The Ecology of Breast Cancer

The promise of prevention and the hope for healing

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Designing for breast cancer prevention and improved outcomes

Breast cancer has long been described as a malignant disease of cells related to hormones, in which an individual's maturation, reproductive history, and behavior play dominant roles. But this narrative is woven into a far more general, complex fabric of communities and society. Breast cancer increases when people in countries with low rates adopt U.S.-Western styles of eating, working, moving around, communicating, making and using consumer products, and general living. This is apparent, for example in Japan, China, and Greenland, where recent breast cancer rates have increased sharply compared to historic patterns.[1,2,3] Breast cancer risk increases in people who migrate from low-incidence to high-incidence countries—particularly when they migrate at a younger age. Within two generations, immigrants are generally as likely to develop breast cancer as people who are native-born. One, two, or even several variables do not explain these realities.

To a large extent breast cancer, like other common complex diseases, arises out of intertwined societal conditions largely of our own making. This chapter looks at steps that people might take in their personal lives as well as other opportunities to re-design community and societal conditions in ways less likely give rise to breast cancer and improve outcomes after diagnosis and treatment.

Generally accepted individual risk factors, briefly discussed in Chapter 2, are simply insufficient to explain differences in breast cancer patterns around the world. An ecological framework is better suited—one in which multiple, multi-level variables collectively inter-

act to create a context in which breast cancer is more or less likely to occur. Appropriate interventions and a more informed research agenda can follow.

Additional breast cancer risk factors for which the strength of evidence varies from strong to probable to plausible—certain kinds of diets, inadequate physical activity, exposures to certain environmental chemicals or contaminants, non-ionizing radiation, inadequate vitamin D status, shift work, light at night, and stress, and their societal determinants, also help shape conditions that foster vulnerability to the disease and less favorable outcomes. Many of these can only partially be addressed by changes in individual behavior. Multi-level public health and policy interventions at the population level are also necessary in order to re-design system conditions in more favorable ways. To illustrate:

- People are often exposed to chemicals that are mammary gland carcinogens in animal studies. These exposures can occur during fetal development, in the workplace, and in the everyday life of children and adults. With virtually no requirement for pre-market safety testing of most chemicals in commerce*, it's difficult to see this as anything but societal failure to protect the general public from exposure to hazardous chemicals almost certain to increase breast cancer risk.

- Over many years, federal subsidies and insurance programs for commodity crops like wheat, corn, and soy beans, but not for fruits and vegetables, have handicapped produce growers and promoted crops used disproportionately in cheaper, processed, unhealthy junk food. The resulting food environment increases the risk of cancer, obesity, diabetes, cardiovascular disease, cognitive decline, and dementia. This is a predictable result of the way we have designed today's dominant food system.

- Lack of safe sidewalks and nearby parks and recreation areas result in reduced physical activity levels of neighborhood residents.[4] Physical activity breaks in school not only improve student fitness but also improve school performance, yet they are increasingly absent because of budget cuts or different priorities.[5,6] Their benefits are lost, and the message to children is that exercise doesn't really matter much.

* Pharmaceuticals and pesticides undergo required safety testing before being allowed onto the market. Even among these chemicals, however, their impacts on the mammary glands of laboratory animals or breasts of humans are poorly evaluated pre-market. Other industrial chemicals, including those produced and used in high volumes in various consumer products, are not required to undergo any pre-market safety testing. The problem is particularly acute for thousands of chemicals that have been on the market for decades without adequate evaluation. Current Federal regulatory authority to address the concern is extremely limited. New legislation, recently introduced in the Senate, is under consideration.

Opportunities to prevent breast cancer and to improve outcomes in breast cancer survivors are readily available. Future research will no doubt help clarify which combinations are most effective, but it's clear that more than individual behavioral change is necessary. Communities and society as a whole must also be involved.

Making sense of complexity

The biology of breast cancers includes differences as well as similarities. Pre- and post-menopausal breast cancers share many but not all risk factors. The distribution of sub-types of breast cancer differs among racial and ethnic groups. Some tumors are more aggressive than others. Treatment varies. Despite this variability we're learned some important general lessons:

- Preventing breast cancer requires an historical, life-course perspective, certainly beginning with fetal development and, in all likelihood, including aspects of the health of parents and grandparents.

- With few exceptions, one, two, or several individual-level risk factors are relatively poor at predicting whether or not a person will develop breast cancer or explaining population trends and variability among populations. This disease is unlike cancer of the lung where a high-impact exposure like cigarette smoking can be a major focus for prevention. When multi-level, interacting variables contribute somewhat similarly to risk, it's a more systemic problem that must be approached differently.

- Multi-level, ecologic models are best suited for understanding the origins of breast cancer and for designing strategies to prevent it and improve outcomes after diagnosis. This is precisely the kind of problem those models are intended to address. Individuals, families, and communities can use an ecological framework to help them decide what to do. Multiple, multi-level interventions, based on a general understanding of system dynamics, are more likely to shift those dynamics in favorable ways, making breast cancer less likely and improve outcomes after diagnosis—in an individual or across an entire population.

- This complexity also means that understanding cause-and-effect relationships in breast cancer development and response to treatment interventions will always be clouded by some degree of uncertainty. It does not yield to precise, granular analysis. That need not be nor should it be a reason for failing to act, based on available information.

Thinking of breast cancer as a disease arising from complex system conditions seems overwhelming at first. Models of interactions among many, multi-level variables related to breast cancer are messy. Graphic representations are usually a tangle of arrows pointing here and there with everything interconnected. They are difficult to interpret and it's worth asking, why even do this?

First, it helps to acknowledge and communicate complexity. It confirms the multi-level, systemic nature of the problem. This highlights the need for broad, diversified efforts to study and change the dynamics of the system. Individuals cannot do this alone.

Second, it helps in making sense of the complexity. Once a general, top-level architecture becomes clear, it can be a screen for sifting through relevant variables in order to plan further study and interventions.

Third, seeing the origins of breast cancer as a problem entailing complex systems dynamics helps to shape thinking about ways and places to intervene most effectively. Systems science highlights leverage points, feedback loops, and causal cascades as particularly influential targets.[7] That is not to say that single, proximate variables are unimportant. We should do what we can, for example, to reduce unnecessary ionizing radiation exposure, particularly in children, adolescents, and young adults when they are more vulnerable to radiation-induced cancer, as a matter of personal choice and medical and public policy. But we can also look upstream at the beginning of causal cascades with multiple downstream impacts—the food system and individual diets, the built environment and physical activity, the material economy and environmental chemical exposures, and so on. Then we can better design interventions with the intention of reaping multiple downstream benefits.

