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Drug Toxicity

Recreational Drug Toxicity

It started about 25 years ago when my college-age son came into my study and asked “MDMA is like alcohol, isn’t it?”

I told him that I had read an article in *Science* that MDMA (“Ecstasy”) “screws-up rats’ brains” (see footnote below). I promised my son that I would get an answer to his question. I have been working on the problem recreational drug toxicity ever since. What has motivated me? Fear, frustration, and hope.

For a semi-popular summary of my findings, go to the PDF of this article in the May-June, 2006, issue of *American Scientist*: [Toxicity of Recreational Drugs](#).

For a more detailed story, scrounge around the references below.

COMPARISON OF ACUTE LETHALITY

My greatest imagined fear was that I would get a call from a hospital saying that my son was dead or irreparably mentally disabled by a drug overdose. Quite naively, I drove over to the UCLA Biomedical Library thinking that a couple hours there would yield the answer to my son’s direct and honest question. No luck. I was puzzled. Hadn’t anyone compared the acute lethality of MDMA and ethyl alcohol? Apparently not. Why? Many reasons.

Although death, as a criterion or dependent variable in an experiment, has the advantage of being a well-defined and indisputable end-state, it has many disadvantages (especially for the “participant”). For example, external conditions (e.g., ambient temperature) and prior health status of the decedents varies greatly and impacts toxic reactions and measurements. Post-mortem redistribution of the drug within a decedent’s body makes estimating of the quantity of administered drug somewhat problematic. Furthermore, the large majority of drug-related deaths involve more than one drug. Multiple drug use increases the risk of adverse reactions. There have been probably under 35 deaths from MDMA reported in English-language medical literature. Most all of the deaths from MDMA involved the use of multiple substances (usually alcohol).

Given the problems of getting “clean” results from deceased humans, researcher often resort to the use of experimental animals (usually rodents) in order to determine the median lethal dose (LD50) of a substance. However, this raises the issue of how to generalize the results from a mouse or rat to a human. There are also ethical issues of sacrificing experimental animals. If you examine any object or phenomenon long enough, it starts to get complex, fascinating, and sometimes downright weird. At any rate, after more than a decade of trying to compare the acute lethality of psychoactive substances, I came up with what I think are empirically defensible estimates.

So back to the original question: “Is MDMA like alcohol?” With respect to causing an acute lethal reaction, Yes. The therapeutic index or safety ratio of alcohol is about 10. That is, if an average non-addicted 70 kg (154 lb) person drinks 10 times as much alcohol (330 grams) within a 15 or 20 minute period as is needed to get a “buzz’ (33 grams—the amount roughly equivalent to two glasses of wine, shots of whiskey, or cans of beer), then there a substantial risk of death. Similarly, if an average person ingests 2 grams of MDMA which is about 16 times the normal recreational dose of 125 mg, then death might occur. More of the details can be found in my article in the journal *Addiction* [June 2004, 99:686-696]. The article summarizes the acute lethality of 20 different psychoactive substances. Click the link if you want to read the article: [Addiction](#). The estimated lethal doses assume that no other drugs are used. Furthermore, it is IMPORTANT to note that none of the doses should be used as a dosage guide because individuals vary greatly in terms of physical and psychological vulnerability.

Finally, drug users or potential drug users should be aware that the health risks from chronic or repeated use of a drug may be different from rare or occasional use. In terms of physiological toxicity per-hour-of-intoxication, smoked cocaine would probably compete with intravenous heroin as the most dangerous, followed by alcohol.

ADDICTION

What drugs have the greatest addiction potential? It depends, in part, on how you define "addiction." There are at least three ways to measure addiction or dependence potential. (1) One criterion is the "capture ratio." That is, of the people who try a drug, what proportion of them will experience situations in which they use the drug despite their sincere intention not to? By this measure, tobacco would probably be ranked near the top, followed by methamphetamine, then cocaine. (2) A different criterion would be the onset of withdrawal symptoms when the drug is not available. Alcohol, heroin and short-acting barbiturates (pentobarbital) get top billing by this standard. (3) Another way is to assess how strongly the person wants to repeat the drug experience as a result of euphoria, confidence, sensuality, novelty, and so forth. Cocaine, opiates, and amphetamines are probably the most addicting drugs by this standard. You might want to check out my estimates of addiction potential of 17 different drugs in a brief chapter, "Acute Toxicity of Drugs versus Regulatory Status," in Jefferson M. Fish (Editor), *Drugs and Society: U.S. Public Policy* (2006), or see my assessment here of four "club drugs" (GHB, ketamine, MDMA, and Rohypnol®) and alcohol in the *Journal of Psychoactive Drugs* (September, 2004; vol. 36:3, pp. 303-310) . [Psychoactive drugs](#).

BENEFITS

If drugs had no perceived benefits, they would simply be ignored. The perceptions may be erroneous or short-sighted, but nonetheless salient enough to induce all of the drug use and abuse that concerns us. Just as drug users tend to overlook possible costs (e.g., chronic illness, economic burden, loss of motivation), nonusers tend to ignore potential benefits. Take, for example the assertion by one government official [F. J. Vocci, Deputy Director, Medication Development Division, NIDA, to Richard Cowan as reprinted in NORML's Ongoing Briefing, Feb. 4, 1995, p.4] that "increased use of marijuana regardless of potency offers a multitude of negative consequences and no benefits." In behavioral economics, costs and benefits are always linked. In addition to mere entertainment or escape from boredom, there are benefits such as elimination of pain or induction of religious experience. For authoritative commentary on religious potential, see T. B. Roberts (Ed.), *Psychoactive Sacramentals: Essays on Entheogens and Religion* published in 2001 by the Council on Spiritual Practices, San Francisco. For a little rant of my own, see my paper, "Opportunity costs of drug prohibition," in *Addiction*, 1997, 92: 1179-1182. In summary, given only one life-time of consciousness, the inability (as a result of prohibition) of an individual to evaluate a safe range of drug-facilitated experiences is a loss of a valuable opportunity. The *New York Times*' opinion section, "Room for Debate," on December 19, 2011, asked the question "Should teenagers get high instead of drunk?" Neither is recommended, but on the basis of acute toxicity, marijuana is clearly the better choice. [New York Times](#)

MISADVENTURES

Some drug fatalities are a result of an overdose of a single drug, but most deaths or cases of serious toxicity involve two or more drugs, misidentification of the substance, or an unusual route of administration. Examples:

Intranasal LSD After a dinner party, eight people snorted a small amount of cocaine. This was followed by two "lines" (3x4x30mm) of white powder believed to be cocaine. It was, instead, pure LSD. Fortunately, LSD is among the least acutely toxic psychoactive substances, and all the individuals were discharged from the hospital within 48 hours. [J. C. Klock, U. Boerner, & C. E. Becker, "Coma, hyperthermia and bleeding associated with massive LSD overdose," *Western Journal of Medicine*, 1974, 120: 183-188.

