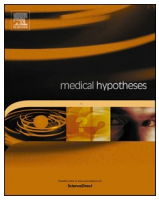
Medical Hypotheses 198 (2025) 111630

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/ymehy



Can serial therapeutic plasma exchange remove synthetic chemicals from humans?

Paul Savage [a,*], Paul S. Anderson [b,c], Jin-Xiong She [d], Pamela W. Smith [e], Patrick Hanaway [f], Ryan Basiorka [a]

[a] MDLifespan Enterprises, LLC, 2400 N. Ashland Ave. Suite 250, Chicago, IL 60614, United States
[b] Anderson Medical Group, DBA P S Anderson LLC, 4110 Cliff Drive, Everett, WA 98203, United States
[c] Bastyr University, 14500 Juanita Dr. NE, Kenmore, WA 98028, United States
[d] Jinfiniti Precision Medicine, Inc., 1235 Walton Way, Augusta, GA 30901, United States
[e] Morsani College of Medicine, University of South Florida, 560 Channelside Dr., Tampa, FL 33602, United States
[f] Family to Family, Functional Medicine: Integrative & Holistic Care, P.O. Box 2256, Weaverville, NC 28787, United States

ARTICLE INFO

Keywords:
Synthetic chemicals
Therapeutic plasma exchange
Chronic exposure
Toxins
Aging

ABSTRACT

Chronic exposure to synthetic chemicals can result in their accumulation in the body and have potentially deleterious effects on physiological functions and cellular processes. Therapeutic plasma exchange (TPE) is generally considered to be a safe outpatient procedure to reduce a number of circulating harmful substances and has been used to treat various autoimmune disorders. We hypothesize that a series of three or five TPE sessions, in conjunction with additional nutritional supplementation, would reduce synthetic chemical levels in adults. To evaluate our hypothesis, a urinalysis of 38 synthetic chemicals (pesticides, herbicides, phenols, volatile organics, parabens, acrylamides, phthalates, and other metabolites) was first conducted in a group of 91 healthy adults; the mean (standard deviation) number of synthetic chemicals detected at moderate or high levels was 3.9 (2.4) per participant. The top three chemicals detected were bisphenol A, a phenolic compound, glyphosate, an herbicide, and butylparaben, a paraben; these chemicals were detected at elevated levels in 60 %, 35 %, and 30 % of the participants, respectively. Subsequently, a subset of 11 participants underwent a series of three or five TPE sessions, combined with nutritional supplementation, and synthetic chemical urinalyses were repeated at 2-weeks, 6-weeks, and 6-months after the last TPE session. Collectively, all synthetic chemical levels elevated at baseline dramatically and significantly ($p \leq 0.0006$) decreased after therapeutic intervention. We conclude that TPE with nutritional supplementation may be a viable therapeutic option to reduce bodily synthetic chemicals. Randomized, controlled trials are warranted to assess potential risks and benefits.

Introduction

Synthetic chemicals were originally created to benefit everyday life, but their widespread presence may have unintentional consequences on the human lives they were intended to improve [1]. Although basic chemical process innovations date back over 17,000 years [2], synthetic chemicals have increased exponentially in the past few decades with approximately 2.3 billion tons of synthetic chemicals produced globally in 2017, a doubling from 2000 [3]. New chemicals are released despite uncertain long-term toxicity [4], and in the U.S. alone, 400 new active chemical components exist in various pesticides [5]. Synthetic chemicals encompass many types of sub-classifications; pesticides, herbicides, phenols, parabens, volatile organic compounds, phthalates, acrylamides, and other related metabolites are examples of synthetic chemical types present in industrialized societies [1,6–8].

Synthetic chemicals can adversely affect health and many are categorized as carcinogens, endocrine disruptors, and/or neurotoxins [1]. Numerous studies have linked pesticides and herbicides, such as glyphosate, to increased cancer risk [9–11]. Phenolic compounds such as bisphenol A and plasticizers, such as phthalates, are endocrine disruptors and are associated with intake of ultra-processed foods due, at least in part, to their packaging material [12,13]. Parabens are considered to be generally safe by the Food and Drug Administration, but recent preliminary research results indicate that chronic, low-level

* Corresponding author at: MDLifespan Enterprises, LLC, 2400 N. Ashland Ave. Suite 250, Chicago, IL 60614, United States.
E-mail address: paul.savage.md@mdlifespan.com (P. Savage).

https://doi.org/10.1016/j.mehy.2025.111630
Received 24 January 2025; Received in revised form 3 March 2025; Accepted 23 April 2025
Available online 24 April 2025

Table 1
The 38 synthetic chemicals assayed, by frequency of occurrence at moderate or high levels, in healthy participants (N = 91).[a]

