Points to cover in this session

• criteria to **diagnose** drug use disorders
  - DSM-IV (old)
  - DSM-5 (new) - (value of these diagnostic guides?)
• **update** on neuroscience 101
  - traditional - (what this means to you)
  - new information
• **programs and treatments** for drug use disorders
  - traditional - (ways to improve future treatment?)
  - new evidence-based
A Global Perspective....

- we don’t all agree on the cause(s) of addiction
- we don’t all agree on whether it should be overcome
- we don’t all agree about how to overcome it

Science works optimistically by assuming that addiction can be overcome and that deaths and suffering can be reduced by finding the causes of addiction and more ways to treat it.

Today is an update on where science is in doing this.
Major Diagnostic Instruments

- DSM-IV, 1994, 2000 (old)
- DSM-5, 2013 (new)
- ICD-10, 2003, 2010 (current)
- ICD-11, 2017 (projected)
- plus, many general diagnostics (e.g., ASI, SASSI, AUDIT)

DSM = Diagnostic and Statistical Manual of Mental Disorders, American Psychiatric Association

ICD = International Classification of Mental and Behavioural Disorders, World Health Organization
• drug abuse is diagnosed by 1 (or more) out of 4 criteria, within the previous 12 month period (“bad choice behavior”)

• chemical dependence is diagnosed by 3 (or more) of 7 criteria, within the previous 12 month period (“brain disease”)

(Old) DSM-IV Diagnosis of Drug Problems
The **main symptom** 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-IV).
Today we want to talk about the disease of “addiction.” (But this word is non-scientific and overused, so it is not the best word to describe the disease.)
The problem with “addiction”

- confusion due to misunderstanding and miscommunication about “addiction”
  - “cell phones are addicting”
  - “antidepressants are addicting”
  - “marijuana is not addicting”
  - “crack babies are addicted”
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!)

😊
Why is DSM important?

- provides **diagnostic criteria** for mental disorders and **drug problems**
- influences **how doctors diagnose and treat** their patients
- insurance companies use it to **determine coverage and reimbursement**
- determines how pharmaceutical companies design **clinical trials**
- determines how **funding agencies decide which research to fund**
DSM-IV Weaknesses

- subjective
- not accurate for adolescent diagnoses
- not accurate for geriatric or infant diagnoses
- often used for diagnosis by computer (e.g., SCID)
- often used by untrained personnel
- does not measure severity of the disorders

Better:
- a trained assessment counselor increases accuracy
- should use as part of a battery of diagnostic tests
the terms “abuse” and “dependence” have been dropped

instead, the phrase “substance-use disorder” (SUD) is described under the general heading “Addiction and Related Disorders”

there is one longitudinal category, with 11 criteria

there are severity specifiers: mild = 2-3 criteria; moderate = 4-5 criteria; severe = 6 or more
• but **do not count tolerance or withdrawal** if medications are **under medical supervision**
• the new category includes **non-substance addictions**
• **gambling disorder** is moved into this category (“addiction”)
• “**internet addiction**” and “**caffeine addiction**” will be considered if more research indicates (until then, placed in an Appendix)
An “addiction” word problem

• For anyone **who wishes to call** the following “addictions”:
  - pornography  - religion
  - exercise  - oil (as in petroleum oil)
  - Butchart Gardens  - tanning booths

• **Science** is not on your side (see DSM-5)

• There’s no doubt that **some compulsive behaviors** exist

• But calling everything an “addiction” **trivializes** the huge amount of work (**research and recovery**) on drug addictions:
  “I’m **addicted** to chocolate chip cookie dough” 😊
  “I’m **addicted** to methamphetamine” 😞

**Dilemma:** It’s not whether compulsive behaviors exist, it’s what to call them! What is their incidence? Do they involve the same brain structures and pathology as addicting drugs?
The media and internet don’t help

“College study finds Oreo cookies are as addictive as drugs”

Fox News (October 15, 2013)
Reasons for the changes in DSM-5

• “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

(or so they say.........)
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......
Problems with the DSM-5 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 and psychological dependence?
- The research cited in making these decisions is **scanty** (severity, craving).
- Where is the “**weight of the evidence**”?
- Where is the **disease** in the new definition?
The New Diagnostics – A Quick Review

**DSM-5**: Substance use disorders (SUDs) lie on a continuum of severity that ranges from “no substance problem” to “severe substance problem”

- no more “abuse” or “dependence” terms
- severity specifiers: mild, moderate, severe
- a separate monograph for each drug/group
- includes gambling, for the first time (but no other compulsive behaviors)
How do we merge the two DSM editions?

