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Iodine-deficient vegetarians: A hypothetical perchlorate-susceptible population?

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Abstract

Recent risk assessments of environmental perchlorate have been subject to much debate. A particular concern is whether appropriate susceptible sub-populations have been identified. Iodine-deficient pregnant women, especially vegetarians, have been proposed as such a potential susceptible sub-population, but there is no evidence of iodine deficiency in the US population and the adequacy of iodine nutrition has not been studied in US vegetarians. To understand the possibility that US vegetarians might be iodine deficient, we reviewed the prevalence, demography, and lifestyle characteristics of US vegetarians as well as the world literature on iodine nutrition in vegetarians. Our findings indicate that strict vegetarians and vegans, who comprise probably less than 0.1% of the US population, have higher education, higher incomes, and healthier lifestyles than the general population. Field studies indicate that vegetarian diets need not lead to iodine deficiency and vegans may suffer excess iodine intake. It is remains uncertain whether there are iodine-deficient vegans or pregnant women in the US. Of more general concern is whether the 10-fold default uncertainty factor is needed for intraspecies (i.e., within human) variability to protect such hypothetical susceptible sub-populations.

Keywords: Perchlorate; Iodine; Vegan; Vegetarian; Susceptible sub-population; Susceptibility; Uncertainty factor

1. Introduction

Perchlorate (ClO_4^-) is a small, stable, naturally occurring anion that has become the focus of animated debate in the risk assessment community (National Academy of Sciences, 2003). Historically prescribed as an anti-thyroid medication, it is now most important as a manufactured substance that is utilized as an oxidizer in munitions and rocket fuel. Environmental releases during manufacture and use have led to detectable perchlorate levels in wells and surface water in a number of states, most notably California, Nevada, and Utah.

The toxicological hazards of perchlorate exposure are known to be limited: it is neither stored nor metabolized; it is not mutagenic or allergenic; and, it poses no apparent human cancer risks. The critical toxicological action of perchlorate is its competitive inhibition of iodine transport by the sodium iodide transporter, a membrane-bound protein responsible for ensuring adequate iodine levels in thyroid and other tissues (Dohan et al., 2003; Wolff, 1998). Inhibition of iodine uptake by pharmacological doses of perchlorate (400–1400 mg/day) was the basis for its use in the treatment of thyrotoxicosis (e.g., Graves disease). Sufficient inhibition of thyroidal iodine uptake necessarily leads to decreased production of thyroid hormones. Thus the effects of perchlorate exposure have been likened to those of iodine deficiency.

Much of the current debate involves the possible thyroidal effects of exposure to environmentally relevant perchlorate levels (e.g., <20–100 μg/L in drinking water). In particular, there is disagreement about the lowest

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perchlorate dose likely to cause iodine uptake inhibition and decreased thyroid activity. Recent studies indicate apparent thresholds in the dose-response between perchlorate exposure and both iodine uptake inhibition and thyroid activity (Greer et al., 2002; Lawrence et al., 2000), with thresholds occurring at doses substantially greater than those expected from ambient exposure. But those studies, which evaluated healthy adults, did not specifically include susceptible sub-populations.

Because perchlorate acts by inhibiting iodine uptake and thus may mimic iodine deficiency, individuals with deficient iodine nutrition have been proposed as such a susceptible sub-population. Even greater concerns have been raised that susceptibility may be enhanced in iodine-deficient pregnant women because pregnant women have greater iodine requirements and iodine deficiency poses risks to the developing fetal nervous system (Delange, 2001; Glinoer, 2001; Hollowell and Hannon, 1997). However, it is not known whether an iodine-deficient population exists in the US. The adequacy of US iodine nutrition has been evaluated periodically by the National Health and Nutrition Examination Surveys (NHANES) (Centers for Disease Control and Prevention, 2003; Hollowell et al., 1998), with most recent results available from 2000. Evaluation of NHANES data according to the consensus criteria developed by the World Health Organization, the United Nations International Children's Emergency Fund and the International Council for the Control of Iodine Deficiency Disorders (WHO/UNICEF/ICCIDD, 2001) indicates that iodine nutrition in the US is adequate (Borak, 2005; Hollowell et al., 1998; Pearce et al., 2004a); there is no evidence of iodine deficiency.