Re-designing the terrain

All levels, individual to societal, contribute to the shape of system conditions—the terrain—that increase or decrease the likelihood of breast cancer, its recurrence, or progression. (see Box 8.1). Opportunities to re-design the topography of that terrain begin with fetal development and continue through childhood, adolescence, and well into adulthood. They feature time-windows of vulnerability, when many influences, independently and collectively, can push breast biology toward malignant transformation and tumor growth or conversely, toward resilience and decreased risk. Efforts to change the design of that terrain can continue throughout life, so that breast cancer or its recurrence after initial treatment is less likely. Well-designed interventions can have the added benefit of helping to reduce the risk of other diseases as well. But they cannot be accomplished by individuals alone. Public health strategies to re-shape the terrain are essential and must include community organiza-

BOX 8.1: The biologic terrain

"Biologic terrain" is a concept that comes from Antoine Béchamp, Claude Bernard, and Louis Pasteur. Bernard described the *milieu intérieur*—the internal physiologic environment and its relevance to health and disease. Pasteur formulated the germ theory of disease and emphasized the invasion of the body by external "germs" as an explanation for illnesses. Béchamp argued that germs could not invade a host and create disease without internal host susceptibility.

It is widely claimed that, on his death bed, Pasteur said, "Bernard [or Béchamp] was right. The pathogen is nothing. The terrain is everything" ("*Le microbe n'est rien, le terrain est tout*"). Pasteur had come to realize how critical the internal terrain is to the susceptibility to infectious diseases. This concept can be broadened beyond the biologic terrain of individuals to include the eco-social terrain in which people live. That, too, helps shape the *milieu intérieur*. It is also applicable to most non-infectious as well as infectious diseases. The eco-social terrain is a major determinant of who gets sick or remains healthy.

tions, governments, businesses, schools, and health care institutions in more comprehensive, multi-level approaches.

These summaries of specific risk factors are based on more detailed material from previous chapters. Supporting references are not repeated here. This is not intended to be medical advice since individuals' needs, health status, and circumstances vary. But, these summaries can offer general guidance, based on what is known about the associations of each variable with breast cancer onset and prognosis after diagnosis and initial treatment.

Diet, nutrition, and the food environment (Chapter 3)

These conclusions are based on the findings of many studies examining links between diet and breast cancer reviewed in Chapter 3. In addition to serving as a guide for individuals and families, health care professionals, food-service providers, local, state, and federal government officials, and other policy makers should be able to identify opportunities they have to use this information to help improve diets and nutritional status in people of all ages. In general, following these guidelines is likely to improve health in other ways as well, although some individuals may have health conditions for which they are not appropriate.

- Beginning in childhood, emphasize consumption of fruits and vegetables. Yellow and orange fruits and vegetables and leafy greens are particularly beneficial as they contain higher levels of carotenoids. Many studies show foods containing higher levels of carotenoids and associated substances to be beneficial for health general-

ly. Studies also find a lower breast cancer risk and improved outcomes following diagnosis and initial treatment with higher baseline carotenoid levels. Whether the observed association between higher levels and reduced breast cancer risk is causal is still somewhat uncertain since the data are largely from observational studies, and carotenoids could also be a marker for other dietary factors associated with decreased risk.[8] But the data are quite consistent, and even in women diagnosed with breast cancer higher baseline serum levels of carotenoids are associated with improved prognosis following initial treatment. This does not mean that carotenoid supplements should be used as a replacement for regular dietary sources since foods containing high levels of carotenoids have other beneficial nutrients as well. Fruits, including berries, also contain a variety of highly beneficial nutrients.

- Total fat should be limited to 20-35 percent of dietary calories. Total dietary fat, at least in adulthood, is only weakly linked to breast cancer risk, but various sub-types of dietary fat have very different health consequences.

    - » Trans fats should be limited as much as possible. They are clearly associated with increased risk of breast cancer and coronary heart disease.

    - » Polyunsaturated fatty acids (FAs) are necessary and beneficial but excessive intake of omega 6 FAs compared to omega 3 FAs may actually increase breast cancer risk. This is clearly true in animal studies, although the evidence from epidemiologic studies is somewhat inconsistent but quite suggestive. Since the diet of most people contains a large excess of omega 6 FAs compared to omega 3s, ingestion of food containing omega 3 FAs should be increased while omega 6 FA consumption is reduced. Certain cold-water fish, like wild salmon and sardines, are a rich source of beneficial long chain omega 3 FAs.* Walnuts also contain beneficial omega 3 FAs. Of the common vegetable oils, soy oil contains only about seven percent omega 3 FAs and canola oil slightly more at 10 percent. Corn, safflower, and sunflower oils generally contain less than one percent omega 3 FAs. Reducing consumption of processed and fast foods and some polyunsaturated vegetable oils—corn, sunflower, safflower, soy, and cottonseed, for example—will help reduce omega 6 FA intake to healthier levels.

* Some marine and freshwater fish are contaminated with hazardous environmental chemicals such as methylmercury, polychlorinated biphenyls, and flame retardants that should be avoided. Consumers should check state fish advisories and information on the Food and Drug Administration website for information about fish species to avoid.

» Monounsaturated fatty acids, such as oleic in extra virgin olive oil, are beneficial and should also be emphasized as a replacement for oils high in omega 6 FAs. Olive oil is prominent in the Mediterranean diet, which is fairly consistently associated with lower breast cancer risk.

» Low-fat dairy is a good option for reducing total energy intake. Some studies show that higher levels of animal fat from dairy and red meat in adolescence and young adulthood are associated with increased risk of premenopausal breast cancer.

- Limit red meat and avoid processed meat consumption, beginning in childhood, as this is likely to reduce breast cancer risk and will have multiple additional benefits throughout life, including reducing the risk of colon cancer and cardiovascular disease.[9,10] Some experts recommend that red meat should be consumed only occasionally, if at all.[11] In addition to saturated fat content, other properties of meat could explain its associations with health effects demonstrated in epidemiologic studies. Some people are concerned about steroid hormone residues present in meat from these animals, even when good veterinary practices are followed.[12] Whether or not these residues are biologically significant to meat eaters is unresolved. Most but not all beef production in the United States utilizes growth promoting hormones. When cooking meat, avoid charring since this creates known carcinogens. Nuts, fish, poultry, and legumes are good protein replacement sources.

- Include consumption of traditional soy products including tofu and fermented miso and tempeh, beginning in childhood, based on evidence of reduced breast cancer risk associated with higher dietary levels. Several studies show that childhood dietary soy is associated with even lower breast cancer risk than soy in adulthood. This does not, however, pertain to infant soy formula, where the impacts on cancer risk are largely unexplored. Nor does it pertain to heavily-transformed soy product additives in processed foods. Processed foods often contain soy oil or soy protein isolates, which don't resemble traditional soy products consumed for centuries in countries with historically low rates of breast cancer. Organic soy products are available for people who want to avoid genetically-modified food and pesticide residues.

- Consider adding seaweed and mushrooms to diets on a regular basis as the few available studies consistently show an association with lower breast cancer risk.

- Dietary carbohydrates are not directly linked to breast cancer risk, but a diet with excessive refined carbohydrates can cause repetitive, exaggerated spikes in insulin secretion and increase the risk of diabetes.[13] Diabetes increases the risk of breast

cancer. Elevated insulin levels can also promote breast cancer. Moreover, in the context of insulin resistance and overweight, a high-carbohydrate diet can also increase triglycerides and reduce high-density lipoprotein (HDL) cholesterol ("good" cholesterol), increasing the risk of coronary heart disease. Compared to refined sugar and carbohydrates common in processed food and beverages, whole grains are healthier as they are a source of fiber and other micronutrients, less likely to cause spikes in insulin secretion, and are associated with lower risk of heart disease and diabetes.

