Not So Hot HOT DOGS?

Fleshing out risks associated with how we treat meat

By JANET RALOFF

Medical research hasn't been offering much encouragement to the steak and potatoes crowd — or, for that matter, to the more plebeian hot dog and chips community.

First came studies indicating that fats — and the cholesterol in meat — can increase an individual's risk of heart disease. Later work linked those fats to a number of cancers, from the breast to the colon. Then analyses indicated that the high protein levels typical of most Western diets pose an independent risk of fostering certain cancers.

Now comes the issue of how meats are cooked or preserved. For instance, a trio of new papers links cured meats — especially hot dogs — to childhood cancers. And last week, new data focused on carcinogens that form in browned meats.

Agricultural Res. Serv., USDA

Cured meats invite one class of carcinogens to dinner, while high temperatures can imbue steaks and other meats with another family of cancer-causing agents.

This can be depressing news for those who like meat — as most Americans do. U.S. livestock producers marketed enough last year to feed every U.S. resident some 112 pounds of red meat and 61 pounds of poultry.

But even for die-hard carnivores the news isn't all bad, if their tastes run to salads and a spot of tea. Such plant-derived foods may fight cancer by targeting the carcinogens that cooked and cured meats bring to the dinner table.

During a study of the reputed link between electromagnetic fields and childhood cancer, Sara Sarasua and David A. Savitz of the University of North Carolina at Chapel Hill looked at possible confounding factors. These included the eating habits of 440 children, 234 of whom had cancer, and of each child's mother during pregnancy.

In the March CANCER CAUSES AND CONTROL, the two epidemiologists report that children of women who ate hot dogs at least once a week during pregnancy faced more than twice the risk of developing a brain tumor as did those whose mothers eschewed frankfurters.

But the kids' diets revealed an even stronger cancer link. Children who ate ground meat at least once a week had twice the risk of suffering acute lymphocytic leukemia as those who ate none; the risk almost tripled for children eating two or more hamburgers weekly. And children noshing on hot dogs once a week or more experienced twice the brain tumor risk of kids who ate none. That risk climbed to almost three times normal if a child ate hot dogs at least twice a week.

Nor were these the only meats linked to cancer. Children who ate the most ham, bacon, and sausage had an 80 percent greater brain tumor risk — and more than three times greater lymphoma risk — than those who ate none of those meats.

But the really big surprise, Savitz told SCIENCE NEWS, "was the apparent synergism between this [meat-linked cancer] and low vitamin intake." Most of the children — and their mothers — took vitamins. Those who didn't appeared much more vulnerable to the meats' carcinogenic potential.

For instance, children who ate the most ham, bacon, and sausage faced 2.9 times the leukemia risk and 4.6 times the brain tumor risk of children who took vitamins and ate the least of these meats. Lunch meats proved a risk factor only among children not taking vitamins.

Says Savitz: "There was a general pattern in which failure to take vitamins conferred a greater increase in risk than eating lots of meats." So within the context of cancer in children, he notes, these data argue that "if there's a benefit to taking vitamins, that benefit is greatest for children who are consuming more of these meats."

While a few previous studies had hinted that cured meats might be linked to childhood cancers, "that's all they were — hints," says John M. Peters at the University of Southern California School of Medicine in Los Angeles. But in the youngsters age 10 and under that his group has just studied — 232 with leukemia, 232 without — the cancer risk was strongly linked to consumption of hot dogs. No other breakfast or lunch meat showed a similar tie.

Dietary questions on cured meats were "added just for completeness' sake" to a large study of risk factors for childhood leukemia, he says. As such, he recalls, these data "were the last things we analyzed. But when we did — lo and behold, this finding jumped out."

Yet even the frankfurter link did not become large until consumption exceeded 12 hot dogs per month. But children who did down dogs that often faced 9.5 times the leukemia risk of those who ate none. And among the offspring of men who ate frankfurters often, the leukemia risk was 11 times normal.

This risk held even among children who, according to their mothers, ate no hot dogs. In other words, the risk conferred by dad's diet appeared independent of that posed by the child's. A report of these findings also appears in the March CANCER CAUSES AND CONTROL.

A third study in the same journal links a pregnant woman's diet to her offspring's subsequent risk of astrocytic glioma, the most common brain tumor in children. Greta R. Bunin of Children's Hospital of Philadelphia and her coworkers focused on 155 glioma victims, all age 6 years or younger. Interviewers surveyed the eating habits of the youngsters' mothers and compared their diets to those of the mothers of a matched group of 155 cancerfree children.

Only hot dogs showed a statistically significant link with the cancer. Mothers who downed frankfurters weekly during pregnancy, compared to those who ate

fewer, appeared to increase their children's risk of brain cancer by 90 percent.

Companies that make processed meats use nitrites and nitrates to prevent the growth of pathogenic bacteria, particularly those responsible for deadly botulism, in their products. In the gut, however, nitrites and nitrates can combine with amines and amides to form potentially cancer-causing N-nitroso compounds.

