Post-Traumatic Stress Disorder

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- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician, behavioral health professional, or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

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 Planners
John M. Leonard, MD
Jane C. Norman, RN, MSN, CNE, PhD
Alice Yick Flanagan, PhD, MSW
James Trent, PhD

Director of Development and Academic Affairs
Sarah Campbell

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

Audience
This course is designed for physicians, physician assistants, nurses, and mental health professionals involved in the identification and treatment of patients with post-traumatic stress disorder.

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NetCE designates this continuing education activity for 15 CE credits.

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Course Objective
The purpose of this course is to provide primary care providers with the knowledge they need to effectively identify, engage, diagnose and treat patients with PTSD.

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

1. Review the historical conceptualization of trauma reactions and post-traumatic stress disorder (PTSD).
2. Analyze the models traditionally used to explain the PTSD disease process and to develop treatment modalities.
3. Define terms related to trauma and stress reactions.
4. Outline the epidemiology of PTSD and related comorbidities in various populations.
5. Review the natural history of PTSD.
6. Describe the personal and societal costs of PTSD.
7. Recognize common presentation and associated comorbid conditions in combat veterans following exposure to trauma.
8. Identify the possible presentations and unique provider considerations involved in the treatment of patients with PTSD following sexual assault.
9. Discuss the impact of minority sexual orientation on the risk for PTSD.
10. Outline the epidemiology and presentation of PTSD following natural disaster or acts of terrorism.
11. Review considerations when assessing and treating PTSD in first responders and trauma care personnel.
12. Describe issues that may arise in persons who develop PTSD in response to injury and/or torture.
13. Analyze the relationship between PTSD and violence and aggression in various populations.
14. Discuss the pathophysiology of PTSD.
15. Evaluate appropriate approaches to assessment and intervention in the immediate post-trauma period.
16. Outline the appropriate assessment and management of patients in the intermediate post-trauma period.
17. Describe the approach to assessment, screening, and diagnosis in the extended post-trauma period, including racial and/or cultural considerations.
18. Identify general management considerations when establishing a treatment plan for persons with PTSD.
19. Evaluate the possible psychotherapeutic interventions for PTSD.
20. Describe the optimal approach to the treatment of complex trauma.
21. Compare and contrast pharmacotherapies and complementary/alternative approaches used in the treatment of PTSD.
22. Discuss key points in the treatment of specific PTSD symptoms and comorbidities.

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 course material for better application to your daily practice.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is a severe, potentially chronic and disabling disorder that develops in some persons following exposure to a traumatic event involving actual or threatened death, serious injury, or sexual assault [1]. Some common symptoms include intrusive thoughts, nightmares and flashbacks of traumatic events, avoidance of trauma reminders, hypervigilance, and sleep disturbance. These symptoms can be highly distressing and substantially impair social, occupational, and interpersonal functioning. The intensely distressing and impairing symptoms of traumatic stress are highly prevalent immediately following traumatic exposure and dissipate over the following days and weeks in most people. Persistence beyond one month post-trauma suggests PTSD [1].

The prevalence of PTSD in the U.S. population is approximately 8%, with incidence as high as 17% in primary care patients and possibly greater than 50% in mental health treatment-seeking populations [2; 3]. PTSD can become chronic in as many as 40% of cases [4]. Roughly 60% of men and 50% of women in the United States have experienced a traumatic event, with the majority reporting trauma exposure also reporting two or more traumatic events [5]. However, PTSD only develops in 10% of those exposed to trauma, a finding that has prompted intense research efforts in identifying risk factors and early intervention to prevent or reduce the development of PTSD [5]. Populations at risk for PTSD include refugee victims of torture, combat veterans, persons released from incarceration, victims of sexual assault, and adults who endured repeated sexual or physical abuse as children [6].

Although these groups are likely to seek physical and mental health care from primary care providers, numerous provider and patient barriers have been identified that impede proper diagnosis and treatment of PTSD in primary care, including stigma or fear of consequences in patients and insufficient knowledge or comfort in caring for post-trauma patients in primary care clinicians. The most prevalent knowledge deficits in PTSD among primary care providers concern cognitive-behavioral interventions, combat stress injuries, mild traumatic brain injury (TBI), neurobiology, and pharmacotherapy [2; 7; 8; 9]. These knowledge deficits are remediable through educational intervention. The purpose of this course is to provide primary care providers with the knowledge they need to effectively identify, engage, diagnose, and treat patients with PTSD and complex trauma/PTSD.

BACKGROUND

HISTORICAL CONCEPTUALIZATION

Humans have experienced tragedies and disaster throughout history, and awareness of adverse effects following trauma exposure have been documented as far back as the 6th century B.C.E. [10]. These sporadic earlier reports focused on the reactions to combat in soldiers. Trauma exposure and subsequent responses became more frequently reported in the 17th century, including descriptions of those who survived the Great Fire of London in 1666 [10].

Traumatic stress has been assigned a variety of labels over the past 200 years, with many reflecting contemporary understanding of causation, as with "soldier's heart" or "irritable heart" in Civil War veterans and "disordered action of the heart" in traumatized veterans of the Boer War [11]. These were followed by 20th century labels for combat and civilian traumatic stress that included battle fatigue, war neurosis, shell shock, gross stress reaction, adjustment reaction of adult life, transient situational disturbance, traumatic neurosis, post-Vietnam syndrome, rape trauma syndrome, child abuse syndrome, and battered wife syndrome. Other labels were intended to stigmatize, as with "lack of moral fibre" assigned to World War II (WWII) British air crews who had lost the will to continue flying into combat [10; 12].

In the late 1800s and into the 20th century, Freud, Janet, Charcot, and Breuer each suggested that PTSD results from an emotional response to environmental events, with hysterical symptoms underlying the psychologic trauma. However, this view was not widely accepted. The dominant view was that traumatic events alone were insufficient to cause symptoms, and many experts suspected an organic cause, such as spinal cord damage in railway accident trauma, brain penetration by exploding artillery microfragments in traumatized combat veterans, and brain damage resulting from starvation in Holocaust survivors [10]. Some doubted the symptom reports and believed malingering and compensation-seeking ("compensation neurosis") were the dominant cause. Many others attributed post-trauma symptoms to pre-existing psychologic dysfunction, hypothesizing that only those with unstable personalities or mental illness developed chronic symptoms because reactions to traumatic events were normally transient [12; 13].

Descriptions of post-trauma symptoms in combat veterans were published following WWI and WWII, with a recognition of shared symptoms between combat veterans, Holocaust survivors, survivors of railway disasters, and Hiroshima and Nagasaki atomic bomb survivors. Increasing acknowledgement of the chronic psychologic problems in many war veterans, especially Vietnam veterans, and of rape survivors convinced clinicians and researchers that significant long-term psychologic problems could develop in people with sound personalities when exposed to horrific stressors. In 1980, PTSD became formalized as a distinct diagnosis by the American Psychiatric Association in the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) [12; 13; 14; 15].

This formal recognition of PTSD was also a major step in spurring traumatic stress research [10]. The DSM-III classed PTSD as an anxiety disorder based on the frequent symptoms of persistent anxiety, hypervigilance, exaggerated startle response, and phobic-like avoidance behaviors [16]. Ongoing research expanded the understanding of PTSD and required revisions in the DSM to reflect current knowledge.

The understanding of trauma and traumatic experience sufficient for PTSD diagnosis has also evolved. The 1980 DSM-III criteria defined a traumatic event as a catastrophic stressor outside the range of usual human experience [14]. This trauma definition was criticized, with research showing the high prevalence of exposure to rape, childhood sexual and physical abuse, domestic violence, and other severe stressors. As a result, the 1994 DSM-IV and its 2000 text revision expanded traumatic event categories to include those within the range of usual human experience, such as automobile accidents and deaths [17; 18]. Also specified was the requirement of an intense emotional reaction to the traumatic event such as panic, terror, grief, or disgust [13].

PTSD research during the years between publication of the DSM-IV-TR in 2000 and the DSM-5 in 2013 changed the understanding of PTSD and prompted the following revisions in the DSM-5 [1; 19]:

- PTSD is no longer an anxiety disorder and is instead placed in a new trauma-specific category.
- Traumatic events are expanded to include actual or threat of death, serious injury, or sexual assault.
- Sexual assault is explicitly named for the first time.
- Fear, helplessness, or horror as initial trauma response is removed because this was found unrelated to PTSD development.
- Symptom clusters expanded from three to four: re-experiencing, avoidance, negative cognitions and mood, and arousal.
- Duration requirement is one month instead of three months.
- A dissociative PTSD subtype has been added.

EXPLANATORY MODELS

Explanatory models of PTSD have been proposed in order to better understand psychotraumatization processes and PTSD. They have also attempted to resolve ongoing debates concerning PTSD, such as the core defining features; qualities of events sufficiently traumatic to produce PTSD; symptoms and their subjective meaning; optimal prevention and treatment approaches; and appropriateness of compensation [20].

The Disease/Illness Perspective

In biologic psychiatry, PTSD is defined as a mental disorder resulting from functional and structural damage to brain structures. PTSD symptoms are linked to specific underlying pathophysiologic processes and treated by psychoactive drugs. Attention to the holistic needs of the patient is discounted [21; 22].

In psychodynamic psychiatry, PTSD is the subjective and interpersonal manifestation of disorder that involves meaning. PTSD results from fear over-conditioning, loss of stimulus discrimination and arousal regulation, progressive neural sensitization, over-consolidation of traumatic memory, and malfunction of harm avoidance mechanisms. Effective treatment involves various neuropsychotherapy approaches and eye movement desensitization and reprocessing (EMDR) [20].

In social psychiatry, attitudes of the community or society shape victim perception of experienced harms and the vocabulary to describe this experience [23]. PTSD possesses a political valence that influences medicine, psychiatry, and society viewpoints of the construct and response to the patient [24]. This perspective stresses the importance in preventing secondary gain and adoption of a sick role [25].

The Dimensional Perspective

From the dimensional perspective, the role of meaning in human behavior, personality, vulnerability, and resilience is emphasized. Vulnerability to emotional distress or disorder is explained by the vulnerability-resilience or stress-diathesis model and by deficits in personality functioning, distress or provocation, and maladaptive response [26]. According to this perspective, PTSD results from the interpretation of meaning related to the event, with distinction of exposure from response. Emotional trauma becomes pathologic when highly threatening or distressful meaning is attached to the event [27].

The Cognitive-Axiologic Perspective

The cognitive-axiologic perspective posits that pathologic processes that underlie PTSD include dysfunctional and conflicting cognitive strategies, misinterpretations, and misrepresentations. The proximal cause of PTSD is thought to involve the explanatory style of individual interpretation of the event [28; 29]. The cause of negative events is attributed by pessimists to permanent, uncontrollable, and pervasive factors, and by optimists to temporary, changeable, and specific factors [29]. According to this approach, errors or biases in thinking (e.g., catastrophic thinking) contribute to the development of PTSD.

With the axiologic perspective, traumatic experiences can provoke the questioning of meaning, values, and purpose within a personal and collective framework. Traumatic events often challenge one's core values and beliefs about safety, self-worth, and the meaning of life. Individuals unable to resolve challenges to their moral and value beliefs can find themselves in a state of demoralization, disillusionment, nonsense, and social alienation [20].

The Behavioral Perspective

Using the behavioral perspective, PTSD is viewed as a disorder of reactivity reflected by maladaptive behavior during interactions with the interpersonal or physical environment. The maladaptive fixation on personal and family safety, anxiety, irritability, and the pervasive sense of threats and danger are explained by classical fear conditioning. The traumatic (unconditioned) stimulus automatically evokes the post-traumatic (unconditioned) emotional response (e.g., fear, helplessness, horror) and/or dissociation. Conditioned stimuli (reminders of the traumatic event) evoke similar conditioned emotional responses, dissociation, flashbacks, and fear-induced avoidance and protective behaviors. Trauma re-experiencing symptoms result from the primacy of traumatic over non-traumatic memory and represent the pathologic exaggeration of the normal adaptive response, whereby traumatic events are memorized for future avoidance of similar threats and dangers [20].

The Spiritual/Transcendental Perspective

Spiritual alienation is frequently reported in patients with PTSD. Many combat veterans report great difficulty in reconciling their religious beliefs with events they experienced and witnessed in the war zone, with many stating they have abandoned their religious faith [30]. Religions differ in their influence on trauma response. For example, traditional Buddhists believe in karma and may be more likely to accept horrific events than Westerners, while Muslims, who believe their fate is in Allah's hands, may feel less compelled to seek any form of relief [20]. Spiritual and religious beliefs are important to many patients and may significantly impact traumatic life events and PTSD as well as valid and legitimate coping mechanisms. Protective and emotional health-promoting spiritual beliefs and concepts include trust in Providence (which is love and wisdom), belief in a higher power as a source of reassurance and hope, ability to find meaning in suffering and illness, gratitude for the gift of life, and the ability to forgive [30].

The Narrative Perspective

The narrative perspective emphasizes the life story of the patient with PTSD in order to better understand the significance, meaning, and processes contributing to the onset and maintenance of clinical symptoms. The importance of life experience, personality organization, and psychologic life script are recognized. Victimization is thought to shatter or severely compromise important basic assumptions, including the belief in personal invulnerability, the perception of the world as meaningful and comprehensible, and the view of selfhood in positive terms. Based on this perspective, recovery from PTSD involves the cognitive rebuilding of a viable assumptive worldview that integrates vulnerability, meaning, and self-esteem [31].

DEFINITIONS

Affect dysregulation: This core symptom of complex trauma describes a durable state of low-threshold and highly intense emotional reactions with a slow return to baseline, becoming easily upset with difficulty in calming down, and feeling overwhelmed by negative emotions [32].

Trauma: An emotional injury or wound that is damaging to one's psychologic health and well-being and mediated by biologic, psychologic, and social factors [33].

Traumatic event: In the DSM-5, a traumatic event is defined as actual or threatened exposure to death, serious injury, or sexual violence. Traumatic events include, but are not limited to, war, torture, sexual or physical assault, natural disasters, accidents, and terrorism. Intentional interpersonal traumatic events such as torture, assault and rape, and prolonged and/or repeated events (e.g., childhood sexual abuse, concentration camp experiences) are more likely than natural events or accidents to result in a traumatic response [1; 34].

Secondary victimization (also referred to as indirect trauma or vicarious trauma): Indirect trauma exposure is inevitable when working with trauma patients. It is common in first responders and relief workers and can also occur in relatives and loved ones of traumatized persons and members of the immediate community or surrounding area following natural disaster, war, or terrorism. Indirect trauma exposure can lead to vicarious traumatization and risk of PTSD [33].

Complex trauma/PTSD: Complex trauma is a result of exposure to repeated, prolonged, or multiple forms of interpersonal trauma, often under circumstances where escape is not possible due to physical, psychologic, maturational, family/environmental, or social constraints [35]. Such traumatic stressors include childhood physical and sexual abuse, coerced conscription as a child soldier, domestic violence, sex trafficking or slave trade, torture, and exposure to genocide campaigns or other forms of organized violence [36].

In addition to core PTSD symptoms, patients with complex PTSD possess self-regulation disturbances in five domains [36]:

- Emotion regulation problems
- Disturbances in relational capacities
- Alterations in attention and consciousness (e.g., dissociation)
- Adversely affected belief systems
- Somatic distress or disorganization

These patients prominently exhibit affect dysregulation, dissociation, and severe interpersonal relationship problems. A constellation of characteristic features has been described that includes impaired emotional control; self-destructive and impulsive behavior; impaired relationships with others; hostility; social withdrawal; feeling constantly threatened; dissociation; somatic complaints; feelings of ineffectiveness, shame, despair or hopelessness; feeling permanently damaged; and a loss of previous beliefs and assumptions of safety and the trustworthiness of others [37; 38]. Issues of chronic self-harm and/or suicidal ideation are also common in this group [35]. The DSM-5 lacks a diagnostic category for complex trauma, and the criteria for PTSD fail to capture important clinical features of this condition. These patients may be diagnosed with complex PTSD or Disorders of Extreme Stress Not Otherwise Specified. The best-fitting diagnostic entity is found in the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) and is termed Enduring Personality Change after Catastrophic Experience (F62.0) [6].

POPULATION-LEVEL EPIDEMIOLOGY AND RISK FACTORS

Incidence and Prevalence

Rates of PTSD should be viewed in the context of broader population-level exposure rates to traumatic events. Large community surveys indicate that 50% to 75% of people report experiencing at least one lifetime traumatic event [39]. A U.S. survey from 2001–2003 of 5,692 participants 18 years of age or older found lifetime PTSD prevalence rates of 6.8% overall—3.6% in men and 9.7% in women. Also found were past-year prevalence rates of 3.5% overall, with 1.8% in men and 5.2% in women. These rates were very similar to those of a large survey in the early 1990s that found a lifetime PTSD prevalence rate of 7.8% overall, with 5% in men and 10.4% in women [39].

A study of the possible influence of changes in DSM-5 PTSD diagnostic criteria on current validity of PTSD epidemiologic data obtained using DSM-IV criteria found little to no effect. Population estimates using DSM-IV criteria remain valid [40].

Risk Factors

As noted, PTSD has long been observed to develop in only a minority of persons exposed to traumatic experience, suggesting that individual differences largely account for variation in PTSD rates that are independent of trauma event factors. This hypothesis has been confirmed in numerous studies and has prompted intensive investigation into individual risk factors to identify opportunities for prevention and early intervention [41].

An under-appreciated risk factor for PTSD is the sudden unexpected death of a loved one. Although an emotionally traumatic event for many, it has been long under-recognized because the origin is interpersonal but lacking violent or other fear-inducing action. The traumatic potential of interpersonal loss was first identified by interviews of 2,181 persons in the Detroit area, which found that sudden unexpected death of a loved one was the most frequent precipitating event in those with PTSD (occurring in 31% of all PTSD cases) and represented a moderate risk factor of PTSD [42]. The authors concluded that the sudden unexpected death of a loved one is an important triggering event of PTSD in the community and is overlooked by the focus on combat, rape, and assaultive violence [42].

Transgenerational trauma was first identified and reported in 1966, based on the clinical observation of offspring of Holocaust survivors [43]. This was quickly followed by many case reports and a growing understanding that "survivor syndrome" was a condition transmitted from one generation to the next. Uncontrolled studies described diverse cognitive and affective symptoms common to survivors and their children, including distrust of the world, impaired parental function, chronic despair, inability to communicate feelings, pervasive fear of danger, separation anxiety, and overprotectiveness within a narcissist family structure. These were followed by the publication of studies identifying resiliency factors [44]. The offspring of Holocaust survivors have been extensively studied to understand the biologic and psychologic contributions to intergenerational PTSD, and the relevance of this research extends to survivors and offspring of genocides in Rwanda, Nigeria, Cambodia, Armenia, and the former Yugoslavia [44; 45]. The study of intergenerational PTSD transmission has broadened to include survivors and offspring of disasters, impoverished high-crime urban environments, and other environments where trauma exposure is prevalent.

There are a number of additional risk factors that predispose persons to experiencing PTSD, often unique to the trauma. These specific risk factors are described in detail later in this course.

COMORBID PSYCHIATRIC AND MEDICAL CONDITIONS

A wide range of other mental health conditions co-occur with PTSD, including anxiety, affective, and substance use disorders. For example, a large study of traumatic injury survivors found that many patients met criteria for a psychiatric diagnosis at 12-month follow-up, including depression (16%), generalized anxiety disorder (11%), substance abuse (10%), PTSD (10%), agoraphobia (10%), social phobia (7%), panic disorder (6%), and obsessive-compulsive disorder (4%) [6]. A 2007 study found that 86% of men and 77% of women with PTSD also met the criteria for another lifetime acute psychiatric disorder, including anxiety disorder (52% of men, 54% of women), affective disorder (50% of men, 51% of women), and substance use disorders (65% of men, 32% of women) [6].

Grief may become a serious health concern for some individuals experiencing bereavement. Although not a DSM-5 diagnostic entity, complicated grief is often comorbid with PTSD, especially in persons following traumatic exposure to disaster with widespread loss of life and in those fleeing war-torn areas as refugees or asylum seekers [46]. Intrusive thoughts are shared symptoms of complicated grief and PTSD, representing painful trauma memories in PTSD and unfulfilled yearning for the deceased person in complicated grief. Both symptoms represent permanent memory states, involving negative sensory or cognitive-emotional elements of the traumatic experience in PTSD, and bittersweet memories and cognitive-emotional appraisals of the deceased person and other related experiences in complicated grief. Common to PTSD and complicated grief is memory duration and exacerbation by anniversaries of the traumatic event or loss [47].

NATURAL HISTORY OF PTSD

A 2013 systematic review helped clarify the longitudinal course of PTSD [48]. In aggregate, mean PTSD prevalence decreased from 28.8% (range: 3.1% to 87.5%) at 1 month to 17% (range: 0.6% to 43.8%) at 12 months post-trauma. Different trajectories followed exposure to intentional (deliberate infliction of harm) trauma versus non-intentional (all others) trauma. With intentional trauma, median PTSD prevalence at 1, 3, 6, and 12 months was 11.8%, 17.1%, 19.0%, and 23.3%, respectively. Of those who developed PTSD following intentional trauma, 35% remitted within three months, while 39% experienced a chronic course of PTSD. This confirms previous findings that PTSD can spontaneously resolve or persist as a chronic disorder. Following exposure to non-intentional trauma, median PTSD prevalence at 1, 3, 6, and 12 months was 30.1%, 17.8%, 12.9%, and 14.0%, respectively [48].

Long-term trajectories based on retrospective population studies in the United States and Australia found that the greatest symptom decrease occurs during the first 12 months following exposure. A substantial minority continue experiencing PTSD for decades, and a 50% to 60% remission rate occurs between 2 and 10 years post-event [34; 49].

An important point is that study design can influence prevalence findings. Studies conducted prospectively with participants assessed at two or more time points following trauma exposure have found lower PTSD remission rates. Australian Vietnam veterans assessed at two points 15 years apart found higher PTSD rates at the later time point [50]. A study of firefighters exposed to the World Trade Center attack found that 10.6% continued to meet diagnostic criteria for PTSD four years later [51]. Israeli veterans followed for 20 years were found to have fluctuating PTSD prevalence rates, with reduced rates 3 years post-combat but substantial increases at the 20-year follow-up [52].

Several other studies suggest that in the absence of effective treatment, persons with a PTSD diagnosis at roughly six months post-trauma are likely to experience a chronic PTSD course with symptoms potentially lasting for decades [34; 53; 54; 55; 56].

The standard-of-care treatment can interrupt the chronic course of PTSD. In aggregate, roughly one-third of patients will achieve good recovery with effective treatment, one-third will moderately improve, and one-third will remain refractory [6].

PERSONAL AND SOCIETAL COST

PTSD can exact a tremendous toll on sufferers and impair their functioning in many (if not all) areas of life, with consequences that extend beyond the individual to impact family members and society as a whole. PTSD can impose one of the greatest levels of disability possibly experienced with any physical or mental disorder. Persons with PTSD may experience decreased role functioning from work impairment or loss; family discord; and reduced educational attainment, work earnings, marriage attainment, and child rearing. PTSD is associated with an increased risk of suicide, high medical costs, and high social costs. As noted, a high percentage of individuals with PTSD have one or more additional psychiatric disorders, most commonly substance use disorders or major depressive disorder. In Iraq and Afghanistan war veterans, PTSD imposed an estimated cost of between $4 billion and $6 billion over two years from medical care, forgone productivity, and lives lost through suicide [57; 58; 59; 60; 61].

Many people with PTSD do not seek treatment, and those who do seek care often receive inadequate treatment. The cost-effectiveness of early diagnosis and appropriate treatment of PTSD has been shown repeatedly, especially compared with the cost of inadequate or ineffective treatment occurring before a correct diagnosis [61; 62].

SPECIFIC TRAUMATIZING EXPERIENCES

Elements of specific traumatizing experiences should be appreciated when working with persons exposed to trauma. The following section is presented according to specific trauma-exposed subgroups or types of traumatic events. This will include the background of trauma experiences and characteristics, epidemiology, risk factors for PTSD, and comorbid conditions, when applicable. The special clinical and provider needs of those exposed to specific traumas are also discussed.

