Addiction Essentials: The Go-To Guide for Clinicians and Patients

Carlton Erickson, Ph.D.
- Distinguished Professor of Pharmacology
- Director, Addiction Science Research and Education Center
- Associate Dean for Research and Graduate Studies

College of Pharmacy
The University of Texas at Austin

July 21, 2011

BIOSKETCH – CARLTON ERICKSON, PH.D.

CARLTON (CARL) K. ERICKSON, a research scientist, has been studying the effects of alcohol on the brain for over 40 years. Carl received his Bachelor's degree from Ferris State College in 1961 and his Ph.D. degree in pharmacology from Purdue University in 1965. He has held tenured teaching and research positions at The University of Kansas (1965-1977) and The University of Texas (1978-present). He presently is Pfizer Centennial Professor of Pharmacology, Associate Dean for Research and Graduate Studies, and Director of the Addiction Science Research and Education Center in the College of Pharmacy at the University of Texas at Austin. He holds memberships in the American Society for Pharmacology and Experimental Therapeutics (ASPET), the Research Society on Alcoholism (RSA), the College on Problems of Drug Dependence (CPDD), and is a member of the Executive Council of the Betty Ford Institute.

Carl is broadly knowledgeable about the neurobiology of alcohol and other drugs, since he is an active scientist and publisher of over 260 scientific and professional articles. He is also co-editor of the book, Addiction Potential of Abused Drugs and Drug Classes (Haworth Press, 1990), co-author of Your Brain on Drugs (Hazelden, 1996), and Drugs, The Brain and Behavior (Haworth Medical Press, 1998). He is the author of The Science of Addiction: From Neurobiology to Treatment (W.W. Norton, 2007), which won a University of Texas Hamilton Book Award in 2008, and a new book, Addiction Essentials: The Go-to Guide for Clinicians and Patients (W.W.Norton, 2011). He is a Field Editor and Highlights Editor of the scientific journal Alcoholism: Clinical and Experimental Research. He is on the science advisory board of Hazelden Foundation in Center City, Minnesota. He has participated in the Professionals in Residence program at the Betty Ford Center in Rancho Mirage, CA and is a recipient of the Betty Ford Center Visionary Award (2000). He is also the recipient of the 2003 Pat Fields SECAD Award, the 2004 Fred French Award for Educational Achievement, the Nelson J. Bradley Award for Lifetime Achievement (2007), and the John P. McGovern Award for Excellence in Medical Education (2009).

Carl has 25 years of biomedical research experience as an active pharmacologist and neuroscientist and 10 years of educational research, all in academic settings. As a non-recovering person who believes "You don't have to have cancer to be a cancer researcher", Carl has tried to learn about addictive disease by attending Twelve Step meetings and becoming knowledgeable about addiction treatment methods. He presents approximately 20-25 lectures annually to health professionals, is a frequent keynote speaker at major conferences in the U.S. and internationally, and has presented Grand Rounds at health science centers to update pharmacy and medical faculty and students about the latest neurobiological research on addictive disease. Public and professional education about the evidence for chemical dependence as a medical disease is extremely important. Carl has spoken to approximately 87,000 professionals and people in recovery since 1978.

THE PRESENTER'S FAVORITE WEBSITES

- University of Texas Addiction Science Research and Education Center: www.utexas.edu/research/asrec
- National Institute on Drug Abuse (NIDA): www.drugabuse.gov
- National Institute on Alcohol Abuse and Alcoholism (NIAAA): www.niaaa.nih.gov
- The Partnership at Drugfree.org/Join Together: www.drugfree.org/join-together
- Faces & Voices of Recovery: www.facesandvoicesofrecovery.org
- NIH/NLM Publications: www.pubmed.gov

Summary of Main Points

- we have a crisis in terminology - it must be clear, to optimize treatment
- there is not just one cause of dangerous drinking and drugging
- some users develop a brain disease
- treatment must attack the cause of the problem

TO BEGIN, LET ME
TELL YOU A STORY…..

