SECTION 1

DIET, MEAT, AND CANCER

While there is scientific consensus that diet plays a significant role in cancer, the evidence regarding specific roles for food groups, individual foods, or food components remains unresolved. For persons who do not smoke, maintenance of a healthy weight may be the single most preventable factor for developing cancer.

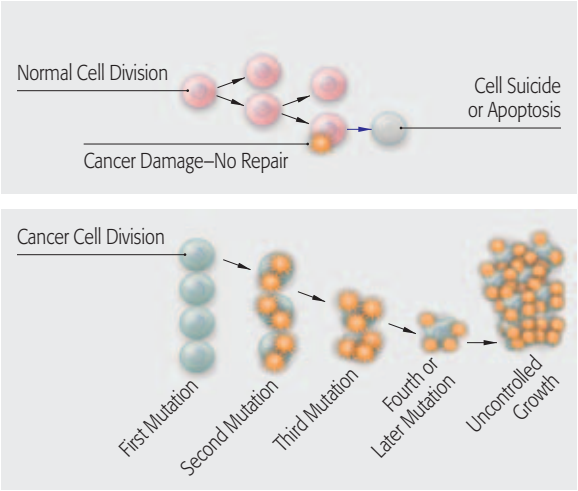
CANCER

Approximately one in every three Americans will be diagnosed with cancer during their lifetime and one in four deaths in the United States is attributable to cancer (Jemal et al. 2008). Cancer is second to heart disease as the leading cause of death in the United States.

Cancer, which may originate from virtually every cell type in the body, is a diverse family of diseases consisting of more than 100 forms (Ecsedy and Hunter 2008). Despite the diversity, several features are common to all cancers, including: unrestricted cellular proliferation, circumvention of cell-cycle control, growth without appropriate signals, escape from programmed cell death, altered interactions between cells and the surrounding environment, evasion of immune-mediated eradication, and the hallmark of malignancy, which is invasiveness into normal tissue (Hanahan and Weinberg 2000). Although the specific etiology of the majority of cancer cases has yet to be identified, it is well-known that the cause of cancer is multifactorial, involving a complex interaction of genetic, lifestyle, infectious, and environmental factors. The progression of cancer commonly takes several years from cancer initiation to diagnosis of disease, thus, enhancing the difficulty in identifying the underlying factors involved in carcinogenesis.

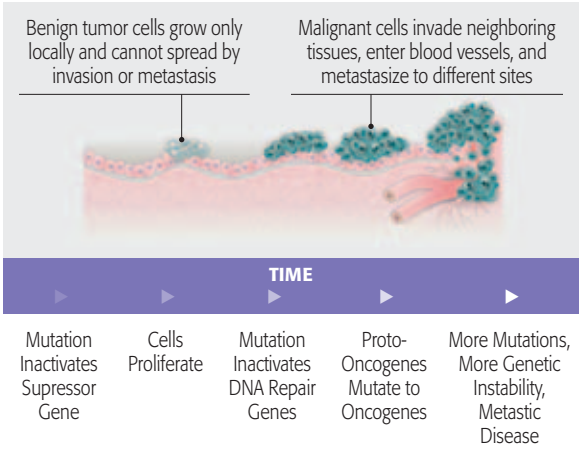
In 2008, a total of 1,437,180 new cancer cases and 565,650 deaths from cancer were projected to occur in the United States (Jemal et al. 2008). Over the past decade cancer incidence rates in the United States have remained relatively stable while cancer death rates have declined (Jemal et al. 2008). Prostate cancer and breast cancer are the most commonly diagnosed cancers among American men and women, respectively, while lung cancer and colorectal cancer rank second and third. Lung cancer, however, is responsible for approximately one-third of all cancer deaths among men and one-fourth of all cancer deaths among women (Jemal et al. 2008), a statistic largely attributable to cigarette smoking.

