

Human Toxic Chemical Exposure

The Bulletin of Pacific Toxicology Laboratories

Proper Use of the Laboratory in Assessing Occupational and Environmental Exposure to Toxic Chemicals

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KEY TOPICS

- I. What test should be ordered?
- II. What type of specimen should be collected?
- III. When should the specimen be collected?
- IV. How often should specimens be collected?
- V. What are the background and toxic levels for the analyte?
- VI. Specimen archiving

Thanks to advances in analytical chemistry, trace amounts of various toxic chemicals can be analyzed accurately in environmental samples by commercial, governmental, and academic laboratories. A few labs even have the ability to measure these chemicals at low levels in human tissues. Having the ability to successfully perform such testing, however, does not necessarily mean that useful information will result. Analysis of human tissues requires an understanding of human biological processes not necessarily required for typical environmental analyses. Important considerations before requesting human toxicological testing are the following:

- What test should be ordered?
- What type of specimen should be collected?
- When should the specimen be collected? - How often should specimens be collected?
- What are the background and toxic levels for the analyte?

While not all of these questions can be answered for each exposure situation; some attention must be given to each of them to assess any health risk.

I. WHAT TEST SHOULD BE ORDERED?

In any investigation of toxic chemical exposure, the chemical(s) suspected at causing the adverse health effect should be identified. The “shotgun” approach of testing for anything and everything is expensive and rarely results in useful data unless numerous

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negative results are of interest. The possible chemical(s) may be well-known to the individual through conscientious efforts - to read container labels of materials used at work. If such information is not easily available, it may be obtained from Material Safety Data Sheets (MSDS) with the employer or manufacturer *as* required by law to supply to workers. If identification of possible chemical exposure is not this straightforward, analysis of environmental samples (wastes, air, water, soil, etc.) may be required. These tests can be prohibitively expensive for a private citizen.

In the workplace, both industrial hygiene air monitoring and wipe test results may be available to workers. If none of these sources of information is available, a realistic, logical evaluation of the individual's medical and job history, including any previous toxic exposures, may suggest likely candidates for testing.

Any list of possible exposure chemicals must be narrowed further based on the availability of an appropriate test and the period of time which has passed since the presumed exposure. This will depend on the chemical and its metabolism in humans. In some cases it is not appropriate to measure the chemical itself (unchanged or as parent compound), since it may be extensively metabolized by the body immediately after absorption. Table 20-1 is a list of some commercially available tests for chemicals and their metabolites.

II. WHAT TYPE OF SPECIMEN SHOULD BE COLLECTED?

Only certain types of human specimens are appropriate for testing. Most commonly tested are urine, blood, and adipose tissue. Table 20-1 lists specimens appropriate to each chemical.

Others, such as breast milk, sebum (from sweat glands), hair and nails are analyzed less often, and therefore, data from such tests may be more difficult to interpret. While some chemicals can be measured in several different *specimens*, Table 20-1 lists the preferred specimens.

III. WHEN SHOULD THE SPECIMEN BE COLLECTED?

In most cases, the specimen should be collected as soon as possible after the exposure. Ideally, in workers, a baseline specimen, which can be analyzed or archived (frozen until needed), should be collected *before* the exposure. However, for chemicals which accumulate in the body, such as polychlorinated biphenyls (PCBs), timing of the analysis is not as critical as for solvents, such as perchloroethylene, which have short half-lives. Table 20-1 indicates the tests which should be done within hours (h), within days (d), within weeks (w), or within months to years (y) of exposure. While it may seem inappropriate to test for a chemical long after that chemical would be metabolized and

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excreted from the body, it may still be useful as a test for its absence to convince a worried patient that the chemical has not been retained. A sensitive, negative test may be worthwhile as reassurance. This, of course, depends on the level of trust the patient has for accepted scientific and medical knowledge.

IV. HOW OFTEN SHOULD SPECIMENS BE COLLECTED?

This depends on the goals of the testing and the subsequent testing results. If the goal of such testing is to investigate an isolated exposure incident, a single sample may be sufficient. If chronic exposure is being monitored, then multiple samples would be necessary to establish the duration of exposure as well as the level of exposure. In general, shorter-lived chemicals (hours, days, weeks) should be tested more often than those which are retained for months or years.

