THE CARB-APPROPRIATE REVIEW

A MONTHLY RESEARCH REVIEW BY

CLIFF HARVEY PHD

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ABOUT CLIFF

Cliff Harvey PhD is an author, clinician, and researcher. He was one of the first clinical nutritionists to begin working with ketogenic and low-carb diets, way back in the 1990s and is also considered a pioneer in the area of mind-body integrative healthcare.

Cliff's early post-graduate work was in mind-body healthcare, while his master's research focussed on the use of medium-chain triglycerides to mitigate 'keto-flu' and encourage faster induction of nutritional ketosis.

His doctoral thesis continued to investigate keto-flu and ketogenesis, and the effects of different types of low-carbohydrate diets along with the individualisation of dietary prescription and how 'carbohydrate tolerance' varies from person-to-person.

He is a former world champion strength athlete, submission grappler, and author of several best-selling books, including *The Carbohydrate Appropriate Diet*, *Carb-Appropriate 101*, *Time Rich Cash Optional* and *The Credo.*

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THIS MONTH

DETOX DIETS...LEGIT OR BS?

Key Findings:

- Detox diets do not promote improved clearance of toxins from the body
- Detox diets achieve weight loss due simply to calorie restriction
- Overall, a detox diet is unlikely to improve the clearance of toxins or weight/fat loss over a healthy diet based on unrefined foods
- Some nutrients can help to support the innate detoxification pathways in the body, but these are typically supplied in greater abundance in a good diet based on natural, unprocessed foods

Detox diets are a fixture of the alternative and complementary health scene. They are extremely common and very popular but it's unclear whether they work, or more importantly, if they work as claimed to help the body eliminate dangerous and damaging toxins.

Detoxification diets and programmes were once more commonly known as *liver cleanses*. They are typically promoted to rapidly 'cleanse' the body of toxins, usually through some combination of fasting or food restriction, and the use of various nutrients and herbs to support the liver and other detoxification pathways and channels. Toxins are poisonous substances produced either within the body or another organism (synthetically created 'toxins' are technically called *toxicants*). While they sound scary (and some are!) we need to also remember that many toxic chemicals are produced as part of normal bodily processes, or are ingested in tiny amounts as part of a normal, healthy diet, or as a result of environmental exposure, so, it's important to remember the old adage, *the dose defines the poison!*

> The dose defines the poison!

How does the body detoxify?

Due to the creation of some toxic by-products in the body from metabolic processes, and the inevitability of exposure to some toxic chemicals and heavy metals in the environment, the body has developed sophisticated detoxification pathways to excrete these chemicals. The liver, kidneys, gastrointestinal system, skin, and lungs all play various roles in the excretion of toxins, with various processes such as methylation, metabolism, or conjugation used to produce chemical end-products that can be more easily excreted. Some chemicals though are difficult to convert to excretable forms and can accumulate in the body, especially in fat tissue (like organophosphate pesticides and herbicides, and heavy metals).

Do detox diets work?

This is an interesting question because we need to first understand a little more about the outcomes of the diets (the ones that have been studied at least) and whether the diets work because of, or despite the claims made by promoters of detox diets.

Let's first delve into whether detox diets work for various outcomes.

Do detox diets help the body to eliminate 'toxins'?

There has been limited research conducted on the many detox diets available. A 2014 review published in the *Journal of Human Nutrition and Dietetics* highlighted the lack of thorough, scientifically robust studies on the various detox diets.

> A 2014 review highlighted the lack of scientifically robust studies on the various detox diets

While one of the studies noted a significant improvement in self-reported symptoms associated with poor health, there was no placebo control and other outcome measures (including some markers of phase 1 and 2 liver detoxification) did not differ significantly between groups. Other studies suffered from similar methodological flaws such as lack of a control group, no randomisation, or inconsistencies in comparison groups.[1]

Will a detox help me to lose weight?

Many people do lose weight on detox diets. It's often claimed that this is because 'toxins' encourage the storage of fat, but in all likelihood, it is actually because while following a restrictive detox diet the person simply eats less. Most detox diets involve some combination of fasting, drastic food restriction or elimination of common foods, or unpalatable foods that all result in less energy intake. As an example, a 2015 study demonstrated that the 'Lemon Detox' diet DID help women to lose weight but this

effect was most likely due to calorie-restriction.[2]

Let's face it, any time you drastically restrict calories you will lose weight...and this aspect of detox diets has little do with toxins.

> Let's face it, any time you drastically restrict calories you will lose weight...

Can certain nutrients improve innate detoxification?

While it's unlikely that specific detox diets will help you to lose weight or detoxify any more than an otherwise good diet based on whole, natural, and unrefined foods, some nutrients might help the body to support its own innate detoxification processes and reduce the damage that toxins may create.

