

# A Case of Delirium in an Opiate Substitution Program

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# 1<sup>st</sup> presentation- 1/02

- 20 yo married WM presents with dysphoria, passive SI and anger problems
- "I've only told the doctors what I thought they wanted to hear; I told them what they wanted to know out of DSM. I have a copy."
- Recurrent episodes of several days of decreased need for sleep, increased GD activity, increased speech and rapid thoughts
- Past trials of sertraline, bupropion, divalproex and gabapentin

# 1<sup>st</sup> presentation- 1/02

- C/o chronic back pain
- Reports distant occasional heroin and cocaine use, heavy past MJ use, heavy ETOh use in active service
- H/o 6 adolescent hospitalizations and 2 in active duty for “depression”
- Accepted lithium trial and low dose risperidone

# 2<sup>nd</sup> presentation- 12/02

- Now reports heroin 2.5-4 gm/day 1993-current, except for active service
- In service, exposed to oxycontin for back injury, resorting to IV oxycodone within 3 weeks
- Regular methamphetamine use 1996-1998; episodic IV cocaine 1999-2000 and last 6 months
- Now reporting heavy ETOH (1/5 QD + 6 pack 16 oz beer) from 1999 until last 2 months

## 2<sup>nd</sup> presentation- 12/02-1/03

- Now 100% SC for depression, also claiming chronic PTSD
- Only lithium helps, but he had stopped it
- LBP 2/10 with heroin, 9/10 without
- Using 90mg QD illicit methadone, starts OST at 110mg, considering LAAM
- Considering restart of lithium

# 1<sup>st</sup> trip in OST- 4/03

- Staying clean with 120mg Qd methadone
- Decreases lithium 300mg Tid -> 300mg Qd
- Reports “seizures,” mainly at night
- Confusion, tremor, sometimes AH, dissociation or LOC
- Wakes up and finds dents in drywall in his apartment

# 1<sup>st</sup> trip in OST- 7/03

- Pt sees ARNP for 2 wks HA, N/V, myalgias, fatigue, dizziness, chills/sweats, plantar surface foot pain -> poor ambulation
- Drastically altered appearance, slow fixed ambulation, poor balance, pallor, latent and blunted
- While seated, RLE noted for akathisia, marked tremor, movement halting and stiff, c/o diplopia
- Cannot raise eyebrows, poor EOM, tongue fasciculation, poor asymmetric strength, clumsy and slow RAM
- Febrile, R/o NMS, referred to PEC

# PES evaluation

- Pts mother notes recent acute behavioral changes, red secretions in rest room, transient R sided weakness; pt reports coughing up dark red
- Initially calm, becomes acutely confused and paranoid, leaves PEC, noted to be ataxic
- Restrained, intermittently lucid, otherwise extremely agitated/combatative, A&O x1
- CPK 375, HCT 30, MCV 101.5, Li <0.1
- NG lavage: "traumatic bilious fluid"





Food Grade Nitrous Oxide Chargers

Photo by Erowid, © 2002 Erowid.org





ENTHEOMATION(C)

### Nitrous Cracker & Balloon

Photo by Entheomation, © 2002 Erowid.org





**Nitrous Oxide cartridge and cracker**  
Photo by Oranges and Stimpysurf, © 2002 Erowid.org



# Medicine Admission- 7/03

- Pt admits to using 10 boxes/day (40 “crackers”/box) for 2 wks PTA
- Reported N<sub>2</sub>O for LBP
- Treated with daily B-12 and thiamine
- Found to have MRSA bacteremia
- MS cleared but truncal and peripheral ataxia remained as well as autonomic neuropathy
- Pt left AMA HD #12

# Nitrous Oxide Abuse

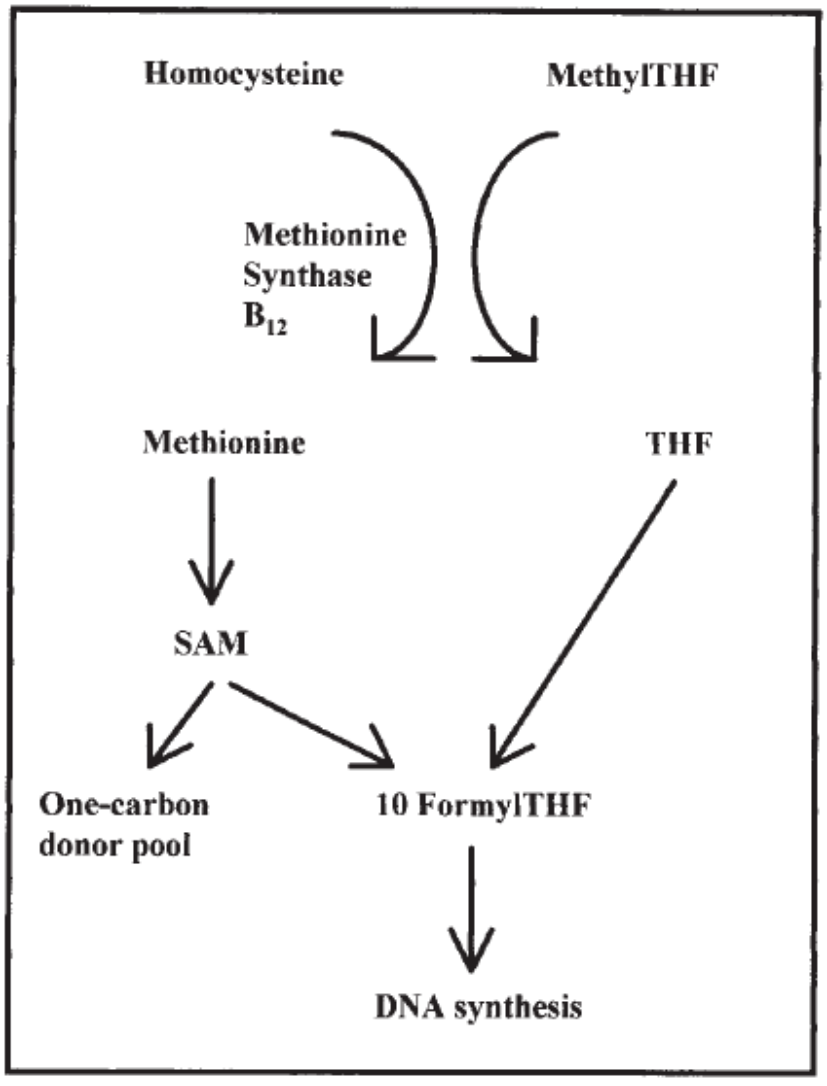
- 6% of 4<sup>th</sup> graders and 18% of 8<sup>th</sup> graders have tried inhalants
- Less common than glue, correction fluid & spray paint in youth
- Abused by nearly 10% of 18-25 year olds, and increasing
- Available in "crackers," "whip its," "charging bottles," tanks from medical or auto supply industry

