Misconception 3—Reducing pesticide residues is an effective way to prevent diet-related cancer

Reduction in the use of pesticides will not effectively prevent diet-related cancer. Diets high in fruits and vegetables, which are the source of most human exposures to pesticide residues, are associated with reduced risk of many types of cancer. Less use of synthetic pesticides would increase costs of fruits and vegetables and, thus, likely reduce consumption, especially among people with low incomes, who spend a higher percentage of their income on food.

Dietary fruits and vegetables and cancer prevention

Two types of evidence, (1) ***epidemiological*** studies on diet and cancer and (2) laboratory studies on vitamin or mineral inadequacy, support the idea that low intake of fruits and vegetables is associated with increased risk of degenerative diseases, including cancer, cardiovascular disease, cataracts, and brain dysfunction (Ames & al. 1995; Ames & al. 1993b; Ames & Wakimoto 2002). Fruits and vegetables are an important source of essential vitamins and minerals (Ames & Wakimoto 2002).

Despite the evidence about the importance of fruits and vegetables, the Canadian campaign "5-to-10-a-Day:

Are You Getting Enough?" reported that 67% of Canadians do not eat 5 or more servings of fruits and vegetables per day, based on a Nielson telephone survey of women (http://5to10aday.com/eng/media_news_nr1.htm; A. Matyas, pers. comm.). Another survey, by interview, reported that about half of Canadians do not eat 5 servings or more per day (Gray-Donald & al. 2000). In the United States, it has been estimated that 80% of children and adolescents, and 68% of adults (Krebs-Smith & al. 1995; Krebs-Smith & al. 1996) do not eat 5 servings or more per day. Publicity about hundreds of minor, hypothetical risks, such as pesticide residues, can result in a loss of perspective on what is important (US National Cancer Institute 1996): only 7% of Canadians surveyed thought that eating fruits and vegetables can reduce the risk of cancer (http://www.5to10aday.com/eng/media_executive_summary.htm). There is a paradox in the public concern about possible cancer hazards from the low levels of pesticide residues in food and the lack of public understanding of the evidence that eating *more* of the main foods that contain pesticide residues—fruits and vegetables—protects against cancer.

Several reviews of the epidemiological literature show that a high proportion of ***case-control studies*** find an inverse association between fruit and vegetable consumption and cancer risk (Block & al. 1992; Hill & al. 1994; Steinmetz & Potter 1996; World Cancer Research Fund 1997). It is not clear from these studies whether individuals who consume very low amounts are the only people at risk, that is, whether there is an adequate level above which there is no increased cancer risk. Table 1 reports the number and proportion of case-control studies for each type of cancer, that show a statistically significant protective effect (World Cancer Research Fund 1997). A recent international panel considered the evidence of a protective effect of fruits and vegetables most convincing for cancers of the oral cav-

Table 1: Review of epidemiological (case-control) studies worldwide on the association between cancer risk and the consumption of fruit and vegetables

Cancer site	Proportion of studies with statistically significant protective effect of fruits and/or vegetables*	Percent of studies with protective effect
Larynx	6/6	100%
Stomach	28/30	93%
Mouth, oral cavity, & pharynx	13/15	87%
Bladder	6/7	86%
Lung	11/13	85%
Esophagus	15/18	83%
Pancreas	9/11	82%
Cervix	4/5	80%
Endometrium	4/5	80%
Rectum	8/10	80%
Colon	15/19	79%
Colon/rectum	3/5	60%
Breast	8/12	67%
Thyroid	3/5	60%
Kidney	3/5	60%
Prostate	1/6	17%
Nasal & nasopharynx	2/4	—
Ovary	3/4	—
Skin	2/2	—
Vulva	1/1	—
Mesothelium	0/1	—
Total	144/183	79%

Source: World Cancer Research Fund 1997.
Note *: $p<0.05$ for test for trend, $p<0.05$ for odds ratio for uppermost consumption level, or 95% confidence interval excluding 1.0 for uppermost consumption level.
Note: "—" = fewer than 5 studies, so no percent was calculated.

ity, esophagus, stomach, and lung (World Cancer Research Fund 1997). In another review, the median relative risk was about 2 for the quarter of the population with the lowest dietary intake of fruits and vegetables compared to the quarter with the highest intake for cancers of the lung, larynx, oral cavity, esophagus, stomach, bladder, pancreas, and cervix (Block & al. 1992). The median relative risk was not as high for the hormonally related cancers of breast, prostate, and ovary, or for the colon.

