Stimulants, Psychosis, & Treatment

David Kan, M.D.
Medical Director, ORT Clinic
San Francisco Veterans Affairs Medical Center
Assoc. Clinical Professor of Psychiatry, UCSF
(415) 812-1092
David.Kan@Gmail.com

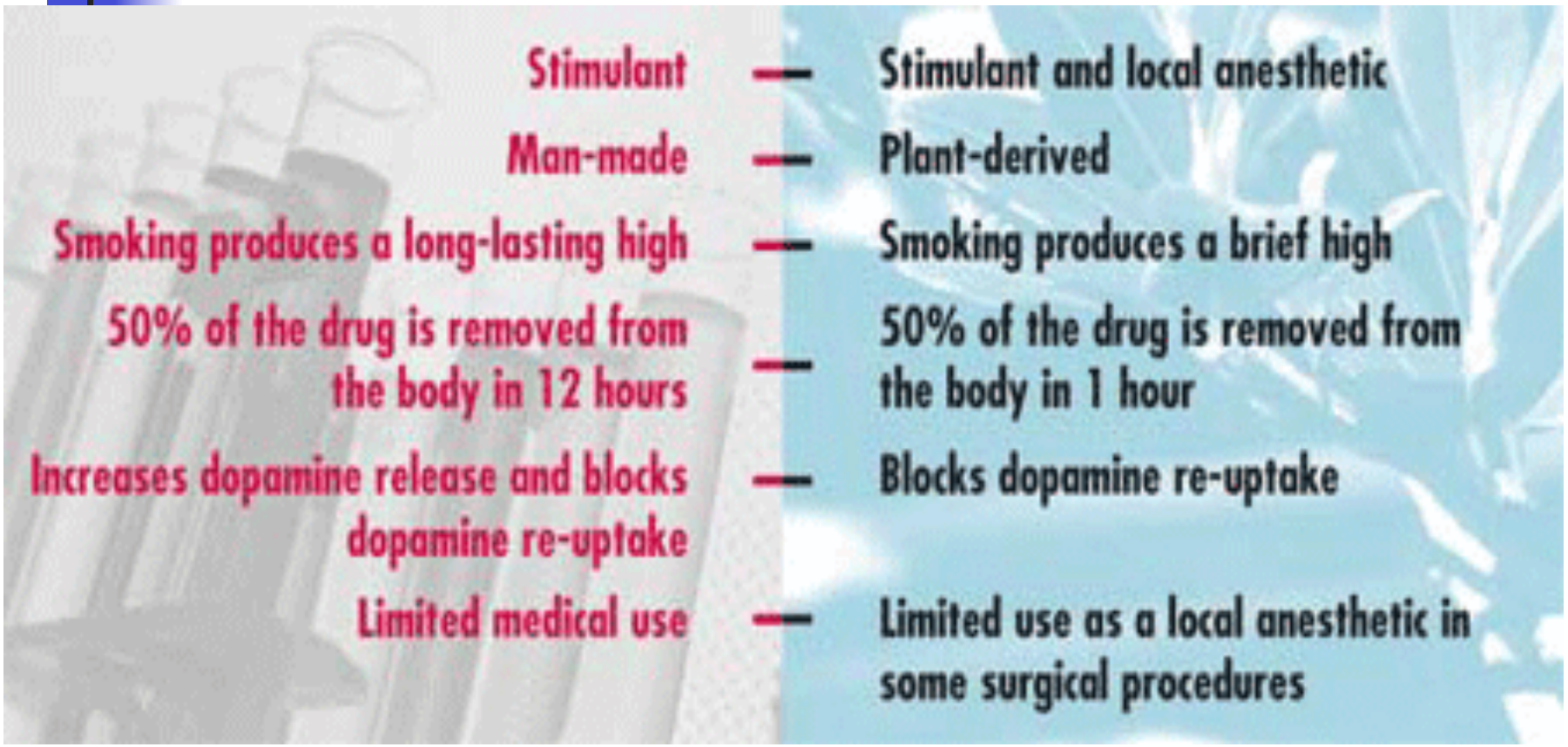
UCSF

Department of Veterans Affairs

Overview

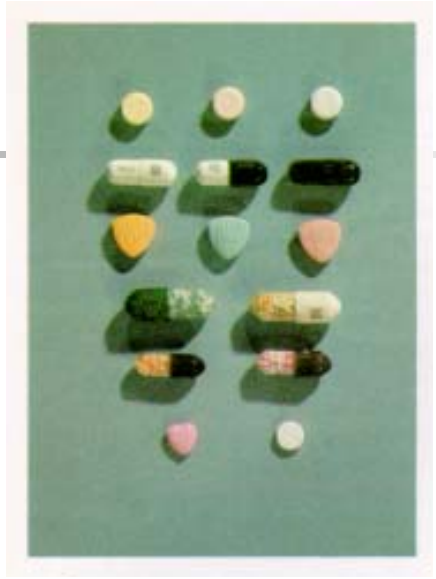
- **Introduction**
  - Epidemiology, Manufacture
- **Usual Effects**
- **Psychosis**
- **Violence**
- **Treatment**

