

## REVIEW

# Detox diets for toxin elimination and weight management: a critical review of the evidence

A. V. Klein<sup>1</sup> & H. Kiat<sup>2</sup>

<sup>1</sup>Faculty of Medicine and Health Sciences, Macquarie University, Sydney, NSW, Australia

<sup>2</sup>Cardiac Health Institute, Sydney, NSW, Australia

### Keywords

energy restriction, detoxification, dietary intervention, toxins, weight loss.

### Correspondence

Hosen Kiat, Faculty of Medicine and Health Sciences, Macquarie University, Building F10A, Ground Floor, 2 Technology Place, Sydney, NSW 2109, Australia.

Tel.: +61 (0)2 9858 9898

Fax: +61 (0)2 9858 2811

E-mail: hosen.kiat@mq.edu.au

### How to cite this article

Klein A.V. & Kiat H. (2014) Detox diets for toxin elimination and weight management: a critical review of the evidence. *J Hum Nutr Diet.* doi: 10.1111/jhn.12286

### Abstract

Detox diets are popular dieting strategies that claim to facilitate toxin elimination and weight loss, thereby promoting health and well-being. The present review examines whether detox diets are necessary, what they involve, whether they are effective and whether they present any dangers. Although the detox industry is booming, there is very little clinical evidence to support the use of these diets. A handful of clinical studies have shown that commercial detox diets enhance liver detoxification and eliminate persistent organic pollutants from the body, although these studies are hampered by flawed methodologies and small sample sizes. There is preliminary evidence to suggest that certain foods such as coriander, nori and olestra have detoxification properties, although the majority of these studies have been performed in animals. To the best of our knowledge, no randomised controlled trials have been conducted to assess the effectiveness of commercial detox diets in humans. This is an area that deserves attention so that consumers can be informed of the potential benefits and risks of detox programmes.

### Introduction

Detoxification or 'detox' diets are short-term interventions designed to eliminate toxins from the body, promote health and assist with weight loss. Detox diets range from total starvation fasts to juice fasts to food modification approaches and often involve the use of laxatives, diuretics, vitamins, minerals and/or 'cleansing foods' <sup>(1)</sup>. A selection of popular commercial detox diets is shown in Table 1. In a recent survey of naturopathic doctors in the USA, 92% of respondents reported using detoxification therapies to treat patients, with 75% reporting the use of diet-based detox measures <sup>(1)</sup>. The most common reasons cited by naturopathic doctors for prescribing detox therapy are environmental exposure to toxins, general cleansing/preventative medicine, gastrointestinal disorders, autoimmune disease, inflammation, fibromyalgia, chronic fatigue syndrome and weight loss <sup>(1)</sup>.

Despite the widespread popularity of detox diets, the term 'toxin' remains ill-defined. In conventional medicine, toxins generally refer to drugs and alcohol, and

'detox' is the process of weaning patients off these addictive substances <sup>(2)</sup>. Approaches to detoxification generally exploit pathways that promote the excretion of chemicals and their metabolites in urine and faeces or extrarenal excretion in sweat or sebum. In the context of commercial detox diets, the term 'toxin' has adopted a much hazier meaning; encompassing pollutants, synthetic chemicals, heavy metals, processed food and other potentially harmful products of modern life. Commercial detox diets rarely identify the specific toxins they aim to remove or the mechanisms by which they eliminate them, making it difficult to investigate their claims. The detox industry finds itself on the notion that chemicals can be neatly divided into 'good' and 'bad' categories; in reality, for the vast majority of chemicals, it is the 'dose that makes the poison'.

To the best of our knowledge, no rigorous clinical investigations of detox diets have been conducted. The handful of studies that have been published suffer from significant methodological limitations including small sample sizes, sampling bias, lack of control groups,

**Table 1** A selection of commercial detox diets

Detox diet	Diet plan	Purported benefits
The master cleanser/lemon detox diet	A 10-day programme in which all meals are replaced with a drink containing lemon juice, purified water, cayenne pepper and tree syrup. Sea salt water and a mild laxative herbal tea are also consumed	Removal of toxins, weight loss, glowing skin, shiny hair and strong nails
The liver cleansing diet	Participants mostly eat vegetarian, high-fibre, low-fat, dairy-free, minimally processed food for 8 weeks. Liver tonics and Epsom salts may also be incorporated	Improved liver function, increased energy levels, removal of toxins, reduction of inflammation and degenerative diseases, better immune function, efficient fat metabolism and weight control
Martha's vineyard Detox Diet® (Martha's Vineyard Diet Detox, Inc., Oak Bluffs, MA, USA)	A 21-day programme in which participants subsist on vegetable juice and soup, herbal tea and specially formulated powders, tablets, cocktails and digestive enzymes	Loss of 9.5 kg (21 lbs), release of toxins and increase of vitality
The Clean Cleanse® (The Clean Program Corp., New York City, NY, USA)	A 21-day programme in which participants consume 'cleanse shakes', 'cleanse supplements' and probiotic capsules for breakfast and dinner. Lunch is a solid meal that must exclude dairy, gluten, processed sugar, soy, corn, beef, pork and some fruits and vegetables	Removal of toxins, improved skin, sleep, digestion, energy, and mental clarity with a reduction in bloating, constipation, headaches and joint pain
Dr Oz's 48-h weekend cleanse	A 48-h programme with quinoa, vegetables, fruit juices and smoothies, vegetable broth and dandelion root tea on the menu	Removal of toxins and improved liver, kidney and colon function
BluePrintCleanse® (BluePrintCleanse, LLC, New York City, NY, USA)	A 3-day programme in which participants subsist on six pre-prepared fruit and vegetable juices per day	Elimination of toxins
Fat Flush® (First Lady of Nutrition, Inc., Post Falls, Idaho, USA)	A 2-week programme in which participants are allowed to consume hot water with lemon, dilute cranberry juice, supplements, pre-prepared cocktails and small meals that are high in protein and vegetables	Removal of toxins, lower stress levels, improved liver function and weight loss
The Hubbard purification rundown	Participants consume increasing doses of niacin in conjunction with a range of A, D, C, E and B vitamins. Minerals including calcium, magnesium, iron, zinc, manganese, copper and iodine are consumed, as well as sodium and potassium electrolytes and a blend of polyunsaturated oils. Participants are also allowed to eat 'balanced meals' but must exercise daily, abstain from drugs and alcohol, and sit in a sauna for up to 5 h per day. The programme generally lasts for several weeks	Removal of fat-stored toxins as well as improved memory, IQ, reaction times, cholesterol levels and blood pressure

reliance on self-report and qualitative rather than quantitative measurements.