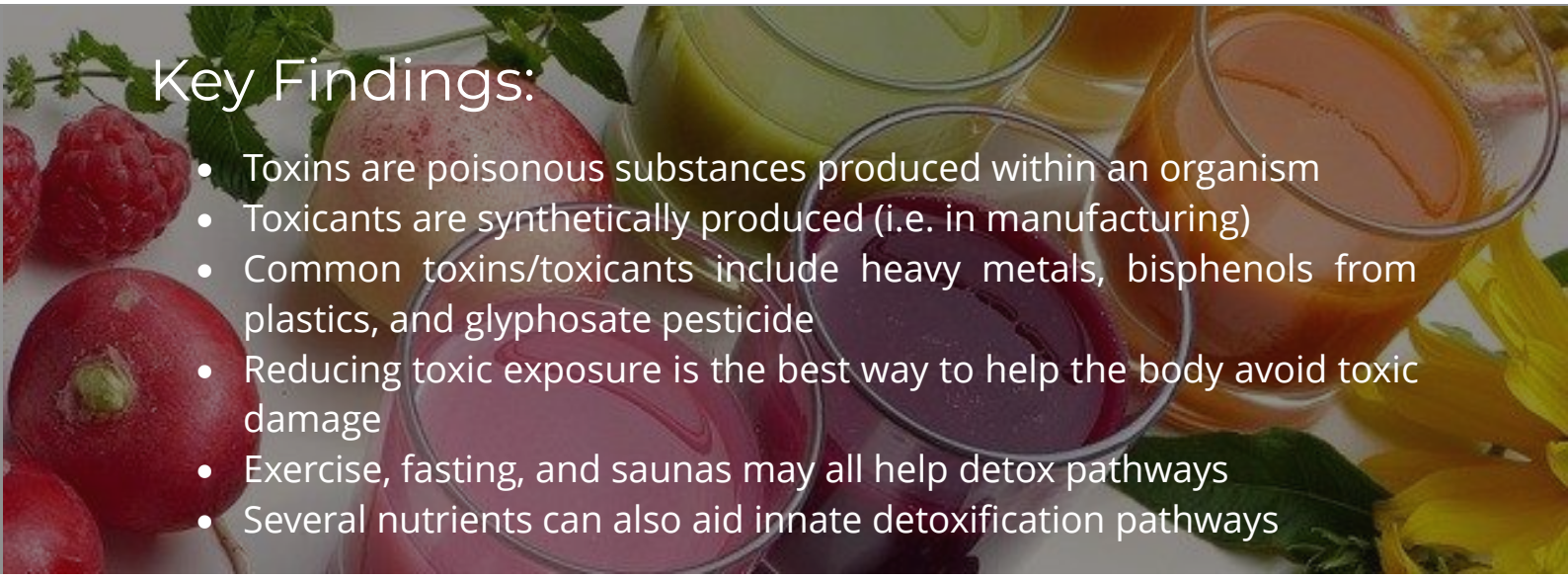
Many nutrients help to support our innate detox pathways and either reduce the toxins that we accumulate or improve their elimination from the body. These include spirulina and chlorella, dandelion,[3-8] folate,[9] alpha-lipoic acid,[10] glycine (in high doses),[11] and a combination treatment of methionine, vitamin C and thiamine.[12]

> It's unlikely that a detox diet will help you to lose more weight than a good nutrition plan

Conclusion

While it's unlikely that a detox diet will help you to lose more weight than a good nutrition plan or remove toxins from the body, eating a natural, unrefined diet that is rich in nutrients and low in toxins and toxicants will help to support the health and performance of the body and support your natural detoxification pathways.

HOW TO SUPPORT THE BODY'S INNATE DETOXIFICATION



Key Findings:

- Toxins are poisonous substances produced within an organism
- Toxicants are synthetically produced (i.e. in manufacturing)
- Common toxins/toxicants include heavy metals, bisphenols from plastics, and glyphosate pesticide
- Reducing toxic exposure is the best way to help the body avoid toxic damage
- Exercise, fasting, and saunas may all help detox pathways
- Several nutrients can also aid innate detoxification pathways

Detoxes and 'cleanses' are some of the most popular diets available and while they probably won't help you to lose any more weight than a good diet or improve your body's ability to remove toxins, certain nutrients and lifestyle changes can help to support your body's own, amazing, innate detoxification pathways.

Toxins are poisonous substances produced either within the body or another organism (synthetically created 'toxins' are technically called *toxicants*). While they sound scary (and some are!) we need to also remember that many toxic chemicals are produced as part of normal bodily processes, or are ingested in tiny amounts as part of a normal, healthy diet, or as a result of environmental exposure, so, it's important to remember the old adage, *the dose defines the poison!*

How does the body detoxify?

Because the body produces some toxic by-products in the body from normal metabolic processes, and the inevitability of exposure to some toxic chemicals and heavy metals in the environment, the body has developed sophisticated detoxification pathways to excrete these chemicals. The liver, kidneys, gastrointestinal system, skin, and lungs all play various roles in the excretion of toxins, through various processes such as *methylation, metabolism*, or *conjugation* which produce chemical end-products that can be more easily excreted.

Some chemicals can be difficult to convert and excrete and can accumulate in the body, especially in fat tissue (i.e. organophosphate pesticides and herbicides, and heavy metals).

Some chemicals can be difficult to convert and excrete and can accumulate in the body

Common toxins and toxicants

Heavy metals

'Heavy metals' are technically metals with high densities, atomic weights, or atomic numbers, but opinions can differ on what exactly constitutes a heavy metal. Heavy metals can include nutrients like iron, cobalt, and zinc, which are essential for health and yet are toxic in large doses, but typically, when people refer to heavy metals in the context of health, they are referring to metals such as lead, cadmium, arsenic, and mercury, which are toxic in even small amounts. Interestingly, in *extremely* small amounts they might act as essential or conditionally essential nutrients too!

In *extremely* small amounts toxic heavy metals might act as essential nutrients

However, modern processing of foods and consumer products, and environmental pollution can accumulate these toxins into dangerous amounts. So, in the case of heavy metals, the old adage, *the poison is in the dose,* is very appropriate!

Arsenic

Elevated levels of this mineral are highly toxic and very dangerous. Arsenic is found in minute doses in many foods and in drinking water and in these minute amounts might be an essential trace nutrient.[13] Based on mammalian studies, a recommended dose of arsenic per day for health is between 12.5 and 25 µg, and people take in around 12-50 µg per day through a normal diet.[13, 14] The World Health Organization (WHO) has set a safe limit of <10 µg /L for drinking water.

Cadmium

Cadmium (Cd) is a heavy metal found commonly in the environment from natural occurrence and contamination. Smokers have the highest exposure to cadmium, while everyday foods are the highest source of cadmium for the non-smoking population. Foods contributing most to dietary cadmium are cereals and cereal products, vegetables, nuts and pulses, starchy roots or potatoes, and meat and meat products. Due to their high consumption of cereals, nuts, oilseeds and pulses, vegetarians can have a higher

dietary exposure to this heavy metal. Cadmium contamination is of concern because it can cause kidney failure, bone demineralisation, and is a carcinogen. The average levels in food have been found to be (approx. 200 µg/kg).[15] A tolerable amount of 7 µg/kg body weight, per week, has previously been set by the European Food Safety Authority, or around 76 µg per day.