COMBAT EXPOSURE AND MILITARY VETERANS

Background

Military personnel may confront numerous potentially traumatizing experiences, including military-specific events and those experienced by civilians. Research suggests the most common traumatic events experienced during active duty are witnessing someone badly injured or killed or unexpectedly seeing a dead body. Events most likely to result in the development of PTSD include witnessing atrocities, accidentally injuring or killing another person, and other interpersonal traumas, such as rape, domestic violence, and being stalked, kidnapped, or held captive [6; 63].

Exposure to multiple traumatic events is not uncommon during deployment, and exposure to real or threatened death and serious physical injury that can lead to PTSD is likely. Fundamental beliefs about self, the world, and humanity can become severely challenged by the nature of wartime traumatic events, such as exposure to the death of civilians and destruction of communities on an unimaginable scale with little preparation. Veterans may themselves have committed acts of violence they deem with hindsight as atrocities, shattering previously held beliefs about the self [6].

More than 2 million members of the U.S. Armed Forces have now served in the Iraq and Afghanistan wars beginning in 2001 and 2003, respectively. In these conflicts, more than 6,000 soldiers died, close to 43,000 were wounded (ranging from shrapnel injuries to amputation and TBI), and more than 100,000 witnessed one or more traumatic events involving horrific injuries or loss of life in members of their unit [64]. Many have returned home with psychologically damaging memories. Combat veterans have often described feeling unable to relate to civilians, including their families, and of having lost the ability for true connectedness except with their comrades, which leads to a sense of loneliness and isolation [64].

With innocent civilians used as human shields, children used as "bait" for attacks, calm moments erupting into death and devastation in seconds, and violations of the rules of engagement, the nature of the Iraq and Afghanistan wars impose on the returning veteran an unnatural recalibration of security and sanity. Among returning war veterans, the most common problems involve somatic, emotional, cognitive, behavioral, interpersonal, and psychosocial components. Somatic concerns appear as primary and middle (sleep-maintenance) insomnia, fatigue, headaches, tinnitus, impotence, restlessness, and chronic pain. Emotional and psychologic complaints may involve nightmares, racing thoughts (particularly at bedtime), generalized and social anxiety, anger and irritability, impulsive hostility, emotional numbing, hypervigilance, complicated grief, and despair [64].

Cognitive problems that may develop from combat trauma exposure include poor sustained and divided attention that partially reflects hypervigilance, poor concentration, impaired memory, rumination, and distorted thinking (e.g., jumping to conclusions, dichotomous decision-making). Common behavioral problems that are underreported include abuse of alcohol, illicit drugs, or prescription medications, and high-risk behaviors such as reckless driving or starting fights. Interpersonal concerns often involve feeling misunder-

stood, intolerance of others, distrust, isolation, and withdrawal. Frequent psychosocial concerns can involve spiritual crisis, domestic violence, child abuse, and general family dysfunction. The most common concerns of veterans seeking primary care are anger, sleep problems, and erectile dysfunction, and all are complicated if there is ongoing substance abuse [64; 65].

Veterans frequently report sensitivity to triggers that stimulate sensory perception, such as sudden or loud sounds, noxious or unusual smells, high temperatures, foreign foods, or uneven terrain. Even less obvious triggers can produce anxiety, panic, fear, anger, and overall sympathetic nervous system arousal, including situations that appear unpredictable (e.g., crowds), beyond control (e.g., a room without an easy exit), or the precursor of potential danger (e.g., traffic or building complexes) [64].

Triggers can activate muscle memory of combat, including the readiness to fight, aggress, and escalate, and none of these are appropriate reactions in the civilian milieu. Combat immersion mode can become stuck in the "on" position, with the defensive or aggressive posture not easily turned off. For others, this heightened state of arousal is experienced as an adrenaline rush of battle that is reinforcing, driving some veterans to seek danger, risk, or excitement to maintain the "high" [64].

Epidemiology

National Vietnam Veterans Readjustment Study

The National Vietnam Veterans Readjustment Study interviewed 3,016 U.S. Vietnam-era veterans between 1986 and 1988 and found a lifetime PTSD prevalence of 30.9% in men and 26.9% in women. The past-year PTSD prevalence was 15.2% in men and 8.1% in women [39; 66].

Gulf War Veterans

From 1995 to 1997, 11,441 U.S. Gulf War veterans were assessed with the PTSD Checklist, with a score ≥50 considered as meeting PTSD criteria. The prevalence of current PTSD was 12.1% [39; 67].

Iraq and Afghanistan War Veterans

Several studies have published PTSD prevalence and incidence rates in Iraq and Afghanistan war veterans. Highly consistent rates have been found with grouping the studies by subpopulation, such as Army or Marine combat infantry units [68]. An early PTSD prevalence study in Iraq and Afghanistan war military personnel using stringent PTSD criteria found three-month post-deployment rates among infantry soldiers and Marines returning from high-intensity combat in Iraq of 12.9% and 12.2%, respectively. Soldiers deployed to Afghanistan who were exposed to very low-intensity combat showed a three-month post-deployment PTSD rate of 6.2%, compared with the pre-deployment baseline population rate was 5% [68; 69]. Subsequent studies of Iraq and Afghanistan war-deployed soldiers found rates of acute stress disorder (ASD) or PTSD of 10% to 20% [68]. Prevalence was directly associated with combat frequency and intensity, with units exposed to minimal combat similar in prevalence to baseline rates in the population, and a linear increase up to 25% in units involved in the highest-intensity combat. Soldiers in Afghanistan showed lower PTSD prevalence earlier in the war, which increased to levels comparable with Iraq combatants from 2007 onward [68].

Soldiers assigned to active and National Guard combat infantry teams showed post-deployment PTSD rates of 15% after 3 months and 17% to 25% after 12 months [68; 70]. A study of previously deployed Iraq and Afghanistan war veterans found a current PTSD rate of 13.8% [39].

Risk Factors

The strongest predictors of increased prevalence of post-deployment PTSD are combat frequency and intensity, which impose greater risk than the actual number of deployments in predicting adverse mental health outcomes [68]. Some evidence indicates that military recruits have a higher prevalence of childhood physical abuse, sexual abuse and neglect, and family dysfunction compared with community averages, with these factors contributing to the higher PTSD risk [71; 72]. Practitioners should assess pre-military history, as these factors can also influence the therapeutic relationship and treatment planning [6].

Comorbid Conditions

Biomechanical Injury/Traumatic Brain Injury

In Iraq and Afghanistan war veterans, biomechanical trauma to the brain caused by explosions and blast waves is the most frequent physical injury [73]. When severe enough, the brain trauma is termed traumatic brain injury or TBI. Even mild TBI elevates patient risk of psychiatric conditions, including PTSD, depression, anxiety, substance abuse, or suicide. TBI is characterized by three symptom types [64; 74]:

- Cognitive: Problems with memory, poor attention, and limited concentration
- Emotional/behavioral: Irritability, depression, anxiety, impulsivity, and isolation
- Somatic: Insomnia, headache, tinnitus, and dizziness

The chaos and possible amnesia surrounding the TBI event can interfere with obtaining a proper history of the injury, but the provider should make an effort to document injury severity and type, previous brain injury history, the extent of symptom overlap between TBI and PTSD. Common overlapping symptoms include depression, anxiety, irritability/anger, trouble concentrating, fatigue, hyperarousal, and avoidance [64; 74].

Risk of Suicide and Violence

Historically, the suicide rates in the Army and Marine Corps consistently surpassed general population rates [75]. From 2014 to 2019, the suicide rate for active-duty military increased from 20.4 to 25.9 suicides per 100,000 service members [76]. Although military suicide rates are comparable with rates in the U.S. adult population (after accounting for age and sex), the Department of Defense reports a continued heightened risk, primarily for enlisted male members who are younger than 30 years of age [77]. Factors with the greatest association to suicide risk include depression, relationship strain, financial and vocational loss, and magnitude of life impairment. Clinical presentations with the highest prediction of potential future suicidal behavior are the presence of overwhelming negative thoughts and hopelessness over the future [78].

The potential for harm to others is another safety concern with veterans to address during assessment. Veterans with pronounced irritability, anger, and impulsivity may act aggressively toward others, and in one study, 63% of veterans seeking care for PTSD had been aggressive to their partners in the last year [64; 79]. To gain a clearer picture of individual veteran risk of suicide or violence, the provider should assess the integrity of the veteran's support system, access to lethal means of self-harm, history of impulsivity and substance use, sleep adequacy, medication regimen, and outlook on the near and distant future [80].

SEXUAL ASSAULT AND ABUSE

Background

The nature of sexual assault varies greatly, from repeated childhood sexual abuse to an isolated event of adult rape, and the adverse effects on mental health are also highly variable. Sexual assault is a unique crime as it usually occurs in private, is shrouded in secrecy, and victims often blame themselves.

Although population-level prevalence rates of childhood sexual abuse are difficult to estimate, the extent of this abuse was captured in a survey of 9,508 predominantly white, middle-class primary care clinic respondents in the San Diego area. One or more childhood sexual abuse experiences were reported by 22% of participants, including being sexually touched or fondled (19.3%) and attempted (8.9%) or completed (6.9%) intercourse or penetration. In comparison, 10.8% reported physical abuse [81].

Compared to PTSD prevalence following single-trauma exposure, adult PTSD prevalence following sustained trauma exposure from childhood sexual abuse is likely substantially higher. One study found 39% of women and 29% of men who reported sustained childhood sexual abuse developed PTSD in adulthood [82].

Most childhood sexual abuse is perpetrated by family members or someone known to the child. Roughly 60% of perpetrators are non-relative acquaintances, such as a family friend, babysitter, or neighbor; 30% are relatives such as fathers, uncles, or cousins; and 10% are strangers [83]. Men are the most common perpetrators with boy or girl victims; women are the perpetrators in 14% of cases against boys and 6% of cases against girls. The Internet is often used to initially contact children by child pornographers and other stranger perpetrators [6].

Many sexually abused children and adult survivors still have contact with their abuser. Intergenerational transmission of abuse results when women abused as children repeatedly select abusive, violent partners who may sexually and/or physically abuse her children [84]. There is also some evidence that male sexual abuse survivors may be more likely to become perpetrators, although this has not been found among female survivors [85; 86]. Children of women experiencing the psychologic impact of abuse (e.g., depression, anxiety, social withdrawal) may receive little protection and/or no positive parenting guidance or strategies. Children may also be taught the world is a dangerous place, and overprotection interferes with the development of resilience [6].

Provider Considerations

Given the societal context of sexual assault reporting, the practitioner should accept the person's account of his or her traumatic experience without investigating the authenticity of the claims. Victims/survivors may anticipate disbelief and denial from the clinician due to past negative responses to their disclosures from friends, family, or the criminal justice system.

Practitioner gender should also be considered when working with sexual assault survivors. Avoid assuming that a female or male patient will prefer a practitioner of either the same or the opposite gender. Instead, discuss this issue with the patient and, if possible, let him or her choose the provider gender [6].

Presentation

In adults with PTSD following sexual assault, the trauma may range from a single adult trauma of rape to repeated sexual abuse during childhood, or a combination of both. The nature of childhood sexual abuse itself is highly variable. Sexual abuse involving penetration (digital or otherwise), as opposed to touching or fondling, has been found to be the most harmful of the abuse experiences [6]. This is also true of sexual abuse involving degradation and violence. Not surprisingly, typical presenting problems differ according to the type and number of sexual assaults experienced. The clinician should be aware of these typical presentations and ensure a comprehensive assessment, especially if a prior history of assault or sexual abuse is suspected. In some cases, the individual who has been sexually abused as a child will present for treatment of PTSD for the first time as an adult [6].

Common presenting problems in survivors of adult sexual assault include [6]:

- Recurrent daytime intrusive memories/flashbacks and distressing dreams
- Physical symptoms of hyperarousal, such as palpitations, sweating, and/or breathing difficulties
- Hypervigilance

PTSD AND TRAUMA EXPOSURE PREVALENCE IN HETEROSEXUALS AND PERSONS WITH MINORITY SEXUAL ORIENTATION

Sexual Identity	PTSD	Childhood Maltreatment	Interpersonal Violence Overall	Unwanted Sex	Attacked or Beaten	Domestic Violence Victim	Witnessed Another Injured or Killed
Men							
Heterosexual	5.03%	10.76%	24.95%	2.23%	11.73%	2.00%	32.45%
HSSP	10.13%	14.98%	33.98%	12.71%	16.64%	3.97%	34.74%
Gay	13.38%	18.26%	50.69%	17.95%	20.70%	11.52%	23.96%
Bisexual	9.00 %	12.15%	31.05%	12.04%	10.42%	0%	33.07%
Women							
Heterosexual	12.50%	13.07%	26.36%	13.41%	3.46%	9.44%	16.13%
HSSP	22.78%	19.55%	46.30%	29.57%	12.88%	23.81%	29.20%
Lesbian	18.04%	27.64%	60.21%	43.98%	10.37%	16.10%	29.39%
Bisexual	25.68%	30.52%	54.06%	47.26%	20.73%	20.17%	30.76%

HSSP = heterosexuals with same-sex partners.

Source: Reprinted with permission from Roberts AL, Austin SB, Corliss HL, Vandermorris AK, Koenen KC. Pervasive trauma exposure among U.S. sexual orientation minority adults and risk of posttraumatic stress disorder. Am J Public Health. 2010;100(12):2433-2441. *Table 1*

- Sleep problems
- Eating difficulties
- Mistrust of men/women, affecting the formation of relationships
- Loss of interest in usual activities
- Shame/guilt associated with memories of assault
- Depression

In adult survivors of childhood sexual abuse, PTSD symptoms are often part of the patient's presentation with prominent avoidance/numbing symptoms [33]. Depressive and anxiety symptoms are also common. Childhood sexual abuse may lead to persistent self-regulation issues, including:

- Affect regulation and impulse control (e.g., self-harming, acting out sexually)
- Attention (e.g., regular dissociative episodes)
- Self-perception (e.g., identity disturbance)
- Relationship difficulties (e.g., attachment, sexual, and parenting problems)

These self-regulation issues can lead to a range of diagnoses, including personality disorders (e.g., borderline personality disorder) and attachment disorders. Substance use problems and eating disorders are also common. Comorbid presentations are the norm for this group. Behavioral problems and disorders (e.g., oppositional defiant disorder) are associated with abuse, particularly in boys. Anxiety, depression, and PTSD may be present in children who have been sexually abused. Interactions with medical or legal systems may trigger trauma memories in survivors of sexual assault, for example, if a medical patient is asked to remove her clothing by a male authority figure [87].

MINORITY SEXUAL ORIENTATION

Data from a national epidemiologic survey of 34,653 U.S. adults were analyzed to examine PTSD and trauma exposure in gay men, lesbians, and bisexuals. The overall finding was elevated rates of PTSD and exposure to traumatic experiences among persons with minority sexual orientation (***Table 1***) [88]. A novel finding was that heterosexuals with same-sex partners had rates of PTSD

and traumatic experiences similar to gays/lesbians and bisexuals in both genders, suggesting that same-sex exposure, rather than same-sex orientation, was a risk factor [88].

CIVILIAN DISASTER EXPOSURE

Background

Natural disasters are large-scale events that impact communities, and the effects can be widespread or relatively localized. For example, earthquakes and wildfires impact a relatively well-defined geographical region, while hurricanes and tsunamis may result in extensive damage. Individuals whose community is affected can experience multiple secondary stressors as a result of disasters, especially from the destruction of home, livelihood, and infrastructure. For others, the traumatic experience is limited to the disaster itself, such as the thousands of tourists exposed to the 2004 tsunami in Southeast Asia. The nature of exposure to disaster trauma varies by the type of disaster and proximity to the focal point. Disaster exposure may result in different psychologic reactions in primary victims compared with secondary victims [6]. An overview of studies assessing trauma following a community-wide disaster reported PTSD prevalence rates ranging from 3.6% to 37% among children and adults living in the affected area (primary victims) and 4.4% to 21.2% among children and adults living near the affected area (secondary victims) [89].

Specific consideration should be given to the issue of traumatic bereavement in disasters producing high fatality rates, because treating PTSD in isolation will not address the full range of distress. The interaction between traumatic memories and the grief process should also be addressed.

Presentation

The immediate post-disaster period involves efforts to mitigate current physical threats, to ensure the physical safety and well-being of the population by providing emergency food and shelter, and to secure people's possessions if homes have been destroyed. Typically, a small group of survivors become acutely distressed. Most survivors become immersed in the practical situational demands and are not overwhelmed by psychologic distress in the immediate post-disaster period. There is also expectation that persons sustaining significant losses or who are displaced will experience some extent of enduring distress. When a degree of normality returns and external demands lessen, distress may persist in those already distressed and others may begin to notice their distress is disproportionate to current circumstances. Both of these groups may seek care for PTSD symptoms.

Psychologic distress following a disaster can manifest as family dysfunction, substance abuse, and/or conflict within the affected community. Disasters may catalyze the development of PTSD and other conditions, including adjustment disorders, major depressive disorder, substance use disorders, and a range of non-specific somatic symptoms. Post-disaster PTSD is characterized by considerable anxiety that a similar event will emerge, and triggers of intense distress are readily observed [90; 91; 92]. One study found that individual- and community-level social cohesion prior to the 2011 earthquake and tsunami in Japan were significantly associated with lower risks of PTSD symptoms, even after adjusting for depressive symptoms at baseline and accounting for experiences during the disaster (e.g., loss of loved one, housing damage) [93].

Provider Considerations

Several specific provider challenges may arise after a natural disaster. Large numbers of people may require treatment over a prolonged period, and the need to treat PTSD with evidence-based methods can be challenged in rural and remote communities with a lack of appropriately trained practitioners. Growing evidence suggests remote Internet-based services can provide effective treatment for PTSD and other common psychologic problems, especially when supported by low-level clinical care [94; 95; 96]. When those experiencing PTSD have sustained substantial economic and social disadvantages from the disaster, their environment may be a constant reminder of the traumatic experience and complicate treatment.

PTSD following a disaster can afflict several members of the same family, and the reactions of other adults in the household can promote the maintenance of PTSD symptoms to a greater extent than the disaster aftermath itself. Treatment should address these relationship dimensions, as they can influence the patterns of withdrawal and avoidance [97].

Chronic PTSD is associated with a greater perception of life threat during the disaster. This can be addressed by cognitive therapy that helps the patient with realistic threat evaluation [98].

COVID-19

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the related disease (COVID-19) has impacted lives across the globe. As of March 2021, more than 114.9 million confirmed cases of COVID-19 had been reported worldwide, with more than 28.7 million cases in the United States alone [99]. Prior to the pandemic, 1 in 10 adults in the United States reported symptoms of anxiety or depressive disorder; during the pandemic, this number rose to 4 in 10 adults [100; 101]. Results of a national poll released in March 2020 found that more than 36% of Americans report that COVID-19 is seriously impacting their mental health [102].

The pandemic also has put healthcare professionals in the undesirable position of having to make difficult decisions about patient, self, and family care and safety while working under extreme pressures due to limited and/or inadequate resources [103]. Psychologic endurance has been a challenge for many people and will likely manifest in the development of a new or exacerbation of an existing psychiatric disorder; development of a trauma or stress-related disorder, such as PTSD; or development of a symptomatic stress response not meeting DSM-5 criteria for a psychiatric disorder [103].

Presentation

According to poll data from July 2020, negative impacts on mental health and well-being reported by U.S. adults included difficulty sleeping (36%) or eating (32%), increases in alcohol consumption or substance use (12%), and worsening chronic conditions (12%) due to worry and stress over the coronavirus [104]. Data from the U.S. Census Bureau's Household Pulse Survey (gathered between April and October 2020) indicate that 41% of U.S. adults reported symptoms of anxiety disorder and/or depressive disorder [105]. Adults in households with job loss or lower incomes reported higher rates of symptoms than those without job or income loss (53% vs 32%). Women with school-aged children were more likely than men (49% vs 40%) to report symptoms of anxiety and/or depressive disorder, and research is beginning to highlight concerns about the mental health and well-being of school-aged children [104]. Although child abuse-related emergency department visits decreased during the COVID-19 outbreak, the severity of injuries among child abuse-related emergency department visits increased and resulted in more hospitalizations [104]. Young adults (18 to 24 years of age) have experienced university closures, social isolation, and loss of income. According to the Survey, 56% of young adults have reported symptoms of anxiety and/or depressive disorder, and they are more than twice as likely as adults to report substance use and suicidal thoughts [105]. Communities of color have historically faced challenges accessing mental health care, and they have been disproportionately affected during the coronavirus pandemic, with non-Hispanic black adults and Hispanic or Latino adults more likely to report symptoms of anxiety and/or depressive disorder than non-Hispanic white adults (48%, 46%, and 41% respectively) [104]. Ongoing public health measures implemented to slow the spread of the coronavirus will continue to expose many people to situations (e.g., isolation, job loss, loss of loved ones) that are linked to poor mental health outcomes [104]. A review of the impact of quarantine identified PTSD symptoms, confusion, and

anger as commonly experienced negative effects [106]. Long-term risk behaviors, distress reactions, and inappropriate coping mechanisms pose a risk of exacerbating mental disorders [103].

Provider Considerations

Physical and social isolation, the disruption of daily routines, financial stress, food insecurity, and numerous other potential triggers for stress response have all been intensified due to this pandemic. The uncertain environment is likely to increase the frequency and/or severity of mental health problems, and there is likely to be a surge in patients experiencing mental health and/or substance use disorder during the pandemic and in its aftermath [104]. Managing the impact of COVID-19 will require a coordinated effort from the entire healthcare system, not just from mental healthcare providers. Critical steps include identifying patients with existing illness who present in acute crisis, identifying new cases of mental illness in people not previously diagnosed, and providing support for those who do not meet diagnostic criteria but who do need help [103]. As stated, growing evidence suggests remote, Internet-based services can provide effective treatment for PTSD and other common psychologic problems, especially when supported by low-level clinical care [94; 95; 96]. Due to COVID-19 social distancing guidelines, Internet-based and telehealth services are becoming more commonly used and accepted among providers, physicians, and patients [103].

TERRORISM

Background

Terrorist acts usually involve the threat or delivery of high levels of destruction to property and human life. There may be exposure to gruesome sights for those involved, including the death and suffering of others that may also include family members and friends. The fear generated by terrorist attacks includes many features characteristic of high-severity traumatic events. The place, timing, and potential victims are usually unpredictable, and the pervasive response of feeling powerless and helpless greatly elevates the risk of perpetual hypervigilance. Bioterrorism carries the added threats of being poorly understood and invisible, with exposed persons difficult to discern from unexposed individuals or groups and uncertainty over the health consequences in those exposed to pathogens. These factors contribute to the objective of terrorist acts, which is to generate terror in the community that is disproportionate to actual risk of exposure or damage from exposure [6].

Epidemiology

The prevalence of PTSD related to the 2001 attack on the World Trade Center decreased from 9.6% one year after the attack to 4.1% at the four-year follow-up among 455 patients in primary care practices in New York City [107]. However, symptoms may persist for years in up to 40% of adults with PTSD triggered by a terrorist attack [4].

Provider Considerations

Sensationalized media reporting and poor communication by public officials can worsen the impact of terrorism, and health professionals can mitigate this effect by accurate communication to the media, public officials, and the general population. Content of such communication may include realistic information on the actual risk of terrorist attack and impact and a summary of terrorism prevention measures that have been implemented. Risk to individuals is typically very low, and the negative health behaviors in response to fear and stress impose a greater health hazard than actual terrorism. The only action required of civilians is vigilance of suspicious activity, which should then be reported to authorities. Early intervention to address mental health problems following trauma is demonstrably effective but only when persons in need can be identified. Therefore, educational material should be distributed to general practitioners to ensure the appropriate assessment and identification of these patients [6; 108].