It is notable, however, that those consensus criteria are meant to identify populations at risk of iodine deficiency, not iodine deficient individuals. There are no consensus criteria for diagnosing iodine deficiency in individuals. For such reasons, a recent California EPA risk assessment concluded that despite the NHANES findings, a sub-population of perchlorate-susceptible iodine deficient individuals might exist:

> [T]here appears to be no iodine deficiency in the general population. However, the data do not preclude the possibility that some women at child-bearing age are not getting the optimal daily amount of iodide. (Office of Environmental Health Hazard Assessment, 2004)

An explanation given for that possibility was that "dietary iodine is known to vary among individuals… Some vegetarian diets may have low iodide content" (Office of Environmental Health Hazard Assessment, 2004).

Thus, the California EPA risk assessment was predicated in part on concerns that vegetarians were prone to iodine deficiency and therefore comprised a susceptible sub-population. However, the sole reference cited in support was a small German study that specifically excluded fish, sea food, iodized salt, and iodine-containing breads and cheeses, while allowing only iodine-free bottled water as beverage (Remer et al., 1999). Not surprisingly, that study found that both vegetarian and non-vegetarian control diets were iodine deficient. The risk assessment provided no data describing the number, the nature, or the nutritional needs of US vegetarians.

Likewise, the most recent US EPA risk assessment of perchlorate raised concerns that iodine-deficient pregnant women comprised a sub-population of "potential susceptibility" (Environmental Protection Agency, 2002). However, the only empirical supporting data provided were by reference to pregnant women in an iodine-deficient part of France (Caron et al., 1997): "over 75% of women had urinary excretion levels below 10 μg/dL." By contrast, NHANES 2000 found that the median value of urine iodine in the US was 161 μg/L (95% CI 147–176) (Centers for Disease Control and Prevention, 2003). No data described the number or nature of iodine-deficient pregnant women in the US population. Accordingly, it seems that both the California and US EPA risk assessments reflect hypothetical concerns about undocumented 'susceptible' sub-populations.

Nevertheless, the possibility of sizeable numbers of iodine-deficient US women of child-bearing age raises important public health concerns that extend beyond perchlorate-related issues. And, given the adequate iodine content of the standard US diet, it is reasonable to suggest that iodine deficiency in this country could result only from adherence to highly restricted diets. Thus, it seems plausible that some vegetarians might be iodine deficient. However, only a handful of published studies have directly examined the sufficiency of iodine in vegetarian diets, none performed in North America.

To better understand the possibility that US vegetarians might be iodine deficient we undertook the following review. We first consider the nomenclature and types of vegetarian diets, then the prevalence, demography, and lifestyle characteristics of US vegetarians, and finally we review nutrition and epidemiology studies relevant to iodine nutrition in vegetarians.

2. Nomenclature, types, and prevalence of vegetarians

The risk of iodine deficiency in vegetarians reflects the extent to which iodine-containing foods are excluded from their diets. For example, those who adhere to highly restricted diets are more likely to suffer deficiency than others who consume dairy products, which are generally iodine-rich. Thus to consider the likely prevalence of iodine deficiency in vegetarians, it is necessary to consider the nature and severity of individual dietary restrictions. However, the scientific and popular literature have adopted an array of variable and sometimes overlapping

Table 1
Types of vegetarian diets including the foods excluded and included by each

Type of diet	Excluded foods	Included foods
Vegetarian	Meat, poultry, fish	Eggs, milk
Lacto-ovo-vegetarian	Meat, poultry, fish	Eggs, milk
Lacto-vegetarian	Meat, poultry, fish, eggs	Milk
Vegan	Meat, poultry, fish, eggs, milk	
Raw food diet	Meat, poultry, fish, eggs, milk	Uncooked fruits, vegetables, seeds, nuts, and grains
Fruitarian	Meat, poultry, fish, eggs, milk	Uncooked fruits and seeds
Pescetarians	Meat, poultry	
Pesco-vegetarian	Meat, poultry	Fish, eggs, milk
Macrobiotic	Meat, poultry, eggs, milk	Fish, vegetables, grains, legumes
Self-defined vegetarian	No strict exclusions	

Source: (ADA, 2003; Applepy et al., 1999; Barr and Chapman, 2002; Dwyer et al., 1974; Freeland-Graves et al., 1986; FF, 2000; Living Foods, 2003; Perry et al., 2002).

nomenclature to describe various types of vegetarian diets (Dwyer et al., 1974; Johnston, 2000; Weinsier, 2000). To standardize our discussion and enhance comparability between the studies considered below, we have adopted the dietary terms and definitions outlined in Table 1.