Meth v. Cocaine



http://www.drugabuse.gov/Researchreports/Methamph/methamph3.html

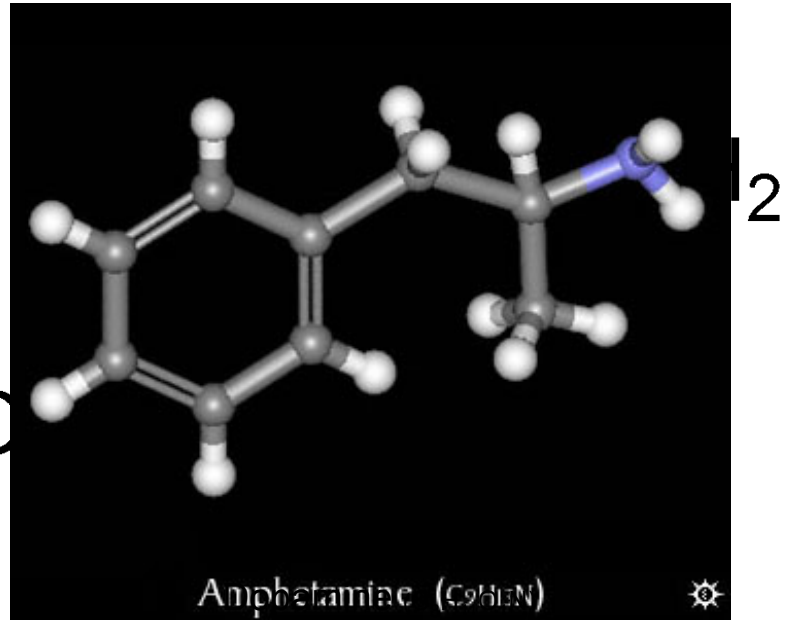
Methamphetamine Preparations

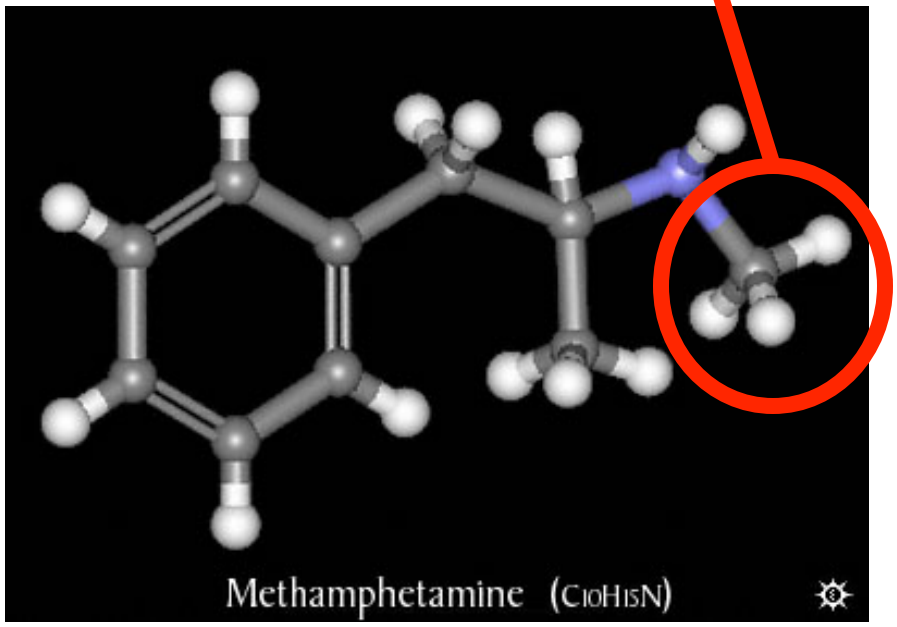


(Meth)Amphetamine

- Pharmacology

Additional Methyl (CH_3) Group





Methamphetamine

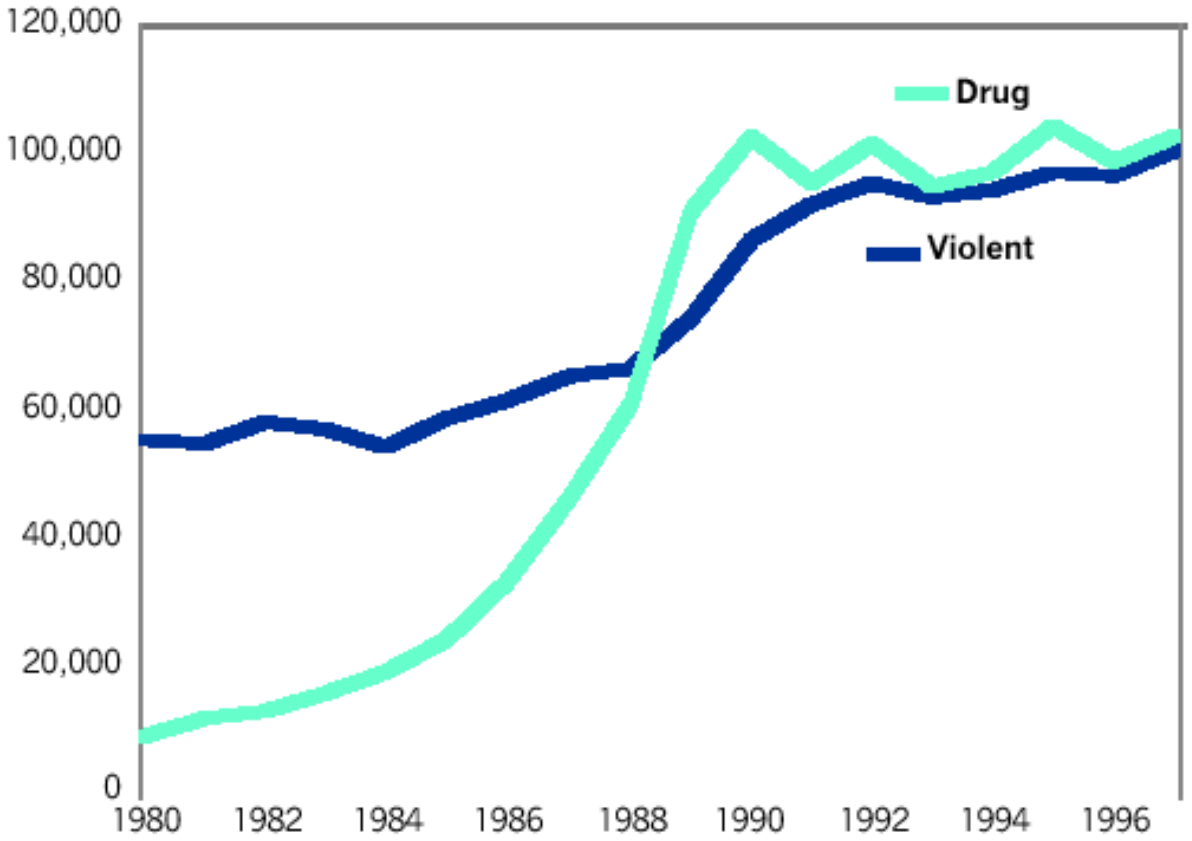
- **Pharmacology**
  - Promotes release of Biogenic Amines
  - Vesicular and Cytosoloic Dopamine, Norepinephrine release and reuptake inhibition
  - Serotonin release + MAOI (at higher doses)