FIGURE 1.1
LOSS OF NORMAL GROWTH CONTROL



Source: Adapted from National Cancer Institute, Understanding Cancer Series

FIGURE 1.2
CANCER TENDS TO INVOLVE MULTIPLE MUTATIONS



Source: Adapted from National Cancer Institute, Understanding Cancer Series

DIET AND CANCER

The role that diet may play in human cancer has received a great deal of attention over the past few decades, leading some researchers to suggest that 35% to even 70% of all cancer deaths may be attributable to dietary factors (Doll and Peto 1981; Willett 2006). Although the exact proportion of cancers attributable to diet remains uncertain, there is scientific consensus that the relationship between diet and cancer is a significant public health issue.

Early evaluations of migrant populations revealed that adopting certain lifestyle and behavioral characteristics led to increased risks of some types of cancer, rather than the burden of cancer resting solely on the shoulders of genetic factors. For example, U.S. immigrants from Japan, a nation with higher rates of stomach cancer, were observed to have decreasing stomach cancer rates that began to reach U.S. rates after two generations of living in the United States (Haenszel and Kurihara 1968). Although genetic factors play a major, and possibly the most important, role in cancer development, observations of secular changes that result in modifying the rates of cancer suggested that diet may influence cancer risk. The hypothesis that diet may contribute to cancer causation began to take hold in the 1970s and was buttressed by experimental and epidemiologic evidence beginning in the early 1980s. Historically, nutrition studies in animals led to hypotheses that the same biological processes occur in humans, and preliminary animal models supported the theory that dietary variations affect cancer outcomes.

Among the first theories involving diet and cancer risk was that fat intake may be involved in carcinogenesis. For example, Tannenbaum and Silverstone (1953) demonstrated that increased intake of dietary fat in rodents increased the rate of mammary tumors. Subsequently, ecologic epidemiology studies of human populations were conducted to evaluate the correlation between the per capita consumption of certain food groups and cancer rates by country. As a result, it was found that countries with higher levels of dietary fat consumption also tended to have higher rates of some common types of cancer, such as breast and colorectal (Carroll 1975; Armstrong and Doll 1978). It wasn't until the 1980s that the majority of more rigorously designed

