

The Journal of Clinical Psychiatry
Audiograph Series

Trauma & Stress
diagnosis & treatment

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Randall D. Marshall, M.D.; Rachel Yehuda, Ph.D.*

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Trauma and Stress: Diagnosis and Treatment

*Mark H. Pollack, M.D.; Kathleen T. Brady, M.D., Ph.D.;
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Posttraumatic stress disorder (PTSD) was not recognized as a distinct disorder until 1980. Since then, much research has focused on its epidemiology, gender differences in prevalence and presentation, diagnosis, comorbidity, biology, and treatment. It can occur after a wide variety of traumatic events, including not only combat and natural disasters but also violent crime, physical or sexual abuse, automobile and industrial accidents, terrorist attacks, and so on. It is a debilitating disorder that can cause impairment in almost every aspect of a person's life. In this Audiograph, experts will discuss some of the main issues surrounding the diagnosis and epidemiology, biology, and treatment of PTSD.

Diagnosis and Epidemiology

Dr. Pollack: PTSD is a condition that affects not only combat veterans but the general population as well. Dr. Brady, what are the current thoughts on epidemiology of PTSD and critical issues in its presentation?

Dr. Brady: PTSD is a characteristic set of signs and symptoms that follow exposure to a traumatic event, and in order to meet criteria for PTSD, individuals not only have to have the symptoms, but those symptoms need to last for at least 1 month after the event and cause considerable functional impairment.

The symptoms fall into 3 clusters.¹ There is the re-experiencing or intrusion cluster, marked by thoughts about

the event that an individual just simply cannot put out of his or her mind—intrusive thoughts and nightmares—as well as physiologic or psychological reactivity when the individual is exposed to anything that reminds him or her of the event. This re-experiencing or intrusion cluster is a particularly important cluster in the differential diagnosis because of an incredible overlap between symptoms of PTSD and symptoms of other psychiatric disorders. But the symptoms in the re-experiencing or intrusion cluster really are unique in that they are all tied very closely to the traumatic event itself.

The avoidant cluster of PTSD symptoms really describes the narrowing of the behavioral repertoire that you often see in individuals with PTSD. They avoid anything—people, places, things—that might remind them of the event. They even do everything they can to avoid thoughts of the event and to push those thoughts out of their mind. They have a very restricted range of affect. They lose interest in things that were previously enjoyable.

Finally, the arousal cluster is marked by symptoms like sleep disturbance, startling easily, poor concentration, and a sense of hypervigilance, always needing to protect oneself. In order to be part of the PTSD syndrome, the avoidant and arousal cluster symptoms should only have appeared after the traumatic event. That is the referral point for PTSD.

PTSD is definitely more prevalent than we previously believed. Traditionally, PTSD was thought of as a disorder that was tied to combat, but we're realizing more and more that civilian traumas can and often do cause PTSD. According to the National Comorbidity



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Survey,² 7.8% of individuals in the United States experience PTSD sometime in their life. PTSD affects about 5% of men and about 10% of women. Different sorts of trauma carry different risks for developing PTSD. Rape has had the highest conditional probability for being associated with PTSD in both men and women. For men in the United States, combat certainly has had high conditional probability for association with PTSD. While factors such as a history of depression or previous traumas might be associated with a vulnerability to the development of PTSD after experiencing a traumatic event, the type and the severity of trauma are really the most important determinants.

Not only do we have this complication of multiple symptoms that overlap with different psychiatric disorders, but PTSD is extremely commonly comorbid with other psychiatric disorders. In fact, it is more common for individuals with PTSD to have other psychiatric disorders than to have PTSD alone. In, again, the National Comorbidity Survey,² 44% of women and

59% of men with PTSD met criteria for 3 or more other psychiatric diagnoses. Forty-eight percent of men and 49% of women who have PTSD have a lifetime major depressive disorder.² Other very prominent disorders in individuals with PTSD include the substance use disorders and other anxiety disorders like social phobia and panic.

The other area of comorbidity is somatic symptoms. Individuals with PTSD often have conditions such as irritable bowel syndrome, chronic pelvic pain, fibromyalgia, or chronic headaches. These individuals often present in a primary care setting rather than a psychiatric setting. Taking a careful trauma history increase the likelihood of appropriate treatment of these patients.

Acute Stress vs. PTSD

Dr. Pollack: The diagnostic criteria require the symptoms to persist for at least 1 month. Do we have a sense of how common more acute stress-related symptoms after a trauma are, and what the difference is between the presentation of PTSD and acute stress-related symptoms? How often do people with acute stress symptoms develop full-blown PTSD?

