

Toxicology News

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Detection of Drug-Impaired Driving can be Difficult

By Sarah Kerrigan

In the United States, it is illegal to drive a motor vehicle under the influence of alcohol or drugs. Compared with alcohol-impaired driving, however, drug-impaired driving is under-reported, often unrecognized, and more difficult to prosecute.

According to the National Highway Traffic Safety Administration (NHTSA), drug-impaired driving is a common factor in serious traffic crashes. The U.S. Department of Transportation (DOT) reports that the full impact of drugs on traffic safety is still unknown. A successful prosecution requires careful coordination of legal, law enforcement, and scientific agencies. "Per se" laws make the prosecution of alcohol-impaired driving straightforward in most states, but the legal situation of drug impairment is inherently more complex. The toxicologist plays a pivotal role in criminal proceedings of this type, and the outcome of the case may depend on the opinion of the expert. To render an opinion of impairment in an individual, the toxicologist may require key information from law enforcement personnel, such as signs and symptoms of drug use, behavioral observations, and driving patterns.

Statistics

According to the 1996 National Household Survey on Drug Abuse conducted by the Department of Health and Human Services (DHHS), 9 million people drove after drug use. A 1995 study by the NHTSA and the DOT showed that drugs were used by 10–22% of drivers involved in crashes, often in combination with alcohol. In a 1990–91 NHTSA study of 1,882 fatally injured drivers in seven states, drugs other than alcohol were found in 17.8% of the cases. Studies of injured drivers taken for medical treatment have shown positive drug rates as high as

40%. Drug use among drivers arrested for motor vehicle offenses is reported to be between 15 and 50%. The highest rates occur among drivers arrested for impaired or reckless driving. These cases were determined not to be alcohol-related, based on low blood alcohol concentrations. Drug prevalence varies by region, but the most frequently reported drugs include cannabinoids, cocaine or cocaine metabolites, and therapeutic depressants.

Drug-impaired driving in young people

The incidence of drug-impaired driving might be even greater in young adults. As many as 22% of young people report drug use prior to driving. In one study funded by the DHHS, 23.5% of drivers under the age of 21 tested positive for drugs other than alcohol. The Ninth Annual PRIDE (Parents Resource Institute for Drug Education) Survey of 129,560 students in 26 states during the 1995–96 school year indicated that 20% of twelfth grade students smoked marijuana in a vehicle. Statistics from NHTSA and the Substance Abuse and Mental Health Services Administration show that driving after drug use is more common among younger drivers. Persons aged 16–20 were more than twice as likely to drive after using drugs (excluding alcohol) compared with those aged 21 or above.

Drugs and fatal crashes

The Fatality Analysis Reporting System posts data on all U.S. car crashes that involve a fatality on a public highway. The analysis of crash data includes alcohol-involved traffic fatalities, but no

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Drug-Impaired Driving

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state-by-state data is available for other drugs. In New Mexico, 449 fatally injured drivers were tested for drugs in 2000. A total of 19% tested positive for drugs other than alcohol. Most of them (12% of the total tested) were positive for drugs alone or in combination with alcohol at concentrations less than 0.08% in blood. Seven percent were positive for both alcohol (>0.08%) and drugs. Eight percent of the fatally injured drivers were positive for multiple drugs, excluding alcohol. The most frequently detected substances were cocaine or benzoylecgonine and cannabinoids, followed by benzodiazepines. Other therapeutics, including antidepressants, muscle relaxants, and non-benzodiazepine-type sedative hypnotics, were detected even more frequently than cannabinoids. This poses a problem for many laboratories because rapid screening tests are not available for many of these medications.

Drug-alcohol or poly-drug combinations compound the complexity of identifying drug-impaired driving. These issues, together with inter- and intra-individual differences, pose a significant challenge to the forensic expert. In the absence of other information, it can be difficult to confirm impairment based on toxicology results alone. Prosecution of a drug-impaired driver is greatly facilitated by the careful documentation of signs and symptoms characteristic of the drug. For this reason, the drug evaluation and classification (DEC) program is extremely useful.

Drug evaluation and classification

The DEC process is a systematic, standardized, post-arrest procedure used to determine whether or not an individual is impaired by one or more categories of drugs. Officers who have completed the DEC training are certified as drug-recognition experts (DREs). The twelve-step DRE evaluation includes observation of behavior, appearance, performance of psychophysical tests, eye movements under different lighting conditions, and measurement of vital signs.

