

Comprehensive Cancer Care: Integrating Complementary & Alternative Therapies  
New Therapies in Breast Cancer

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Dr. Davis: There are a lot of important things we all want to be able to address here today. I'm honored to be asked to try to keep this panel moving along, and I'm looking forward to hearing a lot of the exciting new developments. Without further ado, Dr. Simone.

Dr. Simone: My name is Dr. Charles Simone. I'm a medical oncologist trained at the National Cancer Institute, and also a radiation oncologist trained at the University of Pennsylvania. I got involved in this field a while ago when I got a phone call from a cancer nutritionist. That was in 1981.

Since 1971 when the war was declared on cancer, there are so many thousand deaths – 337; now in 1998 there are well over 560,000 deaths. This is an important slide, very busy, but briefly I want to show you a few things. This is cancer survival, 1930, 1995. One cancer has gone up dramatically, lung cancer, no surprise. One cancer survivorship has come down, stomach cancer. With the advent of refrigeration in the 20's and 30's, less food additives, less stomach cancer. This data is published every year by the American Cancer Society. They obtain the data from the National Cancer Institute. The key is that all these other survival curves are horizontal, which means that there's been no significant progress in the treatment of most cancers, adult. This is the curve culled out for breast cancer, 1930. It means a woman today who gets breast cancer will live as long as a woman who got it in 1930 – despite radioactive

materials, despite combination chemotherapies in the 60's, despite immunotherapies in the 70's – essentially no difference in survivorship since 1930.

We know that breast cancer is related to a high-fat diet as the key factor, and many other factors you've heard already. We know a lot about this issue because of the Japanese data. Women in Japan, the older generation, have much less breast cancer than we do. Younger Japanese women do not. They have the same rates that we have. When you look at their rates of cancer, the number of calories derived from fat is only 20% compared to our 40% dietary fat calories. When they come into this country, after a mere 20 years they have the same rate of colon cancer, and after only two generations, the same rate of breast cancer. Likewise, another corollary to this information is that the Japanese women who do get breast cancer live much longer than our women do. Why? Because they're on a lower fat diet, higher fiber, and few other risk factors that we'll talk about.

Participant: What about green tea?

Dr. Simone: Green tea, black tea, that's a part of it, yes. We know that certain nutrients can be used to prevent disease based on free radical formation, and the neutralization of free radicals. Mother nature gave us some natural protection, like the large protein coat around every cell, certain enzymes and large vitamin E molecules. We had natural protectors against it, but free radicals now are known to be causing all these illnesses, including cancers.

We developed a ten-point plan a number of years ago to show 1) we can reduce the risk of getting cancer and heart disease, and 2) we can actually decrease the breast cancer recurrence rates. Let's go through that. This is a very key piece of information. The survival curve I

showed you before, from 1930 to the present, is pretty much a flat line. Whether a woman has hormonal therapy or chemotherapy, she will live about the same length of time. The life span is unchanged whether you get chemotherapy.

This is not new. In 1991 major articles came out in *Lancet* to discuss this. When we looked at all the data, we found out no matter what systemic therapy you had, if you change your lifestyle, you can change the outcome. If lifestyle changes are implemented, you will increase life span. We know that certain factors influence the immune system. Nutritional factors can enhance it by eating a low-fat, high-fiber diet, antioxidants, exercise, stress modification, a loving situation, clean air, pure water. Corollary, things that suppress the immune system are shown there. I'm just trying to stress the important factors. This is point one of our ten-point plan.

Maintain an ideal weight. We know that people who are overweight will get a higher risk of certain cancers including breast cancer, but also have a higher risk of recurrence rates. Maintain an ideal weight no matter what the issue. Much misinformation is given to patients. One of them is, don't lose weight as a cancer patient. That's wrong. If you're overweight as a breast cancer patient you should bring yourself down to the ideal weight by eating a low-fat diet – fish, poultry without the skin, little or no red meat, little or no dairy products unless you need dairy, then use skim products. If you decrease the fats, you'll decrease risk and weight.

You need to get around a 20% diet in fats compared to what we're normally eating, about a 40% diet. This is simply how to read a food label, a cute little cartoon I saw a long time ago. It says, "Stay away from them. They're very dangerous, loaded with cholesterol." We continue with nutritional factors. High fiber is critical. Four or five vegetables, two or three fruits a day. Vitamins and minerals. People should be taking nutrients during chemotherapy, radiation

therapy. We'll get into the actual data for that. Smoking. Anyone who smokes should not be smoking, as a cancer patient or otherwise. Nobody should be smoking.

Do vitamins and minerals interfere with combination chemotherapy or radiation therapy?

This is an important question I get asked all the time. There is a tremendous amount of misinformation. We know from the late 70's that we used N-acetyl-cysteine at the NCI to help protect the heart against the effects of Adriamycin, a powerful anti-cancer agent used in breast disease. Since then many other agents, all antioxidants have been used – carotene, E, C, selenium, two other agents that are commonly prescribed now by doