Practical Applications of Urine Drug Monitoring in the Addiction Treatment Setting

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Tufts Health Care Institute : Program on Opioid Risk Management
The Role of Urine Drug Monitoring and other Biofluid Assays in Pain Management

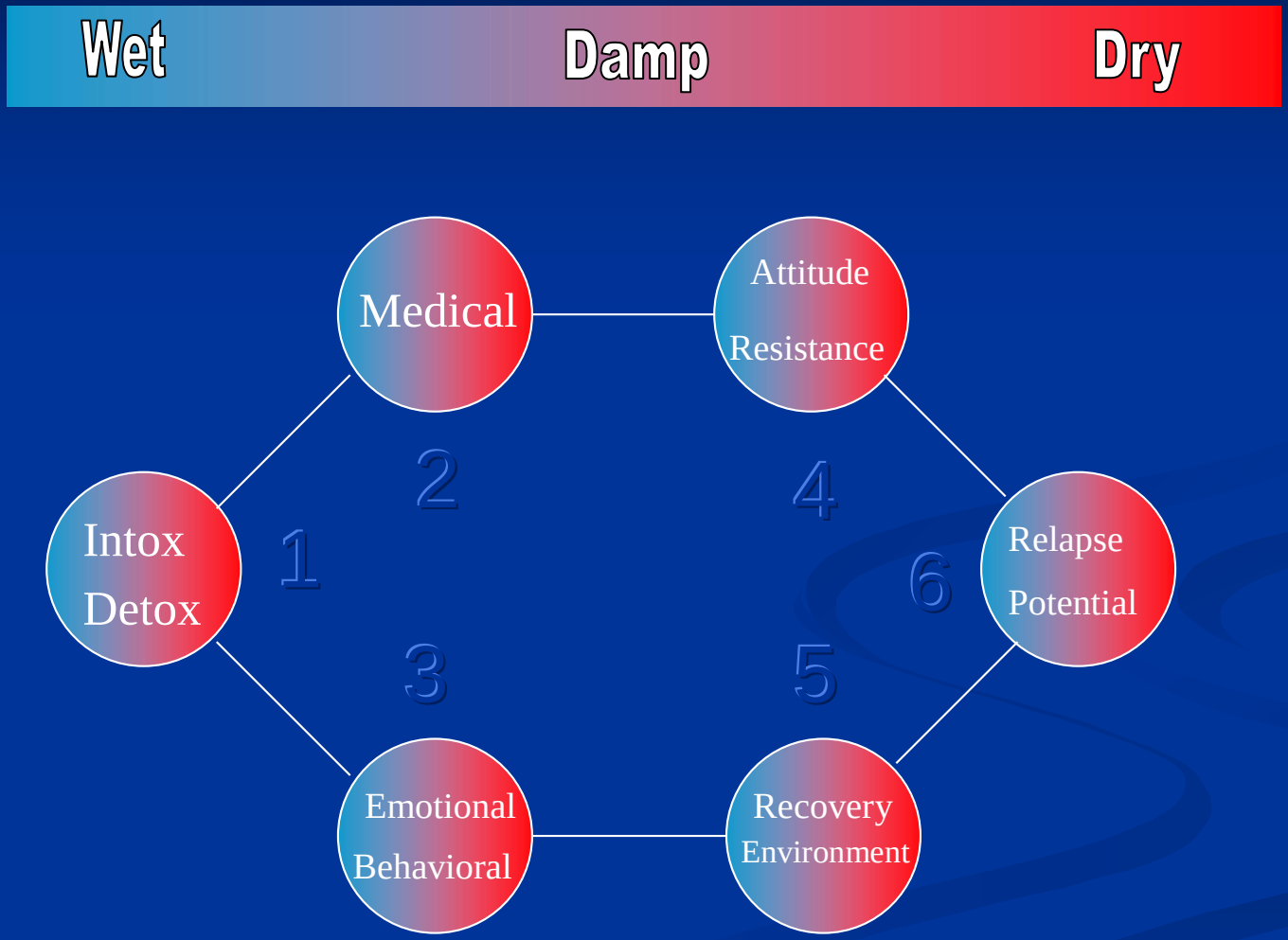
Clinical Assessment Measures

- Clinical Interview : Substance Use History
- Standardized assessment & screening questionnaires
- Physical and mental status examination
- Withdrawal severity assessment scales
- Biological fluid testing
- Psychological and neuropsychological testing
- Imaging studies