The only commercial detox product to have been evaluated clinically is UltraClear® (Metagenics Inc., Aliso Viejo, CA, USA), a medical food supplement that purports to detoxify the liver<sup>(3,4)</sup>. MacIntosh & Ball examined the effects of UltraClear® in 25 naturopathy students, without the inclusion of a placebo control group. A statistically significant (47%) reduction was observed in the volunteers' scores on the Metabolic Screening Questionnaire (MSQ) over the 7-day treatment period. The MSQ comprises a short set of questions designed to gauge the severity of a broad range of health complaints, including headaches,

nausea, genital itch, coughing, chest pain, mood swings, acne and dark circles under the eyes. The rate at which participants cleared a dose of 300–400 mg of caffeine was used to determine the effect of UltraClear® on phase I liver detoxification capacity, whereas the conversion of a dose of 3 g of benzoate was used as a crude measure of phase II glycine conjugation activity. Increases in caffeine clearance and benzoate conversion were observed after the 7-day treatment with UltraClear®, although these changes were nonsignificant.

The only detox programme to have been clinically evaluated is the Hubbard Purification Rundown (Table 1), which was originally developed by L. Ron

Hubbard and the Church of Scientology and used to treat some rescue workers who were exposed to high levels of chemicals after the collapse of the World Trade Center<sup>(5)</sup>. This programme employs niacin supplementation, sweating in a sauna and physical exercise to mobilise stored toxins out of adipose tissue. Participants consume polyunsaturated oils to assist with toxin excretion and are also supplied with a range of vitamins, minerals and electrolytes to 'support healing'. The Hubbard programme was administered to 14 firemen who were suffering from significant memory impairments after exposure to high levels of polychlorinated biphenyls (PCBs) in a transformer fire<sup>(6)</sup>. The firemen's scores on several memory tests reportedly improved after the intervention but the sample size was small and no control group was included.

By applying a similar detox regime, the Foundation for Advancements in Science and Education of the Church of Scientology found statistically significant improvements in blood pressure, cholesterol levels and psychological test scores amongst 103 volunteers compared to a control group of 19 individuals who did not receive treatment<sup>(7)</sup>. The study was limited by lack of randomisation and blinding, and the duration of the intervention period varied widely from 11 to 89 days. The control group did not receive a placebo treatment and the participants were simply re-tested after maintaining their usual lifestyle for 3 weeks. Rather dubiously, the average increase in IQ in the experimental group was reported to be 6.7 points, despite the average intervention length being only 31 days.

Although there is scant clinical evidence available to support the use of commercial detox diets, there are anecdotal reports that they are useful for health promotion and weight loss. Because the lack of research in this field precludes the possibility of a systematic review, we propose preliminary evidence regarding the possible benefits and harms of detox diets and highlight future avenues for research. In particular, attempts will be made to address the following questions:

- What are the specific chemicals to which we are exposed and are they harmful at current exposure levels?
- Is there a role for nutrition in the elimination of toxins?
- Are detox diets useful for weight management?
- Are there any health risks associated with detox diets?

Considering the popularity of detox diets, our opinion is that consumers and medical professionals should be better informed about their possible risks and benefits, and that legislation should be put in place to protect consumers from unsubstantiated claims.

## Exposure to chemicals: should we be concerned?

Global industrialisation has seen a marked rise in the number of chemicals to which we are exposed. In both the European Union (EU) and the USA, approximately 80 000 chemicals are currently in use<sup>(8,9)</sup>. In the EU, regulation introduced in 2007 requires any chemical substance used or produced by companies to be registered<sup>(10)</sup>. For a chemical to be registered, the potential risks and hazards must be assessed (the amount of testing depends on the tonnage produced). To date, the European Chemicals Agency has registered approximately 12 600 substances, meaning that there are thousands still to be tested<sup>(11)</sup>. In the USA, an estimated 2000 new chemicals are introduced into foods and consumer products every year, many of which have not been tested for adverse health effects<sup>(9)</sup>.

It is well-established that some synthetic chemicals accumulate in the human body and that high doses can be toxic<sup>(12)</sup>. Persistent organic pollutants (POPs), for example, are industrial chemicals that accumulate in human adipose tissue<sup>(13,14)</sup>. POPs have been used in flame retardants, pesticides and paints, as well as in coolants and lubricants in electrical equipment. The EU, USA and Australia have been steadily banning POPs since the 1970s, subsequent to studies linking them with endocrine disruption, cardiovascular disease, neurological and developmental defects, metabolic diseases and cancer<sup>(13,15,16)</sup>. The adverse health effects of POPs have mainly been established in animal models and wildlife, although there are several observational studies and cases of accidental poisonings that hint at potential harms in humans<sup>(14)</sup>. For example, in 1973, a group of Michigan residents in the USA were exposed to high levels of POPs known as polybrominated biphenyls (PBBs) when they were mistakenly mixed into cattle feed. Breastfed girls who were exposed to high levels of PBBs *in utero* ( $\geq 7$  parts per billion) during this time had an earlier age of menarche (mean age of 11.6 years) than breastfed girls exposed to lower levels of PBBs *in utero* (mean age of 12.2–12.6 years) or girls who were exposed *in utero* but not breastfed (mean age of 12.7 years)<sup>(17)</sup>. Persistent organic pollutants are known to be transferred to infants via breastfeeding as a result of the accumulation of these chemicals in breast milk<sup>(18,19)</sup>.

The levels of POPs in the ecosystem have been gradually declining since their prohibition, although they are yet to be completely eradicated<sup>(20)</sup>. Even PCBs, chemicals that have been banned or restricted by the EU, USA and Australia since the 1970s, are still detected in almost all human blood, fat and breast milk samples<sup>(20)</sup>. Then again, it should be noted that modern analytical techniques allow very low concentrations to be detected, even down to the subfemtogram scale<sup>(21)</sup>. A study published by the European Food Safety Authority in 2012 reported

that almost all food products contain detectable levels of POPs, particularly fish, meat and dairy products, although these levels have declined since the last assessment in 2002–2004<sup>(22)</sup>. Currently, there is no scientific consensus as to whether current exposure levels to POPs are detrimental to human health, making it unclear whether eliminating them would provide any benefits<sup>(23)</sup>. The detox industry operates on the principle that any level of a foreign chemical in the body should be a cause for concern, although this notion is unsubstantiated. A panel of experts from the United Nations Environment Programme and the World Health Organisation (WHO) concluded in 2012 that, 'although it is clear that certain environmental chemicals can interfere with normal hormonal processes, there is weak evidence that human health has been adversely affected by exposure to endocrine-active chemicals'<sup>(14)</sup>.

Phthalates are another type of chemical to which we are routinely exposed. Phthalates are used in a range of products including cosmetics, food packaging, plastic toys and the capsule coatings of nutritional supplements<sup>(24)</sup>. Concern has been raised over phthalate exposure subsequent to reports that they cause reproductive and developmental problems in laboratory animals<sup>(25)</sup>. Moreover, there are preliminary signs that phthalates have anti-androgenic effects in humans<sup>(26)</sup>. As a result, several phthalates have been restricted for use in children's toys in recent years<sup>(27)</sup>.

Bisphenol A (BPA), which is commonly used in plastic food and drink packaging, has also been linked with numerous health issues, including reproductive changes, cardiovascular disease and diabetes<sup>(28,29)</sup>. BPA is under scrutiny from regulatory bodies in Europe, the USA and Australia; however, at this stage, current exposure levels are not considered to pose any significant health risks<sup>(30–32)</sup>.