- In individuals with insulin resistance or elevated fasting blood sugar (type 2 diabetes or pre-diabetes), efforts to improve insulin sensitivity may be particularly helpful, including after diagnosis and initial treatment of breast cancer. A heart-healthy or Mediterranean-like diet with emphasis on fruits, vegetables, nuts, whole grains, olive oil, low-fat dairy, and fish, with minimal red meat and refined carbohydrates helps to improve insulin sensitivity and reduce diabetes onset, even in people at risk.[14,15,16] In addition to dietary changes, exercise, and weight loss, clinical trials using metformin, a pharmaceutical for treating type 2 diabetes, for prevention or as part of the treatment of breast cancer are currently underway. Metformin improves insulin sensitivity and lowers blood glucose levels. Some clinicians already use metformin as one component of a more comprehensive approach to prevent or treat various kinds of cancer.

- Breast feeding infants for at least six months is not only beneficial for the long-term health of the child but is also associated with multiple maternal benefits, including a reduced risk of breast cancer.[17,18]

- Limit alcohol intake. Alcohol consumption is generally accepted as a risk factor for developing breast cancer. However, the risk of alcohol consumption after diagnosis and treatment is much less clear. Some studies show that the risk of consuming more than three-four drinks/week after breast cancer diagnosis may increase the risk of recurrence[19] while others do not and actually show reduced risk of cardiovascular and all-cause mortality with limited alcohol consumption.[20]

For recipes and further information see *The Cancer Fighting Kitchen: Nourishing big-flavor recipes for cancer treatment and recovery*[21] and cookbooks available through the American Cancer Society.[22]

How well are we doing?

General consensus from virtually every profession finds that today's typical U.S. diet features too many calories and unhealthy and often excessive dietary fats, salt, sugar and other

refined carbohydrates, combined with inadequate fruits and vegetables, healthy fats, whole grains, and micronutrients (see Box 8.2). This dietary pattern contributes substantially to a range of costly diseases and disorders—including obesity, diabetes, cardiovascular disease, cognitive decline, dementia, other neurodegenerative disorders, and various kinds of cancer.[23,24,25,26]

BOX 8.2: A brief summary of current U.S. dietary patterns and trends

- In 2000, on average, individuals in the US consumed roughly 300 more calories every day than in 1985.[27] Since 1970, average daily intake of calories from added fats and oils has increased by 69 percent, driven primarily by increases in salad and cooking oil consumption. Soy oil, in salad dressings, processed food, and for cooking comprises 68 percent of the fats and oils that Americans eat.[28]

- According to the Center for Disease Control and Prevention, fewer than 25 percent of people in the U.S. consume at least five servings of fruits and vegetables daily. This has been relatively constant over the past fifteen years.[29] There is, however, significant variability among states and the CDC encourages states to adopt policies that will promote fruit and vegetable consumption and make them more accessible.[30]

- Total per capita meat consumption in the U.S. is among the highest in the world and steadily rose from 1960 to 2007. It has fallen about 12 percent in the last five years.[31] Declines in beef and increases in poultry consumption are most notable. Twenty-two percent of the meat consumed in the U.S. is processed.

- Per capita consumption of refined sugars and sweeteners has steadily increased. According to the USDA, sugar and sweeteners continue to represent about 36-40 percent of the steadily growing U.S. per capita consumption of carbohydrates.[32]

What people eat is decided by a mix of availability, cost, convenience, taste, and preferences, shaped by agricultural policy, media, advertising, and culture. For decades, agricultural policy has made relatively inexpensive, calorie-rich, nutrient-poor food more readily available to people across the country.[33] Farm policies have favored large commodity crops like soybeans, corn, and wheat, while lacking incentives for growers to increase fruit and vegetable production. A 2008 report from the U.S. Federal Trade Commission concluded that the food industry spent nearly two billion dollars annually marketing food to children and adolescents.[34] The majority of these ads (72 percent) promote foods of low nutritional quality, even though 53 percent include a health-benefit claim.[35]

Individuals can of course be encouraged to make healthier food choices, but clearly there are unrealized opportunities for shaping food and agricultural policy in ways that make healthy choices more affordable, accessible, and desirable. These efforts must address the entire life course—beginning with fetal development. In addition to agricultural policy reforms, state and local governments, individuals and organizations in health care delivery, childcare, schools, and communities more generally have critical roles to play to encourage and enable healthier food consumption.

Physical activity and exercise (Chapter 4)

Strong evidence shows risk reductions of 20-80 percent for post-menopausal breast cancer with increasing physical activity. Evidence for exercise-related prevention of pre-menopausal breast cancer is not as strong. Most studies show that increasing levels and duration of physical activity increase the benefit. For example, one review finds that moderate-to-vigorous intensity physical activity two-three hours/week is associated with an average breast cancer risk reduction of nine percent, compared to 30 percent decreased risk with 6.5 hours/week or more.[36]

Strong evidence, including results from randomized controlled trials, shows that regular exercise also improves numerous measures of health and well-being from the time of a diagnosis of cancer throughout the pre-treatment and treatment periods and beyond. In short, regular exercise not only helps to prevent cancer but also improves health and well-being after the diagnosis and initial cancer treatment.

The American Institute for Cancer Research (AICR) and the World Cancer Research Fund recommend 60 minutes of moderate-intensity or 30 minutes of vigorous-intensity exercise daily to reduce cancer risk.[37] The American College of Sports Medicine recommends healthy adults and cancer survivors perform a minimum of 30 minutes of moderate-intensity exercise five days a week to promote health.[38,39]

Here are some ways people can meet exercise recommendations in a week, according to the Physical Activity Guidelines for Americans:

- Take a brisk walk for 30 minutes on five days (moderate intensity); exercise with resistance bands two days (muscle strengthening).
- Run for 25 minutes three days (vigorous intensity); lift weights on two days.
- Take a brisk walk for 30 minutes two days (moderate); go dancing for an hour one evening (moderate); mow the law for 30 minutes (moderate); do heavy gardening two days (muscle strengthening).

- Do 30 minutes of an aerobic dance class (vigorous); do 30 minutes of running one day (vigorous); take a brisk walk for 30 minutes one day (moderate); do calisthenics (sit-ups, push-ups) on three days.
- Bike to and from work for 30 minutes on three days (moderate); play softball for 60 minutes one day (moderate); use weight machines two days.

How well are we doing?

Unfortunately, most children, adolescents, and adults are not regularly physically active. According to the Centers for Disease Control and Prevention, most children and adolescents aged nine-13 years do not participate in any organized physical activity during nonschool hours.[40] A 2009 survey indicated that only 18 percent of high school students had been physically active for 60 minutes every day in the previous week. Only 33 percent of high school students nationwide attended physical education classes 5 days/week compared to 43 percent of students in 1991. In 2005, fewer than 15 percent of children and adolescents walked or bicycled to and from school.