- **Route of Administration**
  - Binge vs. Constant Use

  - Oral → Nasal → Smoked → Intravenous
    -------*INCREASING POTENCY*------->

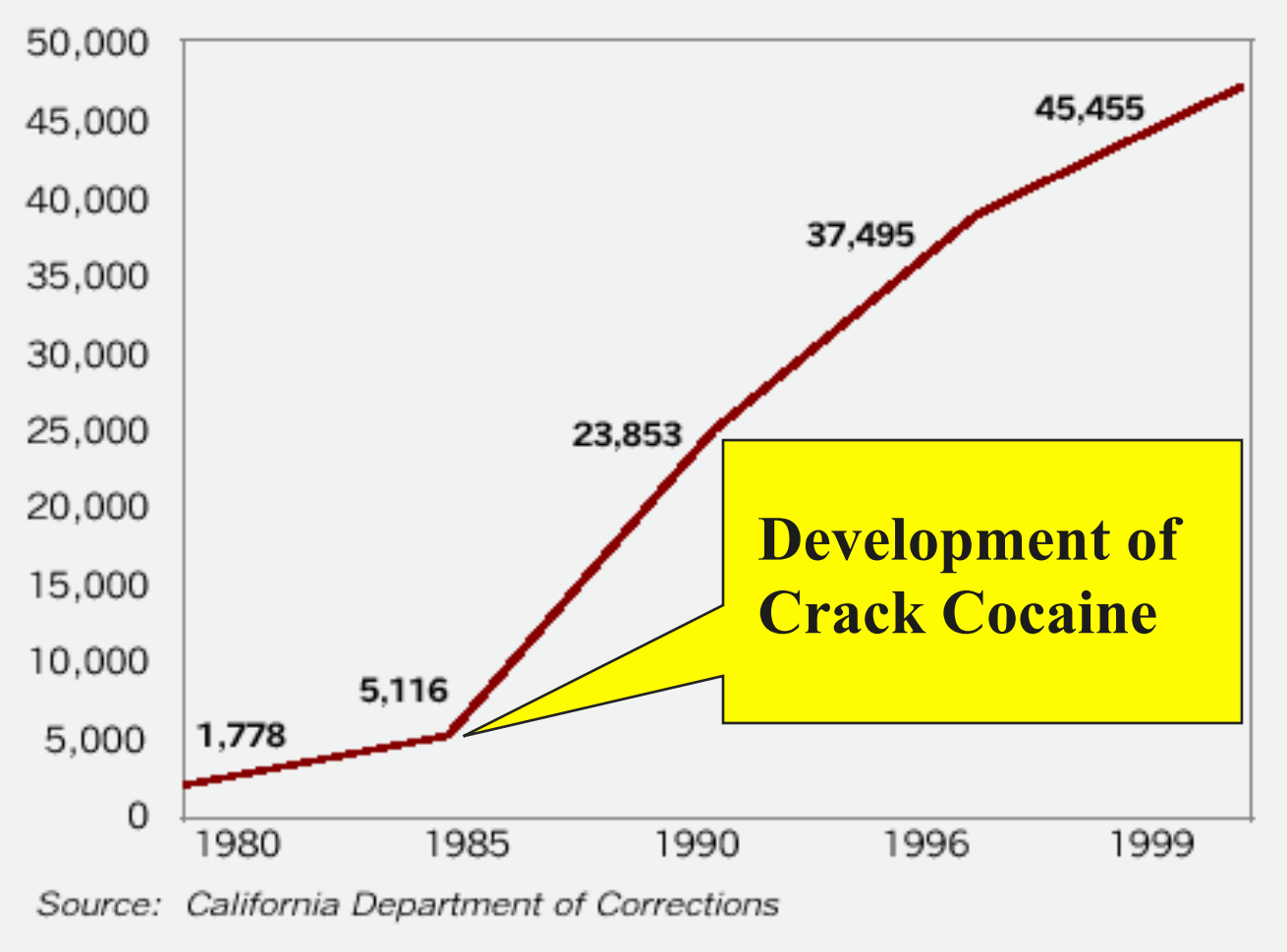
THE MAKERS OF SUDAFED CHANGE THE FORMULA SO THAT IT CAN NO LONGER BE USED TO MAKE METHAMPHETAMINES

Drug vs. Violent Crime Incarcerations



Source: Gililard, Darrel K. Trends in U.S. Correctional Populations, 1992. Washington, D.C.: U.S. Department of Justice, Bureau of Justice Statistics, 1992, and Mumola, Christopher J. and Beck, Alan. Trends in U.S. Correctional Population, 1997. Washington, DC: U.S. Department of Justice, Bureau of Justice Statistics, in press.

Number of Persons Imprisoned in California for Drug Offenses



Cocaine

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Cocaine

- **Pharmacology**
  - Rapid Dopamine + Norepinephrine reuptake inhibition
  - Benzoylmethylecgonine → Benzoylecgonine (inactive)
  - Cocaine + EtOH → Cocaethylene (active)

- **Route of Administration**
  - Oral→Nasal → Smoked → Intravenous
    -------*INCREASING POTENCY*------->

Cocaine Street Prices

- **Powder**
  - $75-$100 a gram
  - 10-12 lines per gram
- **Crack**
  - $10-$25 1/10th gram
  - $40 1/4th gram
  - ~10 “hits” per gram

Cocaine

- **Oral**
  - Chewed Leaves
- **Intranasal**
  - 5-20 min peak effects
- **Smoked**
  - 1.5 min peak
  - 5-15 min duration

Crack Cocaine Manufacture

- **Ingredients**
  - 1-2 grams cocaine
  - 4 Tbs baking soda
  - Bottled Water
- **Directions**
  - Mix well
  - Spread on Baking Sheet
  - Put in oven 350 deg x 25 min or until cracks appear
  - Cut up and enjoy!

