societal myths and stereotypes of aging may prevent practitioners from promoting these values in elderly individuals [95].

Common Myths of Aging

Society holds several myths about the elderly. Many of these myths may be easily disputed based on data from the U.S. Census and other studies.

Myth: Most older adults live alone and are isolated.

Fact: In 2018, 70% of men and 46% of women 65 years and older were married. An estimated 28% lived alone [96]. According to a survey conducted in 2009, 9 out of 10 individuals 65 years of age and older stated they talked to family and friends on a daily basis [97]. In 2016, an estimated 20% of the U.S. population lived in a household comprised of two adult generations or a grandparent or at least one other generation, compared with 12% in 1980 [97; 98]. This multigenerational household trend particularly affects those 65 years and older, with 21% of these individuals living in multigenerational households in 2016. This group was second only to individuals 25 to 29 years of age (33%) [98]. Several factors have contributed to this trend, including growing racial and ethnic diversity and adults getting married later [97; 98].

Myth: Most older adults engage in very minimal productive activity.

Fact: In 2016, 18.6% of persons 65 years and older were employed or actively looking for work, and this population represents approximately 8% of the total labor force in the United States [99]. The elderly are more engaged in self-employed activities than younger persons. In 2016, 16.4% of those 65 years of age and older were self-employed, compared with an average of 5.5% of those 16 years to 64 years of age [100].

Myth: Life satisfaction is low among the elderly.

Fact: Data from the Berkeley Older Generation Study indicate that many elders are quite satisfied with their life [101]. More than one-third (36%) of persons older than 59 years of age and 15% of those older than 79 years of age stated they were currently experiencing the best time in their lives. A 2009 survey found that 60% of individuals 65 years of age and older stated they were very happy. A 2012 survey found that 65% of individuals 65 years of age and older indicated that the past year of their life has been normal or better than normal, and more than 80% of respondents agreed with the statement, "I have a strong sense of purpose and passion about my life and my future" [102]. Most of the factors that predict happiness for the young, such as good health and financial stability, also apply to the elderly. Older adults tend to report higher levels of well-being in part due to the quality of their social relationships [103].

PERSONS WITH MENTAL OR PHYSICAL DISABILITY

Americans with disabilities represent a large and heterogeneous segment of the population. The prevalence of disability varies by age group and definition. Based on the U.S. Census Bureau's 2013 American Community Survey (ACS), which describes disability in terms of functional limitations, 12.6% of the civilian U.S. noninstitutionalized population has a disability, defined as difficulty in hearing or vision, cognitive function, ambulation, self-care, or independent living [104]. The U.S. Department of Education, which uses categorical disability labels, estimates that 13% of children and youth 3 to 21 years of age have a disability (defined as specific learning disabilities, speech or language impairments, intellectual disability, emotional disturbance, hearing impairments, orthopedic impairments, other health impairments, visual impairments, multiple disabilities, deaf-blindness, autism, traumatic brain injury, or developmental delay) [104].

People with disabilities experience many health disparities. Some documented disparities include poorer self-rated health; higher rates of obesity, smoking, and inactivity; fewer cancer screenings (particularly mammography and Pap tests); fewer breast-conserving surgeries when breast cancer is diagnosed; and higher rates of death from breast or lung cancer [104].

Disability cultural competence requires appreciation of social model precepts, which recognize patients' rights to seek care that meets their expectations and values. The social model of disability has been characterized as centering disability as a social creation rather than an attribute of the patient [105]. As such, disability requires a social/political response in order to improve environmental factors affecting access and acceptance [105]. This involves adoption of person-first language, acknowledgement of social and environmental factors impacting persons abilities, and confronting disability-associated stigma.

VETERANS

The effects of military service and deployment to military combat on the individual and the family system are wide-reaching. According to the U.S. Department of Defense, there were 3.5 million current military personnel in 2020 and 18.3 million veterans in 2017 [132; 133]. The Army has the largest number of active duty members, followed by the Navy, the Air Force, and the Marine Corps [132]. Military service presents its own set of risk and protective factors for a variety of mental health issues, including post-traumatic stress disorder (PTSD), traumatic brain injury (TBI), depression and suicide, substance abuse, and interpersonal violence. In particular, transitioning from combat back to home life can be particularly trying for veterans and their families.

As the number of military conflicts and deployments has increased since 2001, the need to identify and provide better treatment to veterans and their families has become a greater priority. The first step in providing optimal care is the identification of veterans and veteran families during initial assessments, with an acknowledgement that veterans may be any sex/gender and are present in all adult age groups [133].

Unfortunately, veterans and military families often do not voluntarily report their military service in healthcare appointments. In 2015, the American Medical Association updated its recommendations for social history taking to include military history and veteran status [134]. In addition, the American Academy of Nursing has designed the Have You Ever Served? Initiative to encourage health and mental health professionals to ask their patients about military service and related areas of concern [135]. This program provides pocket cards, posters, and resource links for professionals working with veterans and their families. Recommended questions for intake include [135]:

- Have you or has someone close to you ever served in the military?
- When did you serve?
- Which branch?
- What did you do while you were in the military?
- Were you assigned to a hostile or combative area?
- Did you experience enemy fire, see combat, or witness casualties?
- Were you wounded, injured, or hospitalized?
- Did you participate in any experimental projects or tests?
- Were you exposed to noise, chemicals, gases, demolition of munitions, pesticides, or other hazardous substances?

PROMOTING CULTURALLY SENSITIVE COMMUNICATION

Communication, the process of sending a message from one party to another, consists of both verbal and nonverbal components. Verbal and nonverbal communications are embedded within the culture of the parties disseminating the information and within the culture of the parties receiving the information. Communication is complex and multilayered because it involves unstated, implicit rules about a variety of factors, including physical distance between parties, tone of voice, acceptable topics of discussion, physical contact, and amount of eye contact [106]. Each of these variables is influenced by the perception of the level of formality/informality of the situation. Frequently, misunderstandings occur because the decoding and interpretation of these nonverbal cues are not accurate.

The verbal component of communication is just as complicated. Certainly, similarity in language shared by both parties enhances communication, but assuming that both parties in a conversation speak the same language, how the information is interpreted is still influenced by a host of factors. Linguists have posited that approximately 14,000 different meanings and interpretations can be extracted from the 500 most common English words [107]. Consequently, practitioners must be aware of the different communication styles held by diverse ethnic minority patients, as the clinical communication process is the primary vehicle by which problems and solutions are identified and conveyed [108].

Styles of communication can be classified from high- to low-context [109]. High-context cultures are those cultures that disseminate information relying on shared experience, implicit messages, nonverbal cues, and the relationship between the two parties [107; 110]. Members of these cultural groups tend to listen with their eyes and focus on how something was said or conveyed [106; 109]. On the other hand, low-context cultures rely on verbal communication or what is explicitly stated in the conversation [107]. Consequently, low-context communicators listen with their ears and focus on what is being said [106; 109; 110]. Western culture, including the United States, can be classified as a low-context culture. On the other hand, groups from collectivistic cultures, such as Asian/Pacific Islanders, Hispanics, Native Americans, and African Americans, are from high-context cultures [109].

Communicators from high-context cultures generally display the following characteristics [106; 107; 110; 111]:

- Use of indirect modes of communication
- Use of vague descriptions
- Less talk and less eye contact
- Interpersonal sensitivity
- Use of feelings to facilitate behavior
- Assumed recollection of shared experiences
- Reliance on nonverbal cues such as gestures, tone of voice, posture, voice level, rhythm of speaking, emotions, and pace and timing of speech
- Assimilation of the "whole" picture, including visual and auditory cues
- Emotional speech
- Use of silence
- Use of more formal language, emphasizing hierarchy between parties

On the other hand, low-context communicators can typically be described as [106; 107; 110]:

- Employing direct patterns of communication
- Using explicit descriptions and terms
- Assuming meanings are described explicitly
- Utilizing and relying minimally on nonverbal cues
- Speaking more and often raising their voices (more animated, dramatic)
- Often being impatient to get to the point of the discussion
- Using more informal language; less emphasis on hierarchy, more equality between parties (more friendly)
- Being more comfortable with fluidness and change
- Uncomfortable using long pauses and storytelling as a means of communicating

Understanding the distinctions between individuals who come from high- and low-context cultures can promote cultural sensitivity. However, it is vital that practitioners take heed of several words of caution. First, it is important not to assume that two individuals sharing the same culture (e.g., low-context culture) will automatically have a shared script for communicating. Second, it is important to not immediately classify an individual into a low- or high-context culture because of their ethnicity. A Chinese American man may not necessarily be a high-context communicator because he is Asian. A host of factors, such as level of acculturation, upbringing and socialization, education, and family immigration history, will all play a role in how one learns to communicate. Third, a major criti-

cism of the discussion of low-/high-context cultures is that they reinforce dualism and ultimately oversimplify the complexities and nuances of communication [112].

Learning to communicate effectively also requires an understanding of how different conversational traits influence the communication process, or how information is conveyed and interpreted. Again, the goal of this section is not to simply dichotomize individuals' conversational styles into categories, but rather to understand the factors that play a role in how someone makes a decision on how to communicate [106].

As long as there are two parties involved in a conversation, nonverbal communication is inevitable, and it becomes salient particularly when it is processed from one culture to another. Nonverbal communication is any behavior (including gestures, posture, eye contact, facial expressions, and body positions) that transcends verbal or written forms of communication [113]. Nonverbal communication can enhance or reinforce what is said verbally, and conversely, it can completely contradict the message communicated verbally. It can also end up replacing what was verbally communicated if both parties do not share a native language [114].

In Western culture, communication is more direct and eye contact is highly valued. When eye contact is not maintained, many Westerners assume that the party is hiding pertinent information. However, in some cultures, reducing eye contact is a sign of respect [108]. Conversely, patients may interpret direct and indirect gazes differently. For example, in one study, Japanese individuals tended to rate faces with a direct gaze as angry and less pleasant compared with Finnish participants [115].

The amount of social space or distance between two communicating parties is culturally charged as well. Depending upon the social context, Westerners tend to maintain a distance of about three feet, or an arm's length, in conversations [107]. In a public setting, where both parties are engaged in a neutral, nonpersonal topic, Westerners will feel encroached upon and uncomfortable if an individual maintains a closer conversational distance. However, in other cultures, such as Latino and Middle Eastern, a closer distance would be the norm [107]. Chung recommends that in a clinical setting the practitioner allow patients to set the tone and social distance [116]. The practitioner can sit first and permit the patient to select where they want to sit.

Cross-cultural communication is by no means simple, and there is no set of rules to merely abide by. Instead, promoting culturally sensitive communication is an art that requires practitioners to self-reflect, be self-aware, and be willing to learn. Therefore, as practitioners become skilled in noticing nonverbal behaviors and how they relate to their own behaviors and emotions, they will be more able to understand their own level of discomfort and comprehend behavior from a cultural perspective [106].

CULTURALLY SENSITIVE ASSESSMENT GUIDELINES

Practitioners may be categorized as either disease-centric or patient-centric [117]. Disease-centered practitioners are concerned with sign/symptom observation and, ultimately, diagnosis. On the other hand, patient-centered practitioners focus more on the patient's experience of the illness, subjective descriptions, and personal beliefs [117]. Patient-centered practice involves culturally sensitive assessment. It allows practitioners to move assessment and practice away from a pathology-oriented model and instead acknowledge the complex transactions of the individual's movement within, among, and between various systems [118].

Practitioners who engage in culturally sensitive assessment nonjudgementally obtain information related to the patient's cultural beliefs, overall perspective, and specific health beliefs [119]. They also allow the patient to control the timing [120].

The goal is to avoid the tendency to misinterpret health concerns of ethnic minority patients. Panos and Panos have developed a qualitative culturally sensitive assessment process that focuses on several domains [119]. Each domain includes several questions a practitioner may address in order to ensure that he or she is providing culturally responsive care.

Alternatively, Kleinman suggests that the practitioner ask the patient what he or she thinks is the nature of the problem [121]. He highlights the following types of questions that may be posed to the patient [121]:

- Why has the illness/problem affected you?
- Why has the illness had its onset now?
- What course do you think the illness will follow?
- How does the illness affect you?
- What do you think is the best or appropriate treatment? What treatment do you want?
- What do you fear most about the illness and its treatment?

Similar to Kleinman's culturally sensitive assessment questions, Galanti has proposed the 4 Cs of Culture [122]:

- What do you call the problem?
- What do you think caused it?
- How do you cope with the problem?
- What questions or concerns do you have about the problem or treatment?

Pachter proposed a dynamic model that involves several tiers and transactions, similar to Panos and Panos' model [123]. The first component of Pachter's model calls for the practitioner to take responsibility for cultural awareness and knowledge. The professional must be willing to acknowledge that they do not possess enough or adequate knowledge in health beliefs and practices among the different ethnic and cultural groups they come in contact with. Reading and becoming familiar with medical anthropology is a good first step.

The second component emphasizes the need for specifically tailored assessment [123]. Pachter advocates the notion that there is tremendous diversity within groups. Often, there are many intersecting variables, such as level of acculturation, age at immigration, educational level, and socioeconomic status, that influence health ideologies. Finally, the third component involves a negotiation process between the patient and the professional [123]. The negotiation consists of a dialogue that involves a genuine respect of beliefs. The professional might recommend a combination of alternative and Western treatments.

Beckerman and Corbett further recommend that recently immigrated families be assessed for [124]:

- Coping and adaptation strengths
- Issues of loss and adaptation
- The structure of the family in terms of boundaries and hierarchies after immigration
- Specific emotional needs
- Acculturative stress and conflict for each family member

Practitioners should seek to understand the sociopolitical context of the origin country [125]. A migration narrative is also recommended, whereby an individual provides a story of their migration history. Asking about how long the family has been in the United States, who immigrated first, who was left behind, and what support networks are lacking gives the practitioner an overview of the individual's present situation [126]. The theme of loss is very important to explore. Types of losses may include family and friends left behind, social status, social identity, financial resources, and familiarity [126]. For refugees and newly immigrated individuals and families, assessment of basic needs (e.g., food, housing, transportation) is necessary [125].

Culturally sensitive assessment involves a dynamic framework whereby the practitioner engages in a continual process of questioning. Practitioners should work to recognize that there are a host of factors that contribute to patients' multiple identities (e.g., race, gender, socioeconomic status, religion) [127].

WELCOMING AND SAFE ENVIRONMENT

Improving access to care can be facilitated, in part, by providing a welcoming environment. The basis of establishing a safe and welcoming environment for all patients is security, which begins with inclusive practice and good clinician-patient rapport. Shared respect is critical to a patient's feeling of psychological well-being. Security can also be fostered by a positive and safe physical setting. For patients who are acutely ill, both the illness experience and treatment process can produce trauma. This is particularly true if involuntary detainment or hospitalization is necessary, but exposure to other individuals' narratives of experienced trauma or observing atypical behaviors from individuals presenting as violent, disorganized, or harmful to themselves can also be traumatic. As such, care environments should be controlled in a way to minimize traumatic stress responses. Providers should keep this in mind when structuring the environment (e.g., lighting, arrangement of space), creating processes (e.g., layout of appointments or care systems, forms), and providing staff guidance (e.g., nonverbal communication, intonation, communication patterns). During each encounter, the patient's perception of safety is impacted by caretakers and ancillary staff.

Experts recommend the adoption and posting of a nondiscrimination policy that signals to both healthcare providers and patients that all persons will be treated with dignity and respect [128]. Also, checklists and records should include options for the patient defining their race/ethnicity, preferred language, gender expression, and pronouns; this can help to better capture information about patients and be a sign of acceptance to that person. If appropriate, providers should admit their lack of experience with patient subgroups and seek guidance from patients regarding their expectations of the visit.

Front office staff should avoid discriminatory language and behaviors. For example, staff should avoid using gender-based pronouns, both on the phone and in person. Instead of asking, "How may I help you, sir?" the staff person could simply ask, "How may I help you?" Offices that utilize electronic health records should have a system to track and record the gender, name, and pronoun of all patients. This can be accomplished by standardizing the notes field to document a preferred name and pronoun for all patients [129]. Some persons who identify as non-binary (i.e., neither or both genders) may prefer that plural pronouns (e.g., they) be used.

Questions should be framed in ways that do not make assumptions about a patient's culture, gender identity, sexual orientation, or behavior. Language should be inclusive, allowing the patient to decide when and what to disclose. Assurance of confidentiality should be stressed to the patient to allow for a more open discussion, and confidentiality should be ensured if a patient is being referred to a different healthcare provider. Asking open-ended questions can be helpful during a history and physical.

The FACT acronym may be helpful for healthcare providers. Providers should:

- **F**ocus on those health issues for which the individual seeks care
- **A**void intrusive behavior
- **C**onsider people as individuals
- **T**reat individuals according to their gender

Training office staff to increase their knowledge and sensitivity toward persons will also help facilitate a positive experience for patients.

CONCLUSION

Culture serves as a lens through which patients and practitioners filter their experiences and perceptions. Patients will bring their unique life stories and concerns to the practitioner, and their cultural values and belief systems will inevitably shape how the problem is defined and their beliefs about what is effective in solving the problem. However, the cultural backgrounds and values of patients are not necessarily scripts that define behavior, and when practitioners view culture as a strength and not a pathology, practitioners will be able to more effectively join with patients to mobilize change.

FACULTY BIOGRAPHY

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families.

Previously acting as a faculty member at Capella University and Northcentral University, Dr. Yick Flanagan is currently a contributing faculty member at Walden University, School of Social Work, and a dissertation chair at Grand Canyon University, College of Doctoral Studies, working with Industrial Organizational Psychology doctoral students. She also serves as a consultant/subject matter expert for the New York City Board of Education and publishing companies for online curriculum development, developing practice MCAT questions in the area of psychology and sociology. Her research focus is on the area of culture and mental health in ethnic minority communities.

Customer Information/Answer Sheet/Evaluation insert located between pages 60–61.

COURSE TEST - #57430 CULTURAL COMPETENCE: AN OVERVIEW

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1. A nurse acknowledges that she still has a lot to learn about different racial and ethnic minority groups. She is willing to learn from her patients and assume the role of learner. This nurse is demonstrating
- A) *diversity.*
- B) *reflexivity.*
- C) *explicit bias.*
- D) *cultural humility.*

2. Which of the following is NOT a risk factor in triggering implicit biases for health professionals?
- A) *Uncertainty*
- B) *Cognitive dissonance*
- C) *Time pressure to make a rapid decision*
- D) *Heavy workload and feeling behind schedule*

3. All of the following are categories of social determinants, EXCEPT:
- A) *Race*
- B) *Economic stability*
- C) *Health care access and quality*
- D) *Social and community context*

4. Which of the following has been identified as a core value of Black culture?
- A) *Spirituality*
- B) *Community*
- C) *Family/kinship*
- D) *All of the above*

5. Male gender identity is related to
- A) *risk avoidance.*
- B) *emotional demonstration.*
- C) *denying pain and weakness.*
- D) *teamwork and help-seeking.*

6. Cultural heterosexism is characterized by
- A) *negative feelings toward oneself and self-hatred.*
- B) *A negative attitude or fear of non-straight sexuality or GSM individuals.*
- C) *considering sexual identity and determining that one does not want to think further about it.*
- D) *the stigmatization in thinking and actions found in cultural institutions, such as educational and legal systems.*

7. Persons with disability experience higher rates of all of the following, EXCEPT:

A) Obesity
B) Smoking
C) Cancer screening
D) Breast and lung cancer mortality

8. Which of the following is a typical characteristic of communication in high-context cultures?

A) Use of more informal language
B) Speaking more and often raising one's voice
C) Assumption that meanings are described explicitly
D) Reliance on interpreting eye contact, gestures, and tone of voice

9. Which of the following is an attribute of patient-centered practice?

A) The practitioner focuses on observed signs and symptoms.
B) The practitioner is concerned with identifying the disease pathology.
C) The practitioner focuses on the subjective description of the illness.
D) The practitioner is not influenced by how the client/patient defines the illness.

10. The basis of establishing a safe and welcoming environment for all patients is

A) security.
B) autonomy.
C) beneficence.
D) maintaining distance.

Be sure to transfer your answers to the Answer Sheet located on the envelope insert.
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Dental Treatment of Pediatric and Adolescent Patients

Audience
This course is designed for dental hygienists and assistants whose patient populations include children and/or adolescents. It may also be of interest to dentists with pediatric patients.

Course Objective
Dental professionals are frequently involved in the care of pediatric and/or adolescent patients. The purpose of this course is to outline the oral health needs and problems unique to the pediatric and adolescent populations.

Learning Objectives
Upon completion of this course, you should be able to:

1. Outline the eruption sequence, anatomy, and morphology of deciduous teeth.
2. List the restorative options for deciduous and permanent teeth in children and adolescents.
3. Evaluate the preventive dentistry options that can benefit deciduous and permanent teeth.
4. Cite the major differences in the use of medications for dental treatment of children and adolescents compared to their adult counterparts.
5. Identify oral lesions that accompany common childhood and adolescent diseases.
6. Evaluate the common oral and maxillofacial signs of child and adolescent abuse.
7. Describe possible oral manifestations of eating disorders.

Faculty
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Faculty Disclosure
Contributing faculty, Mark J. Szarejko, DDS, FAGD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Director Disclosure
The director has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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INTRODUCTION

The goal of achieving and maintaining optimal oral health is one that should begin during childhood, continue during adolescence, and extend into the adult years. Teeth are essential throughout life for mastication, phonation, cosmetics, and support for the tissues that compose the facial form. Dental treatment of pediatric and adolescent dental patients must take into consideration their unique anatomical, physiologic, psychologic, maturational, and emotional differences and needs. This course will highlight these differences and options for preventive dentistry appropriate for this patient population, including a proactive means by which the risk of early childhood caries can be reduced. The need to adjust the dosage and/or frequency of administration of medications used in conjunction with dental treatment of pediatric and adolescent patients will be discussed. Oral lesions associated with common childhood diseases will be identified, as local outbreaks of infectious disease such as the measles and chickenpox still occur. The factors that are integral to the restoration of carious teeth and the oral and perioral signs of child abuse/domestic violence are discussed. Clinicians should consider the extent of their training with pediatric and adolescent patients before they are treated. If the complexity of the case, behavioral concerns, or patient management is beyond the clinician's ability, referral to a pedodontist should be made.

ERUPTION SEQUENCE

The first complete set of teeth to erupt in the oral cavity have been called deciduous, primary, baby, or milk teeth. The eruption of a tooth is a developmental process during which a tooth moves from its position within the alveolar bone through the overlying mucosa into the oral cavity until it achieves a fully erupted position, where it will attain occlusion against an opposing tooth. Most teeth follow this process, although some teeth, most often the third molars ("wisdom teeth"), become impacted as they encounter bony or other anatomical obstructions and never fully erupt. Surgical removal is usually required to relieve pain and to prevent pathology to the adjacent structures.

Infants are usually born completely edentulous (without teeth), but there are rare exceptions. Natal teeth are those that are present at birth, and neonatal teeth erupt within 30 days of birth [1]. These usually occur in the anterior mandible, particularly the early eruption of the mandibular deciduous incisors. Natal and neonatal teeth exhibit minimal root formation and may have a variable range of mobility. This can cause complications during breastfeeding, and sharp edges of the exposed teeth can even traumatize the oral mucosa of the infant. Although these are deciduous teeth, they must be cleaned gently with plain cotton gauze or a cotton swab, as they are subject to colonization by bacteria that can initiate the carious process. Consultation with a dentist or pedodontist can determine the best protocol by which this is accomplished. These teeth are extracted if the mobility presents a risk of aspiration, but this is rare.

The chronology of the eruption of the 20 deciduous teeth will vary widely among children. The mandibular central incisors are usually the first teeth to erupt at 6 to 10 months of age. The maxillary and mandibular second molars complete the sequence and usually appear at 23 to 33 months of age [2]. The lateral incisors, canines, and first molars erupt in the intervening interval. Genetics, systemic illness, and developmental problems are among the many factors that can delay the eruption of the deciduous teeth.

Unlike their permanent counterparts, deciduous teeth have no premolars. The permanent premolars replace the first and second deciduous molars and are the only permanent teeth to have less length in a mesial-to-distal (anterior-to-posterior) dimension than their deciduous predecessors. The permanent molars are the only permanent teeth that do not replace a preexisting deciduous tooth.

The eruption sequence of permanent teeth can also vary. The mandibular central incisors and the mandibular and maxillary first molars are the first permanent teeth to erupt, usually at 6 to 7 years of age. The maxillary and mandibular second molars erupt between 12 and 13 years of age. The third molars are unpredictable but may appear at 17 to 21 years of age, the last teeth to fully erupt during adolescence [3]. Many genetic and physiologic factors can accelerate or extend these eruption patterns.

Teething pain can cause infants and toddlers to drool, become restless and irritable, and even develop a low-grade fever, with treatment designed to palliate symptoms. Caution should be exercised if over-the-counter topical anesthetic preparations are used, as even small doses of these drugs can be toxic to infants and toddlers if swallowed. Similarly, the use of any analgesic medication should be minimized to reflect the limited ability of the infant or toddler to metabolize these substances. Consultation with a pedodontist or pediatrician is advisable to determine a dosing schedule that is efficacious and safe.

ANATOMY AND MORPHOLOGY OF DECIDUOUS TEETH

The 20 deciduous teeth have pronounced differences in the anatomy of their crowns and roots and in the structure and amounts of enamel, dentin, and pulp chamber compared to those of the permanent teeth. These morphologic differences reflect the teeth's design to function for a limited period of time and to be aligned into maxillary and mandibular arches of small dimensions. These differences will also influence the progression of the carious process and the manner in which carious deciduous teeth are restored.

Proportionately, the relationship of the mesial-to-distal dimensions of the crowns of deciduous teeth to the occlusal to gingival dimension is greater than the same relationship among permanent teeth. The occlusal table of the deciduous molars, upon which grinding and crushing of food occurs, is more narrow compared with the wide occlusal tables of the permanent molars. Deciduous molars also feature a prominent bulge in the mesio-buccal area near the gingival crest, which can be conducive to the retention of bacterial plaque at the gingival level and which poses a greater risk of the development of caries [4].

The roots of deciduous anterior teeth are more narrow in a mesial-to-distal direction compared to those of the anterior permanent teeth. The crown-to-root length ratio of deciduous molars is less than the same ratio in the permanent molars, as the roots of deciduous molars are longer in relation to the size of the crowns of these teeth. The apical anatomy of the deciduous molars can feature pronounced but slender curvatures that should be considered if the teeth must be extracted. The roots of the deciduous molars surround the crowns of the developing permanent maxillary and mandibular bicuspids. If an extraction is indicated for any of the deciduous molars, care must be taken to avoid damage to the crowns of their permanent successors. Deciduous molars with fully formed roots can be challenging extractions. These slender and curved roots cannot withstand the degree of pressure utilized for the extractions of permanent molars and can fracture easily if excessive pressure is applied. Deciduous molar roots that fracture in the apical area may be difficult to locate and remove without damaging the permanent bicuspids.

When the roots of the deciduous teeth lose their normal means of attaching to the bone via the periodontal ligament and become fused directly to the bone, this is called ankylosis [5]. Although ankylosis can affect any deciduous tooth, the molars are most often involved. Ankylosis interferes with the normal process of deciduous root dissolution to allow for the normal sequence of shedding of the deciduous teeth and replacement by the permanent teeth. Ankylosed teeth have a dull sound when they are percussed with an instrument and a submerged appearance when adjacent non-ankylosed deciduous teeth are shed and the permanent successors erupt into their proper position. They can delay the eruption of their permanent successor and allow for the unintentional drifting of the adjacent teeth or hypereruption of the opposing tooth. These problems can lead to functional and cosmetic problems that require orthodontic correction. Ankylosed teeth can be difficult extractions because they are fused directly to the bone and excessive pressure can lead to fracture of the deciduous roots, the supporting alveolar bone, and the developing permanent tooth.

Clinicians should not consider the extraction of any deciduous tooth, especially the molars, an easy procedure. High-quality radiographs that show the tooth's root anatomy and its relation to the developing permanent tooth, the age and ability of the patient to withstand a surgical procedure, the surgical skills of the clinician, and the clinician's ability to establish rapport and treat pediatric patients should be considered before a surgical procedure is initiated. Referral to a pedodontist or oral surgeon should be considered if it is in the best interest of the patient.

The enamel and dentin layers of deciduous teeth are thinner than those on permanent teeth. The pulp chamber, which includes the nerve supply, blood vessels, and supporting tissue, is relatively large in deciduous teeth, with a larger pulp chamber-to-clinical crown ratio than in permanent teeth. Pointed extensions of the pulp chamber (called pulp horns) are common in deciduous teeth and are much closer to the external surface of the tooth compared to permanent teeth. Due to these anatomic differences, dental caries spread faster in deciduous teeth and pulpal involvement can occur quickly.

When a carious deciduous tooth will not be shed for a long time, it should be restored. Extension of decay into the pulp chamber will cause pain, necrosis, and local infection; infection can extend quickly between muscular planes to cause regional and even systemic involvement. Thus, carious lesions in deciduous teeth should be restored as quickly as possible to prevent odontogenic infections and tooth loss due to non-restorable caries. Even so, some parents may be reluctant to restore caries in primary teeth because they will ultimately be lost. Clear and complete parental education may help address this.

RESTORING CARIOUS DECIDUOUS AND PERMANENT TEETH IN PEDIATRIC PATIENTS

Dental caries are the most common childhood disease [6; 79]. Although tooth decay is usually managed with no untoward sequelae, complications from dental caries do occur, and if left untreated, caries can lead to meningoencephalitis, subdural empyema, and even death [7]. While this tragic circumstance is rare, it underscores the necessity to restore carious teeth whether they are deciduous or permanent.

Early childhood caries (ECC) are lesions that occur in deciduous teeth between birth and 71 months of age. Deciduous teeth that have been restored or extracted due to extensive caries are also included in this definition [8]. The restoration of carious deciduous teeth or permanent teeth with incompletely formed roots and larger pulp chambers requires different restorative techniques and materials than those used to treat the permanent teeth of adults.

There are numerous dental restorative materials available and several clinically acceptable techniques by which they can be placed. Clinicians should consider patient age, caries risk, ability to cooperate, the expected duration of retention of a carious tooth or the stage of development of a permanent tooth, and the costs involved before any restorative dentistry is begun. Every clinician should be well versed in state laws regarding the consent that is necessary to initiate any treatment for minors.

The prevention of dental caries remains the ideal approach. Teaching patients and their parents about the basic tenets of oral hygiene and motivating them to maintain periodic recall appointments are important parts of this preventive practice.

