

# Treatment of Methamphetamine Psychosis

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# Case 1

- 19 y.o. CM with no previous psych history started using Methamphetamine daily in binge patterns approx. 8 months prior to presentation.
- Used for 3 months, developed paranoia and AH symptoms, lost job as auto electrician.
- Abstinent for 5 months, but now with flattened affect, avolition, depressed mood, irritability, some residual suspiciousness. Unable to work, go to school, living at home with parents.

# Case 1 (cont'd)

- BIB by parents for psychiatric evaluation due to isolation, poor psychosocial functioning, residual psychotic symptoms.
- No family psych history. No previous exposure to psychotropic medications.
- What to do with this patient ?

# Case 2

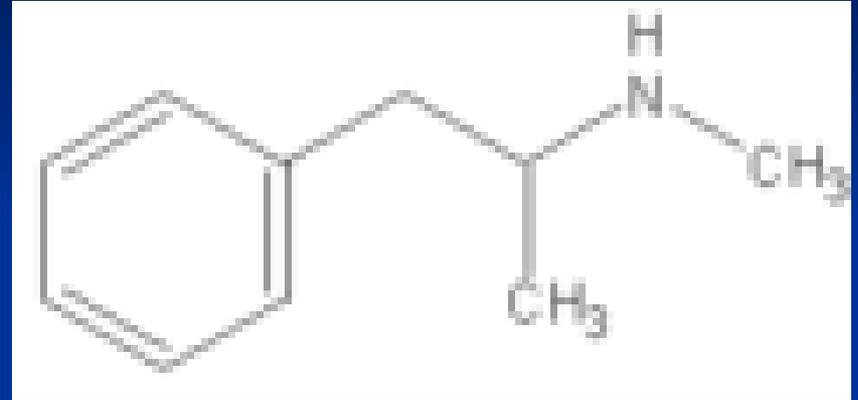
- 52 y.o. AM with a previous history of meth dependence, over 2 years of sobriety, relapsed 2 weeks prior on Meth.
- Developed bizarre behavior, obsessions with security, suspiciousness, paranoia, agitation with some SI, self-injurious behavior over 3 days.
- Admitted to locked psychiatric unit, treated with atypical antipsychotics for 2 days.
- Symptoms resolved completely by day 3-discharged to wife.

# Case 3

- 35 y.o. AAF with a history of alcohol abuse and meth psychosis BIB PD with agitated psychosis, delusional, paranoid, violent towards family, with auditory and visual hallucinations of “mice” after a several month long relapse on meth in binging pattern.
- Symptoms still present after 3 days in psychiatric ER despite IM haldol for emergent treatment and oral atypical antipsychotic use, with persistent delusions and agitation, along with HI.

# Methamphetamine

- Methamphetamine-  
synthetic **stimulant drug**
- Half life 8-14 hours.
- Increases release of DA  
and NE from synaptic  
vesicles.
- Inhibits MOA, increasing  
conc. of released DA, 5-  
HT, NE in synaptic  
clefts.



# Methamphetamine (cont'd)

- Increased DA signaling in NA and VTA projecting neurons leads to euphoria.
- Increased NE signaling from LC neurons leads to increased energy, heightened concentration.
- Acute effects include increased wakefulness, increased physical activity, decreased appetite, increased respiration, hyperthermia, and euphoria. Other CNS effects include irritability, insomnia, confusion, tremors, convulsions, anxiety, paranoia, and aggressiveness.

# Meth Toxicity in Animal Models

- In rodents, sustained high doses of Meth cause persistent DA depletion, nerve terminal degradation, and neuronal loss not seen with cocaine.
- Permanent DA nerve terminal depletion in primate caudate nuclei.
- Damage may be due to toxic DA oxidative metabolites and or glutaminergic overactivation toxicity.

# Meth Toxicity in Humans

- Chronic methamphetamine use resulted in 20-33% decrease in DA transporter binding in 11 former meth users compared to matched controls.
- Duration of Meth use correlated with decrease in DA transporter density and with BPRS psychosis measure.
- BPRS correlated with lower DA transporter density  
*Sekine et al Am J Psych 2001; 158: 1206-1214.*

# Meth Toxicity in Humans 2

- SPECT scans on 21 meth users in Hawaii.
- 16 of 21 had focal perfusion deficits in frontal, parietal, and temporal lobes. Such lesions are associated with violent and aggressive behavior.
- Similar results to previously published scans with cocaine and crack abusers.

Buffenstein et al *Am J Psych* 156 1999

# Meth Toxicity in Humans 3

- 14 Meth using patients with agitation and psychosis admitted to Psych ER showed strong correlation ( $p < 0.10$ ) between plasma or urine drug levels and agitation, positive symptoms of psychosis, thought disorganization, and general psychopathology.

Bakti and Harris *Am J Addict* 13 2004

# Meth Toxicity in Humans 4

- 12 abstinent Meth users studied compared to matched controls.
- Increased aggressive behavior in users vs. Controls
- Reduced Serotonin transporter density in users vs. Controls, correlated with duration of meth use.

Sekine et al *Arch Gen Psych* 63 2006

# Meth Psychosis Syndrome

- Hallucinations are frequently reported in chronic amphetamine users, with over 80% of users reporting the presence of hallucinatory experiences, typically as **visual** or **auditory** experiences. Delusions, paranoia, fears about persecution, hyperactivity and panic are also common.
- Early European and American studies indicated that most of these symptoms would spontaneously resolve within 1 week of abstinence, with a few remaining persistently psychotic which may have had comorbid Schizophrenia.

**Connell 1958; Delay et al Ann Med Psychol 1954.**

# Methamphetamine Psychosis (cont'd)

- However, usage in the US and Europe was fairly limited to medical purposes with little illegal use until recently.
- Japan had legal 100% ampules of Meth available OTC from the end of WWII until 1954, with over 500,000 chronic IV users at the peak of the epidemic. Meth became popular again in Japan in the 1980s and 1990s, being the most frequently abused illegal substance.
- Japanese literature has since the 1960s recognized a persistent psychotic syndrome in chronic meth addicts even after months to years of abstinence that is distinct from Schizophrenia.

# Meth in Japan

- A recent review of acute Meth psychosis studies from 1956, 1982, and 2003 showed that in acutely psychotic meth abusers 190 of 326 (58%) had resolution of their psychosis within 10 days of admission.
- However, 31% of these patients had psychotic syndromes persisting >1 month, with 28% (50 of 170) in 1 study having psychosis lasting >6 months.

Ujike and Sato *Ann NY Acad Sci* 1025:279-287 2004

# Meth Psychosis is not Schizophrenia

- Persistent Meth induced psychotic syndromes are characterized by avolition, anhedonia-asociality, and impaired attention, but with less impairment in reasoning and affective blunting than in Schizophrenia.

Tomiyawa Japan J Psychiatry Neuro (44)3 1990

- Meth induced psychotic states are also more likely to have VH and tactile hallucinations (formication) than in primary psychotic disorders.

Caton et al Arch Gen Psych 62 2005

# Meth Psychosis is not SCZ (cont'd)

- 21 Taiwanese inpatients with severe Meth-induced psychosis were followed for 6 months after discharge while maintaining sobriety.
- SADS scores for positive symptoms and GAS were significantly improved.
- SANS scores were modestly improved, but still somewhat higher than normal

Yeh et al *Zhonghua Yi Xue Za Zhi* 64 2001

# Meth in the West

- Epidemic of Meth use since late 1980s in CA, HI, other western states, now spreading to the midwest.
- The percentage of adult male arrestees testing methamphetamine-positive in 2003 was highest in Honolulu (40.3 percent), Phoenix (38.3) San Diego (36.2), and Los Angeles (28.7).

<http://www.nida.nih.gov/Infofacts/methamphetamine.html>

# Meth in the US

- In the first 6 months of 2004, nearly 59 percent of substance abuse treatment admissions (excluding alcohol) in Hawaii were for primary methamphetamine abuse. San Diego followed, with nearly 51 percent. Notable increases in methamphetamine treatment admissions occurred in Atlanta (10.6 percent in the first 6 months of 2004, as compared with 2.5 percent in 2001) and Minneapolis/St. Paul (18.7 percent in the first 6 months of 2004, as compared with 10.6 percent in 2001).

<http://www.nida.nih.gov/Infofacts/methamphetamine.html>

- Just a matter of time till we see Asian-style persisting Meth-induced Psychotic syndromes...

# Treatment for Acute Meth Psychosis

- No good studies. Frequent usage of typical antipsychotics in literature-textbooks (i.e. IM Haldol for emergent treatment).

Hillard J Clin Psychiatry 59 1998

- 19 patients seen in ER for cocaine or amphetamine-induced psychosis. Severity of psychosis correlated with length of hospitalization, total neuroleptic dose administered.

Harris and Batki Am J Addict 9 2000

# Treatment of Acute Meth Psychosis

## 2

- 202 acutely psychotic patients randomized to IV droperidol or lorazepam.
- 142 (72%) were found post hoc to be Meth+ on toxicology.
- Droperidol (typical antipsychotic) found to produce better and more rapid sedation than lorazepam (benzodiazepine hypnotic).

Richards et al J Emerg Med 16 1999

# Treatment of Persistent Meth Psychosis

- No good studies.
- 2 case reports from same group on treatment of chronic meth psychosis with Risperidone and Olanzapine, providing for resolution of psychotic symptoms after 4 months of treatment.

Misra et al J Clin Psychopharm 20 2000

Misra and Kofoed Am J Psychiatry 1997

# Treatment of Persistent Meth Psychosis 2

- 1 case report of residual Obsessional-Delusional symptomatology after >6 months sobriety resistant to typical antipsychotic treatment, but effectively treated by risperidone.
- May be due to 5-HT<sub>2</sub> effect of atypical antipsychotic- hypothesized to generalize to all atypical antipsychotics.

Iyo et al J Clin Psychiatry 60 1999

# Todd's Ideas

- Duration and amount of meth use loosely correlated with acute meth-induced psychosis. Likely around 50-80% of meth psychotic states with positive symptomatology will resolve within 2 weeks of treatment, given abstinence.
- However, many of the rest will likely continue to experience low-grade positive symptoms for at least months afterwards.
- Treat with low-dose atypical antipsychotics for 2 weeks after resolution of positive symptoms, then consider discontinuing.

# Todd's Ideas 2

- Many former Meth users will have a “meth abstinence syndrome” for months to years after a period of use, consisting of avolition, anhedonia, and social isolation, possibly related to meth-induced changes in brain function.

Newton et al *Am J Addict* 13 2004

London et al *Arch Gen Psychiatry* 61 2004

Newton et al *Clin Neurophysiol* 2003

# Todd's Ideas 3

- How to treat? Effect on ability to maintain abstinence?
- Atypical Antipsychotics- 5 HT 2- D2 pharmacology?
- SSRIs?
- DRIs, Amineptine, Wellbutrin?
- Modafinil, Atomoxetine, Nicotine agonists?

# Last (but not least) Thoughts

- Methylphenidate (ritalin!) post treatment: reverse the effects of Methamphetamine on vesicular DA depletion

Sandoval et al J Pharmacol Exp Ther 304 2003

- Ibogaine

Szumliński et al Pharmacol Biochem Beh 69 2001