ONCE UPON A TIME WE IDENTIFIED ADDICTION BY THE AMOUNT OF DRUG CONSUMED.

TODAY WE DIAGNOSE ADDICTION WITH DIAGNOSTIC CRITERIA. IN THE FUTURE WE WILL HAVE A BRAIN SCAN OR A GENETIC TEST.

THERE ARE TWO TYPES OF OVERDRINKING/OVERDRUGGING: ONE IS A PATHOLOGY OF CELLS IN THE BRAIN, THE OTHER IS A SITUATION OF POOR CHOICE.

WE TREAT THESE TWO CONDITIONS ABOUT THE SAME, WHICH LEADS THE PUBLIC TO ERRONEOUSLY THINK THEY ARE THE SAME.

ONE DRUG OVERUSE CONDITION IS CALLED "DRUG ABUSE"; THE OTHER IS CALLED "CHEMICAL DEPENDENCE" (DSM and ICD).

Drug abuse is voluntary,
the user has control over drug use
and is making bad choices.

(We could say that drug abusers are "good" people making "bad" decisions.)

Chemical dependence is not a choice. It is a disease over which the individual has no control. It is caused by brain dysregulation initiated by drug use.

Today we want to talk about chemical dependence and its treatment. (Some people call this disease "addiction", but this word is non-scientific and overused, so it is not a good word to describe the disease.)

The problem with "addiction"

- erroneous folklore: due to a major misunderstanding about "addiction"
  - "cell phones are addicting"
  - "marijuana is not addicting"
  - "crack babies are addicted"
  - "I'm addicted to you, baby…."

WHERE IS THE CORRECT INFORMATION ABOUT THESE MYTHS?

www.utexas.edu/research/asrec
(the best academic website on the neuroscience of recovery in the whole world!)

Many people believe…

- "addiction", "alcoholism", and "substance abuse" are imprecise and stigmatizing
- "addiction" is somewhat OK when used by scientists and clinicians; but the message is confusing to the public
- "Dr. Erickson, are scientists studying the causes of tanning booth addiction?"

REVIEW THE DIAGNOSTIC CRITERIA IN DSM-IV

DSM-IV Diagnosis of Drug Problems

- drug <u>abuse</u> is diagnosed by 1 (or more) out of 4 criteria, within the previous 12 month period
- chemical <u>dependence</u> is diagnosed by 3 (or more) of 7 criteria, within the previous 12 month period

The <u>main symptom</u> of chemical dependence (a.k.a. "addiction") is "impaired control over the use of a drug".

It is NOT hangover, blackouts, amount of drug taken, withdrawal signs, criminal behavior, or anything else (DSM).

What is the essence of the disease?

Three phenomena:

- like – "I like bananas" ("I like the taste of wine") – social use
- want – "I want her to be my wife" ("I want a Bud Lite") – alcohol abuse
- need – "I need air" ("I need alcohol") – the disease!

  The "need" for a drug is characteristic of chemical dependence. Paradox: in late stages, the person does not want to use the drug, but (he) needs the drug:

  "Please help me, I can't stop!"

REVIEW THE DIAGNOSTIC CRITERIA IN DSM-V

Proposed DSM-V

- the terms "abuse" and "dependence" will be dropped
- instead, "substance-use disorder" under the general heading "Addiction and Related Disorders" has been proposed (UNDER REVISION)
- there will be one category, with 11 criteria
- severity specifiers: moderate = 2 - 3 criteria; severe = 4 or more

Proposed DSM-V (2)

- but do not count tolerance or withdrawal if medications are under medical supervision
- the new category will include non-substance addictions
- gambling disorder will be moved into this category ("addiction") – UNDER REVISION
- "internet addiction" will be considered if more research indicates (until then, Appendix)

Reasons for the changes

- "dependence" is confusing to physicians; they think patients with pain will become "addicted" with more pain medication
- "physical dependence" is a normal response to many medications
- thus, replacing "dependence" with "addiction" is better

W.H.O. (1950) – a terminology reminder

- "For a drug to be addicting, it must have the following:
  - psychological dependence
  - tolerance
  - physiological dependence"

W.H.O. (1950) – a terminology reminder

- ~~"For a drug to be addicting, it must have the following:~~
  - ~~psychological dependence~~
  - ~~tolerance~~
  - ~~physiological dependence"~~
- this is no longer valid! (cocaine, pain)
- these "dependence" terms are dying…….