Drug recognition evaluation was pioneered by the Los Angeles Police Department in the 1970s and 1980s. The program was formally validated in 1984 by a research study at Johns Hopkins University. The NHTSA sponsored a field validation study in 1985 that confirmed the value of the DRE opinion. To date, 5,000 officers in more than 30 states have been certified as DREs.

DREs base their opinions on the characteristic signs and symptoms shown in Table 1. In some

cases, not all of the indicators are present. This may be due to multiple drug use, tolerance or history of drug use, and inter-individual differences. As the number of characteristic signs observed by the DRE increases, the likelihood that he or she will correctly identify the class of drugs responsible for the impairment also increases. This information, together with the driving pattern or behavior, may be of tremendous importance to a toxicologist, who may be required to render an expert opinion.

Drug Effects

Many drugs, particularly those that affect the central nervous system (CNS), can impair driving and result in sensory, motor, attentional, or cognitive deficits. However, inter-individual differences combined with health and metabolic effects, tolerance, and multiple drug use make it extremely difficult to accurately predict the impairing effect of any given drug on a specific individual. From an interpretive standpoint, the toxicologist may rely on a combination of toxicology results, driving behavior, and signs or symptoms documented in the arrest report. Interpretation of the case as a whole, taking into consideration these factors, may allow the toxicologist to reach important conclusions regarding possible impairment. Some common effects of some of the most widely abused drug classes include:

- *Depressants*: Sedation, confusion, poor divided attention, slowed reaction times, memory effects, poor psychomotor skills, droopy eyelids, slurred speech, ataxia, disorientation, decreased pulse, decreased blood pressure.
- *Stimulants*: Hypervigilance, restlessness, excitability, anxiety, self-absorption, body tremors, agitation, paranoia, delusions, obsessive activity, rapid speech, hand-wringing, bruxism, dilated pupils, elevated pulse, elevated blood pressure.
- *Cannabinoids*: Relaxation, sedation, confusion, poor divided attention, slowed reaction times, memory effects, poor information processing, poor coordination, eyelid tremors, reddening of conjunctivae, disorientation, elevated pulse, elevated blood pressure.
- *Hallucinogens*: Dazed, body tremors, blending of the senses, difficulty in speech, poor coordination, poor perception of time/distance, nausea, perspiration, paranoia, disorientation, elevated pulse, elevated blood pressure.
- *PCP*: Difficulty with speech, blank stare, cyclic or repetitive behavior, agitation, perspiration, incomplete verbal response, confusion, repetitive speech, "moon walking."
- *Narcotic analgesics*: Euphoria, sedation ("on the nod"), confusion, mental clouding, stupor, slowed

Table 1. Drug recognition evaluation sign and symptom matrix

Sign or symptom	CNS depressants	CNS stimulants	PCP	Inhalants	Cannabis	Narcotic analgesics	Hallucinogens
Horizontal gaze nystagmus	Present	Absent	Present	Present	Absent	Absent	Absent
Vertical gaze nystagmus	Possibly present	Absent	Usually present	Possibly present	Absent	Absent	Absent
Lack of convergence	Present	Absent	Present	Present	Present	Absent	Absent
Pupil size	Normal range	Dilated	Normal range	Normal/dilated	Normal/dilated	Constricted	Dilated
Reaction to light	Slow	Slow	Normal	Slow	Normal	Slow/no reaction	Normal
Internal clock	Slow	Fast	Fast	Near normal	Distorted	Slow	Fast
Pulse	Below normal	Above normal	Above normal	Above normal	Above normal	Below normal	Above normal
Blood pressure	Below normal	Above normal	Above normal	Near normal	Above normal	Below normal	Above normal
Body temperature	Normal	Above normal	Above normal	Near normal	Normal	Below normal	Above normal

reaction times, poor coordination, constricted pupils, droopy eyelids, nausea, flaccid muscle tone, decreased pulse, decreased blood pressure.

- *Inhalants*: Chemical odor, nausea, slurred speech, disorientation, confusion, bloodshot or watery eyes, lack of muscle control, flushed face, non-communicativeness.

Safe driving involves a high demand for information processing and requires that the individual divide attention between several tasks and operations. Drugs, particularly those that affect the central nervous system, can impair the performance of several functions, including coordination, reaction time, judgment, tracking, attention, and perception.

These functions are necessary for steering, maintaining lane position, braking, acceleration, and manipulation of the vehicle. Cognitive deficits or poor judgment can impair decision-making, avoidance of potential hazards, and anticipation of the risk involved in certain maneuvers. Drug-induced ocular changes, such as pupil constriction or dilation, can affect vision, glare resistance, and adaptation to dark and light conditions.