An initial clinical and radiographic examination will reveal the presence of caries and the risk of developing future caries. Statistics have shown that decay in the pits and fissures causes about 80% to 90% of all caries in the permanent posterior teeth and cause approximately 44% of all caries in deciduous teeth [9]. Pits and fissures are more plentiful and pronounced in the premolars and molars, although pits of varying sizes and depths are also common on the lingual aspects of the maxillary central and lateral incisors as well. These narrow invaginations in the enamel are areas in which bacterial plaque can congregate and into which toothbrush bristles may not reach.

Pit and fissure sealants may be placed to decrease the risk of caries in these areas. Studies have shown that the placement of a second-, third-, or fourth-generation resin-based material can decrease the caries incidence by 88% after two years and by 79% over a span of four years, although the quality of evidence is lower at this interval [10; 80]. Teeth with deeper pits and fissures and patients with poor oral hygiene will have a greater benefit from sealants than those with excellent oral hygiene or shallow pits and fissures. When recall appointments have been kept and oral hygiene has been maintained, sealants have an 80% to 90% retention rate after 10 years and a 65% retention rate after 20 years [11; 66; 80].

Several commercial resin-based sealant products are available. Before any sealants are set, the tooth should be cleaned and the surface etched with an acidic gel that causes the enamel surface to develop microscopic porosities into which the resin will flow. This is very technique-sensitive, as salivary contamination of the etched surface will preclude the development of an adequate bond strength and cause the sealant to detach. A thin layer of material is placed into the desired pit or fissure, with an ultraviolet light used to set the material. Occlusion should always be checked after sealants are placed, as any excess in the sealant height could cause a fracture of the sealant and/or traumatic occlusion of the teeth.

Dental caries can develop despite the best preventive efforts of the patient and the dental staff. The most common materials used to restore deciduous teeth without pulpal involvement are dental amalgam and composite resins. The use of either material has advantages and disadvantages, and the material of choice should be based on the restorative needs of the patient.

DENTAL AMALGAM

Dental amalgam has been used as a restorative dental material since the late 19th century [12]. It has been popular due to its durability, ease of placement, and low cost compared to other dental restorative materials. However, there has been controversy about the safety of dental amalgam use because mercury is one of the composite elements, along with copper, tin, and silver. Patients and parents may have concerns related to the release of mercury during the placement of new amalgam restorations and the removal of deficient restorations, or the continuous release of small amounts of mercury from the material. Numerous studies and reports by the American Dental Association, the American Medical Association, the World Health Organization, the Fédération Dentaire International (FDI), and the U.S. Food and Drug Administration have affirmed the safety and efficacy of amalgam restorative material [14; 82].

Studies have shown that mercury off-gassed from dental amalgam (approximately 2–28 mcg per facet surface per day, with 80% absorbed by the lungs) accumulates in body tissues, particularly the kidneys and brain, with higher levels associated with a greater number of fillings; this represents the most prevalent source of mercury exposure for most individuals [65; 67; 68]. Evidence of debilitating systemic effects from these accumulations is lacking, but there is increasing awareness regarding the impact of cumulative mercury exposure, particularly on cognitive functioning. In 2008, both Norway and Sweden banned the use of amalgam as a dental restorative material [15]. In the United States, amalgam is still used, but some parents will not permit its use for their restorative needs or for those of their children. This debate is global in nature and will continue. Parents of minors who require restorative dentistry should always be presented with options for use of various restorative materials prior to initiation of the procedure.

The preparation of the tooth and placement of an amalgam restoration will depend on whether the carious lesion occurs in the deciduous tooth of a child, the permanent tooth of a child, or the permanent tooth of an adult. Amalgam does not have the capacity to self-adhere to enamel or dentin, and the form of the cavity may not be enough to retain the amalgam restorations. In these cases, auxiliary means of retention (i.e., small slots or grooves placed at the junction of the enamel and dentin) may be necessary. While this is not a problem in the permanent teeth of adults, careful placement is necessary to avoid pulpal involvement in children and adolescents.

A primary advantage of amalgam over composite resins is that it is not as technique-sensitive in its placement. If blood or saliva contaminates a tooth surface, the bond strength of a composite restoration will decrease, causing microleakage and ultimately failure. While a similar circumstance is not ideal for the placement of amalgam, the material is not dependent on a bonding process and contamination will not interfere with its setting.

Amalgam is durable under compressive strength, but its inclusion does not strengthen the tooth. It is a restorative material, not cosmetic, and its appearance will worsen over time as intraoral oxidation reactions cause it to darken. Larger amalgam restorations can also impart a gray or black discoloration to the adjacent enamel.

In children and adolescents, preparation of the outline form for the restoration of deciduous posterior teeth is dependent on several factors. The point at which two adjacent teeth touch (i.e., the contact area) between deciduous molars is broader and flatter than the comparable contact area between permanent teeth, and this is an important consideration when placing class II restorations using amalgam or composite resin. Clinicians who are used to placing class II restorations in permanent teeth should be cognizant of these anatomic and restorative differences. A class II restoration that would provide an adequate interproximal contact in a permanent tooth will not span the contact area of adjacent deciduous molars, which can lead to food impaction and an increased risk of recurrent caries.

COMPOSITE RESIN

Composite resin material was first introduced as a choice for the restoration of class III (interproximal lesions in anterior teeth), class IV (carious lesions or traumatic fractures of anterior teeth that involve the interproximal surface and the incisal edges), and class V lesions of both deciduous and permanent teeth. Numerous composite resin materials have now been developed to restore class I and class II lesions in deciduous and permanent posterior teeth. Beyond the cosmetic benefit, the use of etchants and bonding agents allows a chemical and mechanical bond to develop and secure the composite resin to enamel and dentin. Thus, less tooth structure is removed compared to amalgam, which cannot bond to enamel or dentin and relies on the reduction of additional tooth structure and retentive grooves or slots for mechanical retention.

The primary considerations in the use of composite material for the restoration of posterior deciduous teeth are the additional time required in their placement, the additional cost, and the ability to isolate the tooth. As noted, the placement of composite resin restorations requires that the tooth be isolated from saliva and blood with a rubber dam. While this device provides excellent isolation, some patients will find it uncomfortable, feeling that it is confining and a barrier to communication with dental staff during the procedure. Children can be especially fearful of the rubber dam and may be uncooperative during its placement, which can jeopardize the successful placement of the restoration. Children may also become restless and uncooperative during the longer time required for the placement of composite restorations. If confronted with any of these situations, consider the placement of amalgam restorations in posterior deciduous or permanent teeth or referral to a pedodontist capable of sedating the patient for restorative procedures.

SILVER DIAMINE FLUORIDE

A relatively new product to the United States, 38% silver diamine fluoride (SDF) was approved by the FDA for use in the management of hypersensitivity, and one SDF product, Advantage Silver Arrest (Elevate Oral Care), was the first to be cleared as caries arrest treatment (off-label use) [69; 78]. SDF has been used around the world as an alternative to restorative dentistry (particularly in Japan) for more than eight decades in people of all ages. Because SDF is a newer product in the United States, a committee of researchers and clinicians at UCSF has developed a protocol for using topical 38% SDF for caries treatment at dental clinics. The authors of the protocol describe the mechanism of action of SDF [78]:

> Upon application of silver diamine fluoride to a decayed surface, the squamous layer of silver-protein conjugates forms, increasing resistance to acid dissolution and enzymatic digestion. Hydroxyapatite and fluoroapatite form on the exposed organic matrix, along with the presence of silver chloride and metallic silver. The treated lesion increases in mineral density and hardness while the lesion depth decreases. Meanwhile, silver diamine fluoride specifically inhibits the proteins that break down the exposed dentin organic matrix: matrix metalloproteinases; cathepsins; and bacterial collagenases. Silver ions act directly against bacteria in lesions by breaking membranes, denaturing proteins, and inhibiting DNA replication. Ionic silver deactivates nearly any macromolecule.

SDF may be used for caries preventative therapy in patients with salivary dysfunction secondary to aging, cancer treatment, methamphetamine abuse, polypharmacy, or Sjögren syndrome [78; 83]. SDF therapy is recommended for patients who have complications that preclude invasive restorative treatments. For children, indications for preventative therapy and treatment include extreme caries risk (e.g., xerostomia, severe early childhood caries), treatment challenged by behavioral or medical management, and difficult-to-treat dental carious lesions based on access, isolation, and cleansability (e.g., recurrent caries at a crown margin, root caries in a furcation).

An advantage of SDF is that it can be quickly applied at a diagnostic visit; however, repeat applications are often performed at one- and three-month follow-up visits, and then at six-month semi-annual visits for two to three years [78]. Despite this, a single annual application of SDF is more effective for caries prevention than applying fluoride varnish two to four times per year or, if applied every year, than occlusal sealants [83].

For treatment of a carious lesion, the area is first thoroughly isolated using cotton or gauze; forced air may be used to ensure complete dryness, which improves efficacy. An applicator is used to place a small amount of SDF onto the lesion, where it is left for one to three minutes to soak into and react with the softened enamel and/or dentin; this timeframe is not critical but is a recommended caution for the first application. Uncooperative children have been successfully treated within only a few seconds SDF reaction time.

One disadvantage to SDF therapy is that the product permanently stains the lesion, but no other area, a dark grey color over time as the decay arrests; the color is similar to that of dental amalgam. Patients and/or parents should be informed of this effect [78]. Another disadvantage is that the treatment does not restore function of the tooth; fillings are recommended over SDF therapy if functional restoration is required. A consent form explaining these effects and limitations should be provided and signed by parents. The UCSF protocol and a sample consent form were published in the *Journal of the California Dental Association* and are available online at https://www.cda.org/Portals/0/journal/journal_012016.pdf [78].

CROWNS

Restorative materials such as amalgam and composite resin are not the materials of choice when an extensive amount of deciduous coronal tooth structure has been destroyed by caries. In adults, such teeth are restored with full crowns of cast gold, porcelain-fused-to-metal, or a variety of all-ceramic options. However, when deciduous teeth that will not be shed for several years have extensive coronal caries and occlusal function must be restored, pre-formed stainless steel crowns are the restoration of choice. These stainless steel crowns can also be used to restore grossly carious permanent molars and bicuspids in children and adolescents in whom the roots of the teeth are not completely formed and in which adult occlusion has not yet been completed. In patients for whom amalgam or composite restorations have fractured or who have developed recurrent caries, these crowns may be used. The silver color of stainless steel crowns makes them unaesthetic, and the extended time for the preparation of the tooth, the trial fitting and contouring of the crown, and cementation can be beyond a pediatric patient's ability to cooperate.

Anterior deciduous teeth with extensive coronal caries can be restored with anterior strip crowns. This technique features the use of a pre-formed cellulose acetate strip crown into which the appropriate shade of composite resin material is inserted and then placed onto the tooth [16]. The composite material is light cured, and then the cellulose acetate strip crown is removed. Because this is a bonding procedure, isolation from blood and saliva is mandatory. The restoration of deciduous anterior or posterior teeth with stainless steel crowns or anterior strip crowns is an exacting procedure and should be attempted only by clinicians who have been appropriately trained.

PULP CAPPING AND PULPECTOMY

Carious involvement of the pulp of deciduous and permanent teeth of children and adolescents pose another restorative challenge. Bacterial infiltration of the dental pulp initially presents with an inflammatory response that will culminate in the necrosis of the pulpal tissues. A localized abscess can form and evolve into cellulitis, which follows muscle and fascial planes and can ultimately lead to a disseminated systemic infection. In adults, carious involvement of the pulp of permanent teeth with fully formed roots is treated by root canal therapy or by extraction. While conventional root canal therapy cannot be performed on retained deciduous teeth or permanent teeth in which the roots are not completely formed, other procedures are available to treat pulpal tissue that has carious involvement.

Carious lesions that approach the pulp in a deciduous tooth can be treated by an indirect pulp capping technique. This procedure entails the removal of all of the carious dentin except the layer closest to the pulp. A medicament such as calcium hydroxide or zinc oxide-eugenol (ZOE) is then applied directly against this deepest layer of remaining caries. These compounds stimulate the pulp to produce reparative dentin beneath the carious lesion to stop the progression of caries and maintain pulpal vitality [17]. This technique can be done in one appointment, with amalgam or composite resin restoration placed over the layers of ZOE or calcium hydroxide. Another approach involves the placement of a temporary restoration over the ZOE or calcium hydroxide with a return visit in six to eight weeks to excavate any residual carious dentin and place the final restoration [18].

A direct pulp cap may be used when a carious lesion extends directly into the pulp of an otherwise healthy tooth without symptoms (e.g., pain, sensitivity to extremes of temperature). A material such as calcium hydroxide is applied directly to the area of pulpal exposure to stimulate reparative dentin [19]. This procedure usually has a poor prognosis in deciduous teeth, and if ineffective, a pulpotomy should be utilized.

A pulpotomy is a procedure in which the entire inflamed coronal pulp is removed while the pulpal tissue within the roots is left intact. Upon removal of all caries and the achievement of hemostasis within the pulp chamber, mineral trioxide aggregate (MTA), formocresol, or ferric sulfate is applied with either cotton pellets or a specific carrier directly to the pulpal tissue stumps until a clot forms. The tooth is subsequently restored with a base, such as intermediate restorative material (IRM). The ideal final restoration is a stainless steel crown for deciduous molars or an anterior strip crown for anterior teeth.

The treatment of extensively carious immature permanent teeth, for which root formation and closure are years away, also presents as a unique restorative challenge. Immature permanent teeth with carious lesions that approach the pulp but with no or minimal symptoms can be treated with the one- or two-step indirect pulp technique. If a stainless steel crown or an anterior strip crown is utilized for the immediate restoration, it must be replaced by a permanent crown after root formation is complete. If the removal of the carious lesion causes a small (pinpoint) exposure to the pulp, with symptoms of pain, the direct pulp cap technique can used for immature permanent teeth [20]. Direct pulp caps of immature permanent teeth have a much better prognosis when compared to those of deciduous teeth.

When an extensive carious lesion involves the pulp of immature vital (non-necrotic) permanent teeth, the therapeutic goals are to eliminate pain and to provide treatment that will allow for the complete development of the root, including apexogenesis. This can only occur if the radicular pulp is left in a healthy state. After the inflamed pulpal tissue is removed, a layer of calcium hydroxide or MTA is placed over remaining exposed pulpal tissue [21]. A base (e.g., IRM) and a composite resin restoration complete the coronal seal.

Periodic radiographic assessment is necessary to evaluate the continuity of root formation and apexogenesis. Some teeth restored in this fashion may remain asymptomatic and exhibit no apical pathology, while others will require conventional root canal therapy after the root apex has completed its formation.

EXTRACTION

Caries in deciduous and immature permanent teeth may progress to the point that the tooth is no longer restorable and must be extracted. Although deciduous teeth are designed to be shed, they maintain an important role in occlusion and phonation. Unrestorable deciduous teeth should be extracted before causing drifting of adjacent teeth or creating an obstacle to the eruption of permanent teeth. A classic example of this occurs with the premature loss of deciduous second molars. Because the maxillary and mandibular permanent first molars erupt long before the anticipated exfoliation of the deciduous second molars, which are eventually replaced by the permanent second bicuspids, the premature loss of second deciduous molars allows the permanent first molars to drift mesially and create an obstacle to the eruption of the permanent second bicuspids. A space maintainer may be necessary to prevent this occurrence. The space maintainer is cemented onto the permanent first molar and is removed after the permanent second bicuspid has erupted to a position that will prevent mesial drift.

APEXIFICATION

Carious lesions that are left untreated will eventually cause necrosis of the coronal and radicular pulp. Necrotic (non-vital) immature permanent teeth present a unique challenge, as the non-vital radicular pulpal tissue cannot contribute to further development of the root and apexogenesis. In these cases, an apexification procedure is used. Conventional root canal therapy cannot be completed because the root of the immature permanent tooth has an open apex that cannot provide a definitive stop for obturation material. The apexification procedure is designed to create a definitive calcified stop in the apical region of the root, which would then allow gutta percha to be used to complete definitive root canal therapy. The initial appointment consists of the debridement and removal of the necrotic remnants of the pulpal tissue. A thick paste of calcium hydroxide is placed into the cleansed and debrided canal to stimulate the formation of the calcified stop in the apical region of the root. Whether calcium hydroxide is placed during the initial or second appointment, it is covered with a temporary filling material and left within the canal for approximately six months. If a calcified stop near the apical region of the tooth is confirmed by radiographs and is tactilely encountered by endodontic instruments such as files or reamers, conventional endodontic treatment can be completed [22]. If the stop is not encountered, the canal is retreated with calcium hydroxide paste. The complete loss of pulpal tissue in an immature permanent tooth precludes the continued thickening and developing of the root canal walls even if the apexification technique and subsequent endodontic therapy are successful [23]. This makes the tooth more susceptible to fractures of the crown or the root. A full-coverage crown can decrease, but not eliminate, the potential for coronal fractures. Patients should be reminded to minimize pressure to treated teeth and should be instructed to wear protective mouth guards during athletic activities.

Procedures such as pulpotomies of deciduous and immature permanent teeth and apexification should only be performed by clinicians who have had adequate training. Referral to a pedodontist or endodontist should be considered if the required clinical techniques are beyond the capabilities of the general practitioner.

PREVENTIVE DENTISTRY FOR CHILDREN AND ADOLESCENTS

Of course, the ultimate goal for each child and adolescent is avoidance of dental caries. Unfortunately, many patients in this age range have one or more carious lesions. Infants and children are dependent upon their parents/caregivers to brush and floss their teeth, to bring them to the dental office for exams and routine prophylaxis appointments, and to provide nutrition that is conducive to good oral and general health. There are general guidelines for the prevention of dental caries in children and adolescents that may be helpful for clinicians and parents/patients.

Oral problems that are diagnosed early can be treated conservatively and inexpensively. As such, the American Academy of Pediatric Dentistry has recommended an initial dental examination as early as the first tooth eruption and no later than 12 months, which would include a caries risk assessment, oral hygiene instructions for the parent(s), and a general assessment of the child's oral health [24].

SEALANTS

As discussed, the use and efficacy of pit and fissure sealants can decrease the risk of caries associated with anatomical features in deciduous and permanent teeth. Parents may be unaware of this preventive option, especially if sealants were never used for their own teeth. The benefits of this approach should be discussed with the parents, but it is important that they know that pit and fissure sealants are not a substitute for good oral hygiene. Parents should also understand that the cost of pit and fissure sealants is per tooth and that insurance company reimbursement is variable.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Scottish Intercollegiate Guidelines Network asserts that resin-based fissure sealants should be applied to the permanent molars of all children as early after eruption as possible.

(https://www.scottishdental.org/wp-content/uploads/2014/04/SIGN138.pdf. Last accessed January 19, 2023.)

Grade of Recommendation: A (At least one meta-analysis, systematic review, or randomized controlled trial rated as high quality and directly applicable to the target population; or a body of evidence consisting principally of studies rated as well-conducted, directly applicable to the target population, and demonstrating overall consistency of results)

FLUORIDE TREATMENT

Fluoride is the negatively charged ionic form of the element fluorine, and it is able to form stable bonds with positively charged ions, such as sodium and calcium, to promote remineralization of teeth. Virtually all water naturally contains fluoride, but usually at a concentration that is not sufficient to prevent tooth decay. The use of community water fluoridation began in late 1940s [25]. In 2010, the U.S. Department of Health and Human Services decreased the recommended optimal concentration of fluoride in drinking water for reduction of dental caries from 0.7–1.2 mg per liter of water to 0.7 mg per liter [30]. This change was the result of the widespread availability of fluoride-containing foods, water, beverages, toothpastes, and mouth rinses and to some degree was a response to concerns of overexposure to fluoride, which is neurotoxic at higher doses and can also cause dental and skeletal fluorosis [72]. This recommendation was finalized in 2015, with studies showing that 0.7 mg per liter of fluoride in drinking water maintained decreases of up to 35% of caries in children, while minimizing the risk of skeletal fluorosis [30; 81]. Fluoride is slightly more toxic than lead and slightly less toxic than arsenic and has a narrow therapeutic window that can be difficult to control when all potential sources are considered [74]. Excessive ingestion of fluoride can cause fluorosis, a condition in which the enamel exhibits subtle changes (e.g., white spots) and potentially extensive areas of pitting and discoloration. Swallowed fluoridated toothpaste and drinking water are the primary sources of excessive fluoride intake and are considered the leading causes of fluorosis [71]. To prevent this, parents should receive instructions regarding toothbrushing technique and the amount of toothpaste that is appropriate for children to minimize the unnecessary ingestion of fluoride.

Fluoride's preventive effects are principally topical, rather than systemic, as was previously thought. Fluoride disrupts the activity of cariogenic bacteria (e.g., *Streptococcus mutans*) by decreasing its metabolism of carbohydrates in dental plaque, the action responsible for acidification of the oral environment that causes the demineralization [27]. Acid excreted by cariogenic bacteria stimulates the release of fluoride that is then incorporated into enamel that has undergone initial demineralization. However, mutated strains of *Streptococcus* bacteria resistant to fluoride are known to inhabit the oral cavity (and the environment) in response to fluoride exposure [70]. Fluoride is nonselective and also kills many species of beneficial bacteria.

Topical fluoride inhibits the demineralization of sound enamel and promotes the remineralization of damaged enamel, particularly in the context of dietary fluoride, calcium, and phosphorus deficiency [26]. Fluoride, calcium, and phosphate strengthen the crystal structure of enamel [28]. Beyond a topical effect, ingested fluoride will become incorporated into the enamel and dentin of unerupted teeth and thus increase their resistance to susceptible cariogenic bacteria [22]. New research indicates another important caries-preventing action of topical fluoride is to weaken the ability of bacteria to adhere to tooth enamel [73].

Fluoride concentrations in community water supplies in the United States are not standardized, and some communities have opted not to include fluoride in their water at all. The American Academy of Pediatric Dentistry recommends age-dependent fluoride supplementation only if the fluoride concentration in a child's water supply is less than 0.6 parts per million (ppm) [31]. No fluoride supplement is recommended for children from birth to 6 months, even if community water fluoridation is lacking. A 0.25-mg fluoride supplement is advised for children 6 months to 3 years of age if the fluoride concentration in available water is less than 0.3 ppm. Children 3 to 6 years of age should receive 0.50 mg fluoride if the water fluoride concentration is less than 0.3 ppm or 0.25 mg fluoride if the concentration range is 0.3–0.6 ppm. Children 6 to 16 years of age should receive 1 mg fluoride supplement if the fluoride concentration in the community water supply is less than 0.3 ppm or 0.50 mg if the fluoride concentration is 0.3–0.6 ppm [31]. The American Dental Association Council on Scientific Affairs encourages healthcare providers to evaluate all potential fluoride sources and to conduct a caries risk assessment before prescribing fluoride supplements [74]. Parents should consult with their pediatrician, pedodontist, or general dentist to determine if fluoride supplementation is required for their child.

Due to increasing research and public awareness of the neurotoxic effects of many chemicals, including fluoride, some parents will not want to administer fluoride supplement or fluoride toothpastes. These parents should be advised regarding proper nutritional intake of calcium, phosphorus, and vitamin D and the importance of regular tooth brushing and preventative dental visits [74].

An alternative to fluoride for enamel protection and tooth remineralization is calcium hydroxyapatite, a calcium and phosphorus (phosphate) mineral of which 70% to 80% of tooth and bone are composed. Topical preparations containing hydroxyapatite have been shown to be as or more effective for remineralization, treating tooth hypersensitivity, and reversing carious lesions than fluoride and do not have the detriments of toxicity or tooth fluorosis [84]. Other effects of hydroxyapatite are absorption of oral pathogens and protection against stains and biofilm attachment. The most effective type of hydroxyapatite for topical use is the nanocrystal form (nanohydroxyapatite), which is readily available as toothpastes and rinses. Calcium hydroxyapatite is available as a nutritional supplement and is also included in some dental gels and varnishes.

DENTAL EXAMINATIONS AND PROPHYLAXIS APPOINTMENTS

As noted, children and adolescents are entirely dependent upon their parents or caregivers for access to dental care, and issues with transportation and financial stress may arise. However, regularly scheduled dental examinations can provide a means for oral hygiene instruction for children and their parents and can allow for identification of carious lesions early, when they can be restored by conservative and less expensive means. Beyond the cost-effectiveness of preventive pediatric dentistry, this approach reduces the suffering and morbidity associated with advanced dental problems.

Dental insurance coverage and family income may impact access to care. Families in need of financial assistance may be eligible for dental coverage under the Medicaid program. Unfortunately, the low reimbursement fee schedule for dental procedures precludes many general dentists and dental specialists from accepting patients under this program. The dental divisions of county health departments may provide another low-cost source of dental treatment for pediatric and adolescent patients. Some county and state dental societies also provide periodic pro bono services to those in need. Access to adequate dental care is essential for the appropriate development of children's oral and general health and for their ability to develop and maintain a healthy sense of self-esteem, making this a public health issue.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The U.S. Preventive Services Task Force recommends that primary care clinicians apply fluoride varnish to the primary teeth of all infants and children starting at the age of primary tooth eruption.

(https://jamanetwork.com/journals/jama/fullarticle/2786823. Last accessed January 19, 2023.)

Strength of Recommendation: B (There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.)

MEDICATION USE IN PEDIATRIC AND ADOLESCENT DENTAL PATIENTS

Local anesthetics, analgesics, and antibiotics are used most often before, during, and after the dental treatment of pediatric and adolescent patients. As with any patient, a thorough medical history must be obtained and discussed with the patient and his or her parent or guardian prior to using any medication. Some states require written parental/guardian consent for any medication use in minor children. Medications used for dental purposes should be carefully selected and used to ensure they do not interact adversely with those prescribed to treat a systemic disease. If there are any medical issues that would cause a concern with a proposed dental treatment or the medications used, consultation with the patient's pediatrician or another physician is recommended.

Dental professionals who rarely treat or prescribe medications to pediatric and adolescent patients may give little thought to the profound differences in their ability to metabolize and excrete medications compared with adults. The dosage and frequency of administration may require significant adjustments. History of an adverse reaction to any medication should be discussed with the parent or guardian, as should the presence of pre-existing illness and other medication use. Age and weight should be considered before a medication is recommended or prescribed. For example, a child who is 3 years of age and weighs 30 pounds is often categorized generally as "pediatric," as is an adolescent who is 17 years of age and weighs 200 pounds. But their ability to absorb, distribute, metabolize, and excrete medications will be vastly different. Given these issues, it is not possible to recommend a single dose of any analgesic, antibiotic, or local anesthetic for all pediatric patients. Consultation with a pediatrician is necessary if there is any concern about the type, dose, or frequency of administration of a given medication.

ANALGESICS

Carious involvement of the pulp, localized infections, and trauma to the teeth or surrounding structures may all lead to the use of analgesics for pediatric patients. Acetaminophen is the most frequently used analgesic in this population for mild-to-moderate pain [33]. It is preferred over aspirin, which causes irritation to the gastric mucosa and may cause Reye syndrome. Acetaminophen has analgesic and antipyretic (fever-reducing) capabilities. It blocks the production of prostaglandins in the central nervous system and the generation of pain impulses peripherally [34]. Some younger children and adolescents may have difficulty swallowing tablets or capsules, and acetaminophen is available as a chewable tablet, elixir, or liquid.

An excess use of acetaminophen can lead to hepatic toxicity and even liver failure. The smallest dose for the shortest duration to provide adequate analgesia should be used. Acetaminophen may be combined with other over-the-counter medications (e.g., antihistamines) to provide relief from pain or symptoms of colds, influenza, or sinus congestion. These combinations increase the risk for hepatic toxicity. Parents should be aware that although acetaminophen is an over-the-counter medication, it can be dangerous if used inappropriately in children and adolescents.

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and naproxen may also be used to relieve pain of odontogenic origin. NSAIDs have analgesic, antipyretic, and anti-inflammatory properties. The mechanism of action is twofold, as they decrease prostaglandin synthesis peripherally and decrease the accompanying inflammatory response. In the central nervous system, NSAIDs decrease the synthesis of prostaglandins in the critical pain processing regions and inhibit the ability for pain impulses to be transmitted or received.

The half-life of naproxen is 12 to 15 hours, which allows for it to be taken twice daily. The two- to four-hour half-life of ibuprofen requires that it be administered more frequently [35]. The gastrointestinal side effects that can occur with NSAIDs are decreased if they are taken with food; however, this practice will decrease their systemic absorption. To facilitate easier administration in the pediatric population, ibuprofen is available as infant drops, suspension, or chewable tablet, and naproxen is available as a suspension.

Patients who have experienced an aspirin-induced asthma attack should avoid the use of NSAIDs, as there is a high potential for cross-sensitivity [36]. This group of medications inhibits platelet aggregation and should not be used in patients with a bleeding disorder. NSAIDs are also contraindicated in patients who have gastrointestinal diseases such as inflammatory bowel disease or peptic ulcer.

Codeine, an opioid analgesic, is the most commonly prescribed medication for moderate-to-severe pain in pediatric patients [33]. It may be given alone, but it is usually given in combination with acetaminophen. The recommended pediatric dose of codeine is 0.5 to 1 mg/kg (maximum of 60 mg in adolescents) every four to six hours [33]. The maximum dose of acetaminophen with codeine is based on the acetaminophen dose. Respiratory depression is a serious complication; other common side effects include constipation, nausea, sedation, dizziness, and pruritus.

ANTIBIOTICS

Oral infections that develop from grossly carious teeth require prompt antibiotic treatment before definitive treatment is completed. The rise of resistant bacteria mandates that a conservative approach for the use of antibiotics is used. The extent of the infection, the immunocompetence of the patient, and the age of the patient should be considered before any antibiotic is prescribed. Dental infections contained within the pulpal or gingival tissues immediately adjacent to the tooth and fistulous tracts without signs of systemic involvement generally do not require antibiotic therapy; more extensive involvement and symptomatic presentations do [37]. Dental infections can advance rapidly among pediatric patients, especially younger children, and those who present with signs of systemic involvement should be referred to a pedodontist, oral surgeon, or an emergency department, as intravenous antibiotics and surgical drainage may be required.

Penicillin VK remains the empiric antibiotic of choice for the treatment of odontogenic infections [37]. It is effective against the gram-positive anaerobes commonly associated with these infections. Amoxicillin-clavulanate, a derivative of penicillin VK, is absorbed more rapidly and is more effective against gram-negative bacteria [38; 75]. Both medications are available in suspension formulations, with amoxicillin also available as a chewable tablet. Clindamycin is the alternative antibiotic of choice when a patient is allergic to penicillin VK or amoxicillin, but the development of pseudomembranous colitis is a potential risk when this agent is used. Consultation with the patient's pediatrician is recommended prior to prescribing this medication. Cephalosporins should be considered, particularly if the patient has had a previous course of penicillin or amoxicillin [37].

LOCAL ANESTHETICS

Adequate pain control during restorative or surgical procedures is essential for patient comfort and for the ability to complete the procedure. Many adults have fears or phobias about dental treatment that originate from the pain they experienced during a childhood dental procedure during which pain control was inadequate. Therefore, prevention of pain should be an utmost concern.

