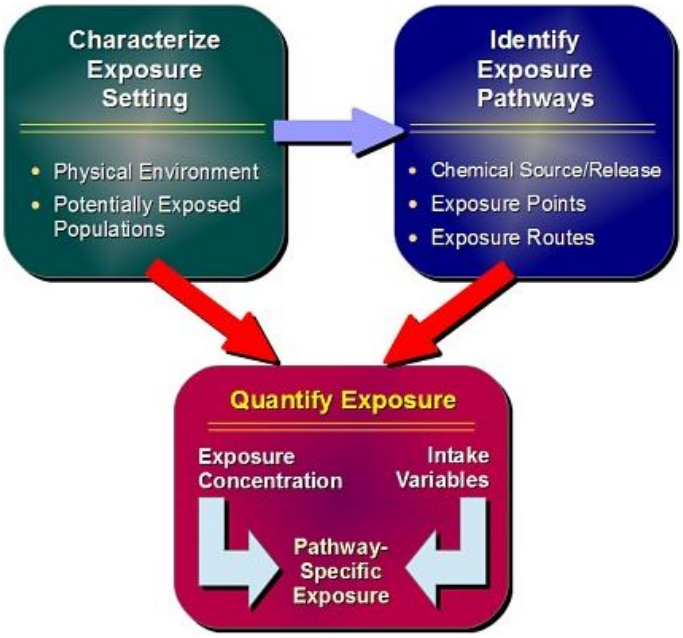
Toxic Exposures

This page outlines some of the basic principles of toxic exposure assessment. ATSDR (U.S. Agency for Toxic Substances and Disease Registry) defines a toxic exposure as *"contact with a toxic substance by swallowing, breathing or touching the skin or eyes. Exposure may be short-term [acute], of intermediate duration or long-term [chronic]."*[1]

The expert toxicologist's primary tasks are to (a) identify toxic substances and/or chemicals of concern (COCs), (b) document and characterize the circumstances under which exposure occurred, (c) identify the pathways, durations and conditions of exposure and (d) determine the respective dosage of each chemical or substance. This process is referred to as an *exposure assessment*. When exposed to a toxic substance, the organ affected at the lowest dose is referred to as the *target organ.*



Components of pathway-specific toxicological exposure assessment. Adapted from U.S. EPA Exposure Factors Handbook [a]

Exposure Assessment in Toxicology

Exposure assessment is merely one step in a multi-step process called risk assessment. Although the precise steps and methods vary according to the type and circumstances of exposure, the underlying principles are the same. Whether the result establishes (or refutes) an excessive blood-alcohol concentration in the driver of a motor vehicle, or addresses a variety of substances over many years in an entire community, the expert toxicologist must follow the same objective steps to arrive at scientifically credible results which must fulfill the criteria of *reasonable toxicological certainty.*

Exposure assessment can be thought of as a process whereby the toxicologist calculates the magnitude, frequency and duration of exposure to a toxic agent. As shown in the chart to the right, this requires compiling sets of information which describe exposure concentrations and intake variables to arrive at a *pathway-specific exposure dose* for each substance. This means characterizing the sources, pathways and routes of exposure as well as the number and characteristics of the person(s) exposed.

In addition, the expert toxicologist must take uncertainties into account. Many factors must be identified and assessed (some of which may have occurred in the distant past). Such an investigation may fall within the realm of forensic toxicology.

Thus, an exposure assessment measures (a) the dose of a toxic agent that was likely to have been absorbed by an exposed individual or population, (b) the form of the toxic agent, (c) the rate at which the agent was delivered, (d) how much of the agent was actually available in the body to produce the biological effect(s) at issue and (e) whether mitigating factors or uncertainties may have altered the outcome. This method produces results which establish the path, transport and anticipated effects of a toxic agent on a biological basis. If a well-documented and recognized cause/effect relationship is demonstrated, this is referred to as a *toxicological endpoint.*