> Vegetarians can have a higher dietary exposure to cadmium

Lead

Lead, is a major contaminant of drinking water and food and is extremely toxic at even small doses, and has been shown to hinder neuronal development, particularly in infants.[13]

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Mercury

Mercury poses severe risks to the development of children in utero and in early life. A tolerable amount has been set by the World Health Organisation of 1.6 µg/kg body weight, per week,[16] or around 17 µg per day for an average weight woman.

Bisphenols

Bisphenols such as bisphenol A (BPA) and bisphenol S (BPS) are chemical 'plasticisers' that function as raw materials for the production of many plastics including storage containers, food and beverage packaging, and lacquers and sealants for a range of other products (such as the BPS containing treatments on thermal cash register receipts).[17] These plasticisers have been found in food, house dust, rivers and lakes, and personal care products,[18, 19] and have been identified in human sera, saliva, and urine.[20] They are known to cause appreciable health harms and are toxic to a range of animals and organisms, including humans.[21, 22]

> Bisphenols are known to be toxic to animals, including humans

As knowledge of the harms of BPA has become more well known, there has been a movement towards using different bisphenols in the place of BPA. This has led to an increase in exposure to other chemicals, in particular, BPAF, BPF, and BPS and this has resulted in similar or even greater levels of exposure and accumulation of these chemicals in humans.[23] The various bisphenols; BPA, BPAF, BPB, BPF, and BPS have been shown to exhibit anti-thyroid, oestrogenic or antiandrogenic properties along with hormone-disrupting effects, toxicity and

damage to both cells and genes, reproductive toxicity, immune dysfunction, dioxin-like effects, nephrotoxicity, and neurotoxicity (toxicity to the brain and central nervous system) and are carcinogens (cancer-causing chemicals).[22-25]

Glyphosate

Glyphosate (commercially often seen as "Roundup") is an extremely common herbicide. Its use has become so common that glyphosate residue can be found in many foods, in water, and in many commonly used products (including medical gauze, tampons, and personal care products). While it has been listed as a probable carcinogen by the International Agency for Cancer Research, its effects on human health are controversial, with some claiming that the chemical is safe in the amount humans are exposed to, while others claim there are very real health risks from low-dose exposure. Overall, the effect of glyphosate on health is likely to be very complex in nature as there are potential effects on hormones, and likely detrimental effects on the microbiome, which require further research.[26]

Reducing toxins in your environment

Choose supplements tested for heavy metals

Many supplement companies test their products to meet stringent guidelines for heavy metal contamination.

Choose organic foods

Organic does not always mean low in toxins and toxicants but they are likely to be lower in pesticide and herbicide residue and environmental pollutants.

Choose foods from countries with more stringent quality controls

Some developing nations can have laxer environmental and pollution controls, and this can affect even 'organic' foods. It is safest to choose foods and materials from countries with more stringent environmental pollution laws and those known to have lower levels of heavy metals in groundwater and soil.

Reduce the use of plastics

Replace plastic storage containers with glass wherever possible. If using plastic, make sure that it is only for short periods of time and try to avoid putting acidic or fat-containing foods and beverages in plastic for any length of time. One of the most important things you can do is to never heat up food in the microwave in plastic containers! Stick to glass or microwave-safe ceramics when using the microwave to heat up food.

Exercise

Exercise can promote greater metabolic activity which might speed the clearance of toxins from the body. It is also useful to offset some of the negative effects that can result from some toxins and toxicants by helping to improve oxidative control, increase insulin sensitivity, and encourage

the clearance of damaged and dysfunctional tissue from the body. Endurance exercise-trained rats are able to maintain glutathione status (an important antioxidant involved in detoxification) during paracetamol toxicity compared to untrained rats.[27]

> Exercise-trained rats are able to maintain glutathione status during paracetamol toxicity compared to untrained rats

Fast

Occasional or intermittent fasting can help the body to deal with some of the effects of environmental toxins and toxicants by modulating inflammation, encouraging the removal of dysfunctional and damaged tissue, and improved antioxidant pathways and insulin sensitivity.[28-32]

Sauna

Saunas have re-emerged in popularity in recent years because various 'heat shock proteins' elicited by higher temperatures might be of benefit to health. Several studies have also shown sauna-based detoxes improved health symptom scores and neurotoxicity scores during detoxification of methamphetamine and other illicit drug exposure.[33, 34]

Nutrients that can aid detoxification

Many of the potential toxins (toxicants) that we can be exposed to promote oxidative and other damage in the body. So, nutrients that might help us to avoid accumulating toxins, encourage their detoxification and excretion, and reduce damage are of particular interest. Oxidation, for example, is a normal and essential part of many cellular processes, however excessive oxidation is damaging. Our natural, internal antioxidant pathways rely on a healthy liver, and various micronutrient and macronutrients co-factors. Most of the research that has been performed on dietary and supplemental interventions that might help in various aspects of detox or resistance to toxic chemicals has been performed in animals (due mainly to the ethics of exposing humans to toxic chemicals!) This research offers a glimpse into some nutrition interventions that might improve the resilience of the body.