Supraperiosteal infiltration with a local anesthetic provides successful anesthesia for maxillary deciduous and permanent teeth. This technique is also successful for all mandibular deciduous teeth but decreases for mandibular molars, as bone density increases with age. An inferior alveolar nerve block (IANB) may be required to provide successful anesthesia for the deciduous mandibular molars in older children and will be required to successfully anesthetize permanent molars. The mandibular bicuspids may be anesthetized by an IANB or by infiltration of the mental nerve.

A topical anesthetic such as benzocaine (available in concentrations up to 20%) can be applied to the mucosa prior to the injection. The minimum required amount is placed on a cotton tip applicator, which is then spread on the isolated and dry mucosa. A staff member should remain with the patient to maintain isolation of the area and minimize swallowing of the topical anesthetic, which can cause nausea in some patients.

As with all medications, the choice of local anesthetic for a pediatric patient must consider the age, weight, medical history, and type and duration of the planned procedure. The margin of safety will be less in smaller, younger children. One can ascertain the safe limit for a pediatric patient by determining the dose (in mg) of a given local anesthetic per kilogram of body weight (mg/kg), which will establish the maximum cumulative dose per appointment. If the maximum dose of lidocaine is 4.5 mg/kg for an entire appointment, a child who weighs approximately 16 kg should not receive more than two carpules of 2% lidocaine per appointment [39]. This is only a guide, as other factors (e.g., hepatic or renal impairment) can decrease a patient's ability to metabolize or excrete a local anesthetic.

Other local anesthetics, such as mepivacaine, prilocaine, and articaine, have established guidelines for the maximum allowable dose per appointment, also expressed as mg/kg. In general, the younger the age and the lower the weight of the pediatric patient, the lower the maximum allowable dose of local anesthetic. Clinicians should begin with these guidelines and use less if the medical history dictates or if a minimal amount of treatment is required.

The vasoconstrictor epinephrine is added to local anesthetics to prolong the duration of anesthesia and to aid in hemostasis in surgical cases. Preservatives such as sodium bisulfite or sodium metabisulfite are also added to local anesthetics that contain epinephrine in order to prolong their shelf life. Patients with allergies to sulfite compounds could develop an allergic reaction if a local anesthetic with epinephrine is used. For these patients, alternative anesthetics, such as mepivacaine plain, are reasonable alternatives.

The use of local anesthetics carries with it the responsibility of heightened safety. Before any local anesthetic is used, the dentist and staff should be fully trained in cardiopulmonary resuscitation for pediatric patients. Equipment and medications necessary in the event of a medical emergency should be easily accessible and all staff members should be trained in their appropriate use. Periodic emergency drills will define the role each staff member should assume during a medical emergency. Clinicians who infrequently use local anesthetics for pediatric patients should be cognizant of the differences in the safe maximum allowable dose of a given anesthetic among different patient populations.

ORAL AND MAXILLOFACIAL LESIONS

HERPES SIMPLEX

Several systemic diseases that affect children and adolescents can present with oral and facial lesions. But the most common cause of oral ulcerations in children is an initial infection with herpes simplex virus-1 (HSV-1). Primary herpetic gingivostomatitis (PHG) usually occurs after 6 months of age and has the highest incidence between 12 and 18 months of age [16]. In children with PHG, the gingival tissues appear red and edematous, with small vesicular lesions and ulcerations on the oral mucosa. Patients will have pain, malaise, and headache and may be febrile. Liquid nutritional supplements and a soft, bland diet may be necessary during this period. Healing occurs spontaneously within 7 to 14 days with no residual scarring from the herpetic lesions. Although this initial attack will resolve, it is not cured. The virus will migrate to a regional nerve ganglion and can become reactivated in the future as recurrent herpes labialis. These recurrent lesions usually occur at the mucocutaneous junction of skin and lips, and unlike PHG, the oral mucosa and gingival tissues are typically uninvolved. Lesions of recurrent attacks heal in 10 to 14 days without scarring. Pediatric patients who are immunocompromised can have a more aggressive course of HSV-1 infection and a protracted healing period. Antiviral medications such as acyclovir can accelerate the healing time. Acyclovir is available as a cream, capsule, tablet, or suspension, with the dosage and frequency of administration adjusted according to the patient's age, weight, and medical history.

MEASLES

Many of the systemic viral diseases that were once common among young children and adolescents, such as measles, mumps, and chickenpox, have been significantly reduced in the United States through the use of effective vaccines. The combined vaccine for measles, mumps, and rubella (MMR) was developed in the late 1960s [41]. In 1995, a chickenpox (varicella) vaccine was introduced, and by 2005, a combination vaccine for all four diseases (MMRV) was introduced [42]. In the 1990s, a study was published implicating the MMR vaccine with the development of autism [43]. Although the basis of this work was later declared fraudulent, many parents refused to have their children vaccinated on the basis of this initial report, which resulted in small increases in the incidence of these diseases [44].

The Centers for Disease Control and Prevention (CDC) has documented several outbreaks of measles in the last decade among unvaccinated groups (e.g., the Amish, orthodox Jewish communities, children of the anti-vaccination movement); one such incidence was the 2015 Disney California theme parks outbreak, which infected at least 125 individuals, most of whom had not been vaccinated due to personal beliefs; others had unknown vaccine status, were undervaccinated, or were too young to have received the vaccine series [76]. Since then, a major increase in the number of cases in the United States has been noted. In the first 10 months of 2019, 1,261 cases of measles in 31 states were reported (compared with a total of 1,958 total cases between 2010 and 2018), 75% of which were in New York. This represents the largest number of cases since 1992 and the second highest number since measles was considered eliminated in the United States in 2000. Of these patients, 89% were either unvaccinated or their vaccination status was unknown [77]. During 2020–2022, there were an additional 180 cases. Travel to or from a foreign country where the disease is endemic can also instigate the spread of measles among unvaccinated persons [76].

The measles virus causes cutaneous, red, maculopapular lesions. Oral manifestations of measles include grayish-white macules surrounded by an erythematous halo, known as Koplik spots. These lesions precede the eruption of the cutaneous lesions [45].

CHICKENPOX

Chickenpox, also known as varicella, is caused by the varicella zoster virus (VZV). This disease is usually seen in children and features lesions that originate on the trunk then spread throughout the body. The oral lesions are white to grayish-white vesicles with an erythematous border involving the tongue, buccal mucosa, gingiva, palate, and oropharynx. They can cause varying degrees of pain, which can complicate eating, swallowing, and maintaining oral hygiene [46]. Nutrition and hydration should be maintained via liquid nutritional supplements, if necessary.

After the primary varicella infection ends, the VZV is transported to the dorsal spinal ganglia and can remain dormant for decades, emerging later as herpes zoster virus, also known as shingles. However, shingles is much more common in older adults, and a vaccine is available for persons 50 years of age and older [47].

MUMPS

The MMR/MMRV vaccines have also been instrumental in significantly decreasing the incidence of mumps. When it does develop, mumps involves the major salivary glands. In particular, the parotid glands' inflammatory response to the mumps virus (known as parotitis) presents as bilateral swelling of variable severity. Children 10 years of age and younger are most commonly affected; however, a larger outbreak in 2006 involved 6,584 college students in multiple states, an outbreak of 3,000 high school students occurred in New York in 2009–2010, and nearly 20,000 cases occurred in 2015–2019 in a variety of settings, including households, schools, universities, athletics teams and facilities, church groups, workplaces, and large parties and events. Since the end of 2019, cases of mumps have declined (likely due to coronavirus preventative measures), but hundreds of cases per year continue to be reported [48]. Rarely, more serious complications such as temporary or permanent deafness, encephalitis, or meningitis, may occur. In some cases, mumps will present as unilateral involvement and swelling of the parotid gland, which can be mistaken for a local odontogenic infection.

HAND, FOOT, AND MOUTH DISEASE

Hand, foot, and mouth disease is usually caused by coxsackievirus A16, although other coxsackievirus genotypes can serve as etiologic agents [32]. The disease primarily affects children during the summer and early fall. It usually begins with fever, loss of appetite, fatigue, and sore throat, followed within one or two days by oral sores.

The oral lesions of hand, foot, and mouth disease feature vesicles that quickly rupture to form shallow ulcerations encircled by an erythematous halo. Any area of the oral mucosa can be affected, but lesions occur most often on the palate, tongue, and buccal mucosa. The lesions can be difficult to distinguish from other oral ulcerative lesions, such as aphthous ulcers. However, hand, foot, and mouth disease usually features similar cutaneous lesions on the hands and feet, although the lesions may be limited to cutaneous or oral manifestations in some cases. Afflicted patients are most contagious during the initial week of their infection. Coxsackievirus A16 remains for weeks after symptoms have dissipated, and the patient remains infectious to others during this time [40].

Treatment for hand, foot, and mouth disease is supportive and palliative. Painful oral lesions can complicate a patient's ability to masticate food and to swallow, so softer, blander foods and liquid nutritional supplements may be required. Analgesics compatible with the patient's medical history may be used to decrease oral discomfort. Patients with hand, foot, and mouth disease should be instructed not to scratch or manipulate fluid-filled vesicles in any manner as the contents are infectious and can inoculate other areas.

There is no current vaccine available to prevent hand, foot, and mouth disease. Recovery from the disease only confers immunity against the viral strain that caused the infection, not against other coxsackievirus genotypes. It is a self-limiting disease, but complications, such as viral meningitis or encephalitis, can occur.

RECURRENT APHTHOUS STOMATITIS

Recurrent aphthous stomatitis features painful ulcerative lesions (also known as recurrent aphthous ulcers or more commonly as canker sores) that generally heal without scarring in immunocompetent patients but can recur at any time. The size is a demarcation for the categorization of these lesions. Minor aphthae are less than 1 cm at the greatest diameter; major aphthae exceed this dimension. Each type of lesion only involves nonkeratinized tissues, such as the buccal and labial mucosa, the soft palate, and the surface layer of the floor of the mouth. Movement of the mucosa affected by lesions of either size is painful and can interfere with speaking, eating, and swallowing. Major aphthae tend to have irregular shapes and borders and more depth. The numbers of both can vary, although solitary lesions are uncommon. Lesions of aphthous stomatitis feature a shallow yellow base and an intense erythematous halo peripherally.

The incidence of these lesions varies from 20% to 60% and can reflect the actual population studied. Many patients develop the condition during the first two decades of life [55]. There has yet to be a bacterial, viral, or fungal etiology that can be attributed to the origin of these lesions, but a genetic predisposition to the occurrence is possible. When both parents have a history of these lesions, there is a 90% chance that their children will be similarly affected [56]. Common predisposing factors include physical and emotional stress and sensitivity to ingredients in toothpaste and/or mouthwash, such as sodium lauryl sulfate and alcohol [57; 58]. Tissue manipulation during dental or medical procedures, during which the oral tissues are stretched or manipulated by instruments, is a source of local trauma that can cause the development of these ulcers. Nutritional deficiencies in vitamin C, folic acid, iron, and vitamin B12 are other potential etiologies [58]. Systemic chemotherapy and radiotherapy targeting malignant lesions of the oropharynx can cause the development of overlapping aphthous ulcers of considerable size that can serve as areas of systemic access of pathogenic organisms. Occasionally, these ulcers occur as part of a disease such as Behçet syndrome. In patients with Behçet syndrome, major aphthae are more frequent than minor aphthae and occur simultaneously on the nonkeratinized oral mucosa, uvula, and genitals [58]. Sensitivity to certain medications, including NSAIDs, angiotensin-converting enzyme inhibitors, and bisphosphonates, may produce an aphthous-like tissue reaction. Given the multitude of medications available and potential untoward effects that can occur in the patients who take them, this could be a potential issue for numerous medications.

Treatment and Prognosis

The lesions of recurrent aphthous stomatitis usually revolve spontaneously. Minor aphthae resolve within 7 to 14 days from onset with no residual scarring. Major aphthae can take three weeks or longer to heal and usually do so with scar formation. Antibiotics are only needed if the involved areas become secondarily infected. Treatment is usually designed to avoid contact with these lesions, as a traumatic incident will exacerbate the pain and prolong healing. Palliation of the symptoms associated with these lesions consists of topical anesthetic preparations and systemic analgesics, as needed. A diet that minimizes both acidity and extreme temperatures and avoids foods with sharp edges will facilitate proper nutritional support and minimize physical trauma to the affected areas [58]. Patients with removable orthodontic retainers may refrain from using them if an aphthous ulcer is adjacent to their extensions.

As the name would suggest, these lesions have periodic recurrences. Because more serious lesions such as squamous cell carcinoma can appear in a multitude of different forms, patients should be advised that lesions that do not heal should be re-evaluated for a biopsy.

ORAL AND MAXILLOFACIAL TRAUMA FROM CHILD ABUSE AND NEGLECT

Traumatic injuries to the teeth and the structures of the oral and maxillofacial complex may be the result of falls, sports injuries, car accidents, or violence. Usually, the maxillary anterior teeth take the brunt of the trauma, as they are the first teeth to encounter traumatic forces. The extent of coronal/radicular (root) fracture, the age of the patient, the degree of root development and apical closure of permanent teeth, the medical history, and access to dental care can all influence the ability to restore traumatized teeth. Of the most concern are oral injuries, cutaneous and intra-oral mucosal bruising, and other injuries to the head and neck that occur due to child abuse and neglect.

The head, neck, and arms of pediatric patients should be assessed for signs of bruising or injuries without plausible explanation. All members of the dental profession should be cognizant of their responsibility as advocates for children and adolescents who are victims of physical and emotional abuse. This is a moral and ethical obligation, as all states require dentists to report suspected cases of child abuse to the appropriate social service or law enforcement agencies.

Many cases of child abuse go unreported, so it is difficult to determine the exact number of children affected by physical, emotional, and psychologic abuse. According to the U.S. Department of Health and Human Services, the rate of child abuse and neglect was 8.4 per 1,000 children in 2020 [29]. Neglect represented the most frequent type of abuse, occurring in 76.1% of victims; physical abuse occurred in 16.5% of victims. Dental professionals are often the practitioners who have the most frequent interactions with children and therefore must be attentive to any signs of physical abuse, as abusive injuries to children often involve the face, jaw, mouth, teeth, and tongue [13]. Studies indicate that approximately 65% of abused children have visible injuries to the head, face, neck, and intraoral regions [49]. Child abuse should be considered as a potential source for injuries that are inconsistent with an explanation as to their origin, when several injuries in various stages of healing are present, when children or adolescents appear reluctant or fearful to discuss their injuries, and if parents or guardians appear evasive or defensive when they are questioned about the origin of the child's injuries.

While there is no single injury to the head, neck, oral, or perioral region that is absolutely indicative of child abuse, some injuries and patterns should be viewed with more suspicion than others. Injuries or bruises in the shape of a distinguishable object, such as a belt buckle, strap, rope, electrical cord, clothes iron, or hand, are cause for concern [49]. The cheeks and lips are the most common site of intentionally inflicted injuries in the oral and perioral region, with injuries to the oral mucosa, teeth, gingival tissues, and tongue following behind [49; 50]. Beyond the oral and perioral region, the neck should be included as a part of the comprehensive examination of the child. Bilateral bruise marks or rope burns on the neck may be the result of an attempt to strangle the child; bilateral bruising on a child's arms may be indicative of shaking injury. Bruising and lacerations of the ears and the adjacent skin may be related to abuse; bilateral lesions and traumatic injuries to the ears are rarely accidental in nature. However, this may not be easily visible if hair extends over the ears. Hematomas within the oral cavity and in the perioral area can develop if a child is struck by a hand or a blunt object. Fractures or loss of multiple permanent or deciduous teeth may be the result of being slapped, punched, or struck.

Child sexual abuse may also have oral and perioral manifestations. Venereal warts (*Condyloma acuminatum*) are suspicious for sexual abuse when they occur in a child's oral cavity [49]. These warts appear as cauliflower-like lesions on the lips, palate, and tongue. Forced oral-genital contact can also produce bruising and petechiae (i.e., small foci of hemorrhagic areas caused by trauma to and the rupture of small blood vessels); this most frequently occurs in the area of the soft palate [49].

REPORTING

In many states, dental professionals are legally required or mandated to report any suspected cases of child abuse, maltreatment, and/or neglect that they encounter in their professional roles. However, studies have shown that many professionals who are mandated to report child abuse and neglect are concerned and/or anxious about reporting. Identified barriers to reporting include [51; 52; 53]:

- Professionals may not feel skilled in their knowledge base about child abuse and neglect. In addition, they lack the confidence to identify sexual and emotional abuse.
- Professionals may be frustrated with how little they can do about poverty, unemployment, drug use, and the intergenerational nature of abuse.
- Although professionals understand their legal obligation, they may still feel that they are violating patient confidentiality.
- Many professionals are skeptical about the effectiveness of reporting child abuse cases given the bureaucracy of Child Protective Services (CPS) and the large caseloads.
- Practitioners may be concerned that they do not have adequate or sufficient evidence of child abuse.
- Practitioners may have a belief that government entities do not have the right to get involved in matters within the family arena.
- There may be some confusion and emotional distress in the reporting process.

The failure to identify and report child abuse may result in continued abuse of the child and potentially severe consequences. Improved and ongoing education about child abuse and maltreatment has been shown to improve identification and reporting rates among dental professionals. The education should include [54]:

- Management and outcomes
- The role of the CPS investigator
- The role of the physician/other reporting professional
- The benefits of CPS involvement
- The benefits of mandated education on identification/reporting
- The benefits of professional debriefing for the reporter
- The benefits of collaboration (e.g., with local emergency departments, pediatric specialists)

Other suggestions for improving reporting include [54]:

- Improving the relationship between CPS and dental providers
- Allowing certain registered professionals with demonstrated expertise in identifying/treating child abuse "flexible reporting options" (e.g., deferring reporting when no immediate threat exists or making the report confidentially and deferring an investigation until deemed necessary)
- Improving interaction with the legal system

EATING DISORDERS AND DENTAL HEALTH

Few behavioral or psychologic problems have as direct an adverse effect upon the teeth and the oral mucosa as anorexia nervosa and bulimia nervosa. There are classic oral manifestations of these eating disorders that members of the dental staff may discover during the course of routine dental treatment.

The exact etiology of eating disorders is unknown, but a combination of genetic, hormonal, social, cultural, and attitudinal factors are believed to be involved. Images in mass media that promote a thin body as a vehicle to success and happiness have been implicated in altering a person's perception of his or her appearance [59].

ANOREXIA NERVOSA

Patients with anorexia nervosa have an extreme obsession with their body weight and the restriction of food intake. Women comprise 90% to 95% of anorexia cases, and it is estimated that 1% of all women between 12 and 25 years of age have anorexia, with the onset usually occurring during the adolescent years [60]. Anorexic patients often view themselves as overweight even though most are 15% or more below ideal weight.

Patients with anorexia go to extreme measures to lose weight and prevent weight gain. The most common mechanism is restricting or halting eating. Other patients may exercise excessively. Some patients with anorexia will use laxatives, enemas, or self-induced vomiting as a supplemental means to control their weight. These behaviors can lead to severe acute and chronic medical problems. Patients may appear emaciated but refuse to acknowledge the serious nature of the problem and do not consider the potential medical consequences of the disease.

Women who are anorexic often have irregular menstrual cycles. The skin can become dry and thin and at greater risk for traumatic injury. The restriction of caloric intake can stunt the physical and mental development of children and adolescents, and cognitive damage is possible in all patients. Problems with the cardiovascular system, including hypotension, bradycardia, and cardiac arrhythmias, are very common. Self-induced vomiting and use of laxatives can cause a severe disturbance in the body's mineral and electrolyte balance, and a drastic reduction of the minerals potassium, sodium, and calcium can interfere with the conduction of nerve impulses and the contraction of smooth, skeletal, and cardiac muscle. Failure of multiple organs and systems can lead to death. If part of the disease process, repeated episodes of self-induced vomiting can cause ulceration of the esophageal lining, with the subsequent development of esophageal varicosities and bleeding. Oral effects are generally limited to those caused by extreme starvation and malnutrition.

BULIMIA NERVOSA

Patients with bulimia nervosa tend to lack the emaciated appearance of patients with anorexia nervosa; their body weight and appearance often appears normal. Bulimia features recurrent binge eating, in which a large quantity of food is consumed in a short time, followed by purging (e.g., self-induced vomiting, use of diuretics, laxatives, or enemas) to compensate for the excessive overeating. During binging episodes, the bulimic patient experiences a loss of control over the quantity and variety of food consumed [62]. The practice of binge eating and purging must continue at least twice a week for three months for a diagnosis of bulimia nervosa to be made [61].

The teeth and the oral mucosa of bulimic patients can undergo damage as the recurrent regurgitation of highly acidic gastric contents can induce pathologic change in both. In addition, the mucosa of the soft palate and the anterior pharyngeal area can be traumatized when fingers or objects are inserted to induce vomiting. Healing of these areas may be prolonged by the physical and chemical assault associated with this repetitious behavior. Ulcerated areas of the oral mucosa may lead to local or regional oral infections. The virulence of infections can be exacerbated when the altered nutritional status of these patients compromises their immune response.

Enamel is the hardest substance in the human body, but the repeated exposure to the hydrochloric acid in regurgitated gastric contents over an extended period of time can lead to a unique pattern of enamel erosion called perimylolysis. Perimylolysis features the loss of enamel on the lingual, occlusal, and incisal surfaces of the teeth. As opposed to attrition, which is the loss of enamel from repetitive tooth-to-tooth contact or abrasion via an external source (e.g., excessive or overly forceful tooth brushing), the gradual dissolution of the enamel matrix in patients with bulimia leaves a glossy, smooth surface, most commonly on the lingual surfaces of the maxillary anterior teeth [63]. Any lost enamel cannot be regenerated. The underlying matrix of dentin is then exposed; it will wear faster than enamel and is more prone to caries. While enamel is devoid of any neural element, dentin contains dentinal tubules whose odontoblastic processes can perceive thermal stimuli as a source of pain. This can cause patients to neglect oral hygiene and increase the risk of caries and periodontal disease. The irreversible loss of enamel will also cause a change in the occlusion, decreasing the vertical dimension of occlusion. The loss of tooth structure requires that more complicated and expensive restorative options, such as crowns, be utilized. The loss of enamel support around composite or amalgam restorations can lead to their weakening and ultimate loss. The amount of time necessary for the enamel to be eroded in such fashion can range from six months to two years [64].

CONCLUSION

Dental treatment of the pediatric patient can be a rewarding experience. Dental schools vary in the amount of pedodontic clinical training undergraduate students receive, and each clinician's expertise and comfort level with pediatric patients will vary, especially the treatment of those who are very young or those with complex dental problems. Professional ethics require the clinician to assess if he or she has the clinical and interpersonal skills required for these patients. Referral to a pedodontist or a general practitioner with excellent skills in the treatment of pediatric and adolescent patients should be considered if it is in the best interest of the patient. Each child and adolescent is unique in their personality, medical history, and psychologic needs and well-being. Recognizing and respecting these qualities is the foundation upon which a relationship of mutual trust and respect is built.

Customer Information/Answer Sheet/Evaluation insert located between pages 60–61.

COURSE TEST - #52163 DENTAL TREATMENT OF PEDIATRIC AND ADOLESCENT PATIENTS

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 6 CE Credit Hour activity must be completed by January 31, 2026.

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1. Which of the following statements about deciduous teeth is TRUE?
- A) *Neonatal teeth are present at birth.*
- B) *All natal and neonatal teeth should be extracted.*
- C) *The deciduous mandibular canines are the first teeth to erupt.*
- D) *The last teeth to erupt are the maxillary and mandibular second molars.*

2. What are the only permanent teeth that do not replace a pre-existing deciduous tooth?
- A) *Molars*
- B) *Canines*
- C) *Incisors*
- D) *Premolars (bicuspids)*

3. Ankylosis of deciduous teeth
- A) *most often involves the deciduous canines.*
- B) *facilitates the extraction of deciduous teeth.*
- C) *has no effect on the eruption of permanent teeth.*
- D) *results in a submerged appearance compared to adjacent teeth.*

4. Early childhood caries are defined as lesions that occur in deciduous teeth between birth and
- A) *13 months of age.*
- B) *31 months of age.*
- C) *51 months of age.*
- D) *71 months of age.*

5. What percentage of caries involve the pits and fissures of permanent posterior teeth?
- A) *30% to 40%*
- B) *40% to 50%*
- C) *60% to 70%*
- D) *80% to 90%*

6. Dental amalgam restorations
- A) *strengthen the tooth.*
- B) *are very technique-sensitive during placement.*
- C) *are the choice for class V restorations in anterior teeth.*
- D) *may rely on features such as retentive grooves for resistance to dislodgement.*

7. Which of the following statements about composite restorations is TRUE?
- A) *They rely on grooves and slots for retention.*
- B) *They are less expensive than amalgam restorations.*
- C) *Rubber dam isolation is required to prevent contamination with saliva and blood.*
- D) *The preparation requires more removal of tooth structure compared to an amalgam restoration.*

8. The apexification procedure is used for
- A) *vital deciduous teeth.*
- B) *vital immature permanent teeth.*
- C) *necrotic (non-vital) deciduous teeth.*
- D) *necrotic (non-vital) immature permanent teeth.*

Test questions continue on next page →

9. Fluoride
- A) *supplements are required for all pediatric patients.*
- B) *exerts its effects topically rather than systemically.*
- C) *does not affect the teeth if excessive amounts are ingested.*
- D) *that naturally occurs in water is sufficient to prevent tooth decay.*

10. Which factors should be considered when using or prescribing medications for pediatric and adolescent patients?
- A) *Pre-existing illness*
- B) *Age and weight of the patient*
- C) *Simultaneous use of other medications*
- D) *All of the above*

11. The analgesic acetaminophen
- A) *has peripheral anti-inflammatory activity.*
- B) *is associated with a high incidence of gastric irritation.*
- C) *blocks the production of prostaglandins in the central nervous system.*
- D) *has been identified as an etiologic agent in the development of Reye syndrome.*

12. Nonsteroidal anti-inflammatory drugs (NSAIDs)
- A) *are ideal for patients with gastrointestinal diseases.*
- B) *exert effects only within the central nervous system.*
- C) *are the medication of choice for patients with bleeding or platelet disorders.*
- D) *should not be used for patients that have had aspirin-induced asthma attacks.*

13. Which of the following statements about antibiotics is TRUE?
- A) *Bacterial resistance to antibiotics is a rising problem.*
- B) *Penicillin VK is absorbed more quickly than amoxicillin-clavulanate.*
- C) *Clindamycin remains the empiric antibiotic of choice for odontogenic infections.*
- D) *Amoxicillin is more active against gram-positive bacteria compared with penicillin VK.*

14. Which of the following statements about the use of local anesthetics in pediatric patients is TRUE?
- A) *Hepatic disease can have an influence on the metabolism of local anesthetics.*
- B) *The dental staff must be trained to respond to adverse reactions to local anesthetics.*
- C) *Patients with sulfite allergies should not be given a local anesthetic with epinephrine.*
- D) *All of the above*

15. Primary herpetic gingivostomatitis (PHG)
- A) *heals spontaneously but with scarring.*
- B) *causes the gingival tissues to become pale.*
- C) *causes pain, malaise, headache, and possibly fever.*
- D) *has the highest incidence among adolescent patients.*

16. Koplik spots are associated with
- A) *mumps.*
- B) *measles.*
- C) *shingles.*
- D) *recurrent herpes labialis.*

17. Hand, foot, and mouth disease is usually caused by
- A) *coxsackievirus A16.*
- B) *herpes simplex virus.*
- C) *varicella zoster virus.*
- D) *the measles, mumps, and rubella vaccine.*

18. Which of the following structures in the oral and perioral region is the most common site of intentionally inflicted injuries in abused children?
- A) *Lips*
- B) *Teeth*
- C) *Tongue*
- D) *Gingival tissues*

19. Which of the following statements about anorexia nervosa is TRUE?
- A) *Women comprise about 90% to 95% of all cases.*
- B) *It is not associated with serious medical consequences.*
- C) *The teeth and oral mucosa are unaffected by this disease process.*
- D) *Patients with anorexia usually have a normal body weight and appearance.*

20. Perimylolysis
- A) *is not seen in patients with bulimia nervosa.*
- B) *develops from repetitive tooth-to-tooth contact.*
- C) *is caused by an abrasive force such as overzealous tooth brushing.*
- D) *is caused by repeated contact of gastric hydrochloric acid with the teeth.*

Be sure to transfer your answers to the Answer Sheet located on the envelope insert.
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Herbal Medications: An Evidence-Based Review

Audience
Considering the widespread availability and increased use of herbal medications, this course is designed for dental professionals who will benefit from the course.

Course Objective
Considering the pharmacologic interactions between herbal medications (HMs) and conventional medications, it is paramount to increase the awareness and knowledge of dental professionals about HMs. The purpose of this course is to increase dental professionals' awareness of the potential risks and benefits of HMs from an evidence-based perspective and promote the planned inclusion of HM use in patients' medical history. This course should allow dental professionals to discuss HMs in a knowledgeable and succinct manner with patients and colleagues.

Learning Objectives
Upon completion of this course, you should be able to:

1. Discuss the prevalent current and historical use of HMs in North America.
2. Explain the need to inquire about the use of HMs during preparation of a patient's medical history, including components of a culturally sensitive assessment.
3. Discuss the pharmacology (i.e., pharmacokinetics, pharmacodynamics, drug interactions, adverse drug reactions, toxicology) of HMs.
4. Describe the differences between the process of development and approval of HMs versus conventional medications, and the implications of health claims and therapeutic efficacy of HMs.
5. Outline the merits and limitations associated with the application of contemporary scientific principles and methodologies (i.e., evidence-based medicine) to assess the efficacy and safety of HMs.
6. Discuss, based on scientific and conventional medical principles, the pharmacologic properties, efficacy, safety, toxicology, therapeutic indications, and recommended dosages of saw palmetto and St. John's wort.
7. Describe the potential risks and benefits of ginkgo.
8. Identify key characteristics of ginseng.
9. Discuss the use of echinacea and kava, including potential adverse effects.
10. Review the use of garlic and valerian as HMs.
11. Outline the potential medical uses of andrographis and English ivy leaf.
12. Analyze the available evidence for the use of peppermint, ginger, soy, and chamomile.

Faculty
A. José Lança, MD, PhD, received his Medical Degree at the University of Coimbra in Coimbra, Portugal, and completed his internship at the University Hospital, Coimbra. He received his PhD in Neurosciences from a joint program between the Faculties of Medicine of the University of Coimbra, Portugal, and the University of Toronto, Toronto, Canada. He was a Gulbenkian Foundation Scholar and was awarded a Young Investigator Award by the American National Association for the Research of Schizophrenia and Depression (NARSAD). (A complete biography appears at the end of this course.)