# Nitrous Oxide Abuse

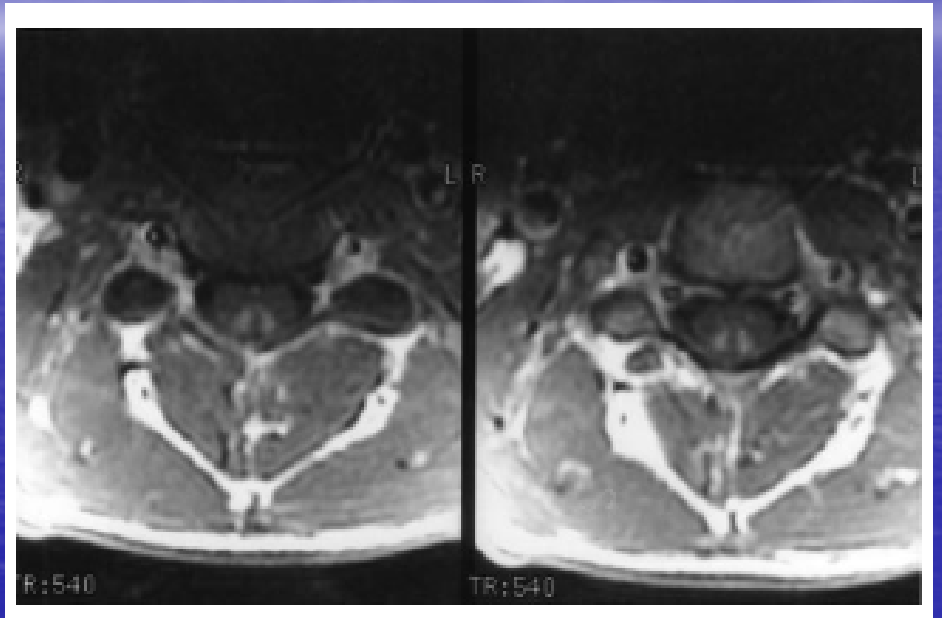
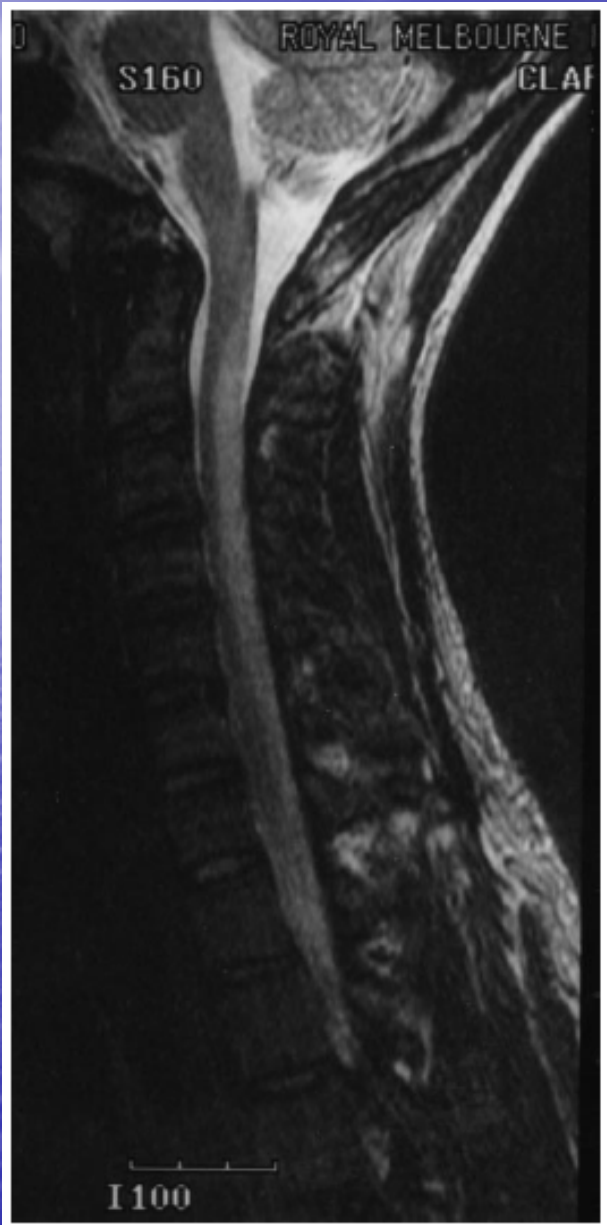
- Acute injury from syncope; death via asphyxiation
- Risk of frostbite or hypothermia
- Brief intense euphoria, lightheadedness, hallucinations, delusions
- HA, drowsiness, n/v, hypoxia
- Disorientation, sensorimotor polyneuropathy, dysarthria, ataxia, loss of vibration and proprioceptive sensation