Reduced accumulation and improved excretion

- **Spirulina** and **dandelion** might help to reduce mercury accumulation.[4] Spirulina with zinc increases the excretion of arsenic in chronic arsenic poisoning,[35] and absorbs cadmium.[8]
- **Chlorella** may be useful in inhibiting the absorption of dioxins via food and the reabsorption of dioxins stored already in the body in the

intestinal tract, thus preventing the accumulation of dioxins within the body. [5] Research performed in mice also suggests that mercury excretion is enhanced by chlorella.[6, 7]

- **Milk thistle** might help to reduce the entry of toxins into cells.[36, 37]
- **Folate** is critical to the metabolism of arsenic.[9]
- **Alpha-lipoic acid** supports detoxification processes.[10]
- **Glycine** was found to be effective for increasing **glutathione** levels, and reduced malondialdehyde levels and decreased lead levels in bone (with extremely high doses of around 1000mg per kg bodyweight in subject animals).[11]

Reduced oxidation and damage from toxins and toxicants

- Treatment with **cysteine, methionine, vitamin C** and **thiamine** can reverse oxidative stress associated with arsenic exposure and result in a reduction in tissue arsenic levels.[12]
- **Spirulina** and **dandelion** enriched diets reduce lead and mercury-related oxidation.[3, 4]
- **Spirulina, ginseng, onion** and **garlic** decrease lipid peroxidation and increase endogenous antioxidant levels.[38, 39]
- **Curcumin, resveratrol, Vitamin C, E, selenium** and **zinc** and the bioflavonoid **quercetin** can effectively protect against cadmium-induced lipid peroxidation and reduce the adverse effect of cadmium on antioxidant status.[40-42]
- **Curcumin** significantly protects against lipid peroxidation induced by both lead and cadmium.[43]
- **Milk thistle** reduces oxidative damage from toxicant exposure.[36, 37]

Conclusion

The body has an amazing capacity to remove toxins and toxicants and while many detox pills and potions won't do anything more than a good diet based on natural and unrefined foods, lifestyle changes and dietary additions can help to support your own internal detoxification pathways to work 'as nature intended'. Eating a varied nutrient-dense, organic diet, exercising, getting enough sleep and occasional fasting can help us to reduce damage from toxins and toxicants and optimise the excretion of any chemical nasties that we might be exposed to.

ALL YOU NEED TO KNOW ABOUT: THE IMPACT OF PLASTICISERS ON HEALTH

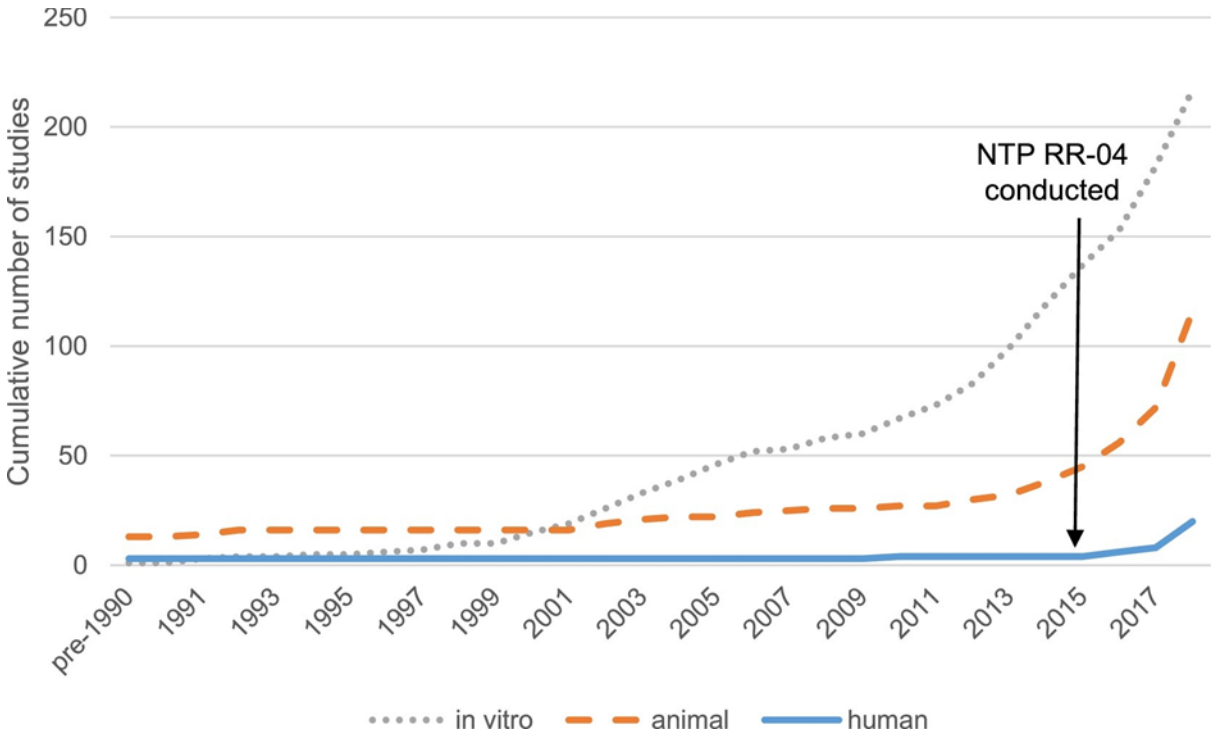
Key Findings:

- The impact of bisphenols on health is becoming more widely studied and understood
- There is now sufficient evidence to consider BPA a significant risk factor for health
- Alternative bisphenols (BPAF, BPF, BPs) are likely to be as toxic as BPA
- Bisphenols are known to be toxic to the kidneys and neurons
- Bisphenols are known endocrine disruptors
- They may increase DNA damage and cancer formation
- Bisphenols may also precipitate weight and fat gain (in children and adults) and increase the risk of diabetes
- Bisphenols might also predispose children to allergy and asthma
- It is unclear whether current intake levels offer an appreciable risk to health, but emerging evidence suggests that previous recommended 'safe' intake levels could still be harmful