Faculty Disclosure
Contributing faculty, A. José Lança, MD, PhD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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DEFINITIONS

The National Center for Complementary and Integrative Health (NCCIH), a division of the U.S. National Institutes of Health, defines complementary and alternative medicine (CAM) as "health care approaches that are not typically part of conventional medical care or that may have origins outside of usual Western practice." [1]. Complementary medicine is non-mainstream practice used together with conventional medicine, and alternative medicine is non-mainstream practice used in place of conventional medicine. Integrative medicine attempts to bring together conventional and complementary approaches to health care [1]. CAM includes a wide range of products including natural health products (NHPs) and practices such as prayer, chiropractic, homeopathy, and massage therapy. In Canada, a similar definition is followed, and regulation of NHPs falls under the jurisdiction of the Natural and Non-Prescription Health Products Directorate (NNHPD), a branch of Health Canada [2].

Herbal medications (HMs), also known as phytochemicals or botanical medications, are considered an integral part of dietary supplements in the United States or natural health products in Canada [3]. Dietary supplements also include other natural compounds, such as vitamins, minerals, amino acids, and essential fatty oils [2].

PREVALENCE OF HERBAL MEDICATION USE

The desire to maintain and promote individual health has contributed to the prevalent use of natural health products, including herbal medications. In 2012, more than 3 out of 10 adults (33.2%) in the United States used complementary medicine approaches and 17.7% used natural products other than vitamin and mineral supplements [1]. In Canada, an estimated 18% of the population takes natural products other than vitamin and mineral supplements [4].

Data from the National Center for Health Statistics (NCHS) indicate that supplement use among U.S. adults 20 years of age and older increased from 48.4% to 56.1% during the period 2007–2008 and 2017–2018, with use more common among women (63.8%) than men (50.8%) [5; 6; 7; 8]. Nonvitamin, nonmineral natural products are the most commonly used category of CAM (17.7%), followed by deep breathing (10.9%), yoga, tai chi, and qi gong (10.1%), chiropractic care (8.4%), meditation (8.0%), and massage therapy (6.9%). The NCHS also found that approximately 12% of children 17 years of age or younger use some form of CAM [5]. Considering the aging of the "baby-boom" generation and increased incidence of chronic health issues, it is likely that the use of CAM, and HMs in particular, will continue to increase in this group. In 2017–2018, dietary supplement use increased with age, both overall and in both sexes, and was highest among women 60 years of age and older (80.2%). The most common types of dietary supplements used were multivitamin-mineral supplements, followed by vitamin D and omega-3 fatty acid supplements [8].

The use of CAM for general health and well-being is greater in people with higher education and income, rather than in individuals with lower education and lower socioeconomic status [5; 9]. However, the National Health Interview Survey revealed that poor adults were more likely to use megavitamin therapy and prayer specifically for a health reason than not poor adults [10]. An estimated 13% of adult CAM users have indicated that they used CAM because conventional medicine was too expensive [10].

It is particularly relevant for medical practitioners that several studies have shown that more than 50% of patients who require conventional health care use CAMs separately or in conjunction with conventional therapies [9; 11; 12]. A published study of men with prostate cancer revealed that one-third of the patients used CAM in conjunction with their conventional therapy [13]. Of those, approximately 30% were taking vitamin and mineral supplements, while 40% were taking herbal compounds either alone or in conjunction with vitamins and antioxidants [13]. It has been estimated that 40% to 70% of patients using CAM fail to disclose this information to physicians or other healthcare professionals [5; 11]. Patients are more likely to disclose CAM use if it is provider-based rather than self-care use [9].

The prevalent use of herbal medications is particularly relevant to medical practice for three main reasons. First, it is commonly and erroneously assumed by patients that by being natural the compound is intrinsically beneficial and devoid of adverse effects. Second, patients often neglect to report to their physicians and other healthcare providers that they are taking HMs, as they think that it is not relevant. Third, pharmacologic interactions between compounds, regardless of whether they are from herbal or conventional origin, may alter therapeutic efficacies and cause negative interactions or serious adverse effects.

It is therefore essential to increase awareness regarding these issues and evaluate the pharmacologic profile and therapeutic properties of the most commonly used herbal medications based on scientific evidence, including clinical trials.

HISTORICAL OVERVIEW OF HERBAL MEDICATIONS IN NORTH AMERICA

Chemical compounds extracted from plants, animals, or micro-organisms, either in raw or purified form, have been used to treat disease for centuries and even millennia. Many of these substances are essential therapeutic tools and widely used in conventional medicine. Aspirin, digitalis, reserpine, morphine, most antibiotics, and anticancer drugs, to name but a few, are perfect examples of the long historical transition between natural medications and mainstream or conventional Western medications. The introduction of new and more effective conventional medications, such as statins, a class of drugs that inhibit 5-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase activity and effectively lower hyperlipidemia, and the antimalarial drug artemisinin, are pertinent examples of identification, extraction, and pharmaceutical application of natural compounds [14; 15]. In fact, it has been estimated that approximately 25% to 50% of marketed drugs are derived from natural sources [16]. One review found that almost 50% of the new small-molecule drugs introduced between 1981 and 2002 were natural products or their chemical derivatives [15]. Consequently, the difference between NHPs/HMs and conventional Western medications is not solely or primarily based on the origin of the compound (i.e., natural versus synthetic) but rather on the process of scientific evaluation of the pharmacologic and biologic properties, toxicologic profile, and therapeutic efficacy of a particular compound prior to its approval for marketing. In Western countries, the process of approval of new conventional drugs is tightly regulated. It falls under the jurisdiction of the U.S. Food and Drug Administration (FDA) in the United States; in Canada, it is regulated by Health Canada.

In the United States, herbal medications are considered dietary supplements and are regulated by the Dietary Supplement Health and Education Act (DSHEA) of 1994 [3]. Under this legislation, some claims, including structure and function, may be made by the manufacturer without requiring proof of safety and efficacy needed for conventional FDA-regulated medications. The product may be advertised as beneficial to maintaining or improving health of a particular organ or system, and the DSHEA states that the manufacturer is responsible for the safety of herbal products [3]. It is, however, the responsibility of the FDA to prove that an herbal compound is unsafe before a product is removed from the market [17]. This has been the case regarding the sale of dietary supplements, including HMs, containing ephedrine alkaloids (e.g., ephedra), which were prohibited in the United States by the FDA in April 2004 [18].

In Canada, herbal medications are classified as natural health products and fall under the jurisdiction of the Natural Health Products Regulations [19]. Canadian regulations provide a regulatory framework similar to the one existing in the United States. It is Health Canada's mandate to regulate the sale and safety of HMs, as illustrated by the ban on products containing ephedra in quantities greater than 8 mg per dose, 32 mg per day, or at any dose in combination with other stimulants, including caffeine.

MEDICAL AND PATIENT PERCEPTIONS AND MISCONCEPTIONS ABOUT THE USE OF HERBAL MEDICATIONS

The pharmacology, therapeutic properties, and toxicologic potential of herbal medications are often the object of inaccurate and biased assessment. Numerous factors contribute to this situation. In some cases, healthcare providers may have limited formal training in the area, which can result in a limited appreciation of the beneficial properties of some phytochemicals and of their potential health risks, including pharmacologic interactions with conventional medications [20]. A survey of community pharmacists in Texas showed that in spite of the fact that 70% of new patients use CAM, pharmacists rarely ask patients about CAM use. This is a particularly troublesome occurrence considering the role played by the pharmacist in assessing potential interactions with conventional drugs [21].

A 2010 United Kingdom-based *Drug and Therapeutics Bulletin* (DTB) survey of 164 healthcare professionals, consisting mostly of hospital physicians and general practitioners, found that while a majority of physician participants (75.3%) considered HMs to be helpful in some circumstances, 72% indicated that the general public had misplaced faith in HMs and 86% felt the general public was poorly informed about HMs [22].

Patients often use herbal compounds based on the misconception that due to being natural, these products are intrinsically beneficial, do not cause adverse effects, and are devoid of any serious toxicologic potential. This is a widespread and inaccurate assessment. Patients need a better understanding of why informing their healthcare providers about CAM, and especially HM, use will be beneficial to their health.

In response to the increasing interest in CAM, including HMs, the U.S. Federation of State Medical Boards has approved guidelines for the use of CAM in conventional medical practice. This document provides information regarding "clinically and ethically responsible use of CAM, within the boundaries of professional practice and accepted standard of care," and provides the methodology to evaluate physicians' adherence to standards of medical practice required by state legislation [23].

CULTURALLY SENSITIVE ASSESSMENT

Because the use of CAM, including HMs, may be tied closely to cultural or ethnic traditions, it is important that any assessment for use of these products be undertaken with an understanding of possible barriers to disclosure. Pachter developed a dynamic model to facilitate culturally sensitive assessments, which involves several tiers and transactions [24]. The first component of Pachter's model calls for the practitioner to take responsibility for cultural awareness and knowledge. The professional should be willing to acknowledge that he/she does not possess enough or adequate knowledge in health beliefs and practices among the different ethnic and cultural groups he/she comes in contact with. Reading and becoming familiar with medical anthropology is a good first step.

The second component emphasizes the need for specifically tailored assessment [24]. Pachter advocates the notion that there is tremendous diversity within groups. For example, one cannot automatically assume that a Nigerian immigrant adheres to traditional beliefs. Often, there are many variables, such as level of acculturation, age at immigration, educational level, and socioeconomic status, that influence health ideologies. Finally, the third component involves a negotiation process between the patient and the professional [24]. The negotiation consists of a dialogue that involves a genuine respect of beliefs. The professional might recommend a combination of CAM and Western treatments. A knowledge of HMs commonly used in different cultures may allow healthcare professionals the opportunity to ask questions about specific products, as many patients do not volunteer information regarding their use of HMs.

DISCLOSURE AND CLINICAL NEED TO IDENTIFY THE USE OF HERBAL MEDICATIONS

As noted, an estimated 40% to 70% of patients fail to report the use of HMs to their physicians and other healthcare providers [5; 11; 13]. Some patients assume that reporting CAM use is not relevant because they are not mainstream medical products or procedures. In one literature review, the major reason for patients' failure to disclose the use of CAM was their concern of a negative reaction by the practitioner [11]. In the same study, lack of interest or assumed lack of knowledge by the medical practitioner were also reported among the main reasons for nondisclosure. This is supported by the 2010 DTB survey, which indicated physicians felt that their personal knowledge about HMs was "quite" or "very" poor (36.2% and 10.4%, respectively), and 89% conceded that their knowledge of herbal medications was "much poorer" than their knowledge of prescription drugs [22].

A number of patients do not disclose the use of HMs simply because their healthcare provider did not inquire [11]. While 77% of physicians worry that their patients may not be informing them about HM use, the DTB survey found that 9% never ask about HM use, 47% occasionally ask, 27% ask most of the time, and only 13% always ask [22]. Thus, considering the prevalent use and the common perception of healthcare professionals' attitudes toward herbal medications, it is essential to change these practices in order to safeguard patients' health.

CLINICALLY RELEVANT PHARMACOLOGY AND TOXICOLOGY OF HERBAL MEDICATIONS

In North America, regulation of HMs is not as strict as that applied to conventional medications. In fact, good manufacturing practices applicable to food manufacturing are some of the only regulations in place to assure standards and quality control of dietary supplements [25]. The concentration of active ingredients in HMs, however, is affected by numerous factors, including [11; 26; 27; 28]:

- The correct identification of the botanical source
- The presence of contaminants or substitution of the intended source or other plants of lower cost with potential toxicologic consequences
- Growing conditions, including temperature, geography and time of harvest, and possible contamination with micro-organisms, heavy metals, pesticides, or prescription drugs
- Collection of the appropriate plant part (e.g., leaves versus root)
- Preparation of specimens (e.g., drying, grinding)
- Laboratory processing (e.g., solvent used for extraction of active ingredients)
- Storage
- Formulation of the final product (e.g., liquid versus solid pill)

These processes vary considerably among manufacturers and influence product quality and concentration of active ingredients in the final product.

Unlike most conventional medications, herbal products often have numerous active ingredients. Pharmacologic and chemical interactions between ingredients may be required for the product to be effective. Accordingly, isolation and purification of a single individual chemical may not lead to the same therapeutic effect as the one described for the original product.

PHARMACOKINETICS

Pharmacokinetics is the study of the effects exerted on drugs by the body, namely the processes of drug absorption, distribution, biotransformation, and ultimate elimination of drugs and their metabolites. All drugs ingested for nutritional, therapeutic, preventive, or diagnostic purposes, regardless of being of natural or synthetic origin, undergo processes of absorption and eventual distribution throughout body tissues and systems prior to reaching their molecular target. Drug distribution does not occur homogeneously throughout the body. Effective availability and concentration of a drug in different organs and tissues is influenced not only by the chemical properties of the drug (e.g., molecular size, electrical charge, ability to bind to plasma proteins, affinity for transporters that will carry the drugs across cell membranes) but also by the anatomic and histologic properties of the tissues themselves (e.g., degree of vascularization and type of capillaries present, including the tightly sealed blood-brain barrier).

Subsequently, all drugs undergo chemical transformation by the body. Briefly, drug transformation is carried out by enzymes leading to the production of metabolites that are either water-soluble (hydrophilic) and excreted mainly through the kidney, or lipid-soluble (hydrophobic). The latter are further metabolized in the liver mainly by a large family of enzymes known as cytochrome P450 (CYP450). Selective CYP450 isoforms, such as CYP3A4 and CYP3A5, are particularly relevant for clinical practice. In fact, CYP3A4 and CYP3A5 account for the metabolism of about 50% of all known drugs. For example, drugs such as digoxin, warfarin, indinavir, cyclosporine A, statins, and some calcium channel antagonists and anticonvulsants are metabolized by these isoforms. Increases or decreases in CYP450 activity therefore influence the processes of drug transformation, alter drug availability, and can have serious clinical implications [29].

PHARMACODYNAMICS

The pharmacologic and therapeutic properties of HMs and conventional medications result from the biologic interaction between an active compound and its target. The mechanisms underlying the drug-target interactions are studied in pharmacodynamics. The precise molecular mechanisms underlying the actions of HMs are, however, more difficult to establish due to the complex composition and presence of numerous chemical elements. For the most commonly used HMs, certain chemical elements have been isolated, their effects studied in vitro, and their therapeutic properties clinically evaluated. Allicin, for example, has been identified as the chemical ingredient in garlic responsible for its cardioprotective and plasma lipid-lowering properties. This effect correlates with the inhibition of HMG-CoA reductase by allicin and other disulfides present in garlic, which is a mechanism of action shared with statins [30; 31; 32].

The beneficial effects of saw palmetto in the treatment of benign prostatic hyperplasia (BPH) have been obtained with standardized lipidosterolic extracts. Several mechanisms of action have been reported, in both in vitro and in vivo models. Although saw palmetto has alpha 1-adrenoceptor antagonistic properties, a mechanism of action common to tamsulosin (Flomax), and anti-inflammatory properties because it inhibits cyclooxygenase, its beneficial effects on BPH correlate with its inhibition of 5-alpha-reductase. This latter mechanism is shared with the conventional drugs finasteride (Proscar) and dutasteride (Avodart) [33; 34].

DRUG INTERACTIONS

Drug-drug interactions, herb-drug interactions, and food-drug interactions can occur when different compounds are concurrently present in the body. These interactions can be either of a pharmacokinetic nature (i.e., absorption, distribution, metabolism, excretion) or a pharmacodynamic nature (i.e., interfering with the interaction between the drug and its molecular target, such as a receptor). Rarely, both pharmacokinetic and pharmacodynamic interactions may occur at the same time.

The complex composition of HMs can, in principle, become the source of various interactions. Multiple chemical compounds can interact either synergistically (i.e., increase the activity of one or more of its chemical constituents) or antagonistically (i.e., decrease the activity of one or more of its components). Furthermore, herbal remedies may include complex mixtures of several herbs, thereby significantly increasing the number of active compounds in the preparation. This makes it particularly difficult to ascertain which of the chemicals is pharmacologically responsible for a particular biologic event. The co-administration of HMs and conventional drugs further increases the possibility of interactions, which can be manifested during experimental conditions or clinically.

Herb-drug interactions apparently occur less frequently and are less serious than drug-drug interactions. This is due to the weaker potency of the herbal medications; however, interactions and adverse events may also be under-reported and relevant information may not be collected [35; 36].

Pharmacokinetic Interactions

Pharmacokinetic interactions between chemical compounds can alter the therapeutic properties of a drug and either increase or decrease the effectiveness of one or both compounds. For example, compounds in grapefruit and grapefruit juice strongly inhibit the liver enzyme CYP3A4 in a dose-dependent manner, thus reducing or preventing the biotransformation of drugs metabolized by this enzyme. This leads to abnormally high and potentially serious or lethal concentrations of these drugs in the blood [35]. Some clinically relevant interactions take place when grapefruit (as well as some other citrus varieties, primarily sour types) are administered with statins, anxiolytic drugs, methadone, or calcium channel blockers [37]. This interaction has led to a ban of grapefruit products in many healthcare facilities.

Goldenseal, used topically as an antiseptic and systemically for the treatment of gastrointestinal disorders and menstrual pain, is also known to strongly inhibit CYP3A4, which prevents the metabolism of drugs such as erythromycin, leading to abnormally high blood levels of this antibiotic [38; 39].

An opposite effect is caused by other medications, including the herbal antidepressant St. John's wort (SJW). SJW induces both CYP3A4 and the intestinal drug transporter P-glycoprotein. Consequently, drugs transformed by CYP3A4 will be degraded faster and their blood levels quickly fall below therapeutic levels with foreseeable clinical implications [36]. These mechanisms have been linked to the low circulating levels of the antirejection drug cyclosporine in patients who received a kidney transplant and were also being treated with SJW [36]. A similar mechanism was reported in a heart transplant recipient and was responsible for the acute rejection of the transplant [40].

Other pharmacokinetic interactions between SJW and prescription drugs have been the subject of several clinical studies, including one that reported the interaction with the anxiolytic alprazolam [41]. Alprazolam is metabolized by CYP3A4 in the liver and intestinal mucosa, and SJW induced the activity of CYP3A4, shortening the elimination half-life of alprazolam from 12.4 to 6 hours.

Pharmacodynamic Interactions

Pharmacodynamic drug-drug or herb-drug interactions result from actions on molecular targets that mediate different processes of a physiologic response. The final result of these interactions can lead to an increase (i.e., synergism or potentiation) or decrease (i.e., inhibition or offset) of the expected response. For example, the antidepressant properties of SJW are associated with hypericin, pseudohypericin, and hyperforin. These compounds have a mechanism of action identical to fluoxetine (Prozac) and paroxetine (Paxil), and inhibit serotonin reuptake [42]. It is therefore not surprising that SJW, like the selective serotonin reuptake inhibitors, has a pharmacodynamic synergistic interaction with drugs that further contribute to increases in serotonin concentration in the synapse, such as monoamine oxidase (MAO) inhibitors (e.g., phenelzine) [41; 43; 44]. The abnormal increase of serotonin resulting from the herb-drug interaction can cause a mild "serotonin syndrome," characterized by confusion, restlessness, high blood pressure, fever, and muscle spasms [45; 46; 47; 48].

Clinically relevant interactions also occur between HMs and conventional medications that affect hemostasis, such as antiplatelet drugs (e.g., acetylsalicylic acid, dipyridamole), anticoagulants (e.g., heparin and vitamin K antagonists such as warfarin), and fibrinolytic drugs (e.g., alteplase, reteplase). A number of HMs contain high amounts of coumarin, salicylates, or other compounds that interfere with hemostasis. Both red clover (*Trifolium pretense*) and sweet clover (*Melilotus alba*) are rich in coumarin. Mold contamination of these plants converts the coumarin into dicoumarol, the vitamin K antagonist from which the potent anticoagulant warfarin is derived. Toxicity has been reported in cattle grazing on moldy clover hay [49; 50; 51]. Although this interaction has not been reported in humans, due to the below-threshold effect of dicoumarol when the herb is administered at the recommended dosage, it is advisable to closely monitor hemostasis in patients undergoing anticoagulant therapy [50; 51].

Another potential herb-drug interaction exists between ginkgo biloba and conventional anticoagulants, as a few cases of hemorrhage have been reported in the literature. One German study, however, has shown that the inhibition of the platelet-activating factor by ginkgo biloba was only observed for amounts at least 100 times higher than the recommended dose [52]. Although, mechanistically, there is the potential for synergistic interaction between ginkgo biloba and anticoagulants, it seems unlikely. Interactions between various HMs and conventional cardiovascular pharmacotherapy, such as anticoagulants, antihypertensives, diuretics, statins, and digoxin, have been reported [53].

ADVERSE EFFECTS/ADVERSE DRUG REACTIONS

As discussed, the pharmacologic properties of HMs and their interactions with prescription drugs can cause adverse effects, also known as adverse drug reactions, and have the potential to cause toxicologic effects. The reporting of adverse effects is the most important tool in post-marketing drug surveillance and accounts for 60% of the data used for adverse effects assessment [54; 55]. In the United States, the FDA has the FDA Adverse Event Reporting System (FAERS). Adverse event reporting for dietary supplements, including HMs, should be directed to FDA's MedWatch. The equivalent agency in Canada is the Canada Vigilance Adverse Reaction Online Database. Reports should be made to MedEffect Canada. An adverse events reporting system, Natural MedWatch, has also been established by the Therapeutic Research Faculty, an independent publisher of evidence-based recommendations for pharmaceuticals (***Resources***).

In both the United States and Canada, adverse effects can also be reported to the manufacturer. In turn, the manufacturer should submit all the collected information to the regulatory agencies. The efficiency of this latter process, however, has been the subject of lengthy debate.

TOXICOLOGY OF HERBAL MEDICATIONS

Systematic analysis of the evidence-based toxicologic properties of HMs is scarce. Toxicologic effects of HMs can result from:

- Administration of a high dose of an HM and consequent abnormal exacerbation of the intended therapeutic effect or occurrence of a toxic effect unrelated to the original therapeutic effect
- Adulteration of the product either by contamination with other plants or with prescription medications illegally included in the product
- Interactions with conventional drugs or other HMs

There is a relationship between the administered amount of a drug and the effect obtained (dose-response curve). As for any drug, very low doses of HMs, below the intended therapeutic threshold, do not have a pharmacologic effect, whereas higher doses within the therapeutic range will elicit the intended effect (therapeutic dose). Above therapeutic doses, the compound may elicit unintended responses, which can result from the exacerbation of the therapeutic effect and the accompanying adverse effects. For example, high doses of an antihypertensive drug can cause abnormally low blood pressure. Alternately, it may stem from the occurrence of another adverse effect not directly related to the primary therapeutic action of the drug. Acetaminophen, the leading cause of acute liver failure in the United States, is a typical example to illustrate the latter type of event [56]. When administered at doses above the therapeutic threshold for analgesia and antipyresis, it causes liver toxicity and can eventually cause death due to liver failure. The smallest dose of a drug that elicits a toxic effect is known as the minimum toxic dose. The lowest drug dose that causes death is known as the minimum lethal dose.

Considering the fact that HMs have a complex and varied chemical composition, and due to the limited knowledge of the precise effects on different constituents of organ systems, healthcare providers should always be aware of their potential toxicity. A relevant example results from chronic ingestion of germander (*Teucrium chamaedrys*). In traditional Chinese medicine, it is used in the form of tea or extract for a variety of purposes, including weight loss. A number of germander-induced cases of severe hepatotoxicity have been reported in the scientific literature, leading to it being banned in France [57]. In 1996, two more cases of hepatotoxicity were reported in Canada [58]. It has been established that its toxicity is caused by the development of autoantibodies that cause immunoallergic hepatitis, and it is strongly advised that it should not be ingested for any reason [59].

Toxicity may also occur as the result of adulteration in the composition of HMs. This may occur by contamination with toxic plants or molds due to improper selection or storage. Adulterations of the intended product may occur either accidentally or deliberately when unscrupulous suppliers replace the intended plant for a cheaper one. Although this substitution may cause physiologic responses that resemble the ones intended, other effects, including toxicity, may occur. Widely reported cases have occurred in several countries, including the United States, where a mixture of plants used in traditional Chinese medicine to detoxify the body contained *Digitalis lanata* instead of plantain and caused digitalis intoxication in two patients. More numerous cases were prevented by the timely intervention of the FDA, leading to the immediate recall of the product [60]. Another well-known case occurred in Belgium, where more than 40 patients developed interstitial fibrosis and progressive renal failure when the nephrotoxic herb *Aristolochia fangchi*, known to contain potent carcinogens, was substituted for the intended *Stephania tetrandra* [61].

On several occasions, it has been found that an HM was deliberately adulterated by adding a prescription drug. Such was the case reported in England, when very high levels of the synthetic drug dexamethasone were found in an herbal cream used to treat eczema [62]. In Saudi Arabia, a complete toxicologic screening of more than 200 samples of traditional products revealed contamination by synthetic drugs (8 cases), micro-organisms (18 cases), toxic substances of natural origin (14 cases), or high heavy metals content (39 cases) [63]. These examples illustrate the need for an increased public and professional awareness, the implementation of appropriate quality control and exhaustive testing of supplies, adherence by the manufacturers to good manufacturing practices, and selection of products manufactured by reputable companies [64].

HERBAL MEDICATIONS: REGULATORY ASPECTS

COMPARISON OF THE PROCESSES OF APPROVAL OF HERBAL COMPOUNDS AND CONVENTIONAL DRUGS

As mentioned, the main difference between HMs and conventional Western medications is neither exclusively nor primarily based on the origin of the compound (i.e., natural versus synthetic) but rather on the process of evaluation regarding efficacy and safety, which the compound should undergo prior to being marketed. In fact, many conventional medications are extracted from natural sources or are the chemical derivatives of naturally occurring molecules.

In Western countries, the process of approval of new conventional medications is tightly regulated. New drugs undergo a process of detailed scrutiny and scientific evaluation prior to being released into the market. Briefly, during the preclinical stages, the physiopathologic mechanisms underlying the disease are identified, and biologic targets (e.g., enzyme, receptor, gene) are identified. Drugs aimed at biologic targets are tested in vitro, and in vivo experiments are conducted under con-

trolled conditions. When the potential therapeutic benefit has been established based on the preclinical studies and the drug is considered ready for human studies, an elaborate application is then submitted to the appropriate regulatory institution: the FDA in the United States and Health Canada in Canada. The application includes:

- Composition and source of the drug
- Manufacturing information
- Data from in vitro and animal studies
- Detailed plans for proposed clinical trials
- Names and credentials of physicians responsible for conducting the clinical trials

If approved, human studies of the investigational new drug (IND) can be initiated. At the institutional level, interdisciplinary review boards are responsible for assuring the ethical and scientific integrity of the clinical trials.

Clinical studies are conducted in four stages or phases (I, II, III, and IV). Phase I is aimed at establishing drug safety, dosage, and pharmacokinetic properties of the drug (e.g., half-life, metabolism). These are open or nonblind studies, in which both investigators and healthy subjects (25 to 100) know what is being administered. Results of human studies are compared with animal studies.

The goal of Phase II is to study the effect of the drug on volunteer patients (100 to 200) with the disease for which the drug was developed. Subjects will either receive the drug, a placebo (negative control), or the standard drug (positive control) used in the treatment of the disease. Further toxicologic studies in animals will continue to assess chronic toxic potential.

Finally, in Phase III, double-blind or cross-over studies are conducted to further evaluate the efficacy of the drug in larger groups of thousands of patients. When Phase III is finished and if the results meet the goals initially established, a new drug application (NDA) will be submitted to the FDA or its congener in another country. After several years of preclinical research, four to six years of clinical trials, and as many as three years after the NDA has been submitted, the FDA may then approve marketing of the drug. At that point, Phase IV is initiated and a mechanism of post-marketing surveillance, including reporting of adverse effects, will be in place.

Compared with this elaborate process of approval, the mechanisms required for the marketing of HMs are extremely simple. To start, in many Western countries, including the United States and Canada, herbal medications are not legally considered drugs, but rather as dietary supplements and natural health products, respectively. Consequently, HMs are not legally required to undergo extensive preclinical investigation, and clinical trial evaluations are not required prior to the marketing of the herbal product. Rather, approval is based on traditional usage.

It should be noted that several herbal medications, namely in the European community, have been thoroughly evaluated, including safety and efficacy, product standardization, and well-conducted clinical trials with comparison to standard treatments (i.e., Phase III). These principles apply to the studies conducted to evaluate the efficacy of standardized preparations of saw palmetto (*Serenoa repens*) in the treatment of BPH [33; 34; 65].

SCIENTIFIC EVALUATION OF HERBAL MEDICATIONS

PRECLINICAL STUDIES AND EVALUATION IN CLINICAL TRIALS

The number of scientific studies aimed at unraveling the mechanism of action of HMs has undergone a remarkable growth in recent decades. Development of new legislation, availability of research funds to study the pharmacologic mechanisms of action and therapeutic efficacy of HMs, drug standardization, and implementation of clinical trials to assess HMs have played a central role in the development of an evidence-based approach to phytotherapeutics. The NCCIH in the United States and the NNHPD in Canada are pivotal in establishing advisory panels, coordinating scientific resources and expertise, and funding quality research on HMs [64; 66]. The American Society for Pharmacology and Experimental Therapeutics has long supported the increase in the National Institutes of Health's NCCIH budget for peer-reviewed research on botanical medications, particularly aimed at studying mechanisms of action and interactions with prescription drugs [67].

Scientific evidence on HMs should also be included in the basic curriculum in medical, pharmacy, dental, and nursing schools. Continuing education of healthcare professionals also contributes to a multidisciplinary and inclusive evidence-based assessment of HMs as part of a broader approach to maintenance of health and disease prevention.

IDENTIFICATION OF ACTIVE COMPOUNDS, ISOLATION, AND STANDARDIZATION

Standardization of the product and its individual chemical constituents is of major importance, and reliability of practices and procedures by the manufacturer is absolutely crucial. Several reports have analyzed the concentration of active ingredients present in herbal medications and compared the values obtained with those reported on the label by the manufacturer. Batch-to-batch variability has also been reported, and in one particular case of a compound containing ephedrine and methyl ephedrine, concentration of these substances varied by 180% and 1,000%, respectively [68].

The lack of standardization may also account for negative results obtained in some clinical trials [69]. One study revealed that, in the case of the antidepressant SJW (*Hypericum perforatum*), the amount of two of its most important chemical constituents, hypericin and pseudohypericin, can vary from 108% to 30% or even to as little as 0.1% of the amount reported on the label when a chemical analysis is conducted in a large number of samples from various manufacturers [70].

