



# Understanding Opiate Addiction

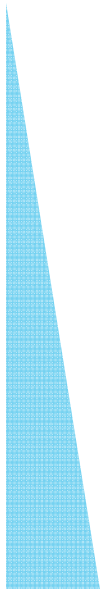
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# Disclosures

▶ None



# Prevalent (incorrect) theories of opiate addiction

- ▶ Opiates are intrinsically addictive, and anyone who takes them long enough will become addicted.
- ▶ Some people just have an "addictive personality", and that explains why they become addicts
- ▶ People with poor will power are unable to quit using drugs once they start, and that's why they are addicts.
- ▶ (We'll discuss these 3 myths at the end of our discussion)



# So, what actually causes addiction?

- ▶ Like diabetes, there are two distinct types of opiate addiction.
- ▶ The first is due to genetic influences, and is referred to as **endogenous opiate dependence**.
- ▶ The second type is due to external influences, such as emotional trauma, and is called **exogenous opiate dependence**.

# Endogenous Opiate Dependence

- ▶ Endogenous opiate dependence is similar to type 2 diabetes in that it is genetically determined and transmitted. For example, if a person has 2 parents who suffer from type 2 diabetes, it is almost inevitable that they too will be at risk for diabetes when they get older.
- ▶ Likewise, if someone has 2 parents who are addicts or alcoholics, they are at very high risk of becoming one themselves.

# Endogenous Opiate Dependence

- ▶ The other similarity with type 2 diabetes is that both addiction and type 2 diabetes are due to receptor dysfunction. With type 2 diabetes, there is plenty of insulin, but the receptors just don't respond to it as they should. Many of the medications used to treat this type of diabetes function by making the receptors work better.



# Endogenous Opiate Dependence

- ▶ Studies have shown that this is exactly what is happening in people who suffer from the genetic form of addiction.
- ▶ Positron Emission Tomography studies show that the receptors in addict's brains that bind our naturally occurring opiates (called endorphins) don't work as well as the non-addicts receptors do.

# Endogenous Opiate Dependence

- ▶ So what is it that these endorphins do?
- ▶ It turns out that endorphins (our naturally occurring opiates) are extremely important *neurotransmitters*, (like serotonin, dopamine, norepinephrine, etc.)
- ▶ Endorphins are responsible for several important functions in the brain, one of the most important being our overall sense of well being. If your endorphin system isn't working correctly, that can interfere with that sense of well being.



# Brain Imaging Evidence of Endogenous Opioid Regulation of Mood and Behavior

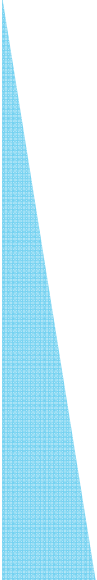
- ▶ Positron emission tomography (PET) of mu-opioid receptors has shown that active changes in mu-opioid neurotransmission occur in response to experimentally-induced negative affective states, thus substantiating the role of the mu-opioid receptor system in the neurophysiological regulation of affective experiences in humans. Further, PET imaging has also shown that sustained sadness was associated with a significant decrease in mu-opioid binding potential in the left inferior temporal cortex of patients with major depressive disorder. These findings clearly show that *endogenous opioid neurotransmission on mu-opioid receptors is altered in patients diagnosed with major depressive disorder*. These findings help explain why some of our chronic pain patients report improved mood and/or remission from depression when treated with opioids, above and beyond any reduction of their pain symptoms." (1)

# Hedonic Tone

- ▶ In Addiction Medicine, we refer to a person's sense of well being as their **Hedonic Tone**. We use this term instead of depression because it allows us to take into consideration a person's baseline emotional state, as well as intrinsic and extrinsic factors that may be coming into play.
- ▶ In a way, Hedonic Tone could be considered the flip side of what we call depression, in that we focus more on a person's happiness than their unhappiness.
- ▶ Another reason to use Hedonic Tone rather than the term depression is that depression refers to a disease state, where Hedonic Tone looks more to the individual's overall emotional health.
- ▶ Everyone's hedonic tone is different, just like everyone's muscle tone is different.