Presentation

Psychologic and behavioral reactions to terrorism are often proportionate to the extent of harmful impact from the attack. Proximity to the attack and the number of attacks are also correlated with symptom severity. Immediate reactions include heightened anxiety, panic attacks, sleep disturbances, substance use problems, absenteeism from work, and retaliatory reactions against minorities groups identified with the terrorists. The initial level of distress often subsides over the first several weeks, although repeated attacks, widespread loss of life, and significant infrastructure damage can elevate and prolong psychologic and behavioral reactions. Significant longer-term mental health problems are usually limited to a small proportion of the population and can include traumatic stress symptoms, anxiety disorders, depression, and substance abuse. A common feature among all levels of distress is an ongoing fear of another attack [6].

FIRST RESPONDERS

Epidemiology

First responders include police, emergency medical service providers, firefighters, and other similar professionals. Although roughly 10% of first responders are estimated to have PTSD, the prevalence rates vary across services, with a meta-analysis finding prevalence rates of 15% in ambulance personnel, 7% in firefighters, 7% to 19% in police, and 13% in other rescue workers [109; 110].

Presentation

First responders can become more distressed by some incidents than others, and the extent an incident is personalized by identification with the event or victim modifies resilience and vulnerability. In fact, police officers who injure or kill another person out of necessity have a greater risk of developing PTSD than depression or an alcohol use problem. The daily, low-level stressors of emergency room personnel, including exposure to long hours, physical exertion, interpersonal conflict, and budgetary constraints, may impose greater risk in developing PTSD than exposure to an isolated traumatic event [111; 112; 113].

Compared to trauma-exposed civilians, typical reactions to traumatic experiences in first responders often involve occupationally appropriate responses such as anger or guilt instead of emotions such as fear or horror. Anger is a significant post-trauma issue in this population, and while pre-existing anger may influence the development of PTSD, PTSD is also associated with an increase in anger. The tangible nature and effect on work and interpersonal relationships make anger more likely to attract attention than internal expressions of distress. Problems with substance use are also very common presenting problems for similar reasons. Prominent hyperarousal is likely in first responders with repeated or frequent exposure to traumatic events. Significant subsyndromal distress is common, which impairs future resilience to traumatic events and increases the risk of developing PTSD [111; 114].

TRAUMA CARE PERSONNEL

Vicarious trauma, also known as indirect trauma, compassion fatigue, or empathic strain, may result from the cumulative emotional impact of working with trauma survivors. Signs and symptoms of vicarious trauma resemble those of direct trauma and include intrusive imagery and thoughts, physiologic arousal, avoidance, or anxiety. Providers may also experience disruptions in personal or professional relationships, managing boundaries, and regulating their emotions. Vicarious trauma may lead to social withdrawal, hopelessness, nightmares or difficulties sleeping, overeating, or alcohol abuse. Work with clients who have experienced specific traumas can influence the expression of vicarious trauma, such as developing sexual problems from working with sexual abuse survivors or travel anxiety from working with transportation accident survivors [115].

At-risk professionals include therapists, counselors, social workers, shelter staff, lawyers, healthcare professionals, clergy, journalists, trauma researchers, and psychologists. Individuals are more likely to develop vicarious trauma when caring for trauma survivors in an open, engaged, empathic, dedicated,

and responsible style. Immersion into experiences of trauma survivors can alter the identity, worldview, spirituality, professional relationships with clients and colleagues, and personal relationships of the trauma professional [115].

Providers may reduce the risk of vicarious trauma, or minimize the severity of impairment if it develops, through basic self-care activities, including balancing work, play, and rest; adequate diet and exercise; appropriate professional training; communicating with colleagues; ongoing consultation; finding a forum to talk about vicarious trauma experiences; adding support staff; and simply acknowledging the difficulties of the work. Some trauma professionals benefit from identifying problems and contributing factors, specific steps to take, and getting support from friends or colleagues in taking these steps. Restoring meaning and hope is essential because these two provider qualities are undermined by vicarious trauma [115].

INJURY, ACCIDENTS, AND MEDICAL TRAUMA

Most studies of accidents, injury, and PTSD have involved severely injured hospitalized patients. Much less is known of PTSD risk in persons with less severe accidents and injury not requiring emergency medical attention.

While many injury survivors experience PTSD symptoms such as nightmares or intrusive memories in the initial weeks after a physical injury, these symptoms tend to resolve within three months in most patients. However, 10% to 15% will go on to develop chronic PTSD [116]. The extent an injury is life-threatening does not predict the development of PTSD; rates of PTSD for certain soft tissue injuries such as whiplash are similar to severe injury. Patients with severe TBI are less likely to develop PTSD compared to those with mild TBI. Low PTSD rates following severe TBI are likely the result of amnesia and absence of trauma memory [117; 118].

Presentation and Comorbidities

Patients with PTSD following severe injury commonly present with distressing memories and nightmares of the accident, insomnia, irritability, elevated startle response, and concentration problems. Situations in which the event happened or that mimic the lead up to the injury are often avoided. Practitioners should be aware that many injury survivors who sustain a TBI have little or no memory of the event. The re-experiencing criteria for PTSD can be met if reminders of the injury-causing event (e.g., returning to driving) trigger distress even if the patient cannot recall critical aspects of the accident. Motivational issues can be problematic in patients with moderate-to-severe TBI and should be assessed because they may diminish engagement in therapy [6].

Depression is frequently comorbid, especially with injuries requiring long-term rehabilitation [119; 120]. Contributory factors include the loss of important roles, financial problems, and uncertainty of the future. Chronic pain is also highly comorbid. Pain and PTSD mutually interact such that pain triggers trauma memories and hyperarousal increases pain perception [119; 120].

As PTSD may contribute to the overall burden of symptoms in some individuals following mild traumatic brain injury (TBI), particularly where problems persist for more than three months, the Scottish Intercollegiate Guidelines Network recommends that mental state should be routinely examined in patients with TBI, with an emphasis on symptoms of phobic avoidance, traumatic re-experiencing phenomena (e.g., flashbacks and nightmares), and low mood.

(https://www.sign.ac.uk/media/1068/sign130.pdf. Last accessed March 18, 2021.)

Level of Evidence: C (A body of evidence including well-conducted case control or cohort studies, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from high-quality systematic reviews of case control or cohort studies)

REFUGEES AND ASYLUM SEEKERS

Epidemiology

Almost 50% of the world's nearly 200 nations torture their citizens, and an estimated 500,000 torture survivors live in the United States [121]. The prevalence of these victims is high in certain refugee groups. Victims of torture are more likely to emigrate than their unmolested fellow nationals, and overall, 6% to 12% of immigrants from countries where torture is practiced say they have been tortured. Those seeking political asylum have the highest rates of torture prevalence, with 20% to 40% of asylum-seeking refugees from Somalia, Ethiopia, Eritrea, Senegal, Sierra Leone, Tibet, and Bhutan reporting being tortured [121].

Among refugee populations, children account for 4% of torture survivors [121]. Their brutalization may have resulted from the police if they lived as street children, or they may have been tortured to terrorize family members or if they lived in "enemy" communities. Older children may have been imprisoned or forced to serve as child soldiers. One meta-analysis reported that 11% of refugee children and 9% of adults met the criteria for PTSD regardless of whether they experienced torture or witnessed war or pandemic political violence [121; 122; 123].

Risk Factors

Among refugees in general, torture is highly correlated with PTSD, while exposure to conflict and displacement have shown a strong correlation with depression [124]. Although the type, severity, or duration of torture has not been found to correlate with the severity of post-torture PTSD, head trauma during torture has been highly associated with post-torture depression and rape during torture is associated with high levels of chronic distress and sexual dysfunction [125; 126; 127].

Comorbid Conditions

The physical symptoms and medical conditions stemming from torture vary by the nature of the torture method. Concussive trauma is nearly universally reported and includes beatings with fists, clubs, and batons. As many as 50% of survivors report beatings on the feet, a technique that produces chronic pain, neuralgia, disability, and heightened risk of PTSD [128]. Among male survivors, sexual torture is substantially underreported, and estimates indicate that 5% to 15% of male survivors were sexually abused by threats of castration or rape, being raped or forced to perform sex in view of others, or receiving electric shock or mutilation to the genitals [129; 130]. Fewer women than men are tortured in aggregate, but around 50% of female torture survivors report sexual torture, typically by rape and sometimes in front of family members [121; 125; 128].

Attempting to distinguish between the consequences of physical and psychologic torture is difficult, as fear of physical violence is a psychologic stressor and psychologic torture often leads to physical sequelae, such as pain and sexual dysfunction. Psychologic torture intends to humiliate, degrade, or induce an extreme state of fear, as through the use of sham executions or forced viewing of torture. Other common psychologic torture methods intend to isolate or disorient a prisoner by blindfolding or sleep deprivation. When physical and psychologic torture are combined, the outcome is often severe and chronic psychologic morbidity [126]. The primary psychiatric diagnoses in torture survivors are PTSD, depression, anxiety disorders, and chronic pain syndromes, with prevalence rates among treatment-seeking torture survivors of 50% to 67% for PTSD, 33% for depression, 10% for generalized anxiety disorders, and 40% to 70% for chronic pain or somatoform disorders [131; 132].

PTSD, AGGRESSION, AND VIOLENCE

The development of PTSD in response to traumatic experiences can increase the risk of aggressive or violent behavior in some populations. In the past decade, this has become an issue of increasing concern, particularly among military veterans.

MILITARY VETERANS

Anger is an emotional state encompassing feelings of variable intensity, ranging from mild annoyance or aggravation to fury and rage. Anger and aggression are related but distinct constructs, and difficulties with anger may not necessarily translate into aggressive behavior. Research has shown that anger is higher among veterans with PTSD relative to those without PTSD, and this relationship between PTSD and anger tends to be stronger in veterans than in civilian populations [133]. When exposed to reminders of their trauma event, these patients show a very strong anger response that differs from the more common anxiety or depressive response in civilians. PTSD is a central and primary risk factor for anger and aggression in military veterans. Clinically, veterans with PTSD often report that anger is the primary problem causing the greatest disruption in their functioning. High levels of anger also interfere with the effectiveness of PTSD treatments [134].

Epidemiology

A study of Iraq and Afghanistan war veterans found that more than 50% of individuals with PTSD reported aggressive behavior in the past four months, such as threatening physical violence, property destruction, and fighting [135]. A 2010 survey of 2,797 U.S. veterans returning from deployment in Iraq or Afghanistan found that 40% reported killing or being responsible for killing during deployment. After controlling for combat exposure, killing was a significant predictor of PTSD symptoms, alcohol abuse, anger, and relationship problems [136].

A study of Vietnam veterans found that combat veterans were not significantly angrier than veterans who did not serve in Southeast Asia and that combat veterans with PTSD scored significantly higher than veterans without PTSD on measures of anger, arousal, range of anger-eliciting situations, hostile attitudinal outlook, and tendency to hold anger in. These results suggest that PTSD, rather than warzone duty, is associated with various dimensions of elevated anger [137].

Anger can be a very difficult emotion to deal with and can lead to legal and interpersonal problems, such as divorce or domestic violence. Research has found that anger negatively influences veterans' PTSD treatment outcomes [138]. To improve treatment effectiveness, clinicians should assess veterans' anger, aggression, alcohol use, and fear of anger to elucidate the relationship between these factors [138].

Veterans with PTSD are at much greater risk for perpetrating partner violence than veterans without PTSD. Studies have found that rates of veteran perpetration of intimate partner violence are up to three times higher than among civilians [139; 140]. The severity of PTSD symptoms, particularly hyperarousal, is significantly associated with intimate partner violence [141; 142]. Most studies have examined rates of aggression among Vietnam veterans several years post-deployment. One study examined partner aggression among male Afghanistan or Iraq veterans who served during Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) and compared it to partner aggression reported by Vietnam veterans with PTSD [143]. Participants were divided into three groups: 27 OEF/OIF veterans with PTSD; 31 OEF/OIF veterans without PTSD; and 28 Vietnam veterans with PTSD. The results suggested that OEF/OIF veterans with PTSD were 1.9 to 3.1 times more likely to perpetrate intimate partner violence than the other two groups [143].

Explanatory Models

The Survival Mode Model

Warzone combatants rapidly learn that survival requires constant vigilance for potential threats in their environment. This includes heightened awareness of small changes, such as a rock formation placed differently than before, and people's facial expressions. They are trained to respond to threats with aggression, and the heightened sense of threat perception is highly adaptive in a warzone setting. Problems arise with return to civilian life when the fully intact threat perception vigilance leads to the misreading of situations as overly threatening when a significant threat is absent, such as the misinterpretation of someone's facial expression. Social situations are viewed through an overly negative, hostile, or threatening lens, and this misread can trigger an aggressive response [143].

The Information Processing Model

Domestic violence perpetrators exhibit information processing deficits at the decoding stage, when input from social interaction is interpreted. This has been validated in studies of men who exhibit violence, in which cognitive deficits at the decoding stage lead to faulty attributions of social situations and irrational beliefs such as an overly hostile interpretation of events. This model is consistent with the survival mode model of aggression in veterans with PTSD, as both state that violence perpetration results from information processing deficits [144].

Hyperarousal Symptoms of PTSD

Hyperarousal symptoms reflect an overactive fight or flight response and include increased anger and irritability, increased startle response, and difficulty sleeping. Hyperarousal symptoms are the result of increased physiologic arousal, and hyperarousal symptoms are most strongly associated with aggression, with physiologic arousal strongly influencing information processing and executive functioning abilities [145].

VIOLENT OFFENDERS

The association of traumatic experience with violence and PTSD is bidirectional. Research has shown much higher PTSD prevalence among incarcerated offenders than the general population; an association between childhood trauma and abuse with subsequent aggressive and criminal behavior, child abuse and neglect, and sexual molestation; and that witnessing a person being killed or seriously injured by another is the most common risk factor for PTSD, aggression, and antisocial behavior in men [146; 147]. Chronic exposure to violence can evolve into a pattern of violence endured and perpetrated [146; 147].

Higher rates of trauma and earlier age of trauma onset are associated with increased violence and victimization in prison [148]. High rates of PTSD and histories of physical and/or sexual abuse have been repeatedly found among incarcerated veterans, inmates in rural prisons and jails, and men in substance abuse treatment. Most studies have suggested a much higher rate of childhood sexual abuse in male inmates than in the general male population [149; 150]. Unlike women, men are rarely safer in prison than before incarceration; their risk of sexual assault is increased exponentially, and the constant threat of potentially lethal violence may trigger greater externalizing trauma responses of aggression and violence and high arousal levels that endanger staff and other inmates [151; 152].

Most studies of trauma and criminality have been descriptive and quantitative. However, 105 young offenders convicted of serious violence were assessed for intrusive memories, ruminations, and PTSD symptoms related to their violent crime [153]. Participants described significant intrusive memories and ruminations related to the assault. The focal point of many intrusive memories involved the moment when the event took a turn for the worse for the perpetrator, demonstrating important implications for risk assessment and therapeutic interventions in violent offenders [153]. Another study examined the prevalence and

characteristics of amnesia in violent offenders and found partial amnesia of offences associated with cognitive processing during the assault [154].

The significance of PTSD in offenders is important to understand. Personality assessment studies have found that PTSD negatively influences impulsivity, aggression, negative emotions, and affect dysregulation, and self-regulation deficits are strongly linked with re-offending risk [155]. Behavioral and emotional dysregulation also elevate the likelihood of high-risk behaviors, exposure to traumatic events, and subsequent PTSD [156; 157]. Some believe that persons with PTSD may be driven to engage in greater risk-taking behavior or to seek danger situations by a compulsion for trauma re-exposure and to re-enact early violence experiences as an attempt to heal unresolved traumatization [158]. Such re-enactments may be reflected by internalizing "acting-in" behaviors of self-harm, suicide, or depression, or by the externalizing "acting-out" behaviors of harming others and criminal activity [159]. This alternating mechanism of acting out and compulsive re-exposure to trauma may help explain the significant role of PTSD in elevating the risk of reoffending [147].

Correctional officers are tasked with managing large numbers of violent offenders, particularly in men's prisons, and trauma is far more likely to be addressed in female than in male inmates. Trauma-informed care is a fairly recent development in the area of PTSD treatment, and in the prison setting, it is implemented to accurately identify trauma and related symptoms, train staff on the impact of trauma, minimize re-traumatization, and help institutions avoid re-enacting the trauma dynamics experienced by many inmates at an early age [160; 161]. Among several lines of supportive empirical evidence are the findings that constant surveillance and authoritative, punitive measures of control, without treatment, represent the least effective means of reducing future criminal behavior, and that treatment and rehabilitation are more successful in reducing recidivism [162; 163; 164; 165].

Prison staff may be reluctant to reduce their use of authoritative, punitive methods when they are believed to be critical enforcement tools and may perceive trauma-informed principles of increasing empathy, compassionate care, grounding, and de-escalation as showing weakness or pandering when, ironically, this approach is more likely to help to create security and a stable environment. A trauma-informed correctional staff provides the necessary environment for effective inmate treatment with trauma-specific clinical interventions that deliver the greatest improvements in inmate stability and reductions in recidivism [146; 166].

RISK AND PROTECTIVE FACTORS

Risk Factors

PTSD is a strong risk factor for aggression, and other contributing risk factors commonly found with PTSD include depression, substance abuse, and TBI. Dysphoric or negative affect contributes to anger-related feelings, thoughts, memories, and aggressive inclinations, and chronic negative affect may lower the threshold that triggers anger and elevate the likelihood for aggressive behavior [167].

Alcohol use problems are the most frequent comorbidity in PTSD, with alcohol often used to self-medicate high hyperarousal symptoms associated with PTSD. Alcohol use alone is a strong risk factor for aggression perpetration, and alcohol leads to aggression, in part, by diminishing executive functioning and altering information processing. Alcohol use also disinhibits violence in persons with hyperarousal or anger problems [167].

TBI is an important consideration in PTSD and aggression risk. One study found that 19% of Iraq and Afghanistan war veterans screened positive for probable TBI during deployment [61]. TBI elevates risks for aggressive behavior by impairing mechanisms that inhibit behavior and regulate emotions; comorbid PTSD further increases this risk. Studies of non-veteran domestic abuse perpetrators found that close to 50% of perpetrators reported brain injury at some previous point, indicating the link between TBI and aggressive behavior occurs independently of veteran status [168; 169].

Protective Factors

Prisoners in Rwanda accused or convicted of participating in the 1994 genocide were evaluated to investigate factors that mitigated PTSD. Of the 269 subjects (66% male, 34% female), many reported suffering from trauma symptoms stemming from their own perpetration of cruelty and violent killing. A subgroup with few or no post-trauma symptoms committed more genocide-related crimes and were significantly more likely to experience rewarding effects from their violence. This reward effect of enjoyment from inflicting cruelty and pain was believed to protect against developing PTSD symptoms [170].

PATHOPHYSIOLOGY

PTSD is viewed as a maladaptive response to a traumatic stressor, characterized by altered fear-related learning (fear conditioning) and extinction, behavioral sensitization and kindling, and alterations in brain regions and neurotransmitter systems closely linked to these processes. The hypothalamic-pituitary-adrenal (HPA) axis is the primary system activated as a stress response and a potential source of vulnerability to trauma-related psychopathology such as PTSD. Normal response to stress exposure initiates a neuroendocrine cascade in the HPA axis, leading to adrenal gland hypersecretion of the glucocorticoid cortisol. HPA axis activity is tightly controlled through complex regulatory mechanisms of glucocorticoid negative feedback. Glucocorticoids regulate the secretion of hypothalamic corticotropin-releasing factor (CRF) and pituitary adrenocorticotropic hormone. HPA axis activity is also regulated by glucocorticoid receptors (GRs) in the hippocampus and prefrontal cortex [171; 172].

Prolonged HPA axis activation from traumatic or chronic stress can induce inappropriate HPA axis adaptation and GR alteration. CRF hypersecretion leads to blunted adrenocorticotropic hormone response to CRF, which suppresses cortisol output. Suppressed cortisol release from dysregulated stress feedback prevents HPA axis self-regulation, which in turn perpetuates a hyperaroused state in stress response pathways. Exposure to single-event traumatic stress upregulates GRs in the hippocampus and prefrontal cortex [171; 172; 173]. HPA stress response pathways are intimately linked with neurotransmitter systems and key brain regions in PTSD.

The neural circuitry that mediates fear memory involves complex interactions among three brain centers: the hippocampus, involved in short-term memory and contextual fear; the amygdala, involved in conditioned fear response; and the medial prefrontal cortex, which mediates suppression of subcortical (e.g., amygdala, hippocampus) responses. Several neurotransmitter systems serve as chemical messengers in this neurocircuit. Alterations in these transmitter systems reflect a dysregulated stress response and substantially impact conditioned fear response and the consolidation and retrieval of traumatic memories [174; 175].

Suppressed cortisol outputs prompt activation of the CRF-norepinephrine cascade, which enhances and prolongs stress response. Stress response is further promoted by degraded regulatory control resulting from alteration in serotonin, gamma-aminobutyric acid (GABA), glutamate, neuropeptide Y, and opioid transmitter systems. Norepinephrine enhances the encoding of fear memories, glucocorticoids block the retrieval of emotional memories, and elevated noradrenergic activity and cortisol suppression enhance the encoding of traumatic memories, suppress the inhibition of memory retrieval, and possibly account for intrusive trauma memories in PTSD. The glutamate/N-methyl-D-aspartate (NMDA) receptor system mediates long-term potential and may further promote conditioning and consolidation of traumatic memories.

An increase and upregulation of GRs in the hippocampus contribute to damage in hippocampal structure and function. Hippocampal damage promotes activation of and failure to shut down stress responses, contributes to impaired extinction of conditioned fear, and facilitates generalization of learned fear to other contexts. This in turn disrupts the ability to discriminate safe from unsafe contexts. Exaggerated amygdala responses promote the activation of stress responses and acquisition of fear associations and underlie hyperarousal and avoidance symptoms in PTSD. Impaired prefrontal cortical function accounts for the loss or reduced ability to suppress stress responses and fear associations generated by the amygdala, thereby interfering with fear extinction [176; 177; 178].

The development of PTSD following trauma exposure results from interactions among genetic variation, early environmental exposures (e.g., childhood abuse), and adult brain function and structure. Chronic stress exposure in childhood leads to altered neurochemical signaling that adversely affects neuronal plasticity and growth in the developing brain, resulting in structural and functional changes in key brain regions that elevate the risk of PTSD. These functional alterations in specific brain regions manifest as poorly contextualized fear memories involving the hippocampus, deficient fear extinction involving the ventromedial prefrontal cortex, reduced reward responsiveness involving the nucleus accumbens, and heightened fear response involving the amygdala and dorsal anterior cingulate cortex [179].

ASSESSMENT AND IMMEDIATE POST-TRAUMA ACTION

Individual reaction to trauma during the immediate postexposure period is varied, complex, and unstable. Based on the available evidence, the care of a patient in the first few days following a traumatic event should focus on the provision of practical and emotional support, approaches to manage distress and access social supports, and promotion of positive expectations [6].

SAFETY AND BASIC NEEDS

In some contexts of repeated trauma exposure, victims presenting for treatment may remain vulnerable to ongoing threat and further trauma. With first responders, victims of domestic violence, and victims of sexual assault perpetrated in their current job setting or by an intimate partner, treatment may be affected by returning to unsafe environments. In the presence of ongoing risk, interventions should initially focus on ensuring safety, stabilization, and symptom management, instead of initiating the trauma-focused components of treatment. Ensure, to the extent possible, the safety, security, and survival needs of the patient by helping secure food, hydration, clothing, hygiene, and shelter. This will include promoting patient stabilization and the importance of sleep and replacing medications that are destroyed or lost. Patients also benefit from education on the process they are experiencing. Patients should be counseled regarding limiting ongoing harm by reducing the use of alcohol, tobacco, caffeine, and illicit psychoactive substances, if needed. Family, friends, and community resources should be identified. From the initial point of contact onward, it is vital to establish a working treatment alliance with the patient and maintain a supportive, nonblaming, non-judgmental stance [6; 68].

