Effect of Drugs on Workplace Exposures

John Elias, MPH, CIH, ROH, CRSP. President, Elias Occupational Hygiene Consulting Inc.
Alison Reineke, BSc, CRSP. Occupational Hygiene Consultant, Environmental Health and Safety Office, University of Manitoba

Abstract

TLVs are guidelines not specification standards. As professionals we must apply them in the context of our workplaces. Among other things we must take into account age and health of workers when applying them. Related to these factors is prescribed medication and over-the-counter medication usage. Medications may contain workplace materials or result in the same metabolites. This may affect routes of entry for workplace chemicals or rates of metabolism. As a guideline or performance standard, the professional is expected to take into account effects such as those from medications. Failure to do so could result in increased susceptibility to workplace materials. Being aware of conditions such as the potential effect of drugs on workplace exposures will help the occupational hygienist to address atypical reactions in the workplace when exposure monitoring shows exposures to be acceptable. When used properly as guidelines TLVs are a tool to help the occupational hygienist to protect all workers.

Keywords TLV, exposure limit, pharmaceuticals, medications, drugs, adjusting exposure limits, interactions is between drugs and workplace materials

Introduction

Occupational hygienists utilize available information to anticipate and recognize unacceptable occupational exposures to chemical, physical, and biological agents.

Occupational exposure limits for acceptable airborne concentrations exist for a large number of chemical and physical agents. Among the best known and widely used occupational exposure guidelines are the threshold limit values (TLVs®) from the American Conference of Governmental Industrial Hygienists (ACGIH®). The TLVs are developed for chemical substances and physical agents. The TLV recommendations represent conditions under which it is believed nearly all workers may be repeatedly exposed, day after day, without adverse effect. TLVs are guidelines for occupational exposures that are intended to be used by individuals trained in the field of industrial hygiene.

Implicit in these values are certain assumptions regarding the conditions of the workplace and health status of the workforce, such as the age and health status of workers, exposure time, physical requirements and hazard mixture in the workplace. There is also the assumption that there are no other similar exposures. It is the job of the occupational hygienist to recognize when these standard conditions are not met, and to interpret the exposure limits in light of the current reality.

One of the conditions that the occupational hygienist must be aware of is the possibility that members of the workforce using drugs (prescribed and over-the-counter). Studies in the Netherlands (Borm and Barbanson, 1988) and United States (Rosenberg, 1994) have shown that 15 to 30% of workers take prescribed drugs. An additional 8% take nonprescribed drugs.

With our aging workforce (or individuals within the workforce) there is likelihood that there will be an increase in illnesses in the workplace due to the aging process (Pleis, Lucas, and Ward, 2009). As the workforce ages, the portion of the workforce that uses prescribed drugs will also increase. Table 1 shows some of the conditions that can affect an aging population.

Table 1: Health Conditions (2008) Shown as a Percent of the Age Group.

Disease	Percent by Age Range		
	18-44	45-64	65-74
Heart Disease (all types)	4.6	12.3	26.7
Cancer (any)	2.3	8.9	19.2
Diabetes	2.3	12.1	20.4
Kidney Disease	0.7	1.8	3.0
Arthritis Diagnosis	7.5	30.9	48.3
Hearing Trouble	6.9	18.4	27.8
Vision Trouble	7.2	13.8	14.3

Unfortunately there is more research studying the effect of other chemicals (workplace, environmental) on drugs than drugs on other chemicals. Although the most comprehensive compilation of interactions is between drugs, there are significant differences in the reporting of interactions between drugs even where there is a regulatory interest in recording such information. It has been found (Litt, 2003) that the reporting of interactions between dugs and workplace chemicals are even sketchier. The literature has some near anecdotal references to workplace exposures and pharmaceutical interaction which have to be checked with references such as the Compendium of Pharmaceuticals and Specialties to determine if such interactions are possible.