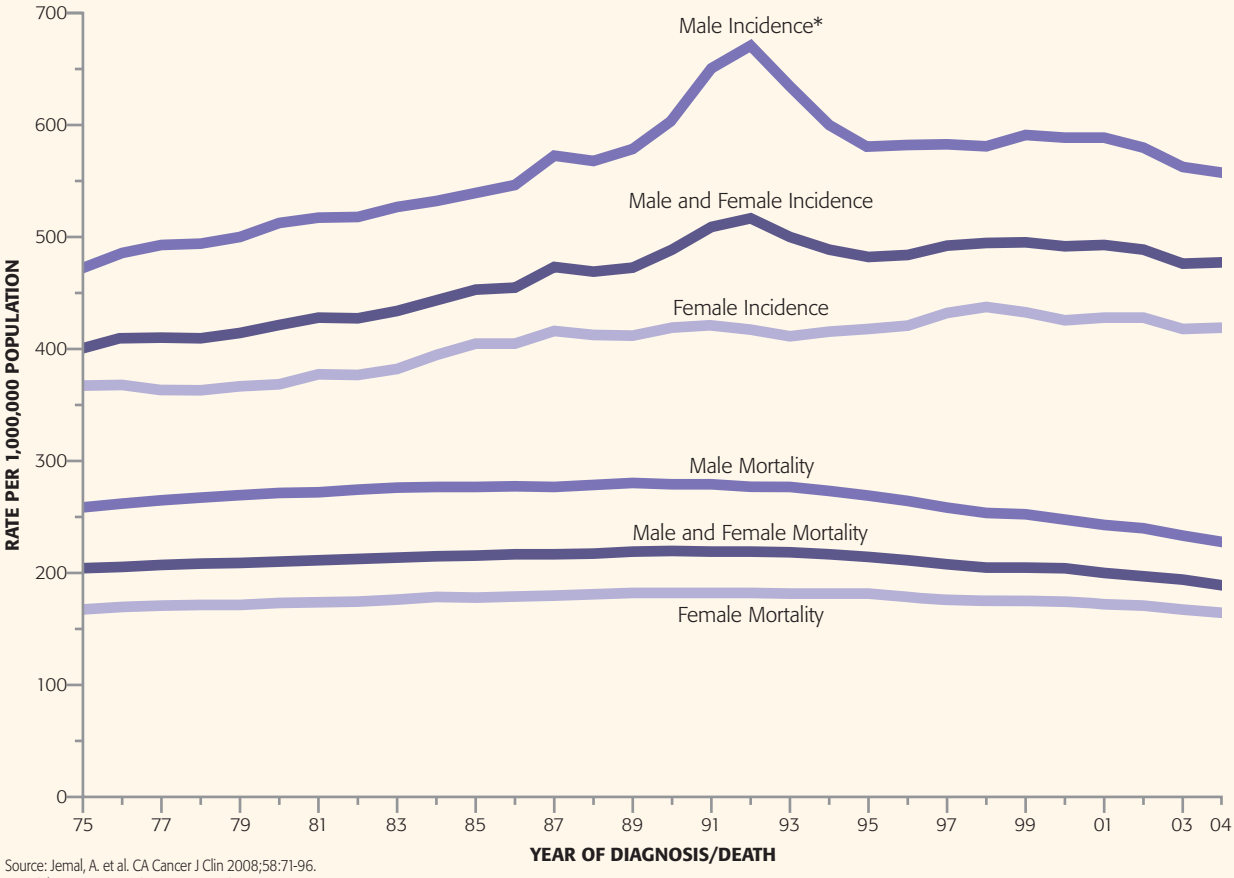
FIGURE 1.3
TEN LEADING CANCER TYPES IN THE UNITED STATES, 2008

MALES		
ESTIMATED NEW CASES*		
Prostate	186,320	25%
Lung and Bronchus	114,690	15%
Colon and Rectum	77,250	10%
Urinary Bladder	51,230	7%
Non-Hodgkin Lymphoma	35,450	5%
Melanoma of the Skin	34,950	5%
Kidney and Renal Pelvis	33,130	4%
Oral Cavity and Pharynx	25,310	3%
Leukemia	25,180	3%
Pancreas	18,770	3%
All Sites	**745,180**	**100%**
ESTIMATED DEATHS		
Lung and Bronchus	90,810	31%
Prostate	28,660	10%
Colon and Rectum	24,260	8%
Pancreas	17,500	6%
Liver and Intrahepatic Bile Duct	12,570	4%
Leukemia	12,460	4%
Esophagus	11,250	4%
Urinary Bladder	9,950	3%
Non-Hodgkin Lymphoma	9,790	3%
Kidney and Renal Pelvis	8,100	3%
All Sites	**294,120**	**100%**

FEMALES		
ESTIMATED NEW CASES*		
Breast	182,460	26%
Lung and Bronchus	100,330	14%
Colon and Rectum	71,560	10%
Uterine Corpus	40,100	6%
Non-Hodgkin Lymphoma	30,670	4%
Thyroid	28,410	4%
Melanoma of the Skin	27,530	4%
Ovary	21,650	3%
Kidney and Renal Pelvis	21,260	3%
Leukemia	19,090	3%
All Sites	**692,000**	**100%**
ESTIMATED DEATHS		
Lung and Bronchus	71,030	26%
Breast	40,480	15%
Colon and Rectum	25,700	9%
Pancreas	16,790	6%
Ovary	15,520	6%
Non-Hodgkin Lymphoma	9,370	3%
Leukemia	9,250	3%
Uterine Corpus	7,470	3%
Liver and Intrahepatic Bile Duct	5,840	2%
Brain and Other Nervous Systems	5,650	2%
All Sites	**271,530**	**100%**

Source: Jemal, A. et al. CA Cancer J Clin 2008;58:71-96.