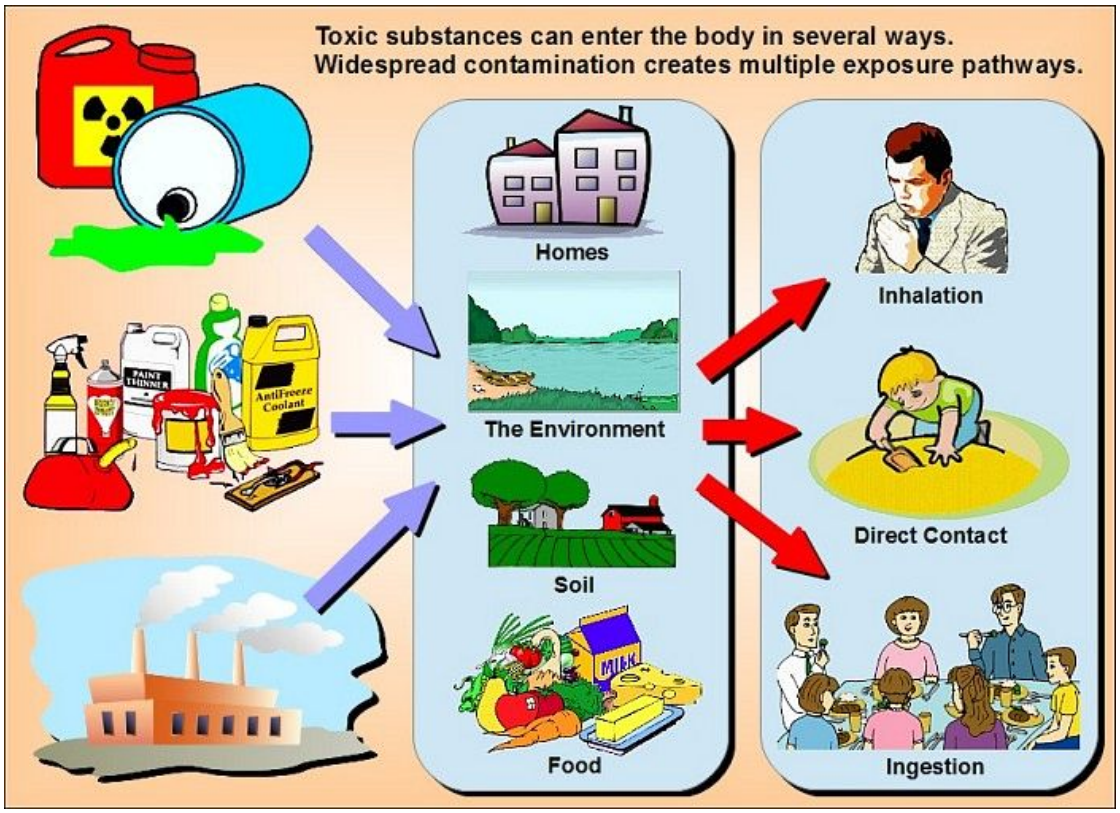
Exposure Pathways

In reviewing a case, the expert toxicologist may find that the route(s) of exposure are self-evident. For example, acute ingestion of a poison, drinking contaminated water or acute inhalation of toxic fumes are often singular events. These can usually be assessed by applying direct dose calculations to established dose-response relationships.

However, widespread environmental contamination, particularly cases involving the release of several toxic substances (sometimes over a period of many years) creates a vastly more complicated situation. In such cases, contamination by (for example) dioxin, trichloroethylene or LNAPL may involve contamination in the air, soil, drinking water, food, dust, etc. In these cases, there are many mechanisms for oral, dermal and inhalation uptake with chemical-specific exposures through multiple pathways.

Thus, the toxicologist must first assess the possible routes of exposure by seeking answers to environmental considerations:

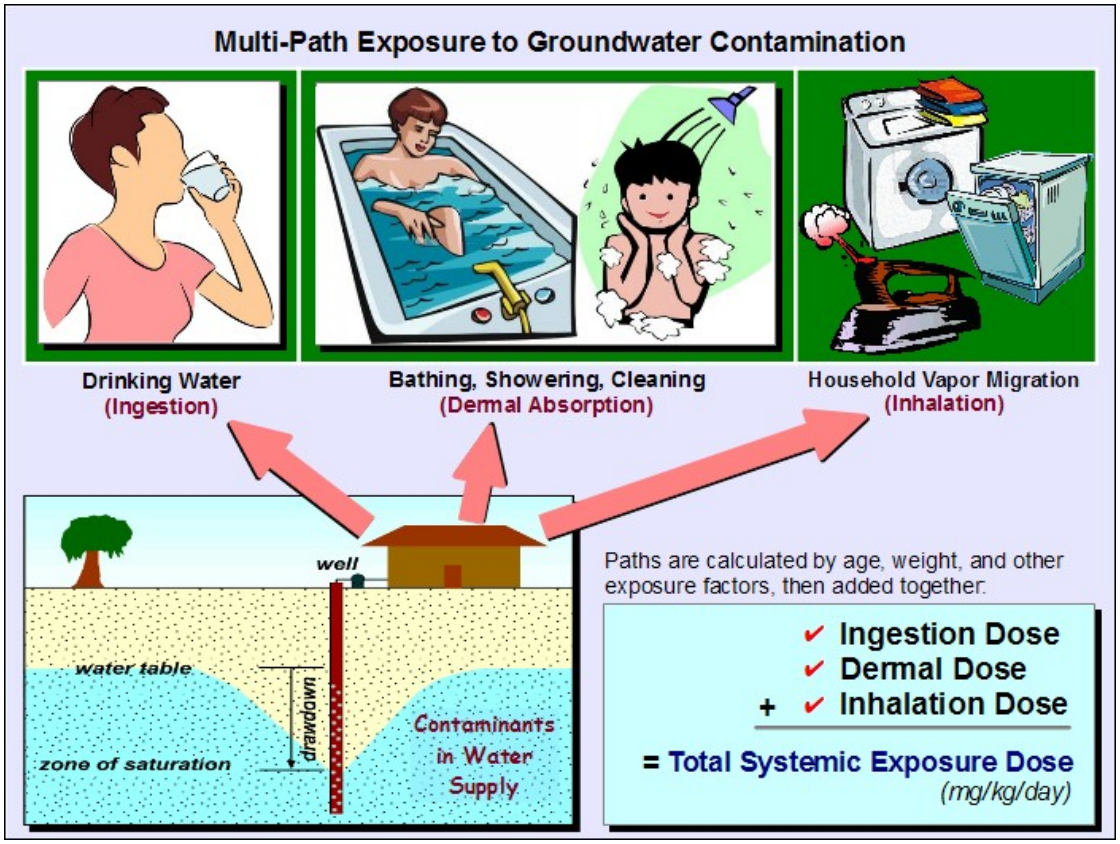
- **Inhalation:** Was the contaminant inhaled or persistent in fine-particle respirable dust within the environment?
- **Dermal Absorption:** Was the contaminant absorbed through the skin?
- **Ingestion:** Was the contaminant ingested through food, drinking, dust, hand-to-mouth behavior, etc.?



Examples of ways toxic substances can enter the human body [b]

Multiple Pathways

In some cases, a primary route of exposure may not be immediately obvious. For example, trichloroethylene (TCE) can be ingested by drinking contaminated water. However, TCE also readily vaporizes and as such, it can be inhaled from hot shower steam and other household sources. TCE can also be absorbed through the skin while swimming or washing.[2] Even inhaling TCE vapors when opening the lid of a washing machine can resuly in a significant quantified dose if the concentration is sufficiently high and if performed with sufficient frequency. These examples underscore the potential complexity of a toxic exposure assessment in a widespread contamination scenario.



Additive exposure pathways from contaminated groundwater [c]

Calculating Cumulative Exposure

In the illustration below, *TCAS* calculated TCE concentrations over time for residents who were exposed through inhaling TCE vapors while showering (among several exposure pathways). As each person aged, they fell into a different group with a different dose absorption factor corresponding to their body weights, water evaporation rates and inhalation rates. Thus, each individual had to be treated as "several" individuals at different points in time. The resulting sums of dosages were then applied to different exposure periods to arrive at a resulting "cumulative inhalation dose" which is itself merely one ledger item in a longer series of *additive* doses.