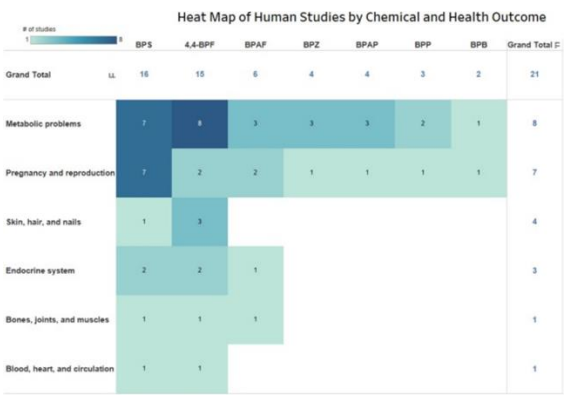
Bisphenols such as bisphenol A (BPA) and bisphenol S (BPS) are chemical 'plasticisers' that function as raw materials for the production of many plastics including storage containers, food and beverage packaging, and lacquers and sealants for a range of other products (such as the BPA or BPS containing treatments on thermal cash register receipts).[17] They are one of the most common industrial chemicals that we come in contact with due to our extraordinary use of products made from plastic. These plasticisers have been found in food, house dust, rivers and lakes, and personal care products,[18, 44] and in a review of 500 studies, BPA was found in greater than recommended levels in effluent, surface water, sewage, sediment, soil, air and other environments in more than 50% of samples from Europe, Asia, and North America.[45] They have also been identified in human blood, saliva, and urine samples.[20] While some

exposure items like thermal paper, may not appreciably increase internal exposure (i.e. we don't know exactly how well it is absorbed through the skin), it is known that BPA is transferred from thermal paper to the skin and can be absorbed,[46] and we ingest the bisphenols as a result of food and beverages stored in plastic or exposed to it during processing.

There were, up until relatively recently, relatively few studies on the toxicity and effects of bisphenols but in recent years, much larger amounts of data are emerging. (See figures below)



BPA had typically been considered a low-risk substance with little potential for harm. However, it is now known that it can cause appreciable health harms, even at low doses,[47] and is toxic to a range of animals and organisms including humans.[21, 22, 48] In a study which evaluated BPA *from milk alone*, exposure levels were considered to be a concern to human health.[19]



As knowledge of the health effects of BPA have become more well known, there has been a movement towards using alternative bisphenols in its place. This has led to an increase in exposure to other bisphenol chemicals, in particular, BPAF, BPF, and BPS, and this has resulted in similar or even greater levels of exposure and accumulation of these chemicals in humans.[23] The various bisphenols; BPAF, BPB, BPF, and BPS (and not just BPA), have been shown to exhibit anti-thyroid, oestrogenic, and antiandrogenic properties. These analogues also exhibit hormone-disrupting effects, toxicity and damage to both cells and genes, reproductive toxicity, immune dysfunction, dioxin-like effects, nephrotoxicity (damage to the kidneys), and neurotoxicity (toxicity to the brain and central nervous system) and are carcinogens (cancer-causing chemicals).[22-25] BPA analogues are, in many cases, even more toxic than the BPA they replace.

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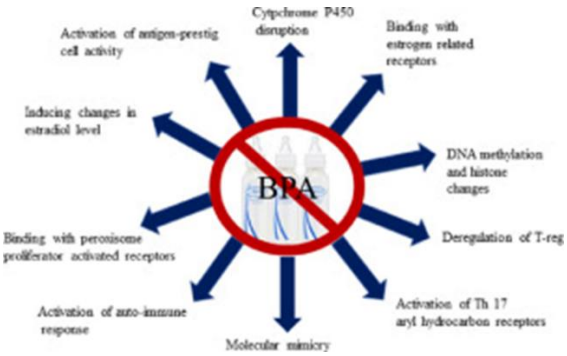
For example, BPB is more acutely toxic and cytotoxic (toxic to cells) and more oestrogenic than BPA,[20] while the evidence for the toxicity of BPS is somewhere between less toxic, but most likely to be at least as toxic as BPA.[44, 49]



Summary of Major Effects of Bisphenols

While there is a suggestion that in utero exposure to bisphenols leads to fat-gain in children, reviews of the evidence show conflicting results for the effects of prenatal bisphenol exposure on children's weight and body fat levels.[50] The other bisphenols used to replace BPA are also likely to increase childhood obesity.[51] Chemical breakdown products from the environmental degradation of bisphenols could also be hormone disruptors.[52] It is only recently (in a 2018 review of 15 studies on metabolomics of BPA) that some of the implications for metabolism in humans have been recognised, with glycolysis, Krebs cycle intermediates, oxidation of long-chain fatty acids, pentose phosphate pathway, nucleoside metabolism, branched-chain amino acid metabolism, aromatic amino

acid metabolism, and sulphur-containing amino acid metabolism significantly changed after BPA exposure.[53] These findings suggest that bisphenols have a complex range of toxic effects in humans.

Bisphenols have a complex range of toxic effects in humans

BPA

The majority of the research on the health effects of bisphenols has come from the study of BPA. Overall, BPA is suspected to be associated with many chronic metabolic diseases. In a major review of observational studies measuring urinary BPA and including at least 100 participants, there was found to be a significant association between BPA levels (highest vs. the lowest urinary BPA) and:

- Diabetes (OR 1.47, 95 % CI: 1.21–1.80)
- Overweight (1.21, 95 % CI: 0.98–1.50), obesity (1.67 , 95 % CI: 1.41–1.98) and waist circumference (1.48, 95 % CI: 1.25–1.76)
- Hypertension (1.41 (95 % CI: 1.12–1.79)

There appears to be a link between BPA and diabetes, coronary heart disease, and weight gain

In prospective studies, there also appears to be a link between BPA exposure and incidence of diabetes, coronary heart disease, and weight gain.[54] And while the link between BPA and type 2 diabetes is controversial, is suggested that this association is not due to chance as the studies typically show either a significant association or a trend towards a likely association.[55]

In reviews of observational studies, there is a consistent finding of reproductive effects, however, the effects on specific hormones and reproductive outcomes are inconsistent.[56] However, there are plausible and proven mechanisms by which BPA acts as a hormone disruptor and the evidence indicates that BPA is likely to increase the risk of infertility in women.[57]

It has also been commonly discussed in the mainstream that hormone disruptors, especially 'xeno-oestrogens' from plastics hasten puberty. In a review of 19 available studies, only seven showed an association between BPA and puberty.[58]

Other outcomes:

Kidney damage

- BPA acts as a biomarker for renal disease and is toxic to the kidneys.[22]