FIGURE 1.4
ANNUAL AGE-ADJUSTED CANCER INCIDENCE AND DEATH RATES FOR ALL SITES, UNITED STATES, 1975 TO 2004



Source: Jemal, A. et al. CA Cancer J Clin 2008;58:71-96.

*The spike in cancer incidence rates among men around 1990 was largely due to the introduction of PSA testing for prostate cancer.

analytical epidemiologic studies, such as cohort and case-control studies, were initiated to examine potential causal relationships between diet and cancer, and the discipline of nutritional epidemiology began to burgeon. Fat consumption continued to be incriminated as a cancer-causing culprit, as well as being implicated as contributing to cardiovascular disease. Other emerging hypotheses included the possible role that fruit and vegetable consumption may play in cancer prevention.

Over the past two decades, improvements in study designs, research methodologies, and analytical techniques have allowed researchers to investigate specific nutrients, foods, food groups, and dietary patterns while better measuring intake and nutritional components of diets. Despite the numerous scientific advancements, there is no conclusive evidence regarding specific roles for food groups and individual foods in cancer causation. In fact, what was thought

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to be a strong and "convincing" association between fruit and vegetable intake and cancer reduction, particularly colorectal cancer, has been weakened somewhat by more recent, large, well-conducted prospective studies, and the scientific evidence has been diluted (Boyle et al. 2008). This is not to say that intake of fruit and vegetables may not reduce the risk of some types of cancer, among other health outcomes, but the available scientific evidence is not as clear today as was thought 10 to 20 years ago. The same can be said for fat intake; large-scale epidemiologic investigations of prospective studies, such as meta- and pooled-analyses, have not supported positive associations between fat consumption and some of the more common types of cancer (Smith-Warner et al. 2001; Alexander et al. 2009; Alexander et al. 2009[submitted]).

Perhaps, researchers need better tools and dietary assessment methods, such as dietary biomarkers, to identify specific sub-groups of the population for which dietary factors may modify the risk of cancer. On the other hand, certain dietary factors once hypothesized to increase or decrease the risk of cancer, may not be directly involved in carcinogenesis. Further confounding the modern thinking on diet and cancer is the uncertainty in the stage of carcinogenesis on which dietary factors may act, and whether such possible risk is dose-dependent (Miller and Linseisen 2009).

It is noteworthy that juxtaposed with examinations of diet and nutrition, there have been epidemiologic evaluations of body mass index, body fatness, exercise and cancer risk. Although findings from epidemiologic investigations of these factors and cancer have not always been consistent, it is becoming increasingly clear that obesity and physical activity are modifiable factors that are essential in decreasing the risk of many types of cancer. Indeed, this is recognized on a global scale, as an increased emphasis has been placed upon the public health infrastructure to make body weight and physical activity a fundamental priority in the prevention of cancer (World Health Organization 2004; WCRF/AICR Policy Report 2009). Thus, findings and epidemiologic summaries presented in this report should be interpreted with the understanding that assessing cancer risk involves a multi-faceted approach whereby several risk factors may be intertwined.

RED AND PROCESSED MEAT CONSUMPTION AND CANCER

To date, the relation between diet and disease has been the subject of thousands of epidemiologic studies, and while these studies have led to the discovery of several important associations between diet and health outcomes, the scientific evidence between dietary factors and cancer prevention have been somewhat underwhelming considering the extent of the research. As such, many questions remain regarding the role of food and nutrition in the prevention and cause of cancer in humans. One such question: "Is there scientific evidence that dietary intake of red meat or processed meat has an effect on developing cancer?" is complex and not only involves factors related to the composition of meat or methods of meat processing and preparation, but also involves accounting for other dietary and lifestyle patterns and choices that may impact the risk of cancer, such as obesity, physical activity, alcohol consumption, smoking, family history of cancer, and adherence to cancer screening recommendations. Addressing this question is one of utmost significance because red meat is a nutrient-rich food that plays an important function in American diets by contributing a unique nutrient package.

