Addiction & Drug Testing

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Faculty Disclosure

Stuart Gitlow MD MPH MBA serves as President of the American Society of Addiction Medicine. He is a solo practitioner specializing in addictive disease. He consults with various industry entities, including Orexo, Unum, MetLife, and Prudential.
What is a disease?

• Is a disease simply a departure from “normal” biologic function?

  – Normal curve with the “departure” being defined as a certain number of standard deviations from the mean

  » Mental retardation
  » Short stature
  » Depression
What is a disease?

• Is disease present if morbidity and/or mortality are impacted?
  – Elevated blood pressure
  – Elevated cholesterol
  – Elevated serum glucose
What is a disease?

- disease /dɪˈziːz/ (dī-zēz´) any deviation from or interruption of the normal structure or function of any body part, organ, or system that is manifested by a characteristic set of symptoms and signs and whose etiology, pathology, and prognosis may be known or unknown.

- But what if we have a manifestation without any known distinct deviation from normal structure or function? Is the manifestation alone sufficient for the definition?
Disease: Diabetes

• Initially, a behavioral syndrome
• Later discovery, a metabolic syndrome
• Still later, an autoimmune syndrome
• Finally, a genetic abnormality causing predisposition combined with an environmental insult giving rise to phenotypic expression

• What is the disease entity?
• When is the disease present?
• Which part should be addressed through treatment?
What is included in the disease definition?

- That is, does an individual with a specific set of symptoms and related findings have one disease, two diseases or many diseases?
Addictive Disease

• Where is the disease?
  – Is the disease defined by the use of substances or by certain behaviors such as gambling?
  – Is the disease defined by the way in which the patient utilizes substances or by the manner in which he engages in certain activities
  – Is the disease present if those behaviors stop?
  – Was the disease present before those behaviors began?
Definition #1 - Alcoholism

Alcoholism is a primary, chronic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. The disease is often progressive and fatal. It is characterized by impaired control over drinking, preoccupation with the drug alcohol, use of alcohol despite adverse consequences, and distortions in thinking, most notably denial. Each of these symptoms may be continuous or periodic.

Note the absence of any reference to quantity or frequency of use.

Morse RM, Flavin DK. The Definition of Alcoholism. JAMA 1992;268:1012-1014.
Definition #2 - Dependence

- Tolerance
- Withdrawal
- Use more/over longer duration than intended
- Desire/unsuccessful effort cut down/control
- Time spent obtaining, using, or recovering
- Social/occupational/recreational reduction
- Continued use despite knowing of persistent physical/psychological problem

- Pick any three from this set, noting that quantity and frequency are absent here as well.

Definition #3 – Alcoholism readdressed

- Alcoholism is a disease characterized by the repetitive and compulsive ingestion of any sedative drug, ethanol being just one of these...
- It is absolutely critical to appreciate that this definition does not in any way specify which sedative agent is used, the frequency of its use, or the amount ingested.
Definition #4 - Addiction

- Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

- Addiction also affects neurotransmission and interactions between cortical and hippocampal circuits and brain reward structures, such that the memory of previous exposures to rewards (such as food, sex, alcohol and other drugs) leads to a biological and behavioral response to external cues, in turn triggering craving and/or engagement in addictive behaviors.

American Society of Addiction Medicine – Public Policy Statement 2011
Cause of Addiction

• **Genetic factors** account for about half of the likelihood that an individual will develop addiction. Environmental factors interact with the person’s biology and affect the extent to which genetic factors exert their influence. Resiliencies the individual acquires (through parenting or later life experiences) can affect the extent to which genetic predispositions lead to the behavioral and other manifestations of addiction. Culture also plays a role in how addiction becomes actualized in persons with biological vulnerabilities to the development of addiction.
What the definition of addiction does not say:

• We’ve talked about a disease of brain reward, motivation, memory, and related circuitry. We’ve talked about genetic abnormalities. We’ve talked about environmental factors.

• What we have not talked about is the drug use or behavior itself. That is simply a manifestation of the disease, not part of the disease itself.
Sedative Pharmacology

![Graph showing level of sedation over time](image)
Human Physiology
Turn the normal curve on its side:
Genetic manifestations

- Stimulus Augmentation is premorbid to addictive illness. Is it a sign that the predisposition to the disease is present?
- This is one likely physiologic basis of addiction, representative of the phenotypic expression but perhaps demonstrating the genotype prior the expression itself.

Addiction definition continued

• The new definition speaks to the importance of environmental factors impacting the extent to which genetic factors are demonstrated.
Sociologic study – Children followed from age 5 to 18

• “Psychological differences between frequent drug users, experimenters, and abstainers could be traced to the earliest years of childhood and related to the quality of parenting received. The findings indicate that (a) problem drug use is a symptom, not a cause, of personal and social maladjustment, and (b) the meaning of drug use can be understood only in the context of an individual's personality structure and developmental history. It is suggested that current efforts at drug prevention are misguided to the extent that they focus on the symptom, rather than on the psychological syndrome underlying drug abuse.”

Dr. Block continued:

- “It would appear that the roots of … substance abuse are discernible, and perhaps modifiable, in early childhood.”