More than 30 large cohort studies of the relationship between diet and cancer are in progress in various countries (Willett 2001). Generally the results of ***cohort studies*** have been less strong and less consistent than case-control studies in their findings about the association between fruit and vegetable intake and cancer risk (Botterweck & al. 1998; Galanis & al. 1998; Giovannucci & al. 2002; Jansen & al. 2001; Kasum & al. 2002; McCullough & al. 2001; Michels & al. 2000; Ozasa & al. 2001; Schuurman & al. 1998; Sellers & al. 1998; Smith-Warner & al. 2001; Terry & al. 1998; Terry & al. 2001; Voorrips & al. 2000; Zeegers & al. 2001). Some cohort studies have shown a lack of association between fruit and vegetable consumption and cancers of the colon, breast, and stomach (Botterweck & al. 1998; Galanis & al. 1998; Kasum & al. 2002; McCullough & al. 2001; Michels & al. 2000; Sellers & al. 1998; Smith-Warner & al. 2001; Terry & al. 1998; Terry & al. 2001; Voorrips & al. 2000). As more analyses are reported from cohort studies, the estimation of relative risks should become more precise.

Observational epidemiological studies have many limitations that make interpretation of results complex. Unlike experiments in rodents, in which a single variable is changed and everything else is controlled for, in epidemiological studies on diet, people eat varied diets and change over time, they may not recall correctly their eating habits, and they have different genetic makeups. Some examples of the kinds of complexities in these studies follow.

The category "fruits and vegetables" is broad and foods contain different amounts of each vitamin or mineral. If a minimum amount of a specific vitamin or mineral is required for protection against a specific cancer, then it may be inadequacy of individual foods that is related to risk (Willett 2001). This is usually not the focus in research investigations; rather, the focus is the combined category, fruits and vegetables. Additionally, use of a multivitamin pill or of a particular vitamin pill has generally not been taken into account in these studies and this may ***confound*** the results because those who take supplements have a healthier lifestyle that includes a greater intake of fruits and vegetables as well as other factors like lower rates of smoking, diets lower in fat, and a belief in the connection between diet and cancer that may affect both their behaviors and their recall of dietary intakes (Block & al. 1994; Patterson & al. 2001). Methodological limitations of case-control studies that may account for findings that are stronger than those of cohort studies include ***recall bias***—controls may remember their dietary habits differently from cases (the people with cancer)—and selection bias—people who choose to participate as controls may have healthier life-styles that include, among other factors, a higher intake of fruits and vegetables, which leads, in turn, to a lower observed relative risk that may not really be due to fruits and vegetables.

Inadequate intake of vitamins and minerals

Laboratory studies of vitamin and mineral inadequacy indicate an association with DNA damage, which suggests that the vitamin and mineral content of fruits and vegetables may underlie the observed association between the intake of fruits and vegetables and the risk of cancer. Maximum health and lifespan require metabolic harmony; and inadequate or sub-optimal intake of essential vitamins and minerals may result in metabolic damage that can affect many functions and hence affect the development of diseases.

Antioxidants such as vitamin C (whose dietary source is fruits and vegetables), vitamin E, and selenium protect against ***oxidative damage*** caused by normal metabolism (Helbock & al. 1998), smoking (Ames 1998), and inflammation (Ames & al. 1993b) (See **Misconception #2**). ***Deficiency*** of some vitamins and minerals can mimic radiation in damaging DNA by causing single- and double-strand breaks, or oxidative lesions, or both (Ames 1998). Those vitamins and minerals whose deficiency appears to mimic radiation are folic acid, B_{12}, B_6, niacin, C, E, iron, and zinc, with the laboratory evidence ranging from likely to compelling. In the United States, the percentage of the population that consumes less than half the recommmended daily allowance (RDA) in the diet (i.e. ignoring supplement use) for five of these eight vitamins or minerals is estimated to be: zinc—10% of women/men older than 50; iron—25% of menstruating women and 5% of women over 50; vitamin C—25% of women/men; folate—50% of women and 25% of men; vitamin B—10% of women/men; vitamin B_{12}—10% of women and 5% of men (Ames & Wakimoto 2002). A considerable percentage of the United States population may be deficient in some vitamin or mineral (Ames 1998; Ames & Wakimoto 2002).