Dr. Brady: I think that a high percentage of individuals who experience a traumatic event have some level of symptoms of PTSD. But the fact that these symptoms are short lived and do not cause functional impairment for a substantial amount of time are probably key features that differentiate pathologic from nonpathologic symptoms.

Dr. Marshall: The development of PTSD is in proportion to the severity of the trauma. Researchers have reported

Table 1. Recovery From Early PTSD*

| Study | Event Sample Size | | | | | | Recovery |
|---|--------------------------------------|---------|------------|-------------|-----------|-----------|------------------|
| | | 1 Month | 2-5 Months | 6-12 Months | 1-3 Years | 3-6 Years | From PTSD |
| Solomon, 1989 ⁶ | Israeli veterans (N = 238) | 100 | ... | 59 | 47 | 42 | 58% |
| Feinstein and Dolan, 1991 ⁷ | MVA (N = 48) | 25 | ... | 14.6 | ... | ... | 42% |
| Rothbaum et al, 1992 ⁸ | Rape (N = 95) | 65 | 47 | ... | ... | ... | ... ^b |
| Perry et al, 1992 ⁹ | Burn victims (N = 51) | ... | 35 | > 32 | > 28 | ... | ... ^b |
| Blanchard et al, 1996 ⁴ | MVA (N = 132) | 39 | 31 | 12 | ... | ... | 66% |
| Shalev et al, 1997 ¹⁰ and Freeman et al, 1999 ¹¹ | Miscellaneous civilians (N = 236) | 30 | 17 | ... | 10 | ... | 66% |

*Reprinted from Shalev, with permission.⁵ Abbreviation: MVA = motor vehicle accidents.

^bRecovery rate not provided for studies lasting less than 1 year.

that virtually 100% of women met criteria for PTSD in the first week after being raped, whereas 3 months later, only 50% continued to meet criteria, suggesting that there is a fuzzy boundary between the normal reaction to a horrible experience and the diagnosis of PTSD.³ With something like a car accident, Blanchard and coworkers⁴ found that only 39% of victims met PTSD criteria 1 month after the accident. By 6 to 12 months after the accident, only 12% had symptoms of PTSD (Table 1).

Dr. Yehuda: When the diagnosis was initially described for the DSM-III, people were not aware of the epidemiologic data that Dr. Brady just reviewed. There was no way for people to know

which of those symptoms were “normal symptoms” that would happen to everybody who was exposed to trauma and which of those symptoms result directly in disability. So when we ask the question about the relationship between symptoms that occur in the acute aftermath of a trauma and symptoms that are seen as part of PTSD, the answer is, of course there’s going to be overlap.

However, the fundamental problem for clinicians goes beyond a description of the symptoms. A person with PTSD is not able to control the memory or the distress that’s associated with an event. For most people, the distress stays for weeks, but the emotional

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impact of a traumatic event generally fades over time, and the trauma takes its place in the tapestry of life experiences. Even though there's going to be a memory of that event, and even though that memory might even cause emotional distress, the person is going to have fundamental control over both when they want to remember the event and how to modulate their distress.

The person with PTSD feels unable to regulate when they're going to have a memory, a flashback, or a dissociative experience, and because of this inability, their lives are restricted. So if we were going back to the drawing board now to describe PTSD on the basis of the epidemiologic data, we might try a different approach. We might want to note which symptoms are pretty common occurrences in response to trauma and which are associated with clinical impairment. The diagnosis of PTSD has symptoms that are both normal and associated with clinical pathology.

Dr. Marshall: One useful analogy is to think about the difference between normal mourning and a pathologic mourning reaction. After you lose someone close to you, it is absolutely normal to be overwhelmed, and then over time, that feeling fades. Bereavement may change your life permanently, but you're eventually able to go back to a day-to-day functional existence.

Dr. Yehuda: Dissociation skills may even be adaptive at the time of trauma. It's an important point to make for clinicians because they're in a position of educating a patient about which reactions are normative and which reactions are pathologic. We can't just list the 17 symptoms of PTSD and say these

are all equally pathologic, because that's just not correct.

Dr. Pollack: If a clinician were called in to see a patient after a major trauma, what might be normative versus potentially a harbinger of bad things to come?

Dr. Yehuda: The most important fact for clinicians and patients to remember is that at first it is normal to experience the memory and have nightmares and continue to feel quite frightened and distressed. People may feel the desire to not talk or think about the



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trauma so as to make the memory and the distress go away. But actually in the acute aftermath of the trauma, the more they can talk to somebody about what happened to them, the more likely it is that avoidance will not set in. I would also tell somebody in the acute aftermath of the trauma that they should gradually see their level of distress decrease over time, and they should monitor it. The people who don't seem to show a gradual decline in their acute symptoms would be at most

risk to have the acute symptomatology turn into full-blown PTSD.