A 2011 survey relying on self-reports found that only about 20 percent of U.S. adults met the 2008 guidelines for both aerobic and muscle-strengthening physical activity. Nationwide, about half of U.S. adults met the aerobic activity guideline—at least 150 minutes per week of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic activity. About 30 percent of adults met the guideline of muscle-strengthening activities at least two times per week.[41] Based on actual measurements of physical activity rather than self reports, only about 10 percent of adults engage in 150 minutes or more of moderate physical activity weekly.[42]

Clearly we have a long way to go to meet generally accepted physical activity guidelines that will not only reduce cancer risk but also the risk of many other chronic conditions, including cardiovascular disease, diabetes, cognitive decline, and dementia. And, it's not just an issue for adults. Increased physical activity improves academic performance among children and is central to efforts to reduce childhood obesity.[43,44]

Physical activity levels are not just a matter of personal choice and behavior; policies at all levels influence them (see Box 8.3). Partnerships are often necessary to improve conditions, services, and environments that enable physical activity. They can establish bike paths, parks, recreation programs, and infrastructure design and maintenance standards. Most studies find that cycling infrastructure, trails, and park upgrades lead to increased physical activity.[45]

According to the Institute of Medicine and the Centers for Disease Control, given the implications for the overall health, development, and academic success of children, schools should also play a primary role in ensuring that all students have opportunities to engage in

vigorous or moderate-intensity physical activity at least 60 minutes daily.[46,47] Churches can also become involved in promoting healthy levels of physical activity for all ages.[48,49]

BOX 8.3: What influences physical activity levels?

Total physical activity levels are a composite of activity at home, in the workplace, in transport, and during leisure time. Most research into influences on physical activity levels has focused on leisure activity and transport. Variables from all levels seem to matter—individual, interpersonal, the social, natural, and built environments, policies, social and cultural norms, global media, and marketing.

At the personal level

- In adolescents, increased physical activity levels correlate with male sex, higher previous physical activity levels, self-efficacy, and family and social support.[50,51] Self-efficacy—confidence in the ability to be physically active in specific situations—seems to be a particularly strong influence in children and adolescents.

- In adults, health status and self-efficacy are the strongest associations with physical activity levels, followed by personal history of physical activity during adulthood and intention to exercise. Male sex, higher education level, and social support are also associated with higher physical activity levels. Self-efficacy is linked to motives related to mastery, physical fitness, social aspects of physical activity, psychological state, enjoyment, and willingness to be fitter and look better than others.[52] Being overweight, perceived effort, job strain, long working hours, and stress are associated with lower exercise levels.

Environmental attributes also influence leisure time physical activity levels

- For children, neighborhood walkability, traffic speed and volume, land-use mix (proximity of homes to destinations such as shops), residential density, and access to recreation facilities are the strongest associations.[53]
- For young people, neighborhood design, availability of recreation facilities, and the transportation environment are the strongest associations.
- For adults, availability and location of recreation facilities, the transportation environment, and aesthetics are most strongly associated with physical activity levels.

Studies have not clearly identified environmental features consistently associated with physical activity levels among older adults. But this is an area of intense interest as part of rapidly growing efforts to develop and implement a national agenda related to the public health aspects of healthy aging.[54] Efforts are underway in cities around the country. There also appear to be cultural differences. Physical activity increases with age as people retire in some Asian nations.[55]

Environmental chemicals and contaminants (Chapter 5)

Historically, interest in exploring connections between environmental chemicals and breast cancer has been slow to develop, even though a chemical, dimethylbenz(a)anthracene, was used to create the first animal model of breast cancer more than 75 years ago. Most laboratory animal and epidemiologic studies have focused on exposures in adults. According to a report from the Institute of Medicine, the strongest existing epidemiologic evidence related to chemical exposures shows increased breast cancer risk from combination hormone therapy products, current use of oral contraceptives, alcohol consumption, and tobacco smoking.[56] Evidence linking passive smoking, other organic solvents, ethylene oxide, polycyclic aromatic hydrocarbons (PAHs), 1,3 butadiene, and some agricultural chemicals to breast cancer is increasingly persuasive. Over 200 chemicals have been identified as mammary gland carcinogens in at least one well-conducted laboratory animal study, but few of these have been examined in epidemiologic studies in people.[57]

Adult exposures are of course important, but a life-course perspective, beginning with *in utero* fetal development, is essential for identifying the connections between chemicals and breast cancer more completely. Laboratory animal studies show that early-life chemical exposures can alter mammary gland development, increasing the risk of cancer in adulthood. Bisphenol A, cadmium, perfluorinated compounds, dioxins, and diethylstilbestrol are examples of this. Human studies are limited, but data show that fetal exposure to diethylstilbestrol (DES) and, in all likelihood, early life exposures to DDT increase breast cancer risk. These examples show that a comprehensive breast cancer prevention agenda must include attention to chemical exposures beginning with fetal development and continuing through childhood, adolescence, and adulthood. This perspective has gained broad support and is slowly leading to fundamental changes in breast cancer research.

Chemicals identified as mammary gland carcinogens as well as those that can modify breast development and increase cancer risk are encountered in consumer products, food, water, various workplace settings, and the general environment. Unfortunately, it is virtually impossible for people to know the identity of or keep records of their exposures to potentially hazardous chemicals in daily life. Bio-monitoring studies of blood, urine, breast milk, or other tissues can identify specific chemicals and levels of exposure in workers or the general population, but with the exception of persistent compounds, they give only a snapshot of what's present at the time of testing and no information about earlier exposures.

Except for substances like alcohol or tobacco smoke, the names of substances linked to cancer in animal or human studies are likely to be unfamiliar to many people. Moreover, manufacturers are not required to disclose the chemical makeup of many consumer products, claiming it to be "confidential business information." And, with the exception of pharmaceuticals, pesticides, and some food additives, no premarket safety testing of chemicals

in consumer products is required, making it difficult for people to make more informed decisions about what they are purchasing.