The exact number of vegetarians in the US remains unclear, in part because of difficulties in agreeing on who and what is being counted. In most surveys, participants were classified on the basis of self-described dietary habits, rather than objective assessments of actual consumption. As discussed below, survey respondents tend to overestimate their vegetarian status, exaggerating the extent of their dietary restrictions and the consistency of their adherence. Despite that, survey results indicate that the prevalence of consistently practicing vegetarians in the US population is small.

An important set of survey findings is found in the Stanford Five City Project, five cross-sectional, household-based surveys, conducted between 1979 and 1990 among participants aged 20–74 who resided in four California cities (Frank et al., 1992; White and Frank, 1994). In those surveys, 14.8–16.9% of the participants said they had not eaten "any meat, poultry, fish, egg yolks or cheese (other than low-fat cheeses like ricotta or low-fat cottage cheese) during the past 1–3 days." When asked about longer periods of dietary restriction, the number of responding participants declined rapidly. For example, 3.0–4.2% had not eaten "any meat, poultry, fish, egg yolks or cheese" during the prior 4–6 days, while only 0.4–1.0% had followed such a diet for 7 days. These data indicate that many people are occasional vegetarians, but few adhere rigorously to restricted diets. Moreover, because the smallest proportion (0.4–1.0%) reflected only a 7-day time span and included some individuals who consumed eggs and dairy products, it overestimated the proportion of strict vegans in that population.

National data are available from the Continuing Survey of Food Intake by Individuals (CSFII), a study conducted by the US Department of Agriculture (USDA) that collected food consumption data from representative samples of non-institutionalized persons in the US (Haddad and Tanzman, 2003; US Department of Agriculture, 2000). Surveys conducted during 1994–1996 and 1998 included 13,341 participants over 6 years of age who were asked about their food consumption on two non-consecutive "recall days." There were 334 participants (2.5%) who described themselves as vegetarians. But, when asked about specific foods consumed on either or both of the recall days, 97 (29%) also said that they had eaten meat (beef, veal, pork or lamb) or poultry, while 234 (70%) said that they had eaten meat, poultry, fish or seafood. Thus, only 30% of the self-described vegetarians had adhered to a vegetarian diet on the two recall days. In another CSFII database of 12,634 survey participants over 6 years of age who provided detailed food consumption information for both recall days, food consumption of 43 individuals (0.34%) was consistent with a vegan diet: no meat, poultry, fish, eggs, or dairy products. Of these, only 14 (33%) identified themselves as vegetarians. Because CSFII considered only two specific recall days, the reported percentages represent upper bounds on the proportion of survey respondents (and of the US population) that is vegetarian; the actual number of true vegetarians is almost certainly smaller. Likewise, although the CSFII data indicate that only a small proportion of the survey population adhered to a vegan diet on two recall days (0.11–0.34%), that proportion almost certainly overestimates the number of consistently practicing vegans.

The CSFII and Stanford Five City Project illustrate the difficulty of characterizing vegetarians on the basis of self-reported dietary practices. Such seemingly inconsistent survey results are likely due to lack of a universally accepted definition of "vegetarian," rather than a lack of understanding or intelligence. Support for that view is found in a survey of US women physicians, a population characterized by both intelligence and knowledge of biology and nutrition (White et al., 1999). When survey subjects were asked about their diets, about 8% identified themselves as vegetarians; when asked to describe their actual food intake, nearly half of the "vegetarian" physicians admitted to eating meat, poultry or fish during the prior week.

Over the past decade the Vegetarian Resource Group (VRG), a non-profit organization dedicated to promoting vegetarianism, sponsored telephone surveys of dietary habits conducted by Roper Organization (1994 and

1997), Zogby (2000) and Harris Interactive (2003) (American Dietetic Association and Dietitians of Canada, 2003; Vegetarian Resource Group, 2003a,b,c). The VRG surveys found that 4–10% of "the country's consumers" call themselves vegetarians, but the numbers that actually follow a vegetarian diet decline as dietary restrictions increase. For example, 6% of respondents to the 2003 survey said that they "never eat meat," 2.8% said they "never eat meat, poultry, fish, seafood" and 1.8% said that they "never eat meat, poultry, fish, seafood, dairy products, eggs, and honey" (Vegetarian Resource Group, 2003a). In discussing this survey, however, VRG discounted its findings:

This number may seem too high, but our theory is that most people who fit the definition of vegetarian (never eat meat, fish, or fowl) are 'very committed to issues' and tend to become vegan. Vegans would be a much smaller percentage of those who self-define as vegetarian—that is, the people who think of themselves as vegetarian but may eat meat, fish, or poultry (Vegetarian Resource Group, 2003a).

