The Role of Epidemiology in Cancer Prevention (44164)

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Abstract. **Cancer is a major cause of morbidity and mortality throughout the world. As the population lives to an older age, cancer incidence and mortality are expected to increase because of the strong relationship between cancer and advancing age. Epidemiology plays a key role in cancer prevention and control by describing the distribution of cancer and discovering risk factors for cancer. Epidemiologic study designs include descriptive, ecologic, cross-sectional, and analytic (cohort, case-control, and intervention) studies. In the past 50 years, epidemiologic research has helped to elucidate many risk factors for cancer. Lifestyle factors such as smoking, diet, alcohol consumption, reproduction (pregnancy, lactation, age at menarche, and menopause), obesity, and inactivity have been suggested as the major contributors to the development of cancer. Epidemiologists have demonstrated that cancer is largely an avoidable disease and estimated that more than two-thirds of cancer might be prevented through lifestyle modification. Epidemiologic research is crucial to public health and cancer prevention. Individuals or communities at increased risk of cancer can be targeted for risk factor modification, as well as for secondary prevention and chemoprevention strategies.** [P.S.E.B.M. 1997, Vol 216]

Cancer is a major cause of morbidity and mortality throughout the world, and in the United States ranks as the second leading cause of death, behind cardiovascular disease (1–5). It is estimated that 1.3 million new cases of cancer will be diagnosed in the United States during 1997 and about 560,000 will result in cancer-related fatalities. The economic cost of cancer to society is tremendous, calculated to be about $104 billion this year (6). Recent trends have indicated that, in the United States, cancer mortality is declining for childhood cancers, Hodgkin's disease, testicular, stomach, cervical, uterine, and colorectal cancer, some smoking-related cancers, and to a lesser extent breast and prostate cancer (3, 7–12). Nevertheless, the overall incidence of cancer is increasing throughout the world, particularly for some of the most common cancers, such as breast, lung, prostate, colon, and rectum (2–5). As the population lives to an older age, cancer incidence and mortality are expected to increase because of the strong relationship between cancer and advancing age (5, 7, 13, 14). Many developing countries are moving toward Westernization, adopting a lifestyle that is similar to that of developed countries, and are thus likely to experience a rise in cancer rates (15). It is projected that in 5–10 years, cancer will become the leading cause of death in the United States and other developed countries (16, 17).

The Role of Epidemiology: Identification of Risk Factors

The discipline of epidemiology plays a key role in cancer prevention and control. In the past 50 years, epidemiologic research has helped to elucidate many risk factors for cancer. Epidemiologic methods have allowed cancer researchers to identify risk factors specific to certain cancers as well as estimate the proportion of cancer deaths attributable to established risk factors (18–20) (Figure 1). Environmental or lifestyle factors have been suggested as the major contributor to the burden of cancer in our society. Epidemiologists have been able to show that cancer is largely an avoidable disease and estimated that more than two-thirds of cancer might be prevented through lifestyle modification (18, 19). This link between lifestyle and cancer has been based on ecologic studies showing differences in cancer rates between and within countries as well as over time, migrant studies illustrating how individuals or their descendants eventually develop cancer at the same rate as those in

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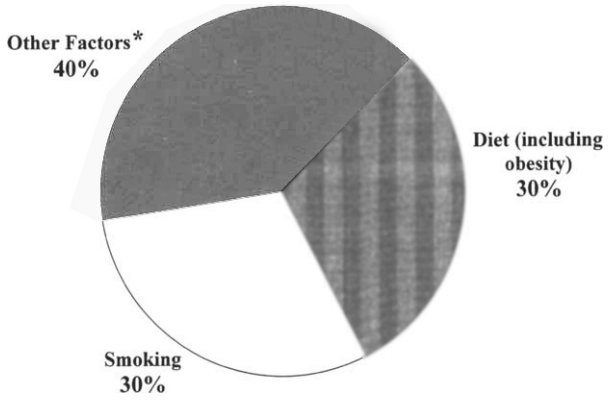

Figure 1. Proportion of cancer deaths attributable to specific risk factors. *Infections and viruses, 5%; heredity, 5%; occupation, 5%; inactivity, 5%; perinatal factors/growth, 5%; reproductive factors/hormones, 3%; alcohol, 3%; socioeconomic status, 3%; environmental pollution, 2%; radiation, 2%; medical drugs and procedures, 1%; food additives, 1%.