# Nitrous Oxide Abuse

- Risk of longterm myeloneuropathy
- Degeneration of lateral and posterior columns
- Megaloblastic anemia due to inactivation of vitamin B-12 by  $N_2O$
- Indirect inactivation of methionine synthase -> impaired DNA synthesis (affecting myelination and hematopoiesis)
- Treat with B-12 supplementation and/or methionine replacement







# More of the same- 10/03

- Presents to PES with AMS, has spent \$30K on N<sub>2</sub>O in last 4-6 mo, apt littered with cannisters, non-ambulatory for past 10 days
- Transferred to 7E General Psychiatry, given haldol and risperidone for delirium, found unresponsive and opisthotonic
- W/u not consistent with NMS, serotonin syndrome or acute EPS, suggestive of toxic encephalopathy
- Prior to MRI, he admits to malingering

# Treatment nonadherence

- Medicine hospitalization 1/04 for continued N<sub>2</sub>O abuse
- Medicine hospitalization 2/04 for R DVT and LLL small PE x2; D/C home on warfarin
- Minimally adherent and INR often subtherapeutic
- Calls GIMC to request help “unpacking boxes, doing dishes, cleaning”; asks PCP to write letter to ATC advocating for fewer visits as “I am half-paralyzed.”

# Treatment nonadherence

- 11/04 UDAs frequently heroin and cocaine+, frequently registering outside prescriptions for opioids,
- 12/04 minimally present for daily OST dosing, unable to obtain OST from PEC, pt and family blame poor decision-making on lack of Rx for BPMD
- 12/04 D/C from ATC

# Treatment nonadherence

- Further hospitalizations:
  - 3/05 Psychiatric hospitalization but does not f/u with ATC
  - 10/05 medicine hospitalization for BLE cellulitis
  - 11/05 LUE abscess I&D; remains somnolent and cocaine+; syringe with illicit substance found in his mattress HD #6
  - 1/06 two medicine hospitalizations for cellulitis & purigo nodularis; found to have loculated sterile fluid collections 2' fibrotic changes LUE form IVDU
- Returns to OST 2/06, barely ambulatory, still needing to straight cath self PRN



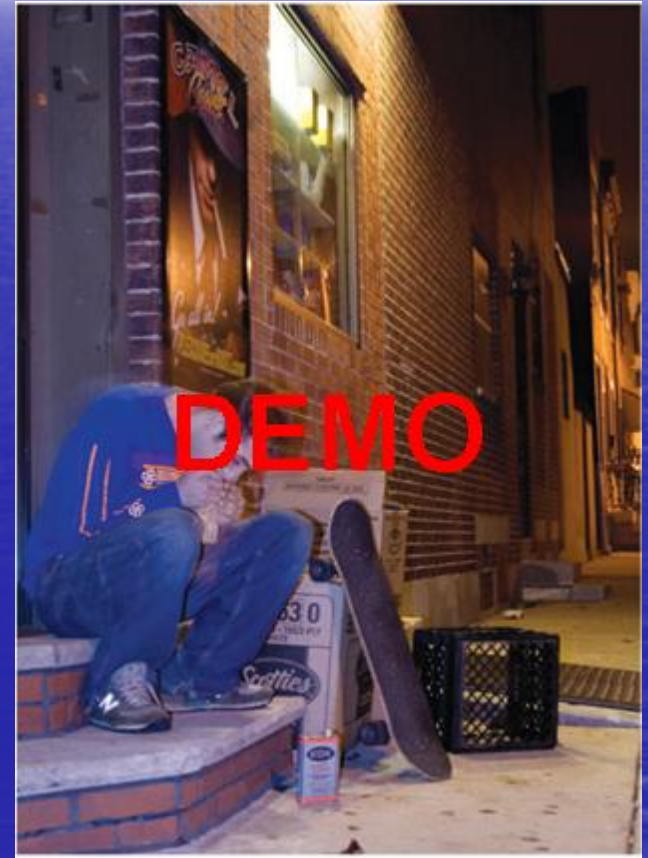
# Case #2

- 34 Yo Native American Male "Don"
- Admitted to HMC with SI in setting of ETOH abuse
- Denies use of other substances except "huffing"



# Clinical history

- Adopted and raised in LDS family
- Multiple hospitalizations at Ryther and PCN
- Very spiritual but little interest in Rx or 12 step programs
- Affect aloof, bizarre, juvenile, and at times apathetic





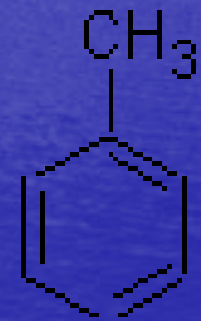
# Clinical history

- Poor judgement
- Threatened to leave AMA, then wavered
- Had been using brother as an alias, then administratively discharged
- In CTU the next day with acute encephalopathy and SI



# Toluene

- Lipophilic aromatic hydrocarbon that is major component of paint thinner, glue, spray paint, gasoline and varnish
- Industrial exposure includes dry cleaning, aviation and chemical industry
- Rapidly concentrates in CNS with high affinity for myelin



# Acute intoxication/encephalopathy

- Bizarre MS changes
- Euphoria, HA and ataxia are most common early Sx
- Reversible
- No known neuroradiological findings; MRI may lack sensitivity to find early changes