There are some differences in the workplace. Under the Hazard Communication requirements of the Occupational Safety and Health Administration regulations, workers are entitled to access to Material Safety Data Sheets (MSDS) that will help them identify the chemicals they may be exposed to at work.[58] Although MSDS are often incomplete with regard to health effects, they do enable workers to identify the name(s) of chemicals produced or used in their workplace. They can then further investigate toxicity concerns in various databases or discuss them with an informed health care provider.[59]

Some states have undertaken efforts to identify and reduce exposure to hazardous chemicals, including carcinogens. For example, California's Office of Environmental Health Hazard Assessment maintains a list of chemicals known by the state to cause cancer or reproductive harm.[60] The Washington state Department of Ecology has generated a list of persistent, bioaccumulative, toxic chemicals (PBTs) with the intent of phasing out their use, release, and exposures in order to reduce and eliminate threats to human health and the environment.[61] Some of the listed PBTs are carcinogens. The Maine Department of Environmental Protection and the Minnesota Department of Health have also generated lists of chemicals of concern.[62,63]

In Massachusetts, the Toxics Use Reduction Act (TURA) program is an effort to reduce the use of toxic chemicals in companies and communities. Under TURA, Massachusetts companies that use or manufacture large quantities of any one of nearly 1,500 listed chemicals are required to: (1) report their use and release of these chemicals every year; (2) prepare a Toxics Use Reduction Plan every two years describing how they can reduce their use of them. A recent report identifies uses and trends of chemicals reported to the TURA program that may cause cancer.[64,65] Those linked specifically to breast/mammary gland cancer in at least one laboratory animal or epidemiologic study include:

1. 1,2-dibromo-3-chloropropane
2. 1,3-butadiene
3. 1,4-dioxane
4. 2-methylaziridine
5. 3.3'-dichlorobenzidine dihydrochloride
6. 4.4'-methylene bis(2-chloroaniline)
7. Acrylonitrile
8. Benzene
9. Carbon tetrachloride
10. Methylene chloride
11. Dioxins
12. Ethylene dichloride
13. Ethylene oxide
14. Hexachlorobenzene
15. Hydrazine
16. Nitrobenzene
17. o-aminoazotoluene
18. Polychlorinated biphenyls
19. Styrene monomer
20. Toluene diisocyanate

Consequently, Massachusetts workers and communities have access to more locally relevant chemical information and can take steps to reduce exposures. State efforts to identify chemicals of concern will hopefully lead to their replacement with safer alternatives.

Recognizing the importance of protecting the developing fetus from chemical exposures, the Royal College of Obstetricians and Gynecologists in the United Kingdom recently published a position paper addressing concerns of expectant parents who want to do what they can.[66] They say:

> "Epidemiological research has linked exposure to some of these chemicals in pregnancy with adverse birth outcomes; pregnancy loss, preterm birth, low birth weight, congenital defects, childhood morbidity, obesity, cognitive dysfunction, impaired immune system development, asthma, early puberty, adult disease and mortality (cardiovascular effects and cancer)."
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> "Under normal lifestyle and dietary conditions, the level of exposure of most women to individual environmental chemicals will probably pose minimal risk to the developing fetus/baby. However, women who are pregnant are exposed to hundreds of chemicals at a low level. Potentially, this exposure could operate additively or interactively and raises the possibility of 'mixtures' effects. On present evidence, it is impossible to assess the risk, if any, of such exposures. Obtaining more definitive guidance is likely to take many years; there is considerable uncertainty about the risks of chemical exposure. The following steps would however reduce overall chemical exposure:
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> - use fresh food rather than processed foods whenever possible;
> - reduce use of foods/beverages in cans/plastic containers, including their use for food storage.* (Comment: This will help reduce exposure to bisphenol A and other additives that can leach into food or liquids resulting in direct human exposure);

* Most food and beverage cans are lined with a resin that can leach bisphenol A (BPA) into the container contents, which is then directly ingested. Recently, the Food and Drug Administration has banned BPA from infant formula packaging but this does not address the problem of fetal exposure resulting from maternal ingestion of BPA-contaminated food or beverages. Free, biologically active BPA has been repeatedly measured in umbilical cord blood and amniotic fluid, showing that the chemical crosses the placenta, exposing the developing fetus. Animal studies show that in utero exposure to BPA alters mammary gland development, thereby increasing cancer risk later in life. (chapter 5)

- minimize the use of personal care products such as moisturizers, cosmetics, shower gels and fragrances (Comment: This will help reduce exposure to chemicals that have been linked to developmental abnormalities, primarily in animal tests. However, some manufacturers have reformulated their products in response to concerns. See the Skin Deep data base referenced below);
- minimize the purchase of newly produced household furniture, fabrics, non–stick frying pans, and cars whilst pregnant/nursing;
- avoid the use of garden/household/pet pesticides or fungicides (such as fly sprays or strips, rose sprays, flea powders);
- avoid paint fumes;
- only take over–the–counter analgesics or painkillers when necessary; and
- do not assume safety of products based on the absence of 'harmful' chemicals in theiringredients list, or the tag 'natural' (herbal or otherwise).

Despite uncertainty surrounding the effects of common environmental chemicals, mothers should be made aware of the sources and routes of exposure, the potential risks to the fetus/baby and the important role that the mother can play in minimizing her baby's chemical exposure. Such information should be conveyed routinely at infertility, antenatal and well woman clinics as well as via the media. In this way, women will be made aware of the uncertainties which will enable them to make informed choices regarding lifestyle changes which can be made to minimize environmental chemical exposure to their unborn child."

This position paper from a large, international medical organization gives good general guidance to people who want to reduce exposures to potentially hazardous chemicals in their daily lives. It could be supplemented with advice to make certain that drinking water is free of dangerous contaminants, particularly for people who have private wells. And, reduction in workplace exposures to potentially hazardous chemicals could also be added to this list. Unfortunately, many women and men who are exposed to known, probable, or possible carcinogens in their workplace are fearful of losing their jobs if they push too hard for exposure reduction or elimination.

This discussion also implicitly acknowledges important chemical safety data gaps and shortcomings in regulatory systems in the U.S. and abroad: fetuses, infants, children, adolescents, and adults are routinely exposed to environmental chemicals of concern and many that have not undergone adequate safety testing before entering the market. In the U.S., Federal regulations are outdated and ineffective for most industrial chemicals.[67]

Recently, interest in regulatory reform in the U.S. has gained some momentum at the state and Federal levels. But, truly protective measures are broadly opposed by many chemical and product manufacturers who are concerned about economic competitiveness and maintaining trade secrets. They argue that requirements for pre-market safety testing and disclosure of results would put them at a competitive disadvantage. Now, consumers make purchasing decisions in the context of considerable ignorance and uncertainty about the safety of what they are buying, and that seems likely to continue.

A number of other organizations concerned about environmental chemicals and their relationship to breast cancer risk have made available resources that will help individuals make more informed personal decisions with respect to purchases and use of consumer products. They include, but are not limited to:

- **The Silent Spring Institute** (http://www.silentspring.org/): This organization has an extensive catalog of resources at http://www.silentspring.org/our-publications.
- **The Breast Cancer Fund** (http://www.breastcancerfund.org/): Among an array of resources, this organization publishes "State of the Evidence: The connection between breast cancer and the environment", which is newly updated and available at http://www.breastcancerfund.org/media/publications/state-of-the-evidence/. Its user-friendly web-based format includes an extensive summary of current science and recommendations addressing chemical exposures.
- **Breast Cancer Action** (http://www.bcaction.org/): This organization makes available a number of resources addressing environmental links to breast cancer and the failure of corporations and governmental agencies to evaluate chemicals for their safety before they are marketed.
- **Environmental Working Group** (www.ewg.org): This organization has assembled a searchable database, Skin Deep, which enables users to identify hazardous chemicals, including carcinogens, in specific personal care products, see http://www.ewg.org/skindeep/. Information about healthy fish consumption and unhealthy fish contaminants associated with adverse health effects is also available on their website.