More than 200 nitrosamines and related nitrosamides have proved carcinogenic in animal studies. Indeed, Savitz notes, the three new studies involving cured meats provide support, "in a very general way, for the hypothesis that it's the conversion of nitrites to nitrosamines that poses a cancer risk."

However, the cancers involved here are extremely rare. For instance, acute lymphocytic leukemia annually strikes only about 3 in every 10,000 children. In absolute terms, then, even a tripling in the frequency of this cancer would increase its incidence only slightly.

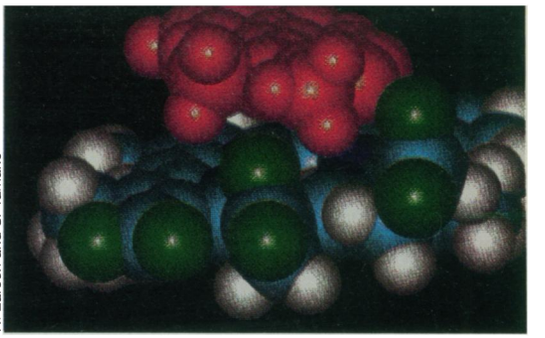
As such, Savitz and the other authors say, their findings do not justify panic among cured-meat eaters. Nor do they argue we should alter our diets – yet – says Steven R. Tannenbaum of the Massachusetts Institute of Technology. But these "extremely preliminary" findings point to the need "to take another look at [the issue] with a larger study that's been designed to test" whether cured meats pose a cancer risk in kids, he adds.

For the past 15 years, the molecular toxicology program that James S. Felton heads at Lawrence Livermore National Laboratory in Livermore, Calif., has examined the heat-induced chemical reactions that cause fried or broiled meats to brown. These so-called Maillard reactions can also create carcinogens known as heterocyclic amines (HCAs). Initially, even at high temperatures, very few of these compounds form.

So searing the exterior of a steak will produce few, if any, HCAs. But as heat begins driving water and fat out, Felton explains, free amino acids, sugars, and creatinine – key ingredients in HCAs – move toward the surface of the meat. Once some critical and as-yet-uncharacterized threshold is reached, he says, "production of heterocyclic amines goes up very fast."

It's not the cooking temperature or time alone, but a combination of the two that determines the type and quantity of HCAs produced, Felton's team reported in San Francisco last week at the annual meeting of the American Association for Cancer Research (AACR).

Moreover, in contrast to the carcinogenic polycyclic aromatic hydrocarbons that can form in char, HCAs can't simply be scraped off a burger or charbroiled chicken. Felton says his data show that HCAs "don't actually occur at the pan-meat interface, but are embedded," tending to form throughout the meat's outer third.



R. Larsen and S. Yamane

Computer model shows potentially detoxifying union that can form between the heterocyclic amine PhIP (upper red ring) and a chlorophyll (lower ring).

Meat type also appears important. One 1988 Livermore study that directly compared ground-meat patties fried identically showed that chicken and beef produce five to eight times more HCAs than fish does.

Felton's team also reported preliminary estimates at AACR of the human risks posed by HCAs in the diet. At least in studies of cancer in animals, the IQ and MeIQx forms seem most potent. A third type, PhIP, is much less potent. However, Felton says, because the chemical reactions in cooking meat overwhelmingly favor production of PhIP, the compound accounts for nearly half the human cancer risk attributable to HCAs.

In work slated for publication this year, Felton's group further refines the upper bounds of this lifetime risk estimate to about 1 per 10,000 exposed individuals – or some 300 of the 155,000 newly diagnosed colorectal cancers in the United States each year. While small compared to the total incidence of this disease, "The magnitude of the predicted population risk is not negligible from a public health standpoint," the scientists argue.

Elizabeth G. Snyderwine and her National Cancer Institute colleagues in Bethesda, Md., reported at AACR that the liver-activated forms of the heterocyclic amines IQ and PhIP form adducts – or covalent bonds to DNA – in human breast cells grown in the lab. Such DNA-altering bonds are often a first step in cancer. Moreover, PhIP produced much higher concentrations of adducts in cultured cells than did IQ. This suggests that among HCAs, "[PhIP] may be the more potent of the mammary carcinogens," Snyderwine says.

What's a well-done-meat lover to do? Felton urges greater use of microwave ovens. His team

Continued on p.269

Coffee: Key to cooked-meat vulnerability?

Heterocyclic amines (HCAs) are not carcinogenic until chemically altered in the liver by a pair of enzymes, each of which controls a separate stage of this two-step process (SN: 1/8/94, p.22). Depending on the genes inherited, a person may produce small, intermediate, or large amounts of the enzymes, notes Fred F. Kadlubar of the National Center for Toxicological Research in Jefferson, Ark. The more enzyme present, the faster the transformation. And individuals possessing genes to carry out both stages rapidly risk activating the most HCAs – the ultimate carcinogens that circulate through the body.