- Are these the roots of substance use disorders, or was Dr. Block observing the environmental and sociologic underpinnings necessary for phenotypic expression?
Definition – Important Points

- Addictive Illness ≠ Substance Use
- Do not look at quantity or frequency measures as being relevant to treatment efficacy, as they are not relevant to the disease definition
- Lifelong illness once initiated, whenever that is.
- Reflect upon the literature with a close eye upon accuracy and relevance.
Drug Testing

- What is standard of care?
  - 16 year old well patient visit
  - 30 year old c/o anxiety or depression
  - 50 year old c/o insomnia
  - 70 year old with episodes of “syncope”
Drug Testing

• A primary prevention, diagnostic, and monitoring tool to identify the presence or absence of drugs of abuse or therapeutic agents related to addiction management in multiple settings.
• Can be conducted using blood, saliva, hair, breath, in addition to the more commonly utilized urine
• Drug Tests do NOT identify substance use disorders, indicate the presence of physiologic dependence, but provide information only about recent use of substances.
Percentage of patients referred to Quest, 2012

- Negative for Any Drug (Including Prescribed Drug) - 25%
- Positive for Prescribed Drug and Negative for Other Drug - 40%
- Negative for Prescribed Drug and Positive for Other Drug - 15%
- Positive for Prescribed Drug and Positive for Other Drug - 20%
Forensic v Clinical

- Forensic testing requires that test results meet rules of evidence in administrative, civil, or criminal proceedings.

- Clinical testing is performed just as any individual laboratory test is conducted.

- Standard workplace drug testing programs are generally set up to follow forensic guidelines.
Methods

• Immunoassay (IA) – these are point of service cups, typically.
  – These have a high rate of clinically false negatives

• IA with gas chromatography-mass spectrometry (GC-MS) for positive result confirmation

• Liquid chromatography-MS (LC-MS)

• Tandem mass-spectrometry (LC-MS/MS)
  – This can be used definitively without initial screening
Hair Testing

- Window of detection is up to 90 days (longer with body hair), but use in the last 5-7 days is not detected.
- Coloring or bleaching hair causes degradation of drugs in the matrix, but doesn’t eliminate the presence of metabolites.
- Shaving head is obvious way around this, but any hair will do.
- Some drug classes such as benzodiazepines are poorly detected.
- No known adulterants
- Typically 1.5” of hair is required.
Alcohol

• BAC is primary test for recent use
• Ethyl Glucuronide will extend window to 72 hours
  – Hair testing possible but uncertain concentration parameters
  – Cannot determine intensity or frequency
• Blood Phosphatidylethanol (PEth) uses fingerstick blood on filter paper and remains positive for 2-3 weeks. Threshold appears to be approximately 1000g over prior 3 weeks with mean daily intake of four drinks.
Nicotine

• Breath testing for CO
  – Note will be positive for marijuana smokers
• Cotinine testing in urine, hair, and saliva
  – Note will be positive in nicotine replacement products
SAMHSA-5

- No longer recommended except where required by regulation.
- Amphetamine, THC, Cocaine metabolites, Opiates, and PCP.
- Note that Opiates will not reflect oxycodone, hydrocodone, buprenorphine, or methadone
Drug Detection Times

- Urine
- Oral Fluid
- Blood
- Sweat
- Hair

Concentration vs. Time:
- Minutes
- Hours
- Days
- Weeks
- Months

Cutoff
Limitations

- IA will often lead to negative results even with substance use. Klonopin and Ativan will not generally show up on benzodiazepine screening. Similarly, Dilaudid and Vicodin may not show up on opioid screening.
- Need to test for normal urine specimen characteristics
  - Temperature 90-100°F, pH 4.5-8, Creatinine>20mg/dL, Specific gravity>1.003
Challenges

• Drug testing will only detect those drugs being sought. Synthetic cannabinoids such as “spice” and synthetic cathinones (“bath salts”) represent a challenge since they will elude standard drug testing.

• Patients will obtain a prescription for, say, Marinol, then indicate that their THC positive result is secondary to prescribed medication. In these cases, THCV, a homologue of THC, will be positive with marijuana but not with Marinol.

• Absence of metabolite testing does not allow certainty as to whether patient may have “spiked” the sample. This is important where diversion of prescribed medication is the concern.
Challenges

• Quantification will not distinguish between recent light use (say, poppy seeds), and remote heavy use.

• Detection periods are quite variable, based upon drug, individual metabolism, and lab testing process and methods.
Costs

- The practice of routinely ordering large arbitrary drug panels with request for LC-MS/MS confirmation and quantification of all results is a significant driver in rapidly increasing costs of drug testing.

- ASAM Policy: Drug testing be determined by the ordering clinician based upon patient-specific medical necessity.
Drug Testing Process

- Key component of assessment and diagnostic workup
- Response to positive testing
- Monitoring procedures (Frequency/Duration)
- Testing panels – which drugs should be tested
- Type of collection – observed/unobserved
- Presumptive (IA) vs Definitive testing
Guidelines

• Routine clinical screening for substance use should be conducted as a universal precaution in all health settings.

• If no risks are present, presumptive test should be performed on two separate occasions within 12 months. If risks are present, definitive testing should be performed, again, twice.

• While in tx for SUD, testing should be conducted regularly/randomly, with high frequency if recent use and lower frequency as sobriety lengthens.

• Testing should be customized for individual patients, reflecting geographically relevant trends. Documentation should reflect reasoning for test selections.