their host country, and etiologic studies identifying carcinogenic agents implicated in cancer. However, efforts to reduce overall cancer rates have not been as successful as those for cardiovascular disease. Epidemiologists contributed to the efforts leading to the reduction in incidence and mortality of cardiovascular disease by identifying markers of risk, such as high blood pressure, obesity, and smoking (21), which enabled prevention programs to be developed targeting individuals at high risk for cardiovascular disease. This same approach could be applied to reduce cancer rates if risk factors amenable to modulation could be identified for cancer. Preventive efforts, screening, chemoprevention, and lifestyle changes, could focus on the management and reduction of the overall incidence and death rate from cancer.

The Discipline of Epidemiology

Epidemiology is the study of the occurrence of illness and the relation between disease and characteristics of people and their environment (22, 23). Cancer epidemiology studies seek to describe the distribution of cancer as well as discover the determinants that may be specific to each cancer or groups of cancer. For instance, it has been shown that smoking causes lung cancer (24–29) and hepatitis B virus causes hepatocellular carcinoma (30, 31). Other examples include risk factors that may or may not cause cancer, but serve to classify individuals at increased risk such as light skin color and risk for melanoma, late age at first birth and breast cancer risk, and family history of colon cancer and risk of this cancer. Cancer epidemiology plays a crucial role in prevention because the study results, when valid, are directly applicable to people, as opposed to laboratory findings in animals, which often cannot be extrapolated to humans.

The substantive area of epidemiology dealing with molecular epidemiology is integral to cancer control and prevention. Molecular epidemiology is based on classical epidemiology methods combined with molecular biology techniques including measurements of carcinogenic dose, biologic response, and susceptibility (32–34). Molecular epidemiologists link epidemiologic observations with biomarkers to document precancerous and cancerous molecular changes or markers of genetic polymorphisms which sometimes represent critical differences, such as metabolism among individuals. Biomarkers may represent exposure to a particular carcinogen, damage to cells, or acquired/inherited susceptibility to carcinogens (32–34).

In the future, molecular epidemiology is likely to make valuable contributions to cancer prevention by identifying individuals and subpopulations at increased risk of developing cancer. These subgroups can then be targeted for lifestyle modification, medical surveillance, and/or chemoprevention. Studies utilizing molecular biology techniques will help in the early identification of cancer-causing agents and increase the precision of exposure measurement. Gene-environment interaction can be studied to evaluate the role environmental factors play in the development of cancer in those who have an inherited susceptibility. The collaboration among epidemiologists, basic scientists, and clinicians will be essential for the conduct of molecular epidemiologic research.

Epidemiologic Measures

To quantify the distribution of cancer, epidemiologists utilize different types of measures. Epidemiologic measures of disease frequency include incidence and prevalence. Incidence measures the occurrence of new cases of disease taking into account the amount of time a person has been disease free. An incidence rate is defined as the number of new cases of disease in the population divided by the sum of the time periods of observation (or time at risk) for all individuals in the population (22, 23). For instance, the incidence rate for breast cancer in white females was 113.2/100,000 women at risk/year and 94.0/100,000 women at risk/year for black females during 1987–1991 (35).

Mortality rates measure the incidence of death and are also used in cancer epidemiology to quantify the frequency of deaths that are attributable to cancer (22, 23). Incidence and mortality rates are important in describing the absolute impact of cancer, and epidemiologists make an important distinction between these two measures of disease frequency. As mentioned, incidence rates reflect the number of new cases of cancer but may also reflect better diagnosis or more complete cancer registration. Screening and other early detection efforts affect these incidence rates. The recently observed increase in incidence rates of prostate cancer is, to a considerable extent, the result of early detection efforts through prostate-specific antigen (PSA) tests leading to increased rates of diagnosis of cancers that may never have progressed to clinical attention. Trends in mortality rates are a function of available treatment modalities and their success in improving survival. In the past few decades progress has been made in the treatment of some cancers,

such as head and neck, thereby reducing cancer-related fatalities.