Thus, VRG provided further evidence that many people call themselves 'vegetarian,' but only a smaller number adhere to such diets and a still much smaller proportion follow strict vegan diets. Unfortunately, the actual numbers are not well characterized by such surveys.

One reason for the difficulty in distinguishing "true vegetarians" from intermittent vegetarians is the increasing access to prepared vegetarian meals (Messina and Mangels, 2001). It has become easy to be a 'part-time' vegetarian. The National Restaurant Association reports that 80% of US table service restaurants offer vegetarian entrees, many fast food restaurants offer vegetarian fare (e.g., veggie burgers), and vegetarian meals are offered at almost every US college and university (National Restaurant Association, 1999). Likewise, many food manufacturers have developed divisions or acquired subsidiaries specializing in 'natural foods' and 'vegetarian alternative' products. As a result, 'alternative' foods are increasingly offered to the wider audience of supermarket consumers: approximately 50% of 'natural foods' and 75% of soymilk are sold in supermarkets (Ginsberg and Ostrowski, 2003). Ease of access, coupled with the positive image of vegetarians (e.g., "very committed to issues"), may encourage occasional eaters of vegetarian foods to self-describe as "vegetarian."

In summary, it seems that the number of people who follow strict vegetarian diets is small, probably less than 0.1% of the US population. These are the vegetarians most likely to be iodine deficient. By contrast, a substantial proportion of self-identified vegetarians regularly consume iodine-rich dairy products and, it seems, many at least occasionally eat meat, poultry or fish.

3. Demographic and lifestyle characteristics of US vegetarians

Surveys of US vegetarians reveal consistent patterns of demographic and lifestyle characteristics. Compared to the general population, self-described vegetarians are more likely to be white females, 20–40 years of age, college-educated, earning relatively high household incomes, and living in East or West coast cities. In the USDA CFSII survey, for example, 67% self-identified vegetarians were female, 79% were white, and 30% were college graduates (compared to 22% in the general population) (US Department of Agriculture, 2000; White and Frank, 1994). Similar patterns were seen among British vegetarians, who were "predominantly from higher social class, and well educated" (Draper et al., 1993). Vegetarians in that study were more than twice as likely to be in the highest socioeconomic category and 51% of vegetarians had a university degree or equivalent, compared to 7% of the Greater London population.

Vegetarians also live healthier lifestyles than do omnivores. Compared to omnivores, vegetarians are significantly less likely to smoke, drink alcohol, or consume fatty and processed foods and more likely to be physically active (Ellis and Montegriffo, 1970; Freeland-Graves et al., 1986; Phillips et al., 1980). There is also evidence that the more restrictive the diets (e.g., vegan vs. vegetarian vs. omnivore), the more likely such demographic and lifestyle patterns will be seen.

Such demographics and lifestyles strongly suggest that those in the US who follow restricted vegetarian diets have adopted those diets as a matter of choice, rather than being imposed by poverty or ignorance. And the health-promoting inclinations of vegetarians also suggest that those who understand their risks of dietary deficiencies (iodine and otherwise) would be inclined to adopt appropriate supplement regimens.

4. Iodine content of omnivore and vegetarian diets

The iodine content of fruits and vegetables reflects the iodine content of the soil, irrigation waters, and fertilizers used in their agricultural production. Likewise, the iodine content of meat, poultry, and dairy products reflects both naturally occurring iodine (e.g., drinking water, livestock feed) and use of iodine-containing supplements. Iodine is often added to feed to prevent endemic iodine deficiency and thyroid-suppressing effects of isoflavone- and thiocyanate-rich feed components (e.g., soy, rapeseed). Also, iodophor sanitizing solutions used to clean cattle and milking equipment increase the iodine content of dairy products. Levels in processed foods depend on naturally occurring iodine and the use of iodized salt and additives. For example, potassium and calcium iodate have been used as "dough conditioners" to improve the texture, appearance, and shelf-life of baked goods; some breads contain more than 300 μg iodine per slice (Dunn, 2003). Another additive, FD&C Red #3 (erythrosine), a dye used in ready-to-eat cereals and other foods, is 58% iodine by weight (National Academy of Sciences, 2001a; Pennington et al., 1995).

