Objective. A number of pharmacological agents have been examined for their possible efficacy at preventing/reducing the development of posttraumatic stress disorder (PTSD). These secondary interventions (administered soon after trauma) have produced mixed results, with the most promising findings being linked to early administration of hydrocortisone. However, effects have been modest, and some previous research indicates that hydrocortisone may be more efficacious in individuals without an extensive mental health history. Due to the extreme heterogeneity of PTSD, it is possible that hydrocortisone differentially impacts different PTSD symptoms. To determine if this is true, we examined whether hydrocortisone differentially impacted the different PTSD symptom clusters. As cortisol has been found to impact memory retrieval, we hypothesized that hydrocortisone would have the greatest impact on re-experiencing symptoms.

Methods. Participants (n=33) were recruited from a level 1-trauma center and were randomized into either the placebo or hydrocortisone group. Participants completed the Peritraumatic Distress Inventory and the Peritraumatic Dissociative Experiences Questionnaire at baseline, and the Davidson Trauma Scale to assess PTSD symptoms at 1- and 3-months.

Results. Using path analyses, hydrocortisone recipients reported significantly fewer re-experiencing symptoms at 1- and 3-months than placebo recipients. With respect to avoidance symptoms, medication groups did not differ at 1-month, but the hydrocortisone group reported
significantly lower symptoms at 3-months. The hydrocortisone group also reported fewer hyperarousal symptoms at 1- and 3-months.

**Conclusions.** Despite a number of limitations, results supported our hypothesis in that hydrocortisone was efficacious at preventing the development of re-experiencing symptoms. However, hydrocortisone also demonstrated efficacy with respect to hyperarousal (at 1- and 3-months) and avoidance (at 3-months). This suggests that early hydrocortisone treatment not only impacted memory retrieval, but also physiological arousal and later avoidance/numbing symptoms. These results suggest that hydrocortisone may broadly impact the development of PTSD symptoms. Though promising, these results are considered preliminary, and should be interpreted with caution.
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Introduction

Although exposure to traumatic events is quite common in the United States (~90% prevalence rate (Alegria et al., 2013), only a minority of individuals who experience a trauma develop posttraumatic stress disorder (PTSD: lifetime prevalence rates of 9-12%: Alegria et al., 2013; Breslau, Kessler, Chilcoat, Schultz, Davis, & Andreski, 1998; Kilpatrick, Resnick, Milanak, Miller, Keyes & Friedman, 2013). This presents challenges to prevention strategies; clinical interventions are costly and time- and labor-intensive, and providing them to all trauma victims would be a waste of resources. As the majority of victims do not develop PTSD, it is necessary to identify high-risk individuals for targeted prevention approaches in order to prevent PTSD symptoms before they impact functioning. PTSD symptoms can be devastating, resulting in extreme impairment and clinical distress (Pietrzak, Goldstein, Southwick & Grant, 2011). PTSD is also often comorbid with other psychiatric disorders and is associated with increased risk of suicide and decreased quality of life (Pietrzak, Goldstein, Southwick & Grant, 2011). Given the debilitating nature of PTSD, research has aimed to develop early interventions that can be administered soon after a traumatic event to reduce or prevent the subsequent development of PTSD.

Initial preventive efforts stemmed from existent successful PTSD treatments, and consisted mainly of administering psychological interventions for chronic PTSD soon after trauma exposure (Bisson, Jerkins, Alexander, Bannister, 1997; Mayou & Hobbs, 2000: Tuckey & Scott, 2014). Unfortunately these initial treatments rendered limited results. Psychological
Debriefing resulted in either no benefit, or in some cases, detrimental effects (i.e., increased rates of PTSD) (Bisson, Jerkins, Alexander, Bannister, 1997; Mayou & Hobbs, 2000; Tuckey & Scott, 2014). Subsequent exposure-based interventions administered within hours of a trauma and cognitive behavioral therapy that was delayed until a few weeks post-trauma produced more promising results (see review: Rothbaum et al., 2012). However, these interventions are time intensive and require trained clinicians to administer. This led researchers to examine whether early pharmacological agents could act as secondary interventions, buffering or preventing the development of PTSD. Of the pharmacological agents examined, hydrocortisone has shown the most promise as a secondary intervention (see review: Amos, Stein & Isper, 2014). A number of randomized controlled trials have found that hydrocortisone results in significantly lower PTSD diagnoses or symptom scores. However, for the most part differences have been modest, and some results have suggested that hydrocortisone may be particularly efficacious in subgroups of participants (Delahanty et al., 2013). One reason that hydrocortisone may not be equally efficacious in all victims with PTSD is that the diagnosis of PTSD contains extraordinary heterogeneity (i.e., there are 636,120 possible symptom combinations that can result in a PTSD diagnosis: Galatzer-Levy & Bryant, 2013). Perhaps hydrocortisone is preferentially beneficial to certain symptoms/patient characteristics. The present paper examined the extent to which hydrocortisone may differentially impact specific symptoms of PTSD in order to suggest whether matching of hydrocortisone administration to symptom presentation may increase treatment efficacy.

**Posttraumatic Stress Disorder**

According to the DSM-IV, a diagnosis of PTSD is considered when an individual experiences a traumatic event that results in intense fear, helplessness, or horror at the time of
exposure, and then develops symptoms grouped into three symptom clusters: (1) re-experiencing, (2) avoidance or emotional numbing, and (3) hyperarousal symptoms (American Psychiatric Association, 2000). Re-experiencing symptoms consist of persistent recollections of the event, distressing dreams, episodic feelings as if one is back in the situation, and experiencing significant distress as a result of these experiences (American Psychiatric Association, 2000). Avoidance symptoms include psychological or physical avoidance of stimuli related to the trauma, while emotional numbing includes symptoms such as a restricted range of affect and feeling detached from others (American Psychiatric Association, 2000). Hyperarousal symptoms are characterized by increased arousal that did not exist prior to the trauma such as difficulty falling or staying asleep, irritability, trouble concentrating, hypervigilance, and an exaggerated startle response.

To incorporate new empirical findings, the DSM-5 (American Psychiatric Association, 2013) updated the criteria necessary to meet a PTSD diagnosis. The new criteria included modifying the definition of a ‘traumatic event’ such that there was no longer the requirement for a subjective reaction of fear, helplessness, and/or horror (Calhoun, Hertzberg, Kirby, Dennis, Hair, Dedert & Beckham, 2012; Carmassi et al., 2013;). Additionally, the DSM-5 eliminated the requirement for specific subjective reactions to the event and broadened the stressor criteria that would qualify as a traumatic event (American Psychiatric Association, 2013). Furthermore, the 3-cluster model of PTSD was changed to a 4-cluster model by splitting the avoidance cluster into two distinct factors: avoidance and alterations in cognitions and mood. This was primarily due to evidence suggesting that these different clusters were associated with distinct effects on psychopathology and mood (Carmassi et al., 2013). Also, three new symptoms were added to the criteria increasing the symptom total from 17 to 20 (two symptoms were added to the
negative alterations in cognitions and mood cluster, and one symptom was added to the arousal cluster). Research has found that discrepancies between DSM-IV and DSM-5 are primarily due to changes in the standard for a PTSD qualifying trauma (i.e. Criterion A), and to changes in the avoidance and negative alteration clusters (Calhoun et al., 2013; Cassmassi et al., 2013).