V. WHAT ARE THE BACKGROUND AND TOXIC LEVELS FOR THE ANALYTE?

The background level or general population range refers to the level below which 95 percent of the values from non-occupationally-exposed individuals will fall. This is the chemical background. As more experience is gained with biological monitoring, background levels may change. Some chemicals, such as PCBs, are ubiquitous so that nearly all specimens will have measurable levels. Therefore, their mere presence in a specimen without a reference range provides the physician with very little new information, or worse, may lead to erroneous conclusions. The purpose of the general population range is to provide the doctor with a perspective from which to distinguish the typically exposed (background) from the atypically exposed. However, levels above or below this range do not imply toxicity or lack of toxicity. Table 20-1 lists general population ranges for commonly ordered tests. These ranges may vary according to the laboratory performing the test because they may be established from a variety of different databases. That general population ranges may be obtained from data published in the scientific literature or developed by the laboratory itself. Investigators involved in large studies often select an unexposed control group for comparison to the study population. This is particularly important when little data has been published concerning background levels of certain chemicals or when demographics may be an important factor.

The question of toxic levels is the most important and the most difficult question of all. The toxic level is the concentration of a chemical above which adverse health effects can occur. Since it is, of course, unethical to dose human beings with chemicals to determine the toxic level, most of our knowledge concerning a chemical's toxicity to humans is from retrospective epidemiological studies and accidental exposures. Some of these sources provide data with a high level of uncertainty, and actual toxic levels, especially from skin absorption, are often unavailable.

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Currently, the most valuable source of guidelines for biological monitoring and limiting the levels of chemical exposure at work is the American Conference of Governmental Industrial Hygienists (ACGIH). This non-governmental organization has developed guidelines which are called "Biological Exposure Indices" or BEIs. BEIs are levels of chemicals or their metabolites in various human specimens which should not be exceeded in order to avoid adverse health effects. These guidelines, with their recommended collection timing, are listed in Table 20-I. The ACGIH documentation should be consulted for proper application of the BEIs.

VI. SPECIMEN ARCHIVING

Specimen archival can be used for the following two purposes:

1. Specimens collected and frozen prior to employment or prior to a change in duties or working conditions can be used if needed at some time in the future to determine a baseline level for comparison to a post-exposure value. These specimens are especially valuable in cases of accidental spills or the appearance of an adverse health effect potentially related to work.
2. Alternatively, specimens may be collected and frozen immediately after a chemical exposure incident and held until more information concerning testing is obtained.

There are several advantages to archiving samples:

- Analytical costs are reduced because only a portion of worker's specimens may need to be analyzed.
- When specimens are eventually analyzed, pre- and post-exposure samples are run together, eliminating day-to-day analytical variability and producing more precise and comparable.
- Test methods, unavailable (even unforeseen) at the time of specimen collection, can be performed at a later date when they are developed.
- A specimen whose value depends on timely collection can be obtained immediately after an exposure. A decision as to which test should be performed (or whether a test should be performed at all) can be made later in a thoughtful, deliberate manner.

Archival of specimens (prior to potential exposure) is most effective for analytes which have the following characteristics:

- Long-term storage stability (months to years)
- long biological half-life
- Blood or urine levels result specifically from chemical exposure and not from variable endogenous production or drugs

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- Potentially present due to work environment and not to environmental exposure or domestic use unrelated to the job

Sore analytes which meet these criteria are PCBs, PEBS, pentachlorophenol, organochlorine pesticides, and related compounds. Serum cholinesterase can be archived, but several baseline samples collected at different times should be stored. Urine trichloroacetic acid, phenol, hippuric acid, and other solvent metabolites can also be archived but should be analyzed within a shorter time frame (three to twelve months). Specimens can be analyzed for other analytes, but the successful use of archiving as a baseline measure depends on individual circumstances. The suitability of archiving specimens following an incident for future analysis depends on the stability of the analyte in the specimen. The holding time for analytes ranges from four days for methylene chloride in blood to five to ten years for PCBs.

Presently available tests, general population range (background), levels of concern, timing of analysis, and specimen requirements are shown in Table 20-1.