TCE Shower Inhalation Exposure Calculations

Shower Inhalation = $\frac{TC \times ED \times EF \times AG \times EI \times EP}{BW}$ = mg/kg/day

Age Group Dose Absorption Factors

0-6 yrs = 0.0531×10^{-2}
7-10 yrs = 0.0875×10^{-2}
11-14 yrs = 0.1185×10^{-2}
Adult = 0.1530×10^{-2}

TC TCE Conc/5 (ug/L) [1]	ED Exposure Duration	EF Exposure Frequency	AG(1) 0-6 Years Dosage	AG(2) 7-10 Years Dosage	AG(3) 11-14 Years Dosage	AG(4) Adult Dosage	EI Exposure Interval	EP Exposure Period	BW Body Weight (kg)	RESULT Inhalation Dose
0.46	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.300	92.3	1.75E-06
9.17	1.040	0.74	0.000266	0.000438	0.000000	0.000000	1	0.057	31.8	8.91E-06
9.17	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.057	59.1	1.04E-05
9.17	1.040	0.74	0.000000	0.000000	0.000296	0.001148	1	0.057	61.4	9.48E-06
9.17	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.057	98.9	6.24E-06
10.20	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.043	81.8	6.29E-06
10.20	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.043	59.1	8.71E-06
10.20	1.040	0.74	0.000531	0.000000	0.000000	0.000000	1	0.043	20.9	8.54E-06
0.78	1.040	0.74	0.000114	0.000250	0.000339	0.000328	1	0.200	40.2	3.07E-06
8.01	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	131.8	2.04E-06
0.00	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.400	57.9	
0.00	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.371	68.2	
9.99	1.040	0.74	0.000133	0.000146	0.000198	0.000638	1	0.343	56.4	5.21E-05
9.99	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.343	73.5	5.49E-05
7.52	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.143	78.2	1.62E-05
8.79	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.143	94.3	1.57E-05
7.52	1.040	0.74	0.000266	0.000350	0.000119	0.000000	1	0.143	45.9	1.32E-05
8.79	1.040	0.74	0.000177	0.000583	0.000000	0.000000	1	0.086	43.9	1.01E-05
1.60	1.040	0.74	0.000266	0.000438	0.000000	0.000000	1	0.086	26.1	2.84E-06
7.52	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.143	74.3	1.70E-05
8.79	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.086	81.8	1.08E-05
1.60	1.040	0.74	0.000531	0.000000	0.000000	0.000000	1	0.071	22.7	2.06E-06
9.99	1.040	0.74	0.000000	0.000000	0.001185	0.000000	1	0.029	68.2	3.82E-06
9.99	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	77.3	4.35E-06
9.99	1.040	0.74	0.000000	0.000000	0.001185	0.000000	1	0.029	63.6	4.09E-06
9.99	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	61.4	5.48E-06
9.38	1.040	0.74	0.000000	0.000583	0.000395	0.000000	1	0.086	70.5	8.59E-06
9.38	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.086	65.9	1.44E-05
9.38	1.040	0.74	0.000000	0.000000	0.000790	0.000510	1	0.086	39.8	2.02E-05
9.38	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.086	65.0	1.46E-05
12.42	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	109.1	3.83E-06
12.42	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	52.3	7.99E-06
12.42	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	65.9	6.34E-06
12.42	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.029	97.7	4.27E-06
0.00	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.014	181.8	
10.59	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.057	125.0	5.70E-06
7.52	1.040	0.74	0.000000	0.000000	0.000356	0.000765	1	0.143	50.8	1.83E-05
7.52	1.040	0.74	0.000000	0.000350	0.000474	0.000306	1	0.143	56.8	1.64E-05
10.59	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.057	79.5	8.96E-06
10.59	1.040	0.74	0.000531	0.000000	0.000000	0.000000	1	0.029	19.5	6.33E-06
5.60	1.040	0.74	0.000228	0.000250	0.000339	0.000000	1	0.200	61.4	1.15E-05
0.78	1.040	0.74	0.000000	0.000000	0.000000	0.001530	1	0.300	62.9	4.37E-06

TCE vapor inhalation concentrations for various age groups while showering (adapted from an actual *TCAS* risk assessment) [d]