# Hedonic Tone

Normal Hedonic  
Tone





# Hedonic Tone

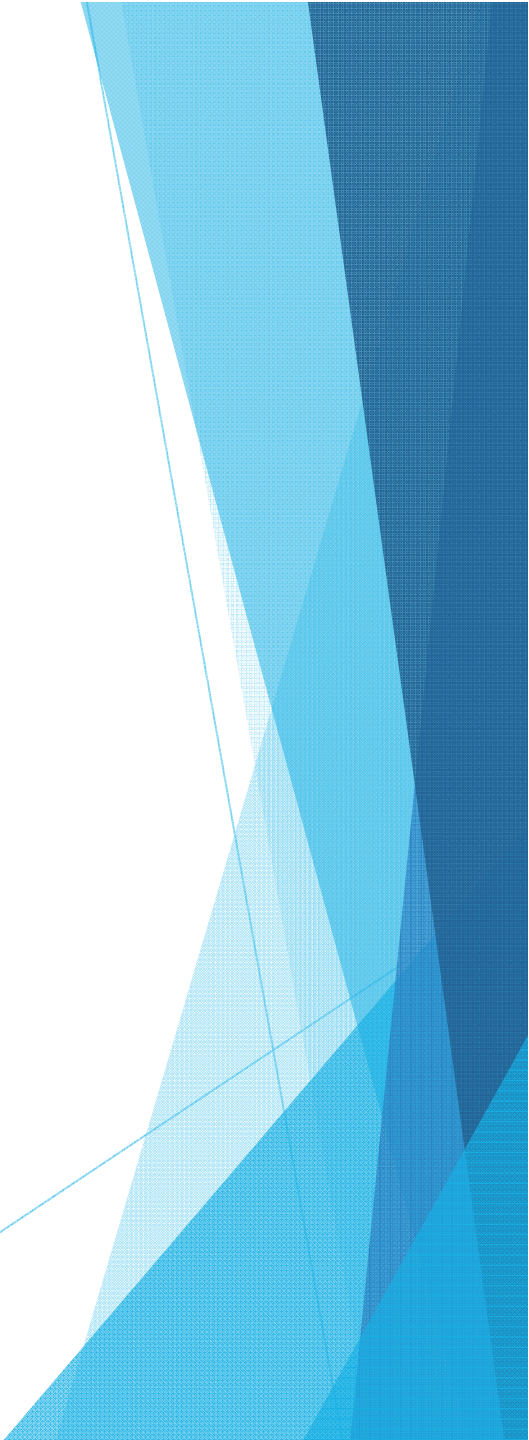
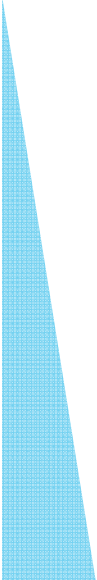
High Hedonic Tone



