AMERICAN MEAT INSTITUTE FACT SHEET

Diet and Cancer Research

Background

What causes cancer? That question has vexed scientists for centuries. Researchers continue to look at genetics, environmental exposure, alcohol consumption, tobacco use, vitamin and supplement use, exercise habits, food consumption and many other factors.

But separating one factor from another can be challenging in the real word. While the life of a laboratory animal can be carefully controlled, humans breathe different air, swim in and drink different water, eat different foods in different combinations, exercise a lot, occasionally or not at all, smoke cigarettes at various frequencies, some filtered and some not and eat elaborate combinations of foods from different farms and ranches, cooked to well done or at other times stir fried lightly. Get the picture? It's not easy to sort one factor from another. And how can these differences be tracked with any degree of accuracy?

These questions illustrate the challenges faced by cancer researchers. It is useful to analyze the different methods that are used to study diet and cancer.

Epidemiology

Epidemiology is the branch of medicine dealing with the incidence and prevalence of disease in large populations and with detection of the source and cause of disease. Epidemiologists use a number of different approaches:

Ecologic study: Using this approach, epidemiologists look at trends occurring in population groups and the corresponding rate of disease. For example, an epidemiologist using this approach might examine the onset of fortification of foods in the U.S. and the rates of disease that occurred during this time period. The challenge with this approach is that because it looks at a population as a whole, it does not look at whether a person who develops a particular disease actually had the exposure. If ten percent of the population developed a disease, were those the same ten percent who did not consume fortified foods?

Case control study: In a case control approach, a group of people with a disease (cases) is compared to a group of people without this disease (controls). Individuals in both groups are interviewed to determine their health habits, environmental exposures, family history, diet and so forth. That data is then compared to determine if an association emerges. For example, did people with heart disease exercise far less than those without it? Did they have a higher body mass index? Did they eat green vegetables? (This is the approach used in investigating foodborne disease outbreaks caused by bacteria such as *Salmonella, E. coli* and *Listeria monocytogenes*.)

This approach is limited by cases' and controls' abilities to recall food consumption and other habits with any degree of accuracy. It is also well-documented that foods and behaviors that have been negatively covered in the popular media – like sugary drinks or fried foods -- tend to be over-recalled. People also tend to overstate their level of exercise. This is called "recall bias."

Cohort study: In a cohort study, a group of people is followed forward in time. They typically record their food consumption, smoking habits and other lifestyle factors in a diary, avoiding the problem of recall bias. Follow-ups are done at regular intervals to determine disease status. For example, a cohort study could determine whether or not women who developed osteoporosis in their 60s began taking calcium sufficiently early. This type of study is considered much more accurate than a case-control, but they are costly and time consuming. They also require a large number of participants.

Meta-analysis: In meta-analyses, researchers look at a group of studies at one time to reach conclusions. They combine overall results together in an effort to assess the weight of the evidence together. However, they do combine the original, underlying data.

Pooled analysis: A pooled analysis is considered to have the greatest statistical power of all epidemiological approaches. Original data from cohort studies is "pooled" together into a single database. Larger numbers of cohorts compared together translate into higher degrees of accuracy. Harvard University is currently managing a large pooling project of 28 studies from an international consortium.

Animal Studies

Animals are often used in studies to determine the impact that an exposure has on them in hopes that scientists can extrapolate the impact that the same

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exposure would have on humans. This approach has distinct benefits because factors like diet, the amount of exercise and the genetic profile can be carefully determined and controlled.

However, questions remain about how precisely animal findings translate to humans. For example, some animals have organs that humans don't have. A mouse has a forestomach, so if a tumor develops in that organ during a study, what is the significance of that finding for humans who don't' have the organ of concern? Most scientists say nothing, while some argue it's reason for concern.

Also, laboratory animals are often exposed to very high doses of substances that may not be applicable to humans.

So What's A Scientist To Do?

Good scientists try to look at the full body of evidence – epidemiological, animal studies and human trials, if they are available. They also try to understand the underlying biology.

That's why a leading thinker in the field, Sir Austin Bradford Hill, in the 1960s proposed that a set of criteria that should be used before any one factor is determined to cause a disease. They include:

Temporality; the suspected cause has to precede the effect.