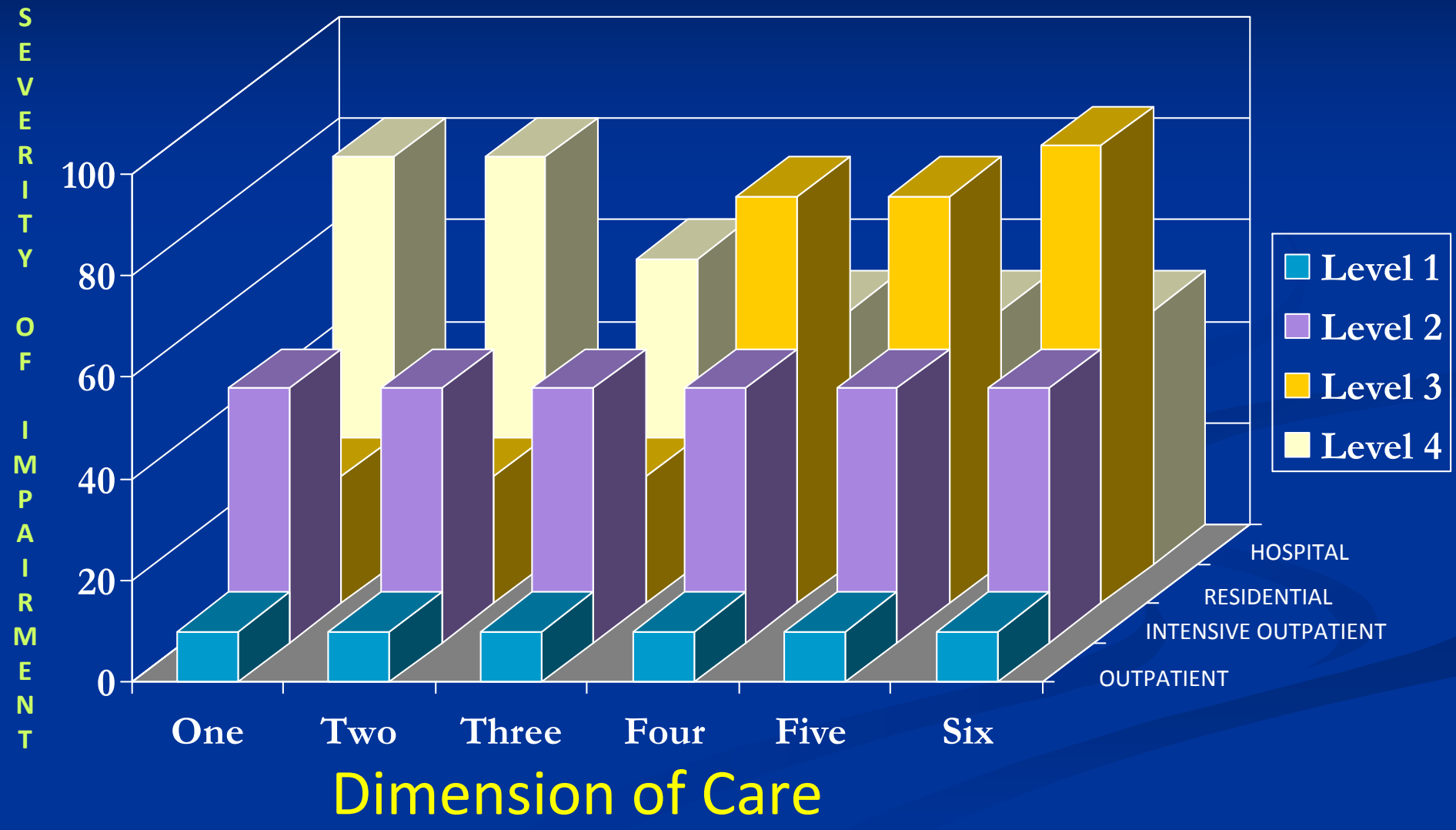
Purpose of Clinical Drug Testing

- Validity of patient history
- Confirmation and documentation of diagnoses
- Assessment of tolerance and physical dependence
- Choice of treatment modalities and level of care
- Treatment planning for opioid addicted pain patient
- Clinical management
- Relapse prevention
- Patient advocacy
- Public safety

ASAM Dimensions of Care



ASAM Dimension vs. Level of Care



Limitations of Substance Use History

- **Self Report is reliably unreliable**
  - Depends upon setting, consequences of self disclosure, and extent of treatment resistance and readiness for change
- **Polysubstance dependence is the norm, not the exception**
  - Patients seeking treatment for one drug class (including alcoholics), frequently use multiple drugs simultaneously – symptom triggered self medication
- **Physicians and providers underestimate use and severity of problems based upon clinical interview, lack of "aberrant behavior", trusting relationship, etc**
- **Physicians and providers are not knowledgeable about interpretation of drug testing and frequently make clinical decisions that may harm patients**
  - Missed diagnoses
  - Under treatment of pain
  - Inappropriate level of care determinations
  - Premature discharge from care
  - Child care and legal consequences
  - Continued care despite prescription abuse and illicit substance abuse and drug diversion

Biological Fluid Testing: What Does It Measure?

- **Measure of presence (detection) of drug in biological fluid only at that moment in time**

  Snapshot = Drug test

  Movie = Serial snapshots over time

- **Frequency of testing depends upon indication**

  If you leave a movie theatre to get something to eat at the snack bar, how long can you be away before you do know what's happening (does not apply to afternoon soap operas)

Take Snapshots : Make Movie

- Drug testing sample = snapshot in time
- Add Clinical information about:
  - What drug(s) taken – amount, route administration, dosage strength, sequential vs concurrent polysubstance use (including alcohol), pattern of use
  - Timing of dose in relation to sample collection
  - Testing Procedures and knowledge of laboratory
  - Patient information – addiction status and severity, concurrent medical and psychosocial problems, legal and family problems
- Drug Testing + clinical information = movie

  Patient =director, Disease = script writer, Clinician = audience

Movie Making : Timing of Sample Collection

- Clinical questions and indications for testing
  - Observed behavior -Reasonable Suspicion Testing
    - Minimal drug effect – Tolerance
    - Withdrawal symptoms – Physical Dependence
    - Desired drug effect (pain relief) - Adherence
    - Excessive drug effect (polysubstance) – Abuse + Addiction
  - Problem behavior - Post Incident Testing