Prevalence measures disease status at a point in time and is the proportion of a population that is affected by disease at that time (22, 23). This type of measure is not generally used in studies of cancer etiology because prevalence is a function of the duration and survival patterns of the disease. Temporal issues related to exposure and disease that are concurrently measured are also important because there is the possibility that the disease process itself may influence exposure assessment (22, 23). For instance, a study comparing the "current" smoking and drinking habits of esophageal cancer cases and disease-free controls may not yield valid exposure data because the cases may have changed their smoking and drinking habits in response to their cancer diagnosis. Prevalence of these two exposures may not accurately reflect "past" smoking and drinking habits, which are most relevant.

Epidemiologic measures of effect, notably relative risks and odds ratios, are used to distinguish risk factors by assessing differences in groups with respect to these factors and measure the strength of the association between a risk factor and cancer. Relative risks and odds ratios are "relative" measures of effect and indicate the increase in risk in the exposed individuals relative to the baseline rates in the unexposed (22, 23). As an example, the relative risk or the odds ratio of lung cancer is about 10 in smokers compared with nonsmokers. This means that smokers are 10 times more likely to develop lung cancer than are nonsmokers.

Attributable risk or risk difference is a measure of association that quantifies the excess risk of disease that can be attributed to a certain exposure (22, 23). Absolute measures are important because they give an indication of the actual burden of disease to society. If a particular cancer is quite rare, even though the relative risk for a specific factor is large, the attributable risk or absolute effect will be relatively small. Prevention efforts to reduce the risk factor will have a minor impact on the overall morbidity from cancer. Conversely, relative risks may be small for an exposure-disease association, but if the exposure is common and the disease is common then the attributable risk will be large.

Epidemiologic measures of disease frequency and association are usually presented with confidence intervals, which give an estimate of the precision. A confidence interval is a range of possible estimates which the "true" parameter is likely to fall in with a specified degree of confidence (22, 23). In a pooled analysis of prospective studies, Hunter *et al.* (36) reported the association between fat intake and breast cancer to be 1.05 (relative risk) with a 95% confidence interval of 0.94–1.16, for women in the highest quintile of total fat intake compared with the lowest. Thus, women who have the highest intake of fat appear to be 5% more likely to develop breast cancer compared with those women who have the lowest fat intake. The 95% confidence interval indicates that the true estimate lies between 0.94 and 1.16 with 95% assurance, suggesting that dietary fat intake at the levels studied may be unrelated to breast cancer risk.

Whether or not the study findings are "statistically significant" and unlikely to be due to chance may also be reported as part of the results. Statistical hypothesis testing, used to derive the level of statistical significance, is controversial in the field of epidemiology (22). Statistical significance has often been misinterpreted to mean that a cause-and-effect relationship exists between the exposure and disease; however, statistical significance is not the same as biological significance. So, in evaluating statistically significant associations, it is important to assess their biological plausibility.

Methodological Design of Epidemiologic Studies

Descriptive Studies. Descriptive studies characterize the distribution of disease by such parameters as age, sex, race, and geographical location by reporting measures of disease frequency: incidence and mortality rates. Results from descriptive studies can be used to formulate hypotheses or allocate health care resources (22, 23). Population-based cancer registries are valuable tools for identifying specific populations at risk, type of cancer, and stage at diagnosis, and for evaluating effect of any prevention efforts. The Surveillance, Epidemiology, and End Results (SEER) Program, a nationwide cancer registry established in 1973, has been crucial to the documentation of cancer incidence, mortality, and trends over time (37).

Ecologic Studies. Descriptive studies can be conducted on populations or individuals. Ecologic or correlational studies compare countries or groups of people on exposure characteristics. For instance, a study on dietary intake and cancer rates might compare diet using per capita consumption of the country or group (a proxy measure which is inherently inaccurate) and cancer rates obtained from vital statistics. These types of studies usually do not take into account potential confounders, other factors such as lifestyle habits that might influence why a particular group has a certain cancer. It has been observed that in countries with high rates of colon cancer, there is also a high consumption of fat compared within countries with low rates of colon cancer (38). People who eat fat tend to eat less fiber and fewer fruits and vegetables (38). They also may exercise less and probably do not have annual colon-cancer screening. It is not clear whether it is fat that causes the increased cancer in these populations or some other confounding factors. Ecologic or correlational studies are hampered by the fact that one cannot directly link the exposure of interest to the person who developed cancer. One can only assess the exposure and cancer rates of the population as a whole. The interpretation of results from these studies is limited because of these problems. However, much of the early data showing a link between diet and cancer among countries was based on this study design, which was quick and inexpensive to implement. The findings were important

because they gave some of the first clues to the link between diet and cancer (39).