Toxin	Moderate Levels		High Levels		% Participants Elevated Levels[c]
	Reference Range (μg/g)[b]	% Participants	Reference Range (μg/g)[b]	% Participants	
Bisphenol A	(2.12–5.09)	25 %	>5.09	35 %	60 %
Glyphosate	(1.65–7.6)	22 %	>7.6	13 %	35 %
Butylparaben	(0.25–4.39)	29 %	>4.39	4 %	33 %
Dimethyl Phosphate	(9.1–33.6)	26 %	>33.6	5 %	32 %
Triclosan	(29.9–358)	30 %	>358	0 %	30 %
Tiglylglycine	(0.09–3.24)	26 %	>3.24	0 %	26 %
Dimethylthiophosphate	(5.91–33.7)	22 %	>33.7	3 %	25 %
Dimethyldithiophosphate	(0.67–6.12)	20 %	>6.12	2 %	22 %
2-Hydroxyisobutyric Acid	(795.93–1215.72)	7 %	>1215.72	12 %	19 %
MEOHP	(8.99–23.4)	9 %	>23.4	4 %	13 %
4-Nonylphenol	(0.42–2.06)	5 %	>2.06	5 %	11 %
Atrazine Mercapturate	(0.02–0.05)	7 %	>0.05	4 %	11 %
Phenyl Glyoxylic Acid	(285–518)	3 %	>518	7 %	10 %
Diethyldithiophosphate	(0.17–0.3)	5 %	>0.3	2 %	8 %
Methylparaben	(180–653)	5 %	>653	2 %	8 %
DDA	(7.9–19)	4 %	>19	2 %	7 %
NAE	(82–199)	4 %	>199	2 %	7 %
Propylparaben	(36.7–222)	5 %	>222	0 %	5 %
Perchlorate	(4.89–10.7)	0 %	>10.7	4 %	4 %
Mono-ethyl Phthalate	(94.2–541)	3 %	>541	1 %	4 %
2,4-Dichlorophenoxyacetic Acid	(0.5–1.55)	1 %	>1.55	1 %	2 %
4-Methylhippuric Acid	(65.51–752.72)	2 %	>752.72	0 %	2 %
3-Phenoxybenzoic Acid	(1.01–5.44)	2 %	>5.44	0 %	2 %
Mono-2-ethylhexyl Phthalate	(2.73–8.47)	0 %	>8.47	2 %	2 %
NADB	(374–583)	1 %	>583	1 %	2 %
2-Hydroxyethyl Mercapturic Acid	(1.7–4.75)	1 %	>4.75	1 %	2 %
N-Acetyl Propyl Cysteine	(11.3–46.1)	2 %	>46.1	0 %	2 %
Diphenyl Phosphate	(1.1–3.7)	2 %	>3.7	0 %	2 %
Diethyl Phosphate	(3.2–15.7)	1 %	>15.7	0 %	1 %
Atrazine	(0.02–0.05)	0 %	>0.05	1 %	1 %
3-Methylhippuric Acid	(64.8–612.83)	1 %	>612.83	0 %	1 %
MEHHP	(14.1–37.7)	1 %	>37.7	0 %	1 %
NACE	(5.28–256)	1 %	>256	0 %	1 %
NAHP	(101–403)	1 %	>403	0 %	1 %
Diethylthiophosphate	(1.24–3.92)	0 %	>3.92	0 %	0 %
2-Methylhippuric Acid	(77.9–248)	0 %	>248	0 %	0 %
N-acetyl Phenyl Cysteine	(1.29–3.03)	0 %	>3.03	0 %	0 %
Ethylparaben	(5.41–99.3)	0 %	>99.3	0 %	0 %

Abbreviations: DDA, 2,2-bis(4-chlorophenyl) acetic acid; MEHHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; NACE, N-Acetyl (2-Cyanoethyl) cysteine; NADB, N-Acetyl (3,4-Dihydroxybutyl) cysteine; NAE, N-acetyl-S-(2-carbamoylethyl)-cysteine; NAHP, N-Acetyl (2,Hydroxypropl) cysteine.

[a] Results were characterized to be "acceptable" (0 to < 75th percentile), "moderate" (75th–95th percentile), or "high" (>95th percentile) based upon the National Health and Nutrition Examination Survey (NHANES) data [43].

[b] Reference ranges are normalized to grams of urine creatinine.

[c] Elevated levels refer to values characterized as either "moderate" or "high."

exposure is linked to breast cancer [14,15]. Volatile organic compounds and acrylamides can also pose significant health risks; various volatile organic compounds display nephrotoxicity and/or neurotoxicity and some have been associated with autoimmune disease [16,17]. Acrylamide has been a well-characterized carcinogen for several decades [18]. Although synthetic chemicals have widespread global presence, and many are known to either cause or have strong associations with adverse health outcomes, no proven therapies exist to actively reduce their presence in the body.

Therapeutic plasma exchange (TPE), an extracorporeal therapy that removes and replaces blood plasma [19], is used to treat acute heavy metal poisoning and various conditions, including autoimmune disorders [20–23]. It is generally considered to be a safe outpatient procedure to reduce a number of circulating toxins or other harmful substances [24]. More recently, TPE is being used as a treatment for other diseases and neurologic conditions, e.g., Alzheimer's disease [22,25–31]. Despite being considered a generally safe procedure, TPE has not traditionally been offered as a preventive measure in otherwise healthy individuals. This may be due, at least in part, to its time and cost commitment on the patient as well as initial investment costs for the clinic.

In addition to TPE, intravenous (IV) infusion of nutrients, antioxidants, and anti-inflammatory supplements is becoming an increasingly popular service offered to individuals seeking novel wellness therapies, although their efficacy and long-term effects are unknown. IV and oral nutrition supplementation has been used in disease management; for example, vitamin C in certain types of cancer [32], iron therapy for iron deficiency anemia [33], and selenium in kidney disease [34]. However, whether additional supplementation with these and other antioxidants and related nutrients can beneficially affect healthy adults as a preventive measure needs further exploration.

The hypothesis

We hypothesize that serial TPE, in combination with an additional nutritional supplementation regimen rich in antioxidants and anti-inflammatory components, will be an effective therapy in reducing the synthetic chemical load in humans.

Evaluation of the hypothesis

In addition to the research described above, the scientific literature supports our hypothesis that TPE is effective in decreasing harmful bodily substances as evidenced in both humans and mice models. One study conducted among older subjects who underwent TPE showed that

apoptotic regulators, myeloid/lymphoid markers in circulating cells, and circulatory regulators of several key inflammatory pathways shifted to resemble those in younger control subjects [35]. Essentially, replacing "older" plasma (analogous to the plasma removed with TPE) with fluids that resemble "younger" plasma (analogous to plasma replacement fluid with additional nutritional supplementation therapy) may promote a more "youthful" profile better equipped at attenuating synthetic chemicals in the body. Other studies also conclude that TPE can reduce immunoglobulins, adipokines, and inflammatory markers in select patient groups [36,37]. In mice, heterochronic parabiosis, or conjoining a younger animal with an older animal, was able to decrease the biological age of "old" mice to be more comparable to that of the younger animals and extend their lifespan [38]. Conversely, exposure of "young" mice to plasma from "old" mice decreased cognitive parameters including synaptic plasticity, contextual fear conditioning, and spatial learning and memory [39]. The results from these studies indicate that TPE may be an effective method to reduce potentially harmful substances, both biologic and non-biologic in nature.