Dr. Brady: When seeing patients a few weeks or sometimes even months after an event, clinicians should ask, “Has it been getting better? Are you thinking of it less?” If the symptoms are going to resolve, that progress should be evident within a month or so.



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Dr. Marshall: It is useful for clinicians to realize that the likelihood of developing a chronic problem is highly correlated with the initial intensity of someone’s reaction. If, for example, there is an incapacitating level of post-traumatic symptomatology and if there was peritraumatic dissociation during the traumatic event, that individual is at much higher risk for having PTSD 3 months down the road.

Dr. Yehuda: There’s also mounting evidence that what happens after a traumatic event can make a difference. Social support is critical. The tendency of a trauma survivor is to want to isolate himself or herself as if somehow by not seeing anybody or talking about it, he or she can erase what has happened. The more you can rally support for the person and make it obvious that support exists—whether it be their family or their friends—the more helpful it is, no matter how acute the distress has been.

Dr. Marshall: Five sessions of time-limited psychotherapy within the first month can reduce rates of PTSD upward of 50%.¹² You encourage patients to allow a genuine emotional experience and reaction to the trauma, whatever that might be, and you encourage them to lean on their available support systems rather than withdraw or avoid.

Gender and PTSD

Dr. Pollack: I wanted to follow up on the issue of the gender distribution of PTSD—both the likelihood of developing PTSD in the face of trauma and the increased overall prevalence in women. Rape is one of the more powerful drivers of development of PTSD, which may account for the increased rate of the disorder in women. What else do we know about the increased rate of PTSD in women?

Dr. Brady: Women are more likely to experience rape, a trauma that is very likely to cause PTSD. The other issue that needs to be taken into account is that having a history of depression or current depression at the time of the trauma is a risk factor for PTSD.¹³ Because depression is twice as common in women as in men,¹⁴ it’s more likely that at the time of traumatization, women have depression or a history of it. So those two factors combined probably account to some extent for the gender differential.

Dr. Yehuda: Rape results in PTSD equally in men and women,² but women are more likely to experience that trauma. Other individual risk factors augment the general rate of PTSD. One is depression, and whatever is the risk factor for increased depression in

women may also be in operation in their increased risk for PTSD.

Biology of PTSD

Dr. Marshall: Although depression is a risk factor, the biology of depression is distinct from that of PTSD.

Dr. Yehuda: Studies of depression have identified increased activation of the hypothalamic-pituitary-adrenal (HPA) system as a major pathophysiologic component of depression.¹⁵ Many people with major depression show some form of hypercortisolemia or increased cortisol levels or activation or nonsuppression on the dexamethasone suppression test.

Depression does exert a different kind of a biological effect than PTSD. PTSD is associated with low cortisol levels and a tendency to show an exaggerated suppression of cortisol in response to dexamethasone administration (Table 2).¹⁶ In persons who have both PTSD and depression, these effects can sometimes cancel each other out after exposure to trauma, so these patients can look like they show neither a hypersuppression nor a nonsuppression of cortisol. These disorders may have very different risk factors and different onsets.

One of our working models of PTSD is that there are biological vulnerability factors that are related to early adverse experiences.¹⁷ Persons who are exposed to trauma early—even if they've recovered from those experiences—may have a different biological profile walking into a traumatic event, which could make normal recovery more difficult for them.

At the initial stress, many biological responses are activated to help a

Table 2. HPA Axis Alterations: PTSD Versus Normal Stress Response^a

| PTSD | Normal |
|--------------------------------|--------------------------------|
| ↓ Cortisol | ↑ Cortisol |
| ↑ Glucocorticoid receptors | ↓ Glucocorticoid receptors |
| ↑ Suppression on DST | ↓ Suppression on DST |
| ↑ Negative feedback inhibition | ↓ Negative feedback inhibition |

^aReprinted from Yehuda,¹⁶ with permission.

Abbreviations: DST = dexamethasone suppression test, HPA = hypothalamic-pituitary-adrenal, PTSD = posttraumatic stress disorder.

person cope. Startle is an orienting response that helps alert the body to the need for a biological response. The sympathetic nervous system releases epinephrine, which is important for the formation of memories, but also helps increase blood pressure and heart rate. The parasympathetic nervous system also is activated so that normative biological activities can cease and desist. Then the activation of the HPA system, which releases cortisol, occurs as a way to put a brake on those other systems once the person has made a response to the stress.