Perceived problems with the changes

- there is no evidence that changing the terminology will lead to changes in doctors' prescribing habits
- is it not possible for doctors to learn the difference between chemical dependence and physical dependence? And also psychological dependence?
- where is the disease in the new definition?
- the research cited in making these decisions is scanty (severity, craving)
- questionable "weight of the evidence"

CHANGES ARE COMING,
BUT NOT UNTIL 2013….

Because DSM criteria are so subjective…..

- we have disagreements over the terms "addiction", "alcoholism", "abuse", and "dependence"
- we really need objective tests for diagnosing who has the brain disease
- we can do this: Georgeopoulos et al., Neuromarker for PTSD, J. Neural Engin., vol. 7 (2010)

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(the terminology of "addiction" is changing….)

RESEARCH VALIDITY ESTIMATE (RVE)

(A Thoughtful Appraisal of High-Quality Scientific Research)

High RVE
- many large, well-controlled studies
- replicable results
- much peer-reviewed, published literature

Low RVE
- few replicable studies
- highly speculative results
- little peer-reviewed, published literature

Who develops
chemical dependence?

Different types of onset

- "instant addiction"
- progression from social use to abuse to dependence
- some people develop the disease, some do not

Who has "what it takes"?

Drug Users Who Will Develop Chemical Dependence

(Lifetime Prevalence Estimates, 1992-98 data):

- nicotine - 32%
- heroin - 23%
- cocaine - 17% (crack - 20%)
- alcohol - 15%
- amphetamines - 11%
- cannabis - 9%
- "sedatives" - 9%
- analgesic opioids - 9%
- psychedelics - 5%
- inhalants - 4%

Anthony et al., 1994
Chen & Anthony, 2004
Hughes et al., 2006

WHERE CAN I GET THESE REFERENCES?

www.utexas.edu/research/asrec

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

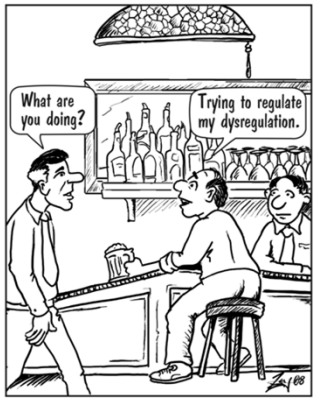
(new research is changing what we know about the disease)

NEUROSCIENCE UPDATE

Chemical Dependence

occurs because of neurochemical <u>dysregulation</u> of the mesolimbic dopamine system (MDS)*

* a.k.a. Medial Forebrain Bundle (MFB)
or "Pleasure Pathway" or "Reward Pathway"



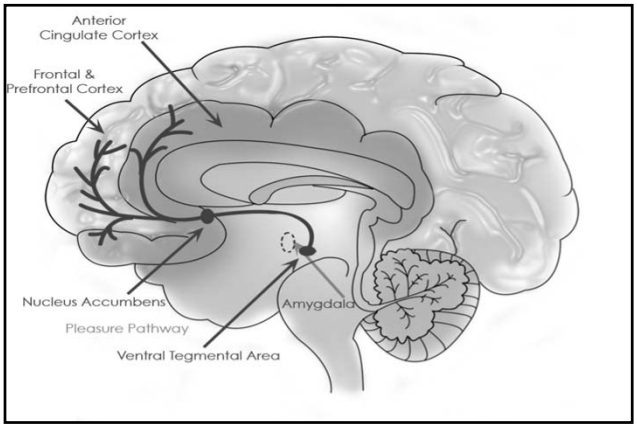
"Addiction" Brain Areas - Historically

- mesolimbic dopamine system
- "key elements of a basal forebrain macrostructure"