The scientific literature also supports our hypothesis that the use of a nutritional supplementation regimen rich in antioxidants and anti-inflammatory components can induce detoxification pathways and potentially reduce the bodily toxin load. Results of a randomized, controlled trial demonstrated that consuming an antioxidant-rich, food-derived, multi-component supplement mix for 28-days can significantly increase antioxidative enzyme activity and total cellular antioxidant capacity in the blood while also decreasing reactive oxygen species [40], all critical detoxification parameters. Although investigators of a recent large-scale observational study concluded that daily oral multivitamin use was not significantly associated with overall health as evidenced by mortality [41], that study only examined basic over-the-counter multivitamins which were not designed to specifically bolster detoxification, anti-inflammatory, and antioxidative pathways. However, a supplementation regimen rich in such nutrients and nutritive components may result in increased detoxification capacity and assist in lowering the synthetic chemical load in the body.

Empirical data

To further evaluate our hypothesis, we first collected empirical data on the prevalence of urinary synthetic chemicals in a cohort of adults without major health conditions and then evaluated whether serial TPE plus a nutritional supplementation regimen rich in antioxidants and anti-inflammatory nutrients reduced their levels versus pre-therapy (baseline). Ninety-one healthy participants (44 female, 47 male) with a mean (SD) age of 57.9 (12.7) years for females and 60.1 (10.6) years for males, who had previously signed up to receive synthetic chemical urine testing for informational and preventive care purposes in the MDLifespan clinic (Chicago, IL), were evaluated. Mean (SD) body mass index (BMI) was 23.9 (6.0) kg/m^2 for females and 26.4 (7.7) kg/m^2 for males. Five participants were black and 86 participants were white. All participants had given informed, written consent for the clinical procedures and analysis. The investigation was conducted in accordance with the Declaration of Helsinki and was exempt from requiring an Institutional Review Board approval under 45 CFR 46.104(d)(4) as determined by WGC IRB Inc., Princeton, NJ (D4-Exemption, November 04, 2024) because only deidentified data were used that were generated as part of clinical care. Participants followed a urine sample collection protocol which included orally ingesting 1500 mg of dimercaptosuccinic acid the evening prior and then collecting the urine sample the following morning with a provided commercial kit; samples were sent to the manufacturer for analysis (Vibrant America, Santa Clara, CA). Thirty-eight synthetic chemicals (Table 1) were assessed in urine samples by a contracted laboratory, Vibrant America (Santa Clara, CA), which quantitatively determined the amount of each urinary synthetic chemical using tandem mass spectrometry methodology [42]. Urine creatinine was assayed using a kinetic colorimetric assay, and the microgram absolute value of each synthetic chemical was then normalized to grams of urine creatinine (μg/g). The creatinine-corrected values were then categorized as "acceptable" (0 to <75th percentile), "moderate" (75th–95th percentile), or "high" (>95th percentile) based on National Health and Nutrition Examination Survey (NHANES) data [42,43]. NHANES data categorizations are presented as the percentiles found in a nationally representative sample and are not indications of their associations with disease or disease risk [43].

Thirty-four of the 38 synthetic chemicals were detected in at least one of the 91 healthy adults who provided samples (Table 1); diethylthiophosphate, 2-methylhippuric acid, N-acetyl phenyl cysteine, and ethylparaben were the four synthetic chemicals not detected in any participant. The mean (SD) number of synthetic chemicals at elevated, i.e., moderate or high, levels per participant was 3.9 (2.4). The top three chemicals detected were bisphenol A, a phenolic compound, glyphosate, an herbicide, and butylparaben, a paraben; these chemicals were detected at elevated levels in 60 %, 35 %, and 33 % of the participants, respectively. Among the other types of chemical classifications, the following were the most frequently detected elevated synthetic chemicals: dimethyl phosphate among pesticides at 32 %, tiglylglycine among other metabolites at 26 %, 2-hydroxyisobutyric acid among volatile organic compounds at 19 %, mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) among phthalates at 13 %, and N-acetyl-S-(2-carbamoylethyl)-cysteine (NAE) among acrylamides at 7 %.

A subset of 11 healthy participants (4 female, 7 male) with a mean (SD) age of 63.8 (10.3) years for females and 61.9 (8.3) years for males chose to undergo the elective, preventive care offered at the MDLifespan clinic. The therapy consisted of either three or five serial TPE sessions, administered at 4-week intervals, and additional nutritional supplementation. Mean (SD) BMI was 21.6 (2.4) kg/m^2 for females and 28.3 (3.1) kg/m^2 for males. All 11 participants were white. Since these were elective therapy services, each of the 11 participants chose which TPE series to undergo; seven participants chose three TPE sessions, and four participants chose five TPE sessions. Pre-therapy, baseline urine samples were collected in the same manner described above, using the urine collection kits. However, for this subset of participants, urine samples were collected and analyzed two weeks and one week prior to commencing the first TPE session. Two baseline samples were collected pre-therapy to mitigate potential fluctuations that may occur either naturally or due to variations in lifestyle, and a synthetic chemical in an individual was only further studied if it was classified as elevated (i.e., "moderate" or "high") at both baseline samplings. Although urine samples may not accurately reflect the total body burden of these chemicals, it is an important component of the body's detoxification system and provided evidence as to whether or not our hypothesis is valid.