Of course, it should not be forgotten that naturally-occurring substances also have the potential to be toxic. Moulds and their volatile metabolites can cause adverse health effects, as well as plant, animal and food allergens<sup>(33)</sup>. Another example is iodine, an element found naturally in the body that can lead to thyroid disorders when consumed in excess<sup>(34)</sup>. In Australia, a class action launched against Bonsoy<sup>®</sup> (Spiral Brands Pty Ltd, Glen Iris, VIC, Australia) in 2010 is continuing to play out, subsequent to the discovery that one of the ingredients in Bonsoy<sup>®</sup> soy milk, a seaweed extract, contained dangerously high levels of iodine.

Finally, certain metals can be toxic to humans. Common examples include mercury, lead, cadmium, arsenic and aluminium<sup>(35–39)</sup>. The level at which each of these metals is considered toxic varies but, in the case of lead, the Centers for Disease Control and Prevention in the USA advise that there is no level that can be considered

to be without some risk to developing infants<sup>(40)</sup>. According to WHO and the Food and Agriculture Organisation of the United Nations (FAO), arsenic levels are problematic in certain regions of the world, such as Bangladesh, where the concentrations in groundwater are relatively high. They assert that, in areas where concentrations of inorganic arsenic in drinking water exceed 50–100 µg L<sup>-1</sup>, there is some evidence of adverse health effects, although lower levels are unlikely to pose serious health risks<sup>(41)</sup>. In the case of mercury, most people have detectable levels, although these levels are not generally sufficiently high to cause adverse health effects<sup>(42)</sup>. Aluminium is ubiquitous in food, air and water, although FAO/WHO advises that an intake of up to 30 mg kg<sup>-1</sup> body weight per day is unlikely to have negative consequences<sup>(43)</sup>. The most common exposure to cadmium is through food; however, the average diet contains less cadmium than the recommended limit<sup>(44)</sup>. As a result, it appears unlikely that the average person would benefit greatly from metal detoxification.

### Is there a role for nutrition in detoxification?

The human body has evolved highly sophisticated mechanisms for eliminating toxins. The liver, kidneys, gastrointestinal system, skin and lungs all play a role in the excretion of unwanted substances<sup>(45)</sup>. The pathways used for detoxification depend on the particular chemical, although they include conversion to a less toxic form (e.g. methylation of arsenic), metabolism or conjugation to produce a water-soluble form for renal excretion, conjugation with glutathione for gastrointestinal elimination, and intracellular metallothionein binding of heavy metals<sup>(33)</sup>.

Foreign chemicals that are not easily removed by these processes include POPs and some metals<sup>(33)</sup>. POPs tend to accumulate in adipose tissue as a result of their lipophilicity and can take years to break down. The half-life of the banned pesticide dichlorodiphenyltrichloroethane (DDT), for example, is 7–8 years<sup>(46)</sup>. Heavy metals can also accumulate in the body, depending on the organic ligands to which they are bound. Mercury has a half-life in blood of approximately 57 days<sup>(39)</sup>, whereas lead has a half-life in bones of 20–30 years<sup>(36)</sup>.

Although there is currently no evidence to support the use of commercial detox diets for removing toxic substances from the body, there are some preliminary studies suggesting that certain nutritional components possess detoxification properties. Considering the vast number of synthetic chemicals to which we are exposed, this is an interesting and worthwhile area of research. It is possible that some of the food items discussed below may provide the basis for an evidence-based detox diet in the future

(if the need for detoxification is established). Table 2 provides a list of these nutritional components.

### Nutritional components for eliminating metals

There is evidence that coriander, malic acid (found in grapes and wine), citric acid (found in citrus fruits), succinic acid (found in apples and blueberries), citrus pectin (found in the peel and pulp of citrus fruits) and *Chlorella* (a type of green algae) exhibit natural chelating properties, suggesting that they may be useful for the elimination of toxic metals <sup>(47–55)</sup>.

Coriander has been shown to reduce cadmium accumulation in the livers of rainbow trout by 20–30% <sup>(50)</sup>. Similarly, when 12-mg doses of coriander were administered to lead-poisoned mice 10 times per week for 25 days, lead concentrations in their bones decreased by approximately 22% compared to the control group <sup>(47)</sup>. However, coriander was not as effective as the clinically approved synthetic chelating agent, meso-2,3-dimercaptosuccinic acid, which decreased lead concentrations by 44%. At this stage, the mechanisms by which coriander enhances heavy metal elimination are unknown, although it is has been proposed that chelating compounds within the herb such as citric acid and phytic acid are responsible <sup>(47,50)</sup>. Because no human studies have been conducted, it is difficult to know how relevant these results are to people.

In mice with aluminium overload, intraperitoneal injections of malic acid, succinic acid and citric acid

significantly increased the faecal excretion of aluminium compared to controls <sup>(48)</sup>. Moreover, citric and succinic acid (but not malic acid) significantly reduced aluminium levels in the bones, which are the main storage sites. It should be noted that the provisional tolerable weekly intake for aluminium set by FAO/WHO is 2 mg kg<sup>-1</sup> body weight <sup>(43)</sup>, whereas the mice in the study received over 50 mg kg<sup>-1</sup> body weight per week. Considering that aluminium intake in humans is markedly lower, it is questionable whether the organic acids used in the study would have any observable detoxification effects in the average person. Consuming adequate levels of iron, calcium and magnesium may be the best way of protecting against excess aluminium storage in the body because deficiencies in these elements are associated with greater aluminium accumulation <sup>(56)</sup>.

*Chlorella* is a unicellular green algae that has been shown to facilitate mercury and lead excretion in mice <sup>(51–53)</sup>. Uchikawa *et al.* <sup>(53)</sup> fed mercury-poisoned mice a powdered form of *Parachlorella beijeirnickii* (a type of *Chlorella*) comprising either 5% or 10% of their diets. After 3 weeks, mercury concentrations in the blood, urine, faeces, brains and kidneys of the mice decreased significantly, whereas a nonsignificant reduction was observed in their livers. In mice dosed with 20 mg of lead, faecal excretion of the metal was increased by 27.7% in those concurrently treated with *P. beijeirnickii* compared to the control group, and blood, kidney and liver levels were significantly lower after 24 h <sup>(51)</sup>. *Chlorella* species contain metal-binding proteins known as

**Table 2** Nutritional components that have been shown to accelerate the elimination of certain chemicals in either experimental animal models or humans