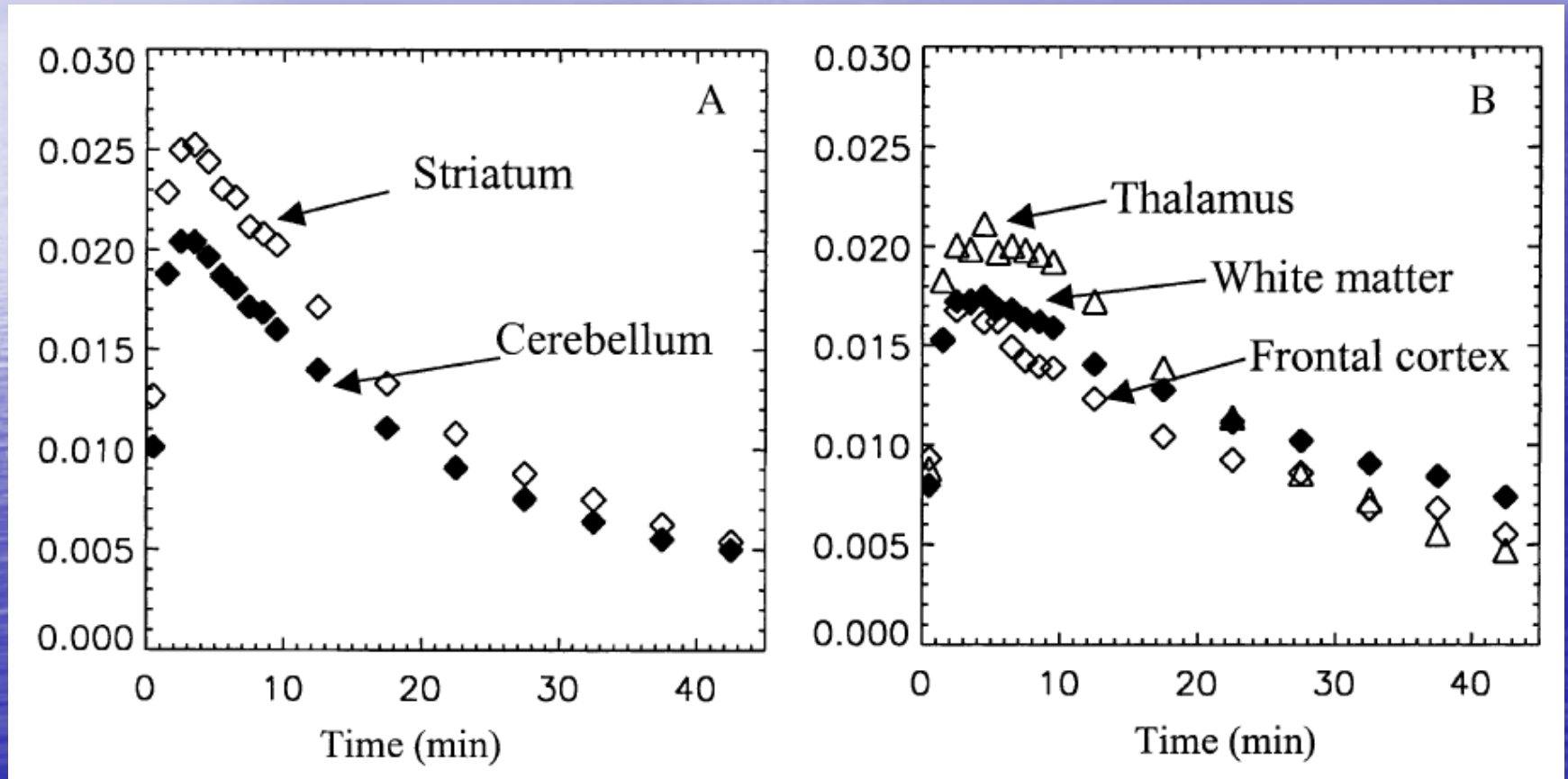


Sniffing an inhalant-soaked rag from a bag is a form of "huffing."

# Acute intoxication/encephalopathy

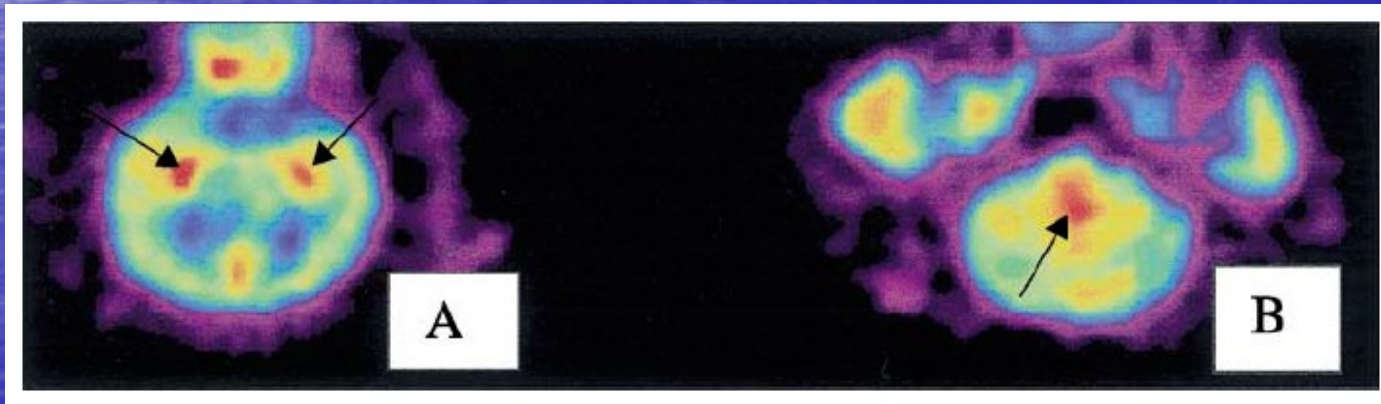
- Other Sx include drowsiness, dizziness, nystagmus, disorientation, and irritability/agitation
- Signs of abuse include red injected conjunctivae, paint stains on body and/or clothing, empty cans
- Cardiotoxicity with lethal dysrhythmia may be cause of “sudden sniffing syndrome”
- Obtundation can lead to suffocation, hypothermia secondary to exposure, or fatal MVA
- Supportive treatment; no direct therapy other than abstinence