This might happen:

- **mild – moderate**: similar to DSM-IV category of “abuse”
- **severe**: similar to DSM-IV category of “dependence”

But the emphasis in DSM-5 is on the idea that “disease” develops somewhere along the continuum – perhaps at **different times** for **different patients**.
WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(Use the word “addiction” carefully, and for professional purposes, use DSM terminology to aid in diagnosis.)
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 a severe SUD?
Drug Users Who Developed Chemical Dependence
(U.S. Epidemiological Estimates, 1992-98):

- nicotine - 32%
- heroin - 23%
- cocaine - 17% (crack - 20%)
- alcohol - 15%
- stimulants other than cocaine - 11%
- cannabis - 9%
- “sedatives” - 9%
- analgesic opioids – 9%
- psychedelics - 5%
- inhalants - 4%

(*Perhaps SUD patients with 6 or more diagnostic criteria)

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 think about the disease
- chemical dependence or severe SUD)
NEUROSCIENCE UPDATE
A severe SUD occurs because of neurochemical dysregulation of the mesolimbic dopamine system (MDS)*

* a.k.a. Medial Forebrain Bundle (MFB) or “Pleasure Pathway” or “Reward Pathway”
What are you doing?

Trying to regulate my dysregulation.
“Addiction” Brain Areas - Historically

- mesolimbic dopamine system
- “key elements of a basal forebrain macrostructure”

**extended amygdala**
- central nucleus of amygdala
- bed nucleus of the stria terminalis
- transition zone, medial (shell) of the nucleus accumbens
“Addiction” Brain Areas - Newer

**binge/intoxication stage:** ventral tegmental area, ventral striatum

**withdrawal/negative affect stage:** extended amygdala

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

Koob and Volkow (2010)
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) NEW!
- marijuana - endocannabinoids (ENCB)
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
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" with the specific dysregulated neurotransmitter system.
- This may be why people have "drugs of (no) choice."
WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(neurobiology explains a lot...)
Let’s think “outside the box”

What causes the disease?
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)
Current research suggests that the site of dysregulation is the cell receptor!

(With nicotine, we are now even discovering subunits of the nicotinic receptor!)
Severe SUD – 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 of SUD range from mild to severe
• remember, this is not mild SUD!
• methadone and nicotine maintenance is evidence that some people require a chemical to overcome the non-normal transmitter system
The problem is: Some scientists contend that addiction is a choice!

- it appears that people who don’t know the complete neurobiological/genetic “addiction” research literature argue against “disease”
- the weight of the research evidence is that “dependence” (not “abuse”) is a disease
- Sources: NIDA, HBO, Koob, Nestler, etc.
- doubters fear that by calling it a disease, we are forgiving addicts from being responsible for what they did – but we’re really not
- Organizations: AMA, ASAM, NCADD, RSA, CMA(?)
Do we treat addiction as a brain disease?

• Not always
• The best treatment centers do (assessment, diagnosis, detox, strategies to change brain function, follow-up) = elements of medical treatment
• Evidence-based (research proven) methods!
• Others in the U.S. don’t care about diagnosis – treat only as if all clients simply need to “rest” - R & R, food, minimal counseling, smiling faces – perhaps placebo?
• Brain disease = long-term care and recovery!
TREATMENT OF SUBSTANCE USE DISORDERS
HARM REDUCTION
What IS harm reduction?

- assuming a person will use drugs; attempt to reduce harm to the user and those around the user
  - methadone
  - needle exchange programs
  - safe injection neighborhoods
  - controlled drinking
  - naloxone auto-injector for heroin overdose (Evzio)
What IS harm reduction?

- assuming a person will use drugs; attempt to reduce harm to the user and those around the user
  - methadone
  - needle exchange programs
  - safe injection neighborhoods
  - controlled drinking
  - naloxone auto-injector for heroin overdose (Evzio)
  - educating the public about the dangers of drunk driving
METHADONE
Characteristics of a Good Methadone Program

Example: to replace street use of heroin with use of an oral opioid in a controlled environment

- methadone taken in front of an employee
- regular drug screens
- steady job
- counseling to get off the medication
MEDICATIONS
Current Medications

- naltrexone (ReVia, Vivitrol*) - alcohol
- acamprosate (Campral, Fr.-Aotal) – alcohol
  * Also used in opioid treatment
- methadone (generic) - opioids
- buprenorphine (Subutex, Suboxone) - opioids, such as heroin
- bupropion (Zyban) - nicotine
- varenicline (Chantix, Champix) – nicotine
- disulfiram (Antabuse) - works on the liver, generally not effective for treating alcohol dependence
What’s new in medication development?

**Alcohol**
- 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)

**Cocaine**
- disulfiram (Antabuse, DA, GABA?)
- methadone (generic, END)
- gabapentin (Neurontin, GABA, anticonvulsant)
- baclofen (generic, GABA, muscle relaxant)
- modafinil (Provigil, GLU, anti-narcolepsy)
Treatment options in the 1960’s (U.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
Today’s treatment options
(Options to initiate recovery....)

- traditional (in U.S.): **12 step programs** (abstinence)
- behavioral: individual/group counseling
- misunderstood (U.S.): **harm reduction**, MM
- new: **motivational interviewing, MET, CBT**, primary care management, vouchers, drug courts
- **medications**: detox meds, meds to enhance abstinence/reward blockers, methadone, buprenorphine, vaccines
  *(evidence-based, or “research proven”)*

(MM= Moderation Management, CBT= cognitive behavioral therapy, MET= motivational enhancement therapy)
What is “evidence based” (EB) treatment?