Measuring impairment

To measure impairment, the toxicologist may rely on a combination of laboratory-based, simulator,

epidemiological, and on-the-road driving studies. For ethical and safety reasons, actual driving studies, in which individuals drive after controlled drug administration, are not widely conducted in the United States.

Laboratory-based measurements can be useful in determining the effect of a drug on the functions necessary for safe driving, for example, reaction time or tracking skills. However, these studies do not allow driving performance to be measured as a "system" of complex tasks performed simultaneously. Simulator studies allow more of a system approach, but are sometimes criticized because they are not "real" and are devoid of consequences.

Epidemiological studies can be extremely useful from a retrospective standpoint. For example, a 1993 study sponsored by the National Transportation Safety Board and the National Institute on Drug Abuse addressed the prevalence of drugs and alcohol among fatally injured truck drivers. They found that one or more drugs were detected in 67% of drivers. The most frequently detected drugs were cannabinoids (13%) and alcohol (13%), followed by cocaine or benzoylecgonine (8%) and methamphetamine or amphetamine (7%). Epidemiological reports can be valuable in terms of characteristic physiological, behavioral, and driving patterns associated with drug-impaired driving.

Drug detection

Most laboratories that test drug-impaired drivers use screening methods such as enzymeimmunoassay, radioimmunoassay, or fluorescence polarization immunoassay to detect drugs in blood or urine samples.

These tests are effective for common drugs of abuse, but may not identify drugs such as designer amphetamines or therapeutic agents. For example, in New Mexico, carisoprodol and meprobamate account for nearly 10% of positive drug findings in drivers apprehended for driving while intoxicated. These samples screen negative on immunoassays for common drugs of abuse. As a result, many cases require either comprehensive or targeted analyses using techniques such as gas chromatography/mass spectrometry.

In October 2000, the U.S. DOT published a report, *Field Test of On-Site Drug Detection Devices*, that evaluated the accuracy and feasibility of on-site drug tests by police officers. Although these devices provide only preliminary results for a limited number of drugs, the concept of a "roadside" drug test is appealing to many law enforcement personnel and DREs who would use them to corroborate field sobriety assessments.

Prevention

Given the scope of drug-impaired driving and the diversity of drugs involved, prevention is a complex problem nationwide. Persons who use illicit drugs and drive are influenced by different factors than those who use prescription or over-the-counter medications for management of chronic pain or seasonal allergies. Successful programs must address public information and education, legislative and enforcement issues, as well as interagency and community cooperation.

Case Studies

Driver #1: A 48-year-old female in a truck was observed weaving from side to side and striking the center divide on a city street. The driver spoke slowly with slurred speech. Her eyes were glossy; her pupils were constricted; and nystagmus was present. The subject failed field sobriety tests. She had trouble following directions and maintaining balance, and was unsteady on her feet. A breath test detected no alcohol.

Blood toxicology: phenobarbital, 8.8 mg/L; chlordiazepoxide, 1.0 mg/L; nordiazepam, 0.62 mg/L; morphine, 0.07 mg/L; codeine, less than 0.025 mg/L.

Driver #2: A 39-year-old male was apprehended for erratic driving. The subject failed the field sobriety tests. A breath test indicated no alcohol was present and a DRE performed an evaluation. The subject was jittery, and both eyelid and body tremors were observed. During the balance test with eyes closed, he stated that he could not close his eyes. He moved rapidly and held on to his pants for support. The subject talked to himself throughout the evaluation. His blood pressure was 158/78; his pulse was 110 bpm; and his body temperature was 100 °F. Muscle tone was rigid and bruxism was present. No nystagmus was present; pupils were 5.0 mm in room light and reacted slowly to light. The DRE opinion was CNS stimulants.

Blood toxicology: methamphetamine, 0.14 mg/L; amphetamine, 0.04 mg/L.

Driver #3: A 46-year-old male was asleep at the wheel at a busy intersection. Witnesses reported the suspect "bouncing" off curbs with his vehicle. Other drivers blocked in the impaired driver with their vehicles until a police officer arrived. The driver was aroused and appeared sleepy but cooperative. The subject failed field sobriety tests but no alcohol was detected. The driver was unsteady and had poor balance and coordination. Horizontal gaze nystagmus and lack of convergence were present. His eyes were bloodshot and watery; his pupils were 2.5 mm in room light and reacted slowly to light. His muscle tone was flaccid. His blood pressure was 120/65; his pulse was 42 bpm. The DRE opinion was narcotic analgesics and CNS depressants.

Blood toxicology: meprobamate, 62 mg/L; carisoprodol, 1.9 mg/L; codeine, 0.39 mg/L; acetaminophen, present.