ACUTE STRESS RESPONSE

Following any extreme stressful event, most of those suffering from acute traumatic stress reactions are easy to identify, as they tend to appear stunned, pale and faint, or tremulous. Some suffering from trauma may not be actual victims, but witnesses or rescuers deeply affected by what they saw. Some may not appear traumatized because they remain highly active. The acute stress response (ASR) is a transient condition that develops in response to trauma exposure, with onset of signs and symptoms occurring during exposure, within minutes of the traumatic event, or several hours to days post-trauma. The physical, cognitive/mental, emotional, and behavioral symptoms of ASR resolve within several days in most cases.

Typical symptoms include depression, fatigue, anxiety, decreased concentration or memory, and hyperarousal. ASR is not a DSM diagnostic entity because it reflects a normal acute response to a terrifying, horrific, or life-threatening experience. The intensity of ASR symptoms is unrelated to the risk of developing PTSD, an important point to convey to patients [68].

Individuals exposed to a traumatic event exhibiting the following responses should be screened for ASR, though no specific screening tool is needed [68]:

- Physical: Exhaustion, hyperarousal, somatic complaints, symptoms of conversion disorder
- Emotional: Anxiety, depression, guilt, hopelessness
- Cognitive: Amnestic or dissociative symptoms, hypervigilance, paranoia, intrusive re-experiencing
- Behavioral: Avoidance, problematic substance use

While many survivors of trauma experience normal stress reactions, some can be overwhelmed by panic or grief and may require immediate crisis intervention. Signs of panic include trembling, agitation, rambling speech, and erratic behavior. Signs of intense grief may be loud wailing, rage, or catatonia. In these cases, practitioners should quickly establish therapeutic rapport, ensure safety, acknowledge and validate the experience, and offer empathy. Medication may be appropriate and necessary [68].

ADDITIONAL ASSESSMENT

Several additional factors involving acute medical/behavioral issues should be considered and assessed in the immediate post-trauma period [68]:

- Address acute medical issues by providing appropriate medical/surgical care or referral, managing substance intoxication or withdrawal, and assessing inability to care for self. Provide medications for specific symptoms, such as sleep or pain, as needed.
- Address acute behavioral issues by stopping self-injury or mutilation, assessing danger to self or others from suicidal or homicidal behavior, helping remove any ongoing exposure to stimuli associated with the traumatic event, and securing any weapons.
- Carefully consider the following interventions if needed to ensure safety:
  - Safe accommodation to protect against further trauma
  - Voluntary inpatient admission if suicidal
  - Restraint/seclusion only if less }restrictive measures are ineffective
- Follow legal mandates, which may include:
  - Reporting of violence or assault
  - Confidentiality of the patient
  - Attending to chain of evidence in criminal cases (e.g., rape, assault)
  - Involuntary commitment procedures, if needed
  - Mandatory testing
- Educate and normalize observed psychologic reactions to the trauma in all persons, including those with few symptoms or no clinically significant symptoms.

PSYCHOLOGIC FIRST AID

Psychologic first aid is widely recognized as a beneficial early intervention in the immediate post-trauma period. It is performed with the objective of protecting victims from future harm, reducing physiologic arousal, mobilizing support for those in greatest distress, keeping families together and facilitating reunion (following disaster or terrorism), providing information and fostering communication and education, and using effective risk communication techniques [68].

The eight core components of psychologic first aid are [180]:

- Engaging the affected person using a non-intrusive, compassionate, and helpful approach
- Ensuring immediate and ongoing safety and providing physical and emotional comfort
- Stabilizing the overwhelmed, distressed patient with reassurance and containment
- Obtaining information that helps prioritize needs and concerns, and selecting subsequent interventions
- Providing the patient with practical assistance to address immediate needs and concerns
- Connecting the patient with social supports by helping structure contacts with primary support persons and/or community helping services
- Educating the patient on stress reactions and coping
- Linking the patient with services and informing of services that might be needed in the future

SECONDARY PREVENTION OF PTSD IN THE IMMEDIATE POST-TRAUMA PERIOD

The long-standing observation that at least 75% of persons exposed to a traumatic event do not develop PTSD, along with the understanding that traumatic event memory is not permanently stored shortly after trauma exposure, has prompted the hypothesis that correctly timed intervention may disrupt trauma memory storage and prevent the development of PTSD. As such, some experts believe that intervention timed for delivery shortly after exposure to a traumatizing event may prevent the development of PTSD. Memory consolidation refers to the transition of trauma event memory from an unstable labile state into a stable state, at which point it becomes stored as long-term memory. Secondary prevention intends to disrupt the process of trauma memory consolidation in the immediate post-trauma period. The "golden hours" of opportunity for intervention to disrupt memory consolidation is thought to range from moments after the event up to 72 hours post-exposure [169; 181]. Selection of approaches for secondary prevention have been informed by the findings that a repressive coping style, whereby the patient utilizes a cognitive and emotional strategy of ignoring and diverting attention from threatening or disturbing memory, offers substantial protection from the development of PTSD [181; 182].

According to the Veterans Health Administration and the U.S. Department of Defense, there is insufficient evidence to recommend the use of trauma-focused psychotherapy or pharmacotherapy in the immediate post-trauma period for the selective prevention of PTSD.

(https://www.healthquality.va.gov/guidelines/mh/ptsd. Last accessed March 18, 2021.)

Strength of Recommendation: N/A

Interventions to Avoid

Research has identified interventions that interfere with the spontaneous recovery process by promoting consolidation and increasing the risk of PTSD [181]. These include psychologic debriefing and benzodiazepines.

Psychologic Debriefing

Psychologic debriefing describes a class of interventions delivered 24 to 72 hours post-trauma, of which ventilation (i.e., describing the experience in detail) is a core component. Because avoidance, suppression, and denial are effective coping responses in reducing post-traumatic distress and facilitating the dissipation of distress symptoms during this period, psychologic debriefing should not be used, as it enhances trauma memories and interferes with spontaneous recovery. No benefit has been found with psychologic debriefing, and patients receiving psychologic debriefing have shown higher rates of PTSD diagnosis, work impairment, and worse overall functioning [181; 183].

Benzodiazepines

Benzodiazepines are commonly used to calm the fear and distress that can follow a traumatic event. Until the 1970s, benzodiazepines (or sodium pentothal) were combined with psychologic debriefing and traumatized persons were administered the "benzodiazepine interview" to help them fully re-experience the event as they recalled the details. Benzodiazepines are associated with enhanced access to emotional memories, and their use in the immediate post-trauma phase interferes with normal spontaneous recovery and is associated with higher PTSD rates [169; 181; 184].

Emerging Pharmacologic Options for Secondary Prevention

Morphine

Studies have suggested that modulation of the endogenous opioid system by μ-opioid pathway activation may inhibit fear consolidation and enhance extinction by impairing the molecular mediators of fear consolidation [185]. Several studies have found that early post-trauma morphine administration may protect against the development of PTSD. As most pharmacotherapies are used for symptom reduction following PTSD onset, these results suggest the potential value of morphine as secondary prevention, such that early post-trauma administration at sufficient dose may help prevent PTSD development.

A prospective study assessed 24 children admitted for hospitalization to an acute burn unit and again six months later [186]. While all received morphine, a significant inverse correlation was found between morphine dose and rate of PTSD, with higher-dose morphine strongly associated with a lower rate of PTSD development [187]. These findings were extended to child burn victims 4 years of age or younger by Stoddard et al., who found at three to six months post-discharge that higher morphine dose correlated with lower parent-assessed PTSD symptoms, with highest correlation found between higher morphine dose and amount of decrease in arousal symptom cluster [186].

Another study assessed 155 consecutive patients during hospitalization for traumatic injury, and again at three months [188]. At follow-up, 14% met the diagnostic criteria for PTSD, and these patients had received significantly less morphine than those who did not develop PTSD. After controlling for injury severity, gender, age, and type of injury, elevated-dose morphine in the initial 48 hours after trauma remained significantly associated with lower rates of PTSD development and severity [189]. The brief three-month follow-up may have prevented findings of greater significance between morphine and PTSD possibly afforded by longer follow-up [188].

The effect of morphine administration during early resuscitation and trauma care on PTSD risk was studied in 696 U.S. military personnel who sustained warzone injuries but not serious TBI in Iraq. At six-month follow-up, 243 were diagnosed with PTSD and 453 were not. Among those who developed PTSD, 61% received morphine; in those who did not develop PTSD, 76% received morphine. Following correction for injury severity, age, amputation status, mechanism of injury, and presence or absence of mild TBI, morphine use was independently and significantly associated with a reduced risk of PTSD. No dose-effect relationship was found, and reduced PTSD rates were solely associated with use or non-use of morphine [188]. The authors of these trials suggest that morphine may favorably affect fear conditioning and consolidation of traumatic memory when given acutely following traumatic exposure.

Hydrocortisone

As discussed, normal response to stress stimulates a chain of reactions in the adrenal cortex to synthesize and release glucocorticoids such as cortisol and hydrocortisone. These hormones are instrumental in adaptation to stress, with a main function involving the regulation and containment of sympathetic and parasympathetic responses to stress [190].

Studies have found significantly lower urinary cortisol levels immediately post-trauma in patients who developed PTSD relative to those who did not. These results, together with several other lines of evidence, suggest that proper HPA axis reactivity and activation to trauma exposure is instrumental for spontaneous remission. A potential explanation is that cortisol may decrease the fear response and possibly interfere with consolidation of the traumatic memory, supported in part by findings that benzodiazepines given immediately post-trauma suppress normal HPA activation to calm and sedate but increase risk of PTSD development [181].

To expand preclinical findings and retrospective studies that found substantially lower rates of PTSD in patients administered hydrocortisone immediately following medical trauma, a prospective study of hydrocortisone as secondary prevention was performed in patients with heightened risk of PTSD (i.e., high distress levels consistent with ASD criteria) in order to produce an enriched sample [191; 192]. Following emergency admission for serious injury, 25 patients were randomized to either IV hydrocortisone 100–140 mg or placebo within six hours of injury. Compared to placebo, hydrocortisone led to reduced rates of ASD (20% vs. 66.7%), PTSD at one-month follow-up (12.5% vs. 37.5%), and PTSD at three-month follow-up (0% vs. 37.5%) [181; 193]. A separate systematic review of pharmacologic interventions for the prevention of PTSD in adults found moderate-quality evidence for the efficacy of hydrocortisone [194].

ASSESSMENT AND MANAGEMENT IN THE INTERMEDIATE POST-TRAUMA PERIOD

When psychologic distress severe enough to interfere with important areas of psychosocial functioning persists during the four weeks after trauma exposure, the post-trauma reaction is no longer a normal adaptive response (ASR) and the patient is considered to have ASD. Assessment should be performed to identify persons who meet the criteria for ASD, sub-threshold yet clinically significant distress and impairment, or incapacitating acute psychologic or physical symptoms [68].

Following exposure, some persons will develop a diagnosable disorder, many will experience sub-threshold symptoms, and others will not develop clinically significant symptoms. Stepped care may be employed to help individuals receive care that matches the severity and complexity of need. This is performed by assessment to identify symptom severity and complexity of need. Triage allows patients with great serious immediate need to be rapidly identified and linked to appropriate resources; others with less severe symptoms and impairment are also identified for care. All patients should be assessed for ASD [6].

ASSESSMENT OF CURRENT MEDICAL AND FUNCTIONAL STATUS

The central goal of post-trauma care is to address immediate physical health problems and assist in initiating a return to pre-trauma level of functioning. This is achieved by understanding the current and pre-trauma state of health and functioning [68]. Medical status should be obtained for all persons who present with trauma symptoms via a complete history, physical exam, and neurologic exam. It is important to inquire about the use of prescribed medications (and adherence), alcohol use, and recreational drugs. Cognitive function can be assessed through a mini-mental status examination.

The history, physical exam, and neurologic exam findings may initiate closer investigation into other factors. For example, a toxicology screen may be indicated by the symptom presentation. Patients with focal neurologic findings or possible head injury should undergo additional radiologic assessment, and laboratory studies may be ordered to rule out medical conditions that may account for symptoms of an acute stress reaction.

A focused psychosocial assessment of active stressors, losses, current social supports, and basic needs (e.g., housing, food, financial resources) should be performed. Pre-existing psychologic conditions, such as past history of PTSD, major depressive disorder, or substance use disorder, should be noted and may indicate a greater risk for PTSD development. Patients with pre-existing psychologic conditions should be referred to a psychologic health specialist or emergency hospitalization, if needed. Finally, a functional assessment of the patient's general appearance and behavior, subjectively impaired function, baseline versus current level of functioning, and family and relationship functioning can be useful in treatment planning.

It is vital to provide all patients with education and normalization. This will help to normalize reactions to trauma, improve coping, enhance self-care, facilitate recognition of significant problems, and increase knowledge of and access to care.

RISK FACTORS

Trauma survivors who exhibit symptoms of functional impairment should be screened for the following risk factors for developing ASD and PTSD [68]:

- Pre-traumatic factors: Ongoing life stress
  - Lack of positive social support
  - Young age at time of trauma
  - Personal or family history of psychiatric conditions or substance misuse
  - History of traumatic events or abuse
  - History of PTSD
- Peri-traumatic or trauma-related factors:
  - Severe trauma
  - Physical injury to self or others
  - High-risk trauma, such as combat, killing another person, torture, rape, or assault
  - High perceived threat to life of self or others
  - Mass trauma
  - History of peri-traumatic dissociation
- Post-traumatic factors:
  - Ongoing life stress
  - Lack of positive social support
  - Bereavement or traumatic grief
  - Major loss of resources
  - Negative social support (i.e., a blaming environment)
  - Poor coping skills
  - Distressed spouse or children

ASD DIAGNOSIS

Persistence of significant distress and/or diminished social or occupational functioning longer than 2 days but less than 30 days post-trauma suggests the presence of ASD. ASD and PTSD share substantial symptom overlap, and the primary distinction is timeframe, as PTSD diagnosis requires symptom presence 30 days or longer post-trauma.

A review of 22 studies found that more than 50% of trauma survivors with ASD subsequently meet the criteria for PTSD but that most individuals with PTSD did not initially have ASD [195]. However, the DSM-5 states that roughly 50% of persons who eventually develop PTSD initially present with ASD and that ASD prevalence varies by trauma [1]. An ASD diagnosis is made in less than 20% of cases following traumatic events without interpersonal assault (including 13% to 21% of cases following motor vehicle accidents, 14% of cases following mild trauma injury, 10% of cases following severe burns, and 6% to 12% of cases following industrial accidents) and 20% to 50% of cases following interpersonal trauma events, such as assault, rape, and witnessing mass shootings [1].

Substantive revisions are evident in the ASD concept and criteria in the DSM-5 compared with the previous DSM-IV-TR. ASD was moved from the anxiety disorders category into a new trauma-specific category. Certain diagnostic criteria, such as the requirements for dissociative symptoms and a fear, helplessness, or horror response, were eliminated, and ASD is now viewed as an acute stress response [6]. Diagnosis is no longer based on

EARLY INTERVENTION FOR PTSD (4 TO 30 DAYS POST-TRAUMA)	
Evidence of Benefit	**Intervention Modality**
Greatest benefit with the highest level of evidence	Brief cognitive-behavioral therapy (four to five sessions)
Some positive benefit	Social support Psychoeducation and normalization
May be effective with multiple group sessions	Groups that provide trauma-related education, coping skills training, social support
Unknown benefit	Spiritual support Psychologic first aid (>4 days post-event)
No evidence for or against the use of these drug therapies to prevent the development of ASD or PTSD	Prazosin Atypical antipsychotics Propranolol Imipramine Other antidepressants Anticonvulsants
Recommend against using	Typical antipsychotics
Strongly recommend against, may be harmful	Individual or group psychologic debriefing Formal psychotherapy in asymptomatic individuals Benzodiazepines
Source: [68]	*Table 2*

specific symptom clusters. Instead, it now requires the presence of nine or more symptoms from any of the five symptom categories of intrusion, negative mood, dissociation, avoidance, and arousal, with these symptoms beginning or worsening following the traumatic event(s) exposure [1].

SECONDARY PREVENTION OF PTSD IN THE INTERMEDIATE POST-TRAUMA PERIOD

For acutely traumatized persons meeting the diagnostic criteria for ASD, those with significant levels of acute stress symptoms more than two weeks post-trauma, and those incapacitated by acute psychologic or physical symptoms, several approaches have been identified that can prevent or minimize the development of PTSD when applied within 30 days post-trauma (***Table 2***). Psychoeducation and normalization should continue during this period, and treatment should only be initiated after psychologic first aid has been provided and basic needs following the trauma have been secured [68].

Psychoeducation and Normalization

Patients and their family members (if appropriate) should be given education on ASD, common symptoms, and the range of effective pharmacologic and nonpharmacologic treatments. Any comorbid medical or psychiatric disorders, the mutual interaction between comorbid and ASD symptoms, and how the treatment plan will address comorbidity should be addressed [68; 196].

Practitioners should work to normalize patient experiences, reduce anxiety, and convey hope that symptoms can be overcome with time and treatment [68]. When medications are prescribed, patients should be given information on the regimen, effects and side effects, and adherence when symptoms begin dissipating [196].

Minimizing social isolation is an important part of treatment, and family and/or other social supports should be identified early in treatment. Patients will benefit from appropriate self-help or treatment groups with peer-to-peer assistance and strategies to counter relationship avoidance [197].

Brief Cognitive-Behavioral Therapy

Brief cognitive-behavioral therapy (bCBT) is the best-validated early intervention for reducing current post-trauma distress symptoms, preventing PTSD, and reducing PTSD severity if it develops [68; 196]. It should only be given to symptomatic patients, especially to those meeting ASD criteria. Delivered in four to five sessions, bCBT combines education, breathing training and relaxation, imaginal and in vivo exposure, and cognitive restructuring. bCBT has been shown to equally benefit survivors of sexual and nonsexual assault and is suggested for initiation not earlier than 14 days post-trauma [68; 196].

ASSESSMENT AND ACTION IN THE EXTENDED POST-TRAUMA PERIOD

Persons with ASD or PTSD may not express concerns over recent traumatic experience in their initial provider contact, but instead may request help for mood disorders, anger, relationship problems, poor sleep, sexual dysfunction, or physical health complaints without mention of trauma. One study found only 11% of primary care patients with PTSD had a medical record mention of their condition. Under-reporting is influenced by PTSD avoidance symptoms, social stigma attached to psychologic problems, fear of discrimination, and added stigma if sexual assault was experienced. Providers should be sensitive to these factors [198].

To understand the origin of presenting problems, providers should routinely ask about recent or remote stressful or traumatic experiences and, if suspected, use a traumatic events checklist. Patients should be administered a brief PTSD screening tool if any checklist events are endorsed. While patients are the focus of assessment questions, clinicians should be sensitive to possible transgenerational trauma, particularly in high-risk groups like children of veterans or holocaust survivors [6].

SIGNS AND SYMPTOMS OF PTSD

In addition to specific PTSD symptoms, the time of onset, frequency, course, severity, distress level, and degree of functional impairment require consideration. The elapsed time following trauma exposure is important in determining PTSD risk and appropriate intervention. Persistence of several symptoms over the initial 30-day postexposure period indicates a developing trauma-related stress disorder, including [68]:

- Recurring thoughts, mental images, or nightmares of the trauma event
- Disrupted sleep
- Changes in appetite
- Anxiety and fear, especially when exposed to trauma-associated events or situations
- Feeling on edge, easily startled, or overly alert
- Feeling depressed or sad or having diminished energy
- Memory problems, including difficulty recalling aspects of the trauma
- Feeling "scattered" and unable to focus on work or activities
- Difficulty making decisions
- Feeling irritable, easily agitated, angry, and resentful
- Feeling emotionally numb, withdrawn, disconnected, or different from others
- Spontaneous crying or feeling a sense of despair and hopelessness
- Feeling extremely protective of, or fearful for, the safety of loved ones

PTSD SCREENING AND ASSESSMENT

Screening and assessment are performed to identify trauma-exposed persons at risk for PTSD. When PTSD is suggested by presentation or screening results, more detailed symptom assessment should follow. Several screening and assessment instruments are available for use when PTSD is suspected. Most are DSM-based, with many upgraded to reflect changes in the DSM-5 from the previous DSM.

Screening tools are used to confirm initial impressions of PTSD but cannot be used for diagnosis. On the other hand, assessment tools are used to confirm positive screening results, provide an indication of symptom or impairment severity, and assist in the arrival of a PTSD diagnosis.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Veterans Health Administration and the U.S. Department of Defense suggest periodic screening for PTSD using validated measures such as the Primary Care PTSD Screen (PC-PTSD) or the PTSD Checklist (PCL).

(https://www.healthquality.va.gov/guidelines/mh/ptsd. Last accessed March 18, 2021.)

Strength of Recommendation: Weak for

Screening Tools

Primary Care PTSD Screen for DSM-5

The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5) is a widely used, five-item questionnaire developed especially for primary care clinicians to screen veterans for PTSD. The prior version of the screen (i.e., PC-PTSD) asked individuals to respond to questions about DSM-IV PTSD symptoms in reference to an experience that was "frightening, horrible, or upsetting," which often led respondents to refer to events that, although stressful, were not considered Criterion A traumas (e.g., divorce). To avoid this, the PC-PTSD-5 asks respondents whether they have experienced prior qualifying trauma(s) (e.g., sexual assault, war). If respondents have not been exposed to any of the qualifying traumatic events, they do not need to complete the remainder of the PC-PTSD-5. If they do endorse prior qualifying trauma(s), they respond to questions about DSM-5 PTSD symptoms related to those trauma(s), including [199]:

- Nightmares or unwanted thoughts about it?
- Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?
- Were constantly on guard, watchful, or easily startled?
- Felt numb or detached from others, activities, or your surroundings?
- Felt guilty or unable to stop blaming yourself or others for the event(s) or any problems the event(s) may have caused?

The PC-PTSD-5 is designed for use as a routine screen for PTSD in primary care. If patient response suggests PTSD, further exploration and additional assessment are required for confirmation [199].

Life Events Checklist for DSM-5

The Life Events Checklist for DSM-5 (LEC-5) is a self-report screen for potentially traumatic events in one's lifetime that assesses exposure to 16 events known to potentially result in PTSD or distress. An additional item is included that assesses for any other extraordinarily stressful event not captured in the first 16 items. The LEC was developed for concurrent administration with the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) and is a valid and reliable stand-alone assessment tool for traumatic exposure, particularly when evaluating the consistency of events that actually occurred with a patient. While effective as a tool to assess exposure to events that can result in PTSD, the LEC-5 cannot assess whether the event was traumatic or measure peri-traumatic emotional experiences [200].

LEC-5 formats include standard self-report to establish if an event occurred, extended self-report to establish worst event if more than one, and interview format to establish if Criterion A is met. For each item (e.g., natural disaster), the respondent checks one of the following:

- Happened to me
- Witnessed it
- Learned about it
- Part of my job
- Not sure
- Does not apply

Assessment Tools

Clinician-Administered PTSD Scale for DSM-5

The CAPS-5 is a 30-item structured interview considered the gold standard in PTSD assessment. It may be used for current past-month PTSD diagnosis, lifetime diagnosis of PTSD, and assessment of past-week PTSD symptoms [201]. The CAPS-5 assesses for all 20 DSM-5 PTSD symptoms and obtains information related to the onset and duration of symptoms, subjective distress, symptom impact on social and occupational functioning, symptom improvement from previous CAPS-5 administration, overall response validity, overall PTSD severity, and dissociative subtypes of depersonalization and derealization [201].

An index traumatic event is initially identified as the basis for symptom inquiry. The CAPS-5 was designed for clinicians and clinical researchers with a working knowledge of PTSD and can also be administered by appropriately trained paraprofessionals. It takes 45 to 60 minutes to administer [201]. The LEC-5 is recommended as a supplement to the Criterion A inquiry in the CAPS-5 [201].