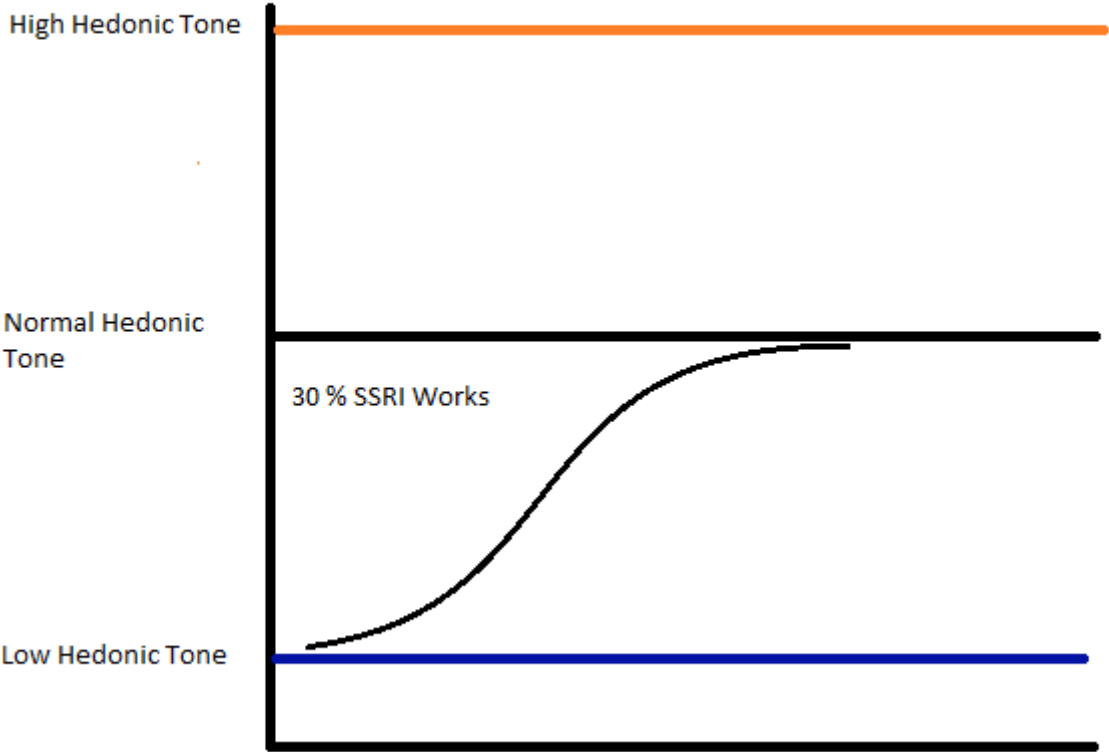
Normal Hedonic Tone



Low Hedonic Tone

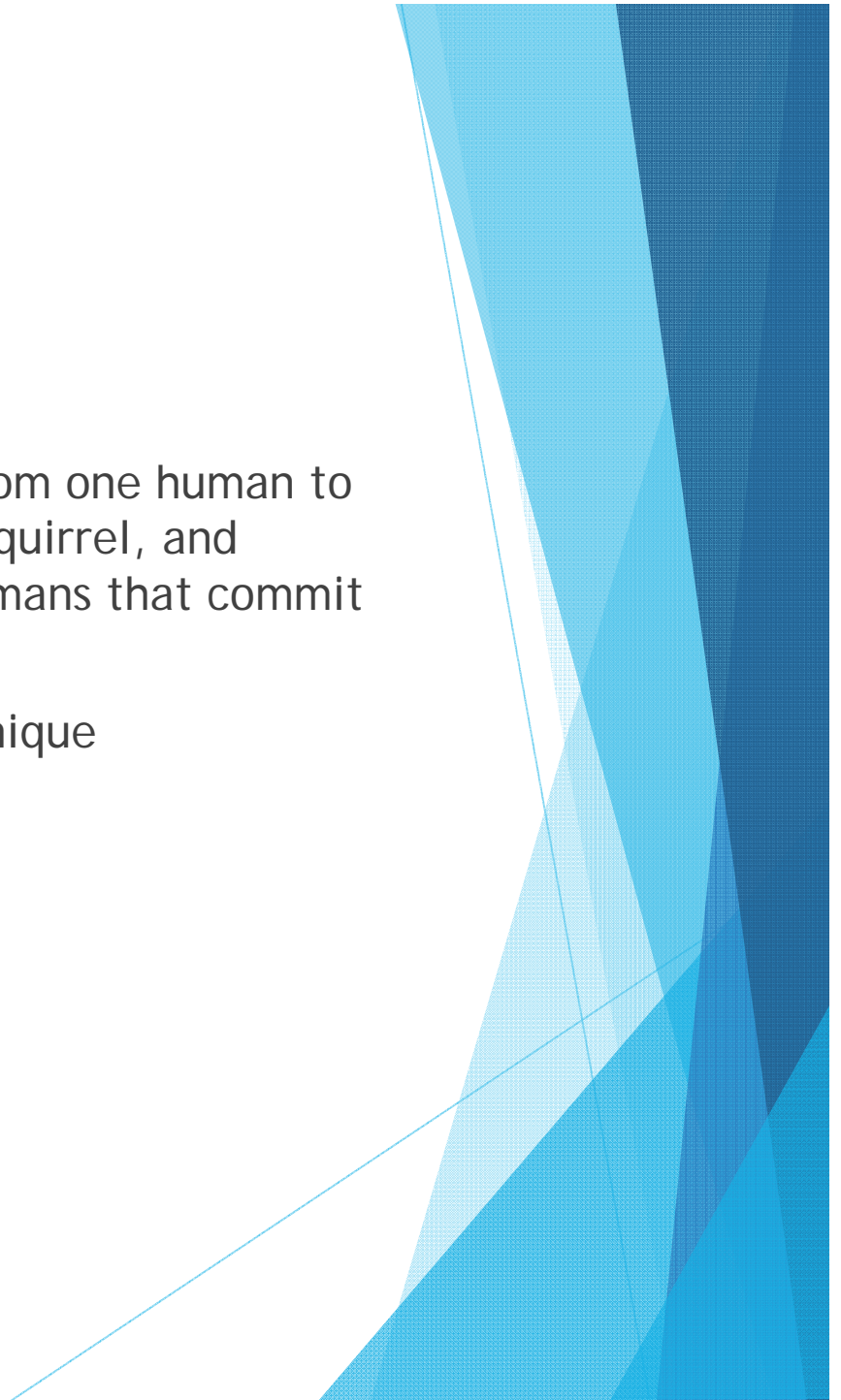
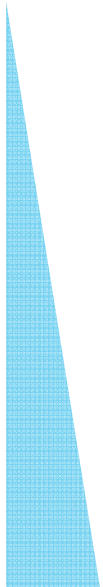