Whether defined by the DSM-IV or DSM-5, PTSD is associated with devastating consequences and comorbidities. PTSD is highly comorbid with a range of mental health disorders including: specific phobia, generalized anxiety disorder, panic, social phobia, major depression, dysthymia, bipolar 1, alcohol use disorder, and drug use disorder (Ouimette et al., 2004; Pietrzak, Goldstein, Southwick & Grant, 2011; Schnurr & Green, 2003). PTSD is also associated with a range of detrimental physiological consequences, having been linked to somatization, chronic pain, circulatory and musculoskeletal disorders, and overall decreased quality of life (Ouimette et al., 2004; Pietrzak, Goldstein, Southwick & Grant, 2011; Schnurr & Green, 2003).

For a diagnosis of PTSD to be considered, symptoms must be present for at least one month (American Psychiatric Association, 2013). Given the negative consequences of a PTSD diagnosis, researchers have sought to develop interventions that could be implemented soon after a trauma to prevent/reduce PTSD symptoms before they have a chance to develop and result in detrimental consequences.

**Psychobiology of PTSD**

Research into secondary pharmacological interventions (interventions implemented after the trauma but before a diagnosis can be considered) has largely been informed by studies examining the psychobiology of PTSD. Not surprising, given the necessity of experiencing a traumatic stressor, PTSD has been associated with abnormal functioning of the body’s primary
stress pathways. More specifically, PTSD has been associated with alterations in the: 1) sympathetic nervous system (SNS), 2) changes in the limbic system, and 3) dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis.

**Sympathetic Nervous System and Locus Coeruleus.** Increased sympathetic arousal has been consistently observed in PTSD, and studies have shown greater excretion of norepinephrine in people with PTSD compared to trauma-exposed controls (Pitman & Orr, 1990). Because norepinephrine is primarily synthesized in the locus coeruleus, it has been suggested that this area underlies autonomic hyperarousal and acts as the “alarm center” in the brain (for a review see van der Kolk, 2001). Further evidence can be seen in functional magnetic resonance imaging (fMRI) research which has indicated that exaggerated startle responses are associated with activation in this brain region (Naegeli, 2017). The locus coeruleus is also thought to facilitate memory retrieval through noradrenergic tracts, possibly resulting in increased physiological arousal during re-experiencing of the trauma (Hageman, Anderson & Jorgensen, 2001; see review: Ravindran & Stein, 2009).

**Limbic System.** Limbic system alterations have also been identified in PTSD. These include specific changes in areas of the brain that are particularly important for the processing of emotionally laden memories: the amygdala and the hippocampus. In a normally functioning brain, the amygdala processes sensory information by giving it emotional meaning. The hippocampus then encodes this emotional meaning into memory (for reviews see: Ravindran & Stein, 2009; van der Kolk, 2001; Yehuda, 2000). In PTSD, there is a hyperactivation of the amygdala when compared to controls. Hippocampal activity is also altered in PTSD though results are inconsistent, with some studies finding greater and some finding decreased activation (Aupperle et al., 2012; Wang et al., 2016). In individuals with PTSD, cognitive and physiological
re-experiencing is often associated with hyperactivation in these brain regions (Stevens et al., 2018). In addition to the role that the limbic system plays in emotion and memory, research has also shown that this system is implicated in the regulation of the HPA axis (see review: Herman, Ostrander, Mueller, Figueiredo, 2005).

**Hypothalamic Pituitary Adrenal Axis.** In a healthy individual, exposure to a stressor activates the HPA axis. Initially the hypothalamus releases regulatory neuropeptides including corticotropin-releasing hormone (CRH) (see review: Herman, Ostrander, Mueller, Figueiredo, 2005). The release of CRH triggers the secretion of adrenocorticotropic hormone (ACTH) from the pituitary, and this prompts the adrenal glands to release the glucocorticoid hormone, cortisol. Through negative feedback inhibition, cortisol works to suppress HPA axis activity at the level of the hypothalamus and pituitary once the threat has been removed, thus stopping the stress response (see review: Yehuda, 2000).

As PTSD is a stress-related disorder, researchers initially hypothesized that PTSD would be associated with heightened activation of the HPA axis and higher levels of circulating free cortisol. Surprisingly, early studies found that individuals with PTSD had significantly lower cortisol levels than trauma-exposed controls (see review: Yehuda, 2001; Yehuda, McFarlane, Shalev, 1998). Similarly, research examining whether biological alterations seen in chronic PTSD could serve as risk factors for the development of PTSD symptoms found low cortisol levels immediately following a trauma in individuals who subsequently developed PTSD (Delahanty et al., 2003; McFarlane et al., 1997). Although contrary to initial hypotheses, one of the actions of cortisol is to modulate arousal; lower cortisol levels could result in increased, excessive sympathetic arousal and perhaps aberrant trauma memory formation characteristic of PTSD (see review: Ravindran & Stein, 2009).
In summary, PTSD is associated with increased sympathetic arousal due to possible alterations in the locus coeruleus, as well as limbic system changes particularly in the amygdala and hippocampus. Dysregulation of the HPA axis also is consistently found in individuals with PTSD, and lower cortisol levels appear to predict PTSD in adults. Consistent findings of altered biological stress pathways led to the exploration of pharmacological agents that could rectify the altered functioning of the SNS and HPA axis.

**Secondary Interventions for PTSD**

Research has examined the efficacy of a number of different pharmacological agents at preventing or buffering the development of PTSD symptoms. The most commonly researched agents include temazepam (benzodiazepine), propranolol (beta-blocker), and hydrocortisone (glucocorticoid) (see review: Amos, Stein, Ipser, 2014).

When used in the immediate aftermath of trauma benzodiazepines such as tamazepam have been found to decrease arousal and anxiety and improve sleep (see review: Guina, Rossetter, DeRhodes, Nahhas & Welton, 2015). However, although tamazepam was efficacious at decreasing acute stress-related symptoms, once the drug was discontinued, symptoms became magnified. Multiple studies found that participants experienced rebound effects, including worsened anxiety, insomnia, and irritability (see review: Guina, Rosseter, DeRhodes, Nahhas & Welton, 2015). While benzodiazepines initially appeared promising in reducing symptoms immediately after traumatic events, they have ultimately been found to be associated with increased PTSD incidence rates (see review: Qi, Gevonden & Shalev, 2016).

The beta-blocker propranolol is typically used to treat hypertension, arrhythmias, and anxiety (Steenen, et al., 2016). It was first explored as an early intervention for PTSD due to its ability to decrease physiological reactivity post-trauma. Propranolol has also been
associated with decreased memory of emotionally evocative information (Cahill, Prins, Weber & McGaugh, 1994). However, findings regarding the efficacy of propranolol at preventing PTSD have been mixed, and results suggesting efficacy have not been successfully replicated (see review: Kearns, Ressler, Zatzick, Rothbaum, 2012). In addition, a 2014 Cochrane review concluded there was no evidence that propranolol prevented PTSD (see review: Amos, Stein & Isper, 2014).

Arguably, the strongest evidence for a secondary pharmacological intervention to prevent PTSD is provided by hydrocortisone. Hydrocortisone is a steroidal drug commonly prescribed for inflammatory and allergy-related conditions. Prior research has demonstrated that it is moderately efficacious as a secondary intervention for PTSD (see review: Amos, Stein, & Isper, 2014). However, the underlying mechanisms for the efficacy of hydrocortisone are not fully understood (see review: Qi, Gevonden & Shalev, 2016). There are two different plausible mechanisms that could explain the efficacy of hydrocortisone: indirectly via decreasing arousal and directly by disrupting memory retrieval.

