VLS-TOX

NON-METALLIC TOXIC CHEMICAL PROFILE

The Non-metallic Toxic Profile test provides information on exposure to toxins in air, water and food. Non-metallic toxic chemicals are invisible and can be found inside drugs, pesticides, packaged foods, household products and in environmental pollution. The increasingly massive presence in these products is counted among the main causes of chronic diseases such as cancer, multiple chemical sensitivity, autism spectrum disorders, autoimmune disorders, chronic fatigue syndrome, heart disease, etc. The Nonmetallic Toxic Chemical Profile provides the quantification of twelve metabolites resulting from exposure to benzene, styrene, pyrethrins, xylene. The test is carried out on a single urine sample analyzed using the refined UHPLC-MS/MS methodology. The test is recommended for subjects who for work reasons and / or in daily life are in contact with these environmental pollutants, anticipating detoxification treatments and preventing the development of chronic diseases.

INDUSTRIAL TOXIC SUBSTANCES

- ✓ **2-Methylhippuric Acid (2MHA) - XYLENE**
- ✓ **3-Methylhippuric Acid (3MHA) - XYLENE**
- ✓ **4-Methylhippuric Acid (4MHA) - XYLENE**

Xylene is an aromatic hydrocarbon produced from petroleum, used as a solvent in printing and paints, it is present in products such as dye, lacquer, indelible markers, pesticides, gasoline, cleaning products, perfumes and repellents. It is also used in analytical laboratories that process histological samples. One of the most common transmission routes for humans is ingestion due to contamination of groundwater for washing oil tanks. It can also be introduced by inhalation causing depression of the central nervous system with symptoms such as headache, vomiting and dizziness. The mechanism of detoxification from xylene occurs by liver oxidation that converts it into methylhippuric acid, a marker of exposure to xylene. Fortunately, the elimination is quite rapid, which is why the side effects are transient. Studies in rats have shown that exposure to styrene induces decreased locomotor capacity, learning and memory loss. These behavioral changes have been associated with decreased beta-endorphins. Treatment involves initial research and removal of sources of xylene and following a detoxification protocol (e.g. Hubbard protocol).

- ✓ **2-Hydroxyisobutyric Acid (2HIB) - MTBE/ETBE**

Methyl-t-butyl ether and ethyl-t-butyl ether are organic compounds used as additives in green gasoline to increase their octane number. Due to its high solubility, it can easily penetrate the aquifers where it remains for a long time if an adequate removal process is not intervened. Its permanence in the ecosystem and the drinking or irrigation use of contaminated water causes it to enter the food chain. Other sources of exposure occur by inhaling gasoline, absorption through the skin or its vapors via car exhaust gases. MTBE and ETBE are metabolized and eliminated as urinary metabolites between 10 and 28 hours or exhaled unchanged. If exposure is prolonged over time, it may cause liver, kidney, and nervous system toxicity in animals, with genetic modifications. In case of ascertained exposure, reduce the time spent in the body by undergoing a sauna and proceed are an adequate detoxification protocol (example Hubbard). 2-Hydroxyisobutyric acid is also an endogenous product of branched chain amino acid degradation and ketogenesis.

- ✓ **Phenylglyoxylic Acid (PGO) - STYRENE-ETHYLBENZENE**

Styrene is an aromatic hydrocarbon used in a lot of chemical synthesis processes and as a solvent. Widely used in the production of plastic (also for food), in building materials and in exhausted car fumes, styrene poisoning can cause irritative effects on the skin and mucous membranes and, at high concentrations, can be toxic on the Central Nervous System causing concentration problems, muscle fatigue, fatigue, nausea. Since 2011 styrene has been officially recognized as a carcinogen. The urinary concentration of phenylglyoxylic acid is well correlated with styrene exposure. This acid has a longer biological half-life than mandelic acid (another metabolite of styrene), allowing more accurate monitoring of styrene exposure. In case of positive result to PGO exposure, immediately remove plastic and polystyrene containers for cooking, eating and drinking, preferring those made of glass, paper or stainless steel. Accelerate elimination through detoxifying treatments (sauna) and reduced glutathione supplementation.