Strength; Epidemiological studies always include a Relative Risk (RR) number. The number 1 means "no effect." If a scientist set out to determine whether peanut butter caused weight gain, he might look at how often various people eat peanut butter and how much weight they gain or lose.

When data is analyzed, a relative risk number greater than one means there is a positive relationship – eating peanut butter would appear to increase the risk of weight gain, while a number less than 1 would mean that eating peanut butter appears to reduce weight gain. The higher the RR, the stronger the association.

When RRs are very close to the neutral "1" number, there is no effect. By contrast, when tobacco was associated with lung cancer, the RRs were very strong in the 15 to 25 range. Few would argue that tobacco use is strongly associated with lung cancer. On the other hand, most experts agree that studies with RRs under 2 are very weak and is very likely mere statistical "noise" and thus the finding may be related to mere chance.

Scientists and policymakers must consider other factors in association with values. If a disease strikes one person in a million then a group with twice the risk means two in a million will get the disease. In both cases the disease is rare.

While Sir Bradford Hill himself never set a precise RR threshold, many scientists since his time have. The World Health Organization and the International Agency for Research on Cancer in 1980 wrote, "Relative risks of less than 2.0 may readily reflect some unperceived bias or confounding factor, those over 5.0 are unlikely to do so." In 1981, esteemed researcher Sir Richard Doll argued that " ... when relative risk lies between 1 and 2 ... problems of interpretation may become acute, and it may be extremely difficult to disentangle the various contributions of biased information, confounding of two or more factors, and cause and effect. In 1994, the National Cancer Institute wrote, "In epidemiologic research, relative risks of less than 2 are considered small and usually difficult to interpret. Such increases may be due to chance, statistical bias or effects of confounding factors that are sometimes not evident."

Most recently, in 1999, Robert Temple MD, director of drug evaluation, U.S. Food and Drug Administration in a letter to the J*ournal of the American Medical Association*, wrote, "Relative risks of 2 have a history of unreliability….My basic rule is if the relative risk isn't at least 3 or 4, forget it."

Dose Response; Scientists also examine the "dose-response." If something truly causes a disease, then the risk should increase with the dose. For example, if five cigarettes double a risk, then ten cigarettes should triple it and so on. The dose-response line should be a smooth curve moving upward in the same direction. But if five cigarettes double a risk, but ten cigarettes only increase the original risk by ten percent, 15 cigarettes increase it slightly then line appears like a bumpy road, then the association may not be a strong one and may also be related to mere chance.

Consistency; Has this effect been observed and replicated over time or do findings contradict each other? If five studies say oranges prevent colds and five say they do not, then there is a lack of consistency and conclusions about cause and effect cannot be drawn. Similarly, if only one study has found that oatmeal reduces cholesterol, then cause and effect also has not been determined.

Biological Plausibility; Could a claim that one

factor causes a disease be supported biologically? Scientists need to be able to explain the biological underpinnings of an epidemiological association.

Meat and Cancer Research

Dozens and dozens of studies have examined the nutrition benefits of meat as well as its potential role in causing diseases like cancer. Nutrition experts believe that taken together, meat has a valuable role to play in a balanced diet. It is a nutrient dense food that offers excellent nutrition per calorie. Meat, whether fresh or processed, is an excellent source of protein, iron, minerals and many vitamins. Meat also provides a feeling of satisfaction and fullness and has proven helpful in weight loss programs that include lean cuts.

Certainly, the media impacts our perception of the healthfulness of many foods. It is much more exciting to report that something DOES cause cancer than to report that it DOESN'T. That's why so many single studies generate exciting headlines like "Deadly Dinners…tune in at 5!" While every cancer researcher no doubt hopes to be the person to unlock cancer's mysteries, the fact is, cancer causes, prevention and treatment remain complex and clouded with uncertainty.

Regrettably, many misleading headlines appeared in November 2007 that gave the public the impression that dramatic new findings related to cancer had been uncovered. At that time, the World Cancer Research Fund published a report on diet and cancer and it was positioned as "the final word" on diet (including meat) and cancer. It certainly was not.