Hormone disruption and sex-effects

- BPA disrupts hormones by increasing oestrogen metabolism in the kidney and upregulating cytochrome p-450 aromatase activity by means of steroidogenesis.[22]
- BPA is an ovarian, uterine and prostate toxicant at a level below the lowest observed adverse effect level (50 mg kg^{-1} body weight) as well as below the proposed safe level (4 µg kg^{-1} body weight).[59]
- Reliable evidence shows a negative effect of BPA on sperm quality and motility.[59]

Cancer formation and DNA damage

- BPA can affect cell signalling processes of growth, division, migration, and autophagy and apoptosis, increasing the risk of cancer formation and growth.[60]
- Low-dose exposure could provide a significant risk for oncogenesis (cancer formation), especially breast cancer risk.[48]
- The epigenetic risks from BPA exposure are typically seen at nM blood ranges (see later in this article for an explanation of how this relates to intakes) and increases in a linear fashion with higher doses.[61]
- A recent (2016) review suggested that "there is substantial evidence from rodent studies indicating that early-life BPA exposures below the oral reference dose lead to increased susceptibility to mammary and prostate cancer. Based on the definitions of "carcinogen" put forth by the International Agency for Research on Cancer and the National Toxicology Program, we propose that BPA may be reasonably anticipated to be a human carcinogen in the breast and prostate due to its tumour promoting properties."[62]

Pregnancy and birth outcomes

- Recent reviews (2017-2019) reviews have demonstrated an association between BPA exposure and birth weight,[63, 64] and developmental defects and miscarriage.[64]

Weight and fat gain

- Higher BPA exposure is likely to increase the risk of obesity in children.[51, 65]
- In adults, reviews of 18 studies (to 2015) were split between no association between BPA exposure and BMI (10 studies) but with a significant association seen in eight studies.[66]

Insulin resistance and metabolic disorders

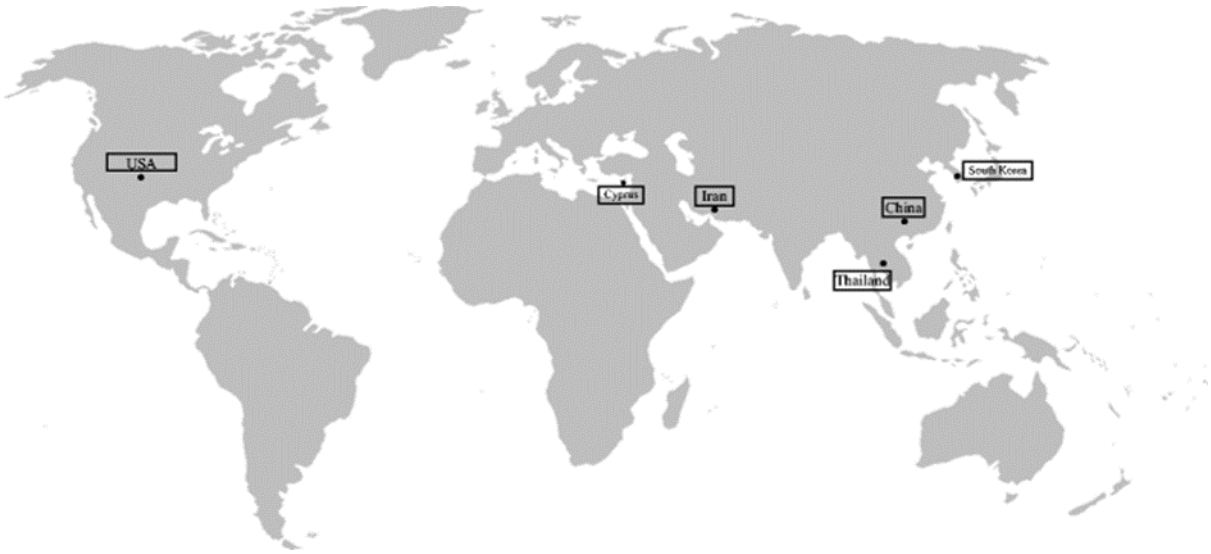
- BPA might be involved in insulin resistance and hyperandrogenism in PCOS.[67]

Behavioural effects

- Early exposure to BPA is linked to increased hyperactivity.[68]
- Prenatal exposure to maternal BPA is associated with higher levels of anxiety, depression, aggression, and hyperactivity in children.[69]

Allergy and asthma

- There is some suggestion that BPA (and phthalates found in plastics) might also predispose children to asthma and allergies.[70, 71]



There have been fewer studies on the alternative bisphenols now being used more commonly than BPA. However, similar effects are now being demonstrated in scientific research.

BPB

- BPB is likely to be anti-androgenic, demonstrating reduced testosterone production in human testes and reducing sperm motility, and number.[20]
- It is similarly oestrogenic, and promotes developmental toxicity, oxidative stress, and reduces cortisol and cortisone.[20]

BPF

- BPF is a potential carcinogen, and genotoxin (causing DNA damage).[20]
- It has a similar oestrogenic activity to BPA and is also anti-thyroid, and results in probable developmental toxicity, and is an oxidative toxicant.[20]

BPS

- BPS has similar or lower toxicity than BPA.[44]
- BPS has similar or less endocrine disruption than BPA.[44]
- It also exhibits similar neurotoxicity and immunotoxicity, and lower reproductive and developmental toxicity[44]

What are suggested safe intakes?

A temporary tolerable daily intake of 4 µg per kilogram of body weight per day and a migration limit of 0.6 mg/kg in food from plastic materials, has been set.[19] To put this in context, the recommended short-term daily tolerable intake for me (an 85kg male) would be ~340mcg.

> The suggestion from animal and human research is that there is a likely risk from exposure levels less than recommended 'safe' amounts

The average daily intake in the US population is estimated to be ~25 ng per day (from BPA alone).[61] This intake amount results in blood levels in the pMol range, while effects are typically seen in *in vitro* at nMol ranges. So, typical levels of ingestion may not result in levels sufficient to induce appreciable damage. However, when we consider the total (and rising) amounts of bisphenols, and other chemicals like phthalates that are incorporated into our food and lifestyle environment, and accumulation in the body, there might be

some cause for concern. As stated earlier, the suggestion from animal and human research is that there is a likely risk from exposure levels less than these apparently 'safe' amounts,[62] and the accumulation of both laboratory and observational evidence showing harm, further urges caution with the use of plastics.