A PTSD severity rating can be determined based on the results of the CAPS-5 [201]:

- 0 Absent: The patient report does not fit DSM-5 symptom criteria.
- 1 Mild/subthreshold: The patient described a problem consistent with symptom criteria but not severe enough to be considered clinically significant. The problem does not satisfy DSM-5 symptom criteria or PTSD diagnosis.
- 2 Moderate/threshold: The patient described a clinically significant problem that satisfies DSM-5 symptom criteria and counts toward a PTSD diagnosis. The problem would be a target for intervention. This severity rating requires a minimum frequency of two times per month or some of the time (20% to 30%) PLUS a minimum intensity of "clearly present."
- 3 Severe/markedly elevated: The patient described a problem that is difficult to manage and at times overwhelming and would be a prominent target for intervention. This severity rating requires frequency of two or more times per week or much of the time (50% to 60%) PLUS a minimum intensity of "pronounced."
- 4 Extreme/incapacitating: The patient described a condition far above threshold that is pervasive, unmanageable, and overwhelming and would be a high-priority target for intervention.

PTSD Checklist for the DSM-5

The PTSD Checklist for the DSM-5 (PCL-5) is a widely used, self-administered assessment validated to confirm suspicion of PTSD from patient screening. The PCL-5 can be used for screening, presumptive diagnosis, or treatment response monitoring in PTSD [202]. Unlike the PCL for the DSM-IV, which had three versions, there is now a single version of PCL-5. The three formats of the PCL-5 include one without a Criterion A component, one with a Criterion A component, and one with the LEC-5 and an extended Criterion A component.

The 20 questionnaire items included in the PCL-5 correspond to DSM-5 symptom criteria for PTSD. Each item is self-rated on a 0–4 scale for each symptom, corresponding to item descriptors of "not at all," "a little bit," "moderately," "quite a bit," and "extremely" [202]. The PCL-5 scores are not compatible with PCL for DSM-IV scores and cannot be used interchangeably.

The PCL-5 can be completed by patients in a waiting room before a session, and it takes 5 to 10 minutes to complete. Interpretation is made by a clinician, and consideration should be given to characteristics of the patient's setting when the PCL severity scores are used to make a diagnosis. The assessment goal should be considered, with a lower cutoff with screening or when it is advantageous to maximize detection of possible cases. A higher cutoff is suggested when the tool is used to make a definitive diagnosis or to minimize false positives [202].

When used to monitor patient progress, research with the previous DSM-IV-based PCL indicated that a 5- to 10-point variation represented reliable change not due to chance and a 10- to 20-point change represented clinically significant change; thus, a minimum threshold of 5 points should be used to determine any treatment response, and a minimum threshold of 10 points used to determine clinically meaningful improvement. Although treatment response scores for PCL-5 are not yet published, a similar scoring range is expected [202].

Cultural/Racial Considerations in Screening

Research involving veterans has explored possible racial/cultural differences in PTSD risk or presentation. While higher PTSD rates have been found in individuals who are black or Hispanic, this is primarily attributable to greater exposure to traumatic stressors. Otherwise, few to no racial or ethnic differences have been found in PTSD prevalence. Researchers have conducted studies of PTSD in ethnic minority Vietnam veteran populations, and while the results are not consistent, the overall finding is that most ethnic minority Veteran groups have a higher rate of PTSD than white veterans [203]. Differences in samples, measures, and whether the interviewer and participant were racially paired affected the results. Ethnic minority veterans were more likely to disclose problems or to engage in treatment when paired with a clinician of the same race [204]. Clinical manifestation and treatment response in combat-related PTSD has also been found to be similar among various races; however, present findings highlight a lack of research focused on understanding cultural factors related to the assessment and treatment of PTSD [68; 205; 206].

DIAGNOSIS OF PTSD

As noted, diagnosis of PTSD is based primarily on the criteria outlined in the DSM, and there have been significant revisions to the criteria with the most recent revision (***Table 3***) [1]. The distinction of acute versus chronic PTSD was removed in the DSM-5. However, the manual does include the subtype of PTSD with delayed expression [1].

The ICD-10 is typically used by administrators, information technology specialists, and coding professionals, while clinicians use DSM-5 diagnoses. For each diagnostic entity in the DSM-5, the ICD code is found in parentheses within the diagnostic criteria box for the given disorder [207].

EVIDENCE-BASED PRACTICE RECOMMENDATION

For patients with suspected PTSD, the Veterans Health Administration and the U.S. Department of Defense recommend an appropriate diagnostic evaluation that includes determination of *Diagnostic and Statistical Manual of Mental Disorders* (DSM) criteria, acute risk of harm to self or others, functional status, medical history, past treatment history, and relevant family history. A structured diagnostic interview may be considered.

(https://www.healthquality.va.gov/guidelines/mh/ptsd. Last accessed March 18, 2021.)

Strength of Recommendation: Strong for

Criticism of DSM-5 Diagnostic Criteria for PTSD

The changes in the DSM-5 have not been without controversy. The absence of complex trauma/PTSD as a PTSD variant or separate diagnostic entity has been criticized [208]. Important dimensions of complex trauma, such as affect dysregulation, are also not included in the diagnostic criteria for PTSD. Impairments in functioning unaddressed by PTSD criteria are frequently referred to as "comorbid conditions," which many consider to be inadequate to describe the wide-ranging symptom constellations of complex trauma [33].

Also absent from the diagnostic criteria is the role of betrayal. When present in the dynamics of the trauma event, betrayal is an important, distinct, and complementary factor that contributes to severity of emotional impact from trauma not attributable to life threat alone. Study of the contribution to PTSD symptom severity from physical injury, perceived life threat, and betrayal found that betrayal was associated with all PTSD symptom clusters and with total severity of PTSD [209].

DSM-5 DIAGNOSTIC CRITERIA FOR PTSD IN ADULTS AND CHILDREN OLDER THAN 6 YEARS OF AGE	
Criterion	**Symptom or Description**
Criterion A: Stressor (both required)	1. Event involving actual or threatened death, serious injury, or sexual violence 2. Exposed to event: Directly; witnessed in person; indirectly by learning close loved one or family member exposed to trauma; repeated or extreme indirect exposure to disturbing details of trauma event, often through work
Criterion B: Intrusion symptoms (one required)	1. Recurrent, involuntary, and intrusive memories 2. Traumatic nightmares 3. Dissociative reactions (flashbacks) that may occur on a continuum from brief episodes to complete loss of consciousness 4. Intense or prolonged distress after exposure to traumatic reminders 5. Marked physiologic reactivity after exposure to trauma-related stimuli
Criterion C: Avoidance (one required)	1. Trauma-related thoughts or feelings 2. Trauma-related external reminders (places, conversations, activities, objects)
Criterion D: Cognitions and mood (two required)	1. Inability to recall key features of the traumatic event (from dissociative amnesia, not from head injury, alcohol, or drugs) 2. Persistent distorted, exaggerated negative beliefs or expectations about oneself, others, or the world ("I am bad," "The world is completely dangerous," "I've lost my soul forever," or "My nervous system is permanently ruined.") 3. Persistent distorted blame of self or others for the cause or consequences of traumatic event 4. Persistent negative trauma-related emotions such as fear, horror, anger, guilt, or shame 5. Loss of interest in (pre-traumatic) significant activities 6. Alienated from others 7. Constricted affect, inability to experience positive emotions
Criterion E: Arousal and reactivity (two required)	1. Irritable or aggressive behavior 2. Self-destructive or reckless behavior 3. Hypervigilance 4. Exaggerated startle response 5. Problems in concentration 6. Sleep disturbance
Criterion F: Duration	Persistence of Criteria B, C, D, and E symptoms longer than one month
Criterion G: Functional significance	Significant symptom-related distress or functional impairment (e.g., social, occupational)
Criterion H: Exclusion	Disturbance not due to medication, substance use, or other illness
Specify if: With dissociative symptoms	The person experiences high levels of either of the following in reaction to trauma-related stimuli: 1. Depersonalization: The experience of being an outside observer of or detached from oneself (e.g., feeling as if "this is not happening to me" or one were in a dream) 2. Derealization: The experience of unreality, distance, or distortion (e.g., "things are not real")
Specify if: With delayed expression	Full diagnosis not met until six or more months post-trauma, though onset of some symptoms may occur immediately
Source: [1]	*Table 3*

Researchers have concluded that when prominent as an element of a traumatic event, betrayal is a core dimension of the psychologic trauma that elevates PTSD risk [210]. However, this is not reflected in the DSM-5 criteria.

Differential Diagnosis of PTSD

Traumatic event exposure can lead to PTSD, PTSD and comorbid psychiatric conditions, or psychiatric conditions absent PTSD. Other common conditions that may develop from trauma experience include depression, anxiety disorders (e.g., panic disorder), generalized anxiety disorder or specific phobias, substance use disorders, and adjustment disorders. A diagnosis of complicated bereavement (formerly traumatic grief) following a traumatic loss should be considered. Associated features commonly found include guilt, aggression, somatic complaints, relationship problems, and impaired occupational functioning. Assessment of associated features is important because they can influence treatment outcome and/or represent therapeutic targets. Specific associated features more common in survivors of prolonged or repeated traumatic events (e.g., childhood sexual abuse, torture) include somatic complaints, interpersonal problems, affective dysregulation, and identity disturbances. The substantial symptom overlap between complex PTSD and borderline personality disorder requires careful assessment for differentiation [6].

While some patients experience several PTSD symptoms, the diagnostic threshold also depends on severity of impaired functioning. In the absence of clinically significant impairment, accurate diagnosis is more likely to be adjustment disorder, anxiety disorder, depressive disorder, or complicated bereavement [64]. PTSD is often diagnosed by providers lacking specialized training in behavioral health, which can lead to overdiagnosis, as when a patient reports one or two post-traumatic stress symptoms, such as nightmares and insomnia. A PTSD diagnosis may also be overlooked in patients with prominent neurocognitive complaints suggestive of TBI. In other patients, prominent neurovegetative symptoms, such as depressed mood and sleep problems, that are more disruptive to daily functioning may overshadow classic PTSD symptoms [64].

GENERAL MANAGEMENT CONSIDERATIONS

FACTORS THAT MAY INFLUENCE TREATMENT OUTCOME

Several factors have been identified that potentially influence treatment retention and outcome and should be considered during treatment planning.

Timing of Treatment

Two randomized trials of single-trauma survivors were designed to address the possible impact on treatment outcome with immediate versus delayed treatment. Both studies found no differences in outcome, and similar outcomes were found in retrospective studies [211; 212; 213; 214]. However, early intervention for PTSD is associated with better depression outcomes, an important finding because this disorder has considerable overlapping clinical and neurobiologic features with PTSD. From a clinical perspective, longer illness duration is associated with a greater level of distress and with other social and occupational problems. For this reason, PTSD treatment should be encouraged as early as reasonably possible. However, it is important to convey the message to patients who experienced trauma some time ago that treatment can be effective regardless of illness duration [6].

Comorbidities

The influence of psychologic comorbidity on treatment response is inconsistent. On one hand, research on depression, generalized anxiety disorder, borderline personality disorder, anger, alcohol use disorder, social alienation, and emotional dysregulation has shown a negative influence on outcome. On the other hand, many other studies have not found this effect, which suggests the influence of comorbidity may be sample-specific [6].

Depression

As discussed, depression is frequently comorbid with PTSD, and early and ongoing suicide risk assessment is essential with this comorbidity. There are as yet no studies examining the sequencing of the treatment of comorbid depression and PTSD. Numerous studies have found that comorbid depression severity negatively influences PTSD outcome, and the outcomes of both conditions were evaluated following an integrating depression and PTSD intervention [215; 216]. Patients received behavioral activation during the first half of treatment and exposure during the second half. Both studies found that behavioral activation improved symptom severity of both disorders. The exposure intervention decreased PTSD severity, and exposure also resulted in significant change in depression accounted for by improvements in PTSD [215; 216]. This suggests that improvements in comorbid depression result from addressing PTSD symptoms; however, patients with severe depression should also be considered for depression-specific techniques [6]. With pharmacologic treatment for comorbid PTSD and depression, patients who show an incomplete or lack of response to antidepressants may benefit from adjunctive treatment with the atypical antipsychotic aripiprazole [217].

An alternative view is that comorbid depression and PTSD represents a trauma-related phenotype (possibly even a subtype of PTSD) that is distinct from depression, reflecting a fundamental dimension of risk for psychopathology following trauma exposure [218]. This has significant implications for treatment. If the comorbidity represents either a distinct phenotype or a subtype of PTSD, then treatment approaches that target only specific aspects of PTSD (e.g., avoidance) may be less effective in the presence of depression [218]. The issue is further complicated by the lack of pharmacotherapy that specifically addresses PTSD. With respect to psychotherapies, treatment recommendations for comorbid depression and PTSD are distinct; there are no clear guidelines for treating the comorbidity [218].

Terminal Illness

Terminally ill patients with PTSD, regardless of cause, are found to exhibit greater emotional distress, lower quality of life, and worse medical prognosis than those without PTSD [219]. The extent that standard treatment for PTSD is appropriate largely depends on the patient's stage of illness. Numerous lengthy and intensive sessions designed for long-lasting PTSD symptom improvement are not appropriate for patients in the final stages of terminal illness; therapy that focuses on maximizing the quality of life is likely to be more beneficial. A stepped care approach is suggested, with initial use of lower-level interventions [220]. In patients lacking response, the decision to increase treatment intensity is guided by patient prognosis. With such an approach, initial treatment can address practical issues such as social connectedness. Subsequent stages may involve providing coping strategies, such as relaxation or cognitive restructuring, with trauma-focused techniques introduced only if required and permitted by prognosis. Standard exposure therapy can be modified to shorten the length of sessions or decrease the intensity of exposure if fatigue is an issue [219].

Traumatic Brain Injury

TBI is often comorbid in combat veterans with PTSD. Both share substantial overlap in symptoms, and when both are present and the TBI is mild, limited research suggests the cognitive deficits are attributable to PTSD. On the other hand, one 2020 study suggests that cognitive deficits are attributable to mild TBI, which increases acute stress symptoms rapidly following trauma and, in turn, results in PTSD development [221].

The effect of mild TBI on PTSD treatment response is unclear due to the absence of high-quality randomized controlled trials. Tentative suggestions support the use of standard CBT, with minor modifications as needed. The authors of one study suggest that prolonged exposure may be helpful for patients with PTSD and a history of mild TBI [222]. The study included 51 veterans, with or without a history of mild TBI, who

had been treated with prolonged exposure at a veterans' PTSD clinic. The analysis also included previously collected data from a controlled trial of 22 veterans randomly assigned to prolonged exposure or present-centered therapy. For both sets of data, the authors found that prolonged exposure reduced PTSD symptom levels; no effect for mild TBI was detected [222]. Therapists can encourage patients to manage mild TBI-related symptoms by using compensatory strategies such as personal digital assistants or scheduling cognitive breaks [223; 224; 225].

Compensation

Studies on whether PTSD treatment outcomes are compromised in patients actively seeking compensation for PTSD have produced mixed findings. However, an investigation of 800 veterans (21% receiving PTSD disability compensation, 30% seeking compensation, and 49% seeking compensation increase) found that veterans pursuing a claim were as likely as veterans with a stable claim to benefit from inpatient care [226].

Therapeutic Alliance and Treatment Expectations

Establishing a good therapeutic alliance is vitally important and improves PTSD treatment outcome, but it is potentially challenging to establish a strong alliance with patients who have experienced traumatic events. Although traumatization and PTSD can challenge a provider's ability to ensure the patient feels safe in the therapeutic relationship, approaches have been identified that ease this process. Patient trust in their provider can be facilitated by conducting the initial assessment and treatment with sensitivity and in the safest environment possible and by conveying genuine empathy and warmth toward the patient. Acknowledging the patient's worst fears of re-exposure to intolerable traumatic memories and the perception of therapy as threatening or intrusive is very important. Patients often experience relief when hearing their provider validate the possible distress from discussing traumatic life events and that the depth and intensity of exploring difficult events and feelings will be their decision. This also helps the patient restore a sense of control, often lost following a traumatizing experience [227; 228; 229].

Importantly, providers should not assume they have any understanding of the traumatic experience or convey this to the patient, unless they have been in armed combat, sexually or physically assaulted, or experienced other similar traumas. Providers should gain a general understanding of the nature of more common trauma experiences by reading relevant material or watching documentaries and/or educational videos. This helps the provider comprehend some of the severity and intensity of the experiences; appreciate the appropriate feelings of rage, fear, and grief expected from these experiences; and improve their ability to meet the expression of these feelings with respect and compassion [68].

The importance of the provider-patient alliance was underscored by a study of 116 PTSD patients receiving prolonged exposure therapy [230]. The strength of the alliance was measured during the course of therapy. Of the 82 study-completing patients, 44 never experienced a rupture in alliance. Of the 38 who experienced a ruptured alliance, 61% experienced a subsequent repair. After controlling for pretreatment PTSD level and total prolonged-exposure session, patients without a rupture in alliance reported the lowest post-treatment PTSD symptom levels, followed closely by patients with repaired ruptures. The highest post-treatment PTSD levels were found in patients with unrepaired alliance ruptures [230].

Patient expectation of treatment outcome is positively associated with actual outcomes, and this effect of treatment expectancy has been found with Vietnam veterans and other patient groups with PTSD and with generalized anxiety disorder, social anxiety, and chronic pain. These findings stress the importance of the clinician taking the necessary time early in the treatment process to clearly explain the nature and expected outcomes of treatment and to convey an attitude of collaboration and optimism [231; 232; 233; 234].

Combat Veterans

Many veterans with PTSD find their relationships with others have changed as a result of their exposure to trauma. They often report difficulty trusting others, are suspicious of authority, dislike even minor annoyances, and generally want to be left alone. The provider may find the veteran with PTSD appearing withholding, negative, or hostile in the initial meeting. Veterans are trained to size people up and will not share what is truly distressing to them if they sense a lack of genuine investment in their well-being. The veteran may prefer to focus on symptoms, which obscures the history behind them and other important details involving psychologic etiology [65; 68].

In addition, seeking behavioral health care has long been stigmatized by military "warrior" culture. Veterans are likely to minimize their impairment and distress as the result of stoic expectations of them when engaging in psychologic trauma-prone activities; training that prepares them for dangerous situations; stoicism and a machismo response instilled by military culture and indoctrination; fear of their diagnosis or avoidance in discussing their war experiences; and fear of negative impact on their military career options. Combat medics are exposed to graphic and horrifying battlefield injuries and deaths and may avoid seeking help because the reliance on them by many others for medical support and psychologic, spiritual, and emotional guidance creates the belief of needing to be self-sufficient [64].

Establishing rapport with these patients can be tenuous, but it is essential on many levels. Providers should not mistake constricted affect or guarded behavior for a personality disorder or defensive character structure. Perceiving the patient as having "an attitude" or personality disorder comorbidity can result in the combat veteran feeling misunderstood, misdiagnosed, and ultimately betrayed by an otherwise competent professional. The provider should adopt a stance of caring and concerned involvement, take what the patient says at face value without judging or labeling this type of behavior, and not withdraw into an "objective professional" role. The provider who can relate honestly and openly is more likely to have a patient who is willing to relate to him/her as a fellow human being and an effective partner in treatment [64; 68].

Refugee Victims of Torture

Therapeutic engagement of refugee and asylum-seeking populations comes with additional issues that may impede the successful development of a therapeutic alliance. Practitioners should be aware of their own ethnocentricity when working with refugees and should strive to be culturally informed, open to culture-specific interpretations of psychologic problems, and aware of differing values and stereotyping, which would make matching treatment with client need easier. Cultural factors influence the decision to seek treatment and interact with social factors, such as region of origin, socioeconomic status, education, and social status, to influence PTSD symptom presentation. While the construct of PTSD is broadly applicable across cultures, the potential existential impact of traumatic experiences may be culture-specific [235; 236].

The need for interpreters may impose problems that can impede therapy if not proactively addressed. To maintain a climate of confidentiality, clients should not know the interpreters. The rationale and potential client response to an intervention should be explained to interpreters to avoid unintended compromise. It is important that clear roles are set and explained. Providers should also understand the risk of vicarious trauma in interpreters, who may have traumatic exposures similar to those described by the patient. Appropriate preparation, debriefing, and clinical supervision can mitigate distress from secondary trauma exposure [237].

Interventions should address other forms of distress potentially resulting from chronic stressors or exposure to war-related violence and loss, including the following issues [238]:

- Violence and uncertainty during trauma may induce anxiety, fear, and helplessness.
- Humiliation from forced impossible choices may lead to feelings of guilt and shame.
- Disrupted relationships, separation, and isolation may lead to grief, depression, and altered interpersonal capacity from fear of relationships, dependency, or extreme self-sufficiency.
- Shattered existential values from trauma may produce loss of faith in humanity, distrust, sensitivity to injustice, and idealizing and/or devaluing of others.
- Anger and aggressive behavior can result from low frustration tolerance, reaction to injustice and betrayal, and defense against shame and guilt.

Individual strengths may emerge with PTSD symptoms during trauma aftermath, with such outcomes as resilience and post-traumatic growth. Clinicians should identify and build on resilience factors in treatment, if appropriate [6].

Motivation for Change

Patient motivation to change has been identified as another variable that influences treatment response. Some patients with PTSD may have difficulty recognizing when their thoughts or behaviors are unhelpful to progress in therapy and will not see any reason to change. The Transtheoretical Model suggests that readiness to change occurs over six stages (pre-contemplation, contemplation, preparation, action, maintenance, and termination) and that each stage requires different therapeutic approaches [239; 240; 241]. According to this model, patients in the early stages of change may not yet recognize their attitudes and behaviors as problematic and are unlikely to benefit from trauma-focused PTSD treatment. These patients may benefit from motivational interviewing techniques that have shown to be useful in facilitating readiness and resolving ambivalence for change in populations such as substance abusers. Motivational interviewing techniques can include psychoeducation, assisting the patient recognizing the pros and cons associated with his or her behavior, and comparing a patient's behaviors to those of the average person without PTSD. Understanding the need to change allows the patient to more seriously consider taking the necessary steps to enact change, such as engaging in trauma-focused therapy [6; 242].

Demographics

The large majority of research in the PTSD field has been conducted on adults between 18 and 65 years of age, with less research on treating PTSD in the elderly and the very young. A long-held assumption is that older adults (65 years of age and older) may be less responsive to PTSD treatment, although there is little supportive evidence. Fortunately, this belief has been refuted by two reviews that found that standard psychotherapies for PTSD (such as CBT) do benefit older adults, with additional benefit obtained by adding a narrative life-review approach to standard CBT [243; 244; 245]. Evidence-based treatments for PTSD, such as CBT, are also considered effective for preschool children (younger than 6 years of age), and other modalities (e.g., play therapy, EMDR) may be useful if applied in developmentally appropriate ways [246; 247].

Treatment outcome is found to be largely unaffected by other demographic variables, such as marital status, employment, and level of education [245; 248; 249]. Epidemiologic studies consistently show higher PTSD prevalence in women versus men, and while the reason for this is not clarified, it is possible the difference may be explained by trauma type, with women more likely to suffer interpersonal violence perpetrated by someone they know and trust. However, this does not entirely account for the gender difference in PTSD, as findings indicate that women are at greater risk for developing PTSD than men even

when they are exposed to similar types of trauma [250]. Some studies of gender and treatment outcome have shown that women respond better to psychotherapy or that gender does not significantly influence outcome [249; 251]. Other studies suggest that women respond better to pharmacologic treatments for PTSD than men, but this finding may be accounted for by other factors [252]. Additional research is needed to draw more definitive conclusions regarding gender differences in treatment outcomes. Overall, women are somewhat more likely to seek PTSD treatment than men [253; 254].

Treatment Setting

In some circumstances, the delivery of PTSD treatment in settings with exposure to ongoing stress and trauma is unavoidable. These settings include immigration detention facilities, refugee camps, correctional facilities, theaters of combat, and where domestic violence is a threat. Treatment delivery under these conditions can be complicated by the degree of stress inherent in the circumstance, as well as by the potential for further trauma exposure, short and unpredictable lengths of stay, lack of access to mental health history, and client reluctance to disclose important information due to fear of compromising their legal status, application for asylum, or deployment status. Although the delivery of care for PTSD in challenging environments has not received sufficient research attention, two studies have shown promising results when delivering PTSD therapy to individuals in a Ugandan refugee camp [6; 255; 256].