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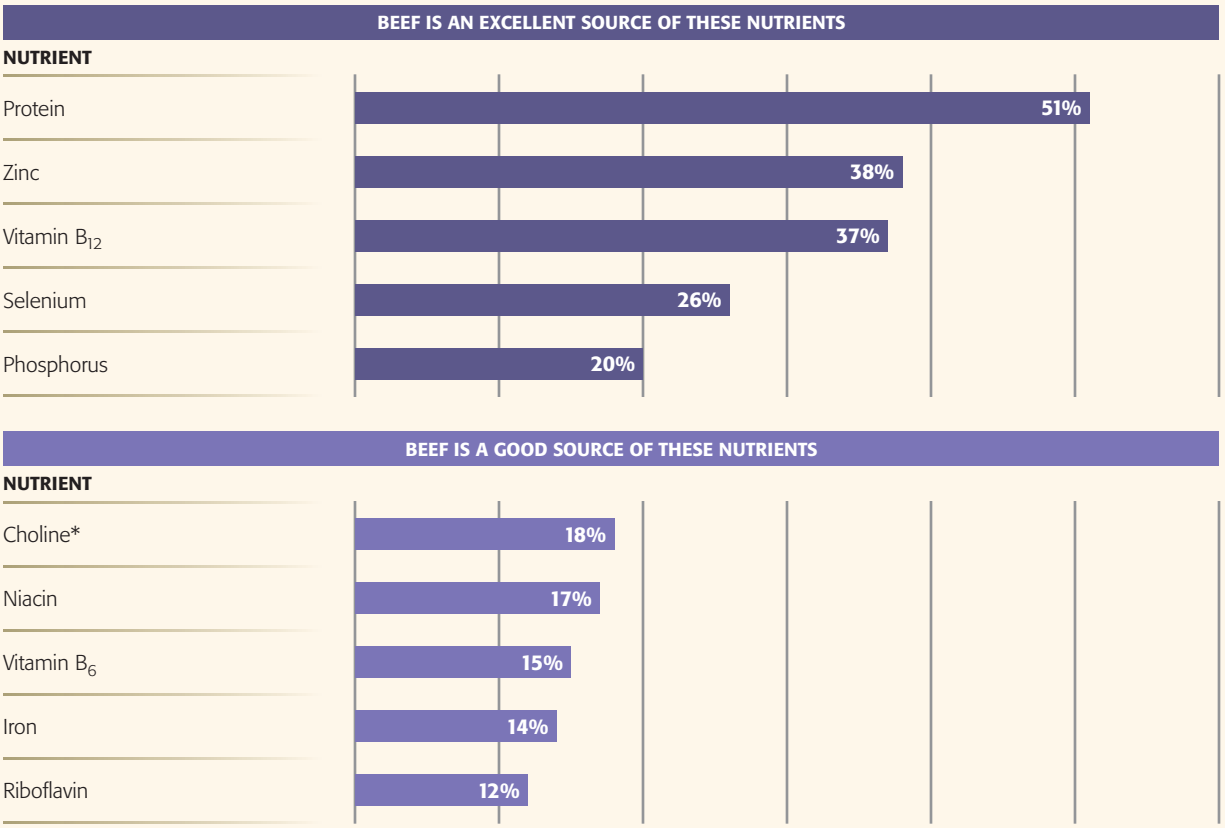
FIGURE 1.5
BEEF'S NUTRIENT VALUE

A 3-ounce serving of beef (179 calories) contributes less than 10 percent of calories to a 2,000-calorie diet, yet it supplies more than 10 percent of the Daily Value for:



U.S. Department of Agriculture, Agricultural Research Service 2009, USDA Nutrient Database for Standard Reference, Release 22. Homepage **www.nal.usda.gov/fnic/foodcomp**. NDB 13364, composite of trimmed retail cuts, 0" trim, all grades, 3 ounces cooked, visible fat trimmed.