Nutritional component	Chemical eliminated	Evidence in animals or humans?	References
Malic acid	Aluminium	Mice	Domingo <i>et al.</i> <sup>(48)</sup>
Citric acid	Aluminium	Mice	Domingo <i>et al.</i> <sup>(48)</sup>
Succinic acid	Aluminium	Mice	Domingo <i>et al.</i> <sup>(48)</sup>
Citrus pectin	Lead	Humans	Zhao <i>et al.</i> <sup>(55)</sup>
Coriander	Cadmium	Rainbow trout	Ren <i>et al.</i> <sup>(50)</sup>
	Lead	Mice	Aga <i>et al.</i> <sup>(47)</sup>
Selenium	Mercury	Birds, fish, mammals	Ralston & Raymond <sup>(58)</sup>
		Humans	Li <i>et al.</i> <sup>(59)</sup> , Seppanen <i>et al.</i> <sup>(60)</sup>
Chlorella	Mercury	Mice	Uchikawa <i>et al.</i> <sup>(52,53)</sup>
	Lead	Mice	Uchikawa <i>et al.</i> <sup>(51)</sup>
	H <sub>6</sub> CDD	Mice	Takekoshi <i>et al.</i> <sup>(61)</sup>
	PCDDs	Rats	Morita <i>et al.</i> <sup>(62,63)</sup>
	PCDFs	Rats	Morita <i>et al.</i> <sup>(62,63)</sup>
Nori	PCDDs	Rats	Morita & Tobiishi <sup>(64)</sup>
	PCDFs	Rats	Morita & Tobiishi <sup>(64)</sup>
Olestra	HCB	Mice	Jandacek <i>et al.</i> <sup>(76)</sup>
	PCBs	Humans	Jandacek <i>et al.</i> <sup>(77)</sup>

HCB, hexachlorobenzene; H<sub>6</sub>CDD, 1,2,3,4,7,8-hexachlorodibenzo-*p*-dioxin; PCBs, polychlorinated biphenyls; PCDDs, polychlorinated dibenzo-*p*-dioxins; PCDFs, polychlorinated dibenzofurans.

metallothioneins which are considered to assist with metal-detoxification<sup>(49,54)</sup>. It should be noted that *Chlorella* has also been shown to be useful for removing heavy metals from wastewater<sup>(57)</sup>.

Selenium supplementation has been shown to attenuate the toxic effects of mercury in mammals, birds and fish<sup>(58)</sup>. Less is known about the potential of selenium supplementation to assist with mercury detoxification in humans, although a recent study of long-term mercury-exposed individuals in China found that 3 months of selenium supplementation (100 µg day<sup>-1</sup>) almost tripled the urinary excretion of mercury<sup>(59)</sup>. An earlier study found that selenium supplementation decreased pubic hair mercury levels by 34% in healthy volunteers<sup>(60)</sup>. The mechanisms by which selenium assists with mercury detoxification are currently unclear. Selenium is known to have a high affinity for mercury, leading to the formation of mercury selenide (HgSe) complexes<sup>(58)</sup>. However, no HgSe complexes were detected in the urine samples collected by Li *et al.*<sup>(59)</sup>, suggesting that there are other factors at play.

#### Diet-based detox measures for eliminating persistent organic pollutants

In addition to facilitating metal detoxification, *Chlorella* has also been shown to assist with the elimination of some POPs. Takekoshi *et al.*<sup>(61)</sup> administered a type of dioxin, 1,2,3,4,7,8-hexachlorodibenzo-*p*-dioxin (H<sub>6</sub>CDD), to mice before feeding them a 10% *Chlorella pyrenoidosa* diet or a basal diet. During the first week, the *C. pyrenoidosa* diet led to 9.2-fold greater faecal excretion of H<sub>6</sub>CDD than the basal diet. After the fifth week, H<sub>6</sub>CDD excretion was still 3.1-fold higher and liver accumulation was significantly lower in mice fed the *C. pyrenoidosa* diet. Similarly, Morita *et al.*<sup>(62,63)</sup> reported that both *Chlorella* and *Chlorella*-derived chlorophyll enhance the elimination of polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) from rats in a dose-dependent manner. Nori (*Porphyra yezoensis*), another type of algae commonly eaten in Japan, has also been shown to markedly increase faecal elimination of PCDDs and PCDFs in rats<sup>(64)</sup>.

The Hubbard Purification Rundown used in the New York rescue workers' detox project (involving vitamin/mineral supplementation, polyunsaturated oils, sauna and exercise) has been reported to reduce adipose tissue concentrations of PCBs and hexachlorobenzene (HCB) in electrical workers. After 3 weeks of treatment, the body burdens of HCB and PCBs decreased by 30% and 16% in the workers respectively<sup>(65)</sup>. Rea *et al.*<sup>(66)</sup> trialed the programme in 210 volunteers who reported suffering from 'chemical sensitivity', although a control group was not

included. The study claims to have tested blood levels of several chemical categories (pentachlorophenols, PCBs, volatile aliphatic and aromatic chlorinated and nonchlorinated hydrocarbons and organochlorine pesticides) before and after treatment, although the specific compounds are not named and no information is provided on how they were quantified. Instead, it is simply stated that blood toxic chemical levels decreased by 63%. The paucity of data and poor methodologies presented in these studies cast uncertainty over the validity of the results<sup>(1)</sup>. Moreover, concerns regarding the safety of this detox programme have arisen subsequent to reports stating that it can lead to severe hyponatraemia<sup>(67)</sup>.

Another detox programme was trialed in Taiwanese patients who had been exposed to dangerous levels of PCBs. During the 7–10-day intervention, they subsisted on fruit and vegetable juice, milk, boiled soybean juice, vitamins, laxatives and water<sup>(68)</sup>. The participants reported improvements in their health, although the study did not control for the placebo effect. The body burdens of PCBs were not measured before or after the study, making it impossible to conclude whether the detox had any effect. It is also unclear whether this programme would be useful for detoxification amongst people who have not been exposed to high levels of PCBs.

An important consideration is that detox diets involving energy restriction may be accompanied by weight loss, which is known to redistribute POPs from fat stores into the circulation<sup>(69–74)</sup>. This phenomenon has mostly been reported in obese individuals after bariatric surgery<sup>(69,72,74)</sup>, although a 15-week weight loss programme involving moderate energy restriction has also been shown to increase plasma concentrations of a range of POPs, particularly in men<sup>(73)</sup>.

Such redistribution of POPs into the circulation is a major concern because transport to sensitive body organs may ensue. In a study of women exposed to PBBs in Michigan, exposure levels were only a predictor of menstrual alterations in those who had lost weight in the past year. This suggests that PBBs must be mobilised into the bloodstream before they can affect normal ovarian functioning, although the sample size in the study was small<sup>(75)</sup>. Jandacek *et al.*<sup>(76)</sup> examined the effects of 'yo-yo dieting' (alternating periods of fasting and *ad libitum* feeding) on the biodistribution of the lipophilic pesticide, HCB, in mice. As the mice shed body fat, HCB was released into the circulation and carried to the brain and kidneys. The brain burden of HCB almost tripled during the fasting period. There was no significant difference between faecal excretion of HCB during fasting and feeding, suggesting that energy restriction merely altered the biodistribution of POPs, rather than aiding in their elimination.

Interestingly, Jandacek *et al.* <sup>(76)</sup> were able to enhance faecal excretion of HCB 30-fold when they fed mice olestra, a nonabsorbable fat substitute used in some snack foods, including fat-free Pringles<sup>®</sup> (Kellogg's, Battle Creek, MI, USA). Brain accumulation of HCB was also reduced by 50%. It was speculated that the lipophilicity of olestra allowed it to absorb HCB and transport it out of the body via the faeces. A recent study demonstrated that olestra is also a safe and effective way for eliminating PCBs in humans <sup>(77)</sup>. Participants consumed 15 g day<sup>-1</sup> of olestra for 1 year in a double-blind placebo-controlled trial, with the results showing that the elimination rates of PCBs increased significantly.

