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EXAMINATION OF DIETARY RECOMMENDATIONS FOR SALT-CURED, SMOKED, AND NITRITE-PRESERVED FOODS

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SUMMARY

Preservation of foods by smoke, salt, and other means has been practiced throughout the history of human civilization. Salted, smoked, and nitrite-preserved foods are descendants of this heritage. In the United States and some other countries, several modern improvements of the traditional processes have been incorporated. This report examines cancer risks associated with consumption of foods preserved by these methods.

Concern about the consumption of salt-cured foods

is due to high rates of gastric cancer in areas of the world in which people consume foods preserved with high concentrations of salt. It is unclear, however, whether the carcinogenic-risk is related directly to these foods or to other components of the diet. Whatever the mechanism, it has been shown that refrigeration of foods is corre-

lated highly with a decline in the rate of gastric cancer. In the United States, salt-cured and pickled foods no longer are consumed in great quantities because of the widespread use of refrigeration. These foods have evolved into forms that are salted to a lesser degree and depend on modern refrigeration and packaging practices for preservation.

Exposure of foods to smoke, which began as a traditional method of preservation, continues to be used today mainly because of taste and other organoleptic prop-

erties. Although wood smoke contains animal carcinogens, levels of these compounds in foods processed by means of traditional methods of smoking are lower than levels in charcoal broiled foods. In addition, these compounds are characterized as animal carcinogens as a result of the feeding of experimental doses greatly ex-

ceeding normal human intake and lifetime feeding regimens. Smoke flavorings now are being used in place of traditional smoking methods in most of the processed meat products produced in the United States because the animal carcinogens known to exist in natural smoke have been removed from the flavorings. These smoke flavorings have been reviewed extensively for safety and have been authorized for use by the U.S. Food and Drug Administration.

Substantial changes also have taken place in the use of nitrite in the processing of cured meats, mainly because of concerns that *N*-nitroso compounds (NOCs) are formed by *N*-nitrosation. Many of these NOCs, particularly nitrosamines, have tested positive in animal carcinogenicity experiments. The residual levels of nitrites in modern nitrite cured meats have decreased five-fold over the last two decades. Perhaps more important, ascorbate or erythorbate has been added and these substances are known to inhibit the *N*-nitrosation reaction.

These improvements led the American Cancer Society to state in 1996 that “nitrites in food are not a significant cause of cancer in Americans.” Recently, attention to the use of nitrite in cured meats has been heightened by epidemiologic reports associating cured meats with childhood cancers. It is important, however, to recognize the limitations and mixed findings resulting from these epidemiologic studies and the very limited evidence of biological plausibility from animal studies.

In conclusion, the scientific evidence does not support restrictions in the consumption of salted, smoked, or nitrite-preserved foods by the U.S. population.

INTRODUCTION

In the last two decades, various authoritative bodies have made a number of human health based recommendations concerning cured meat consumption. In 1981 and 1982, the National Academy of Sciences (NAS)/National Research Council (NRC) issued reports summarizing the available scientific evidence concerning nitrite-cured meat and offered implications and recommendations (National Research Council, 1981,

1982a). Key findings from the first report (National Research Council, 1981) were that nitrite itself was not carcinogenic, but there was some concern about the potential toxicity and carcinogenicity from certain metabolites that might result from its use. Further research to assess this risk was recommended, along with the institution of measures decreasing exposure to nitrite and its metabolites (but not at the risk of jeopardizing the ability of nitrite to protect against botulism and food spoilage).

The follow-up report (National Research Council, 1982a) examined alternatives to the use of nitrite in foods and made suggestions regarding partial or complete nitrite alternatives, along with recommendations about the use of agents for blocking or inhibiting the formation of nitrosamines. Some of these recommendations were implemented, and other changes were made by the cured meat industry; however, an effective replacement for the antibotulinal effects of nitrite has not been found.