Vitamin D (Chapter 6)

Studies addressing the relationship between vitamin D and breast cancer risk are inconsistent, but most using serum levels as a marker of vitamin D status find higher levels associated with lower risk. In 2011 an Institute of Medicine (IOM) expert panel concluded that most Americans had adequate levels of vitamin D, based on their judgment that a serum level of 25OH-D of 20 ng/mL (50 nmol/L) or greater is sufficient. Average levels in the population

sample they studied were slightly greater, although one-third of adults had 25OH-D levels less than 20 ng/mL.[68] Their conclusion was based only on a consideration of vitamin D and bone health. The committee privileged randomized controlled trials as the gold standard, finding the available evidence of insufficiently high quality to make population-wide recommendations for dietary intake of vitamin D based on any other health endpoint.

The Endocrine Society Clinical Practice Guidelines recommend a target level 25OH-D of at least 30ng/mL.[69] They conclude that lower levels are inadequate. Using the Endocrine Society guideline, over 50 percent of the U.S. population has insufficient levels of vitamin D.

People of color, particularly African-Americans, have significantly lower levels than people with lighter skin because skin pigmentation tends to block UV light absorption and vitamin D synthesis. Older peoples' vitamin D levels also tend to be lower.[70] But, compared to normal weight children, those who are overweight or obese are much more likely to have serum 25OH-D levels less than 20 ng/mL.[71]

Vitamin D sufficiency is important throughout life—beginning with fetal development, childhood, and adolescence when cells are rapidly proliferating. The effects of vitamin D are far more widespread than bone health. Vitamin D is a hormone with receptors in many organs.

With regard to breast development, laboratory animal studies show that lack of a vitamin D receptor results in enhanced mammary gland ductal elongation and branching and increased responsiveness to hormonal stimulation.[72] These are precisely the kinds of changes that increase cancer risk. A prospective study also found earlier onset of menarche in girls with low 25OH-D levels. If this finding is confirmed it adds to the evidence for a link between vitamin D and breast cancer and has broader implications for breast cancer research.

Given what we know about current population vitamin D status, the safety of higher levels, and evidence that generally although inconsistently points toward lower breast cancer risk with higher levels of vitamin D, achieving and maintaining serum levels of 25OH-D in the range of 30-40 ng/mL is supportable and highly unlikely to be associated with adverse consequences. This serum level is consistent with conclusions of both the IOM and the Endocrine Society.

For most people, achieving this serum level will probably require vitamin D supplementation, beginning in pregnancy. The modest levels of vitamin D in many prenatal vitamins are insufficient for achieving optimal serum levels.[73,74] The American Congress of Obstetricians and Gynecologists (ACOG) recommends testing pregnant women who are at increased risk of vitamin D deficiency (e.g., women with limited sun exposure, women with darker skin that limits absorption of vitamin D). If a woman's vitamin D levels is 20 ng/mL (50 nmol/

L) or less, ACOG recommends vitamin D supplementation in a dosage of 1,000 to 2,000 IU daily.[75]

The Centers for Disease Control and Prevention and the American Academy of Pediatrics (AAP) also find that most U.S. infants and children are not consuming enough vitamin D according to 2008 recommendations.[76] The AAP recommends that all infants, whether being breast fed or formula fed, receive a vitamin D supplement.

The IOM committee affirmed a recommended daily allowance (RDA) of 600 IU vitamin D daily, except 800 IU daily for men and women > 70 yrs of age, based only on requirements for bone health. The committee also acknowledged that many people are not receiving that amount and recognized a safe upper limit of 1000-1500 IU in infants, 2500-3000 IU in children, and 4000 IU in adolescents and adults

For many people, supplementation will need to continue through adolescence and adulthood. A supplement of 1000 IU- 2000 IU vitamin D daily will bring most people into the range of 30-40 ng/mL, although some people may need more to achieve that level.[77] However, excessive vitamin D intake can have adverse consequences and levels of supplementation beyond recognized safe upper limits should be guided by testing serum levels.

Night work; light at night (Chapter 6)

The International Agency for Research on Cancer (IARC) decision classifying shift work with circadian rhythm disruption as probably carcinogenic to humans led to efforts to identify interventions to mitigate risk, especially related to breast cancer. For studies looking specifically at breast cancer and duration of shift work, significantly increased risk becomes apparent after about 20 years of working night-shifts, but it is unclear if risk also increases with shorter duration. Nevertheless, since night work is a permanent feature of many occupations, certain steps can be taken to minimize circadian disruption that may help to reduce cancer risk:[78]

- Rapidly rotating shifts (one-two consecutive nights) cause less disruption of circadian rhythms than slowly rotating shifts (three or more consecutive shifts). Delay of circadian phase causes less disruption than advance of circadian phase and therefore forward- rather than backward-rotating shifts are preferable.

- Permanent night work is an option to avoid circadian disruption and may be feasible, particularly if a night-oriented rhythm during days off is possible. But, this requires avoiding bright light during the day and making certain that sleep is adequate.

- Modified light intensity during work at night can help, such as working in bright white light to increase adoption of a night rhythm or in dim red light to prevent adoption. Dim red light suppresses melatonin less than bright white light, but there may be a trade-off with alertness that is critical for performing many tasks.

- People working at night should be especially attentive to maintaining adequate levels of vitamin D.

- Considering the potential risks and benefits, most analysts do not recommend earlier or more intensive mammography screening in women night shift workers.

- Women who have breast cancer should be advised not to work night shifts because of the strong experimental evidence showing that suppression of melatonin secretion can facilitate tumor growth.

Ionizing radiation (Chapter 6)

Ionizing radiation is a firmly-established risk factor for breast cancer. In spite of this, excessive exposure to radiation from medical sources, including X-rays, CT scans, and other medical imaging, is a large and growing problem. To reduce exposures:

- Individuals should discuss with their health care providers the need for medical tests or procedures that involve radiation exposure. Key considerations include personal history of radiation exposure, the expected benefit of the test, and alternative ways of obtaining the same information.

- To help limit cumulative medical radiation exposure, individuals and their health care providers can create a record of all imaging or nuclear medicine tests and, if known, the estimated radiation dose for each test.

- Medical and nursing schools, schools training nuclear medicine and radiology health care workers, and professional organizations must undertake systematic education and evaluation of current standards of practice to make certain that radiation exposures are minimized without sacrificing quality of care.

- Improved equipment design, regular calibration, and maintenance can also help minimize exposures.

Electromagnetic fields (Chapter 6)

The International Agency for Research on Cancer (IARC) has classified both extra low frequency (ELF) and radio frequency (RF) electromagnetic fields (EMF) as possibly carcinogenic in humans, but whether or not they increase the risk of breast cancer is an important but unresolved question. But recent case reports of breast cancer in young women who carried cell phones in their bras are extremely disturbing. Proposed mechanisms by which EMFs could influence breast cancer risk for which there are varying levels of support include genotoxic effects, alterations in gene expression, oxidative stress, up-regulation of stress responses, changes in permeability of membranes and the blood brain barrier, reduced melatonin levels, and altered immune function.