More reassuring results have been reported. The chemical composition of five of the most commonly used HMs was studied, and these results were compared to the information provided in the label by the manufacturer [71]. Results of this study, conducted by the University of California, Los Angeles (UCLA) Center for Human Nutrition, are encouraging and reflect a positive trend in increased quality and standardization of HMs by the manufacturers. For each product, three different samples from each of 12 bottles (6 bottles for each of the two separate batches) were collected. Five of the most commonly used HMs in North America were studied, specifically saw palmetto, SJW, echinacea, ginkgo biloba, and kava. Samples were purchased from 8 to 10 different suppliers nationally available in the United States. A greater consistency of composition was observed for samples purchased over the counter than for those purchased by mail order. A drastic decrease in variability of the marker compound was observed between batches; saw palmetto and SJW were the least variable, and the most variable were ginseng and echinacea [71].

In fact, analysis of the saw palmetto specimens revealed that the concentration of the marker compound ranged from 77% to 106%, and for two of the manufacturers the values were within ±10% of their label claim. For SJW, the concentration of the marker compound hypericin ranged from 88% to 110%, and for two of the suppliers it was within ±10% of their claim. In the echinacea compounds studied, the concentration of the marker compound ranged from 78% to 173% of the reported value, and two of the manufacturers were within ±10% of the concentration claimed. Ginseng was the most variable HM, and the amount of the marker varied from 44% to 261% of the claim. Only for one of the manufacturers was the value within ±10% of the claim. For kava, the values were within ±10% of their claim for more than 70% of the suppliers [71].

In the United States, the National Institute of Standards and Technology (NIST), in collaboration with the National Institutes of Health Office of Dietary Supplements, the FDA, the Center for Drug Evaluation and Research, and the Center for Food Safety and Applied Nutrition, is developing procedures regarding the standardization of dietary supplements and natural health products [64; 72]. The development of standardization of active ingredients, accurate evaluation of chemical contaminants, such as toxic metals present in the soil and/or acquired during processing, and screening for microbiologic contaminants, such as *Escherichia coli*, will certainly contribute to an increase in consumer reassurance, and to the acceptance by larger numbers of conventional healthcare providers [73]. In 2007, the FDA issued guidelines to outline requirements and expectations regarding how dietary supplements are manufactured, prepared, and stored [74]. These practices are meant to reduce misidentification and contamination of dietary supplements by manufacturers and to reduce errors in purity, strength, and composition. The guidelines are updated periodically to ensure current safe practices, with the last update conducted in 2013 [74; 75]. Although the practices are expected to be adhered to, to date there is no FDA approval process [74]. Several organizations, including the U.S. Pharmacopeial Convention (USP), NSF International, and Consumerlab.com, offer voluntary dietary supplement verification programs that provide standards and monographs for determining product and ingredient identity, strength, quality, and purity, and award a seal of approval mark to dietary supplement products that meet their criteria [74; 76; 77; 78].

Legislation requiring the standardization of herbal medications has been successfully implemented in several countries of the European Union, with benefits regarding the scientific assessment of pharmacologic properties and conduction of well-controlled clinical trials and mandatory reporting of adverse effects [79]. It has often been argued that a stricter control of phytochemicals further enhances their role as useful complementary rather than alternative therapeutic tools to conventional medications [64; 74; 75].

EVIDENCE-BASED REVIEW OF THE MOST COMMONLY USED HERBAL MEDICATIONS

Considering the large number of available HMs, it is beyond the scope of this course to exhaustively review them all. Fourteen of the most commonly sold HMs will be reviewed following an evidence-based assessment of several parameters relevant to clinical practice (***Table 1***). For each phytomedicine, the following subjects will be presented:

- Common name and scientific name
- Historical and current use
- Pharmacology
- Evidence-based therapeutic use and effectiveness
- Adverse effects and drug interactions
- Toxicology
- Dosage

A REVIEW OF HERBAL MEDICATIONS				
Common Name	**Scientific Name**	**Typical Modern Uses**	**Efficacy**	**Safety**
Saw palmetto	*Serenoa repens* or *Sabal serrulata*	Treatment of benign prostatic hyperplasia (BPH)	★★E	S
St. John's wort	*Hypericum perforatum*	Treatment of mild-to-moderate depression	★★E	AEs/DIs
Ginkgo	*Ginkgo biloba*	Management of age-related memory loss, dementia, early stages of Alzheimer disease	★★E	S
Ginseng	*Panax ginseng, P. quinquefolius, P. japonicus*	Treatment of cardiovascular diseases, diabetes, immunomodulation, menopause	★E	No S data
Echinacea	*Echinacea angustifolia, E. pallida, E. purpurea*	Treatment of common-cold symptoms	★★E	S
Kava	*Piper methysticum*	Treatment of anxiety, stress, insomnia	★★★E	AEs/DIs/UnS
Garlic	*Allium sativum*	Prevention and treatment of hyperlipidemia, hypertension, cardiovascular disease	★★E	AEs/DIs
Valerian	*Valeria officinalis*	Treatment of insomnia, anxiety	★★E	S
Andrographis	*Andrographis paniculata*	Prevention of upper respiratory tract infections	★★E	AEs/DIs
English ivy leaf	*Hedera helix*	Treatment of bronchitis and asthma	★★★E	S
Peppermint	*Mentha x piperita* Lamiaceae	Management of irritable bowel syndrome, dyspepsia	★★E	S
Ginger	*Zingiber capitatum* or *Zingiber officinale*	Treatment and prevention of nausea	★★★E	S
Soy	*Glycine max*	Treatment of cardiovascular disease, osteoporosis	★E	No S data
Chamomile	*Chamaemelum nobilis* or *Matricaria recutita*	Management of inflammatory diseases	★★E	S

Source: Compiled by Author *Table 1*

The therapeutic effectiveness of each medication is based on published scientific data regarding in vitro and in vivo studies of the mechanism of action and clinical studies, including randomized clinical trials, clinical studies, and meta-analyses. Accordingly, each herbal product is ranked into one of the following four categories:

★★★E: Clinically effective: Demonstrated by multiple randomized clinical trials

★★E: Clinically beneficial: Demonstrated by several controlled clinical trials, although some studies show conflicting or inconclusive results

★E: Limited effectiveness: Demonstrated by controlled clinical trials

No E data: Nonexistent or minimal supporting scientific evaluation

Product safety guidelines follow the same general rules applicable to mainstream drugs, and use during pregnancy, lactation, and childhood should be restricted to compounds tested for teratogenicity, carcinogenicity, and general toxicity. Otherwise, it is not advisable for the patient to be exposed to an untested HM. As a guideline, a product is ranked as:

- **S**: Safe
- **AEs/DIs**: Reported adverse effects and/or drug interactions
- **UnS**: Unsafe
- **No S data**: Unknown or limited controversial safety data

SAW PALMETTO

Efficacy: ★★E

Safety: S

Common Name and Scientific Name

Saw palmetto (*Serenoa repens or Sabal serrulata*) is also known as American dwarf palm or cabbage palm. This abundant and scrubby palm is indigenous to Florida and other southeastern states of the United States.

Historical and Current Use

Saw palmetto berries collected in the autumn were used by southeastern Native Americans in the treatment of urinary disorders and as an antiseptic. Saw palmetto extracts are now used in the treatment of BPH. In several European countries, use of this herb has been approved for the treatment of mild-to-moderate BPH. In Germany and Austria, saw palmetto is the most common form of therapy for BPH and represents more than 90% of all drugs prescribed for the treatment of this disorder [51; 65].

Pharmacology

The beneficial effects of standardized liposterolic extracts (phytosterols) in the treatment of BPH are now well established. The extracts represent 85% to 95% of free fatty acids from saw palmetto berries. Although the mechanism of action of saw palmetto is not completely understood, both in vitro and in vivo studies have revealed that the beta-sitosterol component of the extract correlates with its efficacy in the treatment of BPH [80; 81; 82]. Saw palmetto inhibits 5-alpha-reductase, the enzyme responsible for the transformation of testosterone into dihydrotestosterone (DHT), its tissue-active form [82; 83]. This mechanism of action is similar to the one described for finasteride and dutasteride [34; 82; 84]. It should be noted, however, that finasteride only inhibits the type 1 isoform of 5-alpha-reductase responsible for the production of different testosterone metabolites in the tissues, whereas saw palmetto inhibits both type 1 and type 2 isoforms [82; 85].

Other pharmacologic mechanisms of action of saw palmetto have been reported in the literature, namely that it competes with DHT and blocks androgen receptor stimulation, although this mechanism does not seem to correlate with its clinical efficacy [82; 86]. In vitro, saw palmetto extracts have alpha-1 adrenoceptor blocking properties like the standard drug tamsulosin, albeit this mechanism does not seem to account for saw palmetto's therapeutic effects as it is not observed at the lower concentrations, which are equivalent to the doses used in humans [87]. Interestingly, saw palmetto also inhibits cell proliferation and promotes apoptosis (i.e., programmed cell death) of prostate cancer cells, and its anti-inflammatory properties have been linked to its inhibitory actions on cyclooxygenase and lipoxygenase [88; 89; 90]. Together, all of these mechanisms may synergistically contribute to the therapeutic efficacy of saw palmetto extracts.

Evidence-Based Therapeutic Use and Effectiveness

The clinical effectiveness of saw palmetto in the treatment of mild-to-moderate BPH has been extensively studied. A comprehensive review of clinical studies that assessed the efficacy of saw palmetto versus placebo and saw palmetto versus finasteride was published in 2002 [65]. Results from 21 clinical trials, with a total of more than 3,000 patients, were analyzed. Several clinical parameters were evaluated, including urinary symptoms (e.g., dysuria, fullness, bladder residual volume), nocturia, urine flow rate, and prostate size (Boyarsky score, American Urologic Association Score, and International Prostate Symptom Score). The authors concluded that, "men taking saw palmetto were nearly twice as likely to report improvement in symptoms than men taking placebo," [65]. Also, "when compared to finasteride, saw palmetto provided similar responses in urologic symptoms and flow measures and was associated with a lower rate of impotence" [65]. This review, however, lacks information regarding comparisons between saw palmetto and alpha-1 adrenoceptor antagonists such as tamsulosin. Updates of this review, published in 2009 and 2012, found that saw palmetto was not more effective than placebo for treatment of urinary symptoms consistent with BPH [91; 92].

A large study of more than 2,500 patients suffering from mild-to-moderate BPH compared the effectiveness of saw palmetto versus tamsulosin (704 patients), saw palmetto versus finasteride (1,098 patients), and two different doses of saw palmetto (160 mg twice a day versus saw palmetto 320 mg once a day) [34]. The study demonstrated a better outcome for patients taking saw palmetto than those taking either of the conventional drugs. Also, unlike the conventional drugs, no negative impact on sexual function was reported by patients treated with saw palmetto. These results further support other well-conducted studies [84; 93; 94; 95; 96; 97; 98; 99; 100]. Interestingly, saw palmetto was less effective than finasteride in reducing prostate volume, although involution of the prostate epithelium and reduction of inflammation was observed [34; 101]. Co-administration of saw palmetto and finasteride did not improve the treatment outcome. A report in which saw palmetto efficacy was not observed may be attributable to the study being conducted in patients with moderate-to-severe BPH, as opposed to the beneficial effects on patients with a mild-to-moderate condition [102]. In addition to the population cohort difference, the study also failed to conduct an appropriate dose-response study or raise the dose of saw palmetto to adjust for the severity of the medical condition.

In conclusion, evidence demonstrates that saw palmetto is effective in the treatment of mild-to-moderate BPH, is less expensive, and is better tolerated than conventional medications [94; 103]. In addition, it is now well established that saw palmetto does not interfere with the laboratory measurements of prostate specific antigen (PSA), used to assess the progression of prostate cancer [83; 104]. This presents a considerable advantage over 5-alpha-reductase inhibitors finasteride and dutasteride, which are known to mask PSA readings and prevent an accurate assessment of the disease progression and concurrent development of prostate cancer [83; 104]. The efficacy of saw palmetto in the treatment of more severe BPH has not been established.

Saw palmetto has also been used to treat other genitourinary disorders, including chronic prostatitis. However, clinical studies have shown a lack of significant improvement in patients treated with saw palmetto for one year, contrasting with the benefits observed in the group treated with finasteride [103; 105].

It has also been advocated that saw palmetto, either alone or in conjunction with other nutraceuticals, may also play an important role in the prevention of BPH, although the results obtained are inconclusive [106; 107]. The effects of chronic saw palmetto administration on the organization of chromatin structure in patients with BPH provides an insight of the molecular effects of saw palmetto potentially relevant to gene expression and tissue differentiation [108].

Adverse Effects and Drug Interactions

Consistently, all studies revealed the absence of significant side effects. A 2008 meta-analysis of saw palmetto trials found that serious adverse effects (e.g., cancer, sexual dysfunction, hepatotoxicity, respiratory problems) were no more common in treatment groups than in placebo groups [109]. Gastrointestinal symptoms, including nausea or abdominal pain, may occur in less than 2% of patients but seem to decrease when doses are taken with a meal. Because of its antiandrogenic properties, women should not take saw palmetto for treatment of urogenital problems if they take contraceptives, hormone replacement therapy, have breast cancer, or are pregnant [65; 82]. Furthermore, there is no clinical evidence supporting a beneficial effect of saw palmetto in the treatment of urethritis in women. Interactions with anticoagulants are negligible and arise from a single reported case [110]. In clinical trials, 3% of the subjects developed hypertension, compared with 2% treated with finasteride; however, this difference was not statistically significant [84].

Toxicology

Saw palmetto is widely considered a safe phytomedicine, and no serious toxicologic effects are reported in the scientific literature [109]. Results of the Complementary and Alternative Medicine for Urological Symptoms (CAMUS) trial found no evidence of toxicity among 369 patients randomized to 320 mg, 640 mg, or 960 mg daily saw palmetto extract at doses up to three times the usual clinical dose during an 18-month period [111].

Dosage

Standardized lipophilic extracts of saw palmetto are administered at a dose between 100–400 mg twice daily for the treatment of BPH [33; 34; 51; 82]. A dose of 160 mg twice a day is the most commonly used dosage in clinical trials [82]. Therapeutic benefits are observed within three to four weeks after the initiation of treatment, which usually lasts for three to six months.

ST. JOHN'S WORT

Efficacy: ★★E

Safety: **AEs/DIs**

Common Name and Scientific Name

St. John's wort (*Hypericum perforatum*) is also known as amber touch-and-heal, goatweed, and klamath weed.

Historical and Current Use

This perennial, native to Europe, Western Asia, and North Africa, is a resilient weed, widespread in parts of the United States and southern Canada. The plant has golden-yellow flowers that bloom in the summer, which are collected and dried. The medicinal use of SJW as a topical anti-inflammatory and for wound healing has been known since ancient Greece. Extracts have been used in folk medicine for the treatment of depression and other mood disorders and also as a diuretic. Today, SJW is used primarily for the treatment of mild-to-moderate depression and has traditionally been the most commonly prescribed antidepressant in Germany, where it is available as a prescription medication [79; 112].

Pharmacology

Several chemicals, including naphthodianthrones (e.g., hypericin, pseudohypericin), phloroglucinols (e.g., hyperforin), flavonoids (e.g., quercetin), and essential oils, are the primary constituents of SJW [82; 113]. Formulations are standardized to concentrations of hypericin, usually 0.3% to 0.4%, which is considered the active ingredient responsible for the antidepressant properties of SJW. Clinical and pharmacologic studies, however, have shown that hyperforin concentrations of 2% to 4% correlate closely with antidepressant efficacy [114; 115].

The pharmacologic mechanisms of action of SJW extracts relevant to its antidepressant effect are complex. Hypericin may have a minor role in MAO inhibition, a mechanism shared with the classical antidepressant phenelzine [82]. This mechanism, however, is not considered clinically significant because it is only observed at concentrations 100 times higher than those used to treat depression [33]. Hyperforin is generally agreed to be the active component [82]. Both hypericin and hyperforin inhibit synaptic reuptake of serotonin, which is the same action as fluoxetine and paroxetine, but they also inhibit the reuptake of dopamine and noradrenaline, like other antidepressants including venlafaxine [82; 116].

After a single dose, the half-life of hypericin is four to six hours, whereas after chronic administration, the half-life of hypericin is one to two days [117; 118]. These values are comparable to those observed for fluoxetine (one to three days) and the selective serotonin re-uptake inhibitor (SSRI) paroxetine (12 hours) [48].

Long-term administration of SJW extracts increase the synaptic density of serotonin receptors by 50%, whereas the receptor affinity remains unchanged [119]. The increase in number of serotonin receptors was observed after a minimum 10 to 12 days treatment, a time frame that correlates with the well-known therapeutic delay of standard antidepressant drugs [120]. Together, the increased number of serotonin receptors and the increase in synaptic concentrations of neurotransmitters provide a mechanistic explanation for the antidepressant effects of SJW [113; 117; 121].

SJW extracts also have antibacterial properties, accounting for the antiseptic and wound-healing properties of topical formulations. Hyperforin is effective in inhibiting gram-positive bacteria, including penicillin-resistant and methicillin-resistant *Staphylococcus aureus*, but it is not effective against gram-negative bacteria. One randomized trial showed the effectiveness of SJW topical application in the treatment of atopic dermatitis [122; 123; 124]. In one small pilot study, SJW significantly improved erythema, scaling, and thickness in plaques of patients with mild psoriasis [125].

Some in vitro studies have shown that SJW extracts have antiviral properties, namely against influenza virus, and one study has identified a novel protein in SJW that suppresses gene expression in human immunodeficiency virus (HIV) [122; 126]. However, a Phase I clinical trial provided negative results [127]. It is important to emphasize that SJW should not be administered to HIV or acquired immune deficiency syndrome (AIDS) patients because of the pharmacokinetic interactions with antiretroviral protease inhibitors, such as indinavir, saquinavir, and ritonavir, and non-nucleoside reverse transcriptase inhibitors, such as efavirenz, which are metabolized by CYP3A4. Induction of CYP3A4 by SJW drastically reduces drug concentrations in the blood by 50% to 80% with subsequent loss of HIV suppression [128].

Finally, in vitro studies have shown that hyperforin and hypericin inhibit tumor cell growth by induction of apoptosis [129; 130]. The use of SJW extracts in the treatment of triple-negative breast cancer is an area of ongoing research [131; 132]. Although these compounds seem to have high efficacy, their potential clinical usefulness as anticancer agents is, at this point, merely speculative.

Evidence-Based Therapeutic Use and Effectiveness

Several clinical trials have assessed the efficacy and safety of SJW preparations in the treatment of depression. A 2005 Cochrane Review extensively analyzed published randomized, double-blind trials comparing SJW with placebo (26 studies) or with standard antidepressants (14 studies) [133]. SJW was demonstrated to be "more effective than placebo and similarly effective as standard antidepressants for treating mild-to-moderate depressive symptoms" [133]. The treatment period lasted from 4 to 12 weeks.

Two large clinical trials conducted in the United States did not support these findings [134; 135]. Both studies were conducted on patients who suffered from moderate-to-severe depression, and many patents presented with a history of drug-resistant depression, which may have affected the outcomes. The Hypericum Depression Trial Study Group has also been criticized because the response rates for both the SJW-treated and the sertraline-treated groups were not different from the placebo-treated group. In another randomized study, conducted in Germany, the effect of SJW (900 mg/day standardized SJW extract) on moderate-to-severe depression was compared with paroxetine (20 mg/day) [42]. The treatment was continued for 6 weeks, and in initial non-responders, after 2 weeks of treatment the doses were increased by 100%. The results indicated that, in the treatment of moderate-to-severe depression, hypericum extract was, "at least as effective as paroxetine" and was better tolerated [42]. A 2008 Cochrane Review of trials examining the treatment of severe depression with hypericum reached similar conclusions as to its efficacy in comparison to placebo and conventional antidepressants. Also, subjects in the SJW groups had a lower drop-out rate, possibly due to fewer side effects [136].

It is established in the scientific literature that standardized SJW extracts are effective and safe in the treatment of mild-to-severe depression [51; 122; 133; 136; 137; 138; 139].

Adverse Effects and Drug Interactions

SJW is well-tolerated and generally safe. Mild side effects include gastrointestinal symptoms, mild sedation or tiredness, dizziness, headache, and dry mouth. Incidence of side effects in SJW-treated patients (4% to 12%) is similar to that observed in the placebo-treated group and significantly lower than standard antidepressants [51; 82; 140; 141]. Two rare adverse events may occur after administration of SJW. First, transient photosensitivity may occur when administered in higher doses,

and second, the occurrence of a serotonin syndrome when co-administered with SSRIs is possible [82; 142]. The latter results from the synergistic interaction between the drugs raising serotonin to abnormally high levels [45; 46; 47; 48; 143].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the American Psychiatric Association, St. John's wort may be considered for patients with major depression who prefer complementary and alternative therapies, although evidence for its efficacy is modest at best and careful attention to drug-drug interactions is needed.

(https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Last accessed June 10, 2022.)

Strength of Recommendation: III (May be recommended on the basis of individual circumstances)

Pharmacokinetic interactions with SJW are rare and only occur at higher doses. Induction of cytochrome P450 isoforms, namely CYP3A4 and CYP1A2, by SJW results in a decreased bioavailability of drugs metabolized by this liver enzyme. These drugs include the immunosuppressant cyclosporine, the anticoagulant warfarin (bleeding), oral contraceptives (causing breakthrough bleeding), antiretroviral protease inhibitors, and theophylline [36; 51; 82; 128; 138]. A report has also shown a reduction in plasma levels of the HMG-CoA reductase inhibitor simvastatin [144]. Activation of the intestinal P-glycoprotein transporter also accounts for the reduction in plasma concentrations of digoxin [128].

In conclusion, although SJW has consistently been reported to be a safe drug when administered within its therapeutic range, its potential interactions with other drugs or herbs (e.g., kava) require caution and a thorough investigation during patient interview prior to use.

Toxicology

It is widely accepted in the literature that, when used within the normal therapeutic range, SJW is devoid of toxicologic properties. In high doses, SJW can elicit photosensitivity. Phototoxicity results from light-induced transformation of hypericin-derived pigments and has been reported in patients with HIV receiving high doses of intravenously administered SJW [127]. To date, only one study of potential teratogenicity during human pregnancy has been conducted, with data collected from the pregnancies of 54 SJW-treated women and 108 women either treated with conventional antidepressants or receiving no pharmacologic treatment. Rates of fetal malformations were similar among the three test groups and similar to rates of malformations in the general population; additionally, premature and live birth rates among the three test groups were similar [145]. Further research in this area is needed, and SJW administration in pregnant patients should therefore be avoided [82].

Dosage

Standardized preparations of SJW are usually administered from 500–1,800 mg per day [51; 122; 133; 137; 138]. In most studies, 900 mg was administered daily (450 mg twice a day, or 300 mg three times a day) [82].

GINKGO

Efficacy: ★★E

Safety: S

Common Name and Scientific Name

Ginkgo (*Ginkgo biloba*), also known as kew tree, ginkyo, or duck-foot tree (because of the characteristic fan-shaped leaves), is a large, resilient, and long-living tree cultivated by monks in China, where many individual specimens are documented to be more than 1,000 years old. Ginkgo trees, often known as living fossils, are the only survivors of the entire Ginkgoaceae family. Fossils of this tree that date back more than 200 million years have been identified in areas throughout the Northern Hemisphere, including Europe and North America. Ginkgo trees were brought into Japan and other East Asian countries around 1200 C.E., possibly in relation to the spread of Buddhism. In the seventeenth century, they were reintroduced in Europe and, more recently, in North America. Ginkgo is a resilient tree to parasites and diseases and, interestingly, also survived the Hiroshima atomic bombing.

Historical and Current Use

The designation originates from ginkgo, meaning silver apricot, and biloba, which describes the two-lobed shape of the leaf. Historically, leaf extracts have been used in traditional Chinese medicine to treat a variety of disorders, including asthma, allergies, premenstrual syndrome, tinnitus, cognitive impairments resulting from aging and dementia, and vascular diseases including central and peripheral vascular insufficiencies. Standardized leaf extracts are used based on their neuroprotective and vascular regulatory properties in the management of intermittent claudication, age-related memory loss, dementia, and early stages of Alzheimer disease [33; 146]. Plum-like fruits of the female tree are not edible and cause contact dermatitis. Ingestion of the seeds causes headache, nausea, diarrhea, and even seizures when ingested in larger amounts [51; 147].

Pharmacology

More than 40 chemical components of ginkgo have been isolated, including flavonoids, terpenoids, flavones, catechins, sterols, and organic acids. The two most important and active groups of chemicals are the flavonoids, such as quercetin and kaempferol, and the terpenoids, including ginkgolides A, B, C, J, and M and bilobalide. Ginkgo biloba extracts available in

Europe and North America are standardized to 24% flavonoids and 6% terpenoids and have been used in hundreds of in vitro and in vivo studies and numerous clinical trials [33; 51].

The biologic properties of ginkgo biloba extract result from the complex interactions among chemical components, and it is therefore difficult to establish a well-defined cause-effect relationship between specific elements and biologic effect. Nevertheless, it is now well established that flavonoids have antioxidant and free-radical scavenger properties. They also have a protective effect against apoptosis and beta-amyloid neurotoxicity of Alzheimer disease and may play an important role in the prevention of neuronal degeneration in Parkinson disease [148; 149; 150; 151].

Terpenoids, particularly ginkgolides, inhibit the platelet activating factor (PAF), and therefore prevent platelet aggregation, have anti-inflammatory properties, and prevent contraction of smooth muscles in the respiratory tract [146]. The vasodilatory properties of standardized ginkgo biloba extract preparations are attributed to the stimulation of endothelium-derived relaxing factor and regulation of nitric oxide release [51].

Ginkgo biloba extract also stimulates receptor expression and neurotransmitter concentrations in the brain, particularly acetylcholine [152; 153; 154; 155]. This latter mechanism of action is similar to the cognitive enhancer, tacrine, previously used in the treatment of Alzheimer disease [156].

Evidence-Based Therapeutic Use and Effectiveness

There is scientific evidence supporting the beneficial use of standardized ginkgo biloba extract, 120–240 mg/day, in the treatment of mild-to-moderate cognitive impairment, such as age-related dementia, multi-infarct dementia, and possibly Alzheimer disease [33; 157; 158; 159]. Some studies show that ginkgo biloba extract is as effective as the acetylcholinesterase inhibitor donepezil (Aricept) in the treatment of patients with early stages of Alzheimer disease, although these findings are not supported by additional studies [160]. One study reported that the combination therapy of gingko biloba extract plus donepezil was more effective than either therapy alone [161]. A 2015 systematic review noted a positive response (defined as improvement in cognitive function and activities of daily living and reduced neuropsychiatric symptoms) to a 240 mg/day dose in study participants with neuropsychiatric symptoms related to a dementia diagnosis but not in individuals thought to have Alzheimer disease [159]. Although studies have shown that ginkgo biloba extract appears to be safe and with no excess side effects compared with placebo, the evidence that it has predictable and clinically significant benefit for people with dementia or cognitive impairment is inconsistent, and whether ginkgo biloba leaf extract is beneficial for the treatment of Alzheimer disease remains controversial. Researchers recommend that the findings be confirmed by larger clinical trials [33; 162; 163; 164; 165; 166; 167; 168].

Clinical trials have assessed the effectiveness of ginkgo biloba extract in the treatment of cerebral insufficiency, which is a syndrome combining mild cognitive impairment, headaches, confusion, poor concentration, fatigue, and dizziness, and is associated with mood disorders. Long-term treatment with ginkgo biloba extract at 120–150 mg/day reduced symptoms and improved short-term memory [169; 170].

Some evidence supports the effectiveness of ginkgo biloba extract in the treatment of peripheral vascular disorders, including intermittent claudication and, to a lesser degree, Raynaud syndrome [33; 171]. In fact, one clinical trial demonstrated that ginkgo biloba extract is as effective as pentoxifylline, the standard medication for the treatment of intermittent claudication [172]. Despite its ability to improve circulation, multiple clinical trials failed to show the efficacy of ginkgo biloba extract in the treatment of Raynaud disease compared with conventional therapy or placebo [173; 174]. One analysis concluded that while ginkgo biloba treatment did slightly increase treadmill walking time of participants with peripheral artery disease and led to a slight reduction of pain, the therapy produced only modest overall improvements [175].

The beneficial effects of ginkgo biloba extract in a variety of medical conditions, such as tinnitus, cochlear disorders, and vascular retinopathies (including macular degeneration), have also been reported in the scientific literature, although larger studies are required to confirm the clinical outcome. It is possible that in these conditions, ginkgo biloba extract is the most effective when administered in conjunction with standard therapies.

Adverse Effects and Drug Interactions

Consistently, ginkgo biloba extract is considered a safe and well-tolerated drug when used at the recommended dose for periods of up to six months. In most clinical studies, the incidence of adverse effects is similar to placebo. Less than 2% of patients develop side effects, namely headache, nausea, or mild gastrointestinal symptoms [51]. Two cases of subarachnoid bleeding have been reported in patients taking ginkgo biloba extract and warfarin, and one case of subarachnoid bleeding and intraocular hemorrhage has also been reported in a patient taking ginkgo biloba extract and acetylsalicylic acid concurrently. A case of postoperative bleeding has also been reported after laparoscopic surgery [176]. In these cases, however, the causal relationship between ginkgo biloba extract and bleeding was not clearly established. Furthermore, bleeding was not reported in any of the clinical trials involving hundreds of thousands of subjects [51]. Nonetheless, it is advisable to discontinue ginkgo biloba extract administration several days prior to surgery [82].

Toxicology

Although in vivo studies did not report either embryotoxic or teratogenic effects of ginkgo biloba extract, this phytomedicine should be avoided during pregnancy and breastfeeding [33; 82; 177]. As mentioned, severe contact dermatitis, similar to that caused by poison ivy, can result from direct contact with the pulp of ginkgo fruit of the female tree. Ingestion of ginkgo seeds, but not leaves, in large amounts (50 or more) causes headache, nausea, diarrhea, and even seizures. This condition is known in Japan as *gin-nan* [82; 147]. Pollen from the male tree can be allergenic for sensitive individuals [51].

Dosage

Standardized extracts are administered at a daily dose of 120–240 mg, in two or three equal doses, for periods of six months or longer [33; 82; 157; 158].

GINSENG

Efficacy: **★E**

Safety: **No S data**

Common Name and Scientific Name

Ginseng is a designation that applies to an HM that is prepared from the root of different plants of the Araliaceae family. Asian ginseng is obtained from *Panax ginseng,* American or Canadian from *P. quinquefolius*, and Japanese from *P. japonicus*. Siberian (Russian) ginseng is obtained from the root of *Eleutherococcus senticosus*, a plant that, although a member of the same Araliaceae family, is not a member of the *Panax* genus and, hence, is not considered a true ginseng. High-quality ginseng root is harvested in the autumn from plants that are 5 to 6 years old.