A deficiency of folic acid, one of the most common vitamin deficiencies in the population consuming few dietary fruits and vegetables, causes chromosome breaks in humans (Blount & al. 1997). The mechanism of chromosome breaks has been shown to be analogous to radiation (Blount & al. 1997). Folate supplementation above the RDA minimized chromosome breakage (Fenech & al. 1998). Folate deficiency has been associated with increased risk of colon cancer (Giovannucci & al. 1993; Mason 1994): in the Nurses' Health Study women who took a multivitamin supplement containing folate for 15 years had a 75% lower risk of colon cancer (Giovannucci & al. 1998). Folate deficiency also damages human sperm (Wallock & al. 2001), causes

neural tube defects in the fetus, and an estimated 10% of heart disease in the United States (Boushey & al. 1995). Approximately 10% of the American population (Senti & Pilch 1985) had a lower folate level than that at which chromosome breaks occur (Blount & al. 1997). Nearly 20 years ago, two small studies of low-income (mainly African-American) elderly (Bailey & al. 1979) and adolescents (Bailey & al. 1982) showed that about half the people in both groups studied had folate levels that low. Recently in Canada and the United States, flour, rice, pasta, and cornmeal have been supplemented with folate (Health Canada 1998; Jacques & al. 1999).

Recent evidence indicates that a deficiency of vitamin B_6 works by the same mechanism as folate deficiency and this would cause chromosome breaks (Huang, Shultz & Ames, unpublished). Niacin contributes to the repair of DNA strand-breaks by maintaining nicotinamide adenine dinucleotide levels for the poly ADP-ribose protective response to DNA damage (Zhang & al. 1993). As a result, dietary insufficiencies of niacin (15% of some populations are deficient) (Jacobson 1993), folate, and antioxidants may interact synergistically to affect the synthesis and repair of DNA adversely. Diets deficient in fruits and vegetables are commonly low in folate, antioxidants, (e.g., vitamin C), and many other vitamins and minerals, result in DNA damage, and are associated with higher cancer rates (Ames 1998; Ames & al. 1995; Block & al. 1992; Subar & al. 1989).

Vitamins and minerals from dietary sources other than fruits and vegetables

Vitamins and minerals whose main dietary sources are other than fruits and vegetables, are also likely to play a significant role in the prevention and repair of DNA damage, and thus are important to the maintenance of long-term health (Ames 1998). Deficiency of vitamin B_{12} (whose source in animal products) causes a functional folate deficiency,

accumulation of homocysteine (a risk factor for heart disease) (Herbert & Filer 1996), and chromosome breaks. B_{12} supplementation above the RDA was necessary to minimize chromosome breakage (Fenech & al. 1998). Strict vegetarians are at increased risk for developing vitamin B_{12} deficiency (Herbert & Filer 1996).

Epidemiological studies of supplement usage (vitamin and mineral intake by pill) have shown at most only modest support for an association. The strongest protective effect was for vitamin E and cancers of the prostate and colon (Patterson & al. 2001). There are many potential problems in conducting such studies including the need and difficulty in measuring supplement use over a long period of time, potential confounding of supplement usage with many other aspects of a healthy life-style, such as more exercise, better diet, and not smoking (Patterson & al. 2001). Clinical trials of supplements are generally too short to measure cancer risk since cancers usually develop slowly and the risk increases with age; moreover, such trials cannot measure the potential reduction in risk if supplements are taken throughout a lifetime (Block 1995). Additionally, the cancer risks of supplement users may be overestimated because they are more likely to undergo early screening like mammograms or tests for prostate cancer (prostate-specific antigen, PSA) which are associated with increased diagnosis (Patterson & al. 2001). Such confounding factors are not measured in many epidemiological studies.

Intake of adequate amounts of vitamins and minerals may have a major effect on health, and the costs and risks of a daily multivitamin and mineral pill are low (Ames 1998). More research in this area, as well as efforts to improve diets, should be high priorities for public policy.