### Diet-based detox measures for eliminating bisphenol A and phthalates

Compared to POPs, BPA and phthalates have relatively short half-lives in humans of <12 h <sup>(78–80)</sup>. Despite their short half-lives, these chemicals are consistently present in human bodies as a result of their ubiquity in plastic water bottles, food containers and the linings of food and beverage cans. Indeed, BPA can be detected in the urine of >90% of the US population <sup>(81)</sup>. Rudel *et al.* <sup>(82)</sup> have examined whether avoidance strategies can help eliminate BPA and di(2-ethylhexyl)phthalate (DEHP) from people's bodies. Five families ate fresh and organic foods exclusively for 3 days, at the same time as avoiding plastic water bottles. After this detox, the participants' average urinary concentrations of BPA and DEHP fell by 66% and 53–56%, respectively. Interestingly, when Sathyanarayana *et al.* <sup>(83)</sup> attempted a similar intervention in 10 families, they found that DEHP levels rose sharply. Further tests revealed that the coriander and milk used in the detox programme contained high levels of DEHP, suggesting that it is difficult to avoid plastic contamination, even in fresh food.

### Are detox diets effective for weight management?

Currently, no scientific studies have investigated the effectiveness of commercial detox diets for losing weight. Because one of the principal claims of the detox industry is that these diets are useful for shedding weight, this is an area that requires attention. Information regarding the short-term and long-term impact of detox diets on weight and other health measures would be of value to consumers and health professionals, whereas comparisons with other types of dietary modifications are also needed.

In the absence of any clinical evidence, we can only extrapolate from studies of other diets. It is known that dieting in general has an estimated success rate of only 20%

<sup>(84)</sup>. A possible explanation for this lack of success is that animals and humans have evolved mechanisms to defend against weight loss because starvation can lead to reduced fertility and even death <sup>(85)</sup>. Energy restriction is known to alter the expression of certain neuropeptides, particularly in the hypothalamus <sup>(85)</sup>. These changes stimulate appetite and reduce metabolic rate and energy expenditure, leading to the weight loss 'plateau' that is often observed during dieting <sup>(85)</sup>. Moreover, studies in mice have shown that the stressfulness of energy restriction can produce long-term changes in stress neurocircuitry, leading to binge eating later on, although this is yet to be established in humans <sup>(86)</sup>. Mazurak *et al.* <sup>(87)</sup> have shown that fasting for 48 h increases cortisol levels in young, healthy women, whereas Tomiyama *et al.* <sup>(88)</sup> have reported that restricting energy intake to 5.02 MJ day<sup>-1</sup> (1200 kcal day<sup>-1</sup>) for 3 weeks also increases levels of this stress hormone in females. There is convincing evidence that stress stimulates appetite and weight gain through elevations of cortisol <sup>(89)</sup>. Dieting is often a stressful experience because it involves resisting temptation and enduring physically aversive feelings of hunger and deprivation <sup>(88)</sup>.

There are many anecdotal reports of the stressfulness of popular detox programmes. This is not surprising considering the low-energy, nutrient-poor nature of many of these diets. For example, the Excavation Cleanse (part of the BluePrintCleanse<sup>®</sup> (BluePrintCleanse, LLC, New York City, NY, USA) range shown in Table 1) provides only 3.59 MJ (860 kcal) and 19 g of protein per day. According to FAO, the average person's minimum daily energy requirement is approximately 7.03 MJ (1680 kcal) and FAO/WHO recommends that adults should consume 0.83 g kg<sup>-1</sup> body weight of high quality protein per day <sup>(90,91)</sup>. Under these guidelines, the Excavation Cleanse does not meet daily protein requirements for anyone who weighs more than 23 kg. The BluePrintCleanse<sup>®</sup> website warns users that they may experience side-effects such as fatigue, headaches, nausea, insomnia, anxiety and shakiness, although it is claimed that these symptoms result from 'bad stuff leaving the body' rather than from protein or energy deficiencies. Based on the work of Mazurak *et al.* <sup>(87)</sup> and Tomiyama *et al.* <sup>(88)</sup>, it is possible that low-energy detox diets increase stress, elevate cortisol and stimulate appetite, thereby making it difficult to lose weight. The findings of Pankevich *et al.* <sup>(86)</sup> obtained from studies of mice hint that stressful detox diets may set the scene for binge eating and rebound weight gain in the future, although this requires experimental validation.

Although it is plausible that energy-restricted detox diets are able to produce short-term weight loss, it is unclear whether these diets are useful for maintaining a healthy weight in the long-term. There is a vast range of alternative diets that contain adequate protein and

micronutrient levels at the same time as facilitating weight loss, which begs the question of whether detox diets have utility at all. Consumers should be made aware that the weight loss claims of these detox products are not underpinned by any clinical evidence.

### Possible health risks of detox diets

The main health risks of detox diets relate to severe energy restriction and nutritional inadequacy. Extreme fasting can lead to protein and vitamin deficiencies, electrolyte imbalance, lactic acidosis and even death<sup>(92)</sup>. In the late 1970s, 60 people were reported to have died when attempting the 'Last Chance Diet', in which a low-energy liquid protein formula was consumed<sup>(93)</sup>. The protein was of low nutritional value, having been derived from bovine hide, tendons, horns and hooves, and the formula provided only 1.67 MJ day<sup>-1</sup> (400 kcal day<sup>-1</sup>). At least 17 of these individuals had no underlying health conditions. Although the Last Chance Diet does not technically fall into the detox category, it illustrates the risky nature of semi-starvation diets.

Detox dieters are also at risk of overdosing on supplements, laxatives, diuretics or even water. A 19-year-old man developed serotonin syndrome after ingesting a cocktail of tryptophan and St John's Wort when aiming to detoxify himself after 3,4-methylenedioxymethamphetamine (MDMA) use<sup>(94)</sup>. This detox protocol was recommended to him by an Internet site. Because many detox products and programmes are promoted over the Internet, they are difficult to regulate.

The lack of regulation in the detox diet industry is a major concern. At present, the EU has refused to authorise the detoxification claims of a dozen nutritional substances (including green coffee, grapefruit and taurine), although there are hundreds of other 'detox' products that do not yet appear on the Health and Nutrition Claims Register<sup>(95)</sup>. Moreover, there are reports that companies are replacing the words 'detox' and 'cleansing' with alternatives such as 'reinvention' and 'revamp', making it increasingly difficult to regulate the detox industry.

In some cases, the components of detox products may not match their labels, which is a potentially dangerous situation. In Spain, a 50-year-old man died from manganese poisoning after consuming Epsom salts as part of a liver cleansing diet<sup>(96)</sup>. Epsom salts are made from magnesium sulphate heptahydrate, although the supplier had mistakenly sold hydrated manganese sulphate instead.