During the 1990s, FDA analyzed the content of iodine (and other minerals) in 294 "core foods" in the US food supply (Pennington et al., 1995). For prepared foods, all cooking was done with non-iodized salt. Multiple analyses (37 analyses per food) were performed to allow calculation of analytical precision. Of those foods, 49 contained more than 20 μg iodine per portion and 32 contained 10-20 μg iodine per portion. Foods with highest in iodine content, 54–450 μg per serving, included a cross-section of typical American cuisine: fruit-flavored cereal, chocolate milk shake, cheese pizza, cod/haddock, chicken pot pie, low-fat plain yogurt, macaroni and cheese, corn grits, homemade lasagna, white rice, pancakes, chocolate milk, chicken noodle casserole, canned spaghetti in tomato sauce, low-fat milk, apple pie, fish sticks, chocolate pudding, and mashed potatoes. Iodine levels of prepared foods would have been significantly higher if cooked with iodized salt. About 50–70% of US households use iodized salt, which provides about 50 μg iodine per day (American Dietetic Association and Dietitians of Canada, 2003; Dunn, 2003). By contrast, vegetables, fruits, and nuts contained essentially no iodine (Pennington et al., 1995). It must be noted that the actual iodine content of foods can vary greatly across brands and sources (Pearce et al., 2004b).

Iodine is also obtained from dietary supplements. About half of prenatal vitamins and many multi-vitamins are supplanted with 100–200 μg per day, and iodine is often found in 'multi-mineral' and 'multi-vitamin-and-multi-mineral' preparations. In 1986, the National Health Interview Survey considered the use of vitamin and mineral supplements among a representative sample of 13,435 US residents (Moss et al., 1989). That survey found that 36% of US adults (excluding pregnant and lactating women) took non-prescription vitamin and mineral supplements. Use was higher in women (41%) than men (31%). These findings were confirmed by the 1988–1994 NHANES III survey, which included 33,905 people comprising a representative sample of the civilian, non-institutionalized US population (National Center for Health Statistics, 1999). Approximately 42% of adults used one or more supplements; use was greater in women (44%) than men (35%). Among pregnant and lactating women, supplement use was much higher: 76% reported taking at least one dietary supplement daily. Among women of childbearing age (i.e., 20–39 years) who took dietary supplements, about 60% used vitamin/mineral combinations likely to contain iodine. Other non-dietary sources of iodine include 'energy' and 'protein' shakes, which are often iodine-supplemented, antiseptics, and mouth-wash.

In light of such evidence, it is not surprising that iodine deficiency is generally not found in the US. To be iodine deficient, one must avoid not just meat, fish and poultry, but also many processed foods, most dairy products, flavored cereals, commercial baked goods, iodized salt, and iodine-containing vitamins and supplements. In other words, it would require almost deliberate avoidance of iodine.

5. Iodine nutrition in vegetarians

The adequacy of iodine nutrition has apparently not been studied in US vegetarians. Worldwide, we identified seven studies, summarized in Table 2, that evaluated iodine nutrition in vegetarians (Abdulla et al., 1981; Draper et al., 1993; Key et al., 1992; Krajcovicova-Kudlackova et al., 2003; Lightowler and Davies, 1998; Rauma et al., 1994; Remer et al., 1999). [1] Although the informational value of these studies is limited by small sample size and methodological deficiencies, [2] these studies reflect the marked heterogeneity that characterizes vegetarian and vegan diets. For example, in two studies, subjects were directed to avoid iodized salt, fish, seaweed and kelp, and iodine-containing processed foods, while only iodine-free beverages were provided (Abdulla et al., 1981; Remer et al., 1999). The iodine intake of those individuals was generally inadequate. By contrast, vegans in two other studies were allowed, but not required to consume large amounts of seaweed and iodine supplements (Lightowler and Davies, 1998; Rauma et al., 1994). In those studies, iodine intake was variable and often excessive.

