

Mitochondrial membrane TL protein studies [TL]

[TL] scavenges ADP from cytoplasm and returns ATP from re-conversion plus 'new' ATP from oxidative phosphorylation. [TL] can be blocked by xenobiotics and/or partial detoxification products. The site is also pH sensitive and can be affected by local or general acidosis including organic acid accumulation from anaerobic metabolism. [TL] efficiency is also compromised by increases in intracellular calcium. **The test sequence** examines the white cell mitochondria using phase-contrast, dark field and polarising microscopy. We search for [TL] adducts using a micro-plate array of fluorescence probes. Positive indications are explored at the molecular level. Detailed fluorescence microscopy at extreme magnifications employs de-convolution and Helicon FocusPro™ software.

<u>Initial examination:</u>	<u>Patient's result</u> ↓	<u>Fluorescent indicators or micro-electrode studies:</u>			
Mitochondria numbers of:	Normal	Outer membrane pH	< 6.8 (low)	6.8 – 7.4 normal	> 7.4 (high)
Mitochondrial clumping	See #1	Patient's result:	6.6		
Mt-membrane structure	See #2	Outer membrane Ca ²⁺	< 200 normal	200 – 300 borderline	> 300 nmol/l raised
Mt-DNA fluorescence	High #3	Patient's result:	125		
Mt-membrane binding: →	Proteins	Esterases	Lipids	Diolein	Aldehydes
Patient's results: →	Normal	Normal	Normal	ND	High #2

(ND = not detected)

<u>Chemical on TL sites</u>	<u>Amount</u>	<u>Comment</u>
p-dichlorobenzene	Moderate	Acumen lab-notes attached.
CTAB (Cetrimide)	Moderate	Acumen lab-notes attached.
Antimony complex	Mild on TL	#1 Sb-actin binding (high).
#2 Oxidative damage.		#3 ? Antibiotic, other drug or a dye.
Low intracellular pH	(6.6)	Anaerobic shift. Poor ATP-access.

Mt membrane K: Normal

Mt membrane Mg: Low-norm

Mt membrane Zn: Low

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Laboratory notes p-dichlorobenzene

Other names: 1,4-dichlorobenzene, PDB, pDCB, Paracide, Para-zene, Paramoth, Di-chloricide.

Uses: Moth/insecticide in industrial and domestic use including 'moth-proofing' of carpets and some textiles. A space-deodorant in air fresheners intended for domestic environments, cars and some office/industrial enclosures. It is widely used in lavatory-bowl blocks and diaper-pail deodorizers. In the chemical industry it is an intermediate in the production of plastics and electronic components.

Toxic symptoms include: profuse rhinitis, headache, anorexia, nausea and vomiting, weight loss, jaundice and cirrhosis. Eye irritation and periorbital swelling can occur at quite low levels and some people become very sensitive to direct contact that results in skin irritation and, occasionally, signs of systemic toxicity.

Carcinogenesis: 'This chemical is reasonable anticipated to be a human carcinogen'. *Report on Carcinogens*, Eleventh Edition (PB2005-104914, 2004) p III-85. See further comments under Acumen test results*

p-dichlorobenzene in Acumen tests: This chemical is one of the most frequent chemical adducts on genomic DNA where the effect depends more on the location of the adduct than its chemical properties. To date, we have a list of more than 15 different gene-locations where this chemical has been responsible for significant blocking of expression. The findings include a significant number of patients where the p53 gene or DNA-ligase expression have been affected. We have also detected pDCB on translocator-sites in mitochondrial membranes.

***In our results,** pDCB DNA-adducts are strongly associated with testicular cancer and prostate cancer in males and, to lesser extent, hormonally-related cancers in females.

Detoxification: pDCB can be conjugated by liver-derived glutathione-S-transferase (GST). At higher concentrations this can lead to the development of an 'abnormal' form of the enzyme as shown by a discrete enzyme band in the affinity chromatography of serum (liver-derived) GST. Partial detoxification may lead to increased presence of pDCB in aqueous regions but, following both acute and chronic exposure, significant concentration are still 'dumped' into fat cells.

Lymphocyte sensitivity to pDCB is reasonably common and is frequently associated with other test abnormalities as above. However, from the test perspective, chronic exposure sometimes only results in lymphocyte sensitivity without measurable accumulation of the chemical in other Acumen tests. In clinical terms, this is deceptive as some of the known toxic symptoms may feature in the history *and* this finding seems to go hand-in-hand with increased incidence of cancer.

Notes by John McLaren-Howard, last update January 2014

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Lab notes regarding the uses/sources of CTAB (Cetrimide)

Cetyl trimethylammoniumbromide is a disinfectant/detergent.

CTAB has had wide use in **hospital and medical practice**, but the incidence of sensitivity to this chemical and its poor record against some organisms has resulted in a decline in its use.

First-aid. CTAB is a major component of some first-aid creams (Savlon etc).

Hand cleaners/soap-substitutes. CTAB is in some industrial hand-cleaners and home-use products designed for hand-cleaning/disinfection.

Shampoos. Some 'medicated' shampoos use CTAB as both a detergent and a bacteriocidal agent.

Comments:

Sensitivity to CTAB seems to be fairly common. It is frequently limited to skin reactions but there do seem to be cases of systemic problems from re-exposure following sensitisation.

CTAB in Acumen test results. We have seen CTAB as a DNA adduct, where the effect will depend on the position of the adduct on the genome – gene blocking etc.

We have also seen CTAB on the translocator sites of the mitochondrial membranes. This lowers ADP to ATP re-conversion and, potentially, the *de novo* production of ATP.

A lymphocyte-sensitivity test for CTAB is available.

Notes prepared by John McLaren-Howard (June 2014).