### Conclusions

At present, there is no compelling evidence to support the use of detox diets for weight management or toxin elimination<sup>(97,98)</sup>. Considering the financial

costs to consumers, unsubstantiated claims and potential health risks of detox products, they should be discouraged by health professionals and subject to independent regulatory review and monitoring. It is hoped that this review will encourage systematic evaluations of commercial detox diets, so that an evidence base can be established to inform future legislation.

Perhaps an important question to ask is why are detox diets so appealing? The seductive power of detox diets presumably lies in their promise of purification and redemption, which are ideals that are deep-rooted in human psychology. These diets, of course, are highly reminiscent of the religious fasts that have been popular throughout human history. It would be useful for future studies to examine the psychological aspects of detox diets and investigate why people are drawn to extreme diets that have no proven benefits. Unfortunately, equating food with sin, guilt and contamination is likely to set up an unhealthy relationship with nutrition. There is no doubt that sustained healthy habits are of greater long-term value than the quick fixes offered by commercial detox diets.

### Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.

No funding declared.

The salaries of the authors are provided by the Cardiac Health Institute and Macquarie University, Australia. All authors contributed to the writing and editing of the manuscript and approved the final version submitted for publication.

### References

1. Allen J, Montalto M, Lovejoy J *et al.*, (2011) Detoxification in naturopathic medicine: a survey. *J Altern Complement Med* **17**, 1175–1180.
2. Diaper AM, Law FD & Melichar JK (2014) Pharmacological strategies for detoxification. *Br J Clin Pharmacol* **77**, 302–314.
3. Bland JS, Barrager E, Reedy RG *et al.*, (1995) A medical food-supplemented detoxification program in the management of chronic health problems. *Altern Ther Health Med* **1**, 62–71.
4. MacIntosh A & Ball K (2000) The effects of a short program of detoxification in disease-free individuals. *Altern Ther Health Med* **6**, 70–76.

5. Cecchini MA, Root DE, Rachunow JR *et al.*, (2006) Chemical exposures at the world trade center: use of the hubbard sauna detoxification regimen to improve health status of New York city rescue workers exposed to toxicants. *Townsend Lett* **273**, 58–65.
6. Kilburn KH, Warsaw RH & Shields MG (1989) Neurobehavioral dysfunction in firemen exposed to polychlorinated biphenyls (PCBs): possible improvement after detoxification. *Arch Environ Health* **44**, 345–350.
7. Schnare DW, Denk G, Shields M *et al.*, (1982) Evaluation of a detoxification regimen for fat stored xenobiotics. *Med Hypotheses* **9**, 265–282.
8. Brown VJ (2003) REACHing for chemical safety. *Environ Health Perspect* **111**, A766–A769.
9. NTP (2014) About the National Toxicology Program. From <http://ntp.niehs.nih.gov/about/index.html> (accessed September 2014).
10. ECHA (2014a) European Chemicals Agency: Understanding REACH. From <http://echa.europa.eu/web/guest/regulations/reach/understanding-reach> (accessed September 2014).
11. ECHA (2014b) European Chemicals Agency: Registered Substances. From <http://echa.europa.eu/information-on-chemicals/registered-substances> (accessed September 2014).
12. Genuis SJ (2011) Elimination of persistent toxicants from the human body. *Hum Exp Toxicol* **30**, 3–18.
13. Jones KC & De Voogt P (1999) Persistent organic pollutants (POPs): state of the science. *Environ Pollut* **100**, 209–221.
14. UNEP (2012) United Nations Environment Program: State of the Science of Endocrine Disrupting Chemicals. From <http://www.who.int/ceh/publications/endocrine/en/> (accessed September 2014).
15. Porta M & Zumeta E (2002) Implementing the Stockholm treaty on persistent organic pollutants. *Occup Environ Med* **59**, 651–652.
16. Ruzzin J, Lee D-H, Carpenter DO *et al.*, (2012) Reconsidering metabolic diseases: the impacts of persistent organic pollutants. *Atherosclerosis* **224**, 1–3.
17. Blanck HM, Marcus M, Tolbert PE *et al.*, (2000) Age at menarche and tanner stage in girls exposed in utero and postnatally to polybrominated biphenyl. *Epidemiology* **11**, 641–647.
18. Karrman A, Ericson I, van Bavel B *et al.*, (2007) Exposure of perfluorinated chemicals through lactation: levels of matched human milk and serum and a temporal trend, 1996–2004, in Sweden. *Environ Health Perspect* **115**, 226–230.
19. Thomsen C, Haug LS, Stigum H *et al.*, (2010) Changes in concentrations of perfluorinated compounds, polybrominated diphenyl ethers, and polychlorinated biphenyls in Norwegian breast-milk during twelve months of lactation. *Environ Sci Technol* **44**, 9550–9556.
20. Solomon GM & Weiss PM (2002) Chemical contaminants in breast milk: time trends and regional variability. *Environ Health Perspect* **110**, A339–A347.
21. Matsui T, Fukazawa K, Fujimoto M *et al.*, (2012) Analysis of persistent organic pollutants as sub-femtogram levels using a high-power picosecond laser for multiphoton ionization in conjugation with gas chromatography/time-of-flight mass spectrometry. *Anal Sci* **28**, 445–450.
22. EFSA (2012) European food safety authority: update of the monitoring of levels of dioxins and PCBs in food and feed. *EFSA J* **10**, 2832–2914.
23. Damstra T, Page SW, Herrman JL *et al.*, (2002) Persistent organic pollutants: potential health effects? *J Epidemiol Community Health* **56**, 824–825.
24. Schettler T (2006) Human exposure to phthalates via consumer products. *Int J Androl* **29**, 134–139.
25. Kay VR, Chambers C & Foster WG (2013) Reproductive and developmental effects of phthalate diesters in females. *Crit Rev Toxicol* **43**, 200–219.
26. Swan SH (2008) Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans. *Environ Res* **108**, 177–184.
27. ACCC (2014) Australian Competition & Consumer Commission: Phthalates in Consumer Products. From <https://www.productsafety.gov.au/content/index.phtml/itemId/972486> (accessed September 2014).
28. Newbold RR, Jefferson WN & Padilla-Banks E (2007) Long-term adverse effects of neonatal exposure to bisphenol A on the murine female reproductive tract. *Reprod Toxicol* **24**, 253–258.
29. von Saal FS & Myers JP (2008) Bisphenol A and risk of metabolic disorders. *JAMA* **300**, 1353–1355.
30. EFSA (2014) European Food Safety Authority: Bisphenol A. From <http://www.efsa.europa.eu/en/topics/topic/bisphenol.htm> (accessed September 2014).
31. FDA (2012) Food and Drug Administration Continues to Study BPA. From <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm297954.htm> (accessed September 2014).
32. FSANZ (2014) Food Standards Australia New Zealand: Bisphenol A (BPA). From <http://www.foodstandards.gov.au/consumer/chemicals/bpa/Pages/default.aspx> (accessed September 2014).
33. Sears ME & Genuis SJ (2012) Environmental determinants of chronic disease and medical approaches: recognition, avoidance, supportive therapy, and detoxification. *J Environ Public Health* **2012**, 356798.
34. Teng X, Shan Z, Chen Y *et al.*, (2011) More than adequate iodine intake may increase subclinical hypothyroidism and autoimmune thyroiditis: a cross-sectional study based on two Chinese communities with different iodine intake levels. *Eur J Endocrinol* **164**, 943–950.
35. Cooke K & Gould MH (1991) The health effects of aluminium - a review. *J R Soc Health* **111**, 163–168.