At about the time that the NAS/NRC reports were being published, the NRC issued a separate report entitled *Diet, Nutrition and Cancer*, which included dietary guidelines for individuals to “minimize consumption of cured, pickled, and smoked foods” (National Research Council, 1982b). By 1987, however, the processing changes in practice by the cured meat industry were being recognized. As pointed out by the American Cancer Society (ACS) (1987), “the American food industry has developed new processes to avoid possible cancer-causing by-products.” Continued improvements in the cured meat process have led the ACS to conclude in their most recent dietary guidelines (American Cancer Society, 1996) that “nitrites in foods are not a significant cause of cancer among Americans.” In addition, the NRC (1996) recently published a comprehensive report entitled *Carcinogens and Anticarcinogens in the Human Diet*, in which no mention was made of the carcinogenic risk associated with cured meat consumption.

The goal of this report by the Council for Agricultural Science and Technology is to reexamine the health based science associated with the production and consumption of cured, pickled, and smoked foods.

SALT-CURED OR PICKLED FOODS

Salting as a means of preserving foods antedates written history. The Mesopotamians (3000 B.C.) generally used salt to preserve meat and fish (Bottero, 1985). Early Roman writers such as Cato (234–149 B.C.) clearly explained the need to salt perishable meats and vegetables to preserve them. Foods usually were covered with copious quantities of salt or saturated salt brine, and the salt was allowed to infuse into the tissue while dehydrating the product. This process rapidly eliminated the microorganisms causing spoilage or food poisoning and allowed organisms producing lactic acid and other desirable sensory products to flourish.

Salting, pickling, and drying continued as the primary means of preserving foods until the twentieth century and the advent of mechanical refrigeration. When refrigeration became the common means of preservation, consumer taste preferences brought about a decrease in salt concentrations in food. For example, hams produced in the first half of the century had salt concentrations of greater than 6% (Moulton and Lewis, 1948), but today many ham products have salt concentrations of less than 2%. As recently as 1980, major brands of hot dogs frequently exceeded 2.8% average salt content (Hoar, 1996). Today, because of changing consumer tastes and dietary concerns, that level has decreased by nearly one-third.

The preponderance of research linking salt-cured foods with gastric cancers was based on epidemiological studies of populations consuming heavily salted foods such as dried seafood and pickled vegetables (Haenzel et al., 1972; Howson et al., 1986; Kim and Hotchkiss, 1994). These foods traditionally were held unrefrigerated, none of the foods studied was common in the modern American diet, and none represented a food currently consumed in the United States. In contrast, a decline in the gastric cancer rate has been associated consistently with the increased use of refrigeration (Howson et al., 1986). This correlation notwithstanding, international studies continue to link salt-cured and pickled foods with gastric cancer. Careful reading of these research reports reveals that the foods implicated are consumed by a very low proportion of persons in the

United States.

SMOKED FOODS

Smoke processing originated at the beginning of human civilization as a means of preserving foods. It still is used, especially in tropical developing countries, to preserve meat. Smoke imparts attractive and appealing sensory properties to meats, including color and flavor. In addition, traditional smoking protects and preserves the nutritive value of foods (Daun, 1979; Hollenbeck, 1979).

Concern has been expressed about the presence of polycyclic aromatic hydrocarbons (PAHs) and nitrosamines, both known animal carcinogens, in wood smoke. These materials have been found in wood smoke and can be removed by separating the condensate into an aqueous phase and a particulate phase containing the carcinogenic compounds. The levels of these chemicals depend on the methods of smoke generation and application and the conditions of smoke curing, e.g., time, temperature, and moisture. Levels reported in traditionally smoked foods are significantly lower than those reported in charcoal broiled products (Ruiter, 1979; Simon et al., 1969; Sink, 1979). Oral administration of some of these compounds has produced tumors in laboratory animals, but only at doses greatly exceeding normal human intake and under regimens entailing chronic administration for the lifetime of the animal.

Most sausages made in the United States are manufactured in removable, semipermeable casings. If natural wood smoke is used, only low-molecular-weight organic acids, carbonyls, and phenols traverse the casing, thereby flavoring and coloring the meat. Carcinogenic tars do not traverse the casing, seldom contact the sausage, and are discarded.