Driver #4: A 21-year-old male was stopped for a traffic lane violation. The subject failed field sobriety tests. A breath test detected no alcohol. During a DRE evaluation, the officer noticed a strong chemical odor and a shiny substance on the driver's face and hands. The driver was "wide-eyed," slow to respond to questions, and had a "blank stare." He had difficulty standing and walking. The officer noted that the subject's eyes briefly converged, then "dropped to the bottom of the eye socket." The subject stated that he had "done two rags of carb cleaner." His blood pressure was 120/70, and his pulse was 60 bpm. His pupils were 4.0 mm with normal reaction to light. The DRE opinion was inhalants.

Blood toxicology: Methylene chloride, present; toluene, present; benzoylecgonine, 0.03 mg/L.

Driver #5: A 52-year-old female was stopped for erratic driving. She appeared lethargic and moved slowly. She failed the field sobriety tests, and a breath test indicated an alcohol level of 0.03%. Her eyes were droopy, and her speech was slow and thick. During the DRE evaluation she exhibited poor balance and coordination on the psychomotor tests. The subject appeared cooperative throughout the evaluation. Horizontal gaze nystagmus and lack of convergence were observed. Her eyes were bloodshot and watery. Her blood pressure was 150/90, and her pulse was 90 bpm. Her pupils were 5.0 mm in room light and had a normal reaction to light. The subject estimated 30 seconds as 10 seconds. The DRE opinion was CNS depressants.

Blood toxicology: Nordiazepam, 0.22 mg/L; diazepam, less than 0.05 mg/L; hydrocodone, 0.02 mg/L; meprobamate, 20.9 mg/L; carisoprodol, 1.8 mg/L; cannabinoids, present.

Driver #6: A 31-year-old male fled the scene of a crash. Upon apprehension, he was transported to the hospital for medical treatment. He was jittery and could not sit still. There was a burn on his lip and a white residue on his tongue. No nystagmus was present. His pupils were 6.5 mm in room light and had a normal reaction to light. His blood pressure was 150/90, and his pulse was 116 bpm.

Blood toxicology: Cocaine, 0.12 mg/L; ecgonine methyl ester, 0.14 mg/L; benzoylecgonine, greater than 1.0 mg/L.

Suggested Reading

1. Drug impaired driving. Campaign *Safe and Sober*, National Highway Traffic Safety Administration, 2000.
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3. Feasibility assessment of chemical testing for drug impairment. U.S. Department of Transportation, DOT HS 806 920, September 1985.
4. Field test of on-site drug detection devices. U.S. Department of Transportation, DOT HS 809 192, October 2000.
5. Identifying types of drug intoxication: laboratory evaluation of a subject examination procedure. U.S. Department of Transportation, DOT HS 806 753, May 1985.
6. The incidence of driving under the influence of drugs 1985: an update of the state of the knowledge. U.S. Department of Transportation, DOT HS 806 900, March 1985.
7. The incidence and role of drugs in fatally injured drivers. U.S. Department of Transportation, DOT HS 808 065, 1992.
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9. Marijuana and actual driving performance. U.S. Department of Transportation, DOT HS 808 078, 1993.
10. Monitoring the future: national results on adolescent drug use. National Institute on Drug Abuse, U.S. Department of Health and Human Services, 2000.
11. National survey of drug use and driving. National household survey on drug abuse. Substance Abuse and Mental Health Services Administration, 1996.
12. Use of controlled substances and highway safety: a report to Congress. U.S. Department of Transportation, DOT HS 807 261, March 1988.

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ELISA for Ketamine

A new enzyme-linked immunosorbent assay (ELISA) is available for detecting ketamine, a popular club drug that is also used as a "date rape" drug.

The kit is designed to screen for ketamine and the ketamine metabolite norketamine in less than 1.5 hours and can be adapted for manual or automated use. It is intended for forensic screening purposes and not for clinical diagnostic use.

The test joins a line of more than 70 forensic drug detection ELISA kits. The kits are qualitative, one-step, nonradioactive, screening tests.

For information, contact Neogen Corp.; 628 Winchester Road; Lexington, Kentucky 40505; (859) 254-1221; www.neogen.com.

SAMHSA Opens New Website

The Center for Substance Abuse Prevention of the Substance Abuse and Mental Health Services Administration has a new website at www.drugfreeworkplace.com.

The website is designed to provide "centralized access to information about drug-free workplaces and related topics."

It includes information such as the proceedings of the September 2001 Conference on Workplace Substance Abuse Prevention and the list of federally certified laboratories.