Adverse Effects of Drugs on Chemicals

The effect of drugs is similar to the effects of chemicals, conditions, or diet, on the rates of metabolism and toxicity. Illnesses or atypical health conditions can alter the effect that a workplace chemical may have on an individual. As a result of these conditions, a worker may be taking medications to ameliorate the conditions. These medications may bring additional complications to the workplace. It should be noted that, as one would expect, the drug will counteract the symptoms of the illness. An individual may not respond as expected to workplace exposures because of the underlying illness that caused drugs to be taken. Therefore, in assessing the total effect of an illness, not only the illness, but also the treatment must be considered.

Drugs can have many different effects with respect to workplace exposures. Some of these effects are due to the intended purpose of the drug, and in other cases is a side effect of the drug.

Often, the normal drug dose is above the no-observed-adverse-effect level (NOAEL) and undesirable effects can occur. If the drug contains a material that is used in the workplace, then normal drug dosages can result in worker exposure to materials above what would be considered acceptable in the workplace. These drugs will have an additive effect with occupational exposures. It has been noted (Alessio, Apostoli, and Crippa, 1995; American Conference of Governmental Industrial Hygienists, 2001) that where a drug metabolite is the same as that of a workplace chemical, a person taking the drug may show false high exposure where biological testing is based on the same metabolite.

Similarity to workplace chemicals

Taking medications can result in exposures to materials that are the same as those in the workplace (Table 2). This will have an additive effect where the chemicals are the same, or affect the same organ in a similar way. This will exaggerate the workplace exposure or result in false biological tests.

Table 2: Examples of Drugs With the Same Materials as Those Found in the Workplace.

Workplace Chemical	Drugs with the Same Material or Effect
Phenol	Antiseptics (phenol-camphor-petrolatum lotion) Throat lozenges Calamine lotions Antacids
Fluoride	Fluoride supplements Decongestants Tooth paste/mouthwash Fluorosteroids
Aluminum	Antacids
Bismuth	Bismuth subsalicylate
Arsenic	Homeopathic medicines
Mercury	Chinese patent medicine, Dental amalgams
Ethanol	Non-medical part of medicines (Benedryl)
Warfarin	Blood thinners (Coumadin)
Aniline	Aniline as a contaminant in pharmaceuticals (Tipranavir)
Cobalt	Cobalt-containing medication for anemia Implants made from cobalt-containing alloys
Organophosphate and acetylcholinesterase inhibiting-carbamate pesticides	Alkyl sulfates and sulfonates (neostigmine, physostimine, pyridostimine, pethidine, some immunosuppressants, and various cytostatic agents)

Effects of metabolites

Drug metabolites can be the same or similar to those of workplace chemicals (Table 3). Where the metabolite is the toxic material of concern the effects are additive with workplace chemicals. Where Biological Exposure Indices are used to estimate exposures the exposure will be overestimated.

In other cases, a drug can affect workplace chemicals by inhibiting their biotransformation (Table 4). This can be done by competition for existing enzymes, such as antabuse which competitively inhibits aldehyde dehydrogenase. Another way that biotransformation can be inhibited is when the drug destroys or inactivates an enzyme as with antineoplastic drugs. Where biotransformation is inhibited, biological testing may show false low exposures when the testing is based on the same metabolite.

Table 3: Examples of Drugs with the Same Metabolites as Workplace Chemicals.

Workplace Chemicals	**Drug with the Same Metabolite**
Analine	Phenacetin Acetanilide Phenazopyridine
Carbon disulphide	Antabuse
Benzene	Phenylsalicylate, Aspirin
Methemoglobin Inducers (Aniline, *m*-Nitroaniline, o-Chloroaniline, *p*-Nitroaniline [PNA], Dichloroaniline Nitrobenzene, Dimethylaniline, *o*-Nitrochlorobenzene, Dinitrobenzene [DNB]e	Medications (generally prescribed) (Nitrites, benzocaine, lidocane, nitroglycerin, prilocaine, silver nitrate (burn dressing), sulfoamides, dapsone, chloroquine)
p-Nitrochlorobenzene *p*-Dinitrosobenzene, Nitronaphthalene N-Isopropylaniline, Nitrotoluene *n*-Methyl aniline, *n*-Propyl nitrate)	Medications (generally over-the-counter) (Acetanilid, bismuth subnitrate, phenacetin)
PAHs	Ointments and shampoos, are used in some contexts for the treatment of psoriasis and dandruff

Table 4: Effects of Chemicals or Conditions in the Workplace on Rates of Metabolism and Toxicity.