- ✓ **N-Acetyl Phenyl Cysteine (NAP) - BENZENE**

Benzene is a widespread solvent in the environment, present in cigarette smoke and gasoline, it is also a by-product of all types of combustion, even of numerous industrial processes. Its metabolite, n-acetylphenylcysteine (NAP), is found in the urine of subjects who have been exposed to this solvent. Benzene also escapes from synthetic materials (carpets, curtains and furniture), glues and detergents. Benzene causes hematological abnormalities as well as being mutagenic and carcinogenic. High exposure to benzene can cause nausea, vomiting, dizziness, poor coordination, central nervous system depression and even death. N-acetyl phenyl cysteine (NAP) is also a metabolic byproduct of potassium sorbate or sorbic acid, a common and safe food preservative. If a positive result is given to benzene exposure, all sources of exposure should be discharged as far as possible. Accelerate elimination through detoxifying treatments (sauna) and reduced glutathione or NAC supplementation.

- ✓ **Diphenyl Phosphate (DPP) - ORGANOPHOSPHATE**

Diphenyl phosphate is a metabolite of triphenyl phosphate, an organophosphate flame retardant (TPHP) that is used in plastics, electronic equipment, nail polishes and resins. Exposure can result from PVC, rubber, polyurethane, textiles, pigments and paints. TPHP can cause endocrine disruption and reproductive and developmental problems. Diphenyl phosphate is eliminated from the body by glucuronosyltransferase enzymes.

- ✓ **N-Acetyl (Propyl) Cysteine (NAPR) - 1-BROMOPROPANE**

1-Bromopropane is an organic solvent used for metal cleaning, foam bonding and dry cleaning. N-acetyl (propyl)cysteinea (NPAS) is its metabolite. Studies have shown that 1-bromopropane is a neurotoxin as well as a reproductive toxin, it can cause sensory and motor deficits. Chronic exposure can lead to decreased cognitive function and impairment of the central nervous system while acute exposure can lead to headaches. Individuals who have elevated levels of 1-bromopropane should examine their environment to determine their route of exposure. The elimination of 1-bromopropane can be accelerated by supplementation of glutathione (reduced) orally, intravenously, transdermally or its precursor N-acetyl cysteine (NAC).

ORGANOPHOSPHATE INSECTICIDAL METABOLITES

- ✓ **Dimethyl Hydrogen Phosphate (DMP) - ORGANOPHOSPHATE**
- ✓ **Diethyl Hydrogen Phosphate (DEP) -ORGANOPHOSPHATE**

Organophosphate is a pesticide, and DMP and DEP are its major metabolites. Organophosphates are among the most toxic and most widely used groups of substances in the world. Their action occurs through the inhibition of the enzyme acetylcholinesterase and other enzymes in which serine is part of the active site, such as dipeptidyl peptidase IV. When acetylcholine degradation is inhibited, overstimulation can lead to constant nerve transmission or overstimulation of neurons or muscles, resulting in excessive salivation, abnormal behavior, diarrhea, urinary incontinence, vomiting, tremors, muscle paralysis, and even death. Elevated levels of exposure have been associated with attention deficit, memory impairment and pervasive developmental disorders in children who come into contact with them or their mothers during gestation. If levels are elevated, toxicity can be measured by decreased cholinesterase or pseudocholinesterase activity in plasma. Acute toxicity is treated with atropine and/or pralidossima. DMP is an important metabolite of the following pesticides: methyl azinfos, methyl chlorpyrifos, dichlorvos, dicrotophos, dimethoate, fenitrothion, fenthion, methyl isazaphos, malathion, methidathion, methyl parathion, naled, methyl oxydemeton, phosmet and methyl pyrimiphos. Exposure to organophosphates can be reduced by eating organic foods, avoiding the use of pesticides in the house or garden, avoiding residence near agricultural areas or golf courses, and staying indoors if insecticides are sprayed. Shampoos for lice, flea collars for pets and flea sprays are also the main sources of organophosphates. Remove sources of exposure if possible. The elimination of organophosphates can be accelerated by the sauna.