    Association of negative behavioral consequence + drug use
  - Treatment adherence and prevention of problem behavior – Random Testing

Random Testing : Clinical Issues

- Purpose:
  - To prevent prohibited drug and alcohol use
  - Monitor of abstinence and treatment compliance
  - For prevention of relapse
  - Monitor development of drug seeking attitudes as predictor of relapse
  - To identify return to drug use
  - Deterrent effect decreases relapse by lowering craving and
  - treatment effectiveness by deterrence

- Random testing does NOT help you determine
  - Elimination rates
  - Drug-drug interactions
  - Fast or slow metabolizers
  - Absorption problems
  - Adherence
  - Drug diversion

Interpreting Urine Drug Test Reports : Questions to Ask

- What testing methodology was utilized?
- Is the drug(s) class the same as reported?
- Are there more drugs than patient reported?
- Are there drugs NOT present that you expected based upon the patients recent substance use history ?
- Are the levels within the expected range?
- Is the patient's behavior and observed degree of intoxication consistent with drug test reports?
- Is the sample dilute?
- Was the sample collected properly and considered valid?
- Was the timing of the collection within expected range?
- Does any other entity need to know the test results?
- What are the consequences of a positive test result?
- What change in clinical treatment plan will result from your interpretation of the test results?

Methodology Information Needed for Interpretation

- Immunoassay for class of drug
  - Cross reactivity between parent drug, metabolites
  - Cross reactivity and baseline stability vary by assay manufacturers
  - False positive, false negatives rates
  - Sensitivity and Specificity
  - Cut off levels and level of detection of assay
  - Linearity of immunoassay

- Molecular Identification : GCMS + LCMSMS
  - Sensitivity and specificity – LCMSMS = 10 to 1000 x more sensitive
  - Measurement of parent drug and metabolites – Heat for GCMS may change structure of parent drug or metabolite
  - Detection time increases as sensitivity increases – LCMSMS >> GCMS
  - Separation between analytes and other drugs
  - Sample volume – LCMSMS only needs 1 ml – multiple assays with re-collection
  - Improved turn around time – presample preparation for LCMSMS << GCMS

Who and When to Test

- All new patients independent of risk status
  - Comprehensive identification and quantification of any and all substances – prescribed, unprescribed, illicit, OTC's, etc
    - Confirmation of presence of prescribed medications
    - Medications from other sources can cloud diagnostic and therapeutic efforts
  - Identification of illicit substance use and referral to treatment
  - Verification of self report and confirmation of diagnoses
  - Identification of metabolic problems and drug-drug interactions

    Ratio of parent drug to metabolites – tolerance and genetic polymorphism

Who and When to Test

- Established patients and those who have the following:
  - Unexpected detectable drugs on initial UDT
  - Dilute urine samples or problems with collection timeliness / procedure
  - Family, SO or workplace reports of impaired behavior or incidents suspicious of being drug related
  - High tolerance and “not enough” for pain control
  - Withdrawal symptoms despite continued drug prescribing and drug detection
  - Those reporting continued abstinence when clinician believes that this seems “too easy”
  - Those displaying problems with medication adherence
  - Reports of “aberrant behavior” – early refills, lost scripts, not following prescribing instructions, pharmacy reports of concern, etc
  - Those reports relapse or use of OTC medications
  - Those reporting continued high risk behavior
  - When making a major change in treatment plan
  - When treatment progress is inconsistent with expected treatment course
  - To support referral for treatment to a higher level of care or for medical / psychiatric treatment
  - At testing frequency to monitor progress and assist in prevention of relapse

Adapted from Gourley, D. and Heit, H.

Reasons for Clinical Drug Testing

- Validity of patient history
- Documentation of Diagnosis
- Treatment assessment
- Treatment planning
- Clinical management
- Relapse prevention
- Patient advocacy
- Public safety