Arousal is critical in aiding memory; we remember events that increase arousal better than ones that do not. However, excessive arousal may lead to inappropriate or “overconsolidated” memories (Henckens et al., 2010; Sorayia et al., 2006; Pitman, 1988; Putman et al., 2007). One mechanism through which hydrocortisone may be efficacious is by containing or shutting down initial sympathetic responses. Cortisol has been found to normalize amygdala activation, which can stabilize the SNS response after a stressful event (Henckens et al, 2010). Inadequate cortisol levels may lead to persistent SNS activation. This continued arousal has been associated with the cyclical consolidation and reconsolidation of distressing memories leading to a susceptibility to developing PTSD (McCleery & Harvey, 2004).
Therefore, increasing cortisol levels via exogenous administration may decrease arousal during periods of consolidation/reconsolidation. It is important to note that research supporting this has been mixed, as some studies have found that cortisol is also associated with increased arousal ratings (Abercrombie et al., 2005).

Alternatively, it has been hypothesized that hydrocortisone’s efficacy lies in its impact on memory retrieval. When administered after learning, but before retrieval, hydrocortisone decreases memory performance (Het, Ramlow & Wolf, 2005). One study also found a decrease in re-experiencing symptoms after hydrocortisone administration (Aerni et al., 2004), and exogenous cortisol administration has been associated with impaired declarative memory retrieval (see review: de Quervain et al., 2009). Prior literature has established the importance of the medial temporal lobe in the retrieval of memories (Squire, 1992; Ritchey et al., 2015). Imaging studies of the temporal lobe have found that after hydrocortisone administration, there was decreased blood flow and activation of this area, providing evidence for a mechanism in which hydrocortisone is able to decrease memory retrieval. Additionally, animal studies (de Kloet, Oitzl & Joels, 1999; de Quervain, Roozendaal & Mcgaugh, 1998; Roozendaal, Griffith, Buranday, de Quervian & Mcgaugh, 2003) have demonstrated that higher glucocorticoid levels are associated with impaired memory retrieval processes; these findings were also replicated in humans (de Quervain, Roozendaal, Nitsch, Mcgaugh & Hock, 2000).

**Hydrocortisone as an Early Intervention for PTSD**

To date, there have been five randomized controlled trials (RCTs) testing the efficacy of hydrocortisone as a secondary intervention. These studies have differed in methods and study samples examined. Despite this, each found promise for the efficacy of hydrocortisone at preventing PTSD symptoms. Three studies administered hydrocortisone during times of critical
illnesses (Shelling et al, 2001; Shelling et al., 2004; Weis et al., 2006). One of these studies focused on a sample with septic shock (Shelling et al, 2001) and the other two focused on samples undergoing cardiac surgery (Shelling et al., 2004; Weis et al., 2006). Two additional studies targeted injury samples recruited in the emergency department (Delahanty et al., 2013; Zohar et al., 2011).

The studies using critical illness populations (Shelling et al, 2001; Shelling et al., 2004; Weis et al., 2006) used intravenous (IV) infusions of an initially high dose of hydrocortisone (100mg) followed by a taper. For the patients with septic shock (Shelling et al, 2001), 100 mg was initially infused, followed by 18mg every hour, until septic shock was reversed. Once reversed, the participants were tapered off hydrocortisone for the next few weeks. Participants receiving hydrocortisone were significantly less likely to meet PTSD diagnostic criteria than those receiving placebo; however, treatment groups did not differ in continuous PTSD symptom scores.

In the first cardiac surgery study (Shelling et al., 2004), the following dosing methods were used: 100mg administered over 10 minutes intravenously before surgery, followed by continuous IV infusions of 10mg per hour for 24 hours, then 5mg per hour on post operative day (POD) 2, then 20mg administered 3 times on POD 3, then tapered to 10mg administered 3 times on POD 4. Results indicated that the hydrocortisone recipients had significantly less PTSD-related symptoms, but no statistically significant difference in the number and type of traumatic memories (Shelling et al., 2004). Weis (2006) replicated this study in a different cardiac surgery population. These finding were very similar to the first study: significantly fewer stress-related symptoms were identified in the hydrocortisone group; however, no differences were found.
between number and type of traumatic memories related to the patient’s stay in the intensive care unit (Weis et al., 2006).

The above studies suggest the efficacy of hydrocortisone at preventing PTSD in samples of participants with critical illnesses. However, in each of these studies the anti-inflammatory effects of hydrocortisone decreased the severity of the medical event, and it is possible that group differences in PTSD symptoms reflect differences in event severity rather than a direct beneficial impact of hydrocortisone on symptom development.

Two studies examined the efficacy of hydrocortisone at preventing PTSD in heterogeneous samples of traumatic injury patients. Zohar and colleagues (2011) recruited individuals who met DSM-IV criterion A and randomized them to receive either a single injection of hydrocortisone (100-140mg depending on weight) or placebo between 1.5 to 5.5 hours after the traumatic injury. Significantly lower Clinician Administered PTSD Scale (CAPS) scores were observed in the hydrocortisone group two weeks and three months post-trauma. In addition, the hydrocortisone group had significantly lower depression and anxiety scores assessed using visual analog scales 2 weeks, and 1 and 3 months after the traumatic event.

In contrast, Delahanty and colleagues (2013) randomized participants to receive either 20mg of oral hydrocortisone or placebo twice daily. The initial dose of 20mg was administered within 12 hours of the trauma, followed by the same dose for 10 days and a six-day taper. This study found significantly lower PTSD and depression symptoms in the hydrocortisone treatment group three months post-trauma. Additionally, participants who had not received any prior mental health treatment reported the lowest PTSD symptoms, suggesting that hydrocortisone is more efficacious at preventing the development of PTSD symptoms in those without a history of psychopathology (Delahanty et al., 2013).
Existing studies have suffered from small sample sizes and a lack of control over possible spurious variables while examining a wide variety of populations, age ranges, methods, and doses. Despite these limitations, each study demonstrated partial support for the efficacy of hydrocortisone as a secondary preventive intervention for PTSD.

**Current Study**

Although existing RCTs have demonstrated support for the efficacy of hydrocortisone as a secondary intervention for PTSD, results have been modest. It is possible that hydrocortisone differentially impacts some PTSD symptoms more than others. In order to determine if this is true, we examined whether hydrocortisone differentially impacted PTSD symptom clusters in the prior Delahanty et al randomized trial. The current analysis assessed the symptom clusters of the DSM-IV. As research has shown that cortisol impacts memory retrieval, we hypothesized that hydrocortisone would have the greatest impact on re-experiencing symptoms.
Methods

Participants

The sample of 33 participants was between the ages of 18-56 (M=30.58 (10.65)), and predominately male (65.6%). The sample was relatively homogenous with respect to race with 86% Caucasian, and 14% African American. Participants were randomized into the placebo (n = 17) and the hydrocortisone (n = 16) conditions.

Measures

Traumatic Stress Schedule. This self-report checklist includes 8 possible events that encompass interpersonal traumas, nature related traumas, and automobile related traumas. Each trauma also is assessed for the extent to which the participant feared for his/her life, experienced physical injury, and experienced distress. This measure was used to obtain an understanding of trauma history and types of traumas experienced.

Peritraumatic Distress Inventory. This 13-item self-report measure assesses distress during and after the traumatic event. Scores correlate with and independently predict later post-traumatic stress symptoms (Brunet et al, 2001; Nishi, Matsuoka, Yonemoto, Noguchi, Kim & Kanba, 2010). The PDI demonstrated strong internal validity (α = .85) in the current sample.