Cross-sectional Studies. Cross-sectional studies are another type of descriptive study, and they assess the exposure of interest and disease of an individual at the same point in time (22, 23). Although this type of design is an improvement over the correlational study because data are obtained on individuals, a major limitation is that the temporal relationship is questionable. For instance, if a study on residential proximity to power lines and childhood leukemia obtained information on "current" exposure at the time of cancer diagnosis then misclassification may result if current exposure is not a good proxy for past exposure. Cross-sectional designs use prevalence of disease as a measure. This limits interpretation because prevalence measures reflect determinants of survival and duration of disease. However, cross-sectional studies can be useful in cancer epidemiology if variables that cannot change over time, like race, sex, or genetic markers, are being studied.

Analytic Studies (Observational and Intervention). Analytic studies include observational (cohort and case-control) studies and intervention (randomized trial or experimental) studies. These study designs are used to assess the association between a specific exposure of interest and disease to elucidate the determinants of disease (22, 23).

Cohort studies. Cohort studies, also referred to as prospective, longitudinal, or follow-up studies, usually consist of a large number of people that are followed over time. The number of individuals needed is based on disease frequency. At the initiation of the study, subjects are disease free. Subjects may provide information on the factors of interest and other confounding factors by completing a questionnaire or interview. Information may also be obtained from medical or employment records depending on the availability and quality of existing data. The participants are then followed for many years and the occurrence of cancer recorded. Repeated assessments of the exposure of interest (i.e., yearly) can be obtained during this follow-up time period, which will help to give a more precise measure of "true" exposure. For example, it has been shown that multiple assessments of diet over time will provide a more accurate estimate of overall dietary intake (40). Information on cancer occurrence can be obtained using a questionnaire completed by the study subject, state cancer registries, death certificates, or medical records. Investigators then compare the cancer rate in those who were "exposed" with that in those who were "unexposed" to the factor of interest. This type of design is expensive in that a large number of individuals are needed and the duration of follow-up is long because cancer is a rare disease that takes many years to develop. An important advantage to this design is that the temporal sequence between the potential risk factor and cancer is clearly defined. The exposure information is collected prior to the occurrence of cancer thus minimizing the potential for recall and selection bias. However, one of the major limitations of this design is the potential for biased results if many of the subjects initially enrolled cannot be located and their cancer status is unknown. These types of studies are quite expensive and time-consuming. The Nurses' Health Study is an example of a large cohort study that has provided many valuable epidemiologic findings (41).

Cohort studies can also be conducted using existing records of events (both exposure and disease) that have already occurred. Occupational records and cancer registry statistics have been utilized to conduct epidemiologic studies relatively quickly and inexpensively. However, the quality of the information is dependent on availability and integrity of existing records.

Case-control studies. In case-control studies, persons with cancer are identified using state cancer registries, death records, or hospital information (22, 23). Individuals identified as having cancer (cases) complete questionnaire gathering information on pertinent factors. Medical records, employment records, and interviews with surrogate family members can be used to ascertain exposure and confounding information. Subjects without disease (controls) who are similar to the cases are identified and the same information obtained. The two groups are then compared on the exposure of interest.

The case-control design is useful for cancer studies because it can be quick, efficient, and inexpensive. Case-control studies require fewer numbers of people than cohort studies, and the time needed to complete the study is shorter. However, case-control studies have increased potential to give biased or inaccurate results (22, 23). Cases may have predetermined notions about the cause of their disease and may "recall' their exposure patterns differently compared with the nondiseased controls, leading to recall bias. For instance, if people with cancer are asked about their fruit and vegetable intake over the past 10 years they may report their current diet, which is likely to have changed because of their illness. Cases might be aware, because of their diagnosis, of the benefits of eating fruits and vegetables and may over- or underestimate their intake. This is not a problem in the cohort study because information is obtained well in advance of cancer diagnosis. Also, when researchers select the control series they might inadvertently choose an inappropriate comparison group which may lead to a distortion in the results. Those who participate may be different than those who do not choose to be enrolled in the study, affecting the validity of the findings.