# Hedonic Tone



# Hedonic Tone

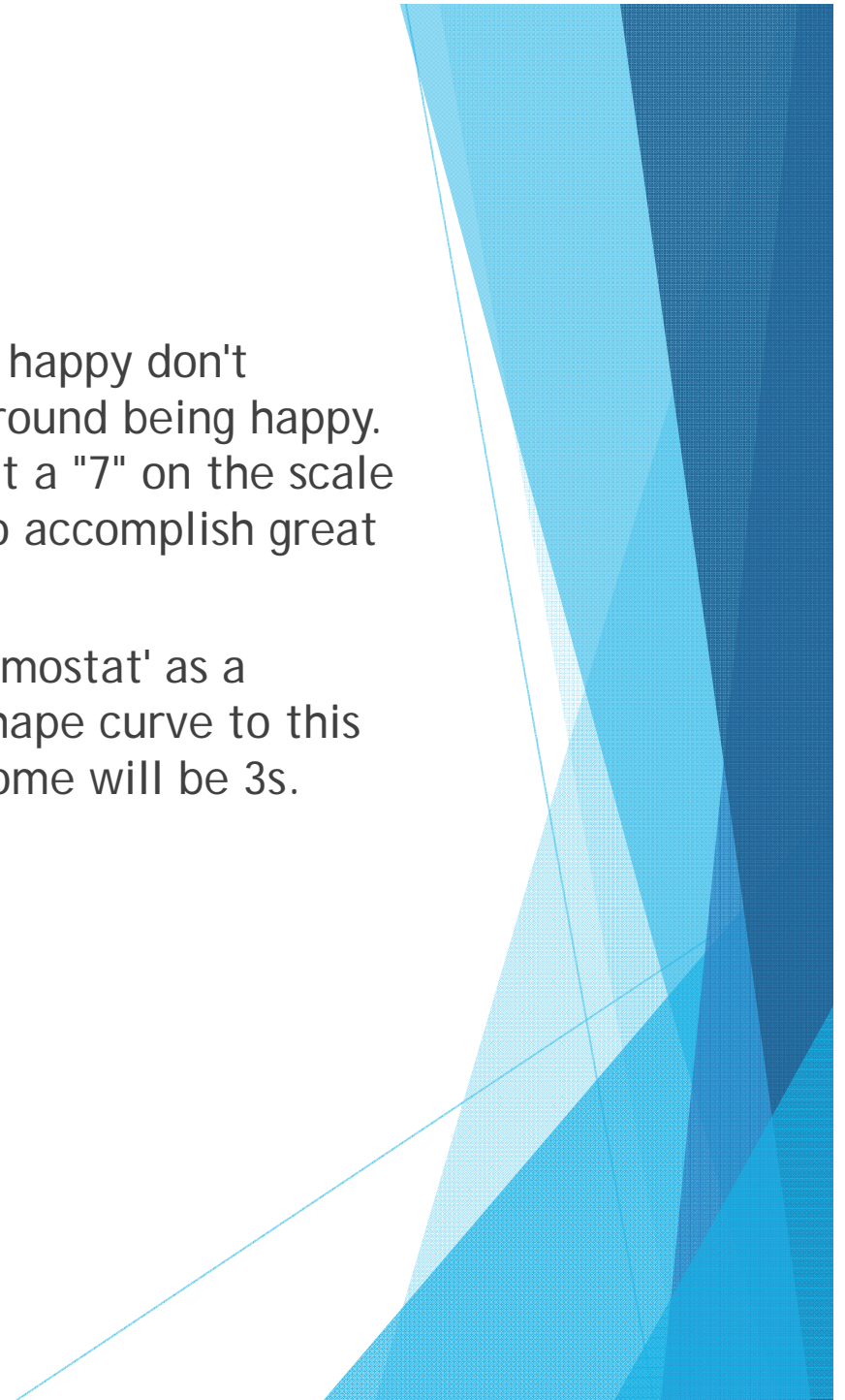
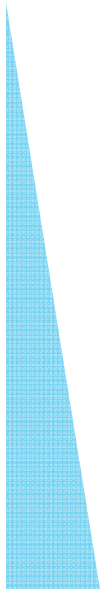
- ▶ So why is it that hedonic tone varies from one human to another? I've never seen a depressed squirrel, and there aren't a lot of animals except humans that commit suicide.
- ▶ As it turns out, depression gives us a unique evolutionary advantage.