Davidson Trauma Scale. This 17-item self-report inventory, measures the DSM-IV symptoms of PTSD (Davidson et al., 1997). The symptoms are assessed on a 5-point frequency and severity scale. In the present sample this measure was used to assess PTSD-related symptoms 1 month and 3 months after the trauma. The internal consistency was strong across all
symptoms with $\alpha = .84$ at one month and $\alpha = .87$ at 3 months. The symptom clusters also had good internal validity (1 month: re-experiencing $\alpha = .77$, avoidance $\alpha = .80$, hyperarousal $\alpha = .83$; 3 month: re-experiencing $\alpha = .89$, avoidance $\alpha = .88$, hyperarousal $\alpha = .85$).

**Procedures**

Participants were recruited from a level one-trauma center. The exclusion criteria included the following: living outside a 25 mile radius of the hospital, a Glasgow Coma Sale (GCS) score of less than 14, inability to initiate the first medication dose within 12 hours of the traumatic event, allergy to cortisol or medical contraindications to cortisol administration, pregnant or breastfeeding, exposure to an ongoing trauma (e.g. domestic violence); injuries requiring delayed operative procedures, use of corticosteroids within the last 6 months, or injuries that required treatment with steroids. All participants had to be non-amnestic and to meet criterion A for exposure to a traumatic event. In order to identify individuals at high risk for PTSD, the Peritraumatic Dissociative Experiences Questionnaire was administered as a screener. All participants had to score equal to or over a 27, a score consistently associated with increased risk for PTSD.

A trauma nurse approached patients and administered the initial screener to determine eligibility. This screener included the Mini-Mental Status Exam to ensure that participants were able to competently consent to the study. The nurse then collected information about each patient’s trauma to confirm that the participant met criterion A for a PTSD diagnosis, and administered the Peritraumatic Dissociative Experiences Questionnaire. Those who consented and had a PDEQ score over 27 were assessed by the trauma physician and randomly assigned to a 10-day medication (20mg hydrocortisone) or placebo regimen taken every 12 hours. Following the 10-day regimen, every 2 days the dose was halved for 6 consecutive days to avoid adrenal
suppression. The 20mg dose was chosen due to prior empirical evidence finding it sufficient to impair memory retrieval, while not interfering with wound healing (Anstead, 1998; De Quervain Roozendaal, Nitsch, McGaugh & Hock, 2000; Kirschbaum, Wolf, May, Wippich & Hellhammer, 1996).

The in-hospital assessment consisted of the PDI, medical chart review and a standard sociodemographic questionnaire. Participants were telephoned every other day for 10 days to evaluate possible medication side effects. Participants also completed daily journals focused on medication adherence and side effects. After 10 days, participants’ medical journals and used pill containers were collected. One-month and three-months post-trauma participants completed the Davidson Trauma Scale.
Results

Overview of Analyses

SPSS Version 20 was used to perform the initial analyses and to prepare the data for the path analyses. List-wise deletion was used to account for missing data. The number of different prior trauma types experienced, total number of prior traumas, age, gender, race, income, injury severity score, peritraumatic distress assessed at baseline, and use of opioid-based pain relievers in the days after the trauma were examined as potential covariates. The placebo group was significantly older ($M_{\text{placebo}} = 36.24 (13.02)$, $M_{\text{treatment}} = 26.73 (8.82)$; $t (28.45) = 2.44$, $p = .021$) and consisted of more non-Caucasian participants ($\chi^2 = 5.23$ $p = .022$) than the hydrocortisone group (see Table 2 & 3). There were no other significant differences between groups (see Table 2 & 3). Thus, age and race were used as covariates in the following models.

Two path models were conducted using AMOS to assess the relationship between the hydrocortisone and re-experiencing, avoidance, and hyperarousal symptoms controlling for the impact of age and race (see Figure 1) (Byrne, 2010). The first model assessed PTSS symptoms at 1-month, the second model assessed symptoms at 3-months. The number of observations in each model was 21, with 18 parameters ($3 = \text{unanalyzed}$, $9 = \text{direct}$, $3 = \text{variance}$, $3 = \text{residual}$), and 3 model degrees of freedom. At a minimum the model would need 180 participants to be sufficiently powered and optimally 360 participants. Though our analysis is severely underpowered, we decided it would be best to model the relationships between the clusters simultaneously to account for collinearity between the symptoms clusters (i.e. re-experiencing, avoidance, and hyperarousal).
Findings

For each model, the following fit indices were assessed: the Chi-Squared Test of Model Fit, the Root Mean Square Error of Approximation (RMSEA), and the Comparative Fit Index (CFI). For both models poor model fit was indicated ($\chi^2 = 12.74, p = .005, \text{CFI} = .816, \text{RMSEA} = .227$; $\chi^2 = 12.74, p = .005, \text{CFI} = .838, \text{RMSEA} = .227$). The model fit was likely impacted by the underpowered sample, therefore the parameter estimates were estimated; however, the following results should be interpreted with severe caution.

In regards to the model evaluating symptoms at 1-month, age was found to impact hyperarousal, such that older participants reported lower symptom severity scores ($\beta = -0.334, p = .015$). Race also accounted for significant variance in avoidance and hyperarousal, respectively ($\beta = -0.326, p = .037$; $\beta = -0.317, p = .021$), suggesting that African American participants reported higher symptom severity compared to Caucasians. With respect to our main variables of interest, hydrocortisone significantly impacted re-experiencing symptoms and hyperarousal symptoms at 1-month ($\beta = -0.438, p = .003$; $\beta = -0.419, p = .002$ respectively), such that the group receiving hydrocortisone reported significantly lower re-experiencing and hyperarousal symptoms at 1 month (see Figure 2).

Next the model for symptoms assessed at 3-months was evaluated; age and race did not account for significant variance in any of the symptoms clusters (see Figure 3). Alternatively, significant group differences were identified and the group receiving hydrocortisone reported significantly lower re-experiencing, avoidance, and hyperarousal symptoms severity ($\beta = -0.464, p = .004$, $\beta = -0.503, p = .001$, $\beta = -0.347, p = .042$ respectively).
Discussion

Prior research has suggested the efficacy of hydrocortisone as a secondary intervention for preventing PTSD. Though results overall have been modest, early hydrocortisone administration has been found to have stronger impact in particular subgroups (i.e. those who have never received prior mental health treatment). Given the heterogeneity of the PTSD diagnosis, it is possible that hydrocortisone is more efficacious at reducing some types of PTSD symptoms more than others. The present study examined whether hydrocortisone differentially impacted the different PTSD symptom clusters (re-experiencing, avoidance/numbing, and hyperarousal). By understanding the types of symptoms affected by hydrocortisone, more effective preventive treatments can be planned and managed.

Based on prior research demonstrating that hydrocortisone impacts memory retrieval, we hypothesized that hydrocortisone would be specifically efficacious at preventing the development of re-experiencing symptoms. Results supported this hypothesis with hydrocortisone recipients reporting lower re-experiencing scores at 1- and 3-months. In contrast, previous research using hydrocortisone as a secondary intervention for PTSD found no differences in number of self-reported traumatic memories between trauma victims receiving and not receiving hydrocortisone (Shelling et al., 2004; Weis et al., 2006). Though related, number of trauma memories and the extent to which one re-experiences the event are different conceptually, and the present findings do not contradict the findings of prior studies on traumatic memories.