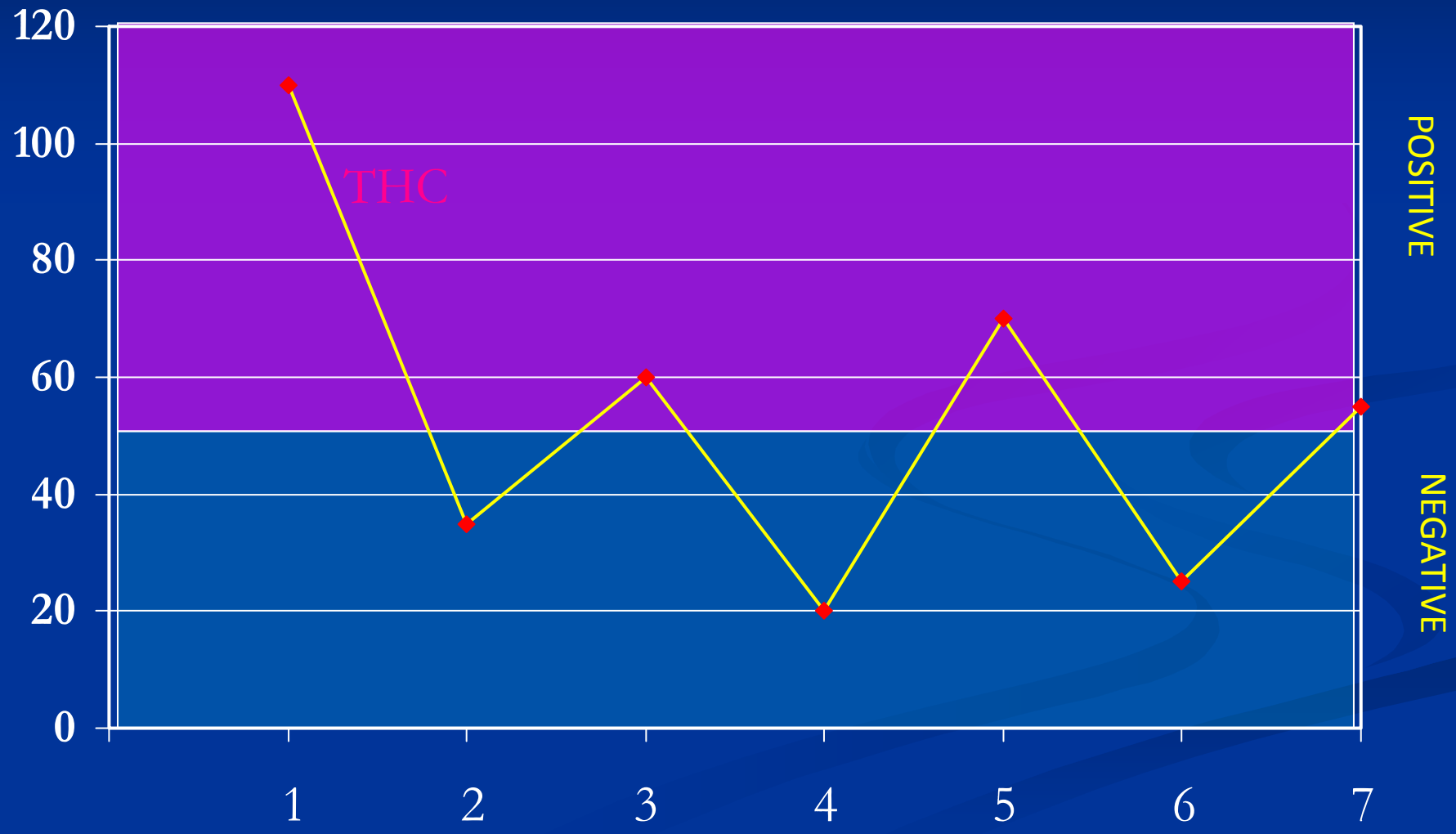
Case Study #1: Child Safety

- 19 year old shows up at hospital in labor and delivers healthy 6.5 lb boy
  - Urine collection obtained during labor is positive for THC
  - Child protective services intervene
  - Child placed in temporary custody with grandmother
  - Referred to your facility for a substance abuse evaluation
  - Need to send report to DCYF regarding treatment recommendations
    - Substance abuse treatment for mom
    - Safety issues regarding potential neglect of child
    - Visitation structure and time frame for re-unitement