Persons who are more likely to develop long-term PTSD seem to show less of a cortisol response in the immediate aftermath of the trauma, which then has the effect of increasing the sympathetic nervous system response, which probably leads to the pairing of the memory and the distress. That is a unique feature of PTSD and probably suggests a long history of HPA challenges and dysregulations, including the possibility of prior depression—it's all compatible.

Dr. Marshall: Would you want to speculate on the potential advantages of having this sort of sensitized HPA access or why the capacity to adapt in this way might actually exist?

Dr. Yehuda: Our systems evolve based on the experiences that happen to us, and people have different sets of experiences, coping skills, and individual traits that they bring to events. By the time somebody has reached early adulthood, a lot has already happened to them, which explains why we don't all respond to things in the same way.

Dr. Brady: What about consistent gender differences in the stress response in the HPA axis?

Dr. Marshall: Men and women experiencing different kinds of trauma have different rates of having PTSD afterward. For example, in the case of physical assault, the rates of PTSD are much higher in women than in men who are physically assaulted, whereas the rates were the same with rape.²

Dr. Yehuda: The cortisol response to stress is also going to be affected by where in the menstrual cycle a woman is and where she is in the reproductive cycle of her life, because estrogen is probably a major mediator of the cortisol response to stress. We have to start looking at this issue carefully. What is the impact of rape before a girl has begun her menstrual cycle and what is the impact of that experience on subsequent traumatizations? Of course, when we're talking about prepubescent girls, we're talking about having to mount a cortisol response in the absence of estrogen. What are the consequences of that? We have a whole horizon that stretches out in front of us in terms of all the things we don't know and still have to learn about biological differences in responsivity to stress and how that interacts with development factors and prior experiences as well as other hormonal risk factors.

Dr. Pollack: In animal models, early stress seems to have permanent effects on the HPA axis and stress response. You had mentioned earlier that women or girls may be particularly prone to certain kinds of early stressors. Were you referring only to sexual abuse?



Our systems evolve based on the experiences that happen to us, and people have different sets of experiences, coping skills, and individual traits that they bring to events.

Dr. Yehuda: Well, it's not just sexual abuse. It could be physical abuse. It could be assault in general. It could be the general feeling of being more vulnerable to attack or threatened than boys or men. Witnessing domestic violence might influence boys and girls differently.

Dr. Pollack: Are there any data on how trauma might affect boys and girls differently?

Dr. Marshall: It probably depends on who the perpetrator is and who the victim is, which certainly could affect role identification and sexual identity for boys and girls differently. Children who are not assaulted but grow up seeing their mother beaten up or threatened often develop the kind of hypervigilance that you see in children who have grown up in war zones or in urban settings where there is a real and constant threat.

Children and PTSD

Dr. Pollack: What happens to the children of Holocaust victims? They themselves didn't live through the Holocaust, but certainly seem to be affected by it.

Dr. Yehuda: Children of Holocaust survivors may be affected in all sorts of ways, because their parents might have PTSD or depression, and living with a parent who has these conditions can certainly have a long-lasting impact. For some children of Holocaust survivors, their experiences are minimized in relation to the Holocaust. This may not necessarily be done for malevolent reasons on the part of the parent, but if a child grows up with a steady diet of "You think this is a problem; it is nothing compared with what happened when I was your age," then this can have a very long-lasting impact. My colleagues and I¹⁸ have found that adult children of Holocaust survivors are 3 times more likely to develop PTSD compared with demographically matched peers, which suggests a certain vulnerability; whether it's transmitted environmentally or genetically is something that we don't know yet.

Adult children of Holocaust survivors complain more about emotional abuse than their peers; emotional abuse is also related to lower cortisol levels,¹⁹ so the risk factor for PTSD may, in fact, be mediated by early experiences of emotional abuse, which might be a more ubiquitous phenomenon. People who experience emotional abuse without other forms of abuse may not realize that they have experienced any abuse because emotional abuse is subtle—few people are aware that emotional abuse can have a negative outcome.

Dr. Pollack: What should parents say to their children about their traumatic experience?

Dr. Yehuda: Holocaust survivors are often motivated to seek treatment when they recognize that there is an adverse outcome on their children. We do have to educate people that exposure to trauma doesn't just affect the person who was exposed, but it also affects all the people with whom that person interacts. Exposure to trauma changes social interactions, and the more dependent a person is on a trauma survivor, the more deeply he or she will be affected. Asking about a trauma survivor's children should be part of routine clinical care, and the psychoeducation process should emphasize the potential impact of the trauma on the trauma survivor's children.



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Dr. Marshall: One of the most fundamental clinical issues in PTSD is the sense of safety in the world. And, of course, the safety of a child's world depends on the existence of the parents and a secure relationship with the parents. Seeing a parent threatened can have profound and disruptive effects on the child's experience of the world and his or her safe place in it.