<u>extended amygdala</u>

- central nucleus of amygdala
- bed nucleus of the stria terminalis
- transition zone, medial (shell) of the nucleus accumbens

70



"Addiction" Brain Areas - Newer

<u>binge/intoxication stage:</u> ventral tegmental area, ventral striatum

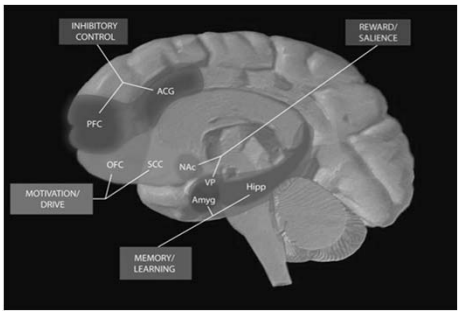
<u>withdrawal/negative affect stage:</u> extended amygdala

<u>preoccupation/anticipation stage:</u> craving: orbitofrontal cortex-dorsal striatum, prefontal cortex, basolateral amygdala, hippocampus, insula; disrupted inhibitory control: cingulate gyrus, dorsolateral prefrontal, inferior frontal cortices

Koob and Volkow (2010)

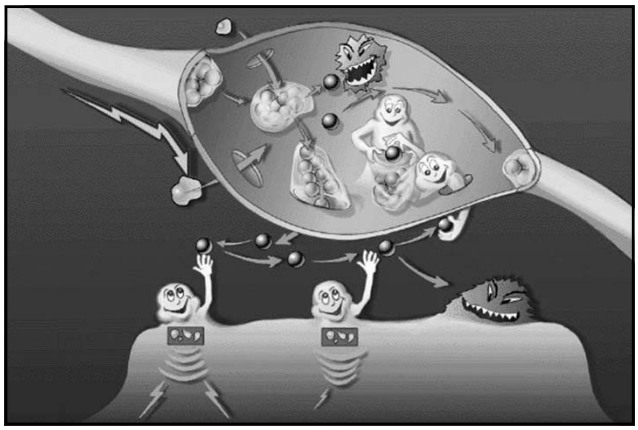
60

Circuits Involved In Drug Abuse and Addiction



All of these brain regions must be considered in developing strategies to effectively treat addiction

WHERE IS THE PROBLEM WITHIN THESE BRAIN AREAS?



What happens?

Drug actions reveal vulnerable brain chemicals

- cocaine, amphetamines - dopamine (DA)
- LSD - serotonin (SER)
- heroin - endorphins (END)
- benzodiazepines – gamma-aminobutyric acid (GABA)
- nicotine - acetylcholine (ACH)
- alcohol (ETOH) - glutamate (GLU)
  - substance P (SUBP)
- marijuana - endocannabinoids (ENCB)

85

The newest….

- Substance P and its receptor, neurokinin 1 (NK1R) - in brain areas involved with stress responses and drug reward
- mice genetically deficient in NK1R = decrease in voluntary alcohol drinking
- alcohol dependent patients given NK1R antagonist or placebo = decreased craving, increased well -being, reduced responses to stress

20

George et al.(Heilig) Science 319:1536-9 (2008)

Emerging "drugs of choice" groupings

- DA - amphetamines, cocaine, ETOH
- END - opioids, ETOH
- ACH - nicotine, ETOH
- GABA - benzodiazepines, ETOH
- SER - LSD, ETOH
- GLU - ETOH
- SUBP - ETOH
- ENCB - marijuana, ETOH

70

20

Thus, drugs are associated with specific neurotransmitters

- we assume that genetics + drug-use lead to "dysregulations" of MDS neurotransmitter systems
- when people use, the drugs "connect" to the specific dysregulated neurotransmitter system
- this may be why people have "drugs of choice"
- multiple dysregulations could explain co-dependence on several drugs

70

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(neurobiology explains a lot…)

Let's think "outside the box"

What causes the disease?

