

# **TOXICOLOGY REPORTER**

## **TOXIC TORTS**

### **PAPE & ASSOCIATES**

*Specializing in Toxicology*

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## TOXIC TORTS: TOPICS

Risk Assessment

Carbon Monoxide

Lead Paint

VX Nerve Gas

Organophosphate Pesticides

Cosmetics - Adverse Reactions

Chemical Burns - Acids and Bases

Food Additives - Allergic Reactions

Acetaminophen (*Tylenol*)

Methyl Salicylate (*Oil of Wintergreen*)

Residential Pesticides (*Dursban*)

Adulterated Foods and Beverages

Estimating Airborne Chemical Exposure

Using the Internet

## Toxic Torts

### Risk Assessment ... Expert opinion based on an evaluation of chemical exposure:

*In the context of a typical civil case, risk assessment is the foundation and analysis leading to an opinion regarding whether or not an exposure to chemical(s) caused or substantially contributed to the plaintiff's injury, disease, or adverse condition.*

**Qualitative Risk Assessment:** Based on the qualitative nature and extent and duration of the chemical exposure(s) and the condition or disease (e.g. the type of cancer) and the clinical onset or diagnosis of that condition (e.g. the latency period for the cancer) ... when there are no reliable quantitative measures of the person's exposure to (e.g. TWA for airborne vapors) or absorption of (e.g. body fluid test results for) the suspect chemical(s).

**Quantitative Risk Assessment:** Based on qualitative and quantitative information allowing for an estimate of the magnitude of the chemical exposure(s) (e.g. ppm-years), comparison with regulatory requirements (e.g. TLV, STEL, etc.), and estimation of the increased risk of adverse effect (e.g. the increased risk of cancer).

### Carbon Monoxide (CO):

#### Absorption-Distribution-Elimination of CO

CO is readily absorbed through the lungs; it binds with hemoglobin in red blood cells; it is distributed throughout the body in proportion to the blood volume and heme-containing proteins; and CO is largely eliminated post-exposure as a result of a relatively slow process involving exchange with oxygen. Blood carboxy-hemoglobin (CO-Hgb) concentration is usually expressed as a percent saturation (i.e. the % of hemoglobin combined with CO).

#### Mechanism of CO Toxicity

Toxicity associated with a decrease in the availability of oxygen at the cellular level is due to a reduction in the oxygen-carrying capacity of red blood cells as a result of the formation of carboxy-hemoglobin (CO-Hgb), a decrease in the dissociation of the available oxygen carried by RBCs (due to a shift in the oxygen dissociation curve), and the binding of CO to other heme-containing proteins including the cytochrome system responsible for cellular respiration.



#### Signs and Symptoms of CO Intoxication

Organs with the highest metabolic rates (oxygen requirements) are the most sensitive. For example, heart and brain tissue. Other factors that relate to target-organ toxicity include rate of respiration, metabolic requirements (exercise), and anemia. As a general rule, CO-Hgb level and effects are related to the level of inspired CO, the degree of physical activity, the duration of exposure, and pre-existing cardiovascular or cerebrovascular disease.

Following CO poisoning, potential neurological effects include change in mental status, coma, decerebrate rigidity, decreased comprehension-coordination-spatial reasoning-visual acuity, and short-term memory loss. Later complications include ARDS, myocardial damage, renal insufficiency, and neurological abnormalities. Longer-term neuropsychological sequelae of CO intoxication include deafness, blindness, impairment of memory, mental retardation, Parkinson-type syndrome, and/or personality change.

#### Diagnosis of CO Poisoning

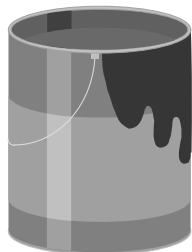
The diagnosis of CO poisoning includes history, physical examination, clinical laboratory testing, response to treatment, and psychometric testing. *Ref.: Comp. Rev. in Toxicology, PD Bryson (1996)*

## Lead Paint in a Home:

Expert review-consultation-report-and-testimony in a lead paint case usually includes the following:

Environmental surveys for lead

Evaluation of the methods used to test for lead or biochemical markers of lead exposure



Computerized biokinetic modeling of factors relating to the exposure-absorption-distribution-and-elimination of lead and comparison with measured blood lead levels