Treatment and Prevention

Dr. Pollack: Let's discuss treatment and early intervention and prevention issues.

Dr. Marshall: The best-established treatment approach for trauma survivors and people with PTSD has been psychotherapy. Perhaps the best studied is exposure therapy, which is an amalgam of psychoeducation, support, provision of hope, and encouragement to face the traumatic memory and process it rather than continue to try to flee it. One of the newer treatments that also seems effective is eye movement desensitization and reprocessing.

The problem with research in psychotherapy and PTSD is that it's generally time limited; regardless of the approach you use, a substantial proportion of individuals will still be symptomatic after the 10 to 15 sessions that are typically studied, suggesting that more treatment is needed. A great gap in our literature is that there are no data on combining medication with psychotherapy or comparing psychotherapy with medications.

Psychotherapy

Dr. Pollack: There's been some concern or controversy about whether or not just having patients talk about what happened to them is in fact helpful or in some cases may retraumatize the individual. Are there ways that we should have patients talk about it?

Dr. Yehuda: Although sometimes talking about the trauma may not be sufficient and other treatment modalities such as pharmacotherapy may have to be used, that doesn't necessarily mean that talking about the trauma is bad for you.

Dr. Marshall: Is there a good way and a bad way to talk about trauma? There's recent controversy surrounding the debriefing model in which immediately after the trauma, the individual is encouraged to talk through it in great detail in an intensive fashion. Rushing people into debriefing can actually be harmful.²⁰ In the literature, there are case reports of individuals in exposure therapy getting worse, relapsing to substance abuse, and becoming acutely suicidal.^{21,22} It's very important to set psychotherapy up in a supportive and safe context with the patient. In the treatment my colleagues and I are studying, there are several sessions that just involve education and winning the patient over, forming a positive alliance, destigmatizing the disorder, and then essentially persuading the individual that therapy is a good idea, so that there's no sense of coercion whatsoever. Inadvertently setting up a coercive feeling within the patient can be damaging.



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Dr. Brady: You need to follow the lead of the patient in terms of how far he or she is comfortable going at any point in time. Even in the midst of exposure therapy, there may be times when both the clinician and the patient need to take a break—have a

session or two in which you retreat and do some different kinds of work—if the patient seems to not be handling it very well.

Dr. Yehuda: Therapists may be unsure about how much they should probe about the traumatic event and when to go along with the patient's statement, "I don't want to talk about it." How much should a therapist engage a patient after that statement is made? The idea is to try to explain to patients why ultimately they are going to have to talk about the trauma. Patients who come to you in the aftermath of a traumatic event are there because, at some level, they do want to talk about it. Their telling you that they don't want to talk about it is the beginning of a process to figure out what they are afraid will happen if they do talk about the trauma. That's essentially what PTSD is about—this fear that thinking about the trauma is the same as re-experiencing it is the same as retraumatization. It's important to understand that having patients relive the traumatic event—even if they have a dissociative experience in your office—is something they can handle. A therapist is competent to handle this and shouldn't be afraid of the material. And if the therapist is not afraid of the material, he or she can help the patients overcome their fear of the material as well.

Dr. Marshall: The patients are confused about the difference between the memory of the trauma and the actual trauma. What therapists essentially do through this treatment is help patients differentiate more and more clearly between the memory and the actual experience.

Dr. Yehuda: People with PTSD can't just tell you how bad they felt. They actually feel how bad they felt every time they have that memory. If you explain to them that what you're going to do is help them have their memory without feeling the emotional distress, they're going to want to work with you, because that's exactly what they want.



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Dr. Marshall: The initial reactions can be incredibly powerful precisely because the patients have never really grappled with the experience. I've seen patients in the first session who become extremely ill, shake, or throw up in the office. It can be overwhelming, but by the second or third or fourth session, the patient is learning from actual experience that each time he or she goes over it, it gets easier.

Dr. Pollack: Education and preparation for what the patient is going to experience early on in treatment are critical to avoid having the patient flee from treatment.

Dr. Marshall: They need to realize that it's going to be really tough in the beginning and then get easier fairly quickly.

Dr. Yehuda: We often fail to talk about shame. For most people who are traumatized, there's a tremendous

feeling of shame that they let it happen or that they were not able to make an attacker stop, or, in the case of the natural disaster, that they just didn't get themselves out of the situation. Even with the therapist, there's quite a degree of embarrassment at describing oneself as being so helpless. So I think that stressing the idea of helplessness and that trauma causes a profound sense of helplessness is an important part of the educational process.