TREATMENT GOALS

Treatment goals should be established collaboratively with the patient after the initial assessment and guided by a comprehensive assessment of the individual and their personal priorities. These treatment goals are then collaboratively reviewed and modified as needed at regular intervals during the treatment process. Optimally, the goals should follow the acronym SMARTER, which stands for specific, measurable, attainable, relevant, time-bound, evaluate, and re-evaluate [6].

The first treatment goal is usually the reduction of PTSD and related symptoms, with other common targets being improvements in comorbid depression, anxiety, anger, and guilt. In patients subjected to protracted child sexual abuse or torture, the initial focus often addresses symptoms of dissociation, impulsivity, affect dysregulation, somatization, and interpersonal problems [6; 257; 258].

The evidence-based literature recommends symptom reduction as the primary overall objective, but practitioners should also address broader patient wellness issues, such as daily functioning and quality of life. Achieving optimal psychosocial functioning is just as vital as symptom reduction, and improved psychosocial functioning may actually be the primary goal for patients with long-term PTSD [6].

Psychosocial rehabilitation can make a valuable contribution to improving functional ability and facilitating recovery by minimizing problems such as homelessness, social inactivity, high-risk behaviors, and unemployment. In appropriate patients, providing targeted clinical and disability management interventions can help reduce or prevent further PTSD-associated disability by improving role functioning and assisting patients in developing the skills and resources specific to their individual needs [6; 258; 259].

Thus, social reintegration and vocational rehabilitation needs should be addressed during the initial assessment and treatment planning. Also during this initial phase, the social support network of the patient should be reviewed and addressed if needed. The family and/or a broader system of care should be engaged, provided with education on PTSD, and involved as an element of collaborative care and the recovery plan [6].

THERAPY SELECTION

The overall objective of PTSD therapy is to treat the four core symptom clusters of intrusive re-experiencing, avoidance, negative alterations in cognitions and mood, and hyperarousal. Psychotherapy is the backbone of PTSD therapy, with pharmacotherapy used as an adjunct if necessary.

Primary care clinicians should be aware of the range of therapeutic options along with their advantages and disadvantages (e.g., time commitment, side effects, risks) and be able to explain these to the patient.

Therapies for PTSD are broadly divided into psychotherapies, pharmacotherapies, and adjunctive or supplemental treatment modalities. Providers and patients alike are faced with important decisions involving the type, number, frequency, and dose of psychotherapy and pharmacologic interventions [68].

Although PTSD therapy research has identified several medications and psychotherapies as first-line treatments, these approaches are much more equivalent in effectiveness than many clinicians realize. Patient preference and treatment approaches with which the provider has the most training or expertise often determine the initial therapeutic approach [68].

The level or intensity of care is guided by illness trajectory, including the degree of chronicity and severity, observed outcomes, and previous therapies. Active follow-up helps determine the level of care each patient requires over time. The provider and patient may determine that psychotherapy alone will be the first-line therapy. If the patient does not sufficiently respond to a period of treatment, the therapeutic intensity can be "stepped up" by adding medication, such as a selective serotonin reuptake inhibitor (SSRI), to the ongoing psychotherapy and reassessing whether additional measures are needed to address comorbid conditions. A helpful approach is to coordinate patient care using a primary care-based collaborative care approach that includes care management, as these approaches have been shown to be useful in the management of depression, chronic pain, chronic fatigue, and other conditions [68].

GENERAL PROFESSIONAL ISSUES

The practice recommendations in PTSD treatment guidelines are made on the assumption of treatment delivery by optimally trained providers, such as specialist trauma-focused interventions by psychiatrists, psychologists, and other specifically trained mental health practitioners, with occupational therapists, rehabilitation counselors, and social workers addressing family, social, and occupational recovery and rehabilitation issues. However, primary care providers often have an established patient relationship that facilitates holistic care and support to the patient and family over time. Chaplains and other pastoral care providers can also play an important role in military settings and following large-scale disasters in the civilian community. Primary care providers are well placed to assume overall care management, make appropriate referrals, and coordinate the contribution of other practitioners when several providers are involved in the care of a patient. The family and carers of the patient can play a critical role in support and recovery. Optimal care of the patient with PTSD involves effective collaboration between all relevant parties [6].

While a practice guideline corollary is that practitioners should not deliver interventions beyond their level of training and experience, this may not always be possible in rural and remote areas where a general practitioner may be the sole health professional in the area. Primary care providers are often responsible for patient care under these circumstances and are unlikely to have the time or training to implement the full range of recommended interventions. They can still play an important role in caring for patients with PTSD through screening, assessment, pharmacotherapy, and possibly by providing general psychologic interventions like psychoeducation and simple arousal management. Primary care practitioners can also support and monitor patients who use self-help materials or Internet-based modalities. When possible, patients should be referred to appropriately-trained mental health practitioners for specialist treatment and ongoing consultation with the primary care practitioner [6].

PROVIDER SELF-CARE

Practitioners involved in post-traumatic health care should have an understanding of the potentially adverse impact on their own emotional wellness. General stress, depression, substance abuse, and professional burnout can result from repeated exposure to the traumatic experiences of others and from the intense distress that often occurs when patients recount their trauma experiences. Also referred to as compassion fatigue, this state can adversely impact the clinical skills of the provider and consequently patient care. Providers are at greater risk when they do not place appropriate limits on the nature and size of their caseload and do not receive sufficient training and support [260]. Self-care responsibilities should be shared by the practitioner, their employer, and their professional body. Providers working in rural and remote communities are more susceptible to developing stress-related problems because isolation is a risk factor. In this type of setting, routine training and support may need to be accessed remotely via the Internet and teleconferencing [261].

PSYCHOTHERAPY APPROACHES

Psychotherapy interventions are aimed at reducing symptom severity, improving overall patient functioning (especially in social and occupational arenas), and improving quality of life. Psychotherapy for PTSD may also have benefits in improving comorbid physical health conditions, but this is not specifically the focus of treatment [68].

For PTSD, psychotherapy approaches with the strongest empirical validation fall broadly within the category of trauma-focused psychotherapy or stress-inoculation training. Trauma-focused psychotherapies for PTSD encompass psychologic interventions based on learning theory, cognitive theory, emotional processing theory, fear-conditioning models, and other theories. They include a variety of techniques commonly involving exposure and/or cognitive restructuring (e.g., prolonged exposure, cognitive processing therapy [CPT], and EMDR) and are often combined with anxiety management or stress-reduction skills focused specifically on alleviating the symptoms of PTSD. Psychoeducation is an important component in all interventions, and CBT that is not trauma-focused is less effective [68].

The approaches most extensively studied in PTSD are grouped into four main categories based on the therapeutic components most emphasized or the specific bundling of therapy components, although there is overlap [6; 68]. These groups are exposure-based therapies, cognitive-based therapies, stress-inoculation training, and EMDR. While these intervention types are described separately, they have overlapping features and are often used in combination, as with the common approach of using psychoeducation, anxiety management, exposure, cognitive restructuring, and PTSD relapse prevention [6].

Exposure-based therapies emphasize in vivo, imaginal, and narrative (oral and/or written) exposure and often include elements of cognitive restructuring (e.g., evaluating the accuracy of beliefs about danger), relaxation techniques, and self-monitoring of anxiety. Examples include prolonged exposure therapy, brief eclectic psychotherapy, narrative therapy, written exposure therapies, and many cognitive therapies that incorporate in vivo and imaginal/narrative exposure.

Cognitive-based therapies emphasize cognitive restructuring (i.e., challenging automatic or acquired beliefs connected to the traumatic event, such as beliefs about safety or trust) and also include relaxation techniques and discussion/narration of the traumatic event orally and/or through writing. Examples include cognitive processing therapy and various cognitive therapies.

Stress-inoculation training emphasizes breathing retraining and muscle relaxation. However, it also includes cognitive elements (e.g., self-dialogue, thought stopping, role playing) and often exposure techniques (e.g., in vivo exposure, narration of traumatic event).

EMDR is distinguished by the use of alternating eye movements but closely resembles other CBT modalities by including an exposure component combined with a cognitive component and relaxation/self-monitoring techniques.

TRAUMA-FOCUSED COGNITIVE-BEHAVIORAL THERAPIES

Trauma-focused CBTs are a group of trauma-focused psychologic treatments derived from behavioral and cognitive theories that involve short-term structured interventions that address the emotional, cognitive, and behavioral sequelae of traumatic event exposure. Although psychoeducation and symptom management strategies (notably arousal reduction) are often included, the two core interventions are exposure and cognitive restructuring [6].

The Veterans Health Administration and the U.S. Department of Defense recommend individual, manualized trauma-focused psychotherapies that have a primary component of exposure and/or cognitive restructuring for patients with PTSD, including prolonged exposure (PE), cognitive processing therapy (CPT), eye movement desensitization and reprocessing (EMDR), specific cognitive behavioral therapies for PTSD, brief eclectic psychotherapy (BEP), narrative exposure therapy (NET), and written narrative exposure.

(https://www.healthquality.va.gov/guidelines/mh/ptsd. Last accessed March 18, 2021.)

Level of Evidence: Strong for

Exposure Therapy

Exposure therapy for PTSD, now termed prolonged exposure, is almost universally considered the cornerstone of effective, evidence-based psychologic treatment of PTSD [6; 68; 262; 263]. Prolonged exposure therapy is based on the fundamental principle of habituation; by exposure to the dreaded fear-provoking stimulus for a sufficient duration, the conditioned emotional response to traumatic stimuli becomes extinguished. By learning that nothing bad, horrible, or catastrophic will occur from exposure to traumatic stimuli, the patient experiences less anxiety when confronted by trauma-related stimuli and avoidance of feared situations is reduced or eliminated [262; 263].

Prolonged exposure is often included as a component with other approaches, termed CBT-mixed therapy. Elements of CBT-mixed therapy may include psychoeducation, self-monitoring, stress management, relaxation training, skills training, exposure (imaginal, in vivo, or both), cognitive restructuring, guided imagery, mindfulness training, breathing retraining, crisis/safety planning, and relapse prevention [263].

This therapy consists of exposure within one session (within-session habituation) or across a series of sessions (between-session habituation) and involves three components:

- Psychoeducation addressing common reactions to trauma and the cause of chronic post-trauma problems
- Imaginal exposure, whereby memories of traumatic experiences are repeatedly confronted in a controlled and safe environment
- In vivo exposure, whereby feared and avoided trauma reminders (situations or activities) are gradually approached and confronted

Effective outcomes are achieved by grading the exposure intensity, typically by using a hierarchy, prolonging the exposure until the anxiety has reduced, and repeating the exposure until the level of evoked anxiety is minimal. Treatment is individualized, with standard treatment consisting of 8 to 15 sessions conducted once or twice weekly for 90 minutes each. Treatment duration can be shortened or lengthened depending on the patient's needs and progress [6; 262].

Adverse effects with prolonged exposure include mild-to-moderate increases in PTSD symptoms, distress, anxiety, depression, and other negative emotions while traumatic experiences are emotionally processed. These increases in distress are often temporary or transient and are not associated with unsuccessful outcomes. A key study found the minority of subjects who experienced consistent symptom exacerbation showed benefit from prolonged exposure therapy comparable to those with less exposure-induced distress. Symptom exacerbation was also unrelated to premature dropout [262; 264].

Comorbid psychiatric conditions are found in the majority of PTSD patients seeking clinical care, and concerns have been raised over the possible negative effect of prolonged exposure in patients with comorbidity. A 2012 study concluded that standard exposure therapy can be applied in PTSD patients with dissociation, moderate-to-severe depression, mild borderline personality disorder, and substance abuse. Prolonged exposure can also be effectively and safely applied within a treatment program that monitors and addresses comorbidity in PTSD patients with comorbid substance dependence, psychosis, severe borderline personality disorder, acute suicidality, and recent suicidal or serious non-suicidal self-injury [265]. A 2015 follow-up review reported similar findings. According to the authors, available research of prolonged exposure as treatment for patients with PTSD indicates that comorbid disorders (e.g., depression, anxiety/substance use/personality/psychotic disorders) and additional symptomatic features (e.g., suicidality, dissociation, negative cognitions/emotions) either decline along with symptoms of PTSD or do not change as a result of prolonged exposure therapy [266].

However, the U.S. Department of Veterans Affairs and the U.S. Department of Defense states the use of prolonged exposure is problematic in some patients with complicated PTSD symptoms [68]. As such, it has been abandoned by some clinicians who cite as rationale the high rates of attrition, suicide, dissociation, destructive impulsivity, and chaotic life problems associated with prolonged exposure.

Cognitive Therapy

Cognitive therapy is based on the theory that the individual's perception of a situation influences the emotional response. In PTSD, cognitive therapy is used to help the patient identify, challenge, and modify biased or distorted thoughts and memories of the traumatic experience and maladaptive beliefs about themselves and the world they have developed following trauma exposure. By assisting patients in identifying distorted thinking and modifying existing beliefs, patients learn to improve their coping skills and change their problematic behaviors. Cognitive therapy is generally brief, goal-oriented, and time-limited. Variants of cognitive therapy have been developed, including cognitive restructuring and cognitive processing therapy [263; 267].

Cognitive-Processing Therapy

CPT is a form of cognitive therapy designed for PTSD based on the premise that affective states such as depressed mood can interfere with emotional and cognitive processing of the trauma memory, which produce or worsen traumatic symptomatology. CPT resolves these maladaptive factors by helping the patient identify and challenge maladaptive thoughts and beliefs ("stuck points") and replace them with rational alternatives. CPT involves psychoeducation, written patient accounts about the traumatic event, and cognitive restructuring to address beliefs surrounding the event's meaning and the implications of the trauma for one's life. Central post-traumatic themes such as safety, trust, power/control, self-esteem, and intimacy are also addressed [263].

This systematic approach to identifying key themes and issues associated with trauma reactions makes CPT highly suited to address some of the complex psychiatric sequelae emerging from recent military conflict exposure in veterans. The exposure component is limited to writing an account of the experience and can also make CPT more acceptable to patients or practitioners as an alternative to purely exposure-focused interventions. CPT has the advantage of addressing the frequently associated problems of depression, guilt, and anger [6; 268].

Stress-Inoculation Training

Stress-inoculation training is a cognitive-behavioral intervention for PTSD in which the basic goal is to help subjects gain confidence in their ability to cope with anxiety and fear stemming from trauma-related reminders. In stress-inoculation training, the therapist helps patients increase their awareness of trauma-related cues for fear and anxiety. In addition, patients learn a variety of coping skills that are useful in managing anxiety, such as muscle relaxation and deep breathing [263].

Coping Skills Therapy

The goal of coping skills therapy is to improve patients' ability to cope with their current situations or environment. Coping skills therapy can help with the management of anxiety or can correct misinterpretations that develop following trauma exposure by delivering a blend of approaches such as education, muscle relaxation training, breathing retraining, role-playing assertiveness training, or biofeedback. Most types of coping skills therapy require at least eight 60 to 90 minute sessions, and 10 to 14 sessions may be needed with more comprehensive interventions that include a stress-inoculation component [263].

BRIEF PSYCHODYNAMIC PSYCHOTHERAPY

Building on traditional psychotherapeutic approaches, psychodynamic therapy encourages the individual to use the supportive relationship with a therapist, and the transference that occurs within that relationship, to verbalize and reflect upon his or her experiences. This process allows unconsciously held thoughts, urges, and emotions to be brought into conscious awareness, which in turn allows the cognitive, emotional, and social aspects of an experience to be integrated into a meaningful structure that helps the person to accept and adapt to his or her experiences. Brief models of psychodynamic psychotherapy have been developed for PTSD following recent traumatic events. This approach focuses on the emotional conflicts caused by a specific traumatic event. The patient is encouraged to put the experience into words and examine the meaning that the event and surrounding circumstances holds. Through this retelling, the therapist assists the individual to integrate the event and re-establish a sense of purpose and meaning in life [6].

EYE MOVEMENT DESENSITIZATION AND REPROCESSING

EMDR is a one-on-one therapy approach designed to reduce trauma-related stress, anxiety, and depressive symptoms associated with PTSD and to improve overall mental health functioning. The theoretical basis of EMDR is that overwhelming emotions or dissociative processes during a traumatic event interfere with information processing, with the stored information "unprocessed" and disconnected from existing memory networks. This can be resolved through a process whereby the person is asked to focus on trauma-related imagery, negative thoughts, emotions, and body sensations as his or her eyes track the back and forth movement of the therapist's fingers across the visual field for 30 seconds or longer. Bilateral audio tones of body movements (e.g., toe tapping) may be used in place of the eye movements. The exact mechanism of action is not fully known, but it is

thought to involve adaptive information processing by which the dual-attention exercises disrupt stored trauma memories to facilitate the elimination of negative beliefs, emotions, and somatic symptoms associated with the trauma memory as it connects the more adaptive information stored in memory networks. When trauma recall ceases to elicit negative beliefs, emotions, or somatic symptoms, and the memory simultaneously shifts to more adaptive beliefs, emotions, and somatic responses, it is stored again and overwrites the original trauma memory [6; 263; 269].

EMDR is typically delivered in 60- to 90-minute sessions, with the number of sessions matching the complexity of the trauma being treated (generally 8 to 12 sessions) [263]. Over time, EMDR has increasingly included treatment components comparable with CBT, such as cognitive interweaving (analogous to cognitive therapy), imaginal templating (rehearsal of mastery or coping responses to anticipated stressors), and standard in vivo exposure. Combined with its initial inclusion of imaginal focus on traumatic images, EMDR now includes most of the core elements of standard trauma-focused CBT. In addition, the protocol has shifted from a single session to eight phases of treatment, comparable in length to standard trauma-focused CBT. The unique feature of EMDR is the use of eye movements as a core and fundamental component throughout treatment [6; 269].

NARRATIVE EXPOSURE THERAPY

Narrative exposure therapy is a standardized, short-term intervention adapted from testimony therapy (traditionally used with survivors of torture and civilian casualties of war) as well as from mainstream exposure approaches. It was originally developed to both treat survivors and to document human rights violations. In narrative exposure therapy, the patient is asked to construct a narrative of his or her life from early childhood to present, focusing in detail on the traumatic events and elaborating on the associated thoughts and emotions. It is proposed that narrative exposure therapy works in two ways: promoting habituation to traumatic memories through exposure and reconstructing the individual's autobiographic memory [6].

MINDFULNESS-BASED THERAPIES

Mindfulness-based therapies are considered part of the "third-wave" of cognitive-behavioral psychotherapies and include acceptance and commitment therapy, mindfulness-based CBT, and mindful meditation. Although relatively new to Western approaches, mindfulness has a long history of practice in Eastern philosophies (e.g., Buddhism, Taoism, yoga). Mindfulness can be defined as "paying attention in a particular way: on purpose, in the present moment, and non-judgmentally" [6; 270].

HYPNOTHERAPY

Hypnotherapy is the therapeutic application of hypnosis to various mental health problems. Hypnosis is achieved through an induction process and may be likened to a form of dissociation. The hypnotic state is characterized by heightened mental focus and suggestibility, allowing the therapist to implant suggestions that aid the individual in better controlling his or her symptoms. It is important to recognize that hypnosis is not an intervention in itself; rather, it is the induction of a state of relaxation and receptivity that (purportedly) makes interventions easier to implement. Thus, hypnosis in PTSD may be used as a precursor to several interventions including imagery, stress management techniques, ego-strengthening self-talk, and exposure [6; 263].

INTERPERSONAL THERAPY

Interpersonal therapy is a time-limited, psychodynamically informed approach that views interpersonal relationships as mediating the formation and maintenance of psychologic problems. This is shown by the strong association between symptoms and social environment, in that interpersonal interactions impact psychologic well-being and vice versa. The goal of interpersonal therapy is to alleviate suffering in patients with PTSD by focusing specifically on interpersonal relationships, to help patients either improve or change their

expectations about their interpersonal relationships, increase patient social supports to improve their management of interpersonal distress, and build interpersonal skills. Interpersonal therapy may address grief over lost relationships, relationship expectations, or changing roles in relationships [6; 263].

IMAGERY REHEARSAL

Imagery rehearsal therapy is a cognitive-behavioral approach for the treatment of chronic trauma-related nightmares. Imagery rehearsal therapy involves recalling the disturbing dream and then changing the imagery of the dream in such a way that the new version is not upsetting, increasing the patient's sense of mastery or control. The individual then rehearses the changed imagery in his or her imagination, particularly just before going to bed [6].

GROUP THERAPY

Group therapy is, of course, not an intervention per se, but rather a vehicle for delivering an intervention. Group therapies for PTSD have included supportive, psychodynamic, and cognitive-behavioral approaches (e.g., exposure, CPT, problem-solving). Common features include a relatively homogenous group membership, provision of mutual support, acknowledgement and validation of the traumatic experience, and normalization of traumatic responses. The presence of other individuals with similar experiences may help to overcome a belief that the therapist cannot be helpful because he or she has not experienced the specific trauma. The group may also be used to promote a non-judgmental approach toward behavior required for survival during the traumatic event [6].

TELEMEDICINE AND WEB-BASED INTERVENTIONS

"Interapy" is a broad term applied to a range of Internet-mediated therapies. Although some web-based interventions operate as purely self-help approaches with no therapist involvement, in most cases there is some limited contact between the therapist and the individual with PTSD via a computer. This approach is likely to be particularly useful for people living in remote areas, for those who are physically disabled and have restricted mobility or who are unwilling to seek face-to-face therapy due to anxiety or fear of stigmatization. Web-based treatment for PTSD usually includes psychoeducation, symptom management, exposure, and cognitive reappraisal, all of which involve structured writing assignments that can be submitted to the therapist for feedback [6].

STRESS MANAGEMENT

The term "stress management" encompasses a broad range of non-trauma-focused cognitive, behavioral, and physiologic interventions used in PTSD to reduce arousal levels, modify lifestyle factors, and address avoidance symptoms that contribute to stress or anxiety. Core components of stress management used in PTSD may include physical strategies, such as relaxation training, controlled breathing (to counter hyperventilation), aerobic exercise, sleep hygiene, and improved diet; cognitive strategies, such as adaptive coping self-statements for use when confronting feared or avoided situations, distraction techniques, and thought stopping; and behavioral strategies, such as structuring daily routines, increasing enjoyable activities, and utilizing social support [6].

SUPPORTIVE COUNSELING AND PRESENT-CENTERED THERAPY

Supportive counseling is a non-trauma-focused approach that centers on the patient's life situation to address and resolve current issues or problems. In PTSD, supportive counseling addresses problems resulting from post-traumatic psychopathology and general life circumstances by employing practical problem-solving and coping strategies. The level of therapist direction and advice is variable [6].

COMPLEX TRAUMA/PTSD

As discussed, acute traumatic responses result from a normal reaction to overwhelming stress and may be construed as a set of adaptive survival mechanisms that become pathologic if the traumatic experience remains unresolved or when the precipitating event(s) have passed. With repeated or chronic trauma exposure, especially in the case of childhood sexual assault, the effects of unresolved trauma are pervasive and become the central organizing structure around which profound neurobiologic adaptations occur [33; 271].

The symptom profile of complex trauma/PTSD recognizes deficits in emotional, social, cognitive, and psychologic competencies as the result of a failure to develop properly or deterioration from prolonged trauma exposure. Thus, treatment for complex trauma emphasizes reduction of psychiatric symptoms and, equally important, improvement in key functional capacities for self-regulation and strengthening of psychosocial and environmental resources. Loss of psychosocial resources, including deficits in self-efficacy, prosocial behaviors, or social support, is common and contributes to the severity and chronicity of PTSD symptoms. Therefore, strengths-based interventions to improve functioning, contribute to symptom management, and facilitate patient integration into family and community structures are integral to each phase of treatment [36; 272].

The development and publication of guidelines for the treatment of patients with complex trauma were prompted by realization that the framework serving as the basis for PTSD guidelines does not include the salient symptoms and problems of persons exposed to prolonged and repeated trauma. As discussed, complex trauma/PTSD is typically the result of repeated or prolonged exposure to interpersonal trauma, commonly under circumstances in which escape is not possible due to physical, psychologic, maturational, family/environmental, or social constraints. Such traumatic stressors include childhood physical and sexual abuse, recruitment or coercion into armed conflict as a child soldier, sex trafficking or sexual/physical slavery, torture, and exposure to genocide or other forms of organized violence [33; 36].