Construction and evaluation of time-lines and test results relating to locations (e.g. residences), sources of lead (i.e. potential exposures), blood lead (BPb) and erythrocyte protoporphyrin (EP) levels and BPb:EP ratios as indicators of the onset-duration-extent of exposure, medical treatments-effects, re-exposure to lead, the effects of lead, and confounding factors

Computer-based searches of the most current scientific literature, a *paper-chase* or search for expert publications or prior inconsistent statements, qualification of experts, trial exhibits, examination of experts, written report, and expert testimony

**A written report usually includes the following:**

**What were the sources, duration, and extent of the person's exposure(s) to lead?**

Factors include residential time-lines, residential and environmental sources of lead and the associated lead levels, as well as time-specific events such as lead abatement(s).

**What were the increases in the person's body burden of lead associated with these exposures?**

Factors include the absorption-distribution-elimination of lead ... allowing for computer-based biokinetic modeling of blood lead (BPb) levels.

**What were the physiological, biochemical, and behavioral indicators that are consistent with lead? How sensitive and selective are these indicators for lead compared to other conditions?**

In some cases, a toxicologist is also asked to report regarding the anticipated effects including neuropsychological effects; however, this would not eliminate the need for a medical expert and a neuropsychologist.

## Lead Paint Case Review: Special Topic

### Corrected BPb and BPb:EP Ratio

**BPb:EP ratio as a biological index to the duration of exposure to lead and/or re-exposure**

Because blood lead (BPb) and erythrocyte protoporphyrin (EP) levels are affected by a variety of metabolic and physiological factors, it may be useful to evaluate these data in non-traditional ways:

Plot a graph of the specimen collection date versus BPb levels that have been corrected for hemoglobin (Hgb) concentration; then,

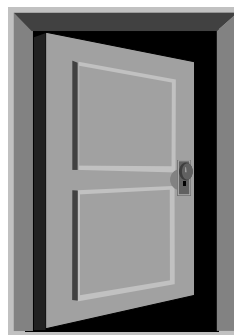
Divide the BPb concentration by the Hgb concentration. For example:

$$\begin{aligned} \text{BPb/Hgb} &= 45 \text{ mg/dl} / 15 \text{ gm/dl} \\ &= 3 \text{ mg Pb per gm of Hgb} \end{aligned}$$

Plot a graph of the specimen collection dates versus the EP or FEP levels that have been corrected for the specimen's Hgb level;

Plot graphs of the specimen collection dates versus BPb or corrected BPb and EP or FEP levels; and,

Overlay these graphs with information including dates of residence, lead abatement, chelation treatments, and Pb-related graphs for siblings.



*If you have general or case-specific questions, feel free to call Dr. Brian Pape.*

*Dr. Pape is a board-certified toxicologist with experience in a wide variety of toxic torts including lead paint, pesticides, carbon monoxide, chemical asthma, chemical burns, cosmetics, and solvent vapors.*

*His direct toll-free phone is (800) 736-0503.*

## Cosmetics - Adverse Reactions:

**A general approach to initial case review includes the following:**

- Review of the patient's medical records
- Comparison of the color, odor, and other physical characteristics of the suspect product with another lot of the same product
- FOI requests for FDA summaries of adverse drug experience reports and product recalls

- Computer-based literature search

*As a general rule, you should resist the initial urge to conduct costly chemical tests.*

*The first step is to gather discovery; then ...*

*Continue to consult with a toxicologist; and then ...*

*Consider your options including testing by FDA laboratories*

## Chemical Burns - Acids and Bases:

Initial evaluation should include a review of ...

**History:** Product-process-exposure  
Chemicals (e.g. MSDS)  
pH and total alkalinity/acidity  
Contact-inhalation-ingestion  
Time-course of adverse effects

**Acute Clinical Symptoms:**

- Ingestion
  - Dysphagia
  - Hypersalivation, drooling
  - Mucous production
  - ARDS, dyspnea
  - Pain (location and character)
  - Edema (location and character)
  - Hematemesis (bloody emesis)
- Inhalation
  - Dyspnea, cyanosis
  - Pulmonary edema
  - Hemoptysis
- Ocular contact
  - Conjunctivitis
  - Corneal abrasion
  - Pain, lacrimation
  - Photophobia

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**Dursban Insecticide continues to be the residential insecticide most often associated with claims of injury.**

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## Food Additives - Allergic Reaction:

### Sulfites

Some individuals experience severe adverse reactions. Ref.: Comp. Rev. in Toxicology, PD Bryson (1996). The first documented report of a reaction to sulfites was in 1796. Since then, sulfites have been reported to produce a wide spectrum of adverse effects.