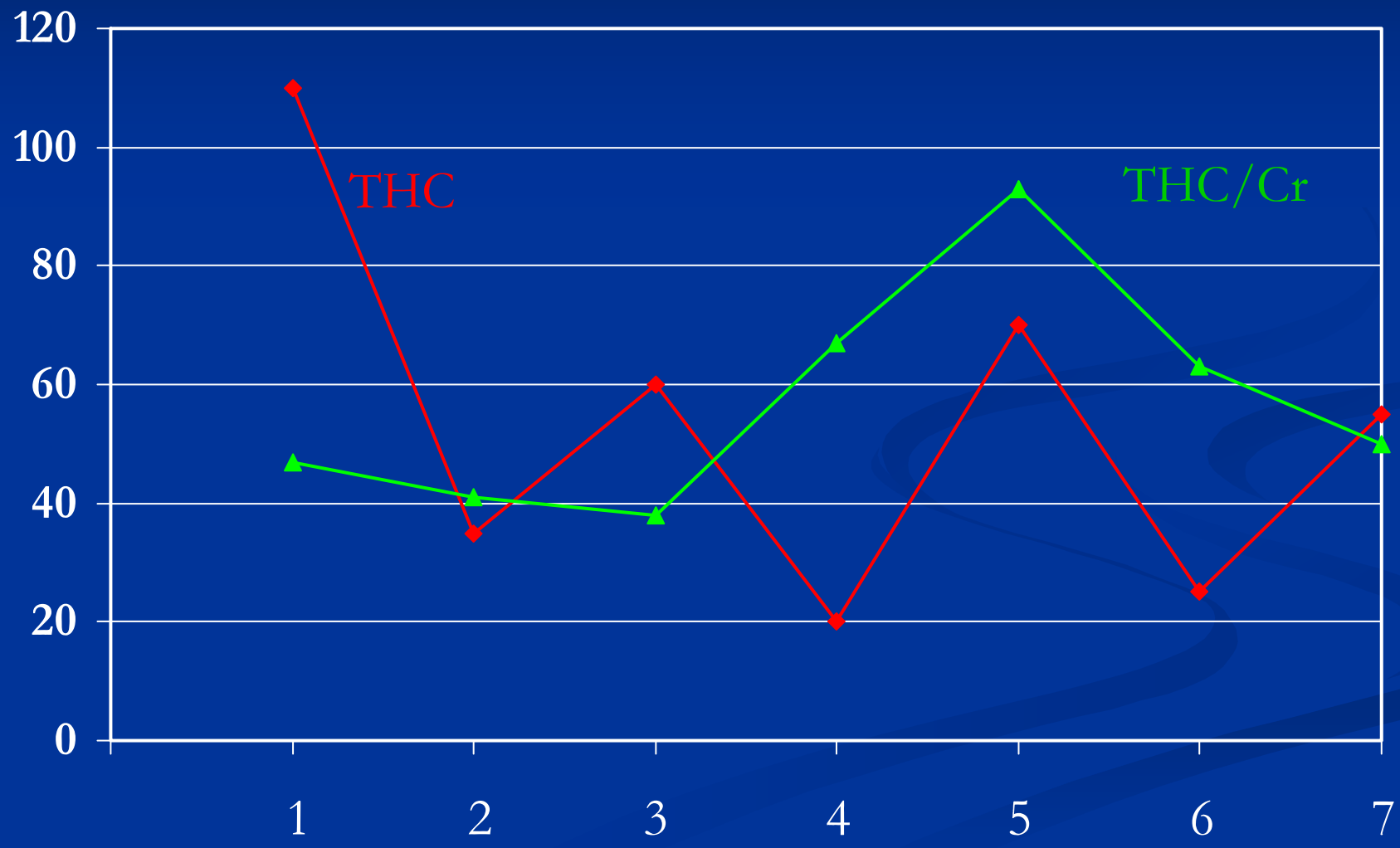
THC Test Results

Sample #	Results
1	Positive
2	Negative
3	Positive
4	Negative
5	Positive
6	Negative
7	Positive

THC ng/ml Levels



THC and THC/Cr Levels



THC Test Results : Clinical Outcome

Sample #	
1	Positive
2	Negative
3	Positive
4	Negative
5	Positive
6	Negative
7	Positive

Clinical Information	
1	24 hrs after last dose
2	Intentional Dilution
3	No use – normal dilution
4	Relapse after false accusation
5	No use – concentrated urine
6	No use – lots of AM coffee
7	Repeat urine : fluid restriction

Qualitative Testing : Problems

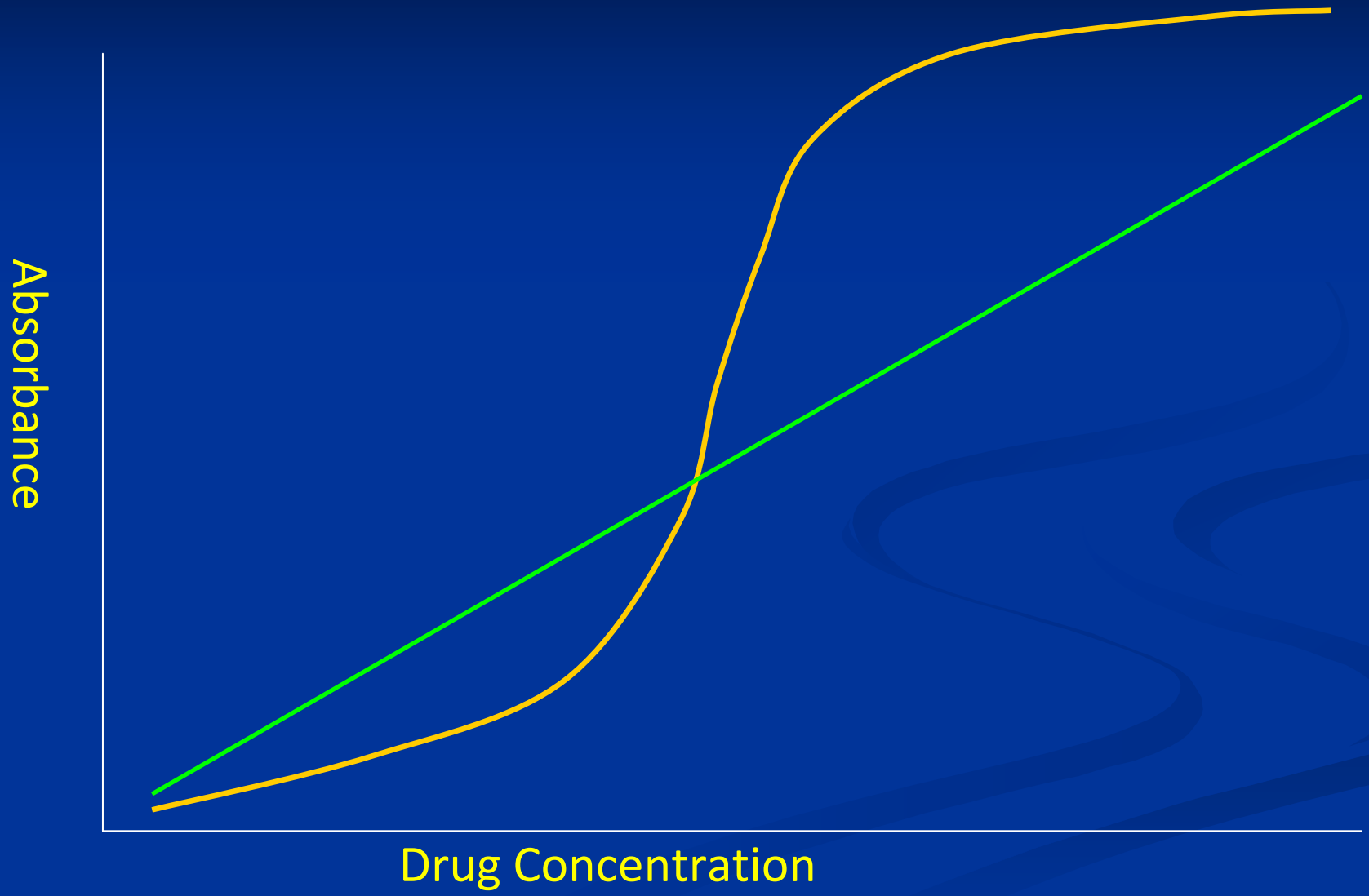
- For post incident samples #2 -#7
  - Positive urine = really was negative
  - Negative urine = really was positive
  - In this example = 100% wrong interpretation, 100% of the time