During this intervention portion of the hypothesis evaluation, each TPE session utilized a continuous flow cell separator (AMICUS Separator, Fresenius Kabi USA, Lake Zurich, IL), and the estimated plasma volume (EPV) was calculated based on individual parameters (height, weight, and hematocrit). A 0.9–1.2 EPV ratio was targeted for plasma removal, since a 1.0 EPV indicates a complete processing of the participant's plasma. Plasma was replaced with an equal volume of 5 % albumin in saline and administered under continuous flow. Citrate (12:1 ratio, 1.25 mg/kg/min infusion rate) served as the anticoagulant. Each TPE session lasted about four hours and employed a standardized protocol. The first hour included ultrasound guided IV placement, pre-procedure meals, and supplemental oral calcium prior to the session. The plasma exchange session lasted two hours, and fluid balance and glucose levels were monitored throughout each session for safety and adverse event prevention. Participants were monitored by medical staff for potential adverse reactions during and for 60 min following each TPE session; IV nutrition supplementation, detailed below, was administered during this period. Though rare, potential adverse reactions include bruising at the catheter site, muscle stiffness and fatigue, hypoglycemia, hypotension, dizziness, vasovagal syncope, and hypocalcemia [44]. All

Table 2
Average percent change of synthetic chemicals detected at moderate or high levels at baseline in healthy participants from baseline to 6-weeks after completing the final TPE session in a series of three or five TPE sessions with additional nutritional supplementation therapy (N = 11).[a–e]

Toxin	Baseline Detection (n)	Mean (SD) or Median (IQR) Baseline, μg/g	6-WeekPost TPE (n)	Mean (SD) or Median (IQR) % Change from Baseline	P-value[f]
2,4-Dichlorophenoxyacetic Acid	2	1.25 (0.69)	2	−76.7 % (21.8)	–
2-Hydroxyisobutyric Acid	4	2431 (1052)	4	−71.9 % (16.0)	0.0029
4-Methylhippuric Acid	1	76.7	1	−95.6 %	–
4-Nonylphenol	1	0.5	1	−45.1 %	–
Atrazine	1	0.08	1	−88.2 %	–
Bisphenol A	6	5.58 (2.96, 13.81)	5	−71.5 % (−71.8, −43.3)	0.0080
Butylparaben	2	3.44 (4.47)	–	–	–
DDA	1	12.0	1	−17.8 %	–
Diethyldithiophosphate	1	0.21	1	−51.2 %	–
Dimethyldithiophosphate	3	1.05 (1.03, 2.22)	3	−59.3 % (−60.1, −42.8)	–
Dimethyl Phosphate	3	14.2 (6.1)	3	−75.3 % (22.3)	–
Dimethylthiophosphate	2	12.6 (6.5)	2	−39.8 % (17.2)	–
Glyphosate	6	10.0 (7.4)	4	−68.0 % (29.3)	0.0188
N-Acetyl Propyl Cysteine	1	60.2	1	−99.2 %	
NAE	1	123	1	−64.2 %	–
Perchlorate	2	19.2 (2.1)	2	−58.9 % (25.7)	–
Phenyl Glyoxylic Acid	1	1318	1	−80.9 %	–
Triclosan	5	57.8 (26.0)	4	−45.4 % (11.9)	0.0047
MEOHP	5	12.3 (11.1, 24.5)	5	−75.7 % (−95.4, −40.1)	0.0121
Mono-2-ethylhexyl Phthalate	1	31.0	1	−94.7 %	–

Abbreviations: DDA, 2-2-bis(4-chlorophenyl) acetic acid; IQR, interquartile range; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; NAE, N-acetyl-S-(2-carbamoylethyl)-cysteine; SD, standard deviation; TPE, therapeutic plasma exchange.

[a] Classification of "moderate" (75th–95th percentile) or "high" (>95th percentile) values are based upon the National Health and Nutrition Examination Survey (NHANES) data [43].

[b] Values are normalized to grams of urine creatinine.

[c] Results are reported as means and standard deviations (a sample size of two or more). Medians and interquartile range (IQR) limits are reported when mean values were markedly different from median values and non-parametric tests were performed (e.g., Wilcoxon signed-rank tests).

[d] Eleven subjects provided baseline data, and 8 subjects provided data for 6-weeks post-final TPE session.

[e] The following toxins were assessed but not present at "moderate" or "high" levels at baseline: tiglylglycine, atrazine mercapturate, methylparaben, propylparaben, mono-ethyl phthalate, 3-phenoxybenzoic acid, N-acetyl (3,4-dihydroxybutyl) cysteine, 2-hydroxyethyl mercapturic acid, diphenyl phosphate, diethyl phosphate, 3-methylhippuric acid, mono-(2-ethyl-5-hydroxyhexyl) phthalate, N-acetyl (2-cyanoethyl) cysteine, N-acetyl (2,hydroxypropl) cysteine, diethylthiophosphate, 2-methylhippuric acid, N-acetyl phenyl cysteine, and ethylparaben.

[f] P-values presented for synthetic chemicals which were detected in at least four participants at baseline.

sessions were conducted at 4-week intervals.

After each TPE session, participants were provided IV nutritional supplementation and sent home with oral nutritional supplementation to take daily throughout the investigation period (Supplemental Material). The IV nutrition supplementation was administered immediately after each TPE, and the oral nutritional supplementation was initiated one day after the first TPE and continued daily for six months after the last TPE in the series. These formulations were created to support one or more of the following: anti-inflammation, anti-oxidation, detoxification, mitochondrial repair, and/or bolstering energizing metabolic pathways including glycolysis, the Krebs cycle, and oxidative phosphorylation. Urine samples were collected following the same protocol detailed above at 2-weeks, 6-weeks, and 6-months after the final TPE session using the provided commercial kits and were shipped to the manufacturer (Vibrant America, Santa Clara, CA) after each collection for analysis.