## Toxic effects in sulfite-sensitive individuals:

<b>Minor</b>	Abdominal pain	Conjunctivitis
	Diarrhea	Dizziness
	Dysphagia	Flushing
	Nausea	Puritis
	Rhinitis	Swelling (tongue)
	Tachycardia	Tingling
	Urticaria	Weakness
<b>Major</b>	Anaphylaxis	Bronchospasm
	Seizures	Death

## Monosodium Glutamate (MSG):

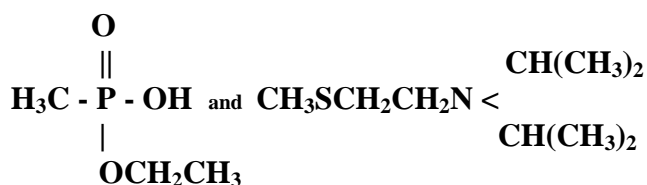
*While MSG is widely used as a food additive and it is on the FDA's GRAS (generally regarded as safe) list, a small percentage of the general public is extremely sensitive to MSG.*

There is a food label loophole: The FDA allows a food label to refer to MSG as hydrolyzed vegetable or plant protein, natural flavoring, flavoring, or seasoning. Ref.: *Comp. Rev. in Toxicology, PD Bryson (1996)*

## VX Nerve Gas ... A Cult Murder:

The Japanese Aum Shinrikyo sect who's homemade Sarin killed 13 people and sickened thousands of commuters in the Tokyo subway in 1995 had earlier killed one of its members with deadly nerve agent VX.

The 28 y.o. victim was attacked in December 1994 on the street in Osaka by two men who sprinkled the nerve agent on his neck. He chased them for about 100 yards before collapsing, dying 10 days later without coming out of a deep coma. VX degradation products were found in the victim:



Cult members also unsuccessfully tried to kill a lawyer who opposed them. They confessed to squirting a mixture of VX and hair oil into a keyhole, hoping the lawyer would touch the nerve agent on his contaminated key. Police later found VX degradation products in the keyhole. Ref.: *C&E News (08/31/98)*

*A brief summary of the toxicology of organophosphate pesticides follows.*

## Organophosphate Pesticides:

Clinical features of intoxication include . . .

### Muscarinic effects

- S** Salivation, sweating
- L** Lacrimation
- U** Urination
- G** Gastrointestinal upset
  
- B** Bowel movement
- A** Abdominal cramps
- M** Miosis

### Nicotinic effects

- M** Mydriasis, muscle twitching
- T** Tachycardia
- W** Weakness
- tH** Hypertension
- F** Fasciculations

### CNS effects

- R** Restlessness
- A** Apprehension
- G** Giddiness
- H** Headache
- A** Ataxia
- T** Tremors
- S** Seizures

**Diagnosis of intoxication** is usually based on chemical exposure, onset-nature-duration of symptoms, laboratory and physiologic testing, and response to treatment. *Ref.: Comp. Rev. in Toxicology, PD Bryson (1996)*

When the nature-severity-duration of acute post-exposure complaints are consistent with toxic effects, there still may be a lot of disagreement regarding residual physiological conditions (e.g. chemical asthma or reactive airways disease) or neurological disorders (e.g. neuropathies or neuropsychological deficits) or immunological conditions (e.g. chemical hypersensitivity or multiple chemical sensitivity).

## Acetaminophen (Tylenol):

While acetaminophen is widely used as an analgesic and antipyretic and is usually thought of as a very safe non-prescription drug, its overuse can result in death:

When the detoxification of an intermediate metabolite of acetaminophen is insufficient due to overuse of the drug or a drug-drug interaction or some physiologic/metabolic insufficiency, the result is liver damage ... potentially fatal liver damage.