Contrary to our hypothesis, hydrocortisone recipients also had significantly lower hyperarousal scores at 1-and 3-months and lower avoidance scores at 3-months. It is possible
that the lower hyperarousal symptom severity scores were produced by the hydrocortisone decreasing SNS activation during periods of consolidation/reconsolidation leading to lower hyperarousal symptom severity and ultimately resulting in weaker emotional memories. As expected, hyperarousal symptom severity decreased in both groups over time; however, the group differences persisted at 3-months. Group differences in avoidance/numbing symptom severity only met statistical significance when assessed at 3-months. It is possible that the lower level of re-experiencing symptom severity and hyperarousal symptom severity at 1-month produced the lower avoidance/numbing symptom severity at 3-months. Overall, hydrocortisone impacted all symptom clusters at 3-months, suggesting that hydrocortisone may not differentially impact symptoms but instead may broadly influence the development of PTSD.

These findings should be interpreted with caution due to the severely underpowered analyses. Though results were significant, the sample size is small leading to a lack of confidence in the parameters estimates. Additionally, lack of model fit is likely due to the small sample size. These two model needs to be replicated in a larger sufficiently powered sample; a minimum of 180 participants and optimally 360 participants are necessary to run these analyses. However, the current parameter estimates were found in the absence of outliers, this leads us to be optimistic that this model may be replicated in a larger sample. Outliers would be particularly impactful in such a small sample, and the lack of outliers suggests a legitimate pattern. However, it is also possible that these findings are just an artifact of the current dataset.

In addition to the underpowered analyses, there are a number of additional limitations. As previously stated, the low base-rates of PTSD create challenges in early intervention studies. Simply stated, it is difficult to show benefit from an early intervention if very few or none of the participants develop the disorder. Also, the current study used the Peritraumatic Dissociative
Experience Questionnaire to screen for high-risk participants. Unfortunately, this also led to a sample that had significant peritraumatic dissociation, suggesting that these results may not generalize to trauma victims/PTSD patients without peritraumatic dissociation.

Similar to other studies that have used hydrocortisone as an early intervention, the sample size in the current study is small and the analyses are underpowered. Given the physical nature of the injuries sustained by the sample and the anti-inflammatory effects of hydrocortisone there are a number of additional explanations for the decrease in re-experiencing, avoidance, and hyperarousal symptoms. Though hydrocortisone has been found to disrupt wound healing, it is possible that it decreased inflammation and overall perception of pain in some participants. This decrease in pain could be related to a decrease in PTSD symptoms.

Noted limitations also draw attention to possible areas of future research. As with all PTSD research, a valid and reliable method of detecting high-risk individuals soon after trauma would be invaluable and allow for more accurate and meaningful secondary intervention research. Also, a replication of these findings in a larger sample would be beneficial and allow for appropriately powered analyses. The possibility that hydrocortisone broadly impacts PTSD symptoms should also be explored. If no differential impact on symptom clusters is identified, then a closer assessment of dosing and timing would also be beneficial due to the variation in the current empirical literature. It is possible that when administered at different times, (ie. 6 hours after a trauma vs. 24 hours after) hydrocortisone may differentially impact the development of PTSD symptoms. Previous literature has demonstrated that when traumatic memories are already encoded, hydrocortisone may disrupt retrieval of these emotionally laden memories (Aernie et al, 2014). However, when administered soon after a trauma, group differences in trauma-related memories were not detected (Shelling et al., 2004; Weis et al., 2006). Although most secondary
pharmacological interventions have attempted to initiate medication administration as soon as possible after the trauma, it is possible that hydrocortisone would be efficacious even if it was delayed a day or so post-trauma.

In addition to dosing and timing suggestions, future research should test the efficacy of hydrocortisone in trauma-exposed samples without physical injuries. Not only would this control for the possible impact of physical pain and anti-inflammatory effects of hydrocortisone, but it would also allow for more control over opioid painkillers and other hospital administered drugs.

In conclusion, this is the first study to suggest that hydrocortisone may decrease intrusion symptoms. In addition, our findings highlight that not only are intrusions significantly lower in the hydrocortisone group, but also hyperarousal symptoms at 1-month and 3-months and avoidance/numbing symptoms at 3 months. This suggests that early hydrocortisone treatment is not only impacting memory retrieval, but also physiological arousal and later avoidance/numbing. It is possible that the lower levels of hyperarousal symptoms precede the development of intrusion symptoms through altering consolidation and reconsolidation; and the resulting lower symptoms in these two clusters later leads to lower avoidance.


http://doi.org/10.1002/da.22012


http://doi.org/10.1002/jts.21848


Pietrzak, R. H., Goldstein, R. B., Southwick, S. M., & Grant, B. F. (2011). Prevalence and Axis I Comorbidity of Full and Partial Posttraumatic Stress Disorder in the United States: Results from Wave 2 of the National Epidemiologic Survey on Alcohol and

http://doi.org/10.1016/j.janxdis.2010.11.010


van der Kolk, B. A. (2001), The psychobiology and psychopharmacology of PTSD. Human Psychopharmacology Clinical & Experimental.16: pp. 49–64. doi:10.1002/hup.270


Table 1. *Summary of intercorrelations for age, peritraumatic distress inventory (PDI), and each symptoms cluster assessed at 1 & 3 (N= 39-64).*

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>PDI</th>
<th>Re-experiencing (1month)</th>
<th>Avoidance (1month)</th>
<th>Hyperarousal (1month)</th>
<th>Re-experiencing (3months)</th>
<th>Avoidance (3months)</th>
<th>Hyperarousal (3months)</th>
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<tbody>
<tr>
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<td>--</td>
<td>-0.143</td>
<td>-0.141</td>
<td>-0.176</td>
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<td>Inventory (PDI)</td>
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* p < .05, ** p < .01, *** p < .001
Table 2. *Descriptive Information.*

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</tr>
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<td></td>
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<tr>
<td>SD</td>
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<tr>
<td>n</td>
<td>17</td>
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</tr>
<tr>
<td>Placebo</td>
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<td></td>
</tr>
<tr>
<td>M</td>
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<tr>
<td>n</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>t</td>
<td>1.44, 11.56</td>
<td>2.58*</td>
<td>56.08</td>
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</table>

* p < .05, ** p < .01, *** p < .00
Table 3. *Chi-Square Comparison of Gender and Race by Experimental Condition.*

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<th>Placebo</th>
<th>$\chi^2$</th>
<th>p</th>
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</tr>
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</table>

* * p < .05, ** p < .01, *** p < .00
Figure 1. Conceptual Model
Figure 2. Results from the path analysis assessed at 1-month predicting group differences (hydrocortisone versus placebo) on symptom severity scores for each cluster of PTSD symptoms, controlling for age and race. Only significant paths are shown for the sake of brevity.

*p < .05, ** p < .01, *** p < .001.
Figure 3. Results from the path analysis assessed at 3-months, predicting group differences (hydrocortisone verses placebo) on symptom severity scores for each cluster of PTSD symptoms, controlling for age and race. Only significant paths are shown for the sake of brevity.