HERBICIDE

- ✓ **2,4-Dichlorophenoxyacetic Acid (2,4-D) - HERBICIDE**

2,4-Dichlorophenoxyacetic acid (2,4-D) may result from exposure to this quite common herbicide, intended to kill unwanted vegetation such as broadleaf weeds and woody plants. 2,4-D acid was part of a chemical mixture called Agent Orange, used by the United States during the Vietnam War to increase the visibility of warplanes by destroying undergrowth and crops. People may be exposed to herbicides by breathing them either by skin contact from their residential use or by living near application sites and/or eating contaminated food and drinking contaminated water. 2,4-D acid has a half-life of about 12-36 h. Exposure through contact or ingestion is associated with neuritis, weakness, nausea, abdominal pain, headache, dizziness, peripheral neuropathy, stupor, seizures, brain damage and impaired reflexes. 2,4-D acid is a known endocrine disruptor and can block the distribution of hormones and cause glands to break. It is also linked to damage to the immune system, birth defects and reproductive problems due to its frequent contamination with dioxins. Reduce exposure by eating organic foods and avoiding the use of pesticides in your home or garden. 2,4-D elimination can also be accelerated by sauna treatment and detoxification protocols with niacin supplementation, vitamin B12 therapy, and glutathione supplementation (reduced).

PYRETHROID INSECTICIDE

✓ 3-Phenoxybenzoic Acid (3PBA) - PYRETHROIDS

3-phenoxybenzoic acid (3PBA) is the result of exposure to pyrethroid insecticides (pyrethrins). Pyrethrins are the collective name of a group of pesticide compounds derived from pyrethrum flowers of the genus Chrysanthemum that includes permethrin, cypermethrin, deltamethrin, cyhalothrin, phenpropatrine and trihalometrine. Pyrethroids are synthetic analogues of pyrethrins. Pyrethroids can affect neurological development, disrupt hormones, induce cancer, and suppress the immune system. Pyrethroids are axon poisons that work by keeping sodium channels in neuronal membranes open. Inhaling elevated levels of pyrethrins or pyrethroids may result in asthmatic breathing, sneezing, stuffy nose, headache, nausea, incoordination, tremors, convulsions, redness and swelling of the face, and burning and itching sensation. Most pyretrin and pyrethroid formulations also contain piperonyl butoxide, which inhibits cytochrome P-450, increasing insecticidal efficacy by slowing the metabolic degradation of pyrethrins and pyrethroids. Therefore, the toxicity of such products may be enhanced by simultaneous exposure to piperonyl butoxide. Exposure of animals to these chemicals causes abnormal behavior and neurological symptoms. Exposure during pregnancy doubles the likelihood of autism. Remove all sources of exposure. Elimination can also be accelerated by sauna treatment and detoxification protocols with niacin supplementation, vitamin B12 therapy and glutathione supplementation (reduced).

REFERENCES:

- National Research Council (US) Committee on Acute Exposure Guideline Levels, Xylenes Acute Exposure Guideline Levels, National Academies Press (US), 2010.
- Kandyala R, Raghavendra SC, Rajasekharan ST. Xylene: An overview of its health hazards and preventive measures. J Oral Maxillofac Pathol 2010; 14:1-5
- Ziegler-Skylakakis, K., Fabri, J., Graeser, U. and Simo, T.A. (2023). Xylenes. In Ullmann's Encyclopedia of Industrial Chemistry.
- Inoue, O., Seiji, K., Kawai, T. et al. Excretion of methylhippuric acids in urine of workers exposed to a xylene mixture: comparison among three xylene isomers and toluene. Int. Arch Occup Environ Heath 64, 533–539 (1993).
- Klaus Weissermel, Hans-Jürgen Arpe, Charlet R. Lindley, *Industrial organic chemistry*, 4th ed., Wiley-VCH, 2003, ISBN 3-527-30578-5.
- Bogen KT, JM Heilman. Reassessment of MTBE cancer potency considering modes of action for MTBE and its metabolites. Crit Rev Toxicol. 2015; 45 Suppl 1:1-56.
- Kenneth T. Bogen & Jacqueline M. Heilman (2015) Reassessment of MTBE cancer potency considering modes of action for MTBE and its metabolites, Critical Reviews in Toxicology, 45:sup1, 1-56
- Rahimian F, Soleimani E. A review of extraction methods and analytical techniques for styrene and its metabolites in biological matrices. Biomed Chromatogr. Oct 2022; 36(10): E5440. doi: 10.1002/BMC.5440. Epub 2022 Jul 18.
- Capella KM, Roland K, Geldner N, Rey deCastro B, De Jesús VR, van Bemmel D, Blount BC. Ethylbenzene and styrene exposure in the United States based on urinary mandelic acid and phenylglyoxylic acid: NHANES 2005-2006 and 2011-2012. Environ Res. 2019 Apr; 171:101-110. Epub 2019 Jan 10.
- Choi AR, Im SG, Lee MY, Lee SH. Evaluation of the Suitability of Establishing Biological Exposure Indices of Styrene. Saf Health Work. 2019 Tue; 10(1):103-108. Epub 2018 Jul 25.
- Medeiros AM, MG Bird, Witz G. Potential biomarkers of benzene exposure. J Toxicol Environ Health. 1997 Aug 29; 51(6):519-39. doi: 10.1080/00984109708984042. PMID: 9242226.
- Carrieri M, Tranfo G, Pigini D, Paci E, Salamon F, Scapellato ML, Fracasso ME, Manno M, Bartolucci GB. Correlation between environmental and biological monitoring of exposure to benzene in petrochemical industry operators. Toxicol Lett. 2010 Jan 15; 192(1):17-21. doi: 10.1016/J.Toxlet.2009.07.015. Epub 2009 Jul 21. PMID: 19628029.
- Funk SP, Duffin L, He Y, McMullen C, Sun C, Utting N, Martin JW, Goss GG, Alessi DS. Assessment of impacts of diphenyl phosphate on groundwater and near-surface environments: Sorption and toxicity. J Contam Hydrol. 2019 Feb; 221:50-57. doi: 10.1016/j.jconhyd.2019.01.002. Epub 2019 Jan 7. PMID: 30642690.
- Cooper EM, Covaci A, van Nuijs AL, Webster TF, Stapleton HM. Analysis of the flame-retardant metabolites bis(1,3-dichloro-2-propyl) phosphate (BDCPP) and diphenyl phosphate (DPP) in urine using liquid chromatography-tandem mass spectrometry. Anal Bioanal Chem. 2011 Oct; 401(7):2123-32. doi: 10.1007/S00216-011-5294-7. Epub 2011 Aug 11. PMID: 21830137; PMCID: PMC3718013.
- Wang D, Zhu W, Chen L, Yan J, Teng M, Zhou Z. Neonatal triphenyl phosphate and its metabolite diphenyl phosphate exposure induces sex- and dose-dependent metabolic disruptions in adult mice. Environ Pollut. 2018 Jun; 237:10-17. doi: 10.1016/J.ENVPOL.2018.01.047. Epub 2018 Feb 20. PMID: 29466770.