Medication Treatment

Dr. Marshall: Medication can often make these psychosocial treatments more comfortable for patients and can make the difference between feeling able to confront their traumatic experiences and process them or feeling essentially unable to face them. Now, there are no data yet on combination treatment or sequencing treatments, but almost every clinician working in the field has probably had the experience that preparing patients for psychotherapy with medication sometimes seems to make the whole treatment process succeed.

We should mention the role of the benzodiazepines in PTSD because, anecdotally, they are still very often prescribed. Trials^{23,24} that examined benzodiazepine use in PTSD systematically showed no effect for PTSD symptoms. The risk of substance abuse is so high in PTSD that clinicians need to be very careful in using these specific medications, and they have certainly not been shown to be effective for PTSD when used alone.

Several multicenter trials now using serotonin reuptake inhibitors (SRIs) have shown efficacy compared with



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placebo, but the interesting thing about this literature is that there's dramatic heterogeneity—placebo response, for example, in PTSD trials varies from 0% to 60%, which suggests that subpopulations and subgroups have very different treatment responses. We're seeing about a 50% reduction in symptoms with SRIs, compared with about a 30% reduction on placebo in the large multicenter civilian trials. The earlier literature is difficult to compare with these newer trials because they were all conducted with U.S. war veterans and generally used other medications.

Sertraline was the first medication the FDA approved for PTSD, and this approval was a major advance in the field.

Two recent studies^{25,26} of paroxetine also showed efficacy in PTSD. In the first study,²⁵ patients were randomly assigned to treatment with 20 mg/day of paroxetine, 40 mg/day of paroxetine, or placebo. Significantly more patients in the paroxetine groups responded to treatment than did placebo patients.

The other study²⁶ was a randomized, placebo-controlled, flexible-dose study of paroxetine in 307 patients, both men and women, with PTSD. Patients who received paroxetine, 20–50 mg/day,

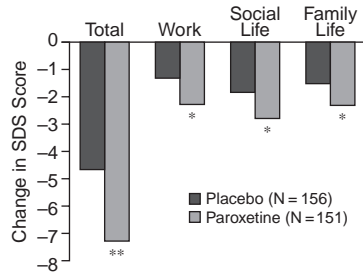
showed significantly greater reduction on all primary and secondary outcome measures than did patients who received placebo (Figure 1). Both trials showed efficacy in both men and women; they were large enough to get a sample of men other than U.S. war veterans.

Dr. Pollack: In addition, both studies^{25,26} reported significantly greater improvement in all 3 symptom clusters in paroxetine-treated patients compared with placebo-treated patients. Paroxetine-treated patients in both studies also experienced improvements in comorbid depression.

Dr. Marshall: A trial²⁷ with fluoxetine in Europe and Africa showed that the agent was effective for war veterans. There's been a real question until recently whether the chronic PTSD due to combat trauma was less treatable than that due to civilian trauma. I think that earlier findings were related to how U.S. war veterans were getting into these clinical trials, rather than the fact that PTSD due to combat trauma is not very treatable with medicine.

Dr. Pollack: In some studies, the entry of veterans has been discouraged—if not even frankly prohibited—because of the perception that they don't respond as well. My understanding is that in some veteran populations, provision of benefits is tied to remaining disabled. There's a disincentive, whether conscious or unconscious, for them to robustly respond to treatment. There's probably also the issue of chronicity; certainly veterans of the Vietnam or Korean wars or World War II with PTSD have been ill now for many decades.

Figure 1. Effect of Treatment on Functional Impairment in PTSD: Change From Baseline in Sheehan Disability Scale (SDS) Scores^a



^aReprinted from Tucker et al.,²⁸ with permission. Negative change in score reflects clinical improvement.
* $p < .05$ vs. placebo; ** $p < .01$ vs. placebo.

Dr. Marshall: The other confound is treatment-refractory status, meaning that the veterans who responded to treatment would already be out of the VA system and would spontaneously have recovered, responded to psychotherapy, or responded to a tricyclic.

Dr. Yehuda: My own experience is that veterans do want to get better. They certainly are somewhat motivated by their compensation issues, but once they're assured that the purpose of a trial isn't tied into their compensation, I think they make very good research candidates. If they're treatment refractory, then they should be excluded from a pharmaceutical trial as part of the standard protocol just like any other treatment-refractory patients should be excluded.

However, even if the war was decades ago, that doesn't mean that veterans have had PTSD that long. The natural history of PTSD is one of peaks and valleys. Many people seek treatment after their symptoms are activated by recent life stressors. I think combat veterans have a lot to teach us, and a lot of the PTSD that we see

among veterans is exactly the same PTSD that we struggle to treat in a civilian setting. What complicates a clinical picture is the presence of substance abuse. If a veteran does not have a substance abuse problem but has PTSD, then that person should be in a trial, or more importantly, should be given an opportunity to be helped by a medication.