*p < .05, ** p < .01, ***p < .001
Project Title: Prevention of PTSD with early hydrocortisone treatment: pilot

Investigators: Douglas L. Delahanty, PhD, Kent State University
William Fallon, MD, Summa Health System
John Bon, PharmD, Summa Health System
Eileen Spoonster, RN, Summa Health System
Stevan Hobfoll, PhD, Kent State University

INTRODUCTION
You are being asked to participate as one of approximately 64 subjects in a National Institute of Health (NIH)-funded research study examining whether a low dose of hydrocortisone is effective at decreasing or preventing symptoms of post-traumatic stress in trauma victims. All participants will have been admitted to the Summa Health System trauma unit to be eligible to participate.

DESCRIPTION OF RESEARCH
People experience a wide range of outcomes following a traumatic event. Although rates differ depending on type of trauma, 20-60% of trauma victims may develop posttraumatic stress disorder (PTSD). However, not all trauma victims develop PTSD. Previous research has found that trauma victims who develop PTSD excrete lower levels of urinary cortisol immediately after a trauma than victims who do not develop PTSD. Other research has suggested that increasing levels of cortisol may protect against the development of PTSD in patients such as yourself—but this has not yet been examined. Cortisol is a naturally occurring hormone in your body, and the present study is designed to test whether increasing cortisol levels can protect against or decrease symptoms of PTSD. Participants in this study will be randomly assigned (as in the toss of a coin) to one of two treatment groups. You will receive either hydrocortisone (20mg, twice per day) or a placebo (a sugar pill) for 10 days with a six-day taper. There is an equal chance of being in either treatment group, and neither you nor the experimenters will know which treatment you received (except in case of an emergency).

INCLUSION/EXCLUSION CRITERIA
Eligible participants will consist of patients aged 18 or older who are admitted to the Summa Health System trauma unit. Participants will be excluded if they do not remember the event leading to their hospitalization, if they have been taking drugs, if they will not be able to start the protocol within 12 hours of their hospitalization, or if administration of hydrocortisone will be contraindicated. A nurse or physician will review medical exclusionary criteria with you.

__________________________ Subject’s initials
__________________________ Date

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NOV 20 2006
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YOUR PARTICIPATION

If you decide to take part in this experiment, the physician will first make sure that you do not have any medical condition or injury that would make you ineligible for this study. Next, a blood sample will be collected to assess your baseline cortisol levels. You will then receive the initial dose orally. This will either be low-dose hydrocortisone or placebo. For the next 16 days (10 days with a 6 day taper) you will need to take 2 pills per day: one in the morning and one in the evening.

We will also meet with you to ask you questions and have you fill out surveys about your thoughts, feelings, and responses to your trauma. The first meeting will occur in the hospital. We will ask you about your memory of the event, your initial responses to the event, and how we can contact you when you leave the hospital. This meeting will last about 15 minutes. We will also need to look at your medical records concerning your current visit to the hospital to record medications you received in the hospital, the extent of your injuries, the time you were admitted, results of blood and urine toxicology reports, and cardiovascular levels upon admission. By signing below you are giving us permission to look at these records.

While you are taking the study medication, a nurse will contact you every day while you are in the hospital and every other day by phone (after discharge) to make sure you are not experiencing any side effects. We will ask you to record the time at which you took the pills in a journal. We will collect the journal on the 10th day that you take the medication (10th day after the trauma), and will ask you to provide us with a urine sample. This sample will consist of all urine produced overnight (from 6PM-9AM), and we will collect the sample the following morning -- the sample will be used to measure levels of cortisol in your body, and will not be used for any alcohol or drug testing.

One and three months after your trauma, one of the members of our research team will come to your house to conduct an interview designed to measure your thoughts, feelings, and reactions to your trauma. To ensure that we don’t miss anything, your answers will be audio taped. The one-month assessment will take approximately 2 hours, and the three-month assessment will take approximately 1.5 hours.

RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS

Risks from the study medication are minimal given proper application of the eligibility criteria. Reported side effects of similar doses and durations of administration of hydrocortisone include difficulty sleeping, euphoria, and fatigue. These side effects have only been reported by a minority of patients. You will be provided with a list of observed side effects to this medication. However, different people tolerate medications differently, and it is possible that you may have more marked reactions to the medication; as with any drug, there may also be unanticipated side effects. There is no risk associated with the urine collection.
Some of the questions we ask will require you to remember aspects of your trauma, and this may lead to increases in distress. The long-term effects of discussing your memories are unknown, but it is possible that some of the questions may provoke stressful memories. In addition, as the long-term effects of early memory recall are unknown, participating in the present study may have no effect on your levels of distress, may lead to longer-lasting distress, or may reduce your levels of distress. If any part of the study causes you to become distressed (symptoms of distress and/or depression include sleep disruption, concentration problems, changes in appetite, and similar disruptions in normal functioning), please call the Center for the Treatment and Study of Traumatic Stress at (330) 379-5094 for an appropriate referral during office hours (9AM-4:30PM). In case of an after-hours emergency, you can contact the Department of Psychiatry at (330) 379-5167 and follow the directions to contact the on-call resident psychiatrist. There also may be unexpected risks resulting from your participation in the study. If any new findings affect your risk to participating, you will be informed of these findings.

POTENTIAL BENEFITS: You may or may not receive hydrocortisone, and the hydrocortisone treatment may or may not decrease symptoms of post-traumatic distress. You personally may not receive any direct benefit from your participation in this study. Your participation in this study may enable us to help future trauma victims. $25 will be provided to you for completing today’s assessment, $100 will be provided at the end of the medication regimen and $100 will be provided to you at each follow-up session ($325.00 total) to compensate you for your time.

CONFIDENTIALITY: All information collected about you will be kept private within the limits of the law. Some of the data may contain sensitive information that could be used in court. You should understand that there are certain legal limits to confidentiality. If you reveal suicidal or homicidal feelings or that a child or fetus (if pregnant) or elderly person is the victim of abuse, actions may be taken to protect others and me.

Paper records are stored in locked cabinets and rooms. Only a subject number will identify the information you provide to us. The Summa Health System IRB, and other federal and/or state agencies may request access to our research records. Results of the study data may be published in scientific journals but your personal information will not be identified in any manner.

VOLUNTARY PARTICIPATION: Your participation in this study is voluntary and you may decline to participate in it without loss of any future services or benefits to which you may be entitled. This study is unrelated to your medical treatment and will have no impact on your medical treatment. Should you choose to participate, you may voluntarily withdraw from it at any time. By signing this form you are indicating that you have been informed about the research study in which you are agreeing to participate, and have had all of your questions satisfactorily answered.

__________ Subject’s initials
__________ Date

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NOV 2 0 2006
INSTITUTIONAL REVIEW BOARD
RESEARCH-RELATED INJURIES: You should also be aware that there are no Federal, State or private programs established to provide research subjects with compensation and/or medical treatment or other financial losses due to physical injuries resulting from research procedures such as the one in which you are being asked to participate. In the event of injury, or any unexpected side effect that is the direct result of the study, emergency treatment is available. However, you and/or your health plan will be billed for this treatment. Summa Health system does not have funds set aside to compensate you for lost wages, disability or discomfort, or psychological or emotional damage, nor is the institution able to pay for the costs of medical treatment if you are injured by participating in this study.

QUESTIONS: If you have any questions now, during or following your participation regarding this study and its associated risks, please contact Douglas L. Delahanty at (330) 672-2395. This project has been approved by Kent State University (5) Institutional Review Board and Summa Health System Institutional Review Board. If you have any questions regarding your rights as a research subject please call the Summa Health System Institutional Review Board, telephone (330) 375-4045. For questions about Kent State University’s rules for research, you may contact Dr. John West, Dean, Division of Research and Graduate Studies, telephone (330) 672-2851.