- Hanley KW, Petersen MR, Cheever KL, Luo L. Bromide and N-acetyl-S-(n-propyl)-L-cysteine in urine from workers exposed to 1-bromopropane solvents from vapor degreasing or adhesive manufacturing. Int Arch Occup Environ Health. 2010 Jun; 83(5):571-84. doi: 10.1007/S00420-010-0524-4. Epub 2010 Mar 14. PMID: 20229238.
- Valentine H, Amarnath K, Amarnath V, Li W, Ding X, Valentine WM, Ichihara G. Globin s-propyl cysteine and urinary N-acetyl-S-propylcysteine as internal biomarkers of 1-bromopropane exposure. Toxicol Sci. 2007 Aug; 98(2):427-35. doi: 10.1093/toxsci/kfm126. Epub 2007 May 21. PMID: 17517825.
- Cheever KL, Marlow KL, B'hymer C, Hanley KW, Lynch DW. Development of an HPLC-MS procedure for the quantification of N-acetyl-S-(n-propyl)-l-cysteine, the major urinary metabolite of 1-bromopropane in human urine. J Chromatogr B Analyt Technol Biomed Life Sci. 2009 Mar 15; 877(8-9):827-32. doi: 10.1016/j.jchromb.2009.02.010. Epub 2009 Feb 11. PMID: 19237326.
- Suratman S, Edwards JW, Babina K. Organophosphate pesticides exposure among farmworkers: pathways and risk of adverse health effects. Rev Environ Health. 2015; 30(1):65-79. doi: 10.1515/reveh-2014-0072. PMID: 25741936.
- Doherty BT, Hammel SC, Daniels JL, Stapleton HM, Hoffman K. Organophosphate Esters: Are These Flame Retardants and Plasticizers Affecting Children's Health? Curr Environ Health Rep. 2019 Dec; 6(4):201-213. doi: 10.1007/S40572-019-00258-0. PMID: 31755035; PMCID: PMC8631201.
- Song Y. Insight into the mode of action of 2,4-dichlorophenoxyacetic acid (2,4-D) as an herbicide. J Integr Plant Biol. 2014 Feb; 56(2):106-13. doi: 10.1111/jipb.12131. Epub 2014 Jan 24. PMID: 24237670.
- CJ Burns, Swaen GM. Review of 2,4-dichlorophenoxyacetic acid (2,4-D) biomonitoring and epidemiology. Crit Rev Toxicol. Oct 2012; 42(9):768-86. doi: 10.3109/10408444.2012.710576. Epub 2012 Aug 10. PMID: 22876750; PMCID: PMC3483058.
- Gaaied S, Oliveira M, Barreto A, Zakhama A, Banni M. 2,4-Dichlorophenoxyacetic acid (2,4-D) affects DNA integrity and retina structure in zebrafish larvae. Environ Ski Pollut Res Int. 2022 Dec; 29(56):85402-85412. doi: 10.1007/S11356-022-21793-8. Epub 2022 Jul 6. PMID: 35794326.
- Wan F, Yu T, Hu J, Yin S, Li Y, Kou L, Chi X, Wu J, Sun Y, Zhou Q, Zou W, Zhang Z, Wang T. The pyrethroids metabolite 3-phenoxybenzoic acid induces dopaminergic degeneration. Ski Total Environ. 2022 Sep 10; 838(Pt 2):156027. doi: 10.1016/J.Scitotenv.2022.156027. Epub 2022 May 20. PMID: 35605864.
- Guvenc D, Inal S, Kuruca N, Gokmen S, Guvenc T. Synthetic pyrethroids common metabolite 3-phenoxybenzoic acid induces caspase-3 and Bcl-2 mediated apoptosis in human hepatocyte cells. Drug Chem Toxicol. 2022 Sep; 45(5):1971-1977. doi: 10.1080/01480545.2021.1894720. Epub 2021 Mar 11. PMID: 33706615.
- Lehmler HJ, Simonsen D, Garcia AQ, Irfan NM, Dean L, Wang H, von Elsterman M, Li X. A systematic review of human biomonitoring studies of 3-phenoxybenzoic acid, a urinary biomarker pyrethroid insecticide exposure, 1997 to 2019. Hyg Environ Healh Adv. 2022 Dec;4:100018. doi: 10.1016/j.heha.2022.100018. Epub 2022 Aug 13. PMID: 36644572; PMCID: PMC9838198.