36. Papanikolaou NC, Hatzidaki EG, Belivanis S *et al.*, (2005) Lead toxicity update. A brief review. *Med Sci Monit* **11**, RA329–RA336.
37. Pinot F, Krepes SE, Bachelet M *et al.*, (2000) Cadmium in the environment: sources, mechanisms of biotoxicity, and biomarkers. *Rev Environ Health* **15**, 299–323.
38. Tchounwou PB, Patlolla AK & Centeno JA (2003) Carcinogenic and systemic health effects associated with arsenic exposure—a critical review. *Toxicol Pathol* **31**, 575–588.
39. Yaginuma-Sakurai K, Murata K, Iwai-Shimada M *et al.*, (2012) Hair-to-blood ratio and biological half-life of mercury: experimental study of methylmercury exposure through fish consumption in humans. *J Toxicol Sci* **37**, 123–130.
40. CDC (2014) Centers for Disease Control and Prevention: Update on Blood Lead Levels in Children. From [http://www.cdc.gov/nceh/lead/acclpp/blood\\_lead\\_levels.htm](http://www.cdc.gov/nceh/lead/acclpp/blood_lead_levels.htm) (accessed September 2014).
41. FAO/WHO (2010) Joint FAO/WHO Expert Committee on Food Additives, 72nd Meeting: Summary and Conclusions. From [http://www.who.int/foodsafety/chem/summary72\\_rev.pdf](http://www.who.int/foodsafety/chem/summary72_rev.pdf) (accessed September 2014).
42. EPA (2014) How People are Exposed to Mercury. From <http://www.epa.gov/mercury/exposure.htm> (accessed September 2014).
43. FAO/WHO (2011) Joint FAO/WHO Expert Committee on Food Additives, 74th Meeting: Summary and Conclusions. From [ftp://ftp.fao.org/ag/agn/jecfa/JECFA\\_74\\_Summary\\_Report\\_4July2011.pdf](ftp://ftp.fao.org/ag/agn/jecfa/JECFA_74_Summary_Report_4July2011.pdf) (accessed September 2014).
44. Satarug S, Haswell-Elkins MR & Moore MR (2000) Safe levels of cadmium intake to prevent renal toxicity in human subjects. *Br J Nutr* **84**, 791–802.
45. Anzenbacher P & Anzenbacherova E (2001) Cytochromes P450 and metabolism of xenobiotics. *Cell Mol Life Sci* **58**, 737–747.
46. Wong MH, Leung AOW, Chan JKY *et al.*, (2005) A review on the usage of POP pesticides in China, with emphasis on DDT loadings in human milk. *Chemosphere* **60**, 740–752.
47. Aga M, Iwaki K, Ueda Y *et al.*, (2001) Preventive effect of *Coriandrum sativum* (Chinese parsley) on localized lead deposition in ICR mice. *J Ethnopharmacol* **77**, 203–208.
48. Domingo JL, Gomez M, Llobet JM *et al.*, (1988) Citric, malic and succinic acids as possible alternatives to deferoxamine in aluminum toxicity. *J Toxicol Clin Toxicol* **26**, 67–79.
49. Huang Z, Li L, Huang G *et al.*, (2009) Growth-inhibitory and metal-binding proteins in *Chlorella vulgaris* exposed to cadmium or zinc. *Aquat Toxicol* **91**, 54–61.
50. Ren H, Jia H, Kim S *et al.*, (2006) Effect of Chinese parsley *Coriandrum sativum* and chitosan on inhibiting the accumulation of cadmium in cultured rainbow trout *Oncorhynchus mykiss*. *Fish Sci* **72**, 263–269.
51. Uchikawa T, Ueno T, Hasegawa T *et al.*, (2009) *Parachlorella beijerinckii* accelerates lead excretion in mice. *Toxicol Ind Health* **25**, 551–556.
52. Uchikawa T, Yasutake A, Kumamoto Y *et al.*, (2010) The influence of *Parachlorella beyerinckii* CK-5 on the absorption and excretion of methylmercury (MeHg) in mice. *J Toxicol Sci* **35**, 101–105.
53. Uchikawa T, Kumamoto Y, Maruyama I *et al.*, (2011) The enhanced elimination of tissue methylmercury in *Parachlorella beijerinckii*-fed mice. *J Toxicol Sci* **36**, 121–126.
54. Yoshida N, Ishii K, Okuno T *et al.*, (2006) Purification and characterization of cadmium-binding protein from unicellular alga *Chlorella sorokiniana*. *Curr Microbiol* **52**, 460–463.
55. Zhao ZY, Liang L, Fan X *et al.*, (2008) The role of modified citrus pectin as an effective chelator of lead in children hospitalized with toxic lead levels. *Altern Ther Health Med* **14**, 34–38.
56. EFSA (2008) Safety of aluminium from dietary intake: scientific opinion of the panel on food additives, flavourings, processing aids and food contact materials. *EFSA J* **754**, 1–34.
57. Wang L, Min M, Li Y *et al.*, (2010) Cultivation of green algae *Chlorella* sp. in different wastewaters from municipal wastewater treatment plant. *Appl Biochem Biotechnol* **162**, 1174–1186.
58. Ralston NVC & Raymond LJ (2010) Dietary selenium's protective effects against methylmercury toxicity. *Toxicology* **278**, 112–123.
59. Li Y-F, Dong Z, Chen C *et al.*, (2012) Organic selenium supplementation increases mercury excretion and decreases oxidative damage in long-term mercury-exposed residents from Wanshan, China. *Environ Sci Technol* **46**, 11313–11318.
60. Seppanen K, Kantola M, Laatikainen R *et al.*, (2000) Effect of supplementation with organic selenium on mercury status as measured by mercury in pubic hair. *J Trace Elem Med Biol* **14**, 84–87.
61. Takekoshi H, Suzuki G, Chubachi H *et al.*, (2005) Effect of *Chlorella pyrenoidosa* on fecal excretion and liver accumulation of polychlorinated dibenzo-p-dioxin in mice. *Chemosphere* **59**, 297–304.
62. Morita K, Matsueda T, Iida T *et al.*, (1999) *Chlorella* accelerates dioxin excretion in rats. *J Nutr* **129**, 1731–1736.
63. Morita K, Ogata M & Hasegawa T (2001) Chlorophyll derived from *Chlorella* inhibits dioxin absorption from the gastrointestinal tract and accelerates dioxin excretion in rats. *Environ Health Perspect* **109**, 289–294.
64. Morita K & Tobiishi K (2002) Increasing effect of nori on the fecal excretion of dioxin by rats. *Biosci Biotechnol Biochem* **66**, 2306–2313.