SIGNATURE LINES: By signing this form I acknowledge that I have read it, understand it, and have had any questions regarding the risks and benefits of this study satisfactorily answered, and I am voluntarily consenting to participate in this study. Further, I realize that by signing this form I do not waive any of my legal rights. I will receive a copy of this form for my records.

Date: ___________ Subject Signature: __________________________

Date: ___________ Researcher Signature: __________________________
(Person obtaining consent)

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Prevention of PTSD with Early Cortisol Treatment
CONTACT INFORMATION

Patient name: ________________________________

Current Address: ________________________________

Do we have your permission to use this address to send you postcards throughout the duration of the study? Yes No

If we are unable to contact you via telephone, do we have your permission to visit your home to inquire about your participation in the study? Yes No

<table>
<thead>
<tr>
<th>Home number:</th>
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<th>Day(s)</th>
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<td>_____________________</td>
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<tr>
<td>Work number:</td>
<td>(<em><strong>)</strong></em>_____</td>
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</tr>
<tr>
<td>Alternate number:</td>
<td>(<em><strong>)</strong></em>_____</td>
<td>_____________________</td>
<td>_____</td>
</tr>
</tbody>
</table>

Can we have the name and number of a close friend or family member that we can contact, if we are unable to get a hold of you? Yes No

Alternate Contact number: (___)________

What time and days of the week can you be reached?

________________________________________

Are you planning on moving within the next month? Yes No

If yes, where can we reach you?

Address: ________________________________

________________________________________

Phone: (___)________

Effective as of what date? ____/____/_______
Prevention of PTSD with Early Cortisol Treatment
DRUG INFORMATION FOR ORAL HYDROCORTISONE

Brand name(s): Cortef; Hydrocortone
Other name(s): Cortisol

Why is this medication prescribed?

Hydrocortisone, a corticosteroid, is similar to a natural hormone produced by your adrenal glands. It is often used to replace this chemical when your body does not make enough of it. It relieves inflammation (swelling, heat, redness, and pain) and is used to treat certain forms of arthritis; skin, blood, kidney, eye, thyroid, and intestinal disorders (e.g., colitis); severe allergies; and asthma. Hydrocortisone is also used to treat certain types of cancer.

How should this medicine be used?

Hydrocortisone comes as a tablet and suspension to be taken by mouth. Your doctor will prescribe a dosing schedule that is best for you. Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand. Take hydrocortisone exactly as directed. Do not take more or less of it or take it more often than prescribed by your doctor.

Do not stop taking hydrocortisone without talking to your doctor. Stopping the drug abruptly can cause loss of appetite, an upset stomach, vomiting, drowsiness, confusion, headache, fever, joint and muscle pain, peeling skin, and weight loss. If you take large doses for a long time, your doctor probably will decrease your dose gradually to allow your body to adjust before stopping the drug completely. Watch for these side effects if you are gradually decreasing your dose and after you stop taking the tablets or oral liquid, even if you switch to an inhalation. If these problems occur, call your doctor immediately. You may need to increase your dose of oral hydrocortisone temporarily or start taking it again.

What special precautions should I follow?

Before taking hydrocortisone,

- tell your doctor and pharmacist if you are allergic to hydrocortisone, aspirin, tartrazine (a yellow dye in some processed foods and drugs), or any other drugs.
- tell your doctor and pharmacist what prescription and nonprescription medications you are taking, especially anticoagulants ('blood thinners') such as warfarin (Coumadin), arthritis medication, aspirin, cyclosporine (Neoral, Sandimmune), digoxin (Lanoxin), diuretics ('water pills'), estrogen (Premarin), ketoconazole (Nizoral), oral contraceptives, phenobarbital, phenytoin (Dilantin), rifampin (Rifadin), theophylline (Theo-Dur), and vitamins.
- if you have a fungal infection (other than on your skin), do not take hydrocortisone without talking to your doctor.
Prevention of PTSD with Early Cortisol Treatment
DRUG INFORMATION FOR ORAL HYDROCORTISONE

- tell your doctor if you have or have ever had liver, kidney, intestinal, or heart disease; diabetes; an underactive thyroid gland; high blood pressure; mental illness; myasthenia gravis; osteoporosis; herpes eye infection; seizures; tuberculosis (TB); or ulcers.
- tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding. If you become pregnant while taking hydrocortisone, call your doctor.
- if you are having surgery, including dental surgery, tell the doctor or dentist that you are taking hydrocortisone.
- if you have a history of ulcers or take large doses of aspirin or other arthritis medication, limit your consumption of alcoholic beverages while taking this drug. Hydrocortisone makes your stomach and intestines more susceptible to the irritating effects of alcohol, aspirin, and certain arthritis medications. This effect increases your risk of ulcers.

What special dietary instructions should I follow?

Hydrocortisone may cause an upset stomach. Take hydrocortisone with food or milk.

What should I do if I forget a dose?

When you start to take hydrocortisone, ask your doctor what to do if you forget a dose. Write down these instructions so that you can refer to them later.

What side effects can this medication cause?

Although side effects from hydrocortisone are not common, they can occur. Tell your doctor if any of these symptoms are severe or do not go away:

- upset stomach
- stomach irritation
- vomiting
- headache
- dizziness
- insomnia
- restlessness
- depression
- anxiety
- acne
- increased hair growth
- easy bruising
- irregular or absent menstrual periods

If you experience any of the following symptoms, call your doctor immediately:

- skin rash
Prevention of PTSD with Early Cortisol Treatment

DRUG INFORMATION FOR ORAL HYDROCORTISONE

- swollen face, lower legs, or ankles
- vision problems
- cold or infection that lasts a long time
- muscle weakness
- black or tarry stool

What storage conditions are needed for this medicine?

Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom).

In case of emergency/overdose

In case of overdose, call your local poison control center at 1-800-222-1222. If the victim has collapsed or is not breathing, call local emergency services at 911.

What other information should I know?

Keep all appointments with your doctor and the laboratory. Your doctor will order certain lab tests to check your response to hydrocortisone.

If your condition worsens, call your doctor. Your dose may need to be adjusted.

Carry an identification card that indicates that you may need to take supplementary doses (write down the full dose you took before gradually decreasing it) of hydrocortisone during periods of stress (injuries, infections, and severe asthma attacks). Ask your pharmacist or doctor how to obtain this card. List your name, medical problems, drugs and dosages, and doctor's name and telephone number on the card.

This drug makes you more susceptible to illnesses. If you are exposed to chicken pox, measles, or tuberculosis (TB) while using hydrocortisone, call your doctor. Do not have a vaccination, other immunization, or any skin test while you are taking hydrocortisone unless your doctor tells you that you may.

Report any injuries or signs of infection (fever, sore throat, pain during urination, and muscle aches) that occur during treatment.

Your doctor may instruct you to weigh yourself every day. Report any unusual weight gain.

If your sputum (the matter you cough up during an asthma attack) thickens or changes color from clear white to yellow, green, or gray, call your doctor; these changes may be signs of an infection.