Alternatives to traditional smoking methods nonetheless have been sought. Smoke flavorings have evolved as a successful alternative imparting the color and flavor of traditional smoking methods.

The use of aqueous liquid smoke flavorings has been increasing in the United States and elsewhere. Liquid smoke flavorings provide the same traits as traditional smoking, e.g., desirable sensory properties, and

preservation through antioxidation or bacteriostasis (Fretheim et al., 1980). Additional benefits of liquid smoke include decreased cooking time; increased consistency of product color and flavor; and the absence of detectable animal carcinogens. Aqueous liquid smoke flavorings are used in most processed meat products, as in, for example, 75% of hot dogs produced in the United States.

Smoke flavorings have been defined as “complex mixtures of components of condensed smoke derived from pyrolysis of hardwoods (usually oak, hickory, beech, alder, and maple) in the absence of or in a limited amount of air” (Joint FAO/WHO Expert Committee on Food Additives [JECFA], 1992). Source materials must be free of pesticides, preservatives, and any extraneous matter that could result in the formation of potentially hazardous components of wood smoke. The specifications published by the JECFA (1992) are rigorous, and a limit of not more than 10 micrograms/kilogram (10 parts per billion) of benzo(a)pyrene is permitted (the limit of detection sensitivity). It also was reported by JECFA (1987) that although nitrosamines were not detected in any of the smoke flavorings tested, some noncarcinogenic PAHs were.

Smoke flavoring solutions may be applied to meat products by dipping the meat, e.g., hams or small meat products, into solutions of smoke flavorings; by showering or spraying in a closed cabinet of the products to be treated, as with frankfurters; or by atomizing/aerosolizing the solutions of smoke flavoring in a traditional smokehouse holding the product, e.g., bacon.

In rodents, acute and subchronic (90-day) feeding studies at very high levels of liquid smoke flavorings have not produced evidence of toxicity (Joint FAO/WHO Expert Committee on Food Additives, 1987). The weight of available evidence indicates that aqueous liquid smoke flavoring is not mutagenic. Long-term and/or carcinogenicity studies of aqueous liquid smoke flavorings have not been reported. The risk of a carcinogenic response is essentially nil because current specifications limit the level of benzo(a)pyrene and because most casings currently used in meat processing are impermeable to the large molecular weight compounds

such as PAHs found in aqueous liquid smoke flavorings. Epidemiological or other human data have not been reported.

A critical review of the available information on smoked food products sold in the United States indicates that these materials are safe and supports their use at current levels. Available data do not support the alleged carcinogenicity of these products. The scientific evidence clearly does not support recommendations to limit the consumption of smoke flavored foods.

NITRITE-PRESERVED FOODS

Introduction

Nitrite, as used to cure meat, functions as a preservative against *Clostridium botulinum* and other spoilage bacteria and imparts palatability and appearance characteristics, namely a specific taste, texture, and pink color. During the 1970s, concerns arose that cured meats contained high levels of residual nitrite and preformed nitrosamines; the former would add to the total body burden of nitrite, and the latter are known animal carcinogens. A decade of research, debate, and technological change in the production of cured meat concluded with the issuance of two reports by the NRC (1981, 1982a). In 1990, Cassens published a complete account entitled *Nitrite-Cured Meat: A Food Safety Issue in Perspective*.

It was established that nitrite is not a carcinogen, and a surveillance program for volatile nitrosamines in bacon was put into place by the U.S. Department of Agriculture. It also is known that green leafy and root vegetables usually contain high levels of nitrate, which may be converted to nitrite during digestion, and thereby expose humans to a much higher level of nitrite than the small amount of residual nitrite (usually < 10 parts per million [ppm]) in modern cured meats. Moreover, endogenous formation of nitrite occurs in humans.

There have been major and important advances in understanding both the endogenous formation of nitrite in humans and the metabolism of ingested nitrite and nitrate. Tracking studies have followed sources of exposure of humans to nitrite and nitrate, and changes have been made in modern cured meats. The role of *N*-nitroso

compounds (NOCs) in cancer has been investigated further, and epidemiological approaches likewise have been undertaken. The following is a summary of this enormous and developing body of scientific literature.