# Hedonic Tone

- ▶ Studies have shown that people who are happy don't accomplish much. They mostly just sit around being happy. On the other hand, people who are about a "7" on the scale of 1 to 10 are the ones who are driven to accomplish great things.
- ▶ So Mother Nature set our 'happiness thermostat' as a species at about 7. If you apply a bell shape curve to this average, some people will be 10s, and some will be 3s.



# Hedonic Tone

- ▶ We call the 3's addicts.
- ▶ And we refer to the 10's as being lazy!
- ▶ But people in the 6 to 8 range tend to grow up to be doctors and lawyers and such.
- ▶ Remember, Mother Nature isn't interested in the survival of the individual, she is only interested in the survival of the species. (How many acorns are produced to get 1 oak tree?)

# Hedonic Tone

- ▶ So it's important to realize that some people just get the short end of the stick from an evolutionary standpoint. But it is no longer necessary to sacrifice these people for the greater good. We treat other diseases that used to be fatal, like type 1 diabetes, instead of just letting natural selection take its toll.
- ▶ So now, let's briefly review the science and history of opiates and depression.



# The use of opioids to treat depression

- ▶ In the US before the 1950's opioids were used to treat depression very successfully
- ▶ If a person responds to nortriptyline and you give them an opioid blocker, the anti-depressant effect goes away
- ▶ Studies using opiates in patients with refractory depression, some of whom with a history of substance abuse, showed robust improvement in their symptoms without concomitant abuse.
- ▶ The primary use for Tramadol in Europe is as an antidepressant.

The SECOND clinically significant issue that occurs with dysfunctional endorphin receptors is an dysfunctional pain response

# Dysfunctional Pain Responses

- ▶ Endorphin receptors are obviously involved in our response to pain, since they bind to opiates
- ▶ If your receptors don't work well, there will be two consequences to that
  - ▶ Exogenous opioids won't bind well to the endorphin receptors, so these people typically require 2-4 times more pain medication than the average person
  - ▶ Those who suffer from addiction are not able to produce endorphins needed to compensate for acute pain
- ▶ Individuals typically compensate for normal chronic pain as we get older