With Nicholas P. Lang of the Arkansas Cancer Research Center in Little Rock, Kadlubar found that the HCA-activating enzymes are the same ones that begin and end the metabolism of caffeine. To learn who carried the genes to complete both stages quickly, they asked 280 people to drink 9 ounces of coffee. Then they scouted for "rapid-rapid" individuals by monitoring their excretion of by-products from the first and last stages of caffeine breakdown. One-third of the people suffered from colon cancer – a malignancy linked to HCAs in animal and human dietary studies.

In the coffee test, "The really striking thing was that only 16 percent of the [cancerfree individuals] were rapid-rapid, while 35 percent of the cancer patients were," Kadlubar says.

Each volunteer also answered a dietary survey. Among its questions: When you have red meat, do you eat it well-done, medium, or rare?

A preliminary analysis shows that, compared with cancerfree people, almost twice as many colon cancer patients – 45 percent – preferred their meat well-done. This pilot study indicates that those with the genes to carry out both phases of HCA transformation rapidly – *and* who like their meat well-done – are six times as likely to develop colon cancer as slow-slow individuals who favor rarer fare, Kadlubar says.

Such high-risk people over age 40 "should be strongly encouraged to have regular colonoscopies" – to diagnose polyps that can be removed before they turn cancerous, Kadlubar says.

In the meantime, Kadlubar observes, their data show "a very rough relationship between the number of cups of coffee an individual consumes each day and whether they're a rapid-rapid metabolizer." He speculates that many heavy coffee drinkers refill their cup to compensate for their body's rapid breakdown of caffeine.

– J.A. Raloff

Continued from p.265

finds that precooking burgers for 2 minutes in a microwave drives off some juice—and most of the precursors of HCAs. When later barbecued, these burgers produce only about 10 percent of the carcinogens seen in patties cooked solely on the grill.

Drinking green or black tea may do much the same thing, says John H. Weisburger of the American Health Foundation in Valhalla, N.Y. His team's new studies show that polyphenols in these brews "powerfully lower the mutagenicity of IQ and PhIP" in bacteria. The teas also inhibited the formation of HCA adducts in cultured cells.

Some sulfur compounds in garlic prevent nitrosamine-induced cancers (SN: 3/19/94, p.190). "But molecule for molecule, selenium analogs of these are several hundred times more powerful than the sulfur ones in cancer prevention — and we have data to support this," says biochemist Clement Ip of the Roswell Park Cancer Institute in Buffalo, N.Y.

Garlic, onions, and other allium family members can't distinguish between selenium and sulfur, so gardeners can fool plants into taking up selenium by fertilizing with it, Ip said at AACR.

His team is currently planning a study in humans of these selenium-enriched alliums in regions of China where selenium deficiency causes a rare form of childhood heart disease. If this shows that people absorb selenium compounds as well as sulfur ones, Ip says, his team may consider a cancer prevention trial using the modified garlic.

But protection from some of these meaty carcinogens may be as simple as grazing at the nearest salad bar, suggest new studies by Roderick H. Dashwood and his colleagues at the University of Hawaii in Honolulu. Their work with chlorophylls (especially the synthetic, water-soluble derivatives known as chlorophyllins) indicates that these plant-derived compounds can inhibit the production of potentially carcinogenic adducts by a number of dietary carcinogens — from polycyclic aromatic hydrocarbons in char and aflatoxin in moldy grains to HCAs in cooked meats.

At the AACR meeting, Dashwood's team reported results from new computer modeling studies that attempt to tease out the mechanism responsible for the chlorophyllins' inhibitory activity. It appears that these compounds form chemical complexes with HCAs and that the stronger this complex, the more potent the inhibition.

More important, Dashwood told SCIENCE NEWS, "We have animal data that suggest this complexing really can be protective." When his team gave IQ and chlorophyllins to rats at the same time, far more of the HCAs were excreted in the feces.

Moreover, his team finds that administering high doses of chlorophyllins and IQ or PhIP to rats prevents the usual development of adducts in the liver, colon, and small intestine. This supplementation also prevents precancerous colon changes in rats exposed to IQ or PhIP, Dashwood's newest studies show — but *only* if given prior to or during HCA exposure. Indeed, when chlorophyllin supplementation followed HCA exposure, it significantly increased the number of "aberrant crypts" — precancerous changes in the colon.

If this cancer-promoting effect varies with the dose, Dashwood says, risks may not occur at low doses or with the natural chlorophyll. The data might also suggest that the large doses of chlorophyllins delivered during his short-term studies were too high.

The take-home message, he suspects, may be as simple as "A little is good; a lot may be deleterious."

Despite the many health concerns about animal protein and the way we preserve and cook it, "It's not at all clear that we can tell people never to eat meat," observes Devra Lee Davis, a toxicologist with the Department of Health and Human Services in Washington, D.C. Indeed, she argues, the oldest advice may still be the best: Eat a varied diet — one rich in fruits, vegetables, and fiber. □