Intervention studies. Intervention studies (also called randomized trials), if conducted properly, are the most powerful tool to measure whether a particular exposure is beneficial and are not limited by potential confounding as other study designs (22, 23). In these studies, each subject is randomly assigned to one of two groups or more (randomization). For example, depending on the focus of the study, one group might receive a vitamin supplement, while the other group receives a placebo. The study ideally is conducted in a "double-blind" fashion; both the study subjects

and the investigators are unaware of who received the vitamin versus the placebo. Study participants are then followed for a designated time period and cancer occurrence ascertained, although a large number of study participants are needed to accrue an adequate number of outcomes. Potential biases may occur if subjects are not compliant with the regimen or if a substantial number are lost to follow-up. The highly publicized studies of β-carotene supplements and lung cancer are examples of chemoprevention intervention studies where natural or synthetic agents were used as the "treatment" to prevent or retard cancer (42–44). Surprisingly, these studies showed that supplemental β-carotene increased the risk of lung cancer among heavy smokers.

Intervention studies are difficult to conduct because of issues of compliance. The amount of time between the intervention and the expected modification on cancer risk is uncertain. The dose needed to affect cancer risk is also largely unknown. Furthermore, the kinds of people who agree to be in a study tend to be healthier, and it may be that the intervention only works in people who are at high risk for the cancer of interest. The logistics of conducting this type of study make it extremely expensive. Due to ethical considerations, intervention studies are not done with factors thought to be harmful.

Limitations of Epidemiology

The limitations of conducting epidemiologic research have been discussed (45). Most epidemiology is observational in nature utilizing cohort and case-control methodology, and few intervention studies have been conducted. Measurement in epidemiologic studies is subject to imprecision, and the appropriate time period for measurement of the exposure may be unknown or reliable information unavailable. Epidemiologic studies take a great deal of effort and resources, and, in the end, results among studies can be confusing and conflicting due to methodological weaknesses, bias, unidentifiable interactions, confounding variables, or simple variation in the populations studied. Statistical methods to increase control of confounding variables have improved greatly, but statistical modeling cannot control for bias in a study design. Sometimes the observed increase or decrease in risk is small and difficult to measure with precision. These "weak" associations are hard to "establish," and the results can easily be misinterpreted.

Cancer Epidemiology—Contribution to Prevention

Cancer epidemiology studies have identified important risk factors for cancer. Subsequent public-policy measures, including education and legislation, aimed at cancer prevention and control have been implemented. The most well known epidemiologic studies are those linking smoking to the development of cancer, especially lung and oral cavity (24–29). Smoking is responsible for about 90% of all lung cancer deaths and about 30% of all cancer deaths (46). During the time period of 1965–1990, the prevalence of adult cigarette smoking declined from 42% to 25%, mainly as a result of increased public awareness about the hazards of smoking (6). Decreased lung cancer death rates in men are a direct result of reduced smoking rates. Epidemiologic research has been the basis for policy efforts aimed at smoking cessation programs to help individuals quit smoking.

Hundreds of studies have shown a relationship between diet and cancer. Diet plays an important role in cancer prevention, and it has been estimated that it accounts for about 30% of total cancer mortality (18–20). Studying the diet-cancer link has been difficult because of the inherent limitations in measuring the dietary intake of free living populations. Many aspects of diet have been studied; key findings from epidemiologic studies are presented.

- Fruit and vegetable consumption have been consistently shown to reduce the risk of many cancers (47).
- Animal products and saturated fat have been associated with an increased risk of colon and prostate cancer (48, 49).
- A high intake of salty, smoked, or cured foods has been shown to increase the risk for stomach cancer (50, 51). The decline of stomach cancer rates in the United States and other countries is most likely related to changes in diet and methods of food preservation (52, 53).
- Beverages consumed at scalding hot temperatures have been linked to esophageal cancer in countries where this practice is common (54).
- Studies have indicated that carcinogenic chemical compounds, notably heterocyclic amines, polycyclic hydrocarbons, and nitorsamines, formed during the cooking process may be related to some forms of cancer (55).
- A high fiber intake is likely to reduce the risk of developing colon and possibly other cancers (56, 57).
- Alcohol, although not originally implicated as a carcinogen in laboratory studies, has been consistently shown to increase rates of many cancers, including liver, oral cavity, upper digestive tract, and probably breast (58, 59). It has also been shown in epidemiologic studies that alcohol combined with smoking acts synergistically to elevate certain cancer risks (60).