- Wrong Clinical Decisions may result
  - Distrust between patient and clinician
  - Improper clinical judgments
    - Discharge from treatment
    - Negative consequences to family –Kids taken from home
    - Increased treatment and societal costs for higher level of care, family court investigations and monitoring, unnecessary child protective services, loss of job, or incarceration

Quantitative Testing : Creatinine

- Total drug concentration in urine=ng/ml
  - Urine dilution vary 10-40 fold (Usual range 20-400 ng/ml)
    - In vivo dilution (excess fluid consumption) 10-20 ng/ml regularly occurs from dietary patterns -Coffee in AM, high volume water for athletes, treatment of kidney or bladder problems, etc
- Creatinine adjusted levels normalize for dilution
  - Calculation of drug / unit creatinine excreted
  - Allows for serial monitoring of drug levels over time
- HOWEVER : Need to know your laboratory qualifications
  - Immunoassays need to be linear over clinically meaningful dosage range in order for calculations to be accurate enough for serial monitoring

Immunoassay Linearity



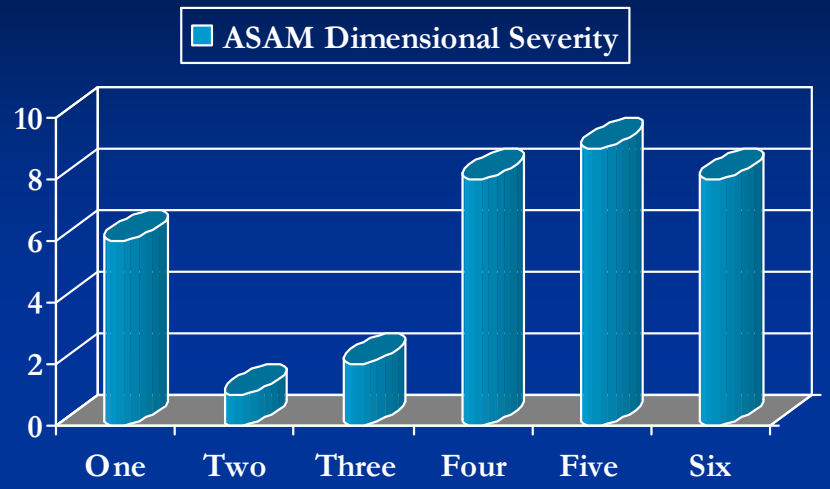
Problems with Immunoassays

- Qualitative results have limited clinical utility
  - Urinary dilution variations make serial measurements difficult if not impossible
  - Need to supervise urine collection to detect in vitro dilution, sample substitution, use of adulterants, etc
  - Many analytes fall below the sensitivity of the assay
  - Many analytes are not detected by the assay

- Immunoassays bind to anything that has a similar shape and/or chemical properties and NEVER identify a compound precisely and unequivacally do not:
  - Separate parent drug from metabolite
  - Determine specific drug within a drug class
  - Identify all drugs or metabolites within a drug class
    - Most opioid assays do not detect oxycodone, methadone, fentanyl

- Cross react with other drugs, foods, etc
  - False positive
    - Drugs within different drug class – Fluoroquinolones antibiotics (+ opiate), Daypro (+benzo)
    - OTC (cold medicines) may react with amphetamine assays
  - True positive
    - Cross reactive with foods (poppy seeds = + opiate assay)
    - Medicines used for other clinical conditions
      - Cocaine for nose bleeds, medical marijuana and Marinol (dronabinol)

Validity of Self Report: Assessment



Progress: 48 yr old nurse

Reported for suspected drug diversion

Has prescription for Percocet + Xanax

Needs fitness for duty report

Needs evaluation for nursing board

Believes needs assessment only

Opiate (EIA= 300ng/ml, FPIA neg),Cr=20, Benzo Positive,

REQUIRE additional testing to be sure if:

Positive opiate inconsistent with oxycodone ingestion history

- Low cross reactivity of oxycodone with traditional opioid immunoassay

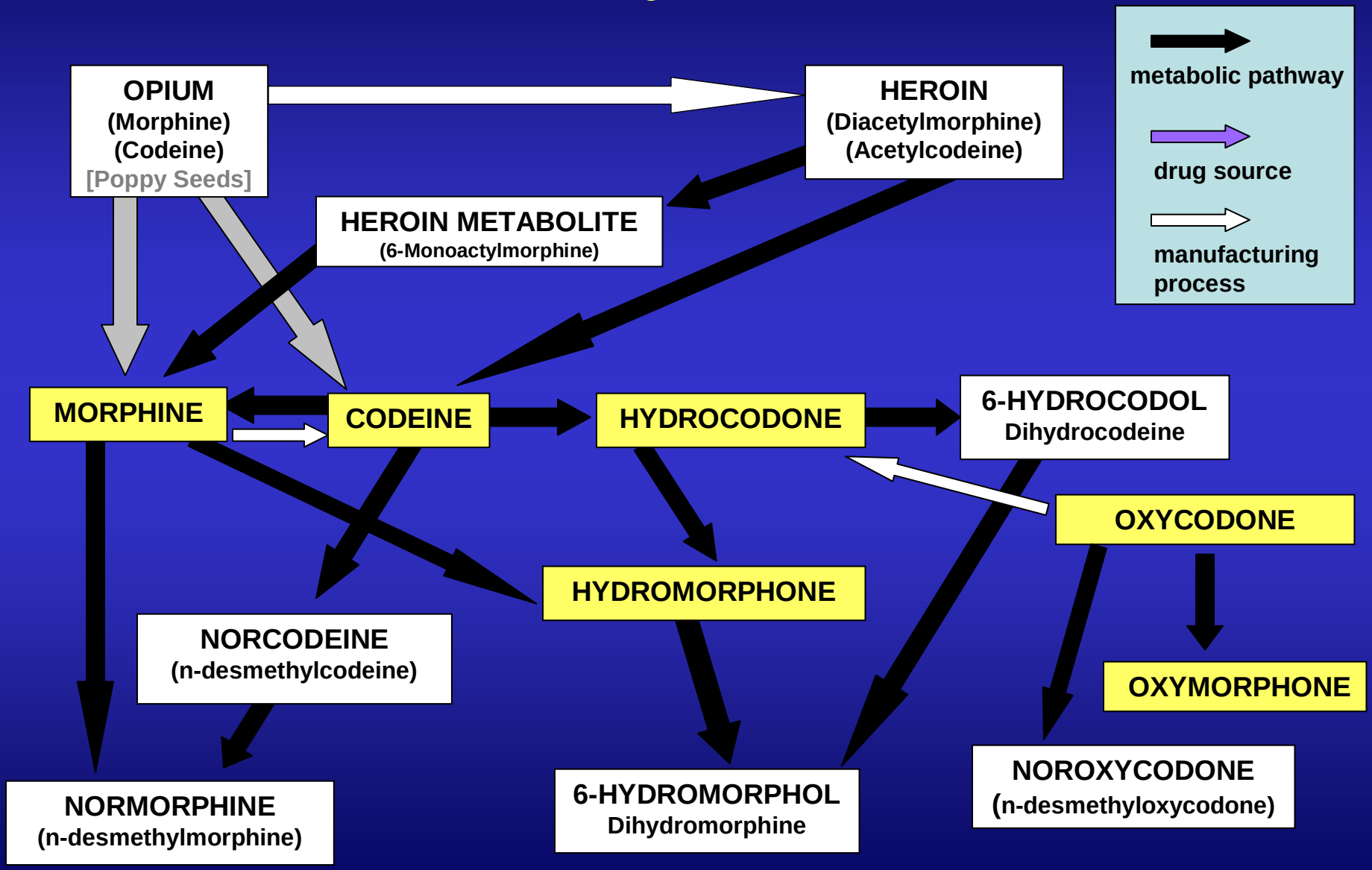
Dilute urine may hide sub-threshold opioids

- Request repeat sample collection until urine more concentrated
- Call lab and ask for sub-threshold components

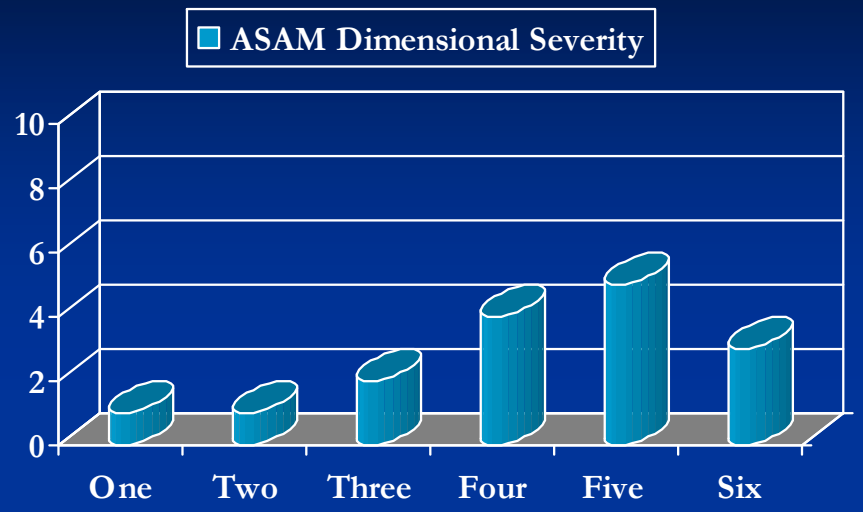
Order test that will identify specific opioids

