J. Med. Toxicol. (2013) 9:1–3
DOI 10.1007/s13181-012-0277-4

EDITORIAL

Commentary on "Transdermal DMPS"

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Published online: 6 December 2012

> Falsehood flies, and truth comes limping after it, so that when men come to be undeceived, it is too late; the jest is over, and the tale hath had its effect.
> The Examiner No. XIV (November 9, 1710)

Thus, did Jonathan Swift, an eighteenth century political activist, author, and satirist, characterize the art of political lying [1] several years before his writing of the allegorical Gulliver's Travels, in which he lampooned the pseudoscientific fads and scams of his day. In this issue of the *Journal of Medical Toxicology*, Jennifer Cohen and colleagues provide a simple, elegant evaluation of a modern-day scam, so-called "TD-DMPS" [2]. The dermal application of a preparation of the chelating agent, sodium 2,3-dimercapto-1-propanesulfonate (DMPS), has been promoted and reportedly patented [3] as a treatment for autism. Data exist on both the oral and parenteral absorption and kinetics of DMPS; and increased urinary excretion of a number of heavy metals occurs, irrespective of metal excess, when this compound (now renamed (*RS*)-2,3-bis(sulfanyl)propane-1-sulfonic acid, 1 H_2O sodium salt) is administered orally or parenterally [4]. However, there were no data available as to the dermal absorption of this compound.

Cohen et al. obtained this non-FDA approved product via a compounding pharmacy and applied it to the skin of eight adult volunteers according to a protocol promoted by a practitioner still licensed in North Carolina [3]. Twelve-hour complete urine collections (and a 24-h collection for one individual) were then assayed for both DMPS and changes in urine mercury excretion as an end point of chelator effectiveness. A positive control was also tracked after oral ingestion of the DMPS. There were no notable changes in urinary mercury excretion following dermal application of the DMPS. No subject had detectable plasma or urine DMPS when measured by the FDA Division of Pharmaceutical Analysis (other than one plasma sample from one patient which was thought to have been contaminated by DMPS on the skin at the time of blood draw).

The manufacturer of DMPS (HEYL Chemisch-pharmazeutishce Fabrik) concludes in their product monograph (dated 2008) that

> I cannot imagine that adequate blood levels of DMPS are achieved by sniffing, transdermal or homeopathic administration in order to mobilise and excrete deposits of heavy metals in the body. Furthermore, the sensitivity of the active substance to oxidation must be taken into account with these methods of administration. DMPS should, therefore, be administered only via the oral or parenteral (i.m. or i.v.) route [5].

As noted by Cohen et al., there are a number of considerations, falling within the science of biopharmaceutics [6], important for determining dermal absorption of compounds. One important consideration is lipid vs water solubility. DMPS has an octanol/water partition coefficient (K_{ow}) of 0.083 and is characterized as "insoluble in non-polar solvents" [5]. Placing it in a "highly specialized micro-

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encapsulated liposomal phospholipid transdermal base" [7] does not, in the absence of testing, guarantee incorporation or absorption of a water-soluble compound, particularly one that is more ionized at physiologic pH. In addition, the combination of glutathione in a 3:1 molar basis with DMPS, as is done with this product, would be expected to result in the formation of acyclic and cyclic sulfide dimers, which may or may not be reduced once (if) absorbed [8]. Again, only in vivo testing would answer that question. Finally, the "transdermal" protocol recommended a dose of 1.5 mg/kg applied topically every other day, which is significantly lower than the 10–30-mg/kg daily divided dose recommended for oral or parenteral use by the manufacturer. While one could argue that a child's skin is overall thinner than that of an adult, the absence of *any* detectable absorption, the potential ex vivo chemical interactions, and the low dose compared to recommended regimens, all convincingly demonstrate that this is no more than a homeopathic administration of a chelator by this process. Although the proponent stated in Congressional testimony that results would be published in 2004 [7], a MedLine search in October 2012 is unrevealing.

Despite the absence of data, and in the face of such concerns about absorption and dose, many advocates of a heavy metal toxic etiology for autism (in particular mercury) have incorporated TD-DMPS into their nontraditional practice [9]. The promotion of the practice in week-long seminars (at a reported cost of $20,000 per practitioner) by its originator has been used by some as a "work around" to avoid discipline by state medical boards which had already prohibited their use of parenteral chelating agents for dubious indications.

So how should the medical toxicology community respond? Certainly, fraudulent practices should be exposed, as has been done by Cohen et al. The basis of many practitioners' arguments for effectiveness and efficacy focuses on comparison of post-chelation challenge urine results to normal ranges from the non-chelated population. Unsupported practices such as metal chelation based on misinterpretation of improperly performed and incorrectly reported laboratory testing should stop. American College of Medical Toxicology (ACMT) has appropriately condemned such practices [10, 11]. The Pediatric Environmental Health Specialty Unit group of the Association of Occupational and Environmental Clinics and the American Academy of Clinical Toxicology also have published a summary guide for the general public on improper chelation practices [12]. Certainly, one barrier to success is overcoming false presumptions about the role of inconsequential environmental exposures in disease [13]. The proceedings of the ACMT Symposium on "Use and Misuse of Metal Chelators" held at the CDC earlier this year [11] should be available in the spring 2013. These will provide ACMT members and public health officials with focused messages to help the public—and our patients—to weigh the evidence behind claims of cause and effect, in both disease and its treatment.

We should recognize, however, the frustration and despair that leads members of the public to embrace homeopathy, "detoxifying regimens," and the like. Perhaps, we should evaluate the larger social phenomenon evident in these relationships. Practitioners who claim they are persecuted by "mainstream medicine" promise hope and cure to patients who have often had unsuccessful interactions with mainstream medicine; they have succeeded in forming a relationship. Even though the treatment itself is ineffective and expensive, a casual reading of internet postings and testimonials makes it clear that—often—an effective therapeutic relationship has been established. The challenge for us is: Let us develop a similarly effective relationship with our patients, without fraudulent practices and without bilking them of their life savings.

Conflict of Interest The author has provided testimony before the CT State Medical Board and a US Senate subcommittee regarding alternative medical practices and has participated in the generation and editing of ACMT documents regarding similar issues. He is a member of the Science Advisory Council for a biomonitoring education group, Environmental Health Research Foundation.

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