Drug That Could Affect Workplace Chemicals	Workplace Chemical	Effect on Metabolism
Aspirin	Xylene	Reduced rate of metabolism
Ethanol	Carbon tetrachloride	Synergistic effect
Ethanol	2-Butoxyethanol, 2-Ethoxyethanol, 2-Methoxyethanol, Dimethylacetamide, Methyl Ethyl Ketone, N-Methyl-2-pyrrolidone, Styrene, Toluene, Trichloroethylene, and Xylene	Reduced rate of metabolism
Isopropanol	Carbon tetrachloride	Synergistic effect
Paracetamol	Toluene	Toluene in blood significantly increased
Cimetidine	Warfarin	Increased blood levels
Some antineoplastic drugs	Various	Inactivates liver enzymes and affects kidney function

Effects on Kidneys

Some drugs can result in impaired kidney function that will affect the kidneys' ability to clear toxic materials from the body. This is a partial list of drugs or drug classes that can have an adverse effect on the kidneys. If a material cannot be effectively removed from the body, its effective half life will be increased and the potential for harm increases.

List of drugs that can affect kidney function.

- Non-steroidal anti-inflammatory drugs (NSAIDS) (Motrin, indomethacin, Ibuprofen, Celebrex, Indocin
- Sulfa drugs
- Antiviral agents
- Ciprofloxacin
- Aminoglycosides
- Radiocontrast media
- Angiotensin - receptor blockers (losartan, telmisartan, candesartan, valsartan)
- Angiotensin - converting enzyme inhibitors (lisinopril, accupril, captopril, ramipril, enalopril)
- Diuretics (amiloride, diazide)

Effects on Liver

Some drugs alter blood flow through the liver either as a primary effect or as a side effect. Propanolol reduces cardiac output while cimetidine inhibits vasodilation; both reduce hepatic blood flow and thus rates of metabolism.

Other drugs may alter hepatic enzyme activity such as antineoplastic drugs or cimetidine which reduces hepatic enzyme activity and thus metabolic processes. For example this interaction may occur between cimetidine and warfarin.

Skin Absorption
Ointments, drug patches and cosmetics can alter dermal absorption of workplace chemicals by acting as a barrier and decrease the rate of absorption. Alternatively, the ointments may act as a reservoir and increase the total absorbed.

Drugs and cosmetics can be applied to the skin. Like drugs there are methods by which they have an effect:

- They remain on the surface – disinfectants, sun screens, insect repellents, decoration
- They penetrate into the skin – moisturizers, anti-wrinkle control
- They penetrate the skin layers – mostly for systemic drugs

Materials that penetrate the skin can act as carriers to help transfer other chemicals through the skin. Where an ointment, drug patch, or cosmetic incorporates materials that penetrate the skin, they can increase the penetration rate of workplace chemicals with skin notations, or can assist a chemical, that will not normally penetrate the skin, to do so. This could increase the effect of workplace materials or cause unanticipated exposures where skin absorption was not expected.

There are many such materials. Osborne and Henko (1997) identified 275 materials as skin penetration enhancers. The following is a list of groups of chemicals that are skin penetration enhancers.

List of groups of chemicals that can penetrate the skin.

- Sulphoxides
- Alcohols
- Polyols
- Alkanes
- Fatty acids, fatty alcohols
- Esters
- Amines and amides
- Terpenes
- Surface active agents

Effect of Drugs on Physical Agents

Just as various medications can affect how an individual will respond to chemical exposure in the workplace, they can also affect how an individual will respond to physical agents such as heat and noise.

Hearing Loss

Examples of drugs that have an ototoxic effect are shown in Table 5. If a worker uses any of these, there is a risk of hearing damage. In some cases, such as aspirin, the effect may be temporary. In most cases, the effect will only be noted when dosages are large. The effect of the drugs can be exaggerated when the individual has kidney or circulatory problems, or when there is previous hearing loss due to noise exposure.