(Meth)amphetamine Manufacture

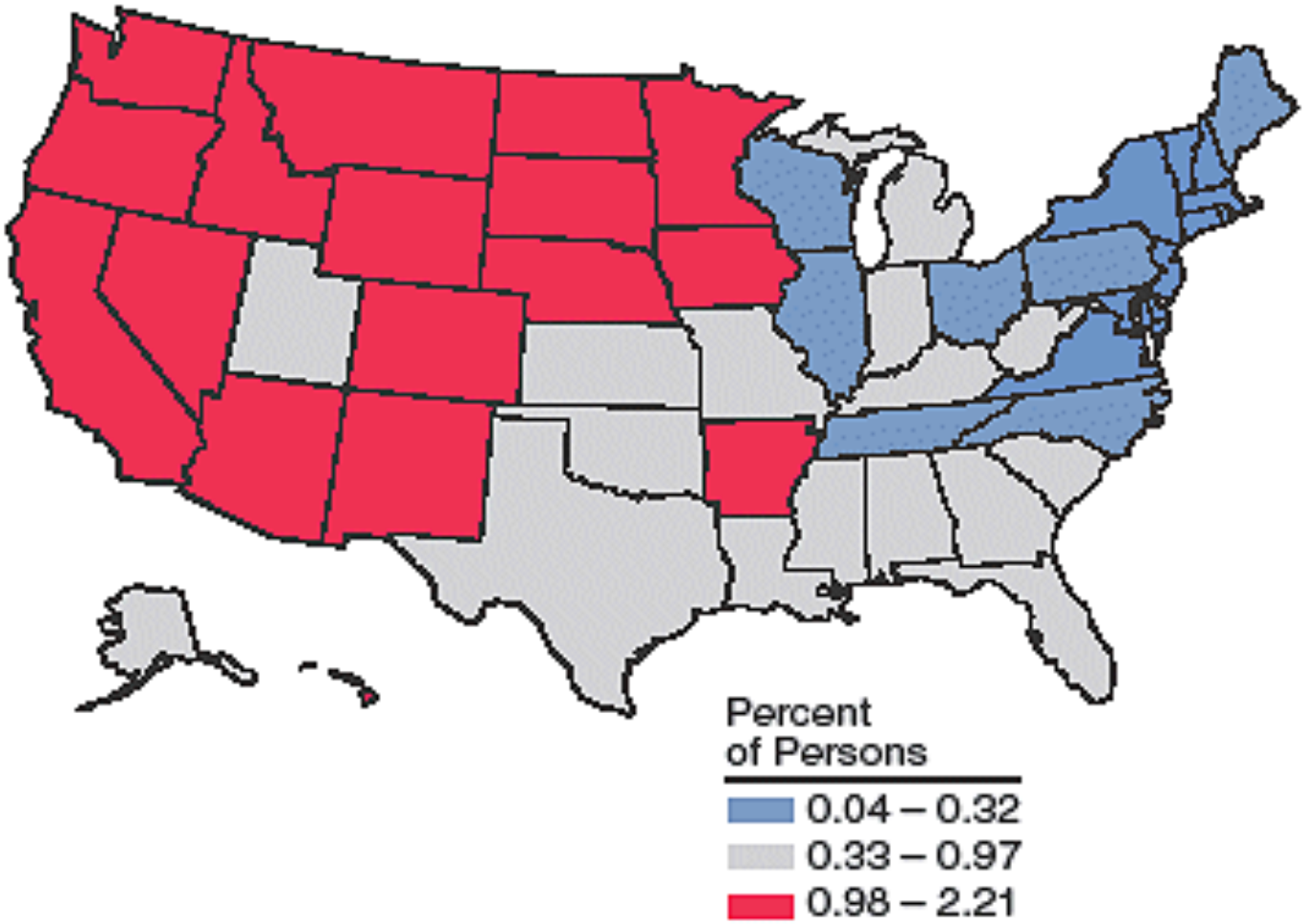
- **Generally two methods of production:**
  1. Reduction of PPA, l-Ephedrine or d-Pseudoephedrine + Red Phosphorous and Hydroiodic acid / Iodine) = 54-82% yield of d-amphetamine
  2. Same Precursors + Sodium or Lithium metal and Ammonia = almost 100% pure d-isomer – more potent and more pure

- **Result usually mixture of amphetamine and methamphetamine**

- **Ratio of amphetamine vs. methamphetamine in blood and urine cannot be interpreted for time since last use**

Logan, BK (2001)

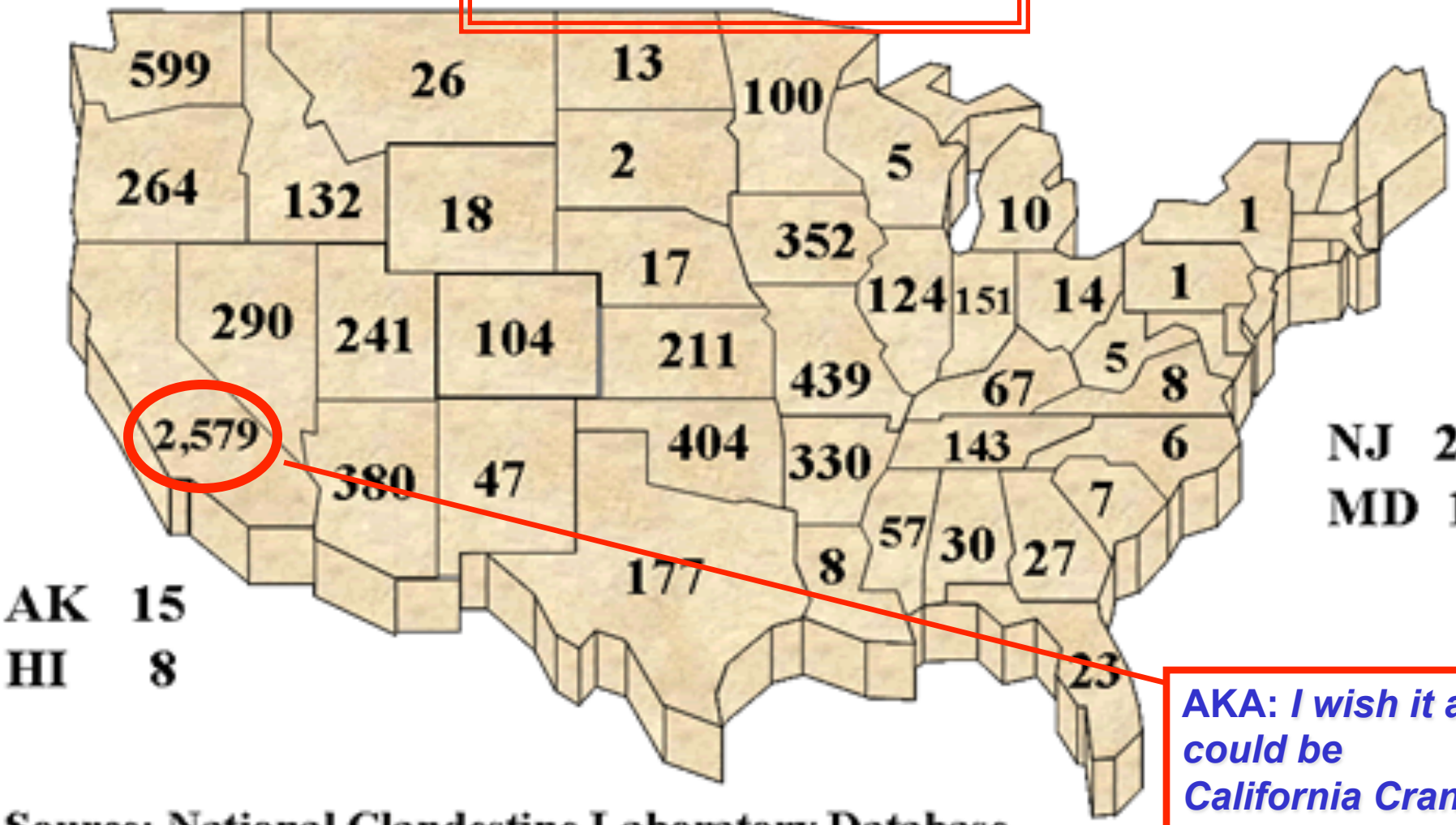
Methamphetamine Use in Past Year among Persons Aged 12 or Older, by State: 2002-04