Labs Should Prepare Now for Chemical Terrorism Dangers

By Jimmie L. Valentine

The recent terrorist attacks in the United States have heightened concerns about future ones. While the recent attackers used aircraft and biological (anthrax) media, a future act might be perpetrated using a chemical agent. In fact, terrorist attacks in Japan in the mid-1990s provide a precedent.

The purpose of this article is to enhance the awareness of laboratory personnel as to the types of chemical weapons or agents that terrorists might use. Such information should aid in preparation in case the laboratory is called on to use its expertise in support of patient care.

Terrorism

There are basically three types of terrorist groups:

(1) Clandestine organizations. Such groups usually seek anonymity, and although they might have a goal, it is not often made known to the victims.

(2) State-supported terrorist groups. These groups have been at the center of the current "War On Terrorism" being waged by the United States. While the participation of the supporting state might be veiled and linkage may be difficult, resources and aid are apparent in what the group is able to accomplish.

(3) Groups with special agendas. Such groups have been seen sporadically in the United States and other countries. Often a pretense of religion is used by such groups, for example, the Branch Davidians and their standoff with the U.S. government in Waco, Texas. Although such groups make their agenda known, it is often so vague and non-mainstream as to be brushed aside by most citizens.

With terrorist attacks receiving so much attention in the news media, it is inevitable that some of the groups described above will attempt to further their agendas through violent, attention-getting acts carried out with potential vehicles of terrorism, that is, biological, chemical, nuclear, conventional (explosives, etc.), and unconventional (aircraft, etc.). This article discusses only chemical agents as vehicles of terrorism.

Chemical weapons

Chemical weapons have been used by various nations because they are relatively easy to deliver to an enemy force. For example, in World War I it was not uncommon for each side to open the valve of

large cylinders of gases, such as chlorine or phosgene, and simply permit the wind to carry the toxic cloud to the enemy's trenches. Obviously, a shift in wind direction might have an undesired effect, but this use does illustrate the simplistic manner in which a toxic chemical can be delivered.

After World War I, many nations, including the United States, searched for more effective ways to deliver potential chemical weapons and hence developed munitions versions of chemical weapons. Munitions such as artillery shells, rockets, and land mines containing various chemicals capable of incapacitating troops were developed. Thankfully, the use of such weapons has been limited, but some instances are known and are discussed below.

Table 1 gives some chemicals studied by the U.S. Army as potential chemical weapons and lists the type of incapacitation caused by each. This table illustrates the diversity of chemical types that a terrorist group could use.

Chemicals in hands of terrorists

Many of the chemicals shown in Table 1 can be produced by such a group, if three key elements are in place. First, the group needs to have access to common starting materials, solvents, and synthesis equipment. Second, those who will conduct the synthetic steps need some modicum of scientific training. And, third, the group needs some financial resources to accomplish the previous steps. However, even a group without access to the foregoing could steal hazardous industrial chemicals or stockpiled weapons. Such theft would be difficult in the United States, where the Army guards the chemical weapons stockpile carefully. However, other countries with weapon stockpiles may not have such safeguards.

Unfortunately, theft of hazardous industrial chemicals might be more feasible because many such products are transported in daily commerce. As arrests of people in the aftermath of September 11 revealed, some potential terrorists had obtained commercial driver's licenses permitting the transport of hazardous materials. Although their exact purpose for obtaining such licenses has not yet been released, a possible scenario would be to open a valve on a tank truck and release its toxic contents while driving through a heavily populated area. Or perhaps another scenario would be to spray the contents over a populated area from a crop-dusting aircraft.

An industrial chemical accident in Bhopal, India, in December 1984 illustrates the effects of a release of a toxic chemical into a densely populated area. After an explosion at a chemical plant released the toxic chemical methylisocyanate, approximately

Table 1. Chemical agents investigated as potential chemical warfare agents

Class of chemical agent	Chemical name	Other or code names
Cyanides	Hydrogen cyanide	AC
	Cyanogen chloride	CK
Nerve agents	Ethyl <i>N,N</i> -dimethyl-phosphoramidocyanidate	Tabun (GA)
	Isopropylmethylphos-phonofluoridate	Sarin (GB)
	1,2,2-Trimethylpropyl-methylphosphono-fluoridate	Soman (GD)
	Cyclohexylmethyl-phosphonofluoridate	GF
	<i>o</i> -Ethyl <i>S</i> -[2-(diisopropyl-amino)ethyl] methyl-phosphonothiolate	VX
Lung toxicants	Carbonic dichloride	Phosgene (CG)
	Trichloromethyl chloro-formate	Diphosgene (DP)
Vesicants	<i>Bis</i> -2-Chloroethyl sulfide	Sulfur mustard (HD)
	2-Chlorovinyl dichloroarsine	Lewisite (L)
Incapacitating agents	Lysergic acid diethylamide	LSD
	3-Quinuclidinyl benzilate	QNB (BZ)
Tear gases	2-Chloro-1-phenylethanone	CN
	2-Chlorobenzalmalono-nitrile	CS
Vomiting gas	10-Chloro-5,10-dihydro-phenarsazine	Adamsite (DM)