# Imaging in acute encephalopathy



# Imaging in acute encephalopathy

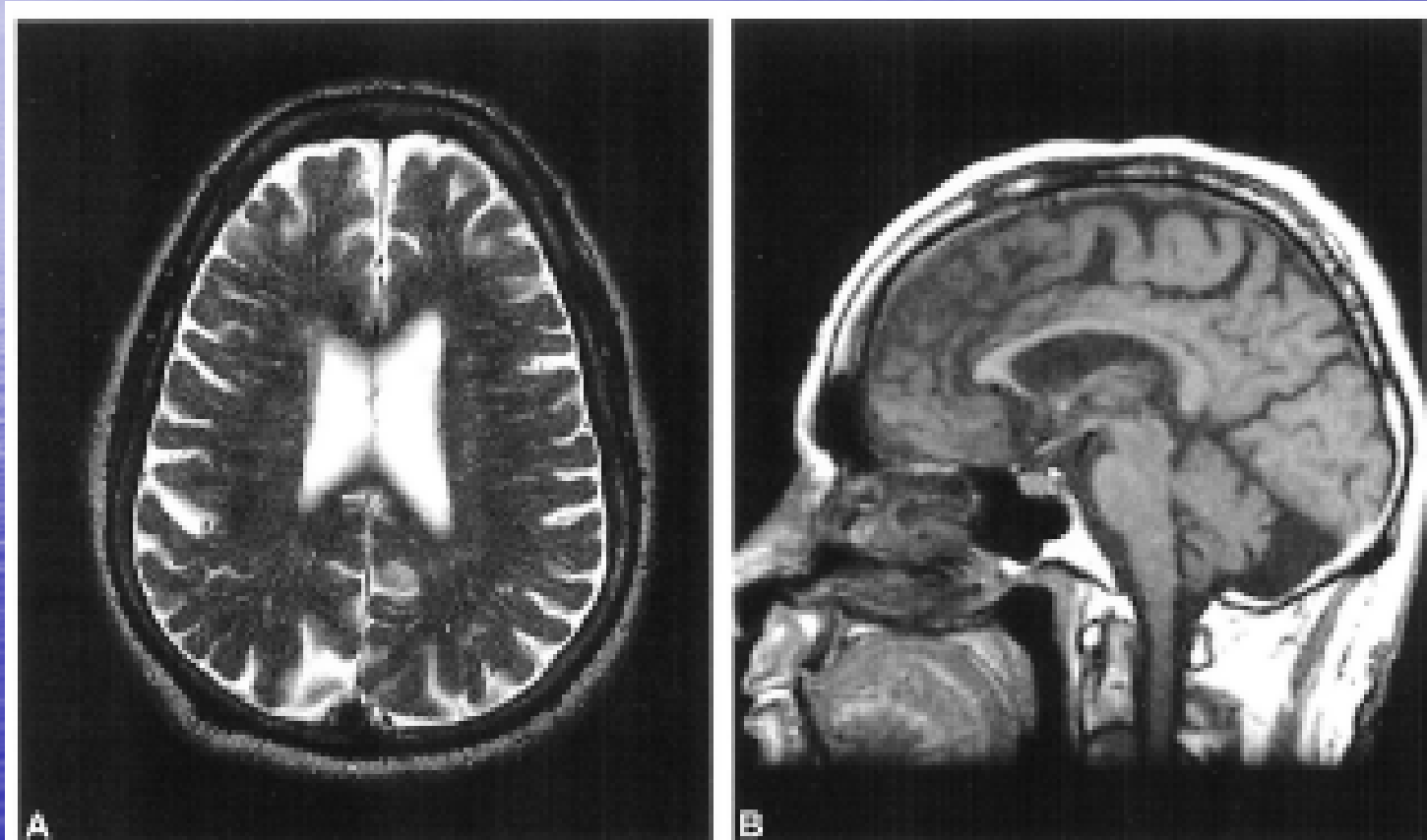
- Toluene is rapidly absorbed, rapidly enters CNS, has short half life, and is rapidly metabolized and cleared
- Rapid uptake and clearance into striatum, cerebellar and frontal cortex



# Chronic encephalopathy

- Imaging reveals irreversible demyelination with minimal gliosis to cerebellar and cerebral white matter
- Known as toluene leukoencephalopathy
- Predominant finding is CNS atrophy
- Marked loss of purkinje cells, also pontine, hippocampal and cerebral atrophy