Total of All Meth Clandestine Laboratory Incidents

Including Labs, Dumpsites, Chem/Glass/Equipment

Calendar Year 1999



Source: National Clandestine Laboratory Database

Total: 7,438 / 43 States Reporting

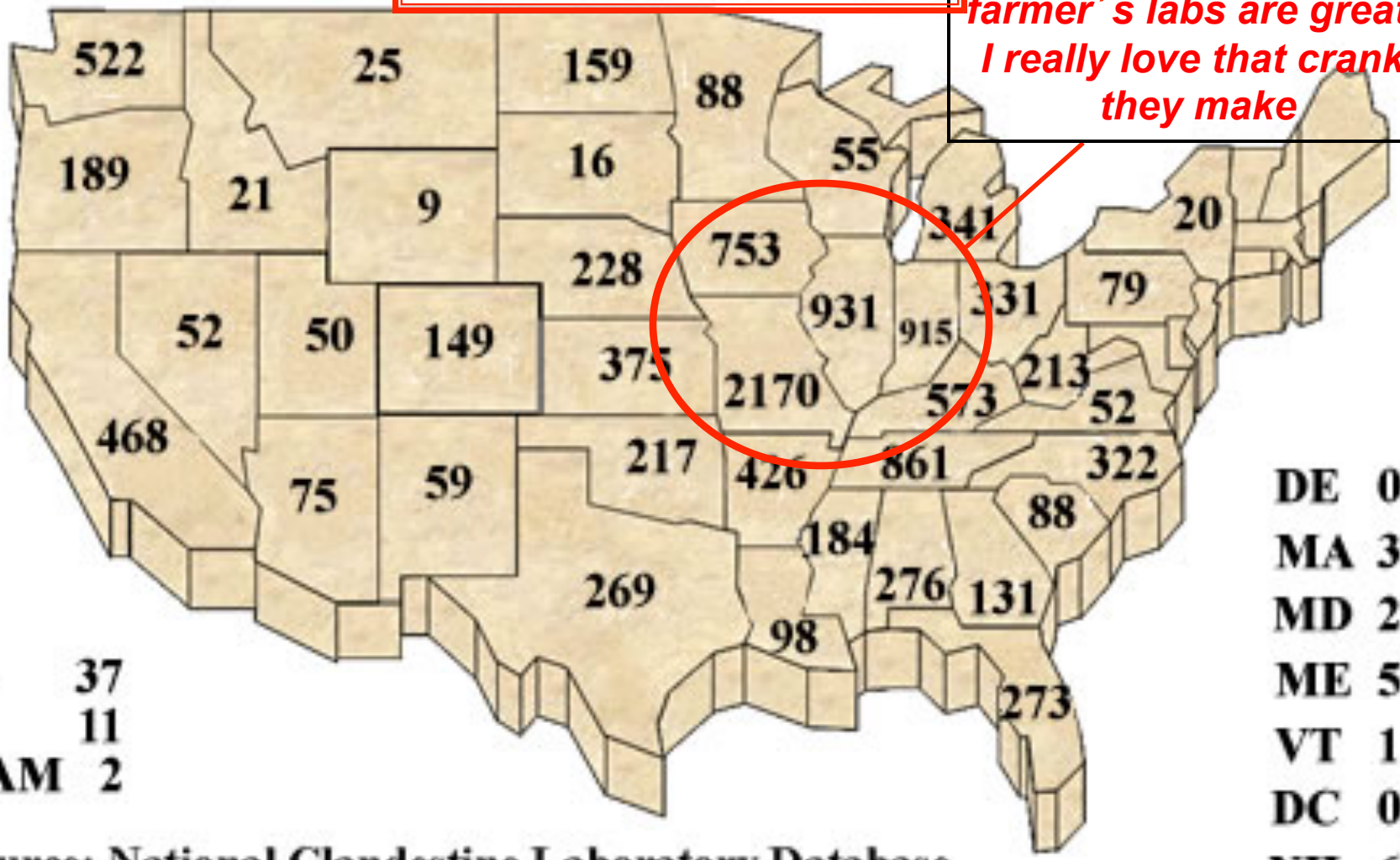
Dates: 01/01/99 to 12/31/99

Total of All Meth Clandestine Laboratory Incidents

Including Labs, Dumpsites, Chem/Glass/Equipment

Calendar Year 2005

Now the midwest farmer's labs are great. I really love that crank they make



AK	37
HI	11
GUAM	2

DE	0
MA	3
MD	2
ME	5
VT	1
DC	0
NH	6

Source: National Clandestine Laboratory Database

Total: 12,139

Dates: 01/01/2005 - 12/31/2005

map last updated June 2006

(Meth)Amphetamine Detection

- **½ Life – 10-12 hours**
- **Detection Period –**
  - **Urine**
    - Amphetamine – 1-3 days (500 ng/ml cutoff for GC-MS)
    - Methamphetamine – 3-6 days (250-500 ng/ml cutoff for GC-MS)
  - **Blood**
    - Methamphetamine - 1-3 days
    - Therapeutic Blood Levels - <50ng/ml
    - >100ng/ml consistent with Abuse
    - Psychosis and Violence 150-1000ng/ml range (blood)[1,2]
    - Cadaveric Heart – unreliable due to diffusion
  - **Frequent false positives**