Adapted from: Textbook of military medicine. Part I. Warfare, weaponry, and the casualty, medical consequences of chemical and biological warfare (1997). Office of the Surgeon General, Department of the Army, United States, p.119.

8,000 people died and more than 30,000 suffered inhalation injuries.

Sarin attacks

The only known intentional releases of a toxic agent into the atmosphere by terrorists occurred in two Japanese cities when the Aum Shinrikyo cult released the nerve gas, sarin, in Matsumoto on June 27, 1994, and in Tokyo on March 20, 1995.

Sarin is an inhibitor or binder of cholinesterases, the endogenous enzymes that terminate nerve conduction by hydrolyzing acetylcholine in the synaptic junction. When a person is exposed to sarin, the inhibition of acetylcholinesterase leads to continual, unimpeded stimulation of the cholinergic nervous system. These dose-related effects include miosis (pupil constriction), salivation, rhinorrhea, secretions, bronchoconstrictions, generalized fasciculations, seizures, urination, and defecation. If the dose is sufficient and the person is not treated with the proper antidote(s), the copious secretions will prevent the exchange of oxygen in the lungs and result in death. Essentially the victims drown in their own secretions.

Antidotes to nerve gases include atropine, which blocks the receptor for acetylcholine; pralidoxime, which reverses the binding of the nerve gas to acetylcholinesterase; and diazepam, which prevents seizures.

Both the Matsumoto and Tokyo releases of sarin illustrate the following points as related to chemical terrorism: (1) a scientifically unsophisticated group

can prepare a toxic chemical for use in a terrorist attack; (2) atmospheric dissemination of a chemical in a toxic dose can be readily accomplished; (3) human toxicity can be profound; (4) recognition that an event has occurred is rapid but the agent used may be unknown initially; (5) the capacity of medical facilities can be overwhelmed; and (6) emergency and medical workers can be in danger of exposure by virtue of caring for victims.

In Matsumoto the sarin was released from the back of a panel truck by using a large fan to blow over two open containers. This rather crude delivery method emitted a plume of sarin sufficient to produce seven deaths, 53 hospitalizations, and 253 outpatient treatments. Retrospectively, it was determined that the release occurred at about 9 p.m. and almost immediately people in the vicinity began to have rhinorrhea. The first call for an ambulance came at 11:09 and by ten minutes after midnight the situation was recognized as a mass disaster. Symptoms observed were (number of victims): marked miosis (124); headache (60); malaise (32); low-grade fever (16); and extremity dysesthesia (16). Eight of the rescue workers had similar, but lesser symptoms, presumably from exposure to the clothing and perhaps breath of the victims. An unknown number of attending nurses complained of malaise and nausea and one physician reported miosis.

An interesting finding in the Matsumoto release of sarin was that two periods of peak exposure occurred. The first came immediately after the fan blew

a plume from the back of the truck. The second came eight hours later, when additional people sought medical care. This latter event was subsequently correlated with persons leaving their homes the next morning to begin their daily activities without knowing that a toxic substance had been released. This event, therefore, provides some evidence to suggest that in-place sheltering is preferable to evacuation if a toxic gas release occurs. Obviously, for a facility to be used as a shelter requires that some precautions be observed, such as taping window and door openings to prevent seepage of a gas into the dwelling.

In the Tokyo attack, cult members brought plastic bags containing sarin into the subway system. They opened the bags under various seats in the subway cars and the subsequent passive diffusion into the enclosed atmosphere of the subway created a major health crisis. Twelve persons died, 1,300 were hospitalized, and approximately 5,500 persons sought medical aid.

Retrospective examination of this event suggested three categories of victims. First, "mild cases," which constituted about 80% of the victims, were victims with eye symptoms that included miosis, eye pain, dim vision, and a decrease in visual acuity. Second, the "moderate cases" had the eye symptoms and in addition had systemic effects such as weakness, difficulty breathing, seizures, and/or fasciculations, but did not require mechanical ventilation. This group represented about 17% of the victims. Third, "severe cases" had these eye and systemic symptoms, and in addition required mechanical ventilation.