Table 20-1 Some Commercially Available Tests for Chemicals and Metabolites in Human Specimens

Chemical	General Population Range	Units	Toxic Level	Timing (half-life)	Specimen Requirements
Solvents					
Benzene					
Benzene	<0.01	Mg/l	N/A	H	7 ml LT
Phenol	<20	Mg/g CR	50	H	25 ml U
Toluene					
Toluene	<0.01	Mg/l	1	H	7 ml LT
Hippuric Acid	<1500	Mg/g CR	2500	H	5 ml U
Cresol, O-	<0.1	Mg/g CR	1	H	25 ml U
Xylene					
Xylenes	<0.01	Mg/l	0.55	H	7 ml LT
Methylhippuric Acids	<50	Mg/l	1500	H	5 ml U
Styrene					
Styrene	<0.01	Mg/l	0.55	H	7 ml LT
Phenynglyoxylic Acid	<50	Mg/l	250	H	5 ml U
Mandelic Acid	<50	Mg/l	1000	H	5 ml U
Ethylbenzene	<0.01	Mg/l	NA	H	7 ml LT
Ethylbenzene					
Phenynglyoxylic Acid	<50	Mg/l	NA	H	5 ml U
Mandelic Acid	<50	Mg/l	2000	H	5 ml U
Hexane					
Hexandione, 2,5-	<0.4	Mg/l	5	H	15 ml U
Perchloroethylene					
Perchloroethylene	<0.003	Mg/l	1	D	5 ml U
Trichloroacetic Acid	<0.1	Mg/l	N/A	D-W	7 ml LT
Trichloroacetic Acid	<0.5	Mg/l	7	D-W	7 ml LT
Trichloroethylene					
Trichloroethylene	<0.003	Mg/l	N/A	H	7 ml LT

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Trichloroacetic Acid	<0.1	Mg/l	100	D-W	5 ml U
Trichloroacetic Acid	<0.5	Mg/l	N/A	D-W	7 ml LT
Trichloroethanol	<0.1	Mg/l	30	H	5 ml U
Trichloroethanol	<0.1	Mg/l	1	H	7 ml LT
Methylene Chloride					
Methylene Chloride	<0.003	Mg/l	1	H	7 ml LT
Carboxybenoglobin	<3%	%Hgb	5%	H	7 ml LT
Dimethylformamide					
N-Methylformamide	<5	Mg/l	50	H	25 ml U
Petroleum Distillates					
Kerosene	<100	Ug/l	N/A	H	7 ml LT
Mineral Spirits	<100	Ug/l	N/A	H	7 ml LT
Ketones and Alcohols					
Methyl Ethyl Ketone	<0.01	Mg/l	2	H	5 ml U
Methyl Ethyl Ketone	<0.01	Mg/l	N/A	H	7 ml LT
Methyl Isobutyl Ketone	<0.01	Mg/l	N/A	H	5 ml U
Methyl Isobutyl Ketone	<0.01	Mg/l	N/A	H	7 ml LT
Methyl N-Butyl Ketone	<0.01	Mg/l	N/A	H	5 ml U
Methyl N-Butyl Ketone	<0.01	Mg/l	N/A	H	7 ml LT
Hexandione, 2,5-	<0.4	Mg/l	5	H-D	15 ml U
Acetone	<3	Mg/l	20	H	15 ml U
Acetone	3-20	Mg/l	N/A	H	7 ml GT
Isopropanol	<1	Mg/l	N/A	H	4 ml
Methanol	<1	Mg/l	15	H	7 ml GT
Organochlorine Pesticides					
DDT	<1.3	Mg/kg	N/A	Y	0.5 gm AT
DDT	<20	Ug/l	N/A	Y	5 ml
DDE	<4.5	Mg/kg	N/A	Y	0.5 gm AT
DDE	<50	Ug/l	N/A	Y	MI S
DDD	<0.150	Mg/kg	N/A	Y	0.5 gm AT
DDD	<20	Ug/l	N/A	Y	5 ml S
Chlordane					
Chlordane, Alpha-	<0.1	Mg/kg	N/A	W	0.5 gm AT
Chlordane, Alpha-	<0.5	Ug/l	N/A	W	5 ml S
Chlordane, Gamma-	<0.01	Mg/kg	N/A	W	0.5 gm AT
Chlordane, Gamma-	<0.5	Ug/l	N/A	W	5 ml S
Oxychlordane	<0.150	Mg/kg	N/A	W	0.5 gm AT
Oxychlordane	<2	Ug/l	N/A	Y	5 ml S
Trans -Nonachlor	<0.173	Mg/kg	N/A	Y	0.5 gm AT
Trans -Nonachlor	<2	Ug/l	N/A	Y	5 me S
Heptachlor	<0.01	Mg/kg	N/A	D-W	0.5 gm AT
Heptachlor	<0.5	Ug/l	N/A	D-W	5 ml S
Heptachlor Epoxide	<0.130	Mg/kg	N/A	Y	0.5 gm AT
Heptachlor Epoxide	<3	Ug/l	N/A	Y	5 ml S
Miscellaneous OC Pesticides					
Lindane (gamma-BHC)	<0.003	Mg/kg	N/A	D-W	0.5 gm AT
Lindane (gamma-GHC)	<13	Ug/l	25	D-W	5 ml S
BHC, Beta-	<0.470	Mg/kg	N/A	Y	0.5 gm AT
BHC, Beta-	<10	Ug/l	N/A	Y	5 ml S
Dieldrin	<0.180	Mg/kg	N/A	Y	0.5 gm AT
Dieldrin	<4	Ug/l	N/A	Y	5 ml S