Fate of Ingested Nitrate and Nitrite in Humans

Ingested nitrate, with a half-life of about five hours, is absorbed rather quickly from the upper gastrointestinal tract and subsequently is eliminated in the urine. Ingested nitrite may react with other substances in the gastrointestinal tract. If absorbed into the blood, it is oxidized rapidly to nitrate or may oxidize hemoglobin to methemoglobin.

A portion of the nitrate in blood is secreted by salivary glands, and the microbial flora of the oral cavity can reduce it to nitrite. About 25% of blood nitrate is secreted into saliva, with about 20% of salivary nitrate reduced to nitrite. About 5% of ingested nitrate therefore is converted in the saliva and reconsumed as nitrite.

Endogenous Formation

Efforts to discover the mechanism of endogenous formation of nitrate and nitrite have engendered considerable uncertainty and debate. Much early work was based on balance studies, and because certain microorganisms can generate nitric oxide by reduction of nitrite or oxidation of ammonia, some confusion arose concerning bacterial conversions. It now is known that the enzyme nitric oxide synthase catalyzes the oxidation of the amino acid L-arginine to nitric oxide and L-citrulline (Culotta and Koshland, 1992) and that the nitric oxide can be converted to nitrite and nitrate and excreted subsequently (Leaf, 1989).

It has been discovered that nitric oxide generated in mammalian cells serves the important role of biological messenger in such important physiological functions as neurotransmission, blood clotting, blood pressure control, and immunity.

Additionally, when nitrite is acidified in the stomach, it has antimicrobial activity that coincides with the formation of nitric oxide. Dykhuizen et al. (1996) concluded that the generation of salivary nitrite from dietary

nitrate may provide significant protection against gut pathogens in humans.

Although nitric oxide has a necessary and positive function, from another perspective it is a risk inasmuch as nitrite may react with amines in the body to form nitrosamines, some of which are animal carcinogens under experimental conditions. (See section "Role of *N*-Nitroso Compounds," below.)

Exogenous Sources of Nitrite and Nitrate

Schuddeboom (1993) concluded that human exposure to nitrite from intake of cured foods was low. He also presented evidence that, when conversion from nitrate is taken into account, nitrite intake from vegetables exceeds that from cured meat. Nevertheless, the benefits of vegetable consumption outweigh concerns about their contribution to nitrite intake.

Several other countries monitor their foods for nitrate, nitrite, and NOCs and have reached the same conclusion, namely, that nitrite and NOCs in the diet represent a relatively small contribution to the total body burden of these compounds (see Cassens, 1995 for review).

Role of *N*-Nitroso Compounds

Nitrite is a reactive chemical and therefore, in addition to reacting with myoglobin, a process resulting in the distinctive characteristics of cured meat, it also can react with other substances found in meat, e.g., amines, amides, amino acids, and related compounds. In so doing, nitrite forms NOCs by a process called *N*-nitrosation. Many of the NOCs investigated, which include nitrosamines or nitrosamides, have tested positive in laboratory animal carcinogenicity experiments. Human stomach cancer risk associated with NOCs and other dietary factors has been reviewed (Nomura, 1996).

It should be realized that the characterization of NOCs, and nitrosamines in particular, as animal carcinogens is based on unrealistic human conditions such as experiments in which dosage far exceeds that to which humans are exposed, continuous lifetime exposure, and other worst-case assumptions. Certainly, some nitrosamines pose a potential carcinogenic risk to humans.

(See Mirvish, 1995 for a discussion of the role that NOCs and *N*-nitrosation have in the etiology of human cancer.) Efforts to decrease exposure to them should be instituted, as should efforts to decrease conditions conducive to their *in vivo* formation. To this end, the level of nitrite in cured meats has been decreased fivefold over the last 20 years (yr), and most cured meats produced in the United States contain ascorbates (Cassens, 1997), which are effective inhibitors of the nitrosation reaction (Mirvish et al., 1995).