GENERAL TREATMENT APPROACHES AND CONSIDERATIONS

Client Safety

The first step of treatment is to establish conditions and an atmosphere of safety to the fullest extent possible. The patient cannot respond to or make progress with therapy if a relative degree of safety is not available or attainable [33; 36].

Affect Regulation

Facilitation of the ability to self-regulate internal states should be a consistent task of therapy, involving, among other things, the teaching of strategies to self-monitor, self-intercept, and self-soothe [33; 36].

Extent of Functional Impairment

It is important that clinicians recognize the breadth of functioning impacted by complex trauma and that acquisition, not just restoration, of some modes of functioning may be necessary. Especially when dating back to childhood, complex trauma can entail developmental deficits in self-organization that are seldom encountered in single-incident PTSD when prior underlying trauma is absent. Developmental and attachment deficits require additional treatment focus and make treatment goals more extensive than those directed at PTSD symptoms alone [33; 36].

Strengths-Based Perspective

Symptoms associated with complex trauma/PTSD are adaptive, and working from a strengths-based approach empowers the patient to access existing resources. Clinical work should be informed by the view of symptoms as "expectable and adaptive" reactions to traumatic childhood experiences and as the persistence of normal responses to abnormal conditions [33; 36].

Neurologic Impact

Experiencing trauma impacts the brain (especially the developing brain), and the far-reaching effects of trauma physiology will impact treatment. Key aspects of this information should be sensitively communicated to the patient to help normalize distressing/problematic internal experiences and responses. The physiologic effects of trauma on the brain, body, and subsequent functioning should form a component of psychoeducation that accompanies effective trauma therapy [33; 36].

Support Networks

The frequent impairment in relational capacity can be reflected in social support that is lacking or sub-optimal. The therapeutic relationship itself can encourage relational capacity as healthy support networks are constructed [33; 36].

Attachment Issues

Although different in presentation and levels of functioning, the ability of patients with complex trauma to connect with themselves and others has been repeatedly assaulted. Attuning to attachment issues is vital to the therapeutic alliance and for effectively working within it, and this approach can assist the provider in recognizing the potential indicators of complex versus single-incident trauma [33; 36].

Dissociation

Practitioners should appreciate the prevalence and varied forms of dissociative responses, the differences between hyper- and hypoarousal, and the need to stay within the window of tolerance. Structural dissociation represents an extreme form of defense in the face of severe and inescapable threat. It is a frequent feature of complex trauma when abuse begins in childhood. The therapist should also be aware of the numerous, milder forms of dissociative response [33; 36].

Hyperarousal is a response to the experience of extreme anxiety and can be characterized by agitation, while hypoarousal appears as passivity, the patient shutting down, and withdrawal. Therapy should always remain within the window of tolerance, which is the threshold of emotional intensity the patient can accommodate without becoming either hyper- or hypoaroused [33; 36].

Addressing Shame

Clinicians should expect and prepare to work with a variety of client responses that may not be obvious. An inability to self-regulate and to draw upon relationships to regain self-integrity can engender deep shame, to which therapists should be attuned [33; 36].

Complex Trauma-Focused Interventions

Standard assessment tools and treatment modalities are limited in relation to complex trauma, and therapists should have a handle on the extent to which these can be modified by incorporating new clinical and research findings. All interventions should originate from the understanding of current clinical and research insights into complex trauma [33; 36].

IMPLEMENTATION OF THERAPY

Phased Treatment

The recommended treatment model for complex trauma is a phase-oriented or sequential treatment, guided by a hierarchy of treatment needs assessed prior to treatment [33; 36].

Phase 1: Stabilization and Skills Strengthening

The first phase of treatment focuses on ensuring safety, reducing symptoms, and increasing important emotional, social, and psychologic competencies. The ability to tolerate emotion by self-soothing and regulated affect is a primary and essential task of treatment phase 1, as re-traumatization can be precipitated when patient efforts are made to process trauma in the absence of self-regulating skills. The critical importance of phase 1 to therapeutic outcomes cannot be overstated, and it is vital in order to realize trauma recovery [33; 36].

The first goal is to ensure that acute mental health treatment needs and patient safety have been achieved. The secondary goals are to strengthen patient capacity for emotional awareness and expression, to increase positive self-concept and address feelings of guilt and shame, and to increase interpersonal and social competencies. Strengthening these domains improves day-to-day functioning, builds confidence, and provides motivation for treatment engagement and continuation. Also, an initial skills-building phase enhances the effectiveness of trauma processing work and contributes to PTSD symptom reduction [33; 36].

Phase 1 introduces psychoeducation about the impact of trauma (particularly when sustained, experienced early in life, or cumulative in nature) as it relates to the development, life course, worldview, relationships, and symptoms experienced by the patient. Interventions in this phase should be evidence-based and matched to individual patient needs. Emphasis should be placed on emotion regulation skills, stress management, social and relational skills building, and cognitive restructuring. Meditation and mindfulness interventions are strong secondary interventions—important and useful but not intended as sole therapy. In phase 1, the therapeutic relationship is important in the development of emotional and social skills through the expression of support, validation, encouragement, and the role modeling of a healthy relationship. While the preferred format for phase 1 treatment is individual therapy, therapist-led group therapy can be an appropriate alternative [33; 36].

Phase 2: Processing

The focus of phase 2 treatment is the review and reappraisal of trauma memories by involving approaches such as narration in the context of an actual and subjectively experienced safe environment. Therapeutic benefit results from patient capacity to maintain emotional engagement with distressing memories while simultaneously remaining physically, emotionally, and psychologically intact. The patient's sense of safety and further exploration of the memory is supported and facilitated by the therapist's presence, encouragement, guidance, and feedback. The experience of safety, and the attendant availability of attentional, cognitive, and emotional resources, comprise the therapeutic circumstances under which reappraisal of the meaning of the traumatic experiences can be conducted. The objective of this process is to facilitate the reorganization and integration of the trauma into autobiographical memory to promote a more positive, compassionate, coherent, and continuous sense of self and relatedness to others. Individual therapy, with or without added group therapy, is recommended for phase 2 [33; 36].

While there are several approaches for successful trauma memory processing, their common feature is an organized recounting of the events, primarily verbally but in some cases supported through other media such as artwork or through other symbols of remembrance and reappraisal of the traumas, as with narrative exposure therapy. During sessions devoted to trauma memory processing, treatment should also include the continued review and use of interventions that strengthen emotion self-management, self-efficacy, and relationship skills [33; 36].

Phase 3: Integration

In this phase, treatment gains in emotional, social, and relational competencies are consolidated to facilitate the transition from the end of treatment to greater engagement in relationships, work or education, and community life. The therapist supports and guides the individual in applying skills to strengthen safe and supportive social networks and to build and enhance intimate and family relationships. Plans for education, employment, recreation, and social activities or meaningful hobbies should be considered and organized. Phase 3 planning also plans for the use of "booster" sessions to refresh skills or address life challenges, articulates relapse prevention interventions, and identifies alternative mental health resources [33; 36].

Neurobiology of Attachment

The therapeutic model/approach should promote integration of functioning based on research findings on the neurobiology of attachment. In the treatment of complex trauma, research emphasizes the importance of engaging the relevant neurobiologic processes of cognitive processing, emotional processing, and sensorimotor processing involving physical and sensory responses, sensations, and movement. While several approaches address these dimensions, they have in common the activation of and engagement with right-brain processes and attentiveness to the role and effects of implicit memory [33; 36].

Adaptation of Standard Therapies

Effective treatment of complex trauma often requires adaptation of, and supplements to, standard psychotherapeutic insight-based and cognitive-behavioral approaches. Attachment neurobiology research establishes the limits and benefits of "talk" therapy, the need to actively address physical, sensorimotor, and experiential processes, and the cognitions and verbal expression of emotion [33; 36].

Individualized Treatment

With patients with complex trauma, therapy should be adapted to the individual rather than expecting the individual to adapt to the therapy. One size does not fit all in terms of using a standardized formulaic approach [33; 36].

Duration and Frequency of Sessions

Therapists should recognize that complex trauma treatment is generally longer than with many other patient populations and is rarely meaningful if completed in less than 10 to 20 sessions. However, if economic or other constraints impose a limit to the number of therapy sessions, therapy should be confined to phase 1 stabilization. In general, therapy is recommended to occur once or twice weekly, with 50 to 75 minutes for individual therapy and 75 to 120 minutes for group therapy, and should not exceed this recommended frequency [33; 36].

While consensus on optimal duration of treatment or its specific course is lacking, and the published treatment research in patients with complex trauma indicates that four to five months is associated with substantial benefits, experts recommend that longer treatment courses than those applied in clinical trials are needed. Most experts consider that a reasonable length involves 6 months for phase 1 and 3 to 6 months for phase 2, for a combined duration of 9 to 12 months for the first two phases [33; 36].

Clinician judgment of the duration of each phase and transitions across phases requires consideration of several factors. Patient progress in phase 1 is gauged by symptom reduction, ability to reduce unhealthy coping or emotion-regulation strategies (e.g., drug abuse, self-injurious behaviors, risk-taking or aggressive behaviors), and demonstrated improvement in executive functioning and life skills. Phase 2 is initiated by clinician/patient agreement that the patient has gained the skills and life stability to safely engage in trauma-focused work. Relapse is expected and planned for, and the patient may return to phase 1 to re-learn or re-consolidate skills before continuing with trauma processing. Advancement to phase 3 occurs when symptoms have been generally and consistently decreasing over time [33; 36].

Establishing Boundaries

Boundaries are especially important in working with clients chronically subjected to violation, exploitation, and dual relationships. Boundaries should be mutually negotiated, and care should be taken to ensure that the client understands their significance and does not view them as punitive. Maintenance of boundaries is also vital for therapist self-care in the demanding work of complex trauma [33; 36].

Collaboration and Continuity of Care

It is important to collaborate with the client and with other professionals and services the patient may contact. Patients with complex trauma are vulnerable to feeling rejected due to histories of betrayal and abandonment. Regardless of the reason, therapy termination is a process that also represents a critical opportunity to support and sustain patient gains in relational, emotional, and behavioral self-regulation. In the event of transfer to a new therapist or provider, interventions that promote a sense of continuity should be integrated into the transition process [33; 36].

Diverse Recovery

Patients differ broadly in their capacity to engage in therapy and resolve symptoms and distress. Along with differences in self- and relational impairment, patients experience differences in healing capacities and resources that contribute to varying degrees and types of resolution and recovery [33; 36].

PROVIDER CONSIDERATIONS

Professional Supervision

The intensity and complexity of transference-countertransference dynamics in complex trauma relationships are such that working without clinical consultation, at any level of helper experience, can pose great hazards for both clients and therapists [33; 36]. Caseload management, training, reflective supervision, and peer supervision or external group processing have been shown to reduce the impact of secondary traumatic stress in professionals caring for persons with PTSD and/or complex trauma [273].

Cultural Competence and Sensitivity

Therapists should be culturally competent and sensitive to gender, sexual orientation, race/ethnicity, age, and other dimensions of difference. Awareness of, and attunement to, the potential impact of "difference" in its various forms (e.g., age, ethnicity, socioeconomic status) is important in all therapeutic work and especially with complex trauma. Because patients themselves can sense therapist ambivalence, therapists should have awareness of their own responses to cultural, gender, and other "differences" in their patients and of resources where they can obtain assistance [33; 36].

EFFICACY

In the treatment of patients with complex trauma/PTSD, stabilization therapies are associated with moderate-to-large treatment effect sizes for PTSD, emotion regulation, and social/interpersonal outcomes. Therapies that include stabilization, skills building, and memory processing are generally superior to those using a stabilization component only. Individual therapies produce larger treatment effect sizes than group therapies [33; 36].

PSYCHOSOCIAL REHABILITATION AND SOMATIC AND ALTERNATIVE THERAPIES

Psychosocial rehabilitation interventions are strongly supported across a broad range of mental disorders, and a growing evidence base confirms the beneficial effect in patients with PTSD. Specific interventions include family psychoeducation, supported education, housing and employment, intensive case management, peer counseling, and "vet to vet" services. Their implementation is associated with positive outcomes in several dimensions, such as symptom reduction, decreased risk of relapse, increased housing stability, improved social and work functioning, reduced stress in families, and enhanced quality of life [274; 275; 276; 277].

PSYCHOSOCIAL REHABILITATION INTERVENTIONS FOR PTSD

Psychosocial rehabilitation interventions have traditionally been used in persons with chronic mental illness (including PTSD) to promote improvements in independent living, socialization, and life management. These approaches may apply a variety of different components, such as social skills training and activities, job skills training, housing support, vocational rehabilitation,

case management, and family support. Its use in PTSD can help offset the extent of impairment and disability by reducing self-care and independent living skills deficits and addressing problems with homelessness, high-risk behaviors, negative interactions with others who lack understanding of PTSD, social inactivity, unemployment, and barriers to services and treatment. While used with other interventions, psychosocial rehabilitation is designed to promote community integration and improved functioning. The importance of introduction at the earliest phase of care is now recognized [6; 68].

Social-Emotional Rehabilitation

Social-emotional rehabilitation was designed specifically for veterans and is comprised of three components. Social skills training helps improve the basic conversational skills important for creating and maintaining social networks. Anger management and problem-solving skills training reduce temper outbursts by introducing alternative expressions for anger, teaching problem-solving and emotion regulation skills, and providing instruction on assertive, non-threatening communication. Veterans' issues management teaches veterans how to discuss combat trauma and other military issues with their significant others in order to improve understanding. Veterans are also taught to identify and challenge negative and dichotomous thinking (e.g., all civilians will not understand them/cannot be trusted because they have never seen combat) that limits their social connections [6].

Vocational Rehabilitation

While the common focus of vocational rehabilitation involves assisting the patient with PTSD in attaining optimal workplace functioning, volunteer work, and other key roles (e.g., parenting) are also a valid focus. Depending on current functioning, vocational rehabilitation can help patients maintain their current role or employment or return to that role using a supported and graded approach. A longer process may involve retraining to improve access to a meaningful occupation [6; 278].

SOMATIC THERAPIES

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) involves applying pulsing high-intensity current through an electromagnetic coil placed on the side of the head. A 2014 review of eight TMS studies in PTSD (including three controlled trials) found this approach was generally well tolerated. Effectiveness was suggested in all studies, and TMS had a significant effect size on PTSD symptoms, possibly correlated with the total number of stimulations [279]. The effects of different frequencies (i.e., high- and low-frequency) of TMS were the focus of a 2017 review and meta-analysis [280; 281]. Results suggest that both high- and low-frequency can alleviate symptoms of PTSD. Low-frequency may reduce overall PTSD and depressive symptoms, whereas high-frequency may improve the main and related symptoms of PTSD [280]. However, the precise treatment location and pulse sequences remain undefined.

Acupuncture

Acupuncture is an alternative medicine treatment that manipulates thin, solid needles inserted into specific points in the skin. By stimulating these points, imbalanced energy flow is corrected through channels known as meridians. The National Institutes of Health in the United States, the National Health Service in the United Kingdom, and the World Health Organization endorse acupuncture for use in the treatment of several types of pain, nausea, and osteoarthritis of the knee. It is considered safe and carries a very low risk of serious adverse effects [6].

Results of a pilot study suggested that acupuncture provided outcomes comparable to CBT in reducing PTSD symptoms, anxiety, and impairment. Positive benefits from both treatments were maintained at three-month follow-up. The researchers stated their findings should be viewed with cautious optimism, with further corroborative and more definitive data needed [282]. More recent reviews and analyses agree with these findings [283; 284].

COMPLEMENTARY AND ALTERNATIVE THERAPIES

Yoga

A review of 12 published studies (including seven randomized controlled trials) on yoga that enrolled participants with recent exposure to trauma following contact with terrorism, combat and war atrocities, disaster from hurricane or tsunami, interpersonal violence, or incarceration was conducted in 2012. Age groups varied, with studies enrolling children, adolescents, and/or adults. The overall findings were that yoga intervention led to reduced levels of post-trauma symptoms and distress that appeared durable at longer-term follow-up. With some of the studies performed in disaster areas and/or countries with limited professional resources, the beneficial effect was considered important, as it was delivered by a trained yoga instructor without advanced education and training in standard post-trauma care [285]. A feasibility study in an outpatient Veterans Affairs PTSD population found that yoga may be effective in improving hyperarousal symptoms of PTSD and some elements of sleep quality [286]. A study conducted to assess the impact of yoga on post-9/11 veterans diagnosed with PTSD found that trauma-sensitive yoga intervention may be effective in this population both as stand-alone and adjunctive therapy [287].

"Power Therapies"

A group of novel PTSD treatments known as "power therapies" have been suggested to work more rapidly than standard treatments, although properly designed research evaluation is lacking. The best known—the emotional freedom technique—involves the patient focusing on traumatic memory while the therapist taps lightly on various traditional acupuncture meridian points. The emotional freedom technique assumes that emotional disturbances from traumatic events are the result of disturbances in the body's energy field (meridian system) that can be restored with this approach. Related approaches include thought field therapy, visual-kinesthetic dissociation, and traumatic incident reduction [6].

The Counting Method

The counting method is an alternative approach whereby the therapist counts aloud from 1 to 100 as the patient mentally recalls the traumatic memory from start to finish. The counting itself is thought to assist the patient in maintaining focus on the traumatic memory and remove avoidance [288].

PHARMACOTHERAPIES

When initiating PTSD treatment, patients should be provided with education about the disorder, the common symptoms, and the range of available and effective pharmacologic and nonpharmacologic treatments. Selection of the initial pharmacologic approach is based on clinician and patient choice and guided by the manifesting symptoms of PTSD, other disorders, and patient preference, with polypharmacy choice dictated by clinical presentation and co-occurring psychiatric disorders [68; 196].

ESTABLISHED PHARMACOTHERAPIES

Selective Serotonin Reuptake Inhibitors

SSRIs are widely recommended as first-line agents in the treatment of PTSD, with demonstrated efficacy in reducing the global, re-experiencing, avoidance/numbing, and hyperarousal symptoms of PTSD [68; 196]. SSRI maintenance therapy has shown a substantial and consistent effect in PTSD by preventing relapse and has demonstrated value in long-term PTSD management. Comparison studies have found efficacy of improving PTSD symptoms with fluoxetine, paroxetine, and sertraline, with clear evidence of patients achieving remission at 12 weeks with paroxetine and insufficient evidence of 12-week remission with fluoxetine and sertraline [68; 263; 289; 290]. Pharmacologic studies generally did not report loss of PTSD diagnosis as an outcome, and studies mostly did not report evidence for other outcomes of interest, such as anxiety symptoms, quality of life, disability or functional impairment, and return to work or active duty [263].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Veterans Health Administration and the U.S. Department of Defense recommend sertraline, paroxetine, fluoxetine, or venlafaxine as monotherapy for PTSD in patients diagnosed with PTSD who choose not to engage in or who are unable to access trauma-focused psychotherapy.

(https://www.healthquality.va.gov/guidelines/mh/ptsd. Last accessed March 18, 2021.)

Strength of Recommendation: Strong for

SSRIs are not without shortcomings. Research now suggests much lower efficacy in veterans with combat-related PTSD, who show lower treatment response to SSRIs than veterans with non-combat PTSD [291]. Only 60% of patients respond to SSRI treatment, and roughly 20% to 30% achieve full remission [292]. Patients may require 12 weeks before responding, and undesirable side effects include loss of sex drive, gastrointestinal effects, or changes in body weight [292]. Discontinuation syndrome can emerge when the SSRI taper is too rapid; this is avoided by a minimum two-month taper [293].

Serotonergic-Noradrenergic Reuptake Inhibitors

Venlafaxine extended-release (ER) (37.5–300 mg per day) is another antidepressant that has been used for PTSD; however, this is an off-label use [294]. Both the Agency for Healthcare Research and Quality (AHRQ) and the American Psychological Association (APA) report moderate-quality evidence for its efficacy, including symptom reduction and symptom remission [263; 290].

Tricyclic Antidepressants

Among the TCAs, nortriptyline, amitriptyline, and imipramine have published evidence supporting their efficacy in PTSD. Although found to reduce PTSD symptoms, the TCAs are toxic and possibly fatal in overdose. TCAs have unfavorable adverse effects, with the prominent anticholinergic side effects particularly risky in patients with cardiac, cognitive disorder, and prostatic hypertrophy comorbidity [293]. For these reasons, TCAs are not recommended as first-line therapy in PTSD [68; 263].

Monoamine Oxidase Inhibitors

Phenelzine is the only agent in this drug class available in the United States that has been studied in PTSD. While phenelzine was found to result in substantial reduction in intrusive thoughts, monoamine oxidase inhibitors (MAOIs) require strict adherence to dietary restriction (i.e., avoidance of tyramine-rich foods) to prevent hypertensive crisis, which may impede patient compliance. Another barrier to wider clinical use is the requirement of a two-week washout with any psychotropic drug that enhances monoamines (including almost all other antidepressants and numerous other agents and classes) to avoid serotonin syndrome [293].

Other Antidepressants

Clinical trials with several other antidepressants have produced favorable results in patients with PTSD. The exact added value of each drug as a treatment option for PTSD remains to be clarified, primarily due to the few published studies relative to SSRIs.

Nefazodone

Several studies have shown nefazodone to be more effective than placebo and equivalent to sertraline in improving PTSD symptoms. Its novel mechanism as a postsynaptic 5-HT and 5-HT2A receptor antagonist and moderate serotonin and norepinephrine reuptake inhibitor confer a superior side effect profile over SSRIs and potential utility in SSRI-resistant PTSD. Its clinical use is constrained by known hepatotoxicity [293].

Mirtazapine

Randomized controlled trials have found mirtazapine to be superior to placebo and comparable to sertraline in the treatment of PTSD and general anxiety symptoms. Mirtazapine possesses a unique mechanism of action, has minimal potential for drug interactions, and is absent serious side effects. It is very useful in sleep promotion [290]. Primary side effects are sedation, constipation, and weight gain [293].

Sympatholytics

Prazosin

Efficacy of the alpha-adrenergic antagonist prazosin in treating PTSD-related nightmares and sleep disruption is demonstrated in several placebo-controlled augmentation trials, and it is considered one of the most promising advances in the pharmacologic treatment of PTSD. The prazosin trials also showed that patients are able to continue maintenance of other PTSD medications, including SSRIs, without interference of benefit. The suggested effective dosage range for prazosin is 6–10 mg at night, initiated at 1–2 mg and slowly increased to avoid hypotension [263; 293].

An evaluation of prazosin monotherapy in 67 active-duty and recently discharged Iraq and Afghanistan war veterans with PTSD and two or more nights of distressing combat-related nightmares per week found prazosin to be superior to placebo for improving overall PTSD symptoms, global function, and sleep quality. However, while PTSD symptoms improved, they did not resolve for most subjects receiving prazosin [295]. A systematic review and meta-analysis found that prazosin improves nightmares and overall PTSD symptoms, including hyperarousal, sleep disturbances, total sleep time, and sleep quality [296].

Guanfacine

Guanfacine has been found ineffective in improving PTSD symptoms, sleep quality, or mood disturbances. It is not recommended as monotherapy for PTSD [68; 297].

Propranolol

Propranolol is a non-selective beta-1 and beta-2-adrenoreceptor antagonist that showed effectiveness in fear reduction in patients with PTSD and memory reconsolidation blockade in animal and healthy volunteer subjects [298]. One randomized controlled trial was conducted to assess the efficacy of trauma memory reactivation with propranolol to reduce PTSD symptoms [299]. The six-week trial included 60 adults diagnosed with long-standing PTSD who received either propranolol or placebo 90 minutes prior to a brief memory reactivation session. Propranolol was administered once per week for six consecutive weeks. Results suggest that pre-memory-reactivation propranolol may be a novel and effective treatment for PTSD [299]. A second and similar randomized controlled trial of 66 adults also evaluated the efficacy of traumatic memory reactivation with propranolol. Results indicate that the efficacy of propranolol was not greater than that of placebo one week post-treatment and that PTSD symptom severity at baseline might have influenced the effectiveness of propranolol [300]. Additional randomized, placebo-controlled trials have not replicated the efficacy of smaller uncontrolled trials as a sole therapy approach for PTSD [263]. Propranolol has been used as an adjunct to reduce stress and intrusive distressing memories in PTSD [68].