• basically – “research proven”
• but to what extent? (what is the research validity?)
• EB is often a term that is thrown out to give credibility to a treatment program
• individual states in the U.S. are now beginning to require EB as a criterion for their treatment
• sometimes confused with “best practices”
• several models for determining EB
Evidentiary hierarchy of weighing evidence (SUNY, 2004)
USPSTF graded model:

• A – high certainty that the net benefit is essential.
  Recommendation: offer or provide this service
• B – high certainty that the net benefit is moderate.
  Recommendation: offer or provide this service
• C – moderate certainty that the net benefit is small.
  Recommendation: offer or provide this service to selected patients depending upon individual circumstances
• D – moderate or high certainty that there is no net benefit or that harms outweigh the benefits. Recommendation: discourage use
• I – insufficient evidence to recommend

[USPSTF = U.S. Preventive Services Task Force, a division of the U.S. Agency for Healthcare Research and Quality (AHRQ)]
USPSTF Levels of certainty regarding net benefit

- **high** – evidence includes consistent results from well-designed, well-conducted studies in representative primary care populations.
- **moderate** – evidence is sufficient to determine benefits, but constrained by a) #, size, or quality of studies, b) inconsistency of findings, c) limited generalizability, etc.
- **low** – evidence is insufficient to assess benefits to health outcomes, due to a) limited # of studies, b) flaws in design or methods, c) inconsistency of findings, etc.
One more level of research evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence
- see handout - steps (levels) of research evidence required

- how **common** is the problem?
- is the testing **accurate**?
- **outcome** if the therapy is **not added**?
- does the **intervention** help?
- **common harms**?
- **rare harms**?
- is the test **worthwhile**?
Level of confidence for EB treatments*

• **12-step programs**: B+, moderate to high certainty of benefit for low to moderate SUD population

• **harm reduction**:
  - methadone – B, moderate for selected heroin UD
  - needle exchange programs – A, high for drug injectors
  - controlled drinking – C, low for severe AUD;
    B, moderate for mild to moderate AUD

* USPSTF model, Erickson ratings 😊
Level of confidence for EB treatments

- **behavioral therapies** (MI, MET, CBT) – B, moderate for mild to moderate SUD; C, moderate for severe SUD

- **medications**
  - B, moderate for moderate to severe AUD
  - C, low for severe nicotine UD
  - B, moderate for moderate nicotine UD
  - B, moderate for severe opioid UD
  - BUT, only about 50% efficacy in most populations; outcomes increase with concomitant behavior therapies
HOT TOPICS
Pharmacogenetics!

- the “personalization” of pharmacotherapy, based upon genetic factors – i.e., predictors of drug response, or to target medication effects
- controversial as to whether pharmacogenetic testing in the clinic should be started, with such preliminary studies
  
  E.g., mu-opioid receptor gene OPRM1; carriers of the G-allele of the A118G polymorphism showed a better response to naltrexone in treating alcohol dependence
Medical education trends (U.S.)

SBIRT:

• **Screening** (At least, SBI...)

• **Brief Intervention**

• **Referral to Treatment**

Also:

• **SIMS: Summer Institute for Medical Students**
  
  (1 week, Hazelden Betty Ford, others)

• some schools: training in addiction medicine during **residencies (U.S.)**
Other hot topics in the U.S.

- Long-term care (Recovery Management)
- Drug courts
- Drug testing as a tool for maintaining abstinence after treatment
- Online tools to reduce relapse (e.g., MORE)
- Decriminalization/legalization of marijuana
- Medical education

No more time for these in this session……️
Overall validity of today’s story

- **Individual validities** add up:
  - neurotransmitter story = medium RVE
  - genetics story = medium RVE
  - medication mechanisms = medium RVE

Three stories **independently** supporting neurotransmitter dysregulation = **very high validity!**
Is there a common mechanism of action for “talk therapies” and medications?
If chemical dependence is a brain disease and people get better with treatment, logic says that:

**Behavioral Therapies Probably Change Brain Chemistry!**
SO, IT APPEARS THAT THE MDS DYSREGULATION BEGINS TO MOVE BACK TOWARDS NORMAL WITH TREATMENT.

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

(For some people, spirituality – or “revelation” - seems to be a very effective way to do this!)
WHAT DOES THIS MEAN FOR CLINICIANS AND TREATMENT PROFESSIONALS?

(The way treatment works is becoming better understood through evidence-based strategies)
CONCLUSIONS
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, Lauder, McCrady, Miller, Moos, Tonigan, others)

• there have been many other research advances, mostly in neurobiology/genetics

• yet some say our field (U.S.) has not moved forward much in the past 70+ years (I disagree)

• choices: 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
- and when we all work together, great things can happen......
References

• Erickson, C.K., “The Science of Addiction: From Neurobiology to Treatment” (W.W. Norton, 2007)
• Brick, J. and Erickson, C.K., “Drugs, The Brain, and Behavior” (2nd Ed., Routledge; October, 2012)
• bibliography: www.utexas.edu/research/asrec