Nitrite-Cured Meat

White (1975) calculated that cured meat manufactured in the United States contained on average 52.5 ppm of residual nitrite. Data used included nitrite values of 0 to 272 ppm. Cassens (1997) sampled bacon, bologna, sliced ham, and weiners at retail and found an average residual nitrite level of 10 ppm; residual nitrate was nondetectable and residual ascorbate was 200 ppm. Because of changing technologies and decreased levels of ingoing nitrite, the residual nitrite content of modern cured meats is about one-fifth of that typically found 20 yr ago. Overall, the dietary intake of nitrite from cured meats constitutes only a minor source of the total exposure. None-the-less, if the total dietary intake of nitrites is too high, even minor sources must be scrutinized.

Epidemiology

In 1982, maternal consumption of nitrite-cured meats was reported as being potentially related to brain cancer in a group of children in Los Angeles, California (Preston-Martin et al., 1982). Several subsequent studies also have reported higher risks of childhood cancer associated with maternal or childhood consumption of cured meats, although the findings have been mixed (Bunin et al., 1993, 1994; Cordier et al., 1994; Filippini et al., 1990; Howe et al., 1989; Kuijten et al., 1990; McCredie et al., 1994a, 1994b; Peters et al., 1994; Preston-Martin et al., 1982; Preston-Martin et al., 1996; Sarasua and Savitz, 1994; Schymura et al., 1996; and Wilkins et al., 1995).

Among the epidemiologic studies reporting associations between childhood cancers and consumption of

specific types of cured meat, relationships have not been consistent for the various types of cured meats (e.g., hot dogs, bacon, and lunch meat) (Bunin et al., 1993, 1994; Peters et al., 1994; Preston-Martin et al., 1982; Preston-Martin et al., 1996; Sarasua and Savitz, 1994).

Moreover, there are major limitations in all studies to date on cured meats and childhood cancers. The first major limitation is that all studies of cured meats and childhood cancers have been case-control studies and therefore have been susceptible to recall bias. After the child was diagnosed with cancer, parents or children were asked to recall consumption of cured meats. Recall bias can occur because parents of children who have cancer may remember their consumption or their children's consumption of certain foods differently due to the stimulus of experiencing cancer. Only a prospective cohort study could eliminate this potentially serious bias in the recollection of dietary exposures.

The second major limitation is that individuals who eat hot dogs have other differences in their diets and lifestyles (Kahn et al., 1996). Potential confounding factors have not been thoroughly investigated in the studies published to date on cured meats, in part due to difficulties in collecting data on a large number of exposures. For example, most, if not all, studies to date do not account for differences in dietary intakes of fat, folate, and fruits and vegetables among individuals who do eat cured meats and those who do not. It is inappropriate to link nitrite-cured meats causally with childhood cancers, for there are serious limitations and mixed findings in the epidemiologic studies. Animal studies provide only very limited evidence of biological plausibility for such a link.

LITERATURE CITED

- American Cancer Society. 1987. *Cancer Facts and Figures*. American Cancer Society, Atlanta, Georgia.
- American Cancer Society. 1996. *Guidelines on Diet, Nutrition, and Cancer Prevention: Reducing the Risk of Cancer with Healthy Food Choices and Physical Activity*. The American Cancer Society 1996 Dietary Guidelines Advisory Committee, American Cancer Society, Atlanta, Georgia.
- Bottero, J. 1985. The cuisine of ancient Mesopotamia. *Biblical Archeology March* 1985:36-47.
- Bunin, G. R., R. R. Kuijten, J. D. Buckley, L. B. Rorke, and A. T. Mead-