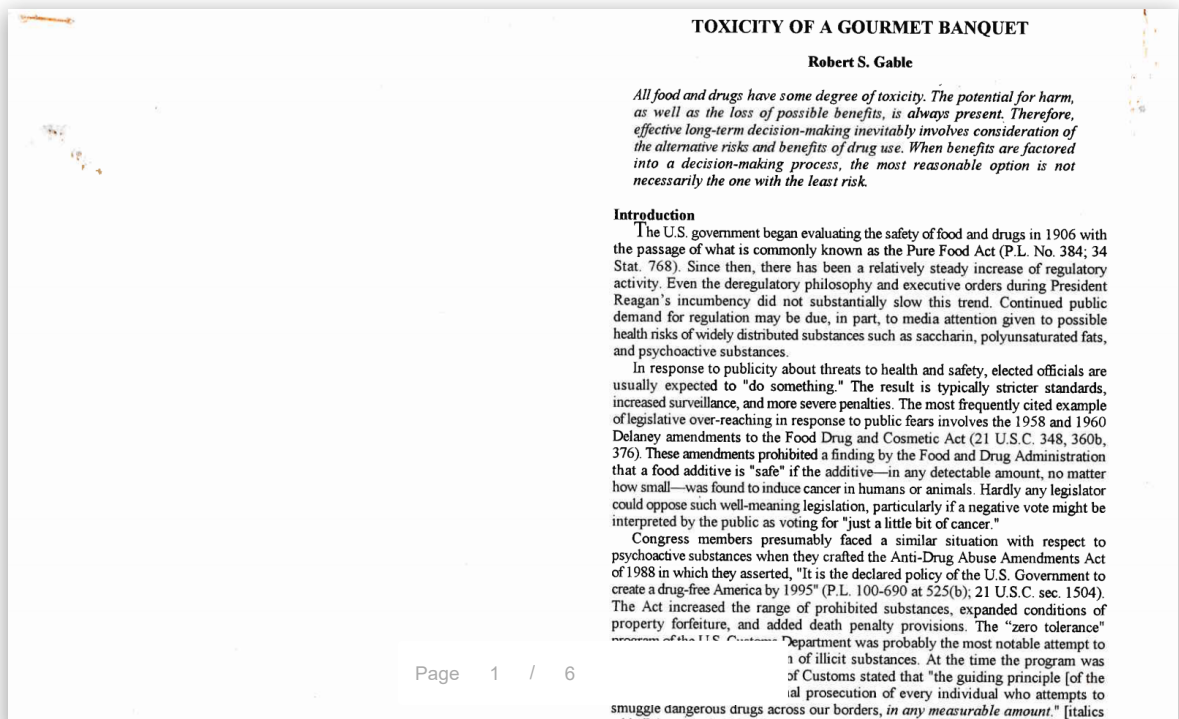
"Laughing Gas" fatalities Three men found dead in the sealed cab of a pickup truck with an empty 80-pound canister of nitrous oxide. [Michael Connelly, "3 found dead after inhaling laughing gas," *Los Angeles Times*, March 1, 1992, p. A1.] M.I.T. student found dead in dormitory as a result of nitrous oxide overdose caused by a plastic bag over his head. [R. Arnaout & D. E. Heimberger, "East campus reacts after student death," *The Tech*, Sept. 1, 1999: 1] Acute toxicity of nitrous oxide is generally minimal when normal air is available.

Intranasal Ritalin® A teenager died when, after drinking ale, he snorted a line of powder consisting of crushed methylphenidate tablets. [W. Massello, and D. A. Carpenter, "A fatality due to the intranasal abuse of methylphenidate," *Journal of Forensic Sciences*, 1999, 44: 220-221.

Smoking fentanyl Fentanyl is a synthetic narcotic analgesic about 30 times more potent than oral morphine. A fentanyl patch is used for continuous delivery of pain relief. A 36-year old male collapsed after just one inhalation of a heated fentanyl patch. [K. A. Marquardt, & R.S. Tharratt, "Inhalation abuse of fentanyl patch," *Journal of Toxicology: Clinical Toxicology*, 1994, 32: 75-78.]

Footnote: My summary, "screws-up rats' brains." was a little less precise than the findings actually reported in the 1985 *Science* article [Ricaurte, G.S., Bryan, G., Strauss, L., Seiden, L.S., Schuster, C.R., "Hallucinogenic amphetamine selectively destroys brain nerve terminals." *Science*, 229:986-988]. There have been many twists, turns, and squabbles in MDMA research in the subsequent decades. For a summary, read an account in the *Chronicle of Higher Education*, "Ecstasy Agonistes," February 27, 2004.

Below is a summary of presumed acute lethal toxicity based on data that I was able to locate. The higher the "Safety Ratio," the safer the drug would seem to be for the specific route of administration indicated for each substance. But note: the information in the table (based on a healthy 70kg/154 lb person) should not be used as a dosage guide because there are significant individual differences in drug reactions. Also be aware that the dosages assume that no other substance (including alcohol) is used.



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For examples of inaccurate regulatory management, see: Gable, R. S. (2006). *Acute toxicity of drugs versus regulatory status*. In J. M. Fish (Ed.), *Drugs and Society: U.S. Public Policy*, pp.149-162, Lanham, MD: Rowman & Littlefield Publishers.

Regarding the marijuana versus alcohol debate, here's the paper comparing acute toxicity: [Addiction journal](#). For a colorful, off-beat YouTube video ("Alcohol, Extacy, [misspelled] Cocaine: Which Drug is the Most Toxic?") summarizing the paper's data, produced by Daniel Keogh for the Australian government-sponsored "Saturday



Night Science" program, check out " [Professor Funk](#)".