- GCMS or LCMSMS

OPIUM'S JOURNEY



Adolescent THC: Dimension 4



Assessment: 16 yr old male

Mother found marijuana in jeans

Good grades and obeys rules

Parents approve of friends / family

Admits to smoking

Urine Toxicology Results: THC = 42ng/ml, CR=215

Toxicology results consistent with reported history

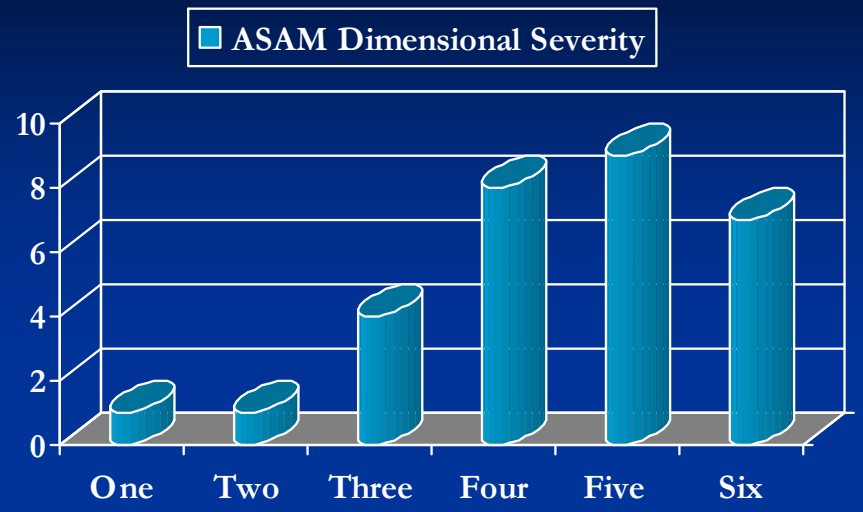
- Would have been negative by forensic standards
- Results allow you to support reliability of patient history

Toxicology results suggest valid collection

Creatinine adjusted levels = 20ng/ml suggest occasional use,

- low quality THC or longer duration since last use

Adolescent THC: Dimension 4



Assessment: 16 yr old male
Mother found marijuana in jeans
Denies smoking – holding it for friend
Grades falling
Disobeys rules / curfews
Parents disapprove of friends

Urine Toxicology Results: THC = 42ng/ml, CR=15

Toxicology results inconsistent with reported history
- Would have been negative by forensic standards
- Results allow you to objectively confront reliability of history

Toxicology results suggest intentional in vivo dilution of sample

Creatinine adjusted levels = 280ng/ml suggest VERY high use,
high quality THC or use prior to session

Drug Testing: Treatment Planning - ASAM 4

- Using Quantitative Toxicology Testing to Estimate:
  - Severity of Dimension Four – Attitude and resistance to treatment
    - Understanding of negative consequences of use and need for treatment
      - Documenting unreliability of self report and explanation of denial/minimization
      - Educate relationship between marijuana effects and failing performance, genetic predisposition and mood and attentional problems
      - Educate parents on use of quantitative testing to enhance trust rebuilding, avoid unnecessary conflict and operationalize behavioral contract to implement treatment goals
    - Enhancing Motivation for Change and Engagement in Treatment
      - Monitoring of drug levels to document abstinence and drug seeking
      - Enhancing motivation for change by objectifying compliance and bi-directional trust rebuilding – allow for adolescent to agree to treatment IF can get something in return short term goal
      - Engage in development of behavioral contract
      - Decrease unnecessary conflict over trust issues by objectifying relationship between behavior and use
      - Rate of elimination may objectify severity of addiction and duration of use
      - Define need for level of care recommended for effective treatment and development of motivation for change in relationship to fear of failure resulting in higher level of care

Purpose of Testing = Trust Rebuilding

- Everyone has to get something positive
  - Person being testing
    - For clean urines-gain privileges, control
    - For improved performance-specific rewards
    - Personal responsibility for actions
    - Vehicle to improve communication
    - Commitment for treatment
  - Person monitoring test results
    - Ease off on degree of control/monitoring
    - Decrease struggle over behavioral observations
    - Decrease fears - rely upon objective confirmation

Behavioral Contracting Issues

- Relationship between testing and results
  - Parenting skills, placement, custody issues
  - Pre and Post testing of “What”
  - How does treatment plan changes with results
- Ability to separate recent from chronic use
  - THC/Creatinine ratios - control of dilution
  - Dropping levels vs. relapse
- Match to natural history of disease
  - Get through urges and high risk situations
  - Maintain trust and job responsibility

Process of Contract Negotiation

- Peace treaty process-cease fire, negotiations, verification and inspection, consequences
- Both sides work on their versions
- Therapists role - specify desired change
- Negotiations regarding details of contracts
- Signing and enforcement of contract
- Anticipatory violation of contract
- Development of treatment options in advance
- Coercive to voluntary participation depending upon previous failure of treatment

Use of Test Results

- Diagnosis Confirmation
- Reduction of Denial and Minimization
- Screening and intervention
- Enhance motivation for treatment (Pt+family)
- Determine need for medical clearance
- Monitoring Treatment Response & Compliance
- Treatment Modification and Decision Making
- Treatment Advocacy
- Assist monitoring in primary care setting
- Reduction of Treatment Costs