Historical and Current Use

The name *Panax* is derived from the Greek *panacea*, meaning cure-all. True to its etymology, the root of the plant has been historically used for a variety of purposes, such as improvement of cognitive and physical performance (i.e., ergogenic effect), cardiovascular diseases (e.g., hypertension), diabetes, cancer, immunomodulation, and menopause. Evidence-based knowledge regarding ginseng's medicinal properties is limited and has generally failed to support historical claims, possibly with the exception of clinical trials assessing the hypoglycemic properties of ginseng [33; 178; 179; 180; 181; 182].

Pharmacology

Several chemicals, including polysaccharides (e.g., ginsan, ginsenans) and a variety of saponins known as ginsenosides, are found in ginseng [82]. Ginsenosides, the most important bioactive compounds, are complex molecules with a steroidal skeleton and modified side chains. The concentration of different ginsenosides varies among species, age of plant, and season of harvest and contributes to the limited understanding of the pharmacologic and physiologic properties of each compound [82]. Adulterants are commonly found in ginseng preparations due to the high cost of authentic ginseng roots, and the presence of natural methylxanthines also may contribute to some reported physiologic effects [82].

Ginsenosides Rb1, Rg1, and Rg2 improve cognitive performance, a mechanism likely related to the stimulation of cholinergic activity implicated in the mechanisms of learning and memory [82; 183; 184]. Both in vitro and in vivo models of Parkinson disease have shown that ginseng extracts have a neuroprotective effect against 1-methyl-1-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced parkinsonism in rodents [185]. Gintonin, a novel glycolipoprotein, is a ginseng derivative found in the root of Korean ginseng [186]. Gintonin holds lysophosphatidic acid (LPA), a serum phospholipid that stimulates cell proliferation, migration, and survival [186; 187; 188]. It is thought that gintonin causes significant elevations in levels of intracellular calcium that promote calcium-mediated cellular effects. Research suggests that gintonin has antioxidant and anti-inflammatory effects against different models of neurodegeneration [186; 187; 189]. In studies of neurodegenerative diseases, such as Alzheimer disease and Parkinson disease, gintonin has demonstrated neuroprotective activity by providing action against apoptosis- and oxidative stress-mediated neurodegeneration [186; 187; 189]. In vitro and in vivo studies have demonstrated that ginseng polysaccharide GH1 and ginsenosides Rb2 and Re effectively reduce hyperglycemia and liver glycogen in genetically obese mice as well as in patients with and without type 2 diabetes [178; 190; 191]. Ginseng also stimulates insulin synthesis and release, an effect possibly caused by the increase in nitric oxide production by ginseng [192]. Preliminary results suggest that ginseng also regulates intestinal absorption of glucose and glycosylation of hemoglobin A1c (HbA1c) [179]. A variety of studies (human, animal, cell) have shown that different processed ginseng extracts and specific ginsenosides possess beneficial effects on type 2 diabetes. Most studies of individual ginsenosides have focused on Rb1, Re, or Rg1 as these are the main components of ginseng and easily obtained. However, their large molecule structure results in poor systemic bioavailability. It is thought that these large-molecule ginsenosides may be a form of storage for saponins in ginseng plants rather than the active form in vivo. The smaller molecule ginsenosides (Rg3, Rh1) may be the ingredient that exerts therapeutic effects [193; 194; 195].

In vitro studies have shown that ginsenosides cause vasodilation and lower blood pressure and that panaxynol, a potent inhibitor of thromboxane A2, prevents platelet aggregation [196; 197]. However, further scientific evidence of the antihypertensive effects of ginseng is required prior to considering its potential benefits in cardiovascular diseases. One double-blind controlled trial found that ginseng significantly improved arterial stiffness and systolic blood pressure but had no noted effect on diastolic blood pressure [198]. Research challenges to

understanding the potential benefits of ginseng in cardiovascular disease include understanding and identifying the distinct cardiovascular properties of the different ginsenoside compositions, identifying what likely are multifaceted mechanisms that account for the effects of the distinct compositions, and determining which ginsenosides mediate which cardiovascular properties [199].The immunostimulatory and antiproliferative properties of ginseng have also been reported in the scientific literature, but further studies are required [200]. Ginseng has been studied for use in the treatment of menopause symptoms, due to the steroid-like chemical composition of ginsenosides, but the results were inconclusive.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Society for Integrative Oncology recommends 2,000 mg daily of encapsulated American ginseng root powder can be considered to improve fatigue during chemotherapy and radiation for breast cancer.

(https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21397. Last accessed June 10, 2022.)

Level of Evidence: C (Recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.)

Evidence-Based Therapeutic Use and Effectiveness

A Cochrane Review has concluded that the beneficial effects of ginseng preparations were "not established beyond reasonable doubt" [184]. Other literature reviews, however, have reported that ginseng extracts effectively reduced blood glucose levels in patients with type 2 diabetes, although information regarding dosage and long-term effects is still incomplete [33; 179; 201]. A modest improvement in cognitive performance has also been reported [33; 179]. Ginseng is also being investigated for use in the treatment of chronic fatigue, respiratory tract infections, stroke, dermatologic diseases, and as an adjuvant to chemotherapy in the treatment of non-small-cell lung cancer [202; 203; 204; 205; 206; 207; 208].

Adverse Effects and Drug Interactions

Ginseng preparations are generally well tolerated when administered within the recommended dosage, and the available animal and human studies suggest that it is safe [82]. As a result of its hypoglycemic properties, it should be used cautiously in patients with type 2 diabetes concurrently treated with oral hypoglycemic drugs. Improvements in blood glucose measures and glycemic control with ginseng use have been inconsistently reported [82].

Anticoagulant properties may also account for a few reports of epistaxis and vaginal bleeding. In contrast, a randomized, controlled clinical trial has shown that ginseng increases the risk of blood clotting in patients treated with warfarin. This pharmacokinetic interaction occurs only after long-term administration of ginseng and results from the induction of hepatic CYP450 isoforms responsible for warfarin metabolism [209].

Interactions between ginseng and MAO inhibitors have also been reported and may cause headaches, insomnia, nervousness, and mood disorders. Pharmacokinetic (e.g., CYP450 induction) and pharmacodynamic potentiation of antihypertensive drugs have also been reported, and it should not be administered to hypertensive patients [33; 82].

A few case reports describe the occurrence of diarrhea, unstable mood, skin rash, or itching after long-term administration. Ginseng has also been associated with loss of menstrual periods and vaginal bleeding in menopausal women. Therefore, ginseng should not be administered to patients with hormone-sensitive conditions, such as breast or uterine cancer and endometriosis [82]. In men, it may be associated with estrogen-like effects, such as reduced libido and gynecomastia [33].

Toxicology

At normal doses, ginseng is reported in the literature as being safe. Nevertheless, ginseng should be avoided during pregnancy and breastfeeding [33; 82; 137]. A case of reversible masculinization of a newborn girl when a mother allegedly took *Eleutherococcus senticosus* (Siberian ginseng) during pregnancy has been reported [210]. In fact, it resulted from the adulteration of the original product and substitution of *Periploca sepium*, a vine of the milkweed family, for ginseng. *Periploca sepium* has been used in traditional Chinese medicine for its stimulatory and libido enhancing effects. Accordingly, it should be emphasized that the mentioned report has been erroneously used as published evidence of ginseng toxicity [211; 212]. Pediatric safety concerns regarding ginseng treatment for upper respiratory tract infections were addressed in a 2008 Canadian trial involving 75 subjects (3 to 12 years of age) given standard doses, low doses, or placebo. The treatments were well tolerated, considered safe, and warrant additional research for use on these and other types of pediatric infections [213].

Dosage

Purified ginseng extracts are generally standardized to 4% or 7% ginsenoside contents. Usually, 100–200 mg of standardized 4% extract is administered orally once or twice daily, for as many as 12 weeks [82]. In traditional Chinese medicine, 0.5–2 g/day of dried ginseng root, equivalent to 200–600 mg of standardized extract, is commonly used. Long-term administration of ginseng should not exceed 1 g/day of the dry root form or 400 mg/day in the extract form. It is administered daily for two to three weeks, then discontinued for one to two weeks. This treatment schedule may be repeated for several months [33; 137].

ECHINACEA

Efficacy: ★★E

Safety: S

Common Name and Scientific Name

The designation echinacea applies to several plants of the Asteraceae/Compositae family, including *E. angustifolia*, *E. pallida*, and *E. purpurea*. Echinacea, also known as coneflower, narrow-leafed cone-flower, or black-eyed Susan, is indigenous to North America. It adapts well and thrives in temperate climates, including Europe and Asia, where it has been planted for decorative and medicinal purposes.

Historical and Current Use

Echinacea was used by Native Americans for a wide variety of conditions, including chewing the roots for toothaches and gingivitis, root and leaf infusion for stomach pain, colds, and infections, and topically as a disinfectant and for wound healing. The use of echinacea was quickly adopted by early European settlers, and shortly thereafter, it became widely used by European herbalists and physicians. In Germany, it has been commonly used in mainstream medicine for almost a century. The German Commission E has approved the use of echinacea for the amelioration of common-cold symptoms, upper respiratory infections, and urinary tract infections, as well as topical administration for treatment of superficial wounds [214]. The scientific literature generally supports a beneficial effect of echinacea extracts in the treatment of cold symptoms, but evidence of its efficacy in the prevention of colds is still limited [215; 216]. Echinacea is the most widely sold HM in the United States and is the third most popular natural product overall (surpassed only by fish oil and glucosamine) [10].

Pharmacology

Preparations from different portions (e.g., root, leaves) of the echinacea plants (e.g., *E. angustifolia*, *E. purpurea*, *E. pallida*) are collected during the blooming season. The products are usually dried, and several chemical components, namely caffeic acid derivatives (e.g., echinacosides, cichoric acid derivatives), flavonoids (e.g., quercetin), alkylamides, and polysaccharides, are identified upon alcoholic extraction [51]. Laboratory analysis of echinacea extracts with high-pressure liquid chromatography provides the chemical fingerprint of different echinacea species. In fact, in *E. purpurea*, no echinacosides are detected, whereas they are abundant in *E. angustifolia* and *E. pallida*. On the other hand, the amount of cichoric acid present in *E. purpurea* is 40- to 60-fold higher than that present in *E. angustifolia* and *E. pallida*, respectively [217]. The relative concentration of various chemicals within the same species also varies in different plant parts. Echinacoside concentrations are higher in the root, whereas cichoric acid concentrations are higher in the flower of all echinacea species than in other plant parts.

Due to its complex chemical makeup, the precise pharmacologic and therapeutic properties of each compound remain to be determined. Naturally occurring phenols, such as the caffeic acid derivatives, are potent antioxidants due to the presence of hydroxyl groups on aromatic rings that scavenge tissue-damaging free radicals [217]. In vitro experiments revealed that alkylamides from echinacea inhibit cyclooxygenase and 5-lypoxygenase, accounting for its anti-inflammatory properties [218; 219].

The immunostimulatory properties of echinacea have been demonstrated both in vitro and in vivo. Nonspecific effects, such as macrophage proliferation, stimulation of interleukin-1, tumor necrosis factor, and interferon stimulation, as well as specific effects, such as increase in numbers of T lymphocytes and natural killer cells, have been reported in several studies [33]. Because the total immunostimulatory effect of echinacea in humans remains to be established, the German Commission E discourages the use of echinacea in patients with autoimmune diseases.

Many preparations are standardized to 4% to 5% echinacosides, while others also report the concentration of cichoric acid. A detailed study conducted by investigators from the University of Colorado Health Sciences Center analyzed 59 samples of echinacea-only preparations purchased from 11 retail outlets in the Denver area [220]. Ten percent of the samples did not contain measurable amounts of echinacea, and the species content only agreed with the label in 52% of the cases. Twenty-one preparations claimed to be standardized, but only nine met the composition reported on the label. Although the efficacy of echinacea in the treatment of some medical conditions has been reasonably established, the lack of species identification and standardization, as well as product contamination/adulteration, should be thoroughly investigated prior to being administered. The poor quality of many available products certainly contributes to, or may account for, the conflicting results and significant number of negative reports published in the scientific journals.

Evidence-Based Therapeutic Use and Effectiveness

The therapeutic effectiveness of echinacea preparations in prevention and treatment of the common cold has been extensively studied. Several extensive reviews and meta-analysis studies have been published, and some have provided conflicting or inconclusive results.

Researchers evaluated the therapeutic effectiveness of echinacea in the treatment of the common cold based on nine placebo-controlled clinical trials and concluded that its effectiveness has not been established [221].

Three randomized, double-blind, and placebo-controlled trials assessed the effectiveness of echinacea on the avoidance of and severity of colds. Consistently, they all revealed that subjects preventively treated with standardized echinacea extracts acquired fewer colds (22%, 58%, 49%) than the placebo group (33%, 82%, 56%) [222; 223; 224]. However, due to the small number of subjects studied in each trial, the decreases were not statistically significant. A meta-analysis evaluated these three clinical trials, and due to the common methodology used, the results of almost 400 subjects were combined [215]. The meta-analysis suggests that the risk of developing a cold was 55% higher in the placebo than in the echinacea-treated group, a statistically significant difference.

A 2014 Cochrane review also evaluated the effects of echinacea on naturally acquired colds [225]. Twenty-four published trials met their inclusion criteria. In the treatment of colds, echinacea was not effective in most clinical trials and beneficial or marginally better than the placebo group in only one trial. In the 12 prevention clinical trials, no significant difference was observed between echinacea and placebo groups, but a later analysis found a 10% to 20% reduction in cold risk [225]. Interestingly, the authors also commented on the pervasive issue of lack of standardization, the variability in bioactive composition of echinacea preparations, and the likelihood that they may contribute to, or account for, the lack of consistency in treatment and prevention outcomes.

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Institute for Clinical Systems Improvement, the evidence on the efficacy of *Echinacea* for the prevention of viral upper-respiratory infection is limited. The studies are either small or of low quality, or the evidence is insufficient to make conclusions. More studies are needed.

(https://www.icsi.org/wp-content/uploads/2019/01/RespIllness.pdf. Last accessed June 10, 2022.)

Level of Evidence: Expert opinion

In vitro and in vivo studies, and in some cases preliminary clinical evidence as well, support other possible therapeutic applications of echinacea preparations (e.g., immunostimulant, anti-infective, wound-healing) [82]. However, due to the limited data, the actual therapeutic outcome is inconclusive.

Adverse Effects and Drug Interactions

In clinical trials, echinacea preparations are generally well tolerated, and the number of patients dropping out of studies is similar to the placebo group. A single study conducted in children 2 to 11 years of age reported the occurrence of an allergic rash [226]. In adults, one review found that the most common adverse effects were nausea and vomiting (<1%), abdominal pain (<1%), and mild drowsiness and headache (<1%) [33]. One case of anaphylaxis has been reported in a patient with a history of atopic reactions [227]. Echinacea should not be administered to individuals with allergies to other plants of the Asteraceae family, including daisies, ragweed, marigolds, and chrysanthemums. It is also recommended to avoid echinacea if currently on immunosuppressants [82].

Toxicology

Both in vitro and in vivo studies suggest that, even when administered at doses several-fold higher than the ones normally used, echinacea is devoid of toxicity. Analysis of 112 pregnant women who were exposed to echinacea preparations during the first trimester of pregnancy showed no difference in fetal health when compared with the nonechinacea-exposed group [228]. Although other studies seem to confirm safety, echinacea preparations should be avoided during the first trimester due to lack of definitive evidence.

Dosage

For treatment of cold symptoms and upper respiratory infections, an initial 300–1,000 mg titrated dose of powdered herb in capsules or its equivalent (tincture or juice) is administered for five to seven days [33; 51; 137; 179]. Use for more than eight weeks at a time should be avoided because of the potential for immunosuppression [82]. Preparations containing 15% pressed herb are used topically as disinfectants.

KAVA

Efficacy: ★★★E

Safety: **AEs/DIs/UnS**

Common Name and Scientific Name

Kava (*Piper methysticum*), a member of the pepper family, is a widely cultivated shrub indigenous to the South Pacific islands. It is also known as kava-kava, kawa, or ava pepper [82].

Historical and Current Use

A drink prepared from the root of the kava plant has been used traditionally in the South Pacific for ceremonial, social, and medicinal purposes for several centuries, if not millennia. It is used for its mild relaxing and calming properties, culturally comparable to alcohol use in Western societies. Following the European trend, the use of kava for the treatment of anxiety has become popular in the United States. In some countries, including Germany, it has been commonly prescribed to treat anxiety, stress, and insomnia, although very serious concerns regarding potential hepatotoxicity have led to warnings and bans in North America.

Pharmacology

The lipid-soluble extract of kava is rich in kava pyrones, including kavain, dihydrokavain, and methysticum [82; 229]. Kava pyrones block voltage-dependent sodium channels, a mechanism responsible for the local anesthetic properties of kava drinks, which causes numbness and tingling of the mouth. Kava also contains antioxidant flavonoids and alkaloids. It has been reported that kava has a direct effect on limbic structures, particularly the amygdala. It does not bind to the gamma-aminobutyric acid $(GABA)_A$ receptors, unlike benzodiazepines, which target the $GABA_A$ receptors abundantly distributed in the cerebral cortex. This may account for the difference in anxiolytic properties of kava, which, unlike benzodiazepines, does not cause sedation [230].

At higher doses, kava lactones also have muscle-relaxant and anticonvulsant properties, which are possibly related to the stimulation of the glycine receptor [231]. Kavain has dose-dependent antiplatelet aggregation and anti-inflammatory properties [232].

Evidence-Based Therapeutic Use and Effectiveness

The clinical effectiveness of kava has been widely studied, and clinical studies strongly support its efficacy in the treatment of moderate and mild cases of anxiety. One meta-analysis included data from 11 double-blind, controlled clinical trials, and the authors concluded that kava, when compared with placebo, is effective in the symptomatic treatment of anxiety [233]. A standardized preparation of kava (LI 150) was as effective as the anxiolytic drugs buspirone and opipramol [234; 235]. An extensive literature review also confirmed the clinical effectiveness of kava preparations in the treatment of anxiety [33].

Several clinical studies assessed the effect of kava on memory and compared it with both the anxiolytic oxazepam and placebo [230]. The studies concluded that kava, unlike oxazepam, does not impair cognitive performance and memory. In fact, an improvement in memory was observed in the kava-treated group, but these interesting results wait for confirmation [33; 236]. A review of at least 10 studies on the effects of kava on cognition have been published, but the heterogeneity of dosages/potency and preparations used precludes meta-analysis. At higher dosages, reaction time may be impaired [237; 238; 239]. Kava has been promoted for use in attention deficit hyperactivity disorder; however, clinical trials are lacking and such use is not recommended [239; 240].

EVIDENCE-BASED PRACTICE RECOMMENDATION

A Cochrane Review found that, compared with placebo, kava extract is an effective symptomatic treatment for anxiety, although, at present, the size of the effect seems small. The effect lacks robustness and is based on a relatively small sample. The data available from the reviewed studies suggest that kava is relatively safe for short-term treatment (1 to 24 weeks), although more information is required.

(https://www.cochrane.org/CD003383/DEPRESSN_kava-extract-for-treating-anxiety. Last accessed June 10, 2022.)

Level of Evidence: Meta-analysis

Adverse Effects and Drug Interactions

In clinical trials, the side effects of kava preparations were rare and mild, with gastrointestinal discomfort, restlessness, headache, and dizziness reported in about 2% of patients. Kava dermatitis, a yellow discoloration of the skin accompanied by scaly dermatitis, is only observed in chronic heavy kava drinkers and reverses after discontinuation of kava administration. This skin condition resembles pellagra but is resistant to niacin treatment [82]. Neurotoxicity, pulmonary hypertension, and choreoathetosis have also been reported in chronic heavy drinkers in the Australian Aboriginal population [241]. A few rare cases of kava-induced Parkinson-like extrapyramidal disorders have been reported, as well as the aggravation of existing Parkinson disease in one patient and one case in the United States of rhabdomyolysis related to the ingestion of a large amount of kava [51; 235]. There are some reports suggesting that kava may cause severe and, in some cases, irreversible liver damage. As a result, the FDA issued an advisory letter to healthcare professionals stating possible health risks [242].

Kava extracts interact with and potentiate the effects of anxiolytic and depressant drugs, such as benzodiazepines, barbiturates, and alcohol. Due to its antiplatelet properties, kavain-containing preparations should not be administered to patients undergoing anticoagulant therapy, although the clinical relevance of this potential interaction has not been established. Kava preparations should also be avoided in patients with extrapyramidal disorders, including Parkinson disease. Finally, due to the potential hepatotoxicity, kava should not be administered to patients with liver disease or those treated with potentially hepatotoxic medications such as acetaminophen, anabolic steroids, or the anticancer agent methotrexate [33; 82; 243]. As a precautionary measure, kava should not be administered during pregnancy and lactation due to the lack of safety studies [82]. Kava administration should be discontinued at least 24 hours prior to surgery because of possible potentiation of the sedative effect of anesthetics [244].

Toxicology

More than 30 cases of kava-induced hepatotoxicity, ranging from hepatitis and cirrhosis to acute liver failure and death, have been reported in the literature. One study of lipid-extractions of kava led researchers to state that rather than being caused by directly toxic mechanisms, reactions to kava likely stemmed from immunologically mediated idiosyncratic mechanisms; therefore, the hepatotoxicity of kava may be similar to benzodiazepines [245]. An Australian trial concluded that water-extracted kavalactones, using dried roots sourced from the island of Vanuatu and prepared in a controlled pharmaceutical manufacturing facility, caused neither an increase in liver enzymes nor hepatotoxic symptoms [246]. Other studies have shown that kava suppresses CYP450 enzymes in the liver, leading to hepatotoxic concentrations of concurrently administered drugs [82; 247]. Although no cases of hepatotoxicity were reported in any of the clinical trials included in a Cochrane Review, it is not recommended for use in the United States [137; 233].

Dosage

Standardized products are available, and the usual recommended daily dose of kavalactones ranges from 120–250 mg/day, divided in two to three equal doses [33; 51]. In the United States, most formulations are standardized to 30% or 55%, meaning that a 100 mg tablet contains 30 mg or 55 mg of kavalactones, respectively. Usually, kava use should be limited to three months to avoid potential habituation, and patients should be advised of the potential adverse effects on motor coordination and capacity to drive or operate heavy machinery [51].

GARLIC

Efficacy: ★★**E**

Safety: **AEs/DIs**

Common Name and Scientific Name

Garlic (*Allium sativum*), also known as allium, is related to chives (*Allium schoenoprasum*) and onions (*Allium cepa*), and all belong to the Liliaceae family, which also includes lilies.

Historical and Current Use

The recorded medicinal use of garlic goes back to ancient Egyptian, Greek, and Roman civilizations. It was used for the treatment of a variety of conditions, including heart problems, headaches, intestinal parasites, and tumors, and as a local disinfectant. In the nineteenth century, Louis Pasteur also reported the antimicrobial properties of garlic. It is now used for its effectiveness in reducing cholesterol and for its antithrombotic and antioxidant properties, as well as for its ability to lower blood pressure. Together, these properties have also provided some support for the use of garlic in the prevention of cardiovascular diseases, including atherosclerosis [33; 37; 51]. The benefits of garlic in the treatment of certain cancers, specifically stomach and colorectal, have also been investigated [248; 249].

Pharmacology

The beneficial effects of garlic have been related to its sulfur compounds. More than 20 different sulfur compounds have been identified in garlic. The sulfur compound allinin (S-allyl-l-cysteine sulfoxide) is transformed to allicin (diallyl thiosulfinate) via the enzyme alliinase when the bulb is crushed or ground. Allicin is an unstable molecule that is converted into more stable compounds. Other sulfur compounds, such as peptides, steroids, terpenoids, flavonoids, and phenols, derive from allicin metabolism and have been the subject of investigations aimed at identifying their biologic role [250]. In vitro and in vivo studies have associated allicin with the antibacterial properties of garlic. Commercially available garlic extracts are standardized to the allicin content. Three water-soluble allicin derivatives, s-allylcysteine (SAC), s-ethylcysteine (SEC), and s-propylcysteine (SPC), are the most effective in reducing in vitro cholesterol synthesis in hepatocytes by 42% to 55% [251].

Methyl-allyl trisulfide (MATS), a lipid-soluble allicin derivative, inhibits cyclooxygenase activity and prostaglandin synthesis and is responsible for the antithrombotic and antiplatelet aggregation properties of garlic [252]. Another sulfur compound, diallyl trisulfide (DATS), is a potent inhibitor of colon and lung human cancer cell proliferation in cell cultures and is at least partially responsible for the anticancer properties of garlic [253; 254; 255; 256].

The antioxidative properties of garlic are exerted indirectly through the sulfur compound-induced stimulation of protective antioxidant enzymes present in the body, including glutathione-S-transferase, superoxide dismutase, and catalase [37; 252].

Evidence-Based Therapeutic Use and Effectiveness

Several clinical trials have reported that garlic lowers total cholesterol levels by 8% to 15% [257; 258]. This effect results from the lowering of the low-density lipoprotein (LDL) and triglycerides, while the high-density lipoprotein (HDL) values remain unchanged. A meta-analysis confirmed that, after 10 to 12 weeks, garlic lowers plasma cholesterol, although the benefits (4% to 6%) were less pronounced than previously reported, and this effect was not statistically significant after a six-month period [259]. In 2001, an extensive meta-analysis of 34 randomized clinical trials including almost 2,000 patients confirmed the previous assertions [260]. A meta-analysis of 26 studies found that, overall, garlic is superior to placebo in reducing serum total cholesterol and triglyceride levels [261]. Compared with placebo, serum total cholesterol and triglyceride levels in the garlic group were reduced by 0.28 mmol and 0.13 mmol, respectively. Garlic powder and aged garlic extract were more effective in reducing serum total cho-

lesterol levels; garlic oil was more effective in lowering serum triglyceride levels. Garlic did not lower LDL cholesterol, HDL cholesterol, apolipoprotein B, or the total cholesterol/HDL ratio [261]. Results of a 2018 meta-analysis found that garlic can reduce total cholesterol and LDL levels, but not HDL and total triglyceride levels [262]. In conclusion, garlic preparations are moderately effective in lowering LDL and triglycerides and do not change the HDL concentration in the plasma [33].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American College of Physicians, the American College of Cardiology Foundation, the American Heart Association, the American Association for Thoracic Surgery, the Preventive Cardiovascular Nurses Association, and the Society of Thoracic Surgeons recommend that treatment with garlic should not be used with the intent of reducing cardiovascular risk or improving clinical outcomes in patients with stable ischemic heart disease.

(http://www.onlinejacc.org/content/64/18/1929. Last accessed June 10, 2022.)

Strength of Recommendation: Strong

The effects of garlic on blood pressure have been studied in several clinical trials. Some studies have shown a small (6%) yet statistically significant effect, although these findings were not replicated by other studies [33]. Garlic is not recommended for the management of hypertension [82; 263].

Garlic has also been shown to inhibit platelet aggregation, as expected by its inhibitory effects on cyclooxygenase and prostaglandin synthesis. The effective dosages are not well established, and comparison with other antiplatelet aggregation drugs is not yet available. Because several reports have associated garlic with bleeding accidents, administration should be limited to lower dosages and co-administration with drugs that affect hemostasis, including antiplatelet aggregation drugs (e.g., aspirin) or anticoagulants (e.g., warfarin), should be avoided [33; 144].

Some clinical studies suggest that garlic preparations slow the progression of atherosclerotic plaques [264]. Although encouraging, these results are preliminary and further studies are required [82].

The anticancer properties of garlic compounds have been reported both in vitro and in vivo, but their clinical effectiveness remains to be established [265]. One small trial in mice showed that garlic extract inhibits growth of certain cancer cells, particularly multiple myeloma. Researchers indicated that the reduced proliferation of cancer cells is at least partly mediated by increased endoplasmic reticulum stress [265]. Another small trial with mice indicated that anticancer properties of garlic are more effective when introduced directly to the cancer cells by injection rather than via oral ingestion [266]. Epidemiologic studies suggest that regular consumption of garlic may be associated with a lower risk of developing gastric and colorectal malignancies [267]. A review of 14 studies of the anticancer properties of garlic and onion supports this association [249]. While the results of one systematic review and meta-analysis suggest a significant inverse correlation between the intake of garlic and the risk of gastric cancer, an analysis of health claims provided to the FDA found no credible evidence supporting the use of garlic for prevention of gastric cancer or breast, lung, or endometrial cancers [261; 268]. Although the epidemiologic evidence is cautiously positive, well-designed clinical trials are needed before a conclusion can be reached [269].

Adverse Effects and Drug Interactions

The most common adverse effects reported are bad breath and body odor [82]. Less commonly, dyspepsia and flatulence are also reported. In rare cases, dermatitis and respiratory difficulty can occur in hypersensitive patients [51]. The highest risk of herb-drug interaction is between garlic and anticoagulant drugs, such as the vitamin K inhibitor warfarin, and antiplatelet aggregation agents, such as ticlopidine and clopidogrel, and results from the pharmacodynamic potentiation of mechanisms of action [144].

Toxicology

Garlic preparations administered within the recommended dosages are safe, although they should not be administered to patients allergic to garlic or to other members of the Liliaceae family, namely chives, onions, leek, or lilies [33; 82; 144]. A dangerous pharmacokinetic interaction between garlic and the protease inhibitor saquinavir has been reported, as it reduces the plasma concentration of the anti-HIV drug by 50% [270].

Dosage

Administration of garlic preparations varies greatly according to the preparation used (i.e., fresh, powder, oil extracts). Standardized preparations to 1.3% allinin or 0.6% allicin are usually administered at 600–900 mg per day. This is considered equivalent to one small clove of fresh garlic [51].

VALERIAN

Efficacy: ★★E

Safety: S

Common Name and Scientific Name

Valerian (*Valeria officinalis*), also known as baldrian, is a member of the Valerianaceae family. Other species of the same family that are also used for medicinal purposes include *V. wallichi* and *V. sambucifolia*.

Historical and Current Use

Historical documents from ancient Greece, China, and India widely report the use of preparations from valerian root and rhizome in the treatment of insomnia and anxiety. This herb, native to Asia and Europe, is found throughout the world. Topically, it has been used in the treatment of acne and wound healing. It has also been used traditionally for the treatment of a variety of disorders, including digestive problems, flatulence, congestive heart failure, urinary tract disorders, and angina pectoris. For the past 200 years, valerian has been widely used in Europe and North America for its mild sedative properties [37; 51].