An exploratory analysis was conducted on creatinine-corrected synthetic chemical values to assess the percent change in levels of elevated synthetic chemicals from baseline, computed as the average of the two baseline values, to 2 weeks, 6 weeks, and 6 months following the last TPE session. A composite score that represents the overall percent change in elevated synthetic chemicals was computed for each participant as the mean of the percent changes in the individual chemicals. One sample t-tests were performed for individual synthetic chemicals with a sample size of four or more and for the composite score to test the null hypothesis that the percent change was 0. Paired t-tests were performed to assess changes in the number of elevated toxins from baseline to each follow-up. Normality was confirmed using Shapiro-Wilk tests with a significance level of 0.01 and by comparing means to medians. Missing data were not imputed. Due to the small size of this investigation, the analyses were not stratified by the number of TPE sessions received. For participants who opted for three TPE sessions and later extended to five sessions, the data following the third and fifth sessions were averaged at each follow-up. All statistical analyses were conducted using R version 4.3.2 (R Core Team, 2023) and a significance level of 0.05, two-sided. P-values were not adjusted for multiple comparisons since this was an exploratory analysis that will be used to inform the design of future studies.

Of the 11 participants, five participants provided empirical data at all post-final TPE time points (2-weeks, 6-weeks, and 6-months post-final TPE), three participants provided only baseline and 6-week post-final TPE data, and three participants provided only baseline, 2-week, and 6-month post-final TPE data. None of the participants reported any side effects or adverse reactions after the TPE sessions, and throughout the follow up. Hemoglobin, fibrinogen, and platelet levels and markers of kidney and liver function remained stable for all participants throughout the entire observational period (data not shown).

Our preliminary empirical data show that TPE with additional nutrition supplementation therapy resulted in a 17.8 %–99.2 % decrease in all detectible synthetic chemicals 6 weeks after the final TPE session compared to baseline (Table 2). T-tests conducted for synthetic chemicals that were elevated in at least four participants at baseline demonstrated that all synthetic chemicals significantly ($p < 0.05$) decreased after participants completed the series of three or five TPE therapies with nutrition supplementation. Specifically, there were median (interquartile range [IQR] limits) percent decreases from baseline of 71.5 (43.3, 71.8) % in bisphenol A ($p = 0.0080$) and 75.7 (40.1, 95.4) % in MEOHP ($p = 0.0121$). And there were mean (SD) percent decreases from baseline of 68.0 (29.3) % in glyphosate ($p = 0.0188$), 71.9 (16.0) % in 2-hydroxyisobutyric acid ($p = 0.0029$), and 45.4 (11.9) % in triclosan