Guidance for Industry, A Food Labeling Guide, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Food Safety and Applied Nutrition, April 2008.

*Dietary Reference Intakes, Institute of Medicine of the National Academies Press, Washington, DC, 2006. (Highest adequate intake for choline (550 mg).

BEEF'S NUTRIENT PROFILE

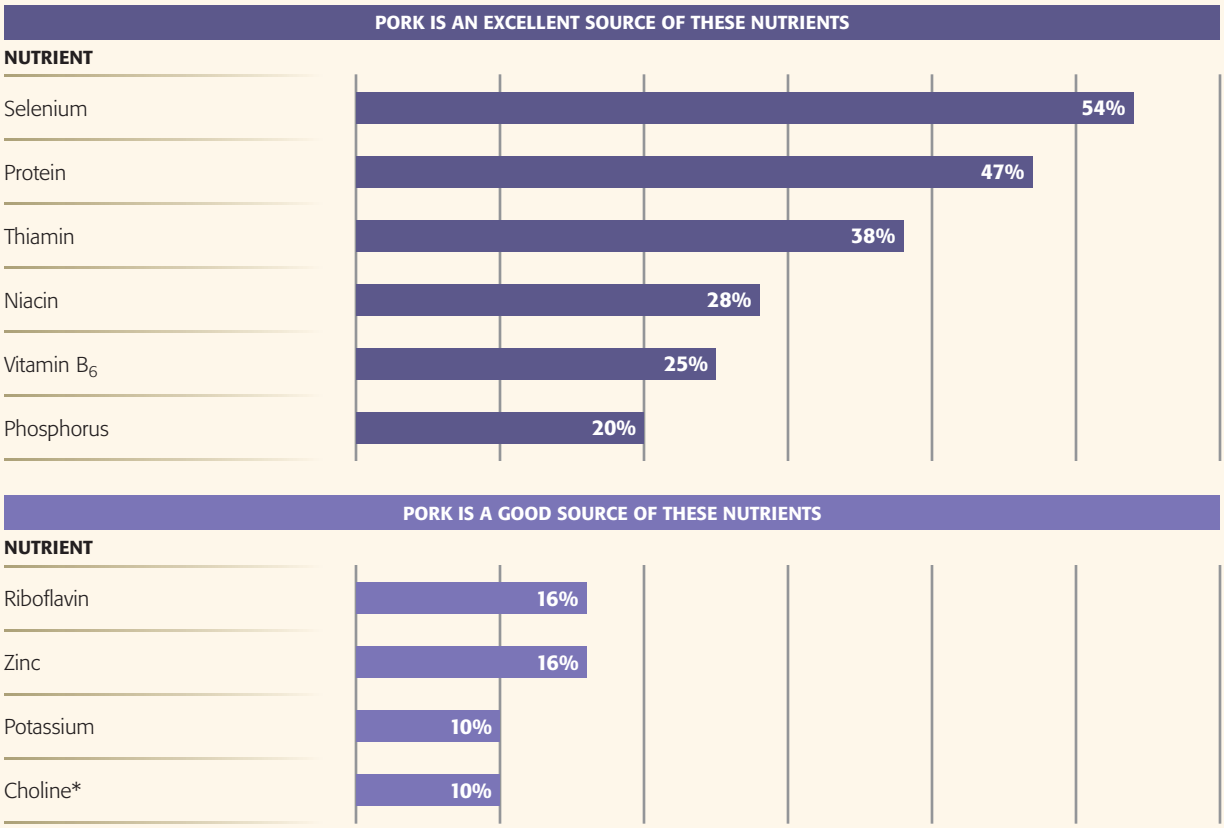
Beef is an important dietary source of several key nutrients, as one 3-ounce serving of beef contributes less than 10% of the daily value of calories in a 2,000-calorie diet, while providing an excellent source (more than 20% of the daily value) of protein, zinc, vitamin B_{12}, selenium, and phosphorous and a good source (more than 10% of the daily value) of choline, niacin, vitamin B_6, iron, and riboflavin (USDA, ARS 2009). In a ranking of nutrient sources in the diet, beef was found to be the number one source of protein, vitamin B_{12}, zinc and monounsaturated fats; number two source of selenium; number three source of iron (behind fortified cereal and yeast bread), vitamin B_6, niacin and phosphorus; and the number four source of potassium and riboflavin (Cotton 2004). In addition, the fat profile of lean beef is comparable to that of skinless chicken.