> Typical levels of ingestion may not result in levels sufficient to induce appreciable damage

Other considerations

Because of its abundance in nature, there is also concern that environmental bisphenol exposure could be damaging to plants, fungi, animals, and entire ecosystems. BPA, for example, might affect the growth and viability of many plants.[72] Conversely, the use of some plants and fungi might aid bisphenol pollution control by metabolising these chemicals into non-toxic ones.[72] Of particular concern is the abundant use of microplastics (pieces of plastic less than 5mm in diameter) which provide bisphenols (increasingly BPS) into the environment, and especially aquatic environments.[73] Microplastics are formed through physical degradation of plastic by sun exposure, heat, and stress (such as 'wave slap'). Bisphenols can biodegrade but this takes a long time. Interestingly, BPS increasingly used to replace BPA degrades more slowly in the environment that BPA (due to its unique bond structure).[73] Breakdown products of BPA and other bisphenols that are created as plastics degrade could also exhibit endocrine activities (affecting the hormonal balance of animals) and could have other environmental and ecosystem effects as they accumulate.[52]

What can I do to reduce my bisphenol exposure?

Avoidance is the key to reducing your exposure to bisphenols and the best way to reduce exposure to bisphenols is to reduce the use of plastics. Some plastics are going to be unavoidable in the modern world, but we can drastically reduce our exposure to bisphenols. Remember that *BPA-Free* does not mean bisphenol-free.

- Use glass storage containers wherever possible
- Use a tempered glass or stainless-steel water container (aluminium containers contain plastic coatings)
- NEVER microwave using plastic containers
- Buy foods, liquids and oils in glass containers
- If you work with thermal paper receipts, wear latex gloves

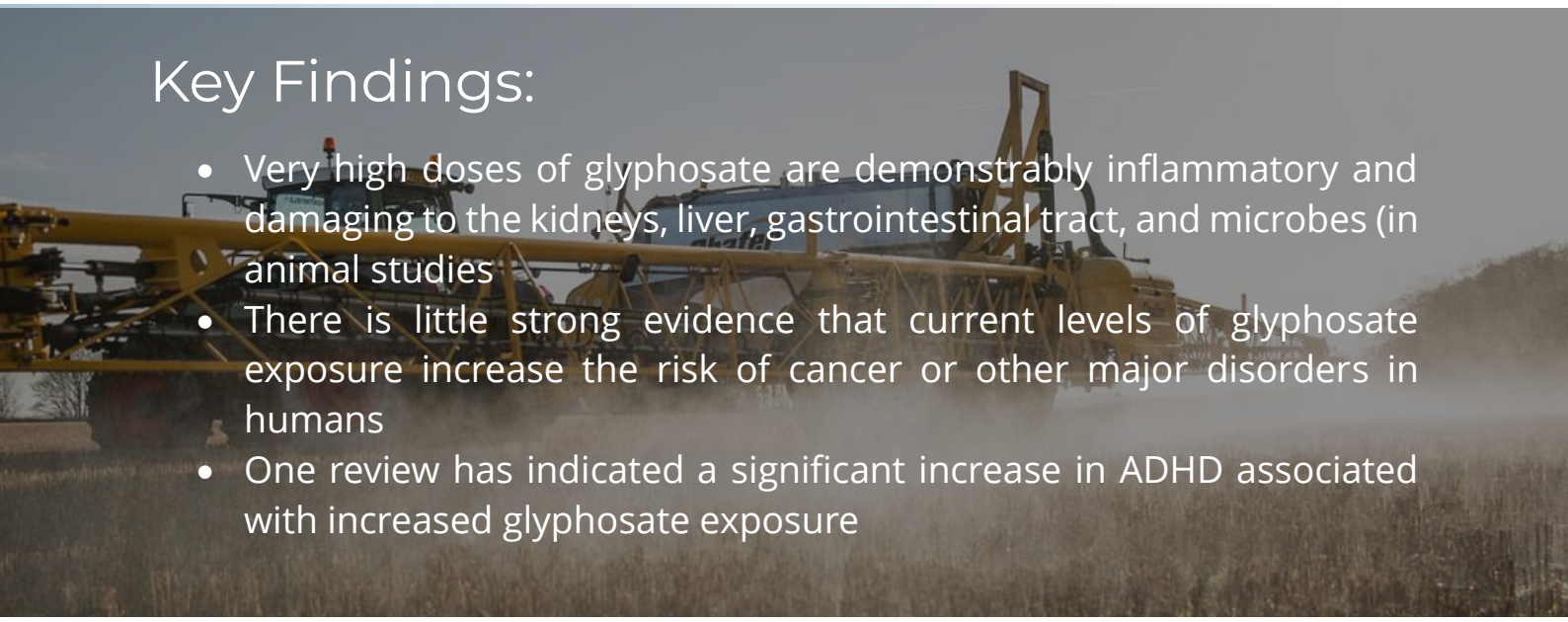
Be especially aware of heating food or beverages in plastic containers. Heat, acid,

and fat all drastically increase the absorption of bisphenols by foods. So, similarly, don't store fatty foods or beverages (like milk), or acidic foods or liquids (i.e. pickles and apple cider vinegar) in plastic bottles.

> Be especially aware of heating food or beverages in plastic containers

It IS OK to store dry foods in plastic, especially bisphenol free plastics like HDTA (such as dry protein powders). However, wherever possible, it is better to store foods in glass, steel, ceramic, or wooden containers (depending on the food of course!).