- ows. 1993. Relation between maternal diet and subsequent primitive neuroectodermal brain tumors in young children. *New Engl J Med* 329:536-541.
- Bunin, G. R., R. R. Kuijten, C. P. Boesel, J. D. Buckley, and A. T. Meadows. 1994. Maternal diet and risk of astrocytic glioma in children: A report from the Children's Cancer Group (United States and Canada). *Cancer Causes Contr* 5:177-187.
- Cassens, R. G. 1990. *Nitrite-Cured Meat: A Food Safety Issue in Perspective*. Food and Nutrition Press, Trumbull, Connecticut.
- Cassens, R. G. 1995. Use of sodium nitrite in cured meats today. *Food Technol* 49:72.
- Cassens, R. G. 1997. Residual nitrite in cured meats. *Food Technol* 51:53-55.
- Cato, Marcus Porcius (234-149 B.C.). *On Agriculture*. Pp. 89-91, 155-157. Loeb Classical Library, Harvard University Press, Cambridge.
- Cordier, S., M. Iglesias, C. LeGoaster, M. Guyot, L. Mandereau, and D. Hemon. 1994. Incidence and risk factors for childhood brain tumors in the Ile de France. *Intl J Cancer* 59:776-782.
- Culotta, E. and D. E. Koshland. 1992. NO news is good news. *Science* 258:1862.
- Daun, H. 1979. Interaction of wood smoke components and foods. *Food Technol* 33:66-70.
- Dykhuisen, R. S., R. Frazer, C. Duncan, C. C. Smith, M. Golden, N. Benjamin, and C. Leifert. 1996. Antimicrobial effect of acidified nitrite on gut pathogens: Importance of dietary nitrite in host defense. *Antimicrob Agents Chemother* 40:1422-1425.
- Filippini, G., A. Artuso, A. Solari, M. Farinotti, G. Lovicu, S. Preston-Martin, and P. Boyle. 1990. Childhood brain tumors and exposure to N-nitroso compounds: A case-control study. *Neurology* 40:420.
- Fretheim, K., P. E. Granum, and E. Vold. 1980. Influence of generation temperature on the chemical composition, antioxidative and antimicrobial effects of wood smoke. *J Food Sci* 45:999-1007.
- Haenzel, W., M. Kurihara, M. Segi, and R. K. C. Lee. 1972. Stomach cancer among Japanese in Hawaii. *J Natl Cancer Inst* 49:969-988.
- Hoar, D. W. 1996. Personal communication.
- Hollenbeck, C. M. 1979. Liquid smoke flavoring—Status of development. *Food Technol* 33:88-90.
- Howe, G. R., J. D. Burch, A. M. Chiarelli, H. A. Risch, and B. C. K. Choi. 1989. An exploratory case-control study of brain tumors in children. *Cancer Res* 49:4349-4352.
- Howson, C. P., T. Hiyama, and E. L. Wynder. 1986. The decline of gastric cancer: Epidemiology of an unplanned triumph. *Epidemiol Rev* 8:1-27.
- Joint FAO/WHO Expert Committee on Food Additives. 1987. *Toxicological evaluation of certain food additives. Smoke flavourings*. Pp. 21-23, 41-57. Thirty-first Report. Technical Report Series 759. Joint FAO/WHO Expert Committee on Food Additives, United Nations.
- Joint FAO/WHO Expert Committee on Food Additives. 1992. *Smoke flavourings. Compendium of Food Additives Specifications* 2:1297-1304, United Nations.
- Kahn, E., G. Bunin, L. Kushi, and J. Brown. 1996. Maternal cured meat consumption and risk of childhood brain tumor: Other explanations. *Am J Epidemiol* 139:S9.
- Kim, S. A. and J. H. Hotchkiss. 1994. Nonvolatile N-nitrosamides in dried squid. In *Nitrosamines and Related N-nitroso Compounds—Chemistry and Biochemistry*. American Chemical Society, Washington, D.C.
- Kuijten, R. R., G. R. Bunin, C. C. Nass, and A. T. Meadows. 1990. Gestational and familiar risk factors for childhood astrocytoma: Results of a case-control study. *Cancer Res* 50:2608-2612.
- Leaf, C. D., J. S. Wishnok, and S. R. Tannenbaum. 1989. L-arginine is a precursor for nitrate biosynthesis in humans. *Biochem Biophys Res Commun* 163:1032.