1. Anggard, E., L. M. Gunne, et al. (1970)

2. Angrist, B. Schweitzer, et al. (1969)

3. Barnhart, FE (2001)

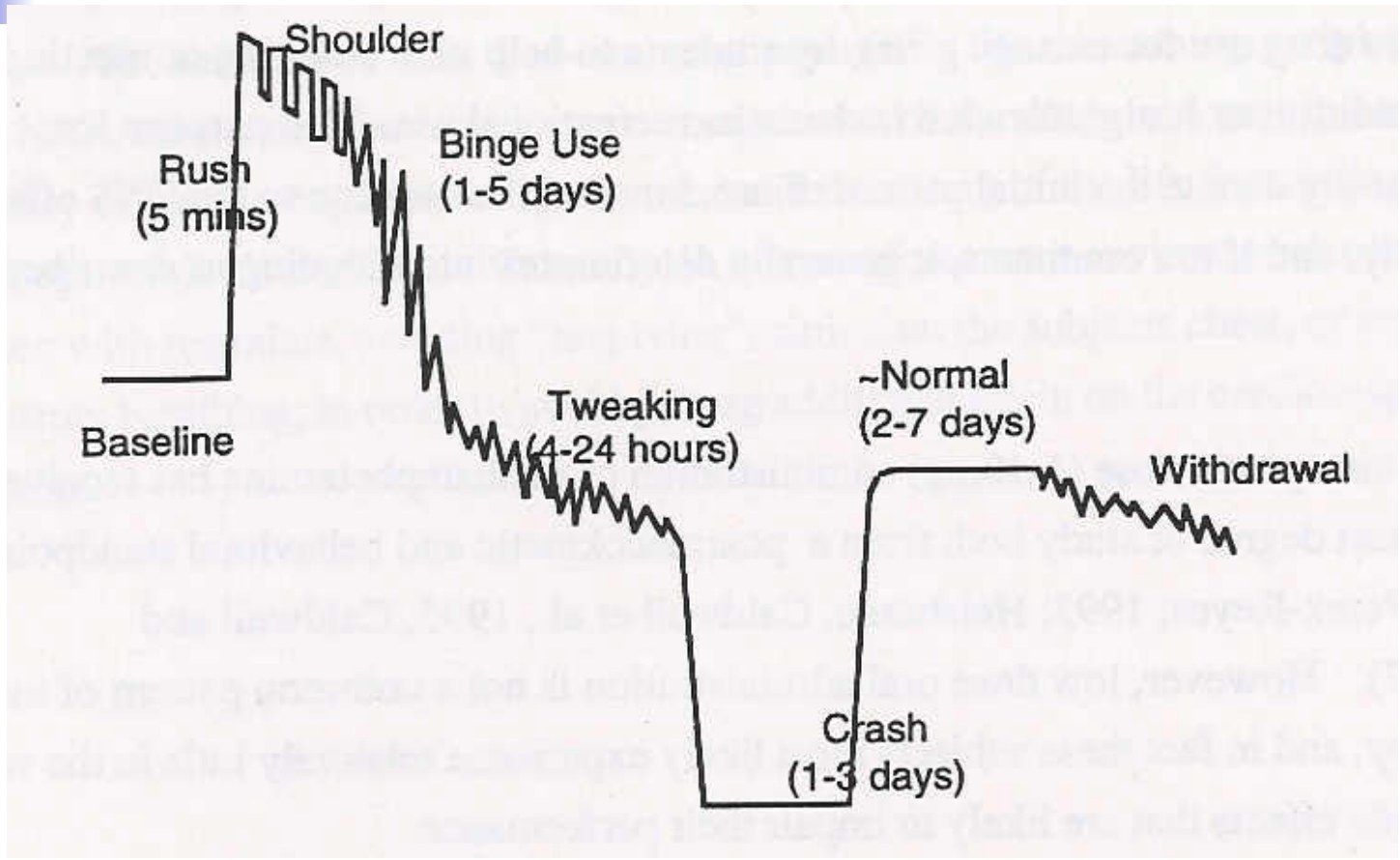
Cocaine Detection

- **½ Life – 1 hour**
- **Detection Period –**
  - **Urine**
    - Cocaine – 6-8 hours
    - Benzoylecgonine – 2-4 days up to 8 days in heavy use
  - **Blood**
    - 5-6 hours post dose – parent c
  - **Infrequent false positives**
    - TAC

Methamphetamine Effects

- Acute Usual Effects
- Acute Adverse Effects
- Mood Disturbance
- Withdrawal Syndrome

The "Meth Run"



Logan BK (1998) "Pharmacology of Methamphetamine and its Relationship to Behavior Impairment" AAFS Meeting, Aug 1998

Acute Meth Usual Effects

- Flash of euphoria, elevated mood
- Insomnia, alertness, increased energy
- Lack of appetite, thirst, diaphoresis
- Loquaciousness, “crystal clear thinking”
- Hyperacute memory – relevant and extraneous stimuli with accurate recall

Ellinwood, E. H., Jr. (1967)

Acute Meth Adverse Effects

- **Anxiety**
- **Progressive stereotyped behavior**
- **Fear, suspiciousness**
- **Awareness of being watched**
- **Peripheral field visual hallucinations**

Ellinwood, E. H., Jr. (1967)
Connell, P H (1958)

Meth Mood Disturbances

- **Depression**
  - 68% Female, 50% Male
- **Suicide Attempt(s)**
  - 28% Female, 13% Male
- **Causality unclear**
- **Pathology Greater in IDU, More frequent users[1]**
- **Anhedonia[2,3]**