Endogenous defenses

The human body has some natural defense mechanisms to protect against toxic exposures. Figure 1 gives a model for airborne exposure. The three major sites of exposure following the airborne release of a toxic chemical are the skin, lungs, and

eyes. While oral exposure could conceivably occur from eating or drinking contaminated food, it is not considered a major route of exposure in this context.

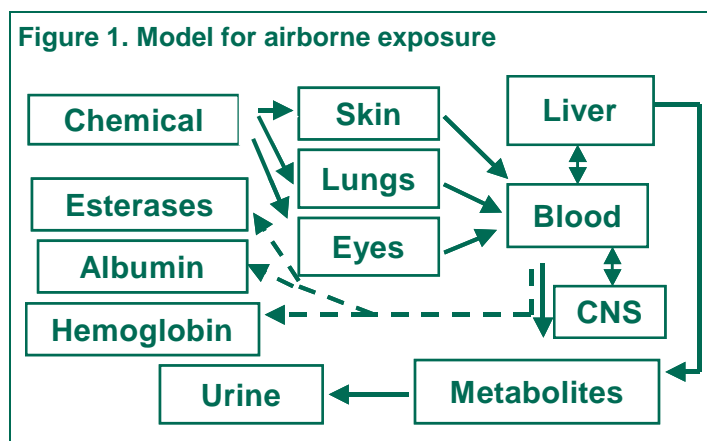
Regardless of the route of exposure, the toxicant undergoes "first-pass metabolism," which can be either pre- or post-systemic. For example, the skin and lungs (the eyes have not been studied as well) contain enzymes that can potentially metabolize the toxicant so that a metabolite is introduced into systemic circulation. If the toxicant is not metabolized in situ in these organs, it can be metabolized on its first pass through the liver, a major site of metabolism. Some liver transformation of the toxic chemical to a more polar and hopefully less toxic compound is to be expected. The portion of the toxicant that is metabolized may be excreted from the central compartment (blood) or it and the parent toxicant may be distributed into peripheral compartments like the central nervous system (CNS).

Entry into the CNS might permit the toxic chemical or metabolite to produce a rapid undesired health effect. Some blood constituents provide a mitigating effect that helps prevent CNS damage. For example, albumin and hemoglobin can bind the offending toxic chemical. Such binding effectively renders the toxicant into a pharmacologically inactive form, that is, it cannot readily traverse membrane barriers in the bound form. Either hypoalbuminemia or anemia in the exposed individual would greatly diminish the effectiveness of this barrier defense. Also, regular use of therapeutic drugs might greatly reduce the number of available binding sites.

The blood butyrylcholinesterases, often referred to as pseudocholinesterases, provide another defense mechanism. This group of enzymes can effectively hydrolyze many toxic compounds, with two factors influencing their ability to do so. First, genetic polymorphisms expressed in about 1 in 1,000 individuals can lead to a deficiency of these enzymes. Such individuals are susceptible to prolonged recovery from anesthetic agents. Second, previous exposure to environmental chemicals can lessen the enzymes' effectiveness. Organophosphate pesticides are metabolized by these enzymes and repeated exposure may diminish their turnover capabilities.

Monitoring for toxic chemical exposure

Laboratories are interested in what types of tests could be used to confirm that a person has been exposed to a toxic chemical. For the organophosphate pesticides and nerve gases discussed above, a rather simple clinical laboratory finding that can indicate exposure is depression of red blood cell (RBC) cholinesterase. This somewhat non-specific test suggests that a person has been exposed to an organo-



phosphate and the subsequent return to a normal range can be followed and correlated with some subjective measures like miosis. Following the Tokyo incident with sarin exposure, it was found that RBC cholinesterase was depressed in relation to the severity of symptoms. That is, those patients who required the most medical support had the largest and most prolonged depression of RBC cholinesterase. Similarly, prolonged miosis was observed in these individuals. Therefore, there is ample evidence to suggest that both miosis and depressed RBC cholinesterase can be correlated with high probability to an organophosphate exposure.

More objective laboratory tests could be used to confirm the exposure and identify the causative agent. For example, consider the metabolism of sarin (which has the military designation of GB) and VX shown in Figure 2. Both are ultimately metabolized to methylphosphonic acid (MPA), so analytical identification of this metabolite alone would indicate exposure to either sarin or VX, but not differentiate between the two agents. However, determination of isopropylmethylphosphonic acid (IMPA) or ethylmethylphosphonic acid (EMPA) would indicate exposure to sarin or VX, respectively.