- McCredie, M., P. Maisonneuve, and P. Boyle. 1994a. Antenatal risk factors for malignant brain tumours in New South Wales children. *Intl J Cancer* 56:6-10.
- McCredie, M., P. Maisonneuve, and P. Boyle. 1994b. Perinatal and early postnatal risk factors for malignant brain tumours in New South Wales children. *Intl J Cancer* 56:11-15.
- Mirvish, S. S. 1995. Role of N-nitroso compounds (NOC) and N-nitrosation in etiology of gastric, esophageal, nasopharyngeal and bladder cancer and contribution to cancer of known exposures to NOC. *Cancer Letters* 93:17.
- Mirvish, S. S., A. C. Grandjean, K. J. Reimers, B. J. Connelly, S.-C. Chen, J. Gallagher, S. Rosinsky, G. Nie, H. Tacatoo, S. Payne, C. Hinman, and E. I. Ruby. 1995. Dosing time with ascorbic acid and nitrite, gum and tobacco chewing, fasting, and other factors affecting N-nitrosoproline formation in healthy subjects taking proline with a standard meal. *Cancer Epidemiol, Biomarkers Prevent* 4:775-782.
- Moulton, C. R. and W. L. Lewis. 1948. *Meat through the Microscope*. University of Chicago Press, Chicago, Illinois. Pp. 247.
- National Research Council. 1981. *The Health Effects of Nitrate, Nitrite, and N-nitroso Compounds*. National Academy Press, Washington, D.C.
- National Research Council. 1982a. *Alternatives to the Current Use of Nitrite in Foods*. National Academy Press, Washington, D.C.
- National Research Council. 1982b. *Diet, Nutrition, and Cancer*. National Academy Press, Washington, D.C.
- National Research Council. 1996. *Carcinogens and Anticarcinogens in the Human Diet*. National Academy Press, Washington, D.C.
- Nomura, A. 1996. Stomach cancer. Pp. 707-724. In *Cancer Epidemiology and Prevention*. 2nd ed. Oxford University Press, New York.
- Peters, J. M., S. Preston-Martin, S. J. London, J. D. Bowman, J. D. Buckley, and D. C. Thomas. 1994. Processed meats and risk of childhood leukemia (California, USA). *Cancer Causes Contr* 5:195-202.
- Preston-Martin, S., M. C. Yu, B. Benton, and B. E. Henderson. 1982. N-nitroso compounds and childhood brain tumors: A case-control study. *Cancer Res* 42:5240-5245.
- Preston-Martin, S., J. M. Pogoda, B. A. Mueller, E. A. Holly, W. Lijinsky, and R. L. Davis. 1996. Maternal consumption of cured meats and vitamins in relation to pediatric brain tumors. *Cancer Epidemiol* 5:599-605.
- Ruiter, A. 1979. Color of smoked foods. *Food Technol* 33:54-59.
- Sarasua, S. and D. A. Savitz. 1994. Cured and broiled meat consumption in relation to childhood cancer: Denver, Colorado (United

States). *Cancer Causes Contr* 5:141-148.

Schuddeboom, L. J. 1993. *Nitrates and Nitrites in Foodstuffs*. Council of Europe Press, Belgium.

Schymura, M. J., D. Zheng, M. S. Baptiste, and P. C. Nasca. 1996. A case-control study of childhood brain tumors and maternal lifestyle. *Am J Epidemiol* 88.

Simon, S., A. A. Rypinski, F. W. Tauber, R. M. Pencyla, and D. O. Westerberg. 1969. Effect of cellulose casing on absorption of polycyclic hydrocarbons in wood smoke by absorbents. *J Agric Food Chem* 17:1128-1134.

Sink, J. D. 1979. Effects of smoke

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processing on muscle food product characteristics. *Food Technol* 33:72-83.

Wilkins, J. C., Pickrel, J. Bunn, and T. Sinks. 1995. N-nitroso compounds and risk of childhood brain tumor: Mother's diet during pregnancy. *Am J Epidemiol*. SER Abstr. P. 615.

White, J. W. 1975. Relative significance of dietary source of nitrate and nitrite. *J Agric Food Chem* 23:886. (See correction in *J Agric Food Chem* 24:202, 1976).

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