Benzodiazepines

Benzodiazepine use in PTSD may potentiate the acquisition of fear responses and worsen recovery from trauma; negatively interact with alcohol and other drug use in a population with high substance use disorder comorbidity; and pose a risk of abuse and dependence in their own right. Following daily alprazolam for five weeks, discontinuation resulted in high rates of rebound anxiety and PTSD symptom exacerbation. Benzodiazepines are not recommended as monotherapy or adjunctive therapy for PTSD [293].

Anticonvulsants

Existing evidence does not support the use of anticonvulsants as monotherapy for the management of PTSD core symptoms. However, they are frequently used as adjunctive treatments [293].

Second Generation/Atypical Antipsychotics

Olanzapine, quetiapine, and risperidone have little positive effect in reducing the core symptoms of PTSD as monotherapy. They do have demonstrated efficacy as adjunctive treatments in patients who have partially responded to SSRI or SNRI treatment of PTSD, and their use as adjuncts in this context is recommended. It is important to monitor patients for side effects, including weight gain and metabolic changes, when using these agents [291].

EMERGING PHARMACOTHERAPY OPTIONS

Ketamine

Glutamate is the primary excitatory neurotransmitter in the brain, and growing evidence indicates that glutamate plays a major role in mediating stress response, traumatic memory formation, and PTSD pathophysiology. Ketamine is a dissociative anesthetic that acts as an NMDA glutamate receptor antagonist. In a 2014 pilot study of 41 patients with chronic PTSD, patients randomly received a single infusion of either IV ketamine hydrochloride (0.5 mg/kg) or IV midazolam (0.045 mg/kg) over 40 minutes, and two weeks later were infused with the alternate medication. Ketamine led to rapid and significant reduction in PTSD symptom severity 24 hours post-infusion, reduction in comorbid depressive symptoms, and improvement in overall clinical presentation. Ketamine was generally well tolerated and did not lead to distressing, persistent dissociative symptoms. In 2021, the results of a randomized controlled trial provided the first evidence of efficacy of repeated ketamine infusions in reducing symptom severity in individuals with chronic PTSD [301]. These results, if replicated, could provide persons with chronic PTSD an effective option for rapid symptom reduction [302].

D-cycloserine

D-cycloserine (DCS) was originally approved for clinical use for the treatment of tuberculosis, but has since been studied in the treatment of anxiety disorders, substance use disorder, and PTSD. Fear extinction has been linked to NMDA glutamatergic receptor activity in the basolateral amygdala, and pre-clinical studies suggest a fear extinction enhancement effect with the partial NMDA receptor agonist DCS [178]. This benefit has been shown in clinical trials of patients with acrophobia, social phobia, and panic disorder when used in conjunction with exposure therapy [303; 304]. DCS efficacy in enhancing extinction is not attributable to possible anxiolytic effects of the drug, because fear expression during exposure and extinction were unaffected [174; 305].

The results of randomized, placebo-controlled trials in PTSD are mixed, with some evidence of particular benefit in severely disordered patients. Overall, there appears to be some benefit in fear extinction success in exposure sessions but also potentially detrimental effects in unimproved patients following exposure [306; 307]. In this last group, DCS may actually contribute to fear memory consolidation [307]. To avoid this outcome, DCS was administered to patients following exposure, and benefit was found in those showing good within-session habituation only [308].

Interestingly, in a study of patients with PTSD following the September 11th attacks given DCS or placebo before 10 virtual reality exposures, DCS led to comparable symptom reduction compared with placebo after the tenth treatment but significantly greater symptom reduction at six-month follow-up (75% vs. 38%) and greater PTSD remission rates at post-treatment (46% vs. 8%) and six-month follow-up (69% vs. 17%) [309].

Individual factors were found to influence treatment response to DCS. A comparison of DCS and placebo augmentation of prolonged exposure found that DCS produced significantly better PTSD symptom outcomes in highly conscientious and low extraversion patients, suggesting that a treatment-matching strategy may improve DCS plus prolonged exposure therapy efficacy for PTSD [309].

DCS has not shown significant side effects in any clinical trial and is easily administered. However, current alcohol abuse is a contraindication for DCS, and negative interaction with stable-dose antidepressants has not been observed [306]. A 2013 review concluded that DCS was a good candidate to implement in routine clinical care of PTSD [178]. A 2018 review suggests that DCS might have a role in the augmentation of exposure therapy [310].

3,4-methylenedioxymethamphetamine (MDMA)

MDMA is a ring-substituted phenethylamine that binds and reverses monoamine transporters to primarily increase serotonin release and activate 5-HT receptors. It also increases the release of norepinephrine and dopamine to a significantly lesser extent than serotonin. While MDMA has become a popular recreational drug due to its potentially profound subjective effects of euphoria, well-being, heightened senses, and closeness and connectedness to others, experimental application of MDMA as a psychotherapy adjunct in the late 1970s to mid-1980s preceded its recreational use [178].

Several lines of evidence suggest that MDMA may benefit patients with PTSD by enhancing extinction learning. MDMA may increase ventromedial prefrontal cortical activity and decrease amygdala activity, two interconnected brain regions essential for extinction learning. MDMA may also enhance extinction learning via enhanced cortisol and norepinephrine levels and increase the level of oxytocin resulting in an enhanced therapeutic alliance [311; 312].

Two randomized placebo-controlled trials of MDMA in patients with PTSD have been published. In one study, 20 patients with severe PTSD unresponsive to previous psychotherapy or medication received MDMA or placebo before two 8- to 10-hour individual psychotherapy sessions. A dramatic reduction in PTSD symptom scores was found in the MDMA group, and 80% of MDMA patients no longer met PTSD diagnosis at two-month follow-up (compared with 25% of those receiving placebo) [313]. All patients subsequently received open-label MDMA before two or three MDMA-enhanced treatment sessions. At an average 3.5-year follow-up, 14 of the 16 subjects showed significant reductions in PTSD severity that persisted to follow-up [313]. Another study randomized 12 patients with treatment-refractory PTSD to MDMA at therapeutic dose (125 mg and 62.5 mg 2.5 hours later) or active placebo dose (25 mg and 12.5 mg 2.5 hours later) before three eight-hour individual psychotherapy sessions. Both groups showed modest symptom improvement, with a trend in the active group of greater improvement. However, all patients still met diagnostic criteria at follow-up [314]. A phase 2 clinical trial assessed the efficacy and safety of MDMA-assisted psychotherapy for treating chronic PTSD among military personnel and first responders [315]. A total of 26 veterans and first responders were randomly assigned to receive 30 mg, 75 mg, or 125 mg of MDMA plus psychotherapy. The 75-mg and 125-mg groups had significantly greater decreases in PTSD symptom severity than the 30-mg group.

PTSD symptoms were significantly reduced at 12-month follow-up compared with baseline after all groups had full-dose MDMA [315]. These tentative results are promising, but more controlled studies are needed on MDMA-enhanced psychologic treatment before reliable conclusions on efficacy can be drawn. Use of MDMA in PTSD poses clinical and pragmatic challenges. SSRI and SNRI antidepressants, the most commonly used antidepressants in PTSD, block the desired effects of MDMA and require discontinuation before MDMA may be initiated. MDMA is a cardiovascular stimulant, and therapeutic use requires stress-electrocardiogram before treatment and physical monitoring and physician presence during MDMA-enhanced treatment [178].

Sirolimus

Sirolimus is a protein synthesis inhibitor. A trial that paired single-administration sirolimus with reactivation of trauma memory in 51 combat veterans with PTSD found that relative to placebo, sirolimus led to significantly fewer and less intense PTSD symptoms at one month post-treatment [316]. These positive effects did not persist at three months, and the researchers concluded that further studies should explore the use of sirolimus beyond a single administration [316].

SYMPTOM-SPECIFIC AND COMORBID APPROACHES TO TREATMENT

Trauma survivors seeking primary care may not specifically complain of core PTSD symptoms, but instead complain of sleeping problems, chronic pain, or anger or substance abuse issues. Addressing these issues is key to effective treatment.

SLEEP DISTURBANCES

Complaints of sleeping problems may be the initial presenting problem in patients with PTSD. Sleep disturbances are highly prevalent in this population, and many patients have had insomnia for years, manifesting in trouble falling asleep, fragmented sleep, frequent awakenings, and nightmares, all of which result in poor sleep quality. Significantly impaired sleep can remain chronic despite therapeutic gains in sleep disruption and other dimensions of PTSD following therapy, as demonstrated by a six-year follow-up study of women with post-rape PTSD who received prolonged exposure therapy and CPT [317]. PTSD symptoms of hyperarousal can be stronger at night and contribute to insomnia. Chronic pain and insomnia frequently co-occur, and most patients with chronic pain experience interrupted or poor sleep quality. Sleep disruption is associated with heightened pain sensitivity and elevated risk of disability. Some patients may use alcohol to self-medicate sleep problems, and excessive alcohol use can impair sleep quality and prevent the development of coping skills for trauma memories and stress.

There is no evidence indicating that insomnia, as a PTSD component, should be managed differently than insomnia in patients without PTSD. However, sleep can be dreaded among psychologically traumatized patients, particularly if they experience intense and highly disturbing nightmares. Nonpharmacologic approaches are associated with equal-to-superior short- and long-term sleep outcomes versus hypnotics alone or hypnotics plus nonpharmacologic approaches. The intent of sleep management is to establish a regular, normalized sleep-wake pattern [68].

Nonpharmacologic Approaches

Sleep Hygiene

Sleep hygiene refers to a group of strategies that eliminate or alter behaviors that promote insomnia and sleep disturbance and add behaviors that promote sleep normalization. The practice of good sleep hygiene involves avoiding [68]:

- Alcohol
- Going to bed too early
- Stimulants, caffeinated beverages, energy drinks, nicotine, and over-the-counter medications
- Stimulating activities, light, noise, and temperature extremes before bedtime or in the sleeping area

Sleep hygiene also involves altering rising from bed to a regular time every day. Nighttime sleep duration should not exceed eight hours, and daytime naps should be eliminated or reduced to 30 minutes maximum. Experts also recommend adding relaxation techniques and moderate exercise, though not immediately before bedtime [68].

CBT for Insomnia

This approach can include educating patients about proper sleep habits and sleep needs, identifying and correcting false and unrealistic beliefs or concerns surrounding sleep, and identifying and addressing anxious, automatic thoughts that disrupt sleep [68].

The Veterans Health Administration and the U.S. Department of Defense recommend cognitive-behavioral therapy for insomnia (CBT-I) for insomnia in patients with PTSD unless an underlying medical or environmental etiology is identified or severe sleep deprivation warrants the immediate use of medication to prevent harm.

(https://www.healthquality.va.gov/guidelines/mh/ptsd. Last accessed March 18, 2021.)

Strength of Recommendation: Strong for

Pharmacologic Approaches

Trazodone or mirtazapine may be helpful in managing insomnia. Trazodone can supplement the action of other antidepressants, and mirtazapine is an antidepressant and anxiolytic. Hypnotics should only be used for short periods of time and if indicated. Use should be restricted to the latest generation of non-benzodiazepines, such as zolpidem, eszopiclone, or ramelteon, as their shorter half-life and lower dependency risk confers a safety advantage. Patients should be monitored for potential acute confusional states or bizarre sleep behaviors [68].

Benzodiazepines may be justified during the immediate post-trauma period to reduce hyperarousal symptoms and anxiety and normalize sleep cycles. However, their use for longer than one month should be avoided, because longer-term use is associated with higher rates of PTSD. In addition, their use is relatively contraindicated in combat veterans with PTSD due to the high prevalence of alcohol and substance use disorders in this group and the elevated dependence risk. Combat veterans may find benzodiazepines very difficult, if not impossible, to discontinue due to significant withdrawal symptoms compounded by the underlying PTSD symptoms [68].

Atypical antipsychotics can be helpful when agitation or other symptoms are severe, but use for insomnia should be avoided due to potential adverse effects. Prazosin is an antiadrenergic drug used for treating hypertension that is considered the treatment of choice for nightmares that remain severe despite non-drug interventions [68].

CHRONIC PAIN

There is now broad recognition that pain and PTSD may mutually maintain or exacerbate symptom severity, and shared neurobiologic processes have been identified [318; 319]. One study found that 66% of veterans with PTSD also met criteria for chronic pain and that effective PTSD treatment diminished pain severity [320]. Comorbid PTSD and chronic pain is highly prevalent, and these

patients often have greater distress and impairment than patients with either condition alone. Pain assessment should be included in the evaluation of patients with ASD or PTSD, and the influence of pain on PTSD symptoms and vice versa should be understood [68].

The objective of one retrospective cohort study was to determine whether the presence of pain affects the diagnosis and treatment of PTSD among Department of Veterans Affairs (VA) patients who have a positive PTSD screening test [321]. Using clinical and administrative data from six Midwestern VA medical centers, the authors identified 4,244 primary care patients with a positive PTSD screen and compared outcomes (e.g., mental health visit, PTSD diagnosis, new SSRI prescription) for those with and without a coexisting pain diagnosis. Patients with coexisting pain were found to have a lower rate of mental health visits than those without pain. There were no significant differences in the rate of PTSD diagnosis or new SSRI prescription between patients with and without coexisting pain [321].

Specific traumas can influence the development of certain pain types. Adult survivors of childhood physical, psychologic, or sexual abuse are more likely to report pain involving the pelvis, lower back, face, and bladder, as well as fibromyalgia, interstitial cystitis, and refractory whiplash syndromes. Chronic pain most common in Iraq and Afghanistan war veterans includes head, neck, back, shoulder, and knee pain [322]. Comorbid physical and emotional problems are also common, and the combination of chronic pain, PTSD symptoms, and post-concussion syndrome is unique to Iraq and Afghanistan war veterans and is prevalent in blast-injured patients [68].

Understanding how chronic pain and PTSD develop, become entrenched, and mutually interact is essential. Both can lead to fear-based avoidance, and avoidance behaviors may exacerbate or maintain the severity of either or both conditions. While pharmacologic agents may be effective for use in pain and PTSD individually, little is known of their impact on functioning in patients with this comorbidity. Pain should be assessed and aggressively treated early in post-trauma recovery, and the optimal strategy is a multidisciplinary approach involving providers across disciplines to develop treatments that are complementary, possess a theoretical basis, and are supported by empirical evidence [68].

Nonpharmacologic Treatment

The initial treatment of PTSD with psychoeducation addresses how fear and avoidance of trauma reminders can maintain symptoms and decrease functional ability. Psychoeducation can also incorporate discussion of how pain may serve as a trauma trigger or reminder; increase arousal, fear, and avoidance; and lead to increased disability and pain [323]. Other nonpharmacologic approaches to manage chronic pain include [68]:

- Relaxation: Focus on the focal point of pain and relax muscle tension
- Increasing activity and fitness: Gradual return to more normal activity levels, slowly increase stamina for physical activities
- Reducing emotional over-reactivity: Practicing specific healthy emotional reactions to stressful triggers
- External focusing/distracting: Learning to shift and manipulate attentional focus away from pain in order to minimize the pain experience

Pharmacotherapy

The most common first-line treatments for pain are analgesics such as opioids, nonsteroidal anti-inflammatory drugs, antiepileptic drugs, TCAs (for neuropathic pain), and antidepressants that target norepinephrine reuptake inhibition. With comorbid chronic pain and PTSD, SSRIs are ineffective in pain management, and sedative and anxiolytic medications are not recommended due to the risk of dependence [68].

The efficacy of opioids in alleviating acute pain is well established, but the safety, efficacy, and effect on patient functioning with long-term opioid use for chronic pain is less established [324]. Opioid side effects of tolerance, physical dependence, and cognitive impairment may contribute to potential decreases in functioning over time [324; 325]. Clinicians should recognize the inter-relationships of chronic pain, PTSD, and opioid abuse. Comorbid psychiatric disorders increase the risk of opioid use disorder with chronic pain, and pain patients with comorbid PTSD may be more likely to use analgesic medications at higher rates than those without PTSD [326; 327].

One retrospective cohort study investigated the effect of mental health disorders, particularly PTSD, on risks and adverse clinical outcomes associated with prescription opioid use [328]. The cohort involved 141,029 Iraq and Afghanistan veterans who received at least one non-cancer-related pain diagnosis within one year of entering the VA healthcare system. More than 15,000 in the cohort were prescribed opioids within one year of their initial pain diagnosis. Compared with 6.5% of veterans with no mental health disorders, 17.8% of veterans with PTSD and 11.7% with other mental health diagnoses but no PTSD were significantly more likely to receive higher-dose opioids, receive two or more opioids concurrently, receive sedative hypnotics concurrently, or obtain early opioid refills. Prescriptive opioids were associated with an increased risk of adverse clinical outcomes for all veterans but was most pronounced in those with PTSD [328]. Providers should weigh the benefits and potential harm of extended opioid therapy for patients with chronic pain subsequent to traumatic injury [68; 329].

IRRITABILITY, SEVERE AGITATION, OR ANGER

Pertinent to this section, post-traumatic anger can become maladaptive or interfere with adaptation to current situations (absent tangible threat). The components of post-traumatic anger are arousal, aggressive behavior, and thoughts/beliefs [68; 330].

Components of Post-Traumatic Anger

Arousal

Anger is marked by increased activation in cardiovascular, endocrine, and brain systems associated with emotion and survival. In some patients with PTSD, this elevated internal activation can become reset as the normal level of arousal [5]. The emotional and physical experience of anger is intensified, and a chronic state is produced of feeling on edge, irritable, and more easily provoked.

Aggressive Behavior

The most effective self-protective response to extreme threat is aggressive action. Many people traumatized at a relatively young age do not learn other responses to threat and tend to react aggressively when feeling threatened. This is further amplified when poor impulse control is present. In some, this reaction to threat began as an adaptive response to their environment that persisted long after removal from threatening circumstances. Behavioral aggression may assume several forms, including aggression toward others; passive-aggressive behavior such as complaining, "backstabbing," deliberate lateness, or doing a poor job; or self-aggression, including self-destructive behavior, self-blame, being chronically hard on oneself, or self-injury.

Thoughts and Beliefs

Thoughts or beliefs are used to understand and make sense of one's environment and can also overexaggerate threat. Persons lacking full awareness of their thoughts and beliefs may perceive greater hostility, danger, or threat than others feel is appropriate. For instance, a combat veteran may become angry when others around him do not "follow the rules." The intensity of his belief is directly related to the importance for him to follow rules during combat to prevent deaths. However, traumatized persons may lack awareness of how their beliefs are linked to past trauma. For example, some individuals with serious trauma exposure develop a deep-seated belief in their need to control their environment. When this results in acting inflexibly, they can provoke others into becoming hostile, creating a self-fulfilling prophecy. Common thoughts in people with PTSD include "No one can be trusted," "If I got out of control, it would be horrible/life-threatening/catastrophic," and "Others are out to get me, or won't protect me, in some way."

Anger Management Treatment

Anger management treatment for post-traumatic anger addresses arousal, behavior, and thoughts/beliefs through specific approaches, and CBT has shown positive results in managing all three post-traumatic anger components [68]. For increased arousal, the treatment goal is to assist the patient in learning skills that reduce overall arousal. These include relaxation, self-hypnosis, and physical exercises to discharge tension.

For behavior, the treatment goal is to evaluate the typical behavioral response to perceived threat or when under stress and to assist the patient in expanding his or her reactions by incorporating more adaptive responses. These include taking a time-out; writing down one's thoughts when angry; improving verbal, assertive communication; and changing the pattern of "act first, think later" to "think first, act later."

For thoughts/beliefs, individuals are instructed and assisted in logging, monitoring, and developing awareness of their thoughts prior to becoming angry. The practitioner may provide the patient with more positive alternative thoughts to replace their negative thoughts or beliefs. Therapy may also include role-playing situations that help patients practice their recognition of anger-provoking thoughts and replace them with more adaptive positive thoughts.

The nature, severity, and dangerousness of symptoms should be evaluated and quantified using a standardized anger scale, such as Spielberger's State-Trait Anger Expression Inventory-2 (STAXI-2). The STAXI-2 is a 57-item inventory that measures the intensity of anger as an emotional state (State Anger) and the disposition to experience angry feelings as a personality trait (Trait Anger) [331]. Any causative factors and change should be monitored during follow-up. Other important aspects of treatment include:

- Involvement in enjoyable activities, especially with family/loved ones
- Adequate sleep and relaxation
- Avoidance of caffeine, alcohol, benzodiazepines, and other substances
- Optimal pain management

If pharmacotherapy is necessary, SSRIs or SNRIs may be considered. For patients who are not responding to SSRIs/SNRIs and nonpharmacologic interventions, low-dose anti-adrenergics or low-dose atypical antipsychotics, such as risperidone or quetiapine, may be initiated. If the patient is still not improving or is worsening, referral to specialty care is indicated.

SUBSTANCE USE DISORDERS

Substance use problems can exacerbate PTSD symptoms, complicate pharmacologic treatment, interfere with psychotherapy effectiveness, and introduce new threats to patient safety and recovery from PTSD. Regardless of whether or not substance use meets the threshold for a diagnosable disorder, problematic patterns of substance use should be addressed early and directly in the treatment planning. Findings that unremitted PTSD symptoms can trigger relapse to substance use in patients attempting durable abstinence underscores the importance of timing in addressing both conditions [196]. Adding to the need of simultaneous treatment of PTSD and substance use disorder are research findings that addressing both conditions reduces the risk of death from all causes, especially in young veterans [332]. One suggested approach for addressing trauma symptoms and substance misuse involves using a trauma-processing model early in treatment. Another stage-based approach for treating PTSD has also been proposed and involves [333]:

1. Establishing safety
2. Remembrance and mourning
3. Reconnection with ordinary life

This process helps establish stability and safety, and substance use can be addressed as a safety component [333].

In one study, patients diagnosed with PTSD and alcohol dependence received CBT that targeted the alcoholism and either sertraline or placebo for PTSD symptoms [334]. This study found that improvements in PTSD symptoms had a greater impact on improving alcohol dependence, but a reciprocal relationship was not found. Of note, improvement in hyperarousal PTSD symptoms was substantially associated with improved alcohol use severity [334].

A stepped-care approach has also been suggested, where either psychotherapy or psychopharmacology is used initially. If acceptable remission has not been achieved after sufficient trials, a complimentary strategy is added [68].

CONCLUSION

PTSD results from experiencing, witnessing, or exposure to actual or threatened death, serious injury, sexual violation, and other events experienced as horrific or terrifying, during which the person felt helpless and powerless. The traumatic event, regardless of cause, leads to clinically significant distress, potential danger to self or others, and impairment in functioning.

Health and mental health providers treat civilians and veterans of all ages with symptoms of PTSD, but many lack the necessary knowledge to identify PTSD and perform differential diagnosis. It is important that healthcare providers understand the unique experiential aspects of exposure to specific trauma events, their impact on the emotional and physical needs of the survivor, and individual risk factors and trauma characteristics that heighten risk of PTSD. Diagnosis and treatment may also be improved with knowledge of the changes in PTSD concept and diagnostic criteria in the DSM-5 and how these changes reflect advances in PTSD research [1]. Complex trauma/PTSD is another consideration. Unlike PTSD from single-event trauma exposure, complex trauma/PTSD results from prolonged or chronic interpersonal traumatization beginning in early life, as with childhood sexual abuse. The diagnostic and treatment implications in patients with complex trauma are substantial, as these patients prominently exhibit affect dysregulation, dissociation, and severe interpersonal relationship problems in addition to core PTSD features. These must be addressed before standard PTSD therapies can be delivered. Improved care of persons with PTSD may result in significant improvements in patients' quality of life.

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