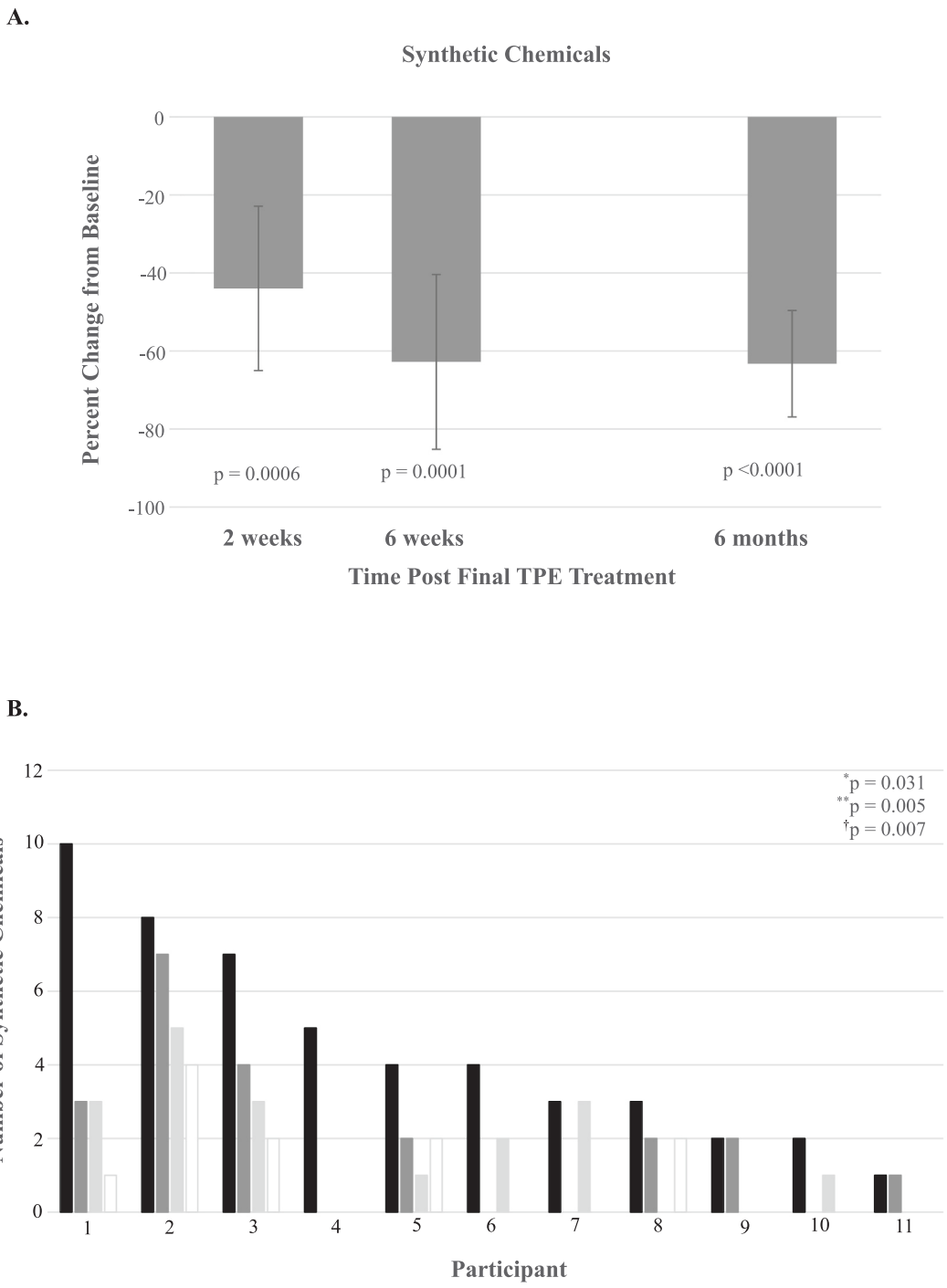


Fig. 1. (A) Average percent change (standard deviation) of all synthetic chemicals, collectively, detected at moderate or high levels at baseline, from baseline to 2 weeks, 6 weeks, and 6 months after completing the final TPE session in a series of three or five TPE sessions with additional nutritional supplementation therapy.[1-3] (B) Number of synthetic chemicals detected in each participant at moderate or high levels at baseline (black bars), 2 weeks (dark gray bars), 6 weeks (light gray bars), and 6 months (white bars) after completing the final TPE session in a series of three or five TPE sessions with additional nutritional supplementation therapy.[1-3] Abbreviations: TPE, therapeutic plasma exchange.
[1]Classification of "moderate" (75th-95th percentile) or "high" (>95th percentile) values are based on National Health and Nutrition Examination Survey (NHANES) data [43]. [2]N = 11 tested participants at baseline; N = 8 tested participants at 2-weeks, 6-weeks, and 6-months post-final TPE session; participants varied for each post-TPE time point assessment, and not all toxins were detected in each participant. Participants 6, 7, and 10 only provided samples at baseline and 6 weeks post-final TPE session, and participants 8, 9, and 11 only provided samples at baseline, 2 weeks and 6 months post-final TPE session. Participants 1 through 5 provided samples at every time point. [3]Signficance in Fig. 1A was assessed using one sample t-tests to test the significance of the overall percent changes. Nominal p-values are reported and not adjusted for multiple comparisons. Significance in Fig. 1B was assessed using paired t-tests to test for differences between the number of synthetic chemicals at baseline versus 2 weeks (*), 6 weeks (**) and 6 months (†) after the final treatment.

($p = 0.0047$). Of note, butylparaben was elevated in two of the 11 participants at baseline but neither of those participants provided urine samples at the 6-week sampling, only at 2-weeks and 6-months post-final TPE session. Mean (SD) percent decreases in butylparaben from baseline to 2-weeks and 6-months post-final TPE in these two participants were 18.8 (16.5) % and 32.2 (0.1) %, respectively. Collectively, the mean (SD) levels of total synthetic chemicals were significantly lower at 2-weeks ($p = 0.0006$) by 44.0 (21.1) %, at 6-weeks ($p = 0.0001$) by 62.8 (22.4) %, and at 6-months ($p < 0.0001$) by 63.3 (13.7) % after the final TPE therapy session (Fig. 1A).

The number of elevated synthetic chemicals ranged from one to 11 when assessing individual participants (Fig. 1B). Notably, the collective synthetic chemical load progressively and dramatically decreased from baseline to 2-weeks post-final TPE therapy session ($p = 0.031$) for the eight participants who provided data at the 2-week post-final TPE. These decreases were also observed for the participants who provided samples at the 6-week post-final TPE therapy session ($p = 0.005$), and for those who provided samples at the 6-month post-final TPE session ($p = 0.007$).

Consequences of the hypothesis

The consequence of our hypothesis that serial TPE, in combination with additional nutritional supplementation, can be an effective synthetic chemical load reduction therapy, is the dramatic, collective, and progressive decrease in all urinary synthetic chemicals detected at elevated levels at baseline throughout the 2-week, 6-week, and 6-month post-final TPE sampling periods in a group of healthy adults. Though preliminary, this observation suggests that serial TPE with nutritional supplementation may substantially reduce the bodily synthetic chemical load. The top three chemicals detected in the original group of healthy adults seeking informational and preventive care were bisphenol A, glyphosate, and butylparaben, and reduction of these synthetic chemicals may have significant health consequences.

Bisphenol A was detected more frequently at elevated levels likely due to the near-ubiquitous presence of this organic, synthetic monomer in the production of polycarbonate plastics commonly used for food and drink packaging, medical devices, and dental material, among others [45]. Given that its hormone-like characteristics may affect body weight, tumorigenesis, metabolism, and male reproductive function, among others [45], investigations of potentially effective reduction methodologies, such as the one presented here, are warranted. Glyphosate, the world's most widely used herbicide [11], was also elevated in the majority of the initial participants in this investigation. Glyphosate is a carcinogen [11], and its presence in urine at elevated levels compared to that of the general population is associated with significantly higher metabolic health risk [46]. Thus, effective reduction methodologies are also warranted for glyphosate. In addition to these two prevalent synthetic chemicals, our empirical data indicated serial TPE with nutritional supplementation may be a viable reduction strategy for other synthetic chemicals since all of those found to be elevated at baseline significantly reduced throughout the sampling period. This includes the pesticide dimethyl phosphate, the volatile organic compound 2-hydroxyisobutyric acid, and the phthalate MEOHP. Preliminary data also show a decrease in at least one acrylamide, although not enough data were available for exploratory statistical analysis. Collectively, these preliminary empirical data and research support from the scientific literature detailed above, validate our hypothesis.