Individuals, families, and communities will need to make their own decisions about how to respond to the concerns raised by a large and growing body of literature addressing potential health effects of ELF- and RF-EMF exposures. This has become a more urgent public health matter as wireless technologies are increasingly deployed in virtually all aspects of our daily lives.

For reducing exposures to ELF-EMF, these simple steps will help:

- Increase your distance from a source. For example, re-position electric alarm clocks and other electric appliances farther away from your body while in bed.
- Use electric blankets only to warm the bed, turning them off before getting into bed.
- Repair faulty wiring which may be generating higher than usual ELF-EMF. If high voltage power lines are close to your house you may want to obtain EMF measurements. In some instances, electric utility companies provide that service for free.
- Turn off electrical devices such as televisions and computers when not in use.

The best ways to reduce RF-EMF exposures from cell phones include:

- Keep conversations on cell phones as short and infrequent as possible; use a land line or send texts instead.
- Do not put it against your body. Put it in your purse, your backpack, or your case.
- Do not keep your cell phone in your bra or pocket.
- Always try to keep it a few inches away from your body. The strength of the antenna signal decreases quickly with increasing distance from the source.
- Do not call in vehicles (car, bus, train). If your mobile does not have an external antenna, the radiation levels go up in moving vehicles. This is because each time the cell phone connects to a new tower (the "handshake") an increase in power follows until an optimal level is established.

- Avoid placing mobile calls in places with poor reception such as cellars or elevators. The cell phone will increase its power (and thus the radiation) in such situations.
- Use the speaker phone feature.
- Plug in earphones while talking.
- Use the hands-free device.
- Keep the phone away from your head.
- Do not sleep with it under your pillow.
- Put your cell phone in airplane mode.

Other steps that will reduce exposures to RF-EMF:

- Avoid using cordless phones.
- Turn off wireless devices when not being used.

Stress reduction (Chapter 7)

Although many people feel that excessive stress can increase the risk of developing breast cancer, the evidence is inconsistent. Yet, based on growing understanding of the underlying biology, it's entirely plausible that unusual or chronic stress could speed the growth and development of an undiagnosed tumor. It is also increasingly apparent that after the diagnosis of breast cancer, stress reduction can be an important part of a comprehensive treatment plan that improves quality of life and can help to prevent or delay recurrence and improve prognosis.

A variety of psychotherapeutic interventions can reduce stress. Techniques subjected to fairly rigorous scrutiny in epidemiologic studies and clinical trials often involve varieties of mind-body-spirit interventions. They include meditation, yoga, mindfulness exercises, guided imagery, music, and cognitive behavioral therapy. Establishing and taking advantage of existing social support networks can also markedly reduce stress and improve outcomes after diagnosis and treatment.

Many studies show that stress reduction can significantly improve quality of life during the initial treatment of breast cancer and thereafter. In general, group therapy, education, structured and unstructured counseling, and cognitive behavioral therapy help to reduce anxiety, depression, and fatigue significantly and generally improve functional ability. For many people, guided imagery, music therapy, meditation, and relaxation training are highly beneficial. A number of these interventions also improve indicators of immune function.

The most significant associations of lower stress levels with improved survival are in women who do not have metastatic disease at the time of initial diagnosis and treatment. But even

with more advanced disease, in some individuals survival is prolonged. Indeed, there will always be individuals who will benefit more or less from a particular intervention.

Improved quality of life is clearly associated with stress reduction in women with all stages of breast cancer. In general, outcomes are more likely to improve when conventional therapy is combined with more comprehensive interventions that include stress reduction along with optimizing diet, exercise, sleep, and social support.

Designing strategies for breast cancer prevention and improved outcomes into daily life

Individual and societal-level variables associated with increased or decreased breast cancer risk do not only act independently. They also combine into an interactive set of system conditions that collectively increase or decrease risk—for individuals, groups of people, and entire populations. To illustrate the importance of interactions, the effects of combinations of dietary fat and chemical carcinogens on the mammary glands of rodents are among the most widely studied. Since the 1970s many investigators have shown that various kinds of dietary manipulations influence the susceptibility of the mammary gland to exposure to the carcinogen DMBA.[79]

For example:

- Sprague Dawley rats fed a diet consisting of 20 percent corn oil (high omega 6:3 fatty acid ratio) from weaning are much more susceptible to developing mammary gland cancer after exposure to the carcinogen DMBA than animals fed a low fat diet exposed to the same carcinogen[80] (see chapter 5 for discussion of DMBA as a mammary gland carcinogen). The rats fed the high corn oil diet also gained slightly more weight and reached puberty earlier. Rats fed a diet consisting of three percent corn oil and 17 percent olive oil were only slightly more likely to develop mammary tumors than low-fat control animals.

- Another rodent study showed that dietary fish oil (a source of long-chain omega 3 FAs) protected against DNA damage caused by exposure to DMBA while dietary corn oil accentuated the DNA damage.[81]

- Pre-pubertal dietary omega 3 FAs can help to protect against DMBA-induced mammary tumors in laboratory rodents, but exceptionally high levels of this kind of fat (39 percent of total calories) can actually promote mammary cancer development.[82]

- One study carried the analysis a step further and administered black tea to rodents that had been treated with DMBA and fed a high-fat corn oil diet. The high-fat diet had the expected promoting effect on DMBA-induced mammary tumors, but there were significantly fewer tumors in tea-drinking rats compared to water-drinking control animals.[83]

- Another rodent study evaluated the effect of vitamin D and calcium on combinations of high fat- and DMBA-induced mammary gland tumors.[84] Inadequate dietary vitamin D and calcium enhanced mammary tumor development with a high-fat diet (20 percent sunflower seed oil, with high levels of omega 6 FAs) while increased dietary levels of vitamin D and calcium were protective. Vitamin D and calcium levels had no significant effect on tumor development in animals fed a low fat diet.

- Demonstrating the importance of a lifespan and trans-generational perspective, a study in rodents found that in utero exposures to a high fat diet (43 percent of maternal calories from corn oil) or a regular rodent diet supplemented with 0.1 ppm ethinyl-estradiol resulted in increased risk of mammary gland tumors not only in offspring daughters but also in granddaughters and great-granddaughters.[85] Epigenetic mechanisms, resulting in heritable changes in gene expression without gene mutations, are likely to explain the findings.

In people the study of interactions among risk factors for breast cancer has been slow to evolve, although we're beginning to see more evidence of the added benefit of combining interventions in adults to prevent the disease or improve outcomes after diagnosis. This is also the case in studies of people at risk of developing diabetes, where combinations of a Mediterranean-like or heart-healthy diet, exercise, and weight control actually prevent the onset of disease more effectively than pharmaceuticals. Based on studies discussed in Appendix A, this is almost certain to decrease breast cancer risk as well. Moreover, comprehensive treatment programs that include a healthy diet, exercise, stress reduction, improved sleep patterns, and social support along with other conventional therapies significantly improve breast cancer prognosis.[86] But, human data addressing combinations of efforts at prevention of breast cancer, across the life course, beginning with fetal development, are virtually non-existent.