Furthermore, one study (Lightowler and Davies, 1998), which analyzed the iodine content of food plus dietary supplements, described three vegan subgroups: those taking no iodine-supplements (mean: 87; range: 25–352 μg/day); those taking iodine-containing supplements (mean: 151; range: 67–246 μg/day); and, those consuming seaweed (mean: 866; range: 521–1467 μg/day). Note that even among those not taking supplements, some had more than adequate iodine intake. The

[1] For purposes of comparison, the current US Recommended Daily Allowance for iodine is 150 μg/day in adults, 220 μg/day in pregnant women, and 290 μg/day in lactating women (National Academy of Sciences, 2001b).

[2] For example, one study had no control or comparison group (Lightowler and Davies, 1998), a second compared vegans from an iodine-deficient area to omnivorous controls from an iodine-sufficient maritime community (Abdulla et al., 1979, 1981), and two other studies had only incomplete dietary histories for a large proportion of their control subjects (Key et al., 1992; Rauma et al., 1994). Only one study (Remer et al., 1999) used an experimental design to compare vegetarian and omnivorous diets.

Table 2
Description of seven studies that evaluated iodine nutrition in vegetarians

Study	Location	Diet types	No. of subjects (m:f)	Urinary iodine	Dietary iodine (μg/d)	Thyroid function
Abdulla (33)	Sweden	Vegan	6 (3:3)	ND	82(± 29) μg/day$^{(5)}$ (male) 58(± 12) μg/day$^{(5)}$ (female)	TSH, T_3, T_4
Draper (34)	UK	Vegan	38 (18:20)	ND	89 (male): 62 (female)$^{(4,7)}$	ND
		Lacto-vegetarian	52 (16:36)		202 (male):156 (female)$^{(4,7)}$	
		Demi-vegetarian	37 (13:24)		204 (male):152 (female)$^{(4,7)}$	
Key (35)	UK	Vegan	48 (48:0)	ND	ND	TSH
		Omnivorous	53 (53:0)			
Krajcovicovi-Kudlackova (36)	Slovakia	Vegan	15 (6:9)	71 (9–204) μg/L$^{(1)}$	ND	ND
		Lacto-ovo and Lacto-vegetarian	31 (12:19)	177 (44–273) μg/L$^{(1)}$		
		Omnivorous	35 (15:20)	210 (76–423) μg/L$^{(1)}$		
Lighthowler (37)	UK	Vegan	30 (11:19)	16.8 μg/L (male)$^{(2)}$ 20.5 μg/L (female)$^{(2)}$	137 (± 149) (male)$^{(6,8)}$ 187 (± 346) (female)$^{(6,8)}$	ND
Rauma (38)	Finland	Vegan	9	<200–1700 μg/day	29 (± 18)$^{(4,7)}$	TSH, T_4
		Omnivorous	8	<150–1200 μg/day	222 (± 93)$^{(4,7)}$	ND
Remer (39)	Germany	Lacto-vegetarian	6 (3:3)	36.6 (± 8.8) μg/day$^{(3)}$	15.6 (12–18)$^{(5,8)}$	
		Omnivorous	(cross-over)	50.2 (± 14) μg/day$^{(3)}$	35.2 (25–45)$^{(5,8)}$	ND
		Omnivorous (protein-rich)		61.0 (± 8) μg/day$^{(3)}$	44.5 (40-48)$^{(5,8)}$	

ND, not done; Urinary iodine: (1) median (range); (2) median; (3) mean (± SD); Dietary iodine: (4) food diary; (5) analysis of duplicate portions; (6) analysis of duplicate portions plus dietary supplements; (7) geometric mean; (8) arithmetic mean (± SD).

other study, which evaluated nine vegans, found urinary iodine excretion >200 μg/day in six, of whom four excreted >900–1700 μg/day (Rauma et al., 1994). These values indicate that iodine intake met or exceeded recommended daily levels.

In addition to iodine measurements, three studies (Abdulla et al., 1981; Key et al., 1992; Rauma et al., 1994) performed thyroid function tests as indirect measures of iodine sufficiency, presuming that physiologically important iodine deficiency would manifest as reduced thyroid function. Thyroid function was normal in two studies (Abdulla et al., 1981; Rauma et al., 1994). The third study reported elevated TSH levels in 5 of 48 vegans, but did not measure dietary or urinary iodine levels (Key et al., 1992). It is noteworthy that the three highest TSH levels were in vegans who "usually took kelp"; it is possible that these three were actually suffering iodine-induced hypothyroidism, a well known condition (Wiersinga and Braverman, 2003) secondary to the consumption of excessive amounts of iodine-rich kelp.