Currently, otherwise healthy individuals who are seeking a robust, minimally-invasive detoxification therapy to reduce potential toxin accumulation due to chronic, day-to-day exposure and to help rejuvenate cellular processes are the ideal candidate for this procedure. Those seeking "rejuvenation" therapies or those who suspect chronic exposure to environmental synthetic chemicals may also be viable candidates since the therapy was developed as a detoxification tool to help eliminate chronic toxin accumulation. As noted, prior research demonstrates that both TPE and intense nutritional supplementation can independently bolster critical cellular and physiological parameters needed for detoxification and "rejuvenation" [35,40]. Ultimately, larger, prospective clinical trials evaluating our hypothesis are needed, as well as studies assessing whether more frequent TPE sessions potentially accelerate clearance, if the amount of TPE sessions affect reduction levels, what portion of the observed reductions are due to the serial TPE sessions versus the intense nutritional supplementation regimen, and if the reductions contribute to health-related outcomes.

Conclusion

To the best of our knowledge, this is the first report that demonstrates that serial (three or five sessions) TPE, in combination with nutritional supplementation, can substantially reduce the amount of urinary synthetic chemicals in otherwise healthy adults. These observations support the potential for health benefits which will need to be confirmed in prospective, randomized, controlled trials.

Funding support

This research was funded by MDLifespan Enterprises, LLC and reports deidentified data collected from patients undergoing the plasma exchange protocol at the MDLifespan Clinic, Chicago, IL.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki and is exempt from requiring an Institutional Review Board approval under 45 CFR 46.104(d)(4) as determined by WGC IRB Inc., Princeton, NJ (D4-Exemption, November 04, 2024) because only deidentified data were used that were generated as part of clinical care. Written, informed consent to participate in the clinical procedures was obtained from all participants involved in the investigation.

CRediT authorship contribution statement

Paul Savage: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Paul S. Anderson:** Resources, Funding acquisition. **Jin-Xiong She:** Writing – review & editing, Validation, Resources, Formal analysis, Conceptualization. **Pamela W. Smith:** Resources, Funding acquisition, Conceptualization. **Patrick Hanaway:** Conceptualization. **Ryan Basiorka:** Validation, Software, Project administration, Formal analysis, Data curation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: MDLifespan Enterprises, LLC, the site clinic of the investigation and the source of funding. P.S. is the owner of MDLifespan Enterprises, LLC. R.B. is an employee of MDLifespan Enterprises, LLC. P.S., P.S.A., J-X.S. and P. W.S. declare stock/stock options from MDLifespan Enterprises, LLC and are members of its Medical Advisory Board. All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

We thank Kevin C. Maki, PhD, Mary R. Dicklin, PhD, Meredith L. Wilcox, MPH, and Orsolya M. Palacios, RD, PhD, of Midwest Biomedical Research for thoughtful discussion and assistance with statistical analyses and technical writing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2025.111630.