Existing evidence shows that consuming a healthy diet beginning in infancy and childhood (see above), maintaining a healthy weight, getting regular exercise, maintaining adequate vitamin D levels, avoiding smoking, limiting alcohol consumption, and avoiding combination hormone replacement therapy and unnecessary radiation exposure are each associated with a significantly lower breast cancer risk. Current oral contraceptive use modestly increases breast cancer risk. For women who are mothers, breast feeding their infants also reduces

their own risk of breast cancer while providing numerous benefits to their children. Risk reduction based on these interventions is best documented for breast cancer developing after age 50, although some of these interventions are clearly tied to reduced risk in younger women as well.[87] Avoiding exposure to carcinogens and chemicals that alter breast development and increase cancer risk is almost certainly going to help as well.

These data help to show how important it is to consider an entire context—a web of interlocking strategic interventions, across the life-course—when looking for opportunities to reduce the risk of breast cancer and improve outcomes. Yet, the complexity of that context means that it will always be difficult to identify precisely what the contribution of each single intervention will be to outcomes. No study has looked at breast cancer links to combinations of childhood and adolescent diet, exercise, and fetal exposures to endocrine disrupting compounds. Nor, has any study examined how vitamin D status might influence those associations. These kinds of studies would be extremely complex and resource intensive—and nearly impossible to carry out. Yet, it is precisely these combinations of variables that influence system conditions, as described in the ecological framework (chapter 1), that make breast cancer more or less likely.

Incomplete data should not prevent us from acting, based on what we already know. Although most established evidence targets steps that adults can undertake, we know enough to conclude that more comprehensive efforts to prevent breast cancer need to begin with fetal development and continue through childhood, adolescence, and throughout adulthood. What might this look like?

- Establish optimal baseline conditions during pregnancy. That means healthy nutrition, appropriate exercise, optimal maternal vitamin status including vitamin D, and avoiding exposures to chemicals and other environmental agents that may alter fetal development, increasing the risk of cancer and other diseases in childhood and years later.

- Infants should be exclusively breast fed if at all possible for at least six months and given a vitamin D supplement as recommended by the American Academy of Pediatrics. When solid food is begun, children should be introduced to a varied, healthy diet, avoiding calorie-rich, nutrient-poor choices that are so commonly pushed onto them by the food industry. Growing evidence shows that unhealthy childhood and adolescent diets are strongly linked to adverse health outcomes in adulthood, including breast cancer.

- Throughout infancy, childhood, adolescence, and adulthood efforts should be undertaken to reduce or eliminate exposures to environmental chemicals and con-

taminants that can alter breast development or otherwise damage breast tissue, increasing cancer risk.

- Avoid unnecessary exposure to both ionizing (e.g., X-rays, CT scans) and non-ionizing radiation, as from cell phones carried close to the body. Early life is characterized by time-windows of vulnerability to environmental influences. As we learn more, it will not be at all surprising to find that breast cancer in younger women is particularly strongly linked to early-life combinations of environmental exposures, unhealthy diets, and sub-optimal vitamin D status, perhaps along with genetic variables that together establish a backdrop for other breast cancer risk factors.

- Regular exercise and physical activity within individual capabilities is an essential part of a healthy childhood and adolescence as well as adult life. Studies show that physical activity levels in early life significantly influence lifelong physical activity patterns. And based on what we know about the benefits of combinations of a healthy diet and regular exercise in adults, it would not be surprising to find them even more beneficial when adopted in childhood.

- Vitamin D supplementation should continue throughout childhood and adolescence and is likely to be necessary throughout life in most people to achieve optimal serum levels.

Individuals and families will of course make their own family planning and medical decisions. But many variables related to breast cancer risk must not only be addressed by individuals but also by communities, businesses, schools, and society more generally. For example, physical activity levels are not just a matter of personal choice. Land use planning and zoning also play an important role by helping to determine neighborhood walkability, access to parks, and availability of bike lanes for transportation. School policies can help to ensure that exercise is a regular part of every student's day. Ready access to farmers markets and other sources of healthy, affordable food influence what people actually eat. Consumer product reformulation, eliminating chemicals plausibly linked to breast cancer, will reduce exposures. Exposure to mammary gland carcinogens in the workplace can be reduced by using safer substitutes and improved worker protection. Individual efforts alone are not sufficient to reduce breast cancer risk.

Multi-level interventions should be combined in integrated breast cancer prevention strategies, just as the integrated approach to breast cancer care and treatment shows great promise.[88,89,90] This typically includes combinations of conventional medical therapy along with nutritional interventions, exercise, stress reduction, and other treatment modalities, depending on individual circumstances. Similarly, integrative approaches to breast cancer

prevention will require combinations of multi-level interventions, beginning with fetal development and continuing throughout the life course.

Historically, we have thought about breast cancer risk in individuals, and risk assessment tools, such as the Gail model, have been developed for individuals to use.[91] But, it looks as if we have collectively although unintentionally also designed current breast cancer patterns into the fabric of communities and society more generally. This argues for widespread interventions at the population level as well as targeted interventions for individuals at higher risk. In this way, we can imagine re-designing various aspects of the eco-social environment to reduce not only breast cancer risk but also the risk of other common, chronic diseases for everyone. Multi-factorial, multi-level changes will be necessary. Properly chosen, they will undoubtedly have co-benefits that will improve public health in many ways.

Conclusions

Reports from two expert committees—one convened by the Institute of Medicine (IOM) and the other a governmental interagency and non-governmental taskforce known as the Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC)—acknowledge the importance of taking a more ecological view of the origins of breast cancer (see chapter 1).[92,93] Many of their observations and recommendations are also explicit in the President's Cancer Panel Report, "Reducing Environmental Cancer Risk: What we can do now?"

These reports and numerous studies discussed throughout earlier chapters make clear that successful efforts at breast cancer prevention must begin with fetal development and continue throughout life. Preventing breast cancer and improving outcomes following diagnosis will require a multi-pronged public health response as well as individual actions. Although we need a revised and expanded research agenda, individuals, communities, and governments do not need to wait to act. Combinations of a lifelong healthy eating, regular exercise, maintaining healthy weight, healthy sleep patterns, maintenance of normal vitamin D levels, avoidance of exposure to chemicals known or suspected to increase cancer risk, avoiding smoking, limited alcohol consumption, avoidance of unnecessary exposure to radiation, and reductions in chronic stress are almost certain to help prevent breast cancer.

Data also clearly show that lifelong healthy diet, regular exercise, healthy weight maintenance, and stress reduction improve quality of life and reduce mortality after initial diagnosis and treatment of breast cancer.

Individuals needing to make changes in their lives to address these opportunities can do that in whatever sequence and combination works for them. They deserve and many will need encouragement from health care providers, family, and support groups. From the perspective of population health, we must also more urgently, consistently, and comprehensively design our communities and public policies in ways that also help to prevent this disease and improve outcomes.

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