Although the informational value of these seven studies is limited, they confirm that the iodine content of vegan diets is often below recommended levels, but they also document that vegans need not be iodine deficient. Vegans who avoid iodized salt and iodine supplements (including seaweed preparations) are at increased risk of iodine deficiency, while those who use such supplements may risk iodine overload (Teas et al., 2004). There is less evidence of iodine deficiency in those who follow less restrictive vegetarian diets. Iodine intake was low in lacto-vegetarians directed to avoid iodized salt, seaweed and iodine-containing processed foods and beverages (Remer et al., 1999), but adequate levels were reported in two other studies of lacto-vegetarians whose diets were not otherwise restricted (Draper et al., 1993; Krajcovicova-Kudlackova et al., 2003). Thus, iodine deficiency seems a concern for vegans, but not other vegetarians, and risks of deficiency seem to depend on their appropriate use of iodized salt and/or dietary supplements.

6. Discussion

The possibility that vegetarian diets lead to iodine deficiency is a public health concern because pregnant women and their fetuses are vulnerable to iodine deficiency and because the vegetarian lifestyle is disproportionately popular among women of child-bearing age. For related reasons, recent perchlorate risk assessments have proposed that vegetarian women of child bearing age are a susceptible sub-population because "vegetarian diets may have low iodide content" (Office of Environmental Health Hazard Assessment, 2004). Although biologically plausible, there is no evidence of an iodine-deficient vegetarian population in the US.

A conceptual challenge underlying this public health concern is the tendency to regard vegetarianism as a homogeneous, rather than heterogeneous practice. That tendency has been challenged by nutritionists:

> The term vegetarian implies a homogeneity which does not exist among Canadian and American vegetarian women. Their diets and nutritional status vary greatly depending upon the particular regime they follow, other dietary proscriptions they include, their attitudes toward and use of the health care system and the presence or absence of other illnesses which compromise nutritional status (Dwyer, 1983).

Such heterogeneity is reflected in the studies discussed above. Among those who describe themselves as "vegetarian," a substantial proportion actually eat meat, chicken or fish. And of those who do avoid meat, chicken, and fish, a large majority consumes dairy products. Thus the number of consistently practicing vegans is very small, probably less than 0.1% of the general population. It is that small group of vegans, not the much larger numbers of lacto-vegetarians and self-defined vegetarians, who might plausibly be at risk of iodine deficiency.

Iodine deficiency has not been documented in US vegans. European studies indicate that the iodine content of strict vegan diets is often below recommended levels, but those who follow such diets need not be iodine deficient; some vegan diets contain adequate iodine and many vegans routinely augment their diets with iodized salt, kelp, and other supplements. Given that vegans generally have higher-than-average education, greater-than-average income, and a general espousal of health-promoting lifestyles, it should not be surprising that many understand the limitations of their diets and routinely use dietary supplements. In studies of European vegans, for example, iodine deficiency was found mainly in those who were specifically directed to avoid iodized salt, seaweed, supplements and iodine-containing beverages.

Despite potentially important public health implications, the number and nature of iodine-deficient pregnant vegetarians in the US has not been documented. Historically, "the majority of pregnant and lactating vegetarian women appear to plan their diets with particular care for these physiological events" (Dwyer, 1983) and that was recently affirmed by the American Dietetic Association and Dietitians of Canada: "well-planned vegan and other types of vegetarian diets are appropriate for all stages of the life cycle, including during pregnancy, lactation, childhood, and adolescence" (American Dietetic Association and Dietitians of Canada, 2003). Thus the issue of concern is not whether there are pregnant vegans, but whether there are any who fail to "plan their diets." Considering their generally higher educational, economic and lifestyle characteristics, along with the generally high use of dietary supplement by pregnant women, it can be expected that the number of iodine-deficient pregnant women in the US is very small. Nevertheless, the actual number of iodine-deficient women in the US should be investigated.

Of more general concern for risk assessment is whether the 10-fold default uncertainty factor is needed for intraspecies (i.e., within human) variability to protect a hypothetical population, i.e. iodine-deficient vegetarians (Strawson et al., 2004; US Environmental Protection Agency, 2002). Use of such a default would be appropriate if there were no data supporting an alternative approach. However, as discussed in this paper, the accumulated data argue that such a population is unlikely to exist in the US. Thus, one has to ask under what conditions is biological plausibility or potential heterogeneity sufficient to justify the adoption of a 10-fold default uncertainty factor? A recent EPA Report addresses "cases where the susceptible population is quite specifically defined" (US Environmental Protection Agency, 2002), but neglects the alternative cases in which, despite theoretical plausibility and reasonable investigative effort, such a population has not be shown to exist.