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Endosulfan I and II	<0.5	UgA	N/A	D-W	5 ml S
Endrin	<0.5	Ug/l	N/A	D-W	5 ml S
Hexachlorobenzene	<0.360	Mg/kg	N/A	Y	0.5 gm AT
Hexachlorobenzene	<5	Ug/l	150	Y	5 ml S
Mirex	<0.043	Mg/kg	N/A	Y	0.5 gm AT
Pentachlorophenol	<0.030	Mg/l	2	W	15 ml U
Pentachlorophenol	0<0.075	Mg/l	5	W	5 ml Plasma
Organophosphorus Pesticides					
Cholinesterase	Varies	IU	-30%	W-M	7 ml GN
Cholinesterase	Varies	IU	-30%	D-W	5 ml S
Alkylphosphate Metabolites	<0.03	Mg/g CR	N/A	D	15 ml U
Malathion Metabolites	<10	Lug/l	N/A	D	15 ml U
Parathion					
Para-Nitrophenol	<0.05	Mg/g CR	2	D	15 ml U
Dursban					
Trichloropyridinol, 3,5,6	<0.01	Mg/l	N/A	D	15 ml U
Herbicides					
2,4,5-T	<0.01	Mg/l	N/A	D	15 ml U
2,4-D	<0.05	Mg/l	N/A	D	15 ml U
Silvex	<0.01	Mg/l	N/A	H-D	15 ml U
Polychlorinated Biphenyls					
PCBs Total	<20	Ug/l	N/A	Y	4 ml S
PCBs Total	<50	Mg/kg	N/A	Y	0.5 G AT
Polybrominated Biphenyls					
PBBs	<1.1	Ug/l	N/A	Y	5 ml S
Anitines					
MBOCA	<10	Ug/l	100-	H-D	15 ml U
Methylenedianiline	<2.5	Ug/g CR	N/A	H-D	1.5 ml U
Heavy Metals					
Lead	<50	Ug/g CR	150	M-Y	15 ml U
Arsenic	<10	Ug/g CR	50	H-D	15 ml U
Cadmium	<3	Ug/l	10	Y	7 ml BT
Chromium	<1	Ug/g CR	30	H-D	15 ml U
Nickel	<5	Ug/g CR	35	D	15 ml U
Mercury	<20	Ug/l	50	D-W	7 ml BT

Ug – Micrograms

G CR – Grams of Creatinine

H – Hours

M – Months

AT – Adipose Tissue

LT – Lavender Top Tube

Mg – Milligrams

IU – International Units

L – Liter

H – Hours

D – Days

Y - Years

U – Urine

GT – Green Top Tube

G- Grams

Kg - Kilograms

DCL – Decileter (100 ml)

W - Weeks

N/A – Not Available

S – Serum

BT – Royal Blue Top Tube

% Hgb – Percent Hemoglobin