References

[1] Naidu R, Biswas B, Willett IR, et al. Chemical pollution: a growing peril and potential catastrophic risk to humanity. Environ Int 2021;156:106616.
[2] Rasmussen SC. Introduction– the role of chemical technology in early civilizations. In: Chemical technology in antiquity. ACS Publications; 2015. p. 1–15.
[3] Valencia RC, Hagan A. The chemical industry under the 4th industrial revolution: the sustainable, digital & citizens one. Wiley-VCH; 2022.
[4] Wang Z, Walker GW, Muir DC, Nagatani-Yoshida K. Toward a global understanding of chemical pollution: a first comprehensive analysis of national and regional chemical inventories. Environ Sci Tech 2020;54:2575–84.
[5] USGS. Pesticide National Synthesis Project: Estimated Annual Agricultural Pesticide Use. https://water.usgs.gov/nawqa/pnsp/usage/maps/county-level/. 2024, Accessed 12-20-2024.
[6] Samarasinghe S, Krishnan K, Naidu R, et al. Parabens generate reactive oxygen species in human spermatozoa. Andrology 2018;6:532–41.
[7] Hales BF, Robaire B. Effects of brominated and organophosphate ester flame retardants on male reproduction. Andrology 2020;8:915–23.
[8] Exon JH. A review of the toxicology of acrylamide. J Toxicol Environ Health B Crit Rev 2006;9:397–412.
[9] Gerken J, Vincent GT, Zapata D, Barron IG, Zapata I. Comprehensive assessment of pesticide use patterns and increased cancer risk. Front Cancer Control Soc 2024;2.
[10] Bassil KL, Vakil C, Sanborn M, Cole DC, Kaur JS, Kerr KJ. Cancer health effects of pesticides: systematic review. Can Fam Physician 2007;53:1704–11.
[11] Cressey D. Widely used herbicide linked to cancer. Nature 2015.
[12] Martínez Steele E, Khandpur N, da Costa Louzada ML, Monteiro CA. Association between dietary contribution of ultra-processed foods and urinary concentrations of phthalates and bisphenol in a nationally representative sample of the US population aged 6 years and older. PLoS One 2020;15:e0236738.
[13] Leti Maggio E, Zucca C, Grande M, et al. Polyphenols regulate the activity of endocrine-disrupting chemicals, having both positive and negative effects. J Xenobiot 2024;14:1378–405.
[14] Tong JH, Elmore S, Huang SS, et al. Chronic exposure to low levels of parabens increases mammary cancer growth and metastasis in mice. Endocrinology 2023;164.
[15] Andersen FA. Final amended report on the safety assessment of methylparaben, ethylparaben, propylparaben, isopropylparaben, butylparaben, isobutylparaben, and benzylparaben as used in cosmetic products. Int J Toxicol 2008;27:1–82.
[16] Tsoukalas D, Fragoulakis V, Papakonstantinou E, et al. Prediction of autoimmune diseases by targeted metabolomic assay of urinary organic acids. Metabolites 2020;10:502.
[17] David E, Niculescu VC. Volatile organic compounds (VOCs) as environmental pollutants: occurrence and mitigation using nanomaterials. Int J Environ Res Public Health 2021;18.
[18] Hogervorst JGF, Schouten LJ. Dietary acrylamide and human cancer; even after 20 years of research an open question. Am J Clin Nutr 2022;116:846–7.
[19] McLeod BC. Plasma and plasma derivatives in therapeutic plasmapheresis. Transfusion 2012;52(Suppl 1):38s–44s.
[20] Yaxley J, Scott T. Dialysis and extracorporeal therapies for enhanced elimination of toxic ingestions and poisoning. Ther Apher Dial 2022;26:865–78.
[21] Rodriguez-Ramirez S, Al Jurdi A, Konvalinka A, Riella LV. Antibody-mediated rejection: prevention, monitoring and treatment dilemmas. Curr Opin Organ Transplant 2022;27:405–14.
[22] Jacob S, Mazibrada G, Irani SR, Jacob A, Yudina A. The role of plasma exchange in the treatment of refractory autoimmune neurological diseases: a narrative review. J Neuroimmune Pharmacol 2021;16:806–17.
[23] Zheng Y, Chou ST. Transfusion and cellular therapy in pediatric sickle cell disease. Clin Lab Med 2021;41:101–19.
[24] Weinstein R. Basic principles of therapeutic plasma exchange. Transfus Apher Sci 2023;62:103675.
[25] Boada M, Kiprov D, Anaya F, et al. Feasibility, safety, and tolerability of two modalities of plasma exchange with albumin replacement to treat elderly patients with Alzheimer's disease in the AMBAR study. J Clin Apher 2023;38:45–54.
[26] Rohrer L, Yunce M, Montine TJ, Shan H. Plasma exchange in Alzheimer's disease. Transfus Med Rev 2023;37:10–5.
[27] Boada M, López OL, Olazarán J, et al. A randomized, controlled clinical trial of plasma exchange with albumin replacement for Alzheimer's disease: Primary results of the AMBAR Study. Alzheimers Dement 2020;16:1412–25.
[28] Bobati SS, Naik KR. Therapeutic plasma exchange – an emerging treatment modality in patients with neurologic and non-neurologic diseases. J Clin Diagn Res 2017;11. pp. Ec35-ec37.
[29] Imbimbo BP, Ippati S, Ceravolo F, Watling M. Perspective: Is therapeutic plasma exchange a viable option for treating Alzheimer's disease? Alzheimers Dement (N Y) 2020;6:e12004.
[30] Escolar G, Páez A, Cid J. Conventional therapeutic plasma exchange versus low volume plasma exchange in chronic pathologies: potential benefit in Alzheimer's disease. Plasmatology 2022;16:26348535221131685.
[31] Edwin Lee MB. Improving biological age, telomere length, and cognition: a case report on the use of therapeutic plasma exchange, peptides, umbilical cord tissue mesenchymal stem cells and exosomes in a patient with cognitive decline. J Restorative Med 2024;14.
[32] van Gorkom GNY, Lookermans EL, Van Elssen C, Bos GMJ. The effect of vitamin C (ascorbic acid) in the treatment of patients with cancer: a systematic review. Nutrients 2019;11.
[33] DeLoughery TG. Iron deficiency anemia. Med Clin North Am 2017;101:319–32.
[34] Iglesias P, Selgas R, Romero S, Díez JJ. Selenium and kidney disease. J Nephrol 2013;26:266–72.
[35] Kim D, Kiprov DD, Luellen C, et al. Old plasma dilution reduces human biological age: a clinical study. Geroscience 2022;44:2701–20.
[36] Guptill JT, Juel VC, Massey JM, et al. Effect of therapeutic plasma exchange on immunoglobulins in myasthenia gravis. Autoimmunity 2016;49:472–9.
[37] Thölking G, Mesters R, Dittrich R, Pavenstädt H, Kümpers P, Reuter S. Assessment of hemostasis after plasma exchange using rotational thrombelastometry (ROTEM). PLoS One 2015;10:e0130402.
[38] Zhang B, Lee DE, Trapp A, et al. Multi-omic rejuvenation and life span extension on exposure to youthful circulation. Nat Aging 2023;3:948–64.
[39] Villeda SA, Luo J, Mosher KI, et al. The ageing systemic milieu negatively regulates neurogenesis and cognitive function. Nature 2011;477:90–4.
[40] Panda C, Komarnytsky S, Fleming MN, et al. Guided metabolic detoxification program supports phase II detoxification enzymes and antioxidant balance in healthy participants. Nutrients 2023;15.
[41] Loftfield E, O'Connell CP, Abnet CC, et al. Multivitamin use and mortality risk in 3 prospective US cohorts. JAMA Netw Open 2024;7:e2418729–.
[42] America V. https://help.vibrant-wellness.com/hc/en-us/categories/10029267716635-Testing-FAQs, Accessed August 15, 2024.
[43] CDC. NHANES 1999-2018: Biomonitoring Data Tables for Environmental Chemicals, Metals and Metalloids. https://www.cdc.gov/exposurereport/data_tables.html. Accessed August 15, 2024.
[44] Balogun RA, Aqui N, Garcia A, et al. Principles of apheresis technology: technical principles of apheresis medicine. American Society for Apheresis; 2020.
[45] Cimmino I, Fiory F, Perruolo G, et al. Potential mechanisms of bisphenol A (BPA) contributing to human disease. Int J Mol Sci 2020;21.
[46] Otaru S, Jones LE, Carpenter DO. Associations between urine glyphosate levels and metabolic health risks: insights from a large cross-sectional population-based study. Environ Health 2024;23:58.