Table 5: Examples of Drugs that may Affect Hearing Loss.

Class of Medication	Medication
Antibiotics	Gentamicin
	Kanamycin
	Neomycin
	Streptomycin
	Tobramycin
	Amikacin
	Erythromycin
	Chloroquin
	Quinine
	Vancomycin
Salicylates	Aspirin
Diuretics	Furosemide (Lasiz)
	Ethacrynic Acid
Antineoplastic Medications	Cisplatinum
	Bleomycin
	Nitrogen Mustard

Heat and Cold Stress

It is reported (Department of the Army and Air Force, 2005) that drugs can have an effect on the body's reaction to physical challenges as well as to chemical challenges in the workplace. Any worker with an illness or taking any medication that interferes with thermal regulation should be carefully monitored when working in cold environments.

Examples of conditions that affect heat production and loss include:

- Cardiovascular
- Peripheral vascular disease
- Endocrinological disorders
- Psychiatric disorders
- Earlier cold injury
- Muscular disorders
- Neural disorders

Examples of conditions that may cause decreased heat production include:

- Hypopituitarism
- Hypoadrenalism
- hypothyroidism

- Hypoglycemia
- Neuromuscular inefficiencies
- Stroke
- Severe arthritis
- Parkinson's disease
- Trauma
- Spinal cord injuries
- Burns
- Disorders that affect sensation in extremities (for example, nerve damage in the feet of people with diabetes)

The following drugs may cause heat intolerance by reducing the ability to sweat or increasing urine production. Workers in hot environments should consult their physician or pharmacist before taking medications (Table 6). The list below shows examples of such drugs, classes of drugs and the means by which they affect heat stress.

Because older individuals often have pre-existing diseases (atherosclerotic heart disease, diabetes mellitus, or alcoholism) and therefore may be receiving medication (phenothiazines, anticholinergics, sedatives, or diuretics) known to predispose the individual to the development of heat stroke; they are more susceptible to heat stroke.

A unique problem reported by Spaul et al. (1985) for outdoor workers is the protective creams or lotions used to prevent sunburn. Oil or alcohol based sunscreens appear to reduce the sweat evaporation rate but not the sweat production rate. This reduces the individual's tolerance to a heat stress environment, particularly at a moderate workload. Therefore workers using such lotions should have a more restricted workload than is currently recommended.

Table 8: Drugs that Affect Heat Tolerance.

Class of Drug	Drug	Mechanism
Anticholinergics	Atropine Scopolamine Pyridostigmine	Impaired sweating
Antihistamines	Diphenhydramine	Impaired sweating
Phenothiazines	Thorazine Stelazine Trilafon	Impaired sweating
Tricyclic Antidepressants	Antitriptyline	Impaired sweating Increased motor activity and heat production
Amphetamines, Cocaine	Ecstacy	Increased psychomotor activity
Ergogenic Stimulants	Ephedrine	Increased heat production

Class of Drug	Drug	Mechanism
Lithium		Nephrogenic diabetes, insipidus, and water loss
Diuretics		Salt depletion and dehydration
Beta-blockers	Propranolol Atenolol	Reduced skin blood flow, and reduced blood pressure
Ethanol		Diuresis
Sedatives		Affects thirst thresholds
Behavioral-modifying Drugs		Increased body temperature
Appetite Suppressants		Increased metabolic heat production and reduced heat distribution by affecting the peripheral circulation

Summary

The impact of most drugs on workplace exposures is unknown. In some cases the effect is known (aspirin on toluene), but the mechanism is unclear. Where it is suspected that a drug has an effect on the impact that a workplace chemical is having, the hygienist should consult with the worker's physician to determine if the drug and the workplace chemical use the same metabolic pathways, or could interact in some other fashion. Given the potential problems, it is surprising that the effects of drugs on workplace exposures have not been explored more fully. These are not rare occurrences. Jerome Z. Litt, M.D. has developed a list of 120 drugs that are known to cause photoallergenic, photosensitive, or phototoxic reactions. These can affect outdoor workers and contain such ingrediants as ibuprofen, saccharin, and streptomycin.

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