There are four clinical phases associated with an acute acetaminophen overdose:

### The first 24-48 hours

- Anorexia
- Nausea
- Vomiting

### The next 24-48 hours

- Liver damage resulting in abnormal liver function tests

### The next 24 to 48 hours

- Clinical and laboratory evidence of hepatic necrosis

### The next 24 to 48 hours

- A resolution phase leading to recovery over time or deterioration leading to death

## Methyl Salicylate (Oil of Wintergreen):

Many over-the-counter products containing oil of wintergreen do not identify the active constituent as methyl salicylate. In fact, some products contain 100% methyl salicylate ... representing a higher salicylate content than pure aspirin.

Five milliliters (one-sixth ounce) of pure methyl salicylate is equivalent to about 21 325-milligram aspirin tablets. The less than cautious use of oil of wintergreen can be dangerous!



*It is important that an expert not attribute an adverse condition to an exposure simply because the condition was reported sometime after the exposure.*

*post hoc, ergo propter hoc*

*"... if condition B temporarily or permanently follows situation A, then A must have caused B." Ref.: JW Snyder (1998)*



## Airborne Chemical Exposure:

### Determination - Simulation - Estimation

**The determination of chemical exposure** is based on the on-site monitoring of airborne chemical concentrations or blood-breath-urine testing following chemical exposure. The disadvantage is that *today's* test result does not necessarily reflect *yesterday's* conditions.

**The simulation of chemical exposure** is based on mathematical modeling of chemical exposure based on product use, chemical volatility, and the distribution-dilution-loss of airborne chemicals due to diffusion and ventilation. Chemical concentration in room air or a subject's breathing zone can be estimated. Unfortunately, computer-assisted simulations are not readily available or adaptable to a case-specific analysis.

**The estimation of chemical exposure** based on hand-calculations is a relatively simple and cost-effective way to approach the initial review of some toxic tort or worker's compensation cases. In many cases, it is the only method that can be cost-justified. A relatively simple example of an estimate of chemical exposure follows.

### Estimation of exposure: An example

Case discovery produced the following:

Employee:	John Doe (JD)
Work schedule:	40 hours a week
Product:	Cleaning solvent
Composition:	n-hexane, 95% vol.
Use:	Cleaning print presses
Product volume:	4 quarts per week
Environment:	13 X 6.5 X 3.8 meters Two closed exit doors No ventilation/exhaust Overhead fans

### The estimation consisted on the following:

Calculation of total n-hexane used each day

$$\begin{aligned}\text{Amount} &= 4 \text{ qt} \times .95 / 5 \text{ days} \\ &= 27 \text{ ounces per day}\end{aligned}$$

Assumption regarding the fraction of the n-hexane that became airborne

$$90\% \text{ or } 24 \text{ ounces}$$

Calculation of the weight of airborne n-hexane

$$\begin{aligned}\text{Weight} &= 24 \text{ ounces} \times 29.6 \text{ milliliters} \\ &\text{per ounce} \times \text{specific gravity of } .85\end{aligned}$$

$$\begin{aligned}\text{Weight} &= 603 \text{ grams} \\ &= 603,000 \text{ milligrams (mg)}\end{aligned}$$

Calculation of the total workplace volume

$$13 \times 6.5 \times 3.8 \text{ m} = 321 \text{ m}^3$$

Calculation of the fully distributed (-fd) airborne concentration of n-hexane without accounting for JD's pattern of product use during the day or the dissipation of airborne n-hexane. This fd-level of n-hexane would be the maximum peak (*end of day*) concentration of airborne n-hexane.

$$\text{Concentration-fd} = 1,878 \text{ mg/m}^3$$

Assumption regarding the actual "end-of-day" n-hexane concentration in room air after accounting for loss due to ventilation or diffusion

$$\text{Assumption: } 50\% \text{ of } 1,878 \text{ mg/m}^3$$

$$\text{Equivalent to } 939 \text{ mg/m}^3$$

Assumption regarding the increase in the fd-concentration during a workday

Assumption: A steady increase

Assuming that all airborne n-hexane is lost overnight, the within-day average airborne concentration would be  $470 \text{ mg/m}^3$

Other important assumptions

The n-hexane concentration in JD's breathing zone was not significantly greater than the fd-concentration in room air. (*Note: This is unrealistic.*)

No significant dermal absorption

**Conclusion:** JD was exposed to increasing concentrations of airborne n-hexane during his workday. The average within-day exposure exceeded mandatory action levels.

A more complex analysis would include the estimation of n-hexane concentrations in his breathing zone. A toxicologist should also compare these and other findings with anticipated clinical effects, relevant case reports, epidemiological studies, and risk assessment models.