The effect of diet on cancer risk is significant. It has been estimated that nearly one-third of all cancer deaths could be prevented by simple diet modification. A major prevention effort to increase fruit and vegetable consumption has been the "5 a Day for Better Health," a national campaign sponsored by the National Cancer Institute to educate the public and motivate behavior change.

There have been many epidemiologic studies showing obesity is related to some forms of cancer, including colon, endometrial, prostate, and breast (19, 20). Obesity is probably influenced by excess caloric intake, inactivity, menopausal status, hormone levels, and insulin resistance. The U.S. National Center for Health Statistics has estimated 31% of men and 35% of women are overweight (61). From

a cancer prevention standpoint, strategies to reduce obesity, preferably through decreasing total calories or increasing activity levels, should make an impact on cancer rates in the society. Efforts to educate the public about the risks associated with being overweight are continuing, although levels of obesity have not been affected (62). Interestingly, recent studies have implicated increased height or stature as a risk factor for cancer (63–66). Increased height may be a marker for growth rates and the result of excess caloric intake during childhood or adolescence.

Certain viruses have also been linked to cancer (19, 20). The human immunodeficiency virus (HIV) is associated with acquired immunodeficiency syndrome (AIDS)–related malignancies, notably Kaposi's sarcoma. Hepatitis B and C are common in Asia and Africa, and cause liver cancer. A vaccine is now available for hepatitis B, which could reduce the prevalence of this virus worldwide. The Epstein-Barr virus has been associated with non-Hodgkin's lymphoma, Hodgkin's disease, and nasopharyngeal cancer. Carriers of the human papillomavirus (HPV) are at increased risk for developing cervical cancer, and strategies have been implemented to educate women about the importance of regular Pap test screening and avoidance of risky sexual practices. The HTLV-1 virus increases the risk for lymphomas and some forms of leukemia. Based on these findings, vigilance in the screening of blood products has been enforced, which will help to decrease the spread of some of these viruses.

Bacteria also are important in the development of cancer. Recently, epidemiologic studies have shown that *Helicobacter pylori* bacteria can cause stomach cancer (67, 68).

Certain occupational exposures have been identified as human carcinogens (19, 20). Studies have shown asbestos, formaldehyde, benzene, aromatic amines, diesel exhaust, arsenic, vinyl chloride, and radon increase the risk of cancer, particularly those of the bladder, lung, bone marrow, and liver, in exposed workers (69). The United States established the Occupational Safety and Health Act in 1970 to protect the workplace, and strict control over and regulations of the level of exposure tolerated in the workplace now exist.

One misconception based on epidemiologic findings is that radiation is a major cause of cancer. In fact, radiation probably accounts for only a very small percentage of all cancer deaths (18–20). Studies done in occupational settings have shown that radon in high doses does cause lung cancer, especially in smokers (70, 71). As well, radiation from nuclear materials and accidents clearly causes cancer, although studies have not been able to convincingly link residence proximal to power plants to high leukemia rates (19, 20). Therapeutic radiation used in high doses increases the risk for some cancers; however, diagnostic x-rays pose very little danger, and the medical benefits far outweigh the risks. Ultraviolet radiation causes the majority of radiation-induced cancer, and epidemiologic studies have demonstrated that 90% of nonmelanoma and melanoma skin cancer are caused by sun exposure (19). Educational strategies focusing on detecting early signs and symptoms, limiting sun exposure, and using sunscreen protection are currently being tested.

Environmental pollution, including tobacco smoke, combustion products, and radon, has been linked to some forms of cancer, but has not been shown to account for a large proportion of all cancer deaths (19, 20). The Environmental Protection Agency was established to set standards and monitor hazardous-waste disposal and water supplies in an effort to control environmental pollution. For instance, aflatoxin, a potent toxin, may interact with hepatitis B virus to cause liver cancer. Federal regulations now limit the amount of this toxin that can be present in U.S. crops.

Evidence supporting the link between exercise and colon cancer is strong (19, 20). Epidemiologists have shown that breast and prostate cancer may also be reduced by regular moderate to vigorous exercise, but the findings are less conclusive. The Surgeon General has recommended that all adult Americans get at least 30 min of moderate to vigorous intensity exercise on most, preferably all, days of the week (72).