# Chronic encephalopathy





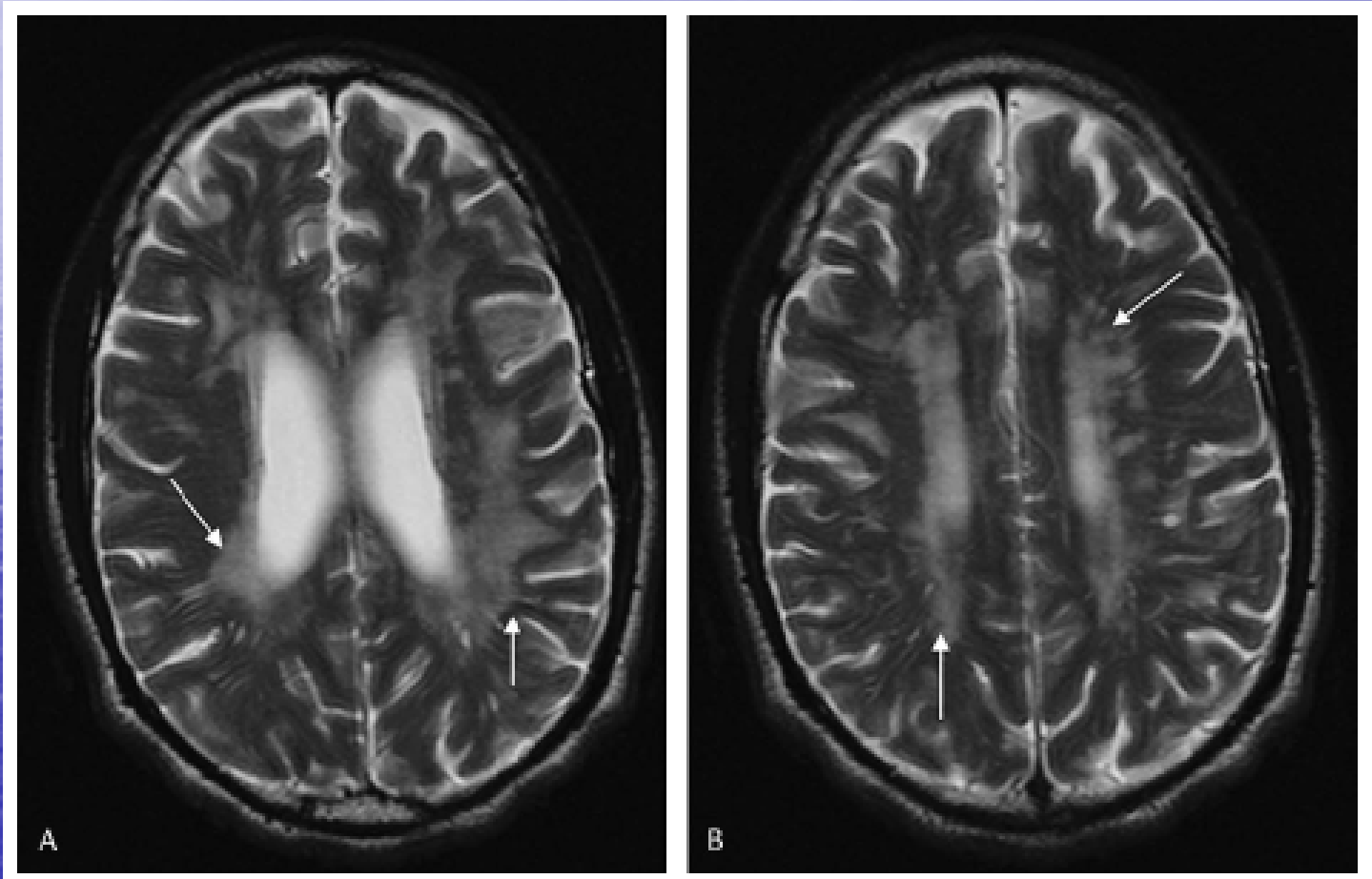
# Chronic encephalopathy



# Chronic encephalopathy

- Diffuse white matter abnormalities and loss of cortical-white matter interface
- Extent of white matter damage is both dose and duration dependent, and correlated with clinical severity
- Organic damage is symmetric