10

Dysregulation =

- continued exposure of the MDS pathways to a drug leads to changes (adaptations) in nerve function, called "neuroadaptations"
- the changes reach a threshold
- ….leading to compulsive use over which the individual has impaired control (symptom of the disease)

70

Current research suggests that the site of dysregulation is the <u>cell receptor!</u>

(With nicotine, we are now even discovering subunits of the nicotinic receptor!)

40

What causes the neurotransmitter systems to become "dysregulated"?

- genetic vulnerability *
- exposure to a drug *
- other aspects of the environment, besides drugs?

60

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(dysregulation of the MDS is the problem, and we are getting closer to understanding where it occurs)

Chemical Dependence – A Brain Chemistry Disease!

- "addicting" drugs "match" the transmitter system that is not normal
- genetic susceptibility is clearly involved - but onset time is variable
- cases range from mild to severe
- remember, this is <u>not</u> drug <u>abuse</u>
- methadone and nicotine maintenance is evidence that some people require a chemical to overcome the non-normal transmitter system

80

WWW.FACESANDVOICESOFRECOVERY.ORG

(there are many pathways to recovery…..)

What do we know about recovery?

- some drugs produce "dependence"
- some people are susceptible to developing the disease
- some people recover fully
- some people recover somewhat
- some people never recover

What is "recovery"?

Recovery from substance dependence is a voluntarily maintained lifestyle characterized by:

- sobriety - abstinence from alcohol and all other non- prescribed drugs (including nicotine)

Betty Ford Institute Consensus Panel (2007)

2 - What is "recovery"?

AND

- personal health - improved quality of personal life as defined and measured by scores on the physical health, psychological health, independence, and spirituality scales of the WHO QOL inst.
- citizenship - improved quality of social function as defined and measured by scores on the social function and environment scales of the WHO QOL instrument

3 - What is "recovery"?

- "Sobriety is best achieved through the practice of abstinence from alcohol and all other drugs of abuse." There is not yet agreement regarding recovery facilitated by psychosocial and pharmacological treatments.
- Early sobriety = 1 - 11 months
  Sustained sobriety = 1 - 5 years
  Stable sobriety = 5 years or more

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(new research is changing what we know about recovery)

Treatment of Drug Abuse and Chemical Dependence

Treatment options in the 1960's

- 12-step programs
- the beginning of inpatient treatment
- the beginning of outpatient treatment
- emergency rooms and jails where people could "sleep it off" – and then go back on the street again

80

Today's treatment options
(Options to initiate recovery….)

- traditional: 12 step programs (abstinence)
- behavioral: individual/group counseling
- misunderstood: harm reduction, MM
- new: motivational interviewing, CBT, MET, primary care management, vouchers
- medical treatments: detox meds, meds to enhance abstinence/reward blockers, methadone, buprenorphine, vaccines

70

(MM= Moderation Management, CBT= cognitive behavioral therapy, MET= motivational enhancement therapy)

Current Medications

- naltrexone (ReVia, Vivitrol) - alcohol
- acamprosate (Campral) - alcohol
- methadone (generic) - opioids
- buprenorphine (Subutex, Suboxone) - opioids, such as heroin
- bupropion (Zyban) - nicotine
- varenicline (Chantix) - nicotine

70

- disulfiram (Antabuse) - works on the liver, generally not effective for treating alcohol dependence

What's new in medication development?