Dr. Marshall: Our literature is confounded by these other factors. I agree that the vast majority of U.S. war veterans want treatment and want to get better.

Psychotherapy vs. Medication Treatment

Dr. Marshall: The recent Expert Consensus Guidelines²⁸ have suggested that the first-line treatments for PTSD should be validated trauma-focused psychotherapy or medication with supportive psychotherapy. You really can give patients a choice. They should be educated about the available psychotherapies and about the availability of medication. You should have a discussion with the patient about his or her fears or fantasies about each of these treatments. Specific fears often accompany the prospect of psychotherapy versus the prospect of taking medication, and a treatment plan can and should be developed in collaboration with the patient.

Dr. Pollack: People sometimes don't want to take medication because of concerns about side effects or dependence. At least initially, patients may also feel so overwhelmed by their symptoms that the idea of trying to explore them may be too much to handle. Step approaches to treatment or combina-

tion treatments can be used in which patients start with medication and experience some reduction in anxiety or depression that may make them more amenable to looking at these issues in therapy.

Dr. Marshall: The other issue is comorbidity. The Expert Consensus Guidelines²⁸ recommended strongly that patients with severe comorbidity also be offered medication initially as well as a trauma-focused psychotherapy.



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Dr. Pollack: Some symptoms may be more or less responsive to treatment or more or less debilitating for the patient. For instance, dissociative symptoms sometimes seem less robustly responsive to treatment. Is that true?

Dr. Marshall: Most of our clinical trials to date are just counting the core PTSD symptoms and measuring reduction, but in many ways it's the associated problems that are much more debilitating. In an open trial with paroxetine,²⁹ we found that the dissociative symptoms were reduced about 50% with paroxetine treatment. It's not surprising, though, because we see dissociation as a state of mind that is triggered by severe fear or anxiety or perception of threat. So when the overall level of fear or anxiety is modulated

by the medication, the dissociation does not get triggered as often. But these are moderately severe dissociative symptoms; we're not talking about the much more severe symptoms seen in dissociative identity disorder.

Dr. Yehuda: Patients do not present for treatment telling us about the 17 symptoms of PTSD that they have. Because not all people have the same symptoms, it's difficult to ascertain whether and to what extent treatments affect different symptoms or symptom clusters. What's very important for the treatment of PTSD is the overall pitch that the clinician gives in the form of psychoeducation that should match the chief complaint of the individual.

Dr. Marshall: How would you present the idea of a psychotherapy versus a medication?

Dr. Yehuda: Whatever the chief complaint is, you have to link the symptom with the event. If one of the problems is the fear of talking about the memory, then the reason that you're going to use behavioral approaches is because we can't get to the avoidance unless we burn through this part of the problem and start talking about the trauma. The avoidance symptoms will dissipate if you're able to do that. If a person's having a lot of hyperarousal symptoms, then you say, "Well look, every time you talk about the trauma, you become very distressed and reactivated and you can't sleep. We're going to give you a medication because a medication can directly help with these kinds of symptoms." If you have an explanation as a clinician for why you do what you do, then patients can understand and be a participant in their treatment in a very active way, which I don't think is possible the

different reasons for the different therapeutic components are not explained.

Dr. Marshall: If patients are wondering why they would need to take a medication if the problem is their psychological reaction, then you can teach patients about the new findings in the biology of PTSD and point out that the distress response is a powerful physiologic reaction that at this point has taken on a life of its own.

Dr. Yehuda: Everybody has a reason that they either do or don't want to take a medication. Some people don't want to take medications because they're afraid of losing control.



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Dr. Marshall: I see the same fear about psychotherapy—the fear that their emotional reaction will get so out of control that they will be devastated or destroyed by it.

Dr. Pollack: Are there particular issues in working with patients with comorbid substance abuse?

Dr. Brady: You can't ignore the problem. For a long time, the mantra in addiction treatment has been to treat the addiction first, then give the patient several months of abstinence before even addressing any other psychiatric disorder. But I think that in individuals with addictions who are

suffering from PTSD, those symptoms can be a big driver of substance abuse relapse— when patients can't sleep, when they have intrusive thoughts, they really want to do something about that pain, and what they know how to do best is use drugs or alcohol. So I've probably been more aggressive in treatment of PTSD symptoms early in the



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course of substance abuse recovery. Generally we do not embark on exposure therapy early in the process because that may be a little stressful for people in early recovery. We've also been very pleased with the use of medications in this population. Again, clinicians certainly need to weigh the risk-benefit ratio carefully because these are individuals more likely to abuse anything you give them and more likely to inadvertently overdose or even intentionally overdose. However, the SRIs are a safer group of drugs than any of the antidepressants that were available before. They also may be helpful in some cases in decreasing alcohol consumption.