65. Schnare DW & Robinson PC (1986) Reduction of the human body burdens of hexachlorobenzene and polychlorinated biphenyls. *IARC Sci Publ* **77**, 597–603.
66. Rea WJ, Pan Y, Johnson Do Faaem AR *et al.*, (1996) Reduction of chemical sensitivity by means of heat depuration, physical therapy and nutritional supplementation in a controlled environment. *J Nutr Environ Med* **6**, 141–148.
67. al-Zaki T & Jolly BT (1997) Severe hyponatremia after 'purification'. *Ann Emerg Med* **29**, 194–195.
68. Imamura M & Tung TC (1984) A trial of fasting cure for PCB-poisoned patients in Taiwan. *Prog Clin Biol Res* **137**, 147–153.
69. Charlier C, Desaive C & Plomteux G (2002) Human exposure to endocrine disruptors: consequences of gastroplasty on plasma concentration of toxic pollutants. *Int J Obes Relat Metab Disord* **26**, 1465–1468.
70. Chevrier J, Dewailly E, Ayotte P *et al.*, (2000) Body weight loss increases plasma and adipose tissue concentrations of potentially toxic pollutants in obese individuals. *Int J Obes Relat Metab Disord* **24**, 1272–1278.
71. Dirtu AC, Dirinck E, Malarvannan G *et al.*, (2013) Dynamics of organohalogenated contaminants in human serum from obese individuals during one year of weight loss treatment. *Environ Sci Technol* **47**, 12441–12449.
72. Hue O, Marcotte J, Berrigan F *et al.*, (2006) Increased plasma levels of toxic pollutants accompanying weight loss induced by hypocaloric diet or by bariatric surgery. *Obes Surg* **16**, 1145–1154.
73. Imbeault P, Chevrier J, Dewailly E *et al.*, (2001) Increase in plasma pollutant levels in response to weight loss in humans is related to in vitro subcutaneous adipocyte basal lipolysis. *Int J Obes Relat Metab Disord* **25**, 1585–1591.
74. Kim M-J, Marchand P, Henegar C *et al.*, (2011) Fate and complex pathogenic effects of dioxins and polychlorinated biphenyls in obese subjects before and after drastic weight loss. *Environ Health Perspect* **119**, 377–383.
75. Davis SI, Blanck HM, Hertzberg VS *et al.*, (2005) Menstrual function among women exposed to polybrominated biphenyls: a follow-up prevalence study. *Environ Health* **4**, 15.
76. Jandacek RJ, Anderson N, Liu M *et al.*, (2005) Effects of yo-yo diet, caloric restriction, and olestra on tissue distribution of hexachlorobenzene. *Am J Physiol* **288**, G292–G299.
77. Jandacek RJ, Heubi JE, Buckley DD *et al.*, (2014) Reduction of the body burden of PCBs and DDE by dietary intervention in a randomized trial. *J Nutr Biochem* **25**, 483–488.
78. Hengstler JG, Foth H, Gebel T *et al.*, (2011) Critical evaluation of key evidence on the human health hazards of exposure to bisphenol A. *Crit Rev Toxicol* **41**, 263–291.
79. Hoppin JA, Brock JW, Davis BJ *et al.*, (2002) Reproducibility of urinary phthalate metabolites in first morning urine samples. *Environ Health Perspect* **110**, 515–518.
80. Koch HM, Bolt HM & Angerer J (2004) Di(2-ethylhexyl) phthalate (DEHP) metabolites in human urine and serum after a single oral dose of deuterium-labelled DEHP. *Arch Toxicol* **78**, 123–130.
81. Calafat AM, Ye X, Wong L-Y *et al.*, (2008) Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol 2003–2004. *Environ Health Perspect* **116**, 39–44.
82. Rudel RA, Gray JM, Engel CL *et al.*, (2011) Food packaging and bisphenol A and Bis(2-ethylhexyl) phthalate exposure: finding from a dietary intervention. *Environ Health Perspect* **119**, 914–920.
83. Sathyanarayana S, Alcedo G, Saelens BE *et al.*, (2013) Unexpected results in a randomized dietary trial to reduce phthalate and bisphenol A exposures. *J Expo Sci Environ Epidemiol* **23**, 378–384.
84. Wing RR & Phelan S (2005) Long-term weight loss maintenance. *Am J Clin Nutr* **82**, 222S–225S.
85. Sainsbury A & Zhang L (2010) Role of the arcuate nucleus of the hypothalamus in regulation of body weight during energy deficit. *Mol Cell Endocrinol* **316**, 109–119.
86. Pankevich DE, Teegarden SL, Hedin AD *et al.*, (2010) Caloric restriction experience reprograms stress and orexigenic pathways and promotes binge eating. *J Neurosci* **30**, 16399–16407.
87. Mazurak N, Guenther A, Grau FS *et al.*, (2013) Effects of a 48-h fast on heart rate variability and cortisol levels in healthy female subjects. *Eur J Clin Nutr* **67**, 401–406.
88. Tomiyama AJ, Mann T, Vinas D *et al.*, (2010) Low calorie dieting increases cortisol. *Psychosom Med* **72**, 357–364.
89. Torres SJ & Nowson CA (2007) Relationship between stress, eating behavior and obesity. *Nutrition* **23**, 887–894.
90. FAO (2008) FAO Methodology for the Measurement of Food Deprivation: Updating the Minimum Dietary Energy Requirements. From [http://www.fao.org/fileadmin/templates/ess/documents/food\\_security\\_statistics/metadata/undernourishment\\_methodology.pdf](http://www.fao.org/fileadmin/templates/ess/documents/food_security_statistics/metadata/undernourishment_methodology.pdf) (accessed September 2014).
91. FAO/WHO (2007) Protein and Amino Acid Requirements in Human Nutrition: Report of a Joint WHO/FAO/UNU Expert Consultation. From [http://www.who.int/nutrition/publications/nutrientrequirements/WHO\\_TRS\\_935/en/](http://www.who.int/nutrition/publications/nutrientrequirements/WHO_TRS_935/en/) (accessed September 2014).
92. Johnstone AM (2007) Fasting – the ultimate diet? *Obes Rev* **8**, 211–222.
93. Isner JM, Sours HE, Paris AL *et al.*, (1979) Sudden, unexpected death in avid dieters using the liquid-protein-modified-fast diet. Observations in 17

- patients and the role of the prolonged QT interval. *Circulation* **60**, 1401–1412.
94. Bryant SM & Kolodchak J (2004) Serotonin syndrome resulting from an herbal detox cocktail. *Am J Emerg Med* **22**, 625–626.
95. EC (2013) European Commission: Register of nutrition and health claims made on foods. From <http://ec.europa.eu/nuhclaims/> (accessed September 2014).
96. Sanchez B, Casaloys-Casado J, Quintana S *et al.*, (2012) Fatal manganese intoxication due to an error in the elaboration of Epsom salts for a liver cleansing diet. *Forensic Sci Int* **223**, e1–e4.
97. Cohen M (2007) 'Detox': science or sales pitch? *Aust Fam Physician* **36**, 1009–1010.
98. Ernst E (2012) Alternative detox. *Br Med Bull* **101**, 33–38.