Although this illustration demonstrates how such calculations may be performed in a community-exposure scenario, it should be noted that this is merely one page from a much longer set of calculations detailing other routes of exposure (water ingestion, dermal absorption, etc.). However, this methodology typifies the requirements imposed upon the expert toxicologist when conducting an exposure assessment in a widespread contamination scenario. Thus, the toxicologist's role is to apply the concise methods necessary to delineate exposure conclusions to *reasonable toxicological certainty.*

Summary

The general information presented herein serves to illustrate the fact that organizing a toxic exposure assessment on the basis of the exposure circumstances is just as important as performing the exposure calculations themselves. U.S. EPA's Exposure Factors Handbook[3] provides a wealth of information regarding methods for applying generally-accepted default values to compile pathway-specific exposure data. This is extremely helpful when investigating and objectively assessing the relevant factors governing the possible exposure pathways including whether exposures occurred simultaneously or at different times. Uncertainties, other possible contamination sources and any relevant historical data should also be taken into account.

When all of the exposure points have been identified and fully characterized, the toxicologist applies a set of generally-accepted equations to the variables (as guided by U.S. EPA, RECAP or other regulatory body). This methodological approach allows all exposure pathways to be quantified with respect to exposure concentrations and their related intake levels and cumulative dose. *This is the last step in the toxic exposure assessment process.* Each exposure pathway must be fully documented and the resulting concentrations applied using generally-accepted, peer-reviewed calculation methods.

Thus, through a meticulous process with concise attention to detail, the expert toxicologist compiles scientifically credible, pathway-specific exposure data. Although pure reasoning can assist in interpreting results, *reasonable toxicological certainty* is largely subordinated to the weight of objective evidence. There should be few (if any) *a priori*[4] determinations in a well-constructed toxic exposure assessment.

Toxic Substances

The universe of toxic substances is vast as there are more than 7 million recognized chemicals in existence. The U.S. General Accounting Office (GAO) references approximately 80,000 chemicals used on a regular basis.[5] The US Agency for Toxic Substances and Disease Registry (ATSDR) has published a large body of information covering a wide range of toxic substances.[6] Armed with the enormous body of toxicological literature and guided by generally-accepted, peer-reviewed methods, the expert toxicologist's goal is to identify and characterize the circumstances of exposure, identify the exposure pathways and determine the dosage of each chemical or substance.

For more than 28 years, *TCAS* has been retained to perform investigative assessments of toxic exposures. We have conducted exposure assessments for a wide variety of substances under many different circumstances. Some of these can be reviewed in our areas of specialization and in our case studies. This website provides reference information for six (6) classes of toxic substances with which *TCAS* has extensive professional experience. Click on your particular area of interest to view additional information.

Hazardous Substances

Heavy Metals

Alcohol Toxicology

Drugs of Abuse

Pharmaceutical Toxicology

Consumer Products

Notes and References

1. Agency for Toxic Substances and Disease Registry, "Health Effects of Exposure to Substances and Carcinogens (Glossary)"
2. U.S. Environmental Protection Agency, "Chemical Summary, TCE"
3. U.S. Environmental Protection Agency, "Environmental Assessment, Exposure Factors Program "
4. *a priori;* A type of conclusion which favors pure reason or intuition over objective evidence.
5. General Accounting Office, "1994b. Toxic Substances Control Act," Federal Register, 1994
6. ATSDR, Division of Toxicology and Environmental Medicine, "Toxic Substances," Evaluations of hazardous substances and their potential health effects (2013)

Images

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A Message from Dr. William R. Sawyer
Chief Toxicologist, *TCAS, LLC*

"A toxic exposure assessment can be a demanding and challenging endeavor. Attention to detail and strict adherence to peer-reviewed methods are essential to producing a scientifically credible assessment."

Toxicology Consultants & Assessment Specialists, LLC
(800) 308-0080 or send a message
6450 Pine Avenue, Sanibel, FL 33957 **(239) 472-2436**
29 Fennell Street, Skaneateles, NY 13152 **(315) 685-2345**
View Dr. Sawyer's profiles on LinkedIn.com, AlmExperts.com and Jurispro.com