The link between hormones and cancer has been studied extensively. The hypothesis that estrogen replacement therapy increases the risk of developing endometrial cancer was initially suggested in the 1970s after rates of this cancer paralleled the increase in prescriptions for exogenous estrogens. Epidemiologists subsequently identified replacement estrogens as a cause of endometrial cancer (73). A finding that was of considerable importance was the diethylstilbestrol (DES)-cancer link. DES, a synthetic estrogen used in the 1940s and 1950s for the prevention of miscarriage, was shown to be associated with a large increased risk of rare types of vaginal and cervical cancer in the female offspring (74). Women who were exposed to this drug *in utero* are now monitored closely for the development of cancer. Epidemiologists have made progress in identifying reproductive factors related to cumulative endogenous estrogen exposure (pregnancy, lactation, age at menarche, and age at menopause) as important in affecting a woman's risk for some cancers. The beneficial effect of oral contraceptive hormones on both ovarian and endometrial cancer has been consistently shown in epidemiologic studies (19, 20).

Studies focusing on genetics and epidemiology have enabled researchers to identify heredity as a major risk factor for most cancers with between 5% and 10% of specific cancers due to familial predisposition (19, 20). Having a family history of cancer increases the risk for the specific cancer by about 1.5- to 2-fold. The role of environmental factors and their interaction with genetic factors is a major focus of ongoing epidemiologic studies. In the future, prevention strategies may be applied to those who have an inherited susceptibility to cancer.

Recently, studies have shown that poverty is a risk factor for developing cancer (19, 75). The reason for this link between socioeconomic status and cancer is probably

related to shared environmental risk factors as well as limited access to preventive care.

Secondary prevention efforts have also been enhanced based upon epidemiologic findings. Screening for premalignant conditions and early detection of malignancies has been shown to be beneficial in decreasing mortality of cancer patients (76). However, a major problem in evaluating screening tests is that early detection may not reduce mortality but, rather, may only increase the length of time a person has a diagnosed cancer.

Case-control methodology was used to identify the benefits of cervical screening using the Papanicolaou test (77, 78). Probably 90% of invasive cervical cancers could be avoided if women adhered to regular Pap test screening (79, 80). While most epidemiologic studies conclude that regular Pap screening would reduce mortality, there has never been a randomized clinical trial to prove it conclusively. Mammography has been shown to reduce the mortality of breast cancer in older women through early detection and subsequent treatment (81, 82). A recent case-control study of skin self-exam showed that it could possibly reduce mortality by 63% (83). Colon-cancer screening by flexible sigmoidoscopy has been shown to be beneficial in reducing cancer deaths (84, 85). Other types of colon screening appear to reduce the incidence but have not been tested for a reduction in mortality. The benefits of prostate screening, PSAs, and digital rectal exams have received considerable attention but are controversial. These tests detect cancer at an earlier stage and theoretically prognosis should be better.

Public Health and Epidemiology

Epidemiology plays a vital role in public health by identifying risk factors for cancer. Knowledge about these determinants can then be used to identify and characterize individuals or communities at increased risk of cancer. These individuals can be targeted for risk factor modification, as well as screening and chemoprevention strategies (86). Because the public is inherently not receptive to behavior change, it is crucial to conduct translational research focusing on how to motivate people to modify their behavior and as well measure these behavior changes on cancer outcomes. Colditz and Gortmaker (87) have suggested strategies for cancer prevention, which include focusing on the biologic process and epidemiology to identify risk factors. Increasing our knowledge of the effectiveness of interventions to reduce modifiable risk factors and overall cancer mortality is paramount. A multidisciplinary approach including biological, epidemiologic, social, behavioral, and economic sciences is necessary.

Public policy has, since the 1980s, emphasized prevention and intervention strategies to modify behavior like tobacco use, dietary practices, and screening behaviors. The process of behavior change has become a major focus (88). People need to be educated about strategies for prevention of cancer. Primary-care physicians, surgeons, and oncologists play an important role not only in detecting and treating cancer but also as conveyors of important public health information. They have the opportunity to make a direct impact because of their personal contact. They can motivate patients to alter their behavior and can communicate the etiology behind the established risk factors. Historically, there has been an emphasis on treatment of advanced disease by these physicians compared with primary prevention of cancer (9). Health-care providers must take an active role, beyond diagnosing and treating the cancer, in educating the public concerning prevention.

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