Dr. Marshall: What would you think about using stress inoculation training techniques, giving these patients an alternative way of controlling their

anxiety by teaching them these techniques as a substitute for an exposure therapy, for example, when you were worried about promoting relapse?

Dr. Brady: Yes, absolutely. A number of cognitive-behavioral strategies teach an individual to manage anxiety and affect in different ways.

Noncompliance

Dr. Pollack: Because of the very nature of PTSD, the risk of noncompliance or nonengagement with either behavior therapy or with medications seems quite high.

Dr. Yehuda: I like the word *non-adherence* better than *noncompliance*. Noncompliance is really making a judgment that a patient is deciding not to take their medication. And nonadherence suggests that they are somehow not able to participate in the treatment the way that you had hoped. A clinician has to be very conscious that trauma survivors feel the need to be in control. So if a patient is not taking medications, it's very important for a clinician to make a distinction between whether this is due to side effects that are intolerable, in which case a change can be made in either the dose or the type of medication, or whether this is more of an overall statement about the fact that the patient feels that he or she is not participating enough in deciding on the trajectory of treatment. There are a lot of psychological issues that might lead patients to not do their homework in psychosocial treatments as well.

Dr. Marshall: With psychotherapy, you assume patients are unlikely to adhere at first because it's so difficult, and discussing noncompliance is really

just a chance to again go over the rationale for doing this.

Dr. Yehuda: Avoidance is one of the key reasons that patients don't do homework for psychosocial therapies. But it's important to recognize that avoidance may be the same reason that they don't take their medication, because the pill reminds them of the PTSD and of the fact that they have been traumatized. And so the statement of not taking a medication is the same kind of statement about not doing homework, for example. There are all sorts of very important reasons that patients don't take their medications; there can't be one assumption about what those reasons are.

Conclusion

Dr. Pollack: All types of trauma can produce PTSD, from terrorist attacks to combat to rape or other personal assault. PTSD can also result from witnessing a traumatic event or learning that such an event has happened to a loved one. Trauma affects people in different ways, some of which are based on gender, but when debilitating effects linger for longer than 1 month, PTSD should be suspected. The clinical pearls discussed by the faculty for man-

aging our patients and trying to help them get better will hopefully help us to take better care of our patients suffering with PTSD. These points include the following:

- PTSD can result from a wide range of trauma and is more prevalent than previously believed.
- Acute response to stress may have some similarities to PTSD symptoms, but normal responses fade over time whereas pathologic symptoms linger and worsen.
- Men and women respond to trauma differently.
- For patients, extensive discussion of the trauma is usually best done in the context of a supportive therapeutic relationship.
- Exposure therapy is effective, but medication treatment may also be necessary to prepare the patient for the rigors of psychotherapy.
- Treatment should target the patient's specific symptoms, and the treatment course should be set with input from the patient.

Thanks to the faculty for wonderful cutting-edge, clinically informed and useful presentations on PTSD.

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Drug Names: *fluoxetine (Prozac and others), paroxetine (Paxil), sertraline (Zoloft).*

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1. Which of the following is not a symptom cluster of posttraumatic stress disorder (PTSD)?
 - a. Re-experiencing
 - b. Avoidance
 - c. Confrontation
 - d. Arousal
2. According to the National Comorbidity Survey, what is the lifetime prevalence of PTSD in the United States?
 - a. 55.7%
 - b. 27.3%
 - c. 7.8%
 - d. 1%
3. The boundary between the normal reaction to a horrible experience and PTSD is always clearly defined.
 - a. True
 - b. False
4. PTSD is associated with what type of change in cortisol levels?
 - a. No change
 - b. Increased
 - c. Decreased
 - d. Unknown
5. Rates of PTSD after rape are
 - a. Much higher in men than women
 - b. Much higher in women than men
 - c. Very low in both men and women
 - d. Similarly high in both men and women
6. The best-established treatment for trauma survivors and people with PTSD is
 - a. Psychotherapy
 - b. Antipsychotic treatment
 - c. Benzodiazepine treatment
 - d. Electroconvulsive therapy
7. For which class of drugs is the strongest evidence of efficacy compared with placebo in the treatment of PTSD?
 - a. Benzodiazepines
 - b. Tricyclic antidepressants
 - c. Serotonin reuptake inhibitors
 - d. Antipsychotics

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