## Adulteration of Food or Beverage:

### Example SOPs for initial case review

It is not unusual for an attorney to call a toxicologist to discuss a case of suspect food poisoning or adulteration. Case examples and appropriate SOPs include the following:

#### (1) Biological material in a bottled beverage

##### Example: Animal material

Report the incident to the point of purchase and appropriate state and federal offices or agencies.

Document product information, incident, and injury by means of photographs, a diary, etc.

Document and preserve the physical evidence.

Discuss these issues with a forensic scientist.

Examine the biological material and record the relevant observations.

Consider requesting an analysis by state or federal laboratories.

Never relinquish all the material.

Follow-up with the forensic scientist.

#### (2) Chemical adulteration of a bottled beverage

##### Example: Noxious material

Discuss the incident with a forensic scientist.

Have the physical evidence available ... you will be asked to describe the odor and compare clarity with another bottle of the product. Some of the likely chemical adulterants include pesticides, cleaning products, and oils used in the bottling facility.

See (1)

#### (3) Food poisoning at a restaurant

##### Example: Salmonella

See (1)

In most cases, you will be asked to follow-up with a food scientist, infectious disease physician, or expert in food sanitation/preparation. It is important that you give this case your prompt attention.

#### (4) Biological material in canned food

##### Example: Animal hide

See (1)

A description of the appearance and condition of animal tissue is a very important part of your initial discussion with a forensic scientist. This is even more important in cases involving bottled beverages.

#### (5) Non-biological material in canned food

##### Example: Broken glass

See (2)

One approach to case analysis would be to use emission spectroscopy to obtain a trace-element fingerprint of the glass and compare this with reference specimens.

## Toxicology<sup>3</sup> :

### Clinical - Analytical - Forensic Toxicology

**Clinical toxicology** is the study of the effects of toxic chemicals on a person. **Analytical toxicology** involves testing for the presence or concentration of specific chemicals and the interpretation of the test results. **Forensic toxicology** involves the application of case findings, research, and study to case-specific questions. **Examples follow.**

#### A negative toxicology screen:

**Hypothetical:** A housewife was acutely poisoned by an organophosphate pesticide; but, her blood and urine “toxic screen” tests at the hospital were “negative”. **Explanation:** The tests did not include analyses for pesticides or metabolites; however, a decreased plasma cholinesterase level would have confirmed the clinical diagnosis.

#### An unexpected increase in blood lead:

**Hypothetical:** Three months after chelation therapy reduced a child’s blood lead levels, the blood lead was again elevated. **Explanation:** The apparent elevation may be due to re-exposure, redistribution of the child’s total body burden of lead, improper specimen sampling, or laboratory error. Comparison of a series of blood lead and FEP levels will often point to the cause of the apparent elevation.

*Is your expert qualified to discuss both clinical and analytical toxicology? Is your expert prepared to analyze your case? One of the best ways to get an initial “reading” regarding abilities is to call the potential expert and discuss your case ... without obligation and without charge.*

## **BRIAN E. PAPE, Ph.D., BCFE, BCFM**

Dr. Brian Pape is the principal consultant with Pape & Associates, specializing in toxicology and related sciences. His professional experience includes the following:

- Associate Professor of Pathology (*Clinical Appointment*), University of Massachusetts School of Medicine.
- Senior Associate Consultant for Mayo Clinic (Rochester, MN) and Director of Toxicology at New England Toxicology Services (Woburn, MA).
- Director of Toxicology and Associate Professor, Department of Pathology, University of Missouri School of Medicine.

Dr. Pape has published more than 50 research papers, abstracts, and professional articles relating to alcohol and drugs, pesticides and toxic chemicals, analytical chemistry, forensic science, and general toxicology. He authors the *Toxicology Reporter*.

He has served as a technical and expert consultant to business, labor, and governmental agencies. He has been qualified as an expert in toxicology and related sciences in State and Federal Courts.

Dr. Pape has been board-certified by the American College of Forensic Examiners (BCFE) and the American Board of Forensic Medicine (BCFM).

He has been qualified on more than 100 occasions in State and Federal Courts. His case testimony has included liquor liability, alcohol and drug related testing-effects-and-accidents, laboratory testing, toxic torts, and product liability.

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