There are few explicit guidelines for characterizing susceptible populations. The Presidential/Congressional Commission on Risk Assessment and Risk Management, for example, observed a need for more frequent considerations of susceptibility ("current regulatory approaches for reducing risks associated with chemical exposures generally do not include information on difference in individual susceptibility"), but also noted that recognition of a group's susceptibility "does not necessarily lead to more stringent regulation" (Presidential/Congressional Commission on Risk Assessment and Risk Management, 1997). Susceptible individuals, for example, might be encouraged instead to modify their behaviors, thereby reducing their susceptibility. As for practical guidance, the Commission stressed the need to identify "the size of the population at higher risk" so as to "characterize the risks more realistically" (Presidential/Congressional Commission on Risk Assessment and Risk Management, 1997). Similarly, National Research Council recommendations in *Science and Judgment in Risk Assessment* urge more extensive empirical studies to characterize more realistically the risks associated with inter-individual variability and susceptibility: "the magnitude and extent of human variability due to particular acquired or inherited [susceptibility] factors should be determined… results of the research should be used to adjust and refine estimates of risks" (National Research Council, 1994).

However, some practical guidance on susceptible populations can be found in the judgments that underlie risk assessments for a number of specific chemicals. For example, EPA has made judgments that reduced the default value of 10-fold for intraspecies (i.e., within human) variability for about 3.6% of the RfDs and RfCs listed in the IRIS database (Dourson et al., 1996; US Environmental Protection Agency, 2002) and a similar default reduction has been recommended for perchlorate (Strawson et al., 2004). Examples of RfDs for which uncertainty factor for within human variability was reduced in light of human data on susceptible populations are shown in Table 3.

Finally, from a public health perspective, the need to document whether iodine-deficiency exists in pregnant US women extends beyond refining perchlorate risk assessments. Sufficient maternal iodine is necessary for normal fetal development, a need that can be met by numerous standard prenatal vitamin preparations. Moreover, most obstetricians and midwives routinely recommend prenatal vitamins to pregnant patients, especially those with restricted diets:

> Almost all pregnant women should be able to obtain the Recommended Daily Allowances for minerals and vitamins through their dietary intake. There is no requirement for routine supplementation, with the possible exception of iron. However, daily supplements should be given if the adequacy of a patient's diet is questionable or if she is at high nutritional risk. *The latter category includes… complete vegans* (Guidelines for Perinatal Care, 1997) (emphasis added).

Table 3
Human-based RfDs with reduced uncertainty factors for intraspecies (i.e., within human) variability on IRIS as of May 2000[a]

Chemical (as on IRIS)	Clinical	Epidemiology	Occupational	Study type for RfD	UF	RfD	RfD confidence
Arsenic, inorganic		✓		Human epidemiology drinking water	3	3 E−4	Medium
Barium	✓	✓	✓	Human experimental and epidemiology	3	7 E−2	Medium
Benzoic acid	✓	✓		Human anecdotal dietary exposure	1	4 E+0	Medium
Fluorine (soluble fluoride)		✓		Human epidemiology	1	6 E−2	High
Manganese		✓		Human data of several types	1	1.4 E−3	Medium
Nitrate	✓	✓		Human epidemiology	1	1.6 E+0	High
Nitrite	✓	✓		Human epidemiology	1	1 E−1	High
Selenium and compounds		✓		Human food and soil epidemiology	3	5 E−3	High
Silver		✓		Human anecdotal studies	3	5 E−3	Low
Zinc and compounds	✓			Human experimental	3	3 E−1	Medium
Perchlorate[b]	✓	✓	✓	Epidemiology study	3	2 E−3	High

[a] Availability of data is defined as studies described in EPA's IRIS RfD file only. Some chemicals are known to have other data for the inhalation route (e.g., manganese).
[b] As per Strawson et al. (2004).

Thus, if significant numbers of pregnant US women are iodine deficient, it would be evidence of substandard prenatal care or failure of pubic health systems. In either event, the most prudent pubic health response would be to address their nutritional needs and prescribe iodine.

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