# The THIRD clinical issue: Circadian Rhythm Dysfunction

- ▶ Day/night cycles are regulated by our endorphin system
- ▶ Our natural sleep cycle at birth is 4 hours, 3 hours awake, 1 hour asleep
- ▶ As we are exposed to light, we acquire a 24 hour cycle
- ▶ Addicts do not have a functional circadian rhythm, so almost all addicts have trouble sleeping

# The FOURTH consequence of a Dysfunctional Endorphin System: Agoraphobia

- ▶ Opiate addicted individuals are more uncomfortable in social situations, and function better in social interactions when taking opiates
- ▶ Addicts have increased perceived social rejection, which exacerbates PTSD, depression, and a sense of being different
- ▶ Addicts tend to self-isolate

# Agoraphobia

- ▶ “Part of the spectrum of depressive disorder syndromes includes symptoms of social withdrawal resulting in subjective psychological pain. Scientific evidence indicates that the psychic pain resulting from broken social ties may arise from the same neurobiological substrates that are involved in the unpleasant experience of physical pain. Functional MRI imaging has demonstrated that a particular polymorphism of the mu-opioid receptor gene was associated with individual differences in sensitivity to social rejection. This mu-opioid receptor polymorphism was also associated with differential neural activity in the dorsal anterior cingulate cortex and insula - both areas known to be the principle sites of activation during a social rejection experience” (2)



# Summary of Endogenous Opioid Dysfunction Syndrome

- ▶ The addict is:
  - ▶ Unhappy
  - ▶ Hurts all the time
  - ▶ Can't sleep
  - ▶ Socially isolated
- ▶ If a pill can cure all of these symptoms, they will have an incredibly strong drive to self-medicate

# These symptoms are frequently called Fibromyalgia

- ▶ Depression, chronic pain and sleep dysfunction are similar to fibromyalgia
- ▶ Studies have shown that people with fibromyalgia have receptor dysfunction as well
  - ▶ Higher incidence in women

# Fibromyalgia Spectrum Disorders

- ▶ Positron emission tomography of mu-opioid receptors in fibromyalgia patients has demonstrated that they exhibit reduced mu-opioid receptor binding potentials within structures typically observed in imaging studies of experimental pain involving healthy controls. These structures included the amygdala, mood control, and the neuro-behavioral effects of drug abuse. (3)



# Summary:

## Endogenous Opioid Dependence

- ▶ 4 major consequences of endogenous opioid dependence
  - ▶ Decreased Hedonic Tone
  - ▶ Increased Acute and Chronic Pain
  - ▶ Circadian rhythm dysfunction
  - ▶ Agoraphobia

# Exogenous Opiate Dependence: The Other Cause of Addiction

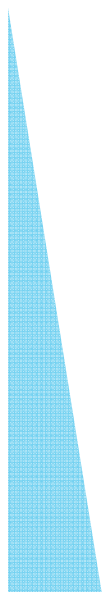
- ▶ Emotional trauma is another cause of addiction
- ▶ 30% of all soldiers with PTSD will become opiate addicts
- ▶ For the vast majority of people, the real cause is emotional trauma in childhood
  - ▶ Linked to ACE study

# Adverse Childhood Experiences Study (ACE)

- ▶ 1990's Kaiser Permanente and CDC partnered to do a study
- ▶ Results were that individuals with dysfunctional childhoods experienced an increase risk of addiction
- ▶ Ace study produced a 10 point questionnaire which covered various causes of emotional trauma in childhood and gave an individual score anywhere from 0 - 10



# ACE Study Video



# Finding Your ACE Score

**While you were growing up, during your first 18 years of life:**

1. Did a parent or other adult in the household **often or very often**...  
Swear at you, insult you, put you down, or humiliate you?  
**or**  
Act in a way that made you afraid that you might be physically hurt?  
Yes No If yes enter 1 \_\_\_\_\_
2. Did a parent or other adult in the household **often or very often**...  
Push, grab, slap, or throw something at you?  
**or**  
**Ever** hit you so hard that you had marks or were injured?  
Yes No If yes enter 1 \_\_\_\_\_
3. Did an adult or person at least 5 years older than you **ever**...  
Touch or fondle you or have you touch their body in a sexual way?  
**or**  
Attempt or actually have oral, anal, or vaginal intercourse with you?  
Yes No If yes enter 1 \_\_\_\_\_
4. Did you **often or very often** feel that ...  
No one in your family loved you or thought you were important or special?  
**or**  
Your family didn't look out for each other, feel close to each other, or support each other?  
Yes No If yes enter 1 \_\_\_\_\_