1. Zweben, J. E., J. B. Cohen, et al. (2004)

2. Angrist, B. M. and S. Gershon (1970)

3. Yeh, H. S., Y. C. Lee, et al. (2001)

Meth Withdrawal Syndrome

- **Anergia, anhedonia, waves of intense craving**
- **"Tweaking" ~24 hours**
  - Dysphoria, scattered, disorganized thought
  - Paranoia/Anxiety/Irritability
  - Hypervigilence
  - Auditory, tactile hallucinations, delusions
  - Normal pupils
- **"Crashing" ~ 24-72 hours**
  - Intense Fatigue, catnapping, uncontrollable sleepiness
  - Continuing stimulation

Logan, BK (1998)

Meth Acute Toxic Confusion / Delirium

- **Uncommon (Involuntary Intoxication)**
- **Clouding of consciousness subtle[1]**
- **Most Experimental reproductions do not note Acute Toxic Confusion [2-5]**

1. *Beamish, P. and L. G. Kiloh (1960)*
2. *Derlet, R. W., P. Rice, et al. (1989) 3. Griffith, J.D. (1970) 4. Bell, D. S. (1973) 5. Angrist, B. M. and S. Gershon (1970)*

Meth Acute Psychosis

- **"Model Psychosis"**
- **Single Dose vs. Repeated High Dose**
- **English Model – Direct Psychotogenesis**
  - Young and Scoville - 1938
  - Connell - 1958
- **Japanese Model –Psychosis from Brain Damage**
  - Sato, Yui, Wada – 1982, 2002, 1976

Meth Acute Psychosis: Risk Factors

- **Premorbid Personality Disorder[1,2,4]**
- **MA and other substance Abuse/ Dependence[1,2,3,4]**
- **Mode of Administration[5]**
- **Previous Psychosis[1,2,3,4,5]**
- **Brain Injury[3]**

1. *Ellinwood, E. H. and S. Cohen (1971)*
2. *Farrell, M., A. Boys, et al. (2002)*
3. *Fujii, D. (2002)*
4. *Iwanami, A., A. Sugiyama, et al. (1994)*
5. *Matsumoto, T., A. Kamijo, et al. (2002)*

Meth Acute Psychosis

- **Psychosis Onset 5-90 hours**
- **Hallucinations Sudden, First to Clear**
  - Visual Hallucinations > Auditory Hallucinations
  - Usually in setting of clear sensorium
- **Paranoid, Reality-Based Delusions**
- **Ideas of Reference**
- **Residual Symptoms Common**
- **Thought Disorder Rare**
- **Restlessness, agitation and excitement**

Bell, D. S. (1965) Bell, D. S. (1973) Angrist, B. Schweitzer, et al. (1969)

Meth v. Cocaine Psychosis

- **Both**
  - Labile Mood
  - Vital Sign Changes
  - Auditory and Tactile hallucinations
  - Residual symptoms common
- **Cocaine**
  - Tends to not last as long
  - Overall Less than meth

Meth Chronic Psychosis

- **Not Recognized by DSM-IV**
- **Japanese Experience**
  - Large “clean populations” 1950’s, 70’, 90’s
  - Brain Damage/Sensitization – DA release in Striatum, Nucleus Accumbens
  - Acute recurrence of previous psychosis in response to psychosocial stress, low dose MA
  - “Settled Psychosis”

Meth Chronic Psychosis

Yui – 116 female prisoners with hx of MAP[1-7]

- 30% had flashbacks
- AH - Comments or threats, IOR, ½ VH
- Paranoid-Hallucinatory symptoms
- Stressful events common precipitant
- Few Negative Symptoms
- Significantly elevated plasma NE and lesser 3-MT elevation with Flashbacks

1. Yeh, H. S., Y. C. Lee, et al. (2001) 2. Yui, K., K. Goto, et al. (2000) 3. Yui, K., S. Ikemoto, et al. (2002) 4. Yui, K., S. Ikemoto, et al. (2002) 5. Yui, K., T. Ishiguro, et al. (1997) 6. Yui, K., T. Ishiguro, et al. (1998) 7. Yui, K., T. Ishiguro, et al. (2000)

Meth Other Long-Term Effects

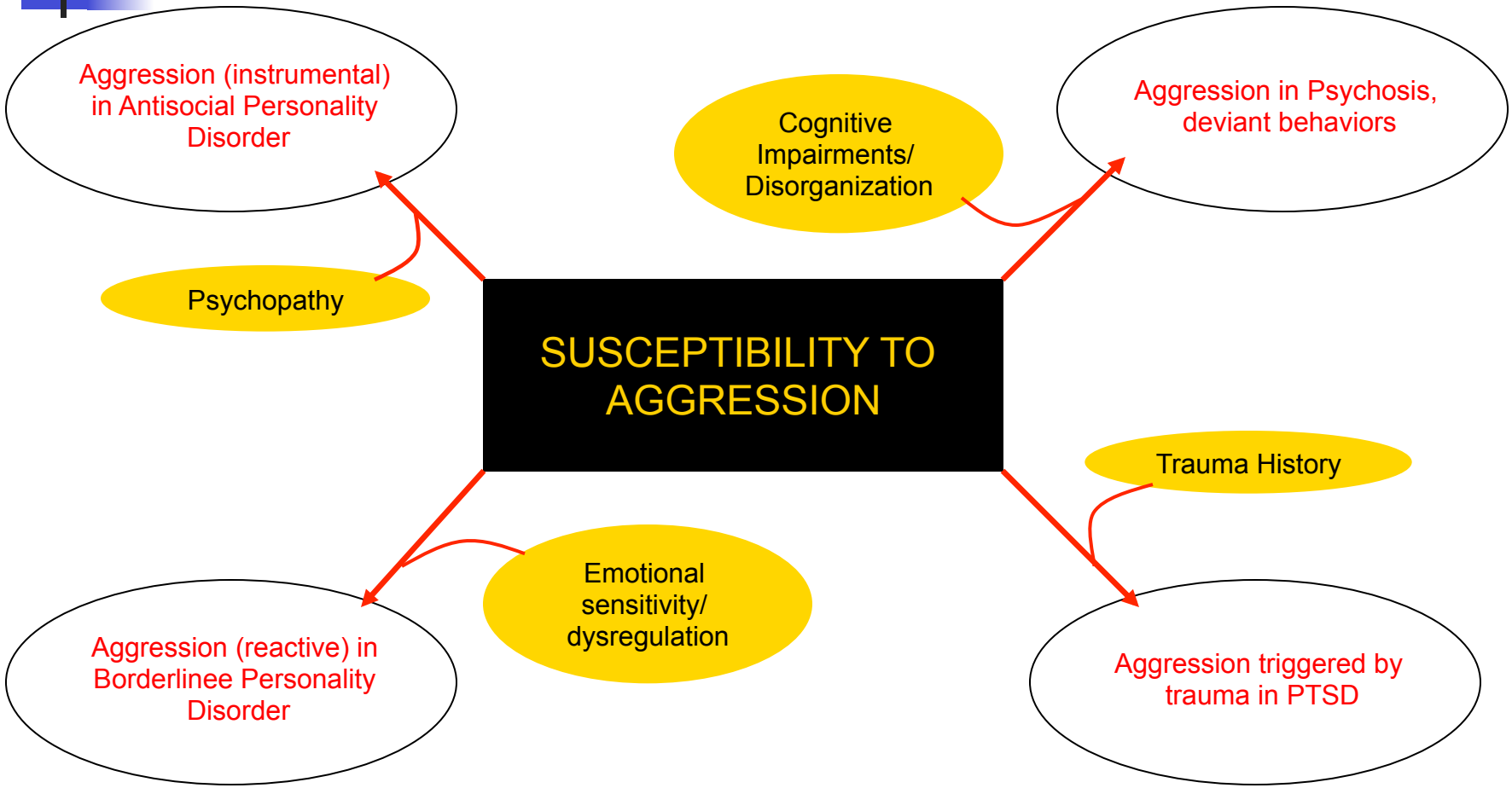
- **Anhedonia**
- **Co-morbid substance abuse**
- **Cognitive and Motor Skills Impairment[1]**
- **Sexuality[2]**
- **Risk Taking[3]**