Pharmacology

A large number of chemicals, including monoterpenes, sesquiterpenes, valepotriates, amino acids, and alkaloids, have been extracted from valerian. Although no single component has been shown to account for its pharmacologic properties, the biologically active valerenic acid has been used as the constituent for standardization. In vivo studies have confirmed the sedative, anxiolytic, and anticonvulsant properties of valerian preparations. Studies have also shown the agonistic effect of valerian and some of its individual compounds on the $GABA_A$ receptors and on the 5-HT5a serotonin receptors [271; 272; 273]. Other studies have revealed that valerian extracts inhibit the presynaptic GABA carrier, further contributing to an increased GABAergic inhibitory activity in the brain [274]. Valerenic acid also inhibits GABA transaminase, the enzyme responsible for GABA metabolism [275]. Together, these findings contribute to a better understanding of the molecular mechanisms underlying the sedative and anticonvulsant properties of valerian. More recently, research has identified valerenic acid and its modulation of the $GABA_A$-ergic system as probable cause of the anxiolytic effects, a mechanism similar to benzodiazepines (e.g., diazepam) [276]. In addition to valerenic acid, isovaleric acid, didrovaltrate, borneol, and some lignans have also been proposed to contribute to the anxiolytic effect of the plant [277].

Evidence-Based Therapeutic Use and Effectiveness

A systematic review of nine randomized clinical trials found that results regarding the effectiveness of valerian in the treatment of insomnia were inconclusive [278]. Some benefits were reported within one to two days, but benefits on sleep were observed only after four weeks of treatment. A larger European clinical trial reported that the valerian had minimal or no effect on sleep regulation [279]. Unfortunately, patients were treated for only two weeks, a time period considered too short when compared with previous studies, which may account for the negative outcome. A 2011 systematic review of CAM practices on insomnia reached a similar conclusion as the European clinical trial regarding valerian [280]. The American Academy of Sleep Medicine suggests that valerian not be used for sleep-onset or sleep-maintenance insomnia as the benefits are considered to be approximately equal to the risks [281].

No well-designed trials of valerian in the treatment of anxiety in humans have been published to date. An investigation of the effect of valerenic acid on rats concluded that valerian use was related to a reduction of anxious behavior, and a small-scale study found that valerenic acid was effective for reducing anxiety before a medical procedure [276; 282].

Adverse Effects and Drug Interactions

In clinical trials, valerian side effects were minor, most commonly headache, stomach upset, or dizziness, and were usually reported as frequently as in the placebo group. Adverse effects on reaction time and alertness were much lower than benzodiazepines. Dependence and withdrawal have not been reported in any of the clinical trials, although a single case report of withdrawal symptoms after discontinuation has been published [283]. As valerian and benzodiazepines similarly target the $GABA_A$ receptor, it is possible that the patient may develop physical dependence after lengthy administration. It is therefore advisable to discontinue valerian administration progressively. Valerian potentiates the effects of other sedatives, such as benzodiazepines, barbiturates, alcohol, kava, and chamomile, and should not be co-administered in conjunction with these drugs or phytomedicines [33].

Toxicology

Valerian is considered safe by the FDA, but administration during pregnancy and breastfeeding is not advised due to the limited availability of safety data [82].

Dosage

In clinical trials, for the treatment of insomnia, 900 mg of a standardized solution equivalent or 1.5–3 grams of dried root was administered 30 minutes to 1 hour before bedtime [51]. Valerian extract, in doses of 400–600 mg, has been used in clinical trials evaluating valerian in insomnia [284; 285].

ANDROGRAPHIS

Efficacy: ★★**E**

Safety: **AEs/DIs**

Common Name and Scientific Name

Andrographis (*Andrographis paniculata*) is also known as *Justicia paniculata*, green chiretta, king of bitters, kan jang, and sambiloto. It is an herb naturally found in Asia, including India, Southeast Asia, and southern China, and it is also cultivated for commercial use in the preparation of traditional HMs. Andrographis is an annual tall herb, up to one meter high, with small white flowers. It thrives in humid climates and shady areas.

Historical and Current Use

The bitter-tasting leaves of andrographis have been used for centuries in traditional Indian and Chinese medicine in the preparation of an infusion used for the treatment of digestive ailments and fever. In Malaysia, andrographis has also been traditionally used for the treatment of hypertension [286]. In northern European countries, andrographis is used for the prevention of upper respiratory tract infections [33].

Pharmacology

Andrographis is rich in diterpenoids and flavonoids. At least nine diterpenoids, including andrographolide, 14-deoxyandrographolide (DA), and 14-deoxy-11-oxoandrographolide (DDA), have been isolated.

In vitro studies revealed that andrographolide has anti-inflammatory, antiapoptotic, and immunomodulatory properties. In vivo studies demonstrated that both DA and DDA effectively lower blood pressure, decrease heart rate, and cause vasodilation [287]. DA and DDA block calcium channels, increase nitric oxide synthesis, and inhibit ß-adrenergic receptors. All of these actions provide the mechanistic explanation for the hypotensive properties of andrographis [287].

Evidence-Based Therapeutic Use and Effectiveness

Several clinical trials, including almost 900 subjects, have assessed the effectiveness of andrographis in the treatment and prevention of upper respiratory tract infection. Two meta-analyses concluded that andrographis was significantly more effective than placebo for the treatment of upper respiratory tract infection symptoms [288; 289]. A 2017 systematic review and meta-analysis also found that andrographis (*A. paniculata*) improved overall symptoms of upper respiratory tract infection compared to placebo, usual care, or other herbal therapies. Andrographis also shortened the time to symptom resolution [290]. Limited evidence also suggests that andrographis preparations may be effective in the prevention of upper respiratory tract infection [291; 292]. Two clinical studies concluded that andrographis is also effective in the treatment of influenza symptoms, although larger and better-designed studies are needed to confirm the results [33].

One randomized controlled trial of 60 patients with mild hypertriglyceridemia found that *A. paniculate* extract reduced triglyceride levels comparable to the effect of 300 mg/day of gemfibrozil, an LDL-lowering agent [293].

Adverse Effects and Drug Interactions

Andrographis is considered safe and well tolerated. Headache, nausea, vomiting, abdominal discomfort, and nasal congestion are the most commonly reported adverse effects [33; 82]. Although data regarding andrographis interactions with other drugs is still limited, due to andrographis' hypotensive and hypoglycemic properties, concurrent administration with antihypertensive and hypotensive drugs should be avoided.

Toxicology

In clinical trials, a dose-response dependent toxicity of andrographis has been identified, and fatigue, headache, and lymphadenopathy have been described [291; 294; 295]. Three cases of anaphylactic reaction have also been reported [288].

Dosage

Usually, 300 mg of standardized preparations of andrographis (4% andrographolides) is taken four times per day, for as long as two weeks [33].

ENGLISH IVY LEAF

Efficacy: ★★★**E**

Safety: **S**

Common Name and Scientific Name

English ivy (*Hedera helix*), also known as common ivy, is an evergreen climbing vine. It is native to Europe and Central Asia, grows easily, and is commonly found in humid environments and in forests. It is often used for decorative purposes. It is different from ground ivy (*Glechoma hederacea*) and American ivy (*Parthenocissus quinquefolia*). It is particularly important not to confuse it with poison ivy (*Rhus toxicodendron*).

Historical and Current Use

The glossy and dark green leaves of common ivy have been traditionally used for the treatment of a wide variety of disorders, including respiratory disease, arthritis, fever, burns, and infections. It is now used as an expectorant and in the treatment of bronchitis and asthma [51].

Pharmacology

Ivy leaves are rich in saponins (e.g., hederin, hederacoside) but also contain sterols, flavonol glycosides, and polyalkenes among other chemicals. Saponins stimulate secretion of mucus in the upper respiratory tract and have a mucokinetic and mucolytic effect [229]. They also prevent acetylcholine-induced bronchospasm [296]. Hederacoside C has antifungal and antibacterial properties [214]. Together, these bronchodilatory and antimicrobial properties of ivy leaf extracts provide the pharmacologic evidence to support their beneficial effects in the treatment of upper respiratory tract infections.

Evidence-Based Therapeutic Use and Effectiveness

The clinical efficacy of ivy leaf extracts has been the subject of one meta-analysis [297]. Five clinical trials, three of which measured its effect on children, indicated that the treated group showed an improvement in chronic bronchial asthma. In another study not included in the previous review, 1,350 children with chronic bronchitis were treated with standardized ivy leaf extracts for four weeks. A significant improvement or cure of the following symptoms was observed, when compared with the baseline: cough (92%), expectoration (94%), dyspnea (83%), and respiratory pain (87%) [298]. A postmarketing study of almost 10,000 patients with bronchitis showed that, after a seven-day treatment with ivy leaf extracts, 95% of the patients had improved significantly [299]. One 2021 systematic review found that while ivy leaf preparations are safe for use in cough due to acute upper respiratory tract infections, the effects are minimal at best and of uncertain clinical importance [300].

Adverse Effects and Drug Interactions

Ivy leaf extracts are generally considered safe. Mild adverse effects, such as gastrointestinal discomfort, eructation, or nausea, are observed in 0.2% to 2.1% of patients [298; 299]. No drug interactions have been reported. Considering the detergent-like actions of saponins, it has been suggested that ivy leaf extracts should not be ingested at the same time as other drugs, considering the unlikely possibility that ivy leaf extracts may facilitate the absorption of the other drugs. However, this warning is not supported by any evidence and should be considered as speculative.

Toxicology

Ingestion of ivy berries can be toxic, and falcarinol present in cut ivy leaves may cause contact dermatitis, particularly in sensitive individuals [144]. In a bizarre case, ingestion of ivy leaves caused mechanical obstruction and suffocation [301]. Toxicology tests confirmed the cause of death as being suffocation, and no toxin was detected in cardiac blood, femoral blood, or urine of the deceased [301].

It has been suggested that ivy leaf products should be avoided during pregnancy because the emetine content in ivy leaf may cause uterine contractions [302]. Data on the effects of ivy leaf extracts during lactation are not yet available, and as a result, ingestion of ivy leaf extracts in these cases should be avoided.

Dosage

Standardized ivy leaf extracts are available as a hydroalcoholic extract syrup (105 mg/day of dried ivy leaf extract), ethanolic extract drops (35–40 mg/day of dried ivy leaf extract), or suppositories (160 mg/day of dried ivy leaf extract) [297].

PEPPERMINT

Efficacy: ★★E

Safety: S

Common Name and Scientific Name

Peppermint (*Mentha x piperita L.*) is a hybrid of *Mentha spicata L.* (spearmint) and *Mentha aquatica L.* of the Lamiaceae (mint) family. It is also known as peppermint oil, menthol, mint, balm mint, brandy mint, and green mint. The plant is native to Europe but is widely cultivated in the United States and Canada [82; 303].

Historical and Current Use

Peppermint leaf and peppermint oil have a history of use for digestive orders that dates back to ancient Egypt. The plant was first described in England in 1696, and both the leaf and the oil have been used in Eastern and Western traditional medicine as antispasmodics, aromatics, and antiseptics. Peppermint oil is used in herbal remedies, cosmeceuticals, personal hygiene products, foods, and pharmaceutical products. Topical preparations have traditionally been used to calm pruritus and relieve irritation and inflammation [303; 304; 305; 306; 307]. Peppermint oil is widely used as a spasmolytic agent in irritable bowel syndrome (IBS) [307; 308; 309].

Pharmacology

Peppermint oil is complex and highly variable, with more than 100 components isolated from the oil. Relative concentrations vary depending on climate, cultivar, and geographic location. Peppermint yields 0.1% to 1% of volatile oil composed primarily of menthol (29% to 48%), menthone (20% to 31%), and menthyl acetate (3% to 10%) [82]. Menthol is rapidly absorbed following oral administration, and elimination is mainly via bile [82; 307]. Peppermint oil has a demonstrated dose-related antispasmodic effect on gastrointestinal smooth muscle, attributed to calcium channel blockade [82; 310; 311]. It reduces intragastric pressure, phasic contractility of the proximal stomach, and appetite, with negligible effects on gastric sensitivity, tone, and nutrient tolerance in health [309].

Evidence-Based Therapeutic Use and Effectiveness

Irritable Bowel Syndrome

The clinical effectiveness of peppermint oil in the treatment of IBS has been extensively studied. A Cochrane review of clinical studies that evaluated the efficacy of bulking agents, antispasmodics (e.g., peppermint oil), and antidepressants for the treatment of IBS was published in 2013 [312]. The review included 56 randomized controlled trials published between 1966 and 2009 involving 3,725 patients with IBS who were older than 12 years of age. The primary outcomes evaluated were improvements of abdominal pain, global assessment, and symptom score. Both antidepressants and antispasmodics demonstrated improvement in outcome measures. Abdominal pain improved in 58% of antispasmodic patients compared with 46% with placebo. Global assessment showed 57% improvement in patients taking antispasmodics compared with 39% with placebo; and 37% of patients taking antispasmodics showed improved symptom score compared with 22% with placebo [313]. A subgroup analysis of different types of antispasmodics, including peppermint oil, revealed statistically significant benefits [312]. Evidence suggests that enteric-coated peppermint oil may be effective in relieving some of the symptoms of IBS [82; 307; 314].

Dyspepsia/Functional Abdominal Pain

The use of peppermint in combination with other herbals for treatment of functional dyspepsia in adults and children has been reviewed in the literature [315; 316; 317]. A study published in 2000 evaluated the safety and effectiveness of enteric-coated capsules containing a fixed combination of 90 mg peppermint oil and 50 mg caraway oil [315]. The study included 96 patients who received either one capsule twice daily or placebo for 28 days. Outcomes measured included change in pain intensity, change in sensation of pressure, heaviness and fullness, and global improvement as rated by the investigators. On the 29th day, the average intensity of pain was reduced by 40% with peppermint use, compared with 22% with placebo; pressure, heaviness, and fullness was reduced by 43%, compared with 22% with placebo; and 67% of patients were very much improved, compared with 21% with placebo.

One randomized trial investigated the pharmacokinetics of menthol use in children 7 to 12 years of age with functional abdominal pain [318]. Thirty children underwent wireless motility capsule testing, and approximately one week later, they were randomized to 180, 360, or 540 mg of enteric coated peppermint oil. The researchers observed a direct linear relationship between peppermint oil dose and menthol systemic exposure with mean elimination half-life 2.1, 3.5, and 4.6 hours for the 180-, 360-, and 540-mg doses, respectively, suggesting that a higher dose of peppermint oil may be needed to achieve maximal response [318].

A choleretic action of peppermint oil has been described, with possible applicability in the management of gallstones [82; 307]. Its antispasmodic action makes it useful in patients with colonic and esophageal spasm and in endoscopy [319; 320; 321; 322; 323].

Adverse Effects and Drug Interactions

Menthol, the major component of peppermint oil, may cause contact dermatitis in some individuals. Mucosal burns and swelling of the tongue and oral cavity have been reported following ingestion of peppermint oil. Other reported incidences include stomatitis and vulval allergic contact; however, such reactions appear to be rare [82; 304; 324; 325; 326].

Toxicology

Peppermint is generally recognized as safe. Comprehensive reports on its safety have identified the constituents pulegone and menthofuran as being of toxicologic concern [327; 328]. Use in pregnancy should be avoided due to emmenagogue effects [82].

Dosage

Doses of peppermint oil of up to 1,200 mg in enteric-coated tablets are used to treat IBS [82]. The tablets should be swallowed whole, not crushed, broken, or chewed, to avoid irritation to the mouth, esophagus, and stomach, and they should be taken 30 to 60 minutes prior to meals on an empty stomach [82; 321; 329]. Doses of 0.1–0.24 mL of peppermint oil have been used as a carminative (relieving flatulence) in clinical studies [82; 313; 330; 331].

GINGER

Efficacy: ★★★E

Safety: S

Common Name and Scientific Name

Ginger (*Zingiber capitatum, Zingiber officinale*) is also known as black ginger, ginger root, and zingiberis rhizoma. Ginger is native to tropical Asia and is a perennial that is cultivated in Australia, Brazil, China, India, Jamaica, West Africa, and parts of the United States. The rhizome is used both medicinally and as a culinary spice [82].

Historical and Current Use

The medicinal use of ginger dates back to ancient China and India. It is referred to in Chinese pharmacopeias, Ayurvedic medicine scriptures, and Sanskrit writings. Its culinary properties were discovered in the 13th century, leading to its widespread use in Europe. Apothecaries in the Middle Ages recommended ginger for travel sickness, nausea, hangovers, and flatulence. Other uses include for the common cold, fever, sore throat, gastrointestinal complications, and indigestion.

Ginger is referenced in the official pharmacopeias of more than one dozen countries. It is approved by Germany's Commission E for indigestion and to help prevent motion sickness. In the United States, ginger is approved as a dietary supplement and commonly used as a treatment for nausea [82; 332; 333; 334].

Pharmacology

Only unbleached ginger is a medicinal-grade drug, containing 1.5% or more volatile oil. More than 400 different compounds have been identified in ginger. The major constituents are carbohydrates (50% to 70%), which are present as starch. Amino acids, raw fiber, protein, phytosterols, vitamins and minerals are among the other constituents. Gingerols, a class of structurally related compounds, form shogaols, the pungent constituents of ginger. The primary shogaols are (6)-gingerol and (6)-shogaol [82; 335; 336]. Ginger exerts in vitro antioxidative, antitumorigenic, and immunomodulatory effects and is an effective antimicrobial and antiviral agent [336].

Evidence-Based Therapeutic Use and Effectiveness

Clinical trials in humans have examined the antiemetic effects of ginger as they relate to nausea of various etiologies (e.g., motion sickness, postoperative, pregnancy-related, chemotherapy-related). In particular, ginger has been found to be more effective than placebo in controlling pregnancy-related nausea and vomiting in randomized controlled trials. The mechanism by which this occurs is unclear, but enhanced gastrointestinal transport, antiserotonin activity, and possible central nervous system effects have been described in animal studies [82]. Although ginger has been shown to be effective in ameliorating pregnancy-related nausea and vomiting, its safety during pregnancy has not been established. In one randomized clinical trial, 102 participants randomly received either 500-mg ginger or placebo two times per day, 30 minutes prior to each dose of antiretroviral therapy for 14 days [337]. Forty-six (90.2%) of the patients in the placebo group and 29 (56.4%) of the patients in the ginger group experienced some degree of nausea, but the frequency of any degree of nausea was significantly lower in the ginger than the placebo group. Results from published studies on the use of ginger for chemotherapy-related nausea are equivocal [82].

Adverse Effects and Drug Interactions

Ginger may enhance the adverse/toxic effect of agents with anticoagulant/antiplatelet properties; bleeding may occur [82]. Adverse reactions reported in trials are uncommon [82]. Case reports of arrhythmia and IgE allergic reaction have been documented [334; 338].

Toxicology

Because there are little data on the toxicity of ginger in humans, there is no consensus on use during pregnancy and lactation [82]. One study found no adverse effects on pregnancy outcomes, and systematic reviews in 2013 and 2018 concurred with this conclusion [339; 340; 341].

Dosage

Ginger has been used in clinical trials in doses of 250 mg to 1 g, repeated three to four times daily [82].

SOY

Efficacy: **★E**

Safety: **No S data**

Common Name and Scientific Name

Soy (*Glycine max*), a plant in the pea family, is also known as soy isoflavones, soya, and soybean. Soy is a common source of dietary phytoestrogens found in American diets as either a food or a food additive [82; 303; 342].

Historical and Current Use

Traditional and folk uses of soy products include for menopausal symptoms, osteoporosis, memory problems, high blood pressure, high cholesterol, and breast and prostate cancer. Soy may be taken as a dietary supplement. Some studies suggest that daily intake of soy protein or soy isoflavones supplements may reduce LDL cholesterol and menopausal symptoms (e.g., hot flashes) in women; however, not enough evidence exists to determine whether soy supplements are effective for any other health uses [342].

Pharmacology

The isoflavones in soybean (i.e., genistein, daidzein, glycitein) have a chemical structure similar to estrogen. They bind to both estrogen receptors (ER alpha and ER beta) and exert estrogen-like effects under some experimental conditions [343]. Genistein, daidzein, and glycitein undergo metabolism to the isoflavandiols, equol, and p-ethylphenol. The metabolism is highly variable (i.e., dependent upon the effect of carbohydrate intake on intestinal fermentation). The isoflavones are secreted into bile via the enterohepatic circulation and eliminated in urine [82].

Evidence-Based Therapeutic Use and Effectiveness

Although soy protein has gained considerable attention for its potential role in improving risk factors for cardiovascular disease, the American Heart Association (AHA) and an expert panel from the American College of Cardiology (ACC) found that the evidence of benefit is uncertain, with a relatively small decrease (3%) in LDL cholesterol concentrations and no effect on other lipid risk factors with soy protein consumption, as compared with milk or other proteins [344].

To assess the effectiveness of phytoestrogens, including soy and soy extracts, for reducing hot flushes and night sweats in postmenopausal women, the authors of a Cochrane review evaluated the results of 30 randomized trials that had a duration of at least 12 weeks and in which the intervention for symptom relief was the use of a food or supplement with high levels of phytoestrogens [345]. However, a strong placebo effect was reported in most of the trials, with a reduction in symptom frequency ranging from 1% to 59%. The authors of the review found no evidence of effectiveness with phytoestrogen use for relief of menopausal symptoms. Authors of other studies confirm this conclusion [346; 347]. In 2017, as a result of inconclusive evidence, the FDA proposed a rule to prevent companies from claiming soy protein can reduce heart disease risk [348].

Several meta-analyses of clinical trials have evaluated the effectiveness of soy preparations in protecting against decreases in bone mineral density (BMD). Some report small improvements in BMD; others report no effect [349; 350]. Soy isoflavones, but not soy protein, may have a beneficial effect on bone turnover during early menopause and in postmenopausal women [351; 352].

Adverse Effects and Drug Interactions

Soybeans and soy products, including supplements, are generally well tolerated.

Toxicology

Concern has been expressed that feeding infants soy formula may adversely affect development of the reproductive system due to the estrogen-like activity of isoflavones; however, data are inconclusive to permit a firm conclusion [353]. In addition, some organizations, such as the American Academy of Pediatrics, assert that "isolated soy protein-based formulas are a safe and nutritionally equivalent alternative to cow milk-based formula for term infants whose nutritional needs are not met from breast milk" [354]. More research and long-term studies are necessary to determine the effects of soy-based formula.

Dosage

The effects of daily doses (40–120 mg) of isoflavones for a variety of conditions have been studied in a large number of clinical trials [82]. A dose of 20–50 g soy protein taken daily by mouth has been studied in individuals with high cholesterol. Isoflavones content has ranged from 60 mg to more than 100 mg daily [355].

CHAMOMILE

Efficacy: ★★**E**

Safety: **S**

Common Name and Scientific Name

Chamomile (*Chamaemelum nobilis*, *Matricaria recutita*) has a variety of common names, including common, English, garden, genuine, German, Hungarian, lawn, Roman, Scotch, sweet, true, and wild types [82].

Historical and Current Use

C. nobilis is a slow-growing perennial; *M. recutita* grows as an upright annual. The fragrant flowering heads of both plants are collected and dried for use as teas and extracts [82]. Both plants have been used since Roman times as antispasmodics and sedatives in the treatment of digestive and rheumatic disorders and as a wash to cleanse wounds and ulcers. Various formulations have been used to treat colic, cystitis, fever, flatulence, and vomiting [356; 357]. German chamomile flower is approved by the German Commission E for use as an inhalant in skin and mucous membrane inflammations, bacterial skin diseases (including those of the oral cavity and gums), and respiratory tract inflammations and irritations. It is also the variety most commonly used in the United States. The flower is approved for use in baths, as irrigation for anogenital inflammation, and for internal use to treat gastrointestinal spasms and inflammatory diseases [358]. *M. recutita* is widely used in Europe as a botanical for wound care. Aqueous extracts are used as washings or wet packs for fresh wounds. Alcoholic extraction yields the most complete blend, which can be transferred to aqueous formulations or ointments [359]. In Europe, traditional phytomedicines such as chamomile play an adjuvant role in acne therapy, either in addition to or in combination with intensive cosmetic care. After cleaning, creams or aqueous decoctions are applied topically [335].

Pharmacology

The chemical compounds of *C. nobilis* and *M. recutita* are similar. Chamomile tea, brewed from dried flower heads, contains 10% to 15% of the plant's essential oil. The blue-colored volatile oil is a complex mixture of sesquiterpenes, sesquiterpene lactones, and acetylene derivatives. Phenolic compounds found in the flowers include hydroxycinnamic acid derivatives, caffeic acid, and flavonoids (i.e., apigenin, luteolin, chamaemeloside). A novel and potent NK1 receptor antagonist has been identified in *Matricaria* flowers. Coumarin has also been identified [82]. The chemical constituents of chamomile (e.g., bisabolol, chamazulene) and the flavonoids apigenin and luteolin possess anti-inflammatory properties. Apigenin has also been shown to reversibly inhibit irritant-induced skin inflammation in animals and to exert antispasmodic effects in the intestines [360]. Bisabolol and the flavonoids have demonstrated antispasmodic effects [82].

Evidence-Based Therapeutic Use and Effectiveness

The chemical components in chamomile (i.e., bisabolol, flavonoids) have demonstrated antispasmodic effects in animal experiments. Chamomile infusions have been used traditionally as gastrointestinal antispasmodics despite the lack of rigorous trials to support this use [82]. Commercial preparations of creams containing chamomile are also widely available despite the paucity of trials to support their use [361; 362].

It has been suggested that chamomile might provide clinically meaningful antidepressant activity [363]. The authors of a Canadian study examined whether commercially available botanicals directly affect the primary brain enzymes responsible for GABA metabolism [364]. Approximately 70% of all extracts tested showed little or no inhibitory effect. However, both *M. recutita* and *Humulus lupulus* (hops) showed significant inhibition of GAD enzyme activity in animals.

Adverse Effects and Drug Interactions

Allergic reactions to chamomile are commonly reported and may be dependent on the route of ingestion. Hypersensitivity reactions include anaphylaxis, dermatitis, gastrointestinal upset, lacrimation, and sneezing. The dried flowering heads may induce vomiting in large amounts. Eye drops containing chamomile have caused allergic conjunctivitis [82]. Chamomile may potentiate the anticoagulant effects of warfarin. No coagulation disorders have been reported, but close monitoring of patients on anticoagulants is advised. In vitro, chamomile has been shown to be bactericidal to some *Staphylococcus* and *Candida* species [365]. Chamomile is considered safe by the FDA, but it should be used with caution in individuals who are allergic to ragweed, as cross-allergenicity may occur. Symptoms include abdominal cramping, tongue thickness, tight sensation in the throat, angioedema of the lips or eyes, diffuse pruritus, urticaria, and pharyngeal edema [366; 367].

Toxicology

Bisabolol toxicity in animal studies is reported to be low following oral administration with no noted teratogenic or developmental abnormalities [82].

Dosage

Because of the sedative effects of chamomile, caution should be used in conjunction with medications with sedative side effects or with alcohol. The oral dose is 400–1,600 mg/day in divided doses, standardized to 1.2% apigenin per dose. Chamomile is commonly consumed as a tea for its calming effect. It can be brewed using one heaping teaspoon of dried flowers steeped in hot water for 10 minutes and may be consumed up to three times per day [368].

CONCLUSION

Herbal medications have become an important issue in North America for a variety of social, economic, and medical reasons, and the use of HMs continues to increase. Data from the National Center for Health Statistics indicates that supplement use among U.S. adults 20 years of age and older increased from 48.4% to 56.1% during the period between 2007–2008 and 2017–2018, with use more common among women (63.8%) than men (50.8%) [8].

In 2012, out-of-pocket expenditures for CAM in the United States were $30.2 billion; this accounts for 1.1% of total national healthcare spending and 8.4% of total out-of-pocket expenditures [369]. The cost of dietary supplements alone was $12.8 billion, or about one-quarter of the $54.1 billion that U.S. adults spent out-of-pocket on prescription drugs [369]. Considering the high price of health insurance and changing attitudes towards CAM, the expenditures today are most likely greater.

In addition, more than 50% of patients receiving conventional medical care also use CAM [11]. An estimated 40% to 70% of patients fail to disclose the use of CAM to their healthcare providers, and concern regarding a possible negative reaction or perceived lack of interest by the healthcare provider have been identified as the main reasons for limited disclosure of CAM use [5; 11; 13]. It is commonly believed by the population in general, and by many healthcare providers as well, that due to their natural origin, these products are intrinsically safe and devoid of adverse effects or toxicity, or that the worst possible outcome is lack of therapeutic effectiveness. This has been proven false.

It is vital that healthcare providers have an understanding of the pharmacologic properties and evidence-based therapeutic efficacy of HMs. Healthcare providers should be aware of the need to inquire about and include current or past use of HMs in the patient's medical history and discuss relevant information with their patients. Providers also should be aware of the possible interactions with conventional medications and evaluate the potential therapeutic benefits of HMs when appropriate.

RESOURCES

MedWatch: The FDA Safety Information and Adverse Event Reporting Program
https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program
1-888-INFO-FDA

MedEffect Canada: Adverse Reaction and Medical Device Problem Reporting
https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html
1-866-234-2345

Natural Medicines
https://naturalmedicines.therapeuticresearch.com/

National Center for Complementary and Integrative Health: Dietary and Herbal Supplements
https://nccih.nih.gov/health/supplements

FACULTY BIOGRAPHY

A. José Lança, MD, PhD, received his Medical Degree at the University of Coimbra in Coimbra, Portugal, and completed his internship at the University Hospital, Coimbra. He received his PhD in Neurosciences from a joint program between the Faculties of Medicine of the University of Coimbra, Portugal, and the University of Toronto, Toronto, Canada. He was a Gulbenkian Foundation Scholar and received a Young Investigator Award by the American Brain & Behavior Research Foundation.

Dr. Lança participated in international courses and conferences on neurosciences. He has contributed to a better understanding of the mechanisms underlying the ontogenetic development of the brain opiatergic system. As a research scientist at the Addiction Research Foundation (ARF) in Toronto, he initiated research on the functional role played by dopaminergic cell transplants on alcohol consumption, leading to the publication of the first research reports on cell transplantation and modulation of an addictive behavior. Subsequently, he also investigated the role played by other neurotransmitter systems in the limbic system and mechanisms of reward, co-expression of classical neurotransmitters and neuropeptides and potential role in neuropsychiatric disorders.

He is an Assistant Professor in the Department of Pharmacology and Toxicology at the Faculty of Medicine and at the Faculty of Dentistry at the University of Toronto, where he lectures and directs several undergraduate and postgraduate pharmacology and clinical pharmacology courses. He was the Program Director for Undergraduate Studies in the Department of Pharmacology and Toxicology of the University of Toronto. He has developed clinical pharmacology courses for the Medical Radiation Sciences and Chiropody Programs of The Michener Institute for Health Sciences at the University of Toronto.

Dr. Lança's commitment to medical education started while a medical student, teaching in the Department of Histology and Embryology, where he became cross-appointed after graduation. In Toronto, he has contributed extensively to curriculum development and teaching of pharmacology to undergraduate, graduate, and medical students.