# Finding Your Ace Score Cont'd

5. Did you **often or very often** feel that ...  
You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you?  
**or**  
Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?  
Yes No If yes enter 1 \_\_\_\_\_
6. Were your parents **ever** separated or divorced?  
Yes No If yes enter 1 \_\_\_\_\_
7. Was your mother or stepmother:  
**Often or very often** pushed, grabbed, slapped, or had something thrown at her?  
**or**  
**Sometimes, often, or very often** kicked, bitten, hit with a fist, or hit with something hard?  
**or**  
**Ever** repeatedly hit at least a few minutes or threatened with a gun or knife?  
Yes No If yes enter 1 \_\_\_\_\_
8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?  
Yes No If yes enter 1 \_\_\_\_\_
9. Was a household member depressed or mentally ill, or did a household member attempt suicide?  
Yes No If yes enter 1 \_\_\_\_\_
10. Did a household member go to prison?  
Yes No If yes enter 1 \_\_\_\_\_

**Now add up your "Yes" answers: \_\_\_\_\_ This is your ACE Score.**



# Relationship of ACE Score

- ▶ “The relationship of ACE score to IV drug use is particularly striking, given that male children with ACE score 6 or more have a 4600% increased likelihood of later becoming an injection drug user, compared to an ACE Score 0 male child; this moves the probability from an arithmetic to an exponential progression. Relationships of this magnitude are rare in epidemiology. This, coupled with related information, suggests that the basic cause of addiction is predominantly experience-dependent during childhood and not substance-dependent. This challenge to the usual concept of the cause of addiction has significant implications for medical practice and for treatment programs. ”
- ▶ “The Hidden Epidemic: The Impact of Early Life Trauma on Health and Disease” Felitti /Anda ACE study chapter

# Women, ACE and Addiction

- ▶ “Analysis of our Study data for injected drug use shows a powerful relation to ACEs. Population Attributable Risk analysis shows that 78% of drug injection by women can be attributed to adverse childhood experiences.”  
“The Origins of Addiction: Evidence from the Adverse Childhood Experiences Study”  
Vincent Felitti,MD

# More From Ace Study

- ▶ “American soldiers in Vietnam provided an important although overlooked observation. Many enlisted men in Vietnam regularly used heroin, however, only 5% of those considered addicted were still using it 10 months after their return to the US. Treatment did not account for this high recovery rate. Why does not everyone become addicted when they repeated inject a substance reputedly as addicting as heroin? If a substance like heroin is not inherently addicting to everyone, but only to a small minority of human users, what determines this selectivity? Is it the substance that is intrinsically addicting, or do life experiences actually determine its compulsive use? Surely chemical structure remains constant. Our findings indicate that the major factor underlying addiction is adverse childhood experiences that have not healed with time and that are overwhelmingly concealed from awareness by shame, secrecy, and social taboo.” (4,5)



# Again - Prevalent (incorrect) theories of opiate addiction

- ▶ Opiates are intrinsically addictive, and anyone who takes them long enough will become addicted.
- ▶ Some people just have an "addictive personality", and that explains why they become addicts
- ▶ People with poor will power are unable to quit using drugs once they start, and that's why they are addicts.

# Redefining Addiction



# Drugs Don't Cause Drug Addiction

## ▶ 3 Question Study

- ▶ Do you remember the 1<sup>st</sup> pain you took
- ▶ Did it give you energy
- ▶ Were you sexually or physically abused before the age of 18



# References

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- ▶ 5. Robins LN. Vietnam Veterans' rapid recovery from heroin addiction: a fluke or normal expectation? *Addiction* 1993; 88:1041-1054.