Practical laboratory preparation

Obviously, hospital-based clinical laboratories are not equipped at present to perform all the tests required to ascertain what type of terrorist agent has been used. The Centers for Disease Control and Prevention (CDC) has been charged with developing and placing on-line the necessary testing methods to identify potential chemicals that terrorists might use. The CDC responds to requests from state health departments, not individual hospital laboratories. Therefore, it is extremely important that hospital laboratory personnel identify the appropriate state health department contact. Now is the time to talk to that individual and determine what telephone number should be called if the hospital suddenly receives patients believed to have been victims of a terrorist at-

tack. By pre-arranging the guidelines for response, the laboratory will be in position to aid the institution in caring for the victims.

Laboratory personnel have to become proactive in their work environment. In hospitals, laboratory personnel need to establish rapport with the emergency department director and staff. The emergency department will be port of entry into a hospital following a terrorist event. Most laboratory tests that will be needed are probably in place, things like blood gases, electrolytes, etc. But a decision needs to be made as to whether an RBC cholinesterase assay should be added, because most clinical laboratories do not have this test available. Pseudocholinesterase testing is not recommended because, as was pointed out above, genetic variants can lead to a false-positive exposure indication. Advance consultations with the emergency department medical staff will help each facility determine its individual needs.

Laboratory personnel can also meet with their institution's safety director and offer to help in planning for decontamination and response following arrival of terrorist victims. The terrorist attacks in Japan clearly show the need for advance planning, because hospitals there were overwhelmed with persons seeking medical aid, and health workers can become victims as well if appropriate exposure precautions are not taken.

Suggested Reading

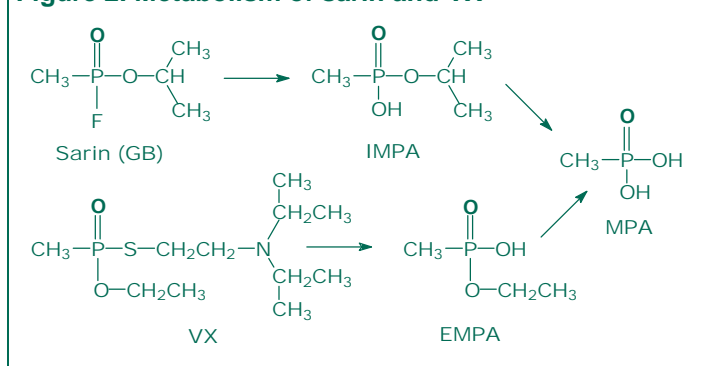
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Figure 2. Metabolism of sarin and VX



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New Toxicology Textbook

The Clinical Toxicology Laboratory: Contemporary Practice of Poisoning Evaluation was recently released by AACC Press.

Topics covered in the book include the epidemiology of poisoning and substance abuse; pharmacokinetic and toxicokinetic behavior of the most prevalent drugs of abuse, medications, and environmental poisons; clinical manifestations of poisons and approaches to diagnosis; critical appraisal of laboratory and point-of-care testing methods, sample types, and tests for sample adulteration; biological monitoring of chemical exposures; pharmacogenetic principles and toxicity risk assessment; and principles and applications of advanced analytical techniques.

Other topics include the dramatic advances in the care of the poisoned patient due to improved standards in emergency medicine, the advent of regional poison centers over the past 25 years, and

successful efforts of clinical toxicologists in adapting cost-effective technologies to support the changing diagnostic and treatment modalities.

Edited by Leslie M. Shaw, Tai C. Kwong, Thomas G. Rosano, Paul J. Orsulak, Bryan A. Wolf, and Barbarajean Magnani, the book includes contributions from an outstanding group of experts in laboratory medicine, emergency medicine, and toxicology; from poison control centers; and from academic, governmental, and private laboratories.

The 538-page softcover costs \$95 (\$76 for AACC members) and can be ordered from AACC customer service at (800) 892-1400 or (202) 857-0717 or online at www.aaccdirect.org.

DATIA Conference

The Drug and Alcohol Testing Industry Association holds its annual meeting May 2–5 in San Antonio, Texas.

For information, contact DATIA; 1600 Duke Street, Suite 220; Alexandria, Virginia 22314; (703) 548-0901; www.datia.org.

SOFT Meeting

The Society of Forensic Toxicologists will hold its annual meeting October 13–17 in Dearborn, Michigan.

Information is available at www.soft-tox.org.

The purpose of *Clinical & Forensic Toxicology News* is to provide practical and timely information on the clinical, forensic, technical, and regulatory issues faced by toxicology laboratories.

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