If you have diabetes, hydrocortisone may increase your blood sugar level. If you monitor your blood sugar (glucose) at home, test your blood or urine more frequently than usual. Call your doctor if your blood sugar is high or if sugar is present in your urine; your dose of diabetes medication and your diet may need to be changed.
Prevention of PTSD with Early Cortisol Treatment
DRUG INFORMATION FOR ORAL HYDROCORTISONE

Do not let anyone else take your medication. Ask your pharmacist any questions you have about refilling your prescription.
Last Revised - 04/01/2003

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Kent State University Hydrocortisone Study
DEMOGRAPHICS

1. Age: __________

2. Sex: Male Female

3. Race/Ethnicity: ______________________

4. How would you characterized where you live now?
   ____ Rural community
   ____ Small town
   ____ Suburban neighborhood
   ____ Urban neighborhood
   ____ Other (specify) ______________________

5. What is your relationship status, and how long has this been the case?
   ____ Single How long ______
   ____ Long-term Live-in How long ______
   ____ Married How long ______
   ____ Separated How long ______
   ____ Divorced How long ______
   ____ Widowed How long ______

6. What is the highest educational level you have completed?
   ____ Elementary
   ____ Jr. High
   ____ GED
   ____ High School
   ____ Trade School (Years beyond HS: _______)
   ____ Some College or 2-year Degree
   ____ 4 Year Degree
   ____ Advanced College Degree
   ____ Other (specify ______________________)

-------- Subject No.
Kent State University Hydrocortisone Study
DEMOGRAPHICS

1. Age: __________

2. Sex: Male  Female

3. Race/Ethnicity: ______________________

4. How would you characterized where you live now?
   ___ Rural community
   ___ Small town
   ___ Suburban neighborhood
   ___ Urban neighborhood
   ___ Other (specify) ______________________

5. What is your relationship status, and how long has this been the case?
   ___ Single  How long _____
   ___ Long-term Live-in  How long _____
   ___ Married  How long _____
   ___ Separated  How long _____
   ___ Divorced  How long _____
   ___ Widowed  How long _____

6. What is the highest educational level you have completed?
   ___ Elementary
   ___ Jr. High
   ___ GED
   ___ High School
   ___ Trade School (Years beyond HS: _________)
   ___ Some College or 2-year Degree
   ___ 4 Year Degree
   ___ Advanced College Degree
   ___ Other (specify __________________________)

_________________ Subject No.
Kent State University Hydrocortisone Study
DEMOGRAPHICS

7. What is your approximate annual income?
   ____ Under $10,000/year
   ____ $10,000 - $15,000/year
   ____ $15,001 - $20,000/year
   ____ $20,001 - $30,000/year
   ____ $30,001 - $40,000/year
   ____ $40,001 - $50,000/year
   ____ $50,001 - $60,000/year
   ____ $60,001 - $70,000/year
   ____ Over $70,001/year

8. What is your occupation? ____________________________

9. What is your spouse/partner's occupation? ________________

10. Is there someone available to help you with any medical care that you might need?
    Yes       No       Doesn't apply

11. Is there someone available to drive you on errands or to work, if you are unable to do this for yourself?
    Yes       No       Doesn't apply

12. Do you smoke
    Yes       No

13. If you smoke, approximately how many cigarettes did you smoke the day of the trauma: ____________

14. Approximately how many cigarettes do you smoke on an average day? ____________

------------------- Subject No.
15. Please list any medications, over-the-counter medications, or drugs that you are currently taking.

Height: _______  Weight: _______

-----------Subject No.
Instructions: Please complete the items below by circling the choice that best describes your experiences and reactions during and immediately following the incident leading to your hospitalization. If an item(s) does not apply to your experience, please circle “not at all true”.

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Not at all True</th>
<th>Slightly True</th>
<th>Somewhat True</th>
<th>Very True</th>
<th>Extremely True</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I had moments of losing track of what was going on -- I “blacked out” or “spaced out” or in some way felt that I was not part of what was going on.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. I found that I was on “automatic pilot” -- I ended up doing things that I later realized I hadn’t actively decided to do.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. My sense of time changed – things seemed to be happening in slow motion.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. What was happening seemed unreal to me, like I was in a dream or watching a movie or play.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. I felt as though I were a spectator watching what was happening to me, as if I were floating above the scene or observing it as an outsider.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. There were moments when my sense of my own body seemed distorted or changed. I felt disconnected from my own body, or that it was unusually large or small.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. I felt as though things that were actually happening to others were happening to me – like I was being trapped when I really wasn’t.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. I was surprised to find out afterwards that a lot of things had happened at the time that I was not aware of, especially things I ordinarily would have noticed.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. I felt confused, that is, there were moments when I had difficulty making sense of what was happening.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>10. I felt disoriented, that is, there were moments when I felt uncertain about where I was or what time it was.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
**Directions**: Rate the extent to which you experienced each item during your traumatic event and immediately afterward.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Not at all</th>
<th>Slightly</th>
<th>Somewhat</th>
<th>Very</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I felt helpless to do more.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. I felt sadness and grief.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. I felt frustrated or angry I could not do more.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I felt afraid for my safety.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. I felt guilt that more was not done.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. I felt ashamed of my emotional reactions.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. I felt worried about the safety of others.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. I had the feeling I was about to lose control of my emotions.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. I had difficulty controlling my bowel and bladder.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10. I was horrified by what happened.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11. I had physical reactions like sweating, shaking, and pounding heart.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12. I felt I might pass out.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13. I thought I might die.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
DAVIDSON TRAUMA SCALE
by Jonathan R.T. Davidson, M.D.

Name: ___________________________ Age: _____ Sex: [ ] Male [ ] Female

Date: ______/_____/______

Please identify the trauma that is most disturbing to you.

Each of the following questions asks you about a specific symptom. For each question, consider how often in the last week the symptom troubled you and how severe it was. In the two boxes beside each question, write a number from 0 - 4 to indicate the frequency and severity of the symptom.

<table>
<thead>
<tr>
<th>FREQUENCY</th>
<th>SEVERITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = Not At All</td>
<td>0 = Not At All Distress</td>
</tr>
<tr>
<td>1 = Once Only</td>
<td>1 = Minimally Distress</td>
</tr>
<tr>
<td>2 = 2 - 3 Times</td>
<td>2 = Moderately Distress</td>
</tr>
<tr>
<td>3 = 4 - 6 Times</td>
<td>3 = Markedly Distress</td>
</tr>
<tr>
<td>4 = Every Day</td>
<td>4 = Extremely Distress</td>
</tr>
</tbody>
</table>

1. Have you ever had painful images, memories, or thoughts of the event? [ ] [ ]
2. Have you ever had distressing dreams of the event? [ ] [ ]
3. Have you felt as though the event was recurring? Was it as if you were reliving it? [ ] [ ]
4. Have you been upset by something that reminded you of the event? [ ] [ ]
5. Have you been physically upset by reminders of the event? (This includes sweating, trembling, racing heart, shortness of breath, nausea, or diarrhea.) [ ] [ ]
6. Have you been avoiding any thoughts or feelings about the event? [ ] [ ]
7. Have you been avoiding doing things or going into situations that remind you of the event? [ ] [ ]
8. Have you found yourself unable to recall important parts of the event? [ ] [ ]
9. Have you had difficulty enjoying things? [ ] [ ]
10. Have you felt distant or cut off from other people? [ ] [ ]
11. Have you been unable to have sad or loving feelings? [ ] [ ]
12. Have you found it hard to imagine having a long life span and fulfilling your goals? [ ] [ ]
13. Have you had trouble falling asleep or staying asleep? [ ] [ ]
14. Have you been irritable or had outbursts of anger? [ ] [ ]
15. Have you had difficulty concentrating? [ ] [ ]
16. Have you felt on edge, been easily distracted, or had to stay "on guard"? [ ] [ ]
17. Have you been jumpy or easily startled? [ ] [ ]