Beef lipids encompass numerous fatty acids, and although animal fats are often considered synonymous with saturated fats, less than half of all fatty acids in beef fat are saturated (USDA, ARS 2009). In fact, beef typically contains a greater proportion of monounsaturated fat than saturated fat.

Beef is an important source of conjugated linoleic acid (CLA). Experimental animal models and *in vitro* studies have supported an anti-carcinogenic effect of CLA at a variety of anatomic sites, such as the colon, prostate, and mammary gland (Wahle et al. 2004; Bhattacharya et al. 2006). In experimental animal studies, CLA has been shown to inhibit the initiation, progression, and

FIGURE 1.6
PORK'S NUTRIENT VALUE

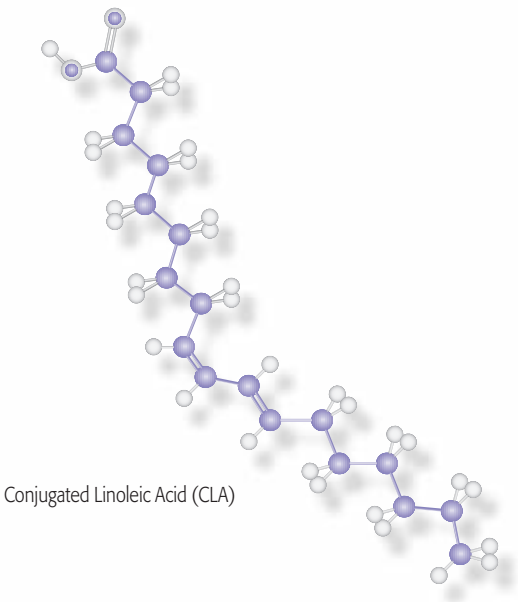
A 3-ounce serving of pork (171 calories) contributes less than 10 percent of calories to a 2,000-calorie diet, yet it supplies more than 10 percent of the Daily Value for:



U.S. Department of Agriculture, Agricultural Research Service 2009, USDA Nutrient Database for Standard Reference, Release 22. Homepage **www.nal.usda.gov/fnic/foodcomp**. NDB 10093, pork, composite of trimmed retail cuts, 3 ounces cooked, visible fat trimmed.

Guidance for Industry, A Food Labeling Guide, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Food Safety and Applied Nutrition, April 2008.

*Dietary Reference Intakes, Institute of Medicine of the National Academies Press, Washington, DC, 2006. (Highest adequate intake for choline 550 mg.)