<u>Alcohol</u>
- nalmefene (END, no other major use)
- topiramate (Topamax, GABA/GLU, migraine etc.)
- ondansetron (Zofran, SER, nausea/vomiting)
- quetiapine (Seroquel, DA?, antiSZP, bipolar)
- aripiprazole (Abilify, DA?, antiSZP, bipolar)

<u>Cocaine</u>
- disulfiram (Antabuse, DA, GABA?)
- methadone (generic, END)
- gabapentin (Neurontin, GABA, anticonvulsant)
- baclofen (generic, GABA, muscle relaxant)
- modafinil (Provigil, GLU, anti-narcolepsy)

20

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(the emphasis today is on evidence-based treatments)

Medical education trends

SBIRT:
- <u>S</u>creening (At least, SBI…)
- <u>B</u>rief <u>I</u>ntervention
- <u>R</u>eferral to <u>T</u>reatment

<u>Also</u>:
- SIMS: Summer Institute for Medical Students (1 week, Betty Ford, Hazelden, others)
- some schools: training in addiction medicine during residencies

Is there a common mechanism of action for "talk therapies" and medications?

YES – If chemical dependence is a brain disease, logic says: Behavioral Therapies Probably Change Brain Chemistry!

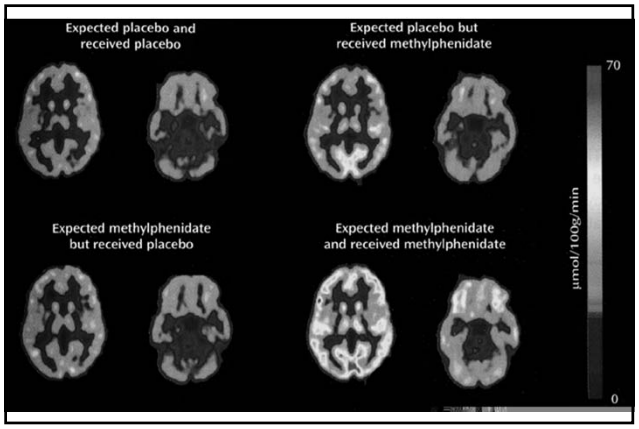
70

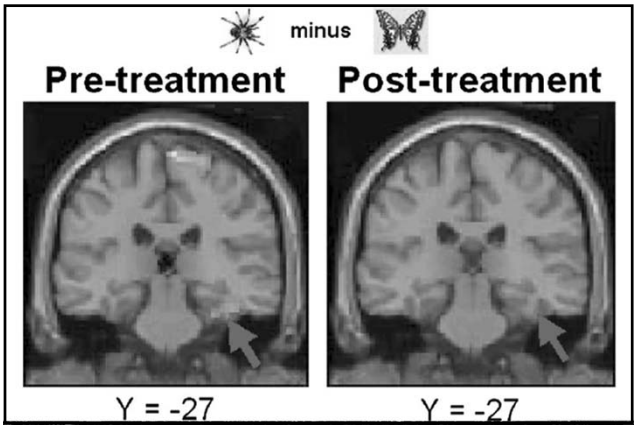
BRAIN IMAGING STUDIES ARE FLOURISHING

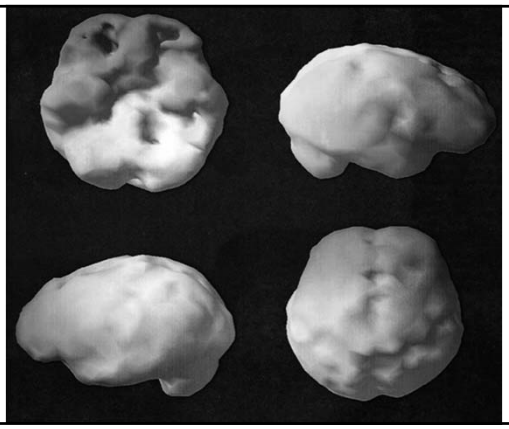
New Brain Scan Research…

- Psychotherapy and meds work on the basal ganglia in the treatment of depression
  Martin et al., 2001
- CBT and meds work on the same brain areas in treating social anxiety Furmark et al., 2002
- CBT appears to modify "bad circuits" associated with anxiety disorders
  Paquette et al., 2003

50







SO, IT APPEARS THAT THE MDS DYSREGULATION BEGINS TO MOVE BACK TOWARDS NORMAL

It cannot be totally normalized, just "pushed back" towards normal, in much the same way that medications change brain chemistry.