He has authored research and continuing education in peer-reviewed publications and is the author of six chapters in pharmacology textbooks. Dr. Lança has conducted research in various areas including neuropharmacology, pharmacology of alcoholism and drug addiction, and herbal medications.

He has developed and taught courses and seminars in continuing medical education and continuing dental education. His commitment to continuing education emphasizes an interdisciplinary approach to clinical pharmacology.

Customer Information/Answer Sheet/Evaluation insert located between pages 60–61.

COURSE TEST - #58394 HERBAL MEDICATIONS: AN EVIDENCE-BASED REVIEW

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 10 CE Credit Hour activity must be completed by June 30, 2025.

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1. What percentage of adults in the United States used complementary/alternative medicine (CAM) in 2012?
- *A) 7.7%*
- *B) 17.7%*
- *C) 33.2%*
- *D) 53.2%*

2. Which of the following statements regarding CAM and herbal medication (HM) use is TRUE?
- *A) In Canada, more than 50% of the population take HMs.*
- *B) The most commonly used CAM modality is homeopathy.*
- *C) Approximately 2% of children 17 years of age or younger in the United States use CAM.*
- *D) In the United States, supplement use increased from 48.4% to 56.1% between 2007–2008 and 2017–2018.*

3. The prevalent use of HMs is particularly relevant to healthcare practice because
- *A) it is important to reassure patients that no adverse effects are possible.*
- *B) patients often report their use of HMs to physicians and seek guidance.*
- *C) patients often assume that HMs are intrinsically beneficial and devoid of potential adverse effects because they are natural.*
- *D) All of the above*

4. Which of the following statements regarding the differences between HMs and conventional medications is TRUE?
- *A) HMs are of natural origin, whereas conventional medications are man-made chemicals.*
- *B) Only a few small-molecule drugs approved as conventional medications since 1981 are natural products or their chemical derivatives.*
- *C) In the United States, therapeutic benefits of HMs can only be made by the manufacturer after proof of safety and efficacy have been assessed by the FDA.*
- *D) The difference between HMs and conventional medications is primarily based on the process of scientific evaluation prior to approval for human therapy.*

5. Which of the following contributes to the inaccurate and biased perceptions of the use of HMs?

A) Patients are usually well informed of the potential risks of HMs.
B) Unbiased and scientifically sound information on HMs is readily available.
C) There is usually limited communication between patients and healthcare providers, particularly pharmacists, regarding HMs.
D) HMs, and their clinical applications, are an integral part of the medical curriculum and give the clinician a solid knowledge of the topic.

6. An estimated 40% to 70% of patients neglect to report HM use to healthcare providers. According to a review of the literature, the major reason for this failure to disclose CAM use is

A) concern about a negative reaction by the practitioner.
B) belief that CAM use is the same as mainstream products/procedures.
C) perception that healthcare providers are very knowledgeable about CAM.
D) None of the above

7. The concentration of active ingredients in HMs is affected by

A) growing conditions.
B) collection of the appropriate plant part.
C) solvent used for extraction of active ingredients.
D) All of the above

8. Which of the following statements regarding pharmacokinetics is TRUE?

A) Drug distribution occurs homogeneously throughout the body.
B) Pharmacokinetic principles only apply to conventional medications.
C) Pharmacokinetics is the area of pharmacology that studies the effects of the drug on the body.
D) Effective availability and concentration of a drug in different organs is affected by the histologic properties of the tissues.

9. Herb-drug interactions

A) are usually identified and properly reported by the healthcare provider.
B) are rare because herbal remedies contain only one active compound.
C) rarely occur because herbal medications and conventional drugs are not usually co-administered.
D) occur less frequently than drug-drug interactions, due in part to HMs having a weaker potency than conventional medications.

10. Adverse effects caused by HMs

A) should not be reported to the manufacturer.
B) are never caused by interactions between HMs and conventional drugs.
C) are an important tool in post-marketing drug surveillance when properly reported.
D) should never be reported to the FDA because they are not conventional medications.

11. Toxicologic effects of HMs can result from

A) adulteration of the product.
B) administration of a high dose of an HM.
C) interactions with conventional drugs or other HMs.
D) All of the above

12. In the United States,

A) granting of investigational new drug (IND) status allows for the drug to be commercialized.
B) safety and efficacy of HMs must be tested in Phases I and II clinical trials prior to being commercialized.
C) data collected in the preclinical phase are gathered and presented to the FDA to seek approval for the granting of Herbal Medication status.
D) compared with the elaborate process of approval for pharmaceuticals, the mechanisms required for the marketing of HMs are extremely simple.

13. All of the following are measures that contribute to an evidence-based approach to HMs, EXCEPT:

A) Drug standardization
B) Further promoting a deregulation of HMs
C) Implementation of controlled clinical trials
D) Increasing the funding for research aimed at studying the pharmacologic and therapeutic properties of HMs

Test questions continue on next page ➜

14. Batch-to-batch variability of HMs is
- A) *highest among saw palmetto products.*
- B) *lowest among ginseng and echinacea products.*
- C) *always within 10% of the concentration claimed.*
- D) *a contributing factor to the lack of therapeutic efficacy of some phytochemicals observed in some clinical trials.*

15. Saw palmetto
- A) *has not been shown to inhibit proliferation of prostate cancer cells.*
- B) *contains beta-sitosterol, the component that correlates with its efficacy.*
- C) *shares the same mechanism of action as alpha-1-adrenoceptor agonists.*
- D) *inhibits only the type 1 isoform of 5-alpha-reductase, the same action as finasteride.*

16. St. John's wort does NOT inhibit synaptic reuptake of
- A) GABA.
- B) *serotonin.*
- C) *dopamine.*
- D) *noradrenaline.*

17. Clinical trials of ginkgo biloba
- A) *do not suggest a therapeutic effectiveness of ginkgo biloba in the treatment of tinnitus.*
- B) *support that ginkgo biloba has a beneficial effect in the management of early stages of cognitive impairment.*
- C) *demonstrating improvement of cognitive functions in older healthy individuals have been large and conclusive.*
- D) *have demonstrated that ginkgo biloba is less effective than pentoxifylline in the treatment of intermittent claudication.*

18. In regard to adverse effects and toxicology, ginkgo biloba
- A) *has been proven to be teratogenic.*
- B) *is considered safe when administered at the recommended dose and for periods of up to six months.*
- C) *causes serious adverse effects, and large clinical trials revealed that there is a significant increase in abnormal bleeding.*
- D) *extracts derived from the plum-like fruits of the female tree may be safely used in the topical treatment of dermatitis.*

19. Which of the following statements regarding ginseng is TRUE?
- A) *The polysaccharide ginsenan is the most biologically active and studied compound present in ginseng.*
- B) *The immunostimulatory properties of ginseng have been reported in the scientific literature, but further studies are required.*
- C) *Ginseng should not be administered to patients with type 2 diabetes because it inhibits insulin release and causes hyperglycemia.*
- D) *Evidence-based knowledge of ginseng's therapeutic usefulness supports the historical claims as a panacea for a variety of medical conditions.*

20. Echinacea is
- A) *the most widely sold HM in the United States.*
- B) *an effective prophylaxis for the common cold, a use supported by clinical trials.*
- C) *indigenous to Asia, where it has historically been used for decorative purposes.*
- D) *not approved by the E Commission in Germany for the treatment of common colds.*

21. In regard to adverse effects, echinacea
- A) *is safe to co-administer with immunosuppressants.*
- B) *causes nausea, vomiting, and abdominal pain in a moderate number of patients (5% to 10%).*
- C) *is generally well tolerated, even at doses several fold higher than the ones recommended.*
- D) *may be administered to patient allergic to daisies, ragweed, or other plants of the Asteraceae family.*

22. Kava
- A) *blocks the effects of anxiolytic drugs.*
- B) *has been proven safe for pregnant and/or breastfeeding individuals.*
- C) *is not metabolized in the liver and, therefore, does not result in liver damage.*
- D) *can cause yellow skin discoloration with scaly dermatitis, resembling pellagra, if taken chronically.*

23. Garlic extracts
- A) *do not display antiplatelet aggregation action.*
- B) *have been proven, in clinical studies, to inhibit lung and colon cancer.*
- C) *have a statistically significant and therapeutically dramatic antihypertensive effect.*
- D) *lower LDL and triglycerides, while HDL concentrations remain unchanged.*

24. For patients taking garlic, the highest risk of herb/drug interaction is with
- A) *anticoagulants.*
- B) *antidepressants.*
- C) *anticonvulsants.*
- D) *antihypertensives.*

25. Valerian use
- A) *has traditionally been limited to the treatment of depression.*
- B) *as an effective cardiovascular agent has been supported by clinical trials.*
- C) *in the treatment of anxiety has been widely used in Europe for at least a century.*
- D) *All of the above*

26. Andrographolide, a compound found in *Andrographis paniculata*, has been shown to
- A) *cause vasoconstricton.*
- B) *block nitric oxide synthesis.*
- C) *potentiate β-adrenergic receptors.*
- D) *have anti-inflammatory properties.*

27. *Andrographis paniculata* may be taken for as long as
- A) *two days.*
- B) *two weeks.*
- C) *two months.*
- D) *two years.*

28. English ivy leaf (*Hedera helix*)
- A) *is now used in the treatment of burns.*
- B) *is native to North and South America.*
- C) *has been traditionally used in the treatment of respiratory diseases and infections.*
- D) *can be substituted for American ivy (Parthenocissus quinquefolia) or ground ivy (Glechoma hederacea).*

29. Peppermint oil has a demonstrated dose-related
- A) *anti-inflammatory effect.*
- B) *effect on gastric sensitivity.*
- C) *in vitro antioxidative effect.*
- D) *antisposmodic effect on gastrointestinal smooth muscle.*

30. Chamomile
- A) *may be cross-allergic with ragweed.*
- B) *is not associated with allergic reactions.*
- C) *may inhibit the anticoagulant effects of warfarin.*
- D) *None of the above*

Be sure to transfer your answers to the Answer Sheet located on the envelope insert.
DO NOT send these test pages to NetCE. Retain them for your records.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Course Availability List

These courses may be ordered by mail on the Customer Information form located between pages 60–61.
We encourage you to **GO GREEN**. Access your courses **online** or download as an **eBook** to save paper.
Additional titles are also available.
www.NetCE.com

ORAL AND MAXILLOFACIAL TRAUMA
#50002 • 5 CE Credit Hours • $45
Purpose: The purpose of this course is to provide dental professionals with a deeper understanding of and appreciation for oral and maxillofacial trauma.
Faculty: Mark J. Szarejko, DDS, FAGD
Audience: This course is designed for all dental professionals, especially those who work in emergency and trauma care.
AGD Subject Code: 070

AIRWAY MANAGEMENT: BASICS FOR HEALTHCARE PROVIDERS


#50010 • 5 CE Credit Hours • $45
Purpose: Gaining control of the airway in a compromised patient is absolutely crucial. The purpose of this course is to provide dental professionals with the clinical knowledge needed to rapidly and effectively assess the patient's airway and intervene efficiently to begin to ventilate the patient in distress.
Faculty: Richard E. Haas, PhD, CRNA (Retired), LTC US Army Nurse Corps (Retired)
Audience: This course is designed for dental professionals involved in monitoring and maintaining patients' airways.
AGD Subject Code: 142

MIGRAINE: DIAGNOSIS AND THERAPEUTIC ADVANCES
#50072 • 5 CE Credit Hours • $45
Purpose: The purpose of this course is to provide an integrated update of the recent developments on the pathophysiology of migraine and resulting "mechanism-related" therapies, to evaluate the clinical benefit-ratio of antimigraine medications, and to summarize the current and evidence-based guidelines for the clinical management of migraine. The information provided should contribute to a more positive interaction between patients and dental professionals, through fostering patient awareness, implementation of lifestyle changes, and compliance to therapy.
Faculty: A. José Lança, MD, PhD
Audience: This course is designed for all dental professionals involved in the care of patients with known or suspected migraine.
AGD Subject Code: 200

HIPAA PRIVACY AND SECURITY


#51140 • 5 CE Credit Hours • $45
Purpose: The purpose of this course is to provide information that will allow dental professionals to more easily comply with the Privacy and Security Rules defined by HIPAA.
Faculty: Carol Shenold, RN, ICP
Audience: This course is designed for all dental professionals.
AGD Subject Code: 566

SMOKING AND SECONDHAND SMOKE


#51784 • 10 CE Credit Hours • $90
Purpose: The purpose of this course is to provide dental professionals with a formal educational opportunity that will address the impact of tobacco smoking and secondhand exposure in public health and disease as well as interventions to promote smoking cessation among their patients.
Faculty: Mark S. Gold, MD, DFASAM, DLFAPA
Audience: This course is designed for dental professionals who may intervene to stop patients from smoking.
AGD Subject Code: 158

DENTAL CARE FOR SPECIAL NEEDS PATIENTS
#51913 • 5 CE Credit Hours • $45
Purpose: The purpose of this course is to focus awareness upon the difficult oral health issues that special needs patients face on a daily basis and to provide dental professionals with the necessary information to improve patients' oral and systemic health.
Faculty: Mark J. Szarejko, DDS, FAGD
Audience: This course is designed for dental professionals involved in assessing and promoting optimum oral care for special needs patients.
AGD Subject Code: 750

Prices are subject to change. Visit www.NetCE.com for a list of current prices.

Course Availability List *(Cont'd)*

ORAL HEALTH ISSUES DURING PREGNANCY

UPDATE

#53073 • 2 CE Credit Hours • $18

Purpose: The purpose of this course is to provide dental professionals with the information necessary to appropriately intervene to promote good oral health in pregnant patients, with lasting positive effects to the patient and fetus.

Faculty: Mark J. Szarejko, DDS, FAGD

Audience: This course is designed for all dental professionals involved in the care of pregnant patients.

AGD Subject Code: 750

ORAL AND MAXILLOFACIAL INFECTIONS

#54032 • 5 CE Credit Hours • $45

Purpose: The purpose of this course is to emphasize to dental professionals the importance of quickly identifying and treating oral and maxillofacial infections.

Faculty: Mark J. Szarejko, DDS, FAGD

Audience: This course is designed for all dental professionals involved in the identification and treatment of oral and maxillofacial infections.

AGD Subject Code: 310

MULTIDRUG-RESISTANT MICROBIAL INFECTIONS

UPDATE

#54214 • 5 CE Credit Hours • $45

Purpose: The purpose of this course is to provide an overview of the basics of antimicrobial resistance mechanisms and to review the classes of multidrug-resistant pathogens currently prevalent in healthcare facilities and the community, including guidelines for prevention and options for therapy.

Faculty: Carol Shenold, RN, ICP; John M. Leonard, MD

Audience: This course is designed for dental professionals involved in the treatment and care of patients with infections.

AGD Subject Code: 148

MEDICAL EMERGENCIES IN THE DENTAL SETTING

#54354 • 5 CE Credit Hours • $45

Purpose: Patients, those who accompany them, or members of the dental staff can be stricken suddenly and without warning by any of a variety of medical emergency issues. The purpose of this course is to provide all members of the dental staff with the training necessary to provide immediate assistance to a patient that experiences any problem that constitutes a medical emergency.

Faculty: Mark J. Szarejko, DDS, FAGD

Audience: This course is designed for all members of the dental profession, including dentists, dental hygienists, and dental assistants.

AGD Subject Code: 142

HIV/AIDS: UPDATE FOR FLORIDA

FL HIV/AIDS

#54703 • 2 CE Credit Hours • $18

Purpose: HIV infection is now endemic in the United States and throughout much of the world, and HIV/AIDS has become less about cure and more about management and control. As with most chronic diseases, treatment protocols and management strategies change over time. The purpose of this course is to provide a basic, practical review and update of knowledge concerning HIV/AIDS, addressing the key issues that impact clinical care and public health practice.

Faculty: Jane C. Norman, RN, MSN, CNE, PhD; John M. Leonard, MD

Audience: This course is designed for all Florida dental professionals involved in the care of patients with HIV/AIDS.

AGD Subject Code: 148

Special Approval: This course fulfills the Florida requirement for 2 hours of HIV/AIDS education.

ORAL COMPLICATIONS OF DIABETES

#54963 • 2 CE Credit Hours • $18

Purpose: Diabetes can have a significant impact on oral health, which in turn affects patients' overall health and quality of life. The purpose of this course is to provide dental professionals with the information necessary to identify oral complications of diabetes and educate patients with diabetes regarding the steps necessary to prevent periodontal disease.

Faculty: Diane Thompson, RN, MSN, CDE, CLNC

Audience: This course is designed for all dental professionals involved in the care of patients with diabetes.

AGD Subject Code: 750

ANTIBIOTICS REVIEW

UPDATE

#55073 • 5 CE Credit Hours • $45

Purpose: The purpose of this course is to provide a review of the major classes of antibiotics and their characteristics as well as an overview of selected individual agents within each class that are most useful for today's clinical practitioner.

Faculty: Donna Coffman, MD

Audience: This course is designed for dental professionals who prescribe or administer antibiotics to patients.

AGD Subject Code: 148

MEDICATION USE IN DENTISTRY

#55253 • 5 CE Credit Hours • $45

Purpose: As the number of medications and range of uses grow, dental prescribing has become increasingly complex. The purpose of this course is to provide dental professionals with the knowledge necessary to effectively prescribe and to monitor the effects of commonly used drugs.

Faculty: Mark J. Szarejko, DDS, FAGD

Audience: This course is designed for all dental professionals.

AGD Subject Code: 010

Prices are subject to change. Visit www.NetCE.com for a list of current prices.

Course Availability List *(Cont'd)*

SUBSTANCE USE DISORDERS AND PAIN MANAGEMENT: MATE ACT TRAINING

Federal MATE Act

#55300 • 8 CE Credit Hours • $64

Purpose: The purpose of this course is to provide dental professionals who prescribe or distribute controlled substances with an appreciation for the complexities of managing patients with substance use disorders and comorbid pain in order to provide the best possible patient care and to prevent a growing social problem.

Faculty: Mark Rose, BS, MA, LP

Audience: This course is designed for all dental professionals who may alter prescribing practices or intervene to help meet the needs of patients with substance use disorders.

AGD Subject Code: 340

Special Approval: This course is designed to meet the Federal MATE Act requirement for new or renewing DEA licensees to complete 8 hours of training on opioid or other substance use, disorders, and the appropriate treatment of pain.

COCAINE USE DISORDER

#56944 • 5 CE Credit Hours • $45

Purpose: The purpose of this course is to provide a current, evidence-based overview of cocaine abuse and dependence and its treatment, in order to allow dental professionals to more effectively identify, treat or refer cocaine-abusing patients.

Faculty: Mark Rose, BS, MA, LP

Audience: This course is designed for dental professionals who are involved in the evaluation or treatment of persons who use cocaine.

AGD Subject Code: 157

CANNABINOID OVERVIEW

NEW!

#58010 • 3 CE Credit Hours • $27

Purpose: The purpose of this course is to provide dental professionals in all practice settings the knowledge necessary to increase their understanding of the various cannabinoids.

Faculty: Chelsey McIntyre, PharmD

Audience: This course is designed for dental professionals whose patients are taking or are interested in taking cannabinoid products.

AGD Subject Code: 149

ALLERGIC REACTIONS IN DENTAL PATIENTS

#58612 • 2 CE Credit Hours • $18

Purpose: The purpose of this course is to provide dental professionals with the information necessary to recognize, treat, and prevent allergic reactions in their patients.

Faculty: Mark J. Szarejko, DDS, FAGD

Audience: This course is designed for all dental professionals who may encounter allergic reactions in their practice.

AGD Subject Code: 142

SLEEP DISORDERS

#58883 • 10 CE Credit Hours • $90

Purpose: Many of the complications associated with sleep disorders are preventable, making early diagnosis and appropriate treatment vital. The purpose of this course is to provide dental professionals with the information necessary to identify and contribute to the treatment of sleep disorders, thereby improving patients' quality of life and preventing possible complications.

Faculty: Teisha Phillips, RN, BSN

Audience: This course is designed for all dental professionals who are involved in the care of patients experiencing a sleep-related disorder.

AGD Subject Code: 730

OSTEOPOROSIS: DIAGNOSIS AND MANAGEMENT

#59143 • 5 CE Credit Hours • $45

Purpose: To appropriately prevent, diagnose, and treat osteoporosis, healthcare providers should understand the epidemiology, physiology, and management. The purpose of this course is to provide dental professionals with the information regarding causes and treatment of osteoporosis necessary to effectively provide patient-centered care.

Faculty: John J. Whyte, MD, MPH; Peter Peraud, MD

Audience: This course is designed for dental professionals, especially those working with patients who present with suspected osteoporosis.

AGD Subject Code: 010

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☐	57923	Domestic Violence: The Florida Requirement / 2 CE Credit Hours	$18
☐	55121	Strategies for Appropriate Opioid Prescribing: The Florida Requirement / 2 CE Credit Hours	$18
☐	57430	Cultural Competence: An Overview / 2 CE Credit Hours	$18
☐	52163	Dental Treatment of Pediatric and Adolescent Patients / 6 CE Credit Hours	$54
☐	58394	Herbal Medications: An Evidence-Based Review / 10 CE Credit Hours	$90

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☐	51140	HIPAA Privacy and Security / 5	$45
☐	51784	Smoking and Secondhand Smoke / 10	$90
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- A passing grade of at least 70% must be achieved on each course test in order to receive credit.
- Darken only one circle per question.
- Use pen or pencil; please refrain from using markers.
- **Information on the Customer Information form must be completed.**

#51334 MEDICAL ERROR PREVENTION AND ROOT CAUSE ANALYSIS—2 CE CREDIT HOURS

Please refer to pages 14–15.

Expiration Date: 08/31/25 *May be taken individually for $18*

	A	B	C	D		A	B	C	D
1.	❍	❍	❍	❍	6.	❍	❍	❍	❍
2.	❍	❍	❍	❍	7.	❍	❍	❍	❍
3.	❍	❍	❍	❍	8.	❍	❍	❍	❍
4.	❍	❍	❍	❍	9.	❍	❍	❍	❍
5.	❍	❍	❍	❍	10.	❍	❍	❍	❍

#57923 DOMESTIC VIOLENCE: THE FLORIDA REQUIREMENT—2 CE CREDIT HOURS

Please refer to page 26.

Expiration Date: 07/31/25 *May be taken individually for $18*

	A	B	C	D		A	B	C	D
1.	❍	❍	❍	❍	6.	❍	❍	❍	❍
2.	❍	❍	❍	❍	7.	❍	❍	❍	❍
3.	❍	❍	❍	❍	8.	❍	❍	❍	❍
4.	❍	❍	❍	❍	9.	❍	❍	❍	❍
5.	❍	❍	❍	❍	10.	❍	❍	❍	❍

#55121 STRATEGIES FOR APPROPRIATE OPIOID PRESCRIBING: THE FL REQ.—2 CE CREDIT HOURS

Please refer to pages 43–44.

Expiration Date: 08/31/24 *May be taken individually for $18*

	A	B	C	D		A	B	C	D
1.	❍	❍	❍	❍	6.	❍	❍	❍	❍
2.	❍	❍	❍	❍	7.	❍	❍	❍	❍
3.	❍	❍	❍	❍	8.	❍	❍	❍	❍
4.	❍	❍	❍	❍	9.	❍	❍	❍	❍
5.	❍	❍	❍	❍	10.	❍	❍	❍	❍

#57430 CULTURAL COMPETENCE: AN OVERVIEW—2 CE CREDIT HOURS

Please refer to pages 62–63.

Expiration Date: 02/28/25 *May be taken individually for $18*

	A	B	C	D		A	B	C	D
1.	❍	❍	❍	❍	6.	❍	❍	❍	❍
2.	❍	❍	❍	❍	7.	❍	❍	❍	❍
3.	❍	❍	❍	❍	8.	❍	❍	❍	❍
4.	❍	❍	❍	❍	9.	❍	❍	❍	❍
5.	❍	❍	❍	❍	10.	❍	❍	❍	❍

#52163 DENTAL TREATMENT OF PEDIATRIC & ADOLESCENT PATIENTS—6 CE CREDIT HOURS

Please refer to pages 81–82.

Expiration Date: 01/31/26 *May be taken individually for $56*

	A	B	C	D		A	B	C	D		A	B	C	D		A	B	C	D
1.	❍	❍	❍	❍	6.	❍	❍	❍	❍	11.	❍	❍	❍	❍	16.	❍	❍	❍	❍
2.	❍	❍	❍	❍	7.	❍	❍	❍	❍	12.	❍	❍	❍	❍	17.	❍	❍	❍	❍
3.	❍	❍	❍	❍	8.	❍	❍	❍	❍	13.	❍	❍	❍	❍	18.	❍	❍	❍	❍
4.	❍	❍	❍	❍	9.	❍	❍	❍	❍	14.	❍	❍	❍	❍	19.	❍	❍	❍	❍
5.	❍	❍	❍	❍	10.	❍	❍	❍	❍	15.	❍	❍	❍	❍	20.	❍	❍	❍	❍

#58394 HERBAL MEDICATIONS: AN EVIDENCE-BASED REVIEW—10 CE CREDIT HOURS

Please refer to pages 114–117.

Expiration Date: 06/30/25 *May be taken individually for $90*

	A	B	C	D		A	B	C	D		A	B	C	D
1.	❍	❍	❍	❍	11.	❍	❍	❍	❍	21.	❍	❍	❍	❍
2.	❍	❍	❍	❍	12.	❍	❍	❍	❍	22.	❍	❍	❍	❍
3.	❍	❍	❍	❍	13.	❍	❍	❍	❍	23.	❍	❍	❍	❍
4.	❍	❍	❍	❍	14.	❍	❍	❍	❍	24.	❍	❍	❍	❍
5.	❍	❍	❍	❍	15.	❍	❍	❍	❍	25.	❍	❍	❍	❍
6.	❍	❍	❍	❍	16.	❍	❍	❍	❍	26.	❍	❍	❍	❍
7.	❍	❍	❍	❍	17.	❍	❍	❍	❍	27.	❍	❍	❍	❍
8.	❍	❍	❍	❍	18.	❍	❍	❍	❍	28.	❍	❍	❍	❍
9.	❍	❍	❍	❍	19.	❍	❍	❍	❍	29.	❍	❍	❍	❍
10.	❍	❍	❍	❍	20.	❍	❍	❍	❍	30.	❍	❍	❍	❍

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Please read the following questions and choose the most appropriate answer for each course completed.

1. Was the course content new or review?
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3. Would you recommend this course to your peers?
4. Did the course content support the stated course objective?
5. Did the course content demonstrate the author's knowledge of the subject?
6. Was the course content free of bias?
7. Before completing this course, did you identify the necessity for education on the topic to improve your professional practice?
8. Have you achieved all of the stated learning objectives of this course?
9. Has what you think or feel about this topic changed?
10. Did evidence-based practice recommendations assist in determining the validity or relevance of the information?
11. Are you more confident in your ability to provide patient care after completing this course?
12. Do you plan to make changes in your practice as a result of this course content?

#51334 2 CE Credit Hrs	**#57923** 2 CE Credit Hrs	**#55121** 2 CE Credit Hrs	**#57430** 2 CE Credit Hrs	**#52163** 6 CE Credit Hrs	**#58394** 10 CE Credit Hrs
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2. ____ Hours	2. ____ Hours	2. ____ Hours	2. ____ Hours	2. ____ Hours	2. ____ Hours
3. ☐ Yes ☐ No	3. ☐ Yes ☐ No	3. ☐ Yes ☐ No	3. ☐ Yes ☐ No	3. ☐ Yes ☐ No	3. ☐ Yes ☐ No
4. ☐ Yes ☐ No	4. ☐ Yes ☐ No	4. ☐ Yes ☐ No	4. ☐ Yes ☐ No	4. ☐ Yes ☐ No	4. ☐ Yes ☐ No
5. ☐ Yes ☐ No	5. ☐ Yes ☐ No	5. ☐ Yes ☐ No	5. ☐ Yes ☐ No	5. ☐ Yes ☐ No	5. ☐ Yes ☐ No
6. ☐ Yes ☐ No	6. ☐ Yes ☐ No	6. ☐ Yes ☐ No	6. ☐ Yes ☐ No	6. ☐ Yes ☐ No	6. ☐ Yes ☐ No
7. ☐ Yes ☐ No	7. ☐ Yes ☐ No	7. ☐ Yes ☐ No	7. ☐ Yes ☐ No	7. ☐ Yes ☐ No	7. ☐ Yes ☐ No
8. ☐ Yes ☐ No	8. ☐ Yes ☐ No	8. ☐ Yes ☐ No	8. ☐ Yes ☐ No	8. ☐ Yes ☐ No	8. ☐ Yes ☐ No
9. ☐ Yes ☐ No	9. ☐ Yes ☐ No	9. ☐ Yes ☐ No	9. ☐ Yes ☐ No	9. ☐ Yes ☐ No	9. ☐ Yes ☐ No
10. ☒ N/A	10. ☐ Yes ☐ No	10. ☐ Yes ☐ No	10. ☒ N/A	10. ☐ Yes ☐ No	10. ☐ Yes ☐ No
11. ☐ Yes ☐ No	11. ☐ Yes ☐ No	11. ☐ Yes ☐ No	11. ☐ Yes ☐ No	11. ☐ Yes ☐ No	11. ☐ Yes ☐ No
12. ☐ Yes ☐ No	12. ☐ Yes ☐ No	12. ☐ Yes ☐ No	12. ☐ Yes ☐ No	12. ☐ Yes ☐ No	12. ☐ Yes ☐ No
13. ☐ Yes ☐ No	13. ☐ Yes ☐ No	13. ☐ Yes ☐ No	13. ☐ Yes ☐ No	13. ☐ Yes ☐ No	13. ☐ Yes ☐ No

#51334 Medical Error Prevention and Root Cause Analysis — If you answered YES to question #12, how specifically will this activity enhance your role as a member of the interdisciplinary team? _____

#57923 Domestic Violence: The Florida Req. — If you answered YES to question #12, how specifically will this activity enhance your role as a member of the interdisciplinary team? _____

#55121 Strategies for Appropriate Opioid Prescribing: The Florida Requirement — If you answered YES to question #12, how specifically will this activity enhance your role as a member of the interdisciplinary team? _____

#57430 Cultural Competence: An Overview — If you answered YES to question #12, how specifically will this activity enhance your role as a member of the interdisciplinary team? _____

#52163 Dental Treatment of Pediatric and Adolescent Patients — If you answered YES to question #12, how specifically will this activity enhance your role as a member of the interdisciplinary team? _____

#58394 Herbal Medications: An Evidence-Based Review — If you answered YES to question #12, how specifically will this activity enhance your role as a member of the interdisciplinary team? _____

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