ALL YOU NEED TO KNOW ABOUT: THE IMPACT OF GLYPHOSATE ON HEALTH



Key Findings:

- Very high doses of glyphosate are demonstrably inflammatory and damaging to the kidneys, liver, gastrointestinal tract, and microbes (in animal studies
- There is little strong evidence that current levels of glyphosate exposure increase the risk of cancer or other major disorders in humans
- One review has indicated a significant increase in ADHD associated with increased glyphosate exposure

Glyphosate is a herbicide ("Roundup") that has become the most commonly used agricultural chemical in the world. There has been a large amount of controversy around the use of this herbicide, especially its possible relation to cancer with the International Agency for Research on Cancer (part of the World Health Organisation of the United Nations) concluding that it is likely to be carcinogenic, while other reviews have disputed this finding, and further papers debating the likely or possible health risks and safety of the herbicide for other health outcomes.[74]

It is clear that the use of glyphosate is enormous and that the chemical can be found ubiquitously in the environment, in water, and in the foods we eat. Glyphosates ubiquitous use has led to it being found in many common products including cereals and grain products, human milk, tampons, medical gauze, honey (both organic and non-organic), and it has also been detected in human urine, demonstrating exposure.[26, 74] There are also very important considerations not just to health, but the environmental impacts on ecosystems from the presence of glyphosate runoff and accumulation in soil and bodies of water.[75, 76]

What health effects have been demonstrated in animal research?

High doses administered to animal subjects can cause kidney damage, reduced growth rates, liver enlargement and inflammation, and gastrointestinal disorders,[74] and is likely to be both genotoxic,[77] and reduce sperm concentrations (based on mouse research).[78] It is also likely that glyphosate through inhibition of the EPSPS enzyme, can destroy bacteria important to human health as part of the intestinal microbiome,[26, 74] and this has provided a controversial hypothesis that glyphosate use may be linked to autism spectrum disorder through the inhibition of the microbiome and resultant growth in clostridia species in the gut.[79]

> It is likely that glyphosate can destroy bacteria important to human health as part of the intestinal microbiome

Animal studies have shown that doses upwards of 100 mg/kg of body weight per day could cause a range of detrimental effects on the liver, bladder, thymus and might be associated with weight gain, colonic ulceration, stomach inflammation, cataracts, liver enlargement, hyperkeratosis, and kidney cell death.[80] However, many of these adverse effects were observed at much higher dosages.

What health effects have been demonstrated in humans?

Overall, systematic reviews and meta-analyses of the effect of glyphosate on cancer are inconclusive and there is no strong evidence that glyphosate causes cancer.[81, 82] Despite the evidence being unclear at best or showing no real association between glyphosate and cancer, the International Agency for Research on Cancer listed glyphosate as a probable carcinogen. Subsequent analyses by the European Union and by the World Health Organisation and Food and Agriculture Organisation suggested no risk.[80, 83] Further reviews, taking into account additional data also disagreed with the IARC report and found no reliable cancer risk.[80, 84, 85] Other reviews have shown no reliable or significant genotoxic risk.[86]

Debate still rages among practitioners and researchers on the carcinogenic potential of glyphosate. If glyphosate is carcinogenic in the amounts that people are regularly exposed to, the reasons are probably complex in nature and may include effects on the microbiome and endocrine system, some of which may take some time to express in observational evidence. It is therefore important that research

continues into the use and rising exposure of humans to glyphosate.[26]

Does glyphosate pose a cardiovascular risk?

Based on results from several mammalian studies (in rats and rabbits), it has been suggested that glyphosate overdose (in workers) might cause conduction disturbances in the heart, and arrhythmias, leading to possible cardiac events.[87]

Glyphosate and pregnancy outcomes

A review of 12 studies on the effects of glyphosate on birth defects, abortions, pre-term deliveries, small for gestational date births, childhood diseases, altered sex ratios, and time-to-pregnancy in glyphosate-exposed populations found no significant associations between this herbicide and adverse pregnancy outcomes.[88]. There was a significant association however in people who apply glyphosate occupationally and Attention Deficit Hyperactivity Disorder (ADHD) (OR = 3.6, 1.3-9.6). However, a recent (2018) review by graduate students at George Washington University found a significant association with neurodevelopmental effects in infants.[89]

What are the 'safe' exposure levels in humans?

A review of studies (> 3000 subjects) found that the average urinary levels of glyphosate in occupationally exposed subjects varied from 0.26 to 73.5 µg/L, while urinary levels from environmental exposure ranged from 0.16 to 7.6 µg/L. Of the studies reviewed, two also measured trends in exposure over time, with both showing increasing numbers of people with detectable glyphosate in their urine over time. [90] So, it is clear that exposure is increasing over time and occupational exposure results in a 2- to 10-fold increase in glyphosate levels in the body.

> It is clear that exposure is increasing over time

A European Union toxicological assessment set an Acceptable Daily Intake level of 0.5 mg per kg of body weight per day in humans,[80] while the United States Environmental Protection agency suggested a 'no adverse effects level' (NOEL) of 100 mg per kg per day and an adjusted daily intake level of 1 mg per kg body weight per day.

However, a 2018 review discussing the implications of the IARC categorisation of glyphosate as a carcinogen proposed that the daily intake thresholds be reduced to 0.175 mg/kg/day to bring the recommendations into line with those recommended by multiple research groups.[26]

Summary and conclusions

1. High doses of glyphosate are demonstrably inflammatory and damaging to the kidneys, liver, gastrointestinal tract, and microbes
2. There is little strong evidence that current levels of glyphosate exposure increase the risk of cancer or other major disorder in humans
3. Significant increases in ADHD have been associated with increased glyphosate exposure

Overall, the evidence shows a demonstrable effect of high dose glyphosate on a range of health outcomes in animals and it could be assumed that these are likely to occur in humans. However, at current exposure levels, there does not appear to be an appreciable risk to humans but exposure to glyphosate is increasing over time and there may be a significant effect on attention and hyperactivity in children and there is a plausible risk for other health outcomes. It seems prudent to limit exposure to glyphosate by:

- Reducing its use around the home (by using non-herbicide/pesticide gardening techniques),
- Using water filters that remove glyphosate
- Choosing organic foods (more likely to contain less glyphosate residue)
- Wearing protective clothing and breathing apparatus if occupationally exposed to glyphosate

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