In fact, the report didn't consider one of the largest studies ever done on red meat and colon cancer -- a 2004 Harvard School of Public Health analysis involving over 725,000 men and women and presented at the 2004 American Association for Cancer Research Conference. This study, "Meat and fat intake and colorectal cancer risk: A pooled analysis of 14 prospective studies," showed no relationship between meat and colon cancer. In fact, this federally funded data shows that red meat and processed meat are not associated with colon cancer and uses what is considered perhaps the most reliable approach to analyzing relationships: pooling original data together and analyzing it.

Other studies that also dispute the meat cancer link include:

- Meat, fish and fat intake in relation to subsite-specific risk of colorectal cancer: The Fukoka Colorectal Cancer Study, 2007
- Low-Fat Dietary Pattern and Risk of Colorectal Cancer, 2006
- Meat, Fat, and Their Subtypes as Risk Factors for Colorectal Cancer in a Prospective Cohort of Women, 2003
- Diet and risk of Colorectal Cancer in Finnish Men, February 1999
- Dietary Fat and Fatty Acids and Risk of Colorectal Cancer in Women, 2004

Given the many different findings on meat, many have asked whether it is possible to suggest cause and effect as WCRF did. It is instructive to apply the Bradford Hill criteria to the WCRF report.

Red Meat and Cancer: Applying the Bradford Hill Criteria and Standards of Epidemiology to the WCRF Reports Conclusions on Red Meat and Cancer

Temporality	Yes. Temporality exists. Meat consumption appears to have preceded the onset of cancer in the studies reviewed.
Strength	No. Strength is weak. The "summary estimate" of the relative risk of red meat and colon cancer according to the WCRF report was 1.43 per each additional time/per week and 1.29 per 100g (3.5 ounces) consumed /per day. The "summary estimate" of the relative risk of processed meat and colon cancer according to the WCRF report is 1.21 per 50g (1.8 ounces) consumed per day. These relative risks fall well below the numbers generally regarded as needed to declare cause and effect.
Dose-Response	Yes and no. Dose response lines for both red meat and colon cancer and processed meat and colon cancer are relatively flat or up and down. The lines stand in sharp contrast to the clear, upward curves shown for the relationship between alcohol and oesophageal cancer, in the same report.
Consistency	No. Of the 16 cohort studies of red meat and colon cancer examined by the WCRF, only four reported statistically significant findings of increased risk (and these were small). Fourteen cohort studies were examined on processed meat and cancer, but only four showed a statistically significant increased risk (and these, too, were small).
Biological Plausibility	No. A 2000-page systematic literature review of research on colon cancer that formed the basis for the WCRF report concluded, "Overall, mechanisms explaining the data are far from plausible biological mechanisms."

National Cancer Institute Guidance

The National Cancer Institute (NCI) has evaluated cancer extensively and continues to support efforts around diagnosis, treatment and research into prevention with an annual budget of over $250 million a year specifically addressing colorectal cancer.

NCI has specific information for health professionals posted on its Web site, including a section discussing the scientific studies that looked at diet and colorectal cancer. The patient information summarizes this information for the general public and says:

"It is not known if a diet low in fat and high in fiber, fruits, and vegetables lowers the risk of colorectal cancer. Some studies have shown that a diet high in fat, proteins, calories, and meat increases the risk of colorectal cancer, but other studies have not."

Of note is that this information was updated in November 2008 -- a full year after the WCRF report was released. A number of NCI scientists with expertise in colorectal cancer were active members in the preparation of the WCRF summary report.

NCI recently (December 2008) created a new Web site tool called "The Colorectal Cancer Risk Assessment Tool" for individuals to examine their ownpersonal risk of colorectal cancer (www.cancer.gov/colorectalcancerrisk/).

This tool does not include meat or processed meat as a factor related to risk, which is an acknowledgement that the scientific knowledge regarding colorectal cancer does not support any recommendations to reduce meat or processed meat consumption.

Conclusion

Confused? You aren't alone. The good news is that federal officials monitor research in its totality and make policy recommendations based upon all the evidence. It's far better to focus on the big picture than the study of the week reported in a way that draws one in to a news broadcast.

Just as your broker may tell you to diversify your investments to reap the maximum benefits, the U.S. Dietary Guidelines say to eat a balanced diet that includes lean meat. In this way, you derive a wide array of nutrients from many different sources. It's the best return on a nutritional investment you can get.

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