(For some people, spirituality seems to be a very effective way to do this!)

10

WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(The way treatment works is becoming better understood through research)

We now have a choice

- there is now research evidence for the effectiveness of the 12-step mutual-help programs (Donovan, Galanter, Humphreys, Kaskutas, Kurtz, Laudet, McCrady, Miller, Moos, Tonigan, others)
- there have been many other research advances, mostly in neurobiology/genetics
- yet some say our field has not moved forward much in the past 60+ years (I disagree)
- choice: continue what works, or look to the science for new ideas to help those still suffering…… (or both!)

Finally, please remember…

- our field is in transition, and previously erroneous folklore is becoming clearer - through new research
- this new information requires an open mind and the curiosity to learn new things - while we continue to help those who are still suffering….

References

- Erickson, C.K., " The Science of Addiction: From Neurobiology to Treatment" (W.W. Norton, 2007)
- Erickson, C.K., "Addiction Essentials: The Go-to Guide for Clinicians and Patients" (W.W. Norton, 2011)
- bibliography: www.utexas.edu/research/asrec

200!

Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV)

Table. Criteria for Drug Abuse and Dependence

Chemical (Drug) *Abuse*

I. A maladaptive pattern of drug use leading to impairment or distress, presenting as one or more of the following in a 12-month period:
   1. recurrent use leading to failure to fulfill major obligations
   2. recurrent use which is physically hazardous
   3. recurrent drug-related legal problems
   4. continued use despite social or interpersonal problems

II. The symptoms have never met the criteria for chemical dependence.

Chemical (Drug) *Dependence*

I. A maladaptive pattern of drug use, leading to impairment or distress, presenting as three or more of the following in a 12-month period:
   1. tolerance to the drug's actions
   2. withdrawal
   3. drug is used more than intended
   4. there is an inability to control drug use
   5. effort is expended to obtain the drug
   6. important activities are replaced by drug use
   7. drug use continues despite knowledge of a persistent physical or psychological problem

II. Two types of dependence can occur:
   A) with physiological dependence (including either items 1 or 2), or
   B) without physiological dependence (including neither items 1 nor 2).

Source: Adapted from *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition - Text Revision,* 2000.

Substance-Use Disorder

A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:

1. recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)

2. recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)

3. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)

4. tolerance, as defined by either of the following:

    a. a need for markedly increased amounts of the substance to achieve intoxication or desired effect

    b. markedly diminished effect with continued use of the same amount of the substance
    (Note: Tolerance is not counted for those taking medications under medical supervision such as analgesics, antidepressants, ant-anxiety medications or beta-blockers.)

5. withdrawal, as manifested by either of the following:

    a. the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for Withdrawal from the specific substances)

    b. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
    (Note: Withdrawal is not counted for those taking medications under medical supervision such as analgesics, antidepressants, anti-anxiety medications or beta-blockers.)

6. the substance is often taken in larger amounts or over a longer period than was intended

7. there is a persistent desire or unsuccessful efforts to cut down or control substance use

8. a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects

9. important social, occupational, or recreational activities are given up or reduced because of substance use

10. the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

11. Craving or a strong desire or urge to use a specific substance.

Severity specifiers:

Moderate: 2-3 criteria positive

Severe: 4 or more criteria positive

Specify if:

With Physiological Dependence: evidence of tolerance or withdrawal (i.e., either Item 4 or 5 is present)

Without Physiological Dependence: no evidence of tolerance or withdrawal (i.e., neither Item 4 nor 5 is present)

Course specifiers (see text for definitions):

Early Full Remission

Early Partial Remission

Sustained Full Remission

Sustained Partial Remission

On Agonist Therapy

In a Controlled Environment