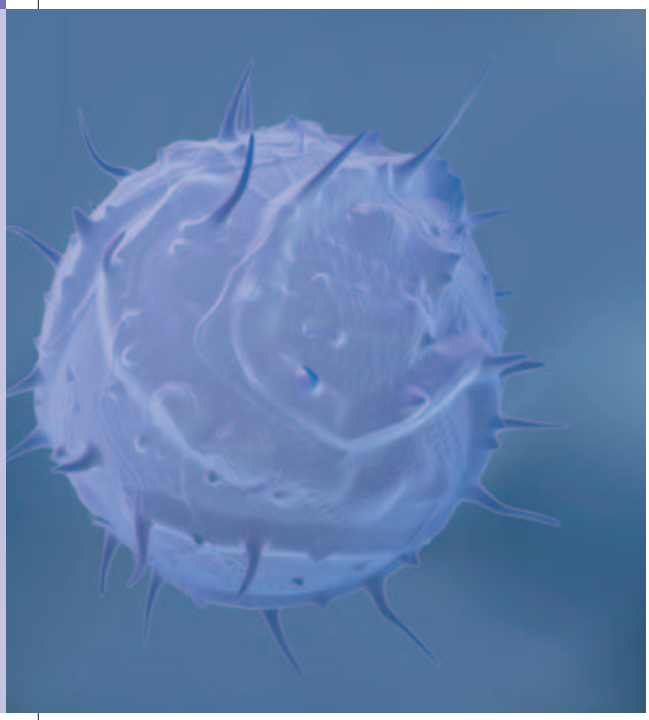


Conjugated Linoleic Acid (CLA)

metastasis of chemically-induced cancer (Wahle et al. 2004; Bhattacharya et al. 2006). However, data for CLA and cancer in human studies are limited, and additional research is necessary to fully understand the potential anti-carcinogenic effects of this fatty acid. Emerging research continues to provide further foundational support for beef's position in a balanced and healthy diet.

As with beef, pork is a nutrient-dense food that can play an important role in helping achieve the recommendations of the Dietary Guidelines for Americans. In fact, a 3-ounce serving of roasted, trimmed pork contributes less than 10% of calories to a 2,000-calorie diet, although it is an excellent source of selenium, protein, thiamin, niacin, vitamin B_6, and phosphorus and a good source of riboflavin, zinc,

potassium and choline (USDA National Nutrient Database 2009). In addition, six common cuts of pork have, on average, 16% less fat and 27% less saturated fat than the same cuts had in the 1990s. Today, the average saturated fat content of the six leanest cuts of pork (based on 3-ounce portions) is only 1.8 grams, and recent data indicate that pork contains no *trans*-fatty acids (USDA National Nutrient Database 2009). Moreover, total fat, saturated fat, cholesterol, and calories from lean pork compare favorably to skinless chicken; a 3-ounce serving of trimmed pork tenderloin has 2.98 grams of total fat compared to 3.03 grams of total fat in a skinless chicken breast (USDA National Nutrient Database 2009).



Human white blood cell

Although beef and pork, as specific sources of food, may provide several key nutrients to an individual's daily dietary intake, persons do not consume isolated foods or only specific nutrients; rather, the human diet comprises a wide variety of foods and patterns of foods that people typically consume on a day-to-day basis. Thus, analyses of dietary intake patterns have emerged as a complementary method to evaluate the relationship of overall diet and health outcomes. Dietary pattern analysis examines the broad spectrum of dietary habits among individuals, and scientists can estimate the risk of certain disease outcomes based on adherence to a particular dietary pattern. It has been argued that dietary patterns may be more relevant to understanding the relation between diet and chronic diseases, such as colorectal cancer, because they offer a broader representation of the diet than individual nutrients or foods. Numerous studies have examined dietary patterns characterized by higher intakes of red and processed meat and cancer outcomes, and while collectively, associations have been inconsistent, the majority of studies observed increased risks of cancer. Despite the nutritional value of beef and pork, meat consumption is typically classified under a "Western" dietary pattern, characterized largely by intake of refined sugars, sugary drinks, and high-fat dairy products. Moreover, persons classified in this rubric generally are more sedentary, have a higher body mass index, consume greater amounts of alcohol, and are more likely to smoke. In comparison a "prudent" dietary pattern is characterized by higher intakes of fruits, vegetables, legumes, fish, and whole grains.

Interpretation of dietary patterns studies is limited by a lack of specificity because "meat" is not analytically isolated, rather, it is included with numerous dietary factors (and associated with several possible confounding factors) that may be indicative of an overall unhealthy lifestyle. The purpose of this technical report is to provide a comprehensive summary of epidemiologic studies that specifically evaluate the relationship between red meat and processed meat consumption and cancer.