*1. Zickler, P. NIDA Notes **17**(1): 1,6*
2. Angrist, B. and S. Gershon (1976)
3. Hurst, P.M, et al (1967)

Methamphetamine and Injury

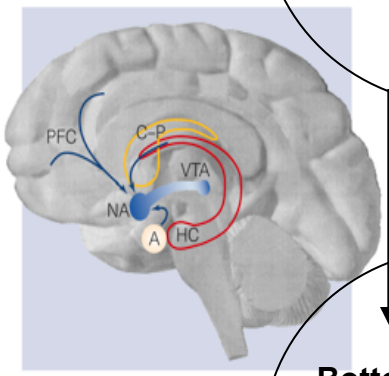
- **Motor Vehicle**
  - More common in withdrawal state
  - “Meth Rage”
  - Impairment similar to Alcohol
- **Manufacture**
  - Chemical Exposure
  - Explosions
- **Distribution**
  - Turf Wars
  - Regional Phenomena

Susceptibility to Aggression & Psychiatric Diagnosis



Adapted from Siever, L. (2008)

Initiation and Modulation of Aggression



Top Down "Brakes":
Suppression/regulation
(orbital frontal cortex,
anterior cingulate gyrus)
SLOW

Bottom-up "Drive":
Signal, trigger
(amygdala, insula)
FAST

Early Information Processing/cognitive appraisal

Sensory Processing

Stimulus/Challenge (Provocation)

Cultural/Social Factors
(Perception of Aggressor)

Sensory Disturbances
(**drugs, alcohol**,
metabolic disturbances)

Cognitive Impairment
(e.g. paranoid ideation,
conspiracy theories)

Developmental Stress/Trauma
(negative schema)

Sensory Deficits
(hearing, vision loss)

Methamphetamine and Violence

- **Relationship Controversial**
  - Drugs and Alcohol combination increases violence and crime risk[1]

- **Methamphetamine**
  - Association at population level often speculative and not well studied[2]
  - Violence itself is not pharmacological attribute of methamphetamine[3]

1. *Klee H, Morris J(1994)*
2. *Sheridan J, et al (2006)*
3. *Bialer PA(2002)*

Methamphetamine and Violence

- **Domestic/Intimate Partner[1, 2, 3]**
  - Greatest Association

- **Methamphetamine vs. Heroin[4]**
  - Meth - Thrill seeking
  - Heroin - Violence in Drug Seeking Behavior

1. Sheridan J, (2006)
2. Ernst, A. A., S. J. Weiss, et al. (2008)
3. Cohen, J. B., A. Dickow, et al. (2003)
4. Klee H, Morris J (1994)

Methamphetamine and Violence

- **Theories**
  - **Disinhibiting influence**
    - Cognitive Distortion
    - Perceptual Disturbance
  - **Differential Association**
  - **Integrative Model**
    - Individual
    - Situational

Methamphetamine

TREATMENT WORKS!

Methamphetamine Treatment – Relapse Prevention

- **MATRIX Model**
  - No significant differences in substance use and functioning between TAU and Matrix groups at discharge and at 6-month followup.
  - Had consistently better treatment retention rates than did TAU participants
  - 27% greater treatment completion
  - 31% greater to have meth-free urine test results while in treatment
  - At 6-month followup, > 65% of both Matrix and TAU participants had negative urine tests for methamphetamine and other drugs
  - (800) 729-6686 / www.ncadi.samhsa.gov
- **Contingency Management**
- **Limited Medication evidence**
  - Modafinil (Provigil)
  - Disulfiram (Antabuse)

Methamphetamine Treatment – Medications

- **Psychosis**
  - Atypical and Typical Neuroleptics
    - Acute
    - Chronic
- **Mood Disorder**
  - ?
  - Exercise

Clinical Assessment of Stimulant Effects

- **Spectrum of Symptoms**
- **Variability**
  - Tolerance
  - Dosage
- **Clinical History is Best Guide**
- **Toxicology not well correlated with psychosis**

Angrist, B. Schweitzer, et al. (1969)

Summary

- Stimulant induced states best evaluated by clinical interview, collateral, etc.
- Toxicology helpful but not definitive
- Controlled studies of Stimulants and Violence limited
- Individual hx and specific situation must be taken into account
- Pure MA states rare