# Chronic encephalopathy



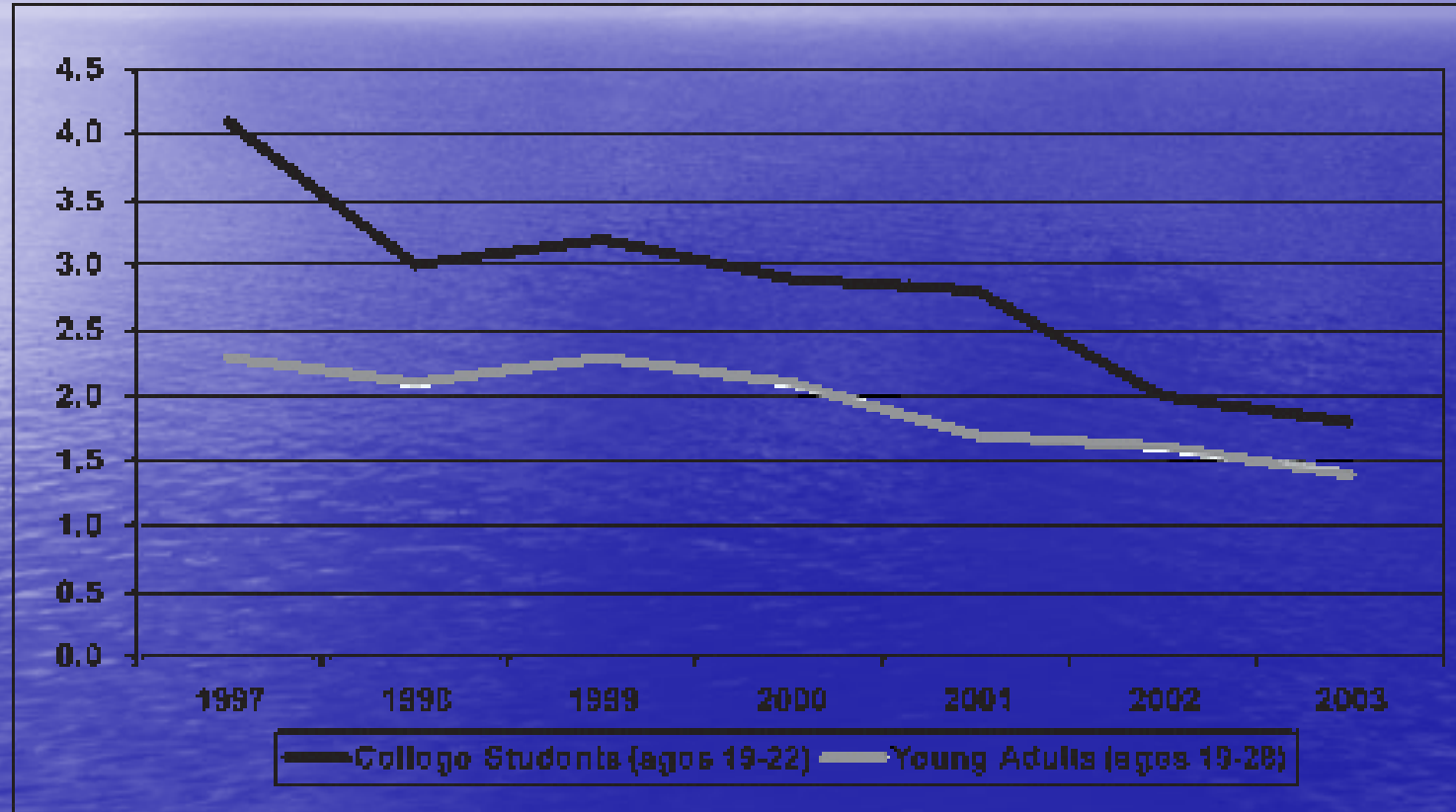
# Chronic encephalopathy

- Characteristic dementia of cerebral white matter:
  - Language, extrapyramidal function and procedural memory are preserved
  - WAIS-R IQ declines, verbal IQ does not
  - Impaired frontal lobe function, visuospatial skills and sustained attention
  - Pervasiveness in slowed information processing

# Who is using inhalants?

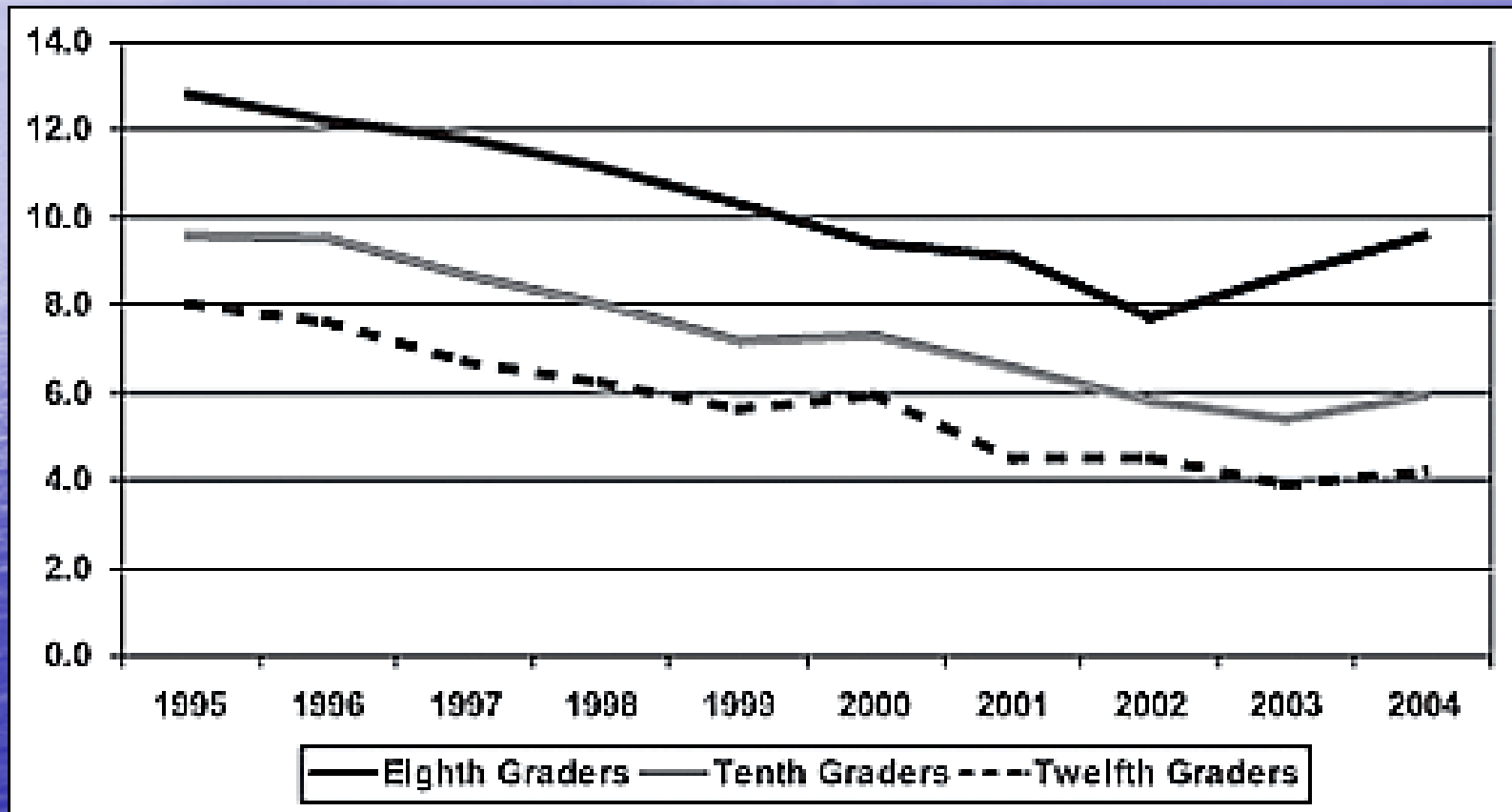
- Inhalants are volatile compounds of four types: aerosols, nitrites, solvents and other gases
- Easy availability, low cost and absence of withdrawal symptoms make for potent starter drug
- Highest rates of abuse in adolescents

# Who is using inhalants?



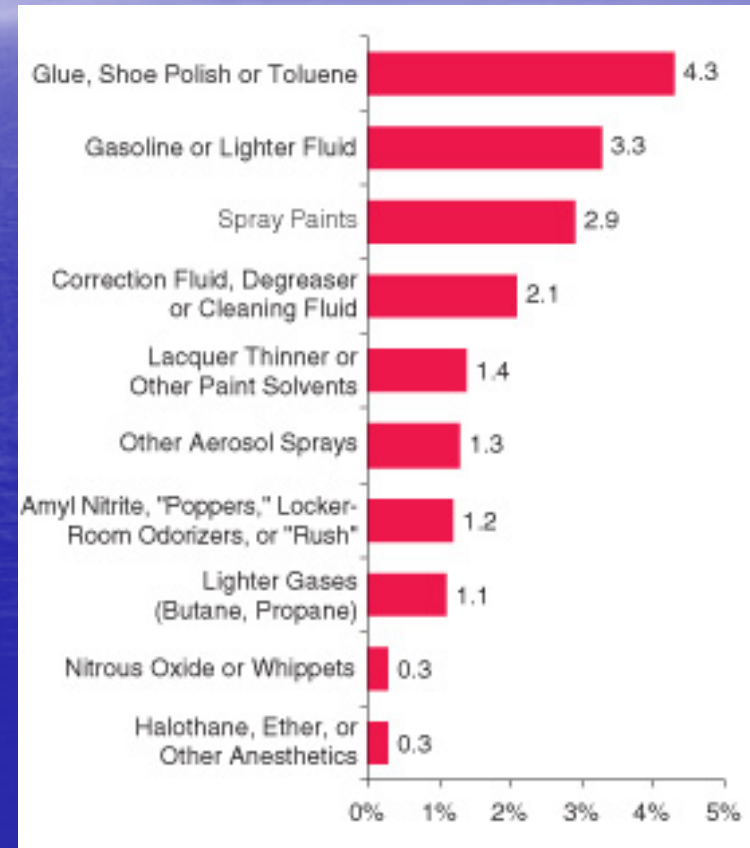
MTF survey

# Who is using inhalants?



MTF survey

# Who is using inhalants?



Percentages of Youths Aged 12 or 13 Reporting Lifetime Use of Inhalants, by Inhalant Type: NSDUH 2002 & 2003



# Who is using inhalants?

Drug or Method of Administration	Total	AGE GROUP (Years)		
		12-17	18-25	26 or Older
<b>Inhalants</b>	9.7	10.5	15.7	8.6
Amyl Nitrite, "Poppers," Locker Room Odorizers, or "Rush"	3.8	1.7	2.9	4.2
Correction Fluid, Degreaser, or Cleaning Fluid	1.0	2.2	1.7	0.7
Gasoline or Lighter Fluid	1.7	3.5	2.9	1.3
Glue, Shoe Polish, or Toluene	1.9	4.5	2.6	1.5
Halothane, Ether, or Other Anesthetics	0.5	0.4	0.8	0.4
Lacquer Thinner or Other Paint Solvents	0.9	1.7	1.6	0.6
Lighter Gases (Butane, Propane)	0.4	1.1	1.0	0.3
Nitrous Oxide or "Whippets"	5.0	2.1	10.7	4.4
Spray Paints	0.9	2.5	1.5	0.5

2002 NSDUH

# Who is using inhalants?

- 11% of recent adolescent users meet DSM criteria for dependence or abuse
- Adolescent inhalant use is a risk factor for criminality, conduct disorder and initiation of opioid use
- Adolescents most commonly use glue, shoe polish and gasoline
- 80% of adolescent users initiate by age 15

# Substance Dependence

- (1) tolerance, as defined by either of the following:
  - (a) a need for markedly increased amounts of the substance to achieve Intoxication or desired effect
  - (b) markedly diminished effect with continued use of the same amount of the substance
- (2) Withdrawal, as manifested by either of the following:
  - (a) the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for Withdrawal from the specific substances)
  - (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
- (3) the substance is often taken in larger amounts or over a longer period than was intended
- (4) there is a persistent desire or unsuccessful efforts to cut down or control substance use
- (5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
- (6) important social, occupational, or recreational activities are given up or reduced because of substance use
- (7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

# Substance Abuse

- (1) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
- (2) recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
- (3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
- (4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of Intoxication, physical fights)

# Who is using inhalants?

- Adult users are more likely to use only one substance (nitrous oxide or amyl nitrites)
- Adult users are much less likely to use weekly or more
- Only 22% initiate by age 15; 59% initiate in adulthood
- Adult users have much less connection to criminal behavior

# Who is using inhalants?

- Adult inhalant users who are most likely to meet criteria for inhalant abuse or dependence are:
  - Aged 25-39
  - Less educated
  - Often in psychiatric Rx for comorbidity
  - Higher rates of coexisting alcohol use disorders

# Summary

- Signs and Sx of acute inhalant abuse frequently include somnolence, confusion, euphoria, acute cerebellar intoxication, peripheral nerve effects, and agitation/irritability (similar to alcohol inebriation)
- Signs and Sx of chronic abuse include cognitive deficits (particularly toluene) or effects on PNS (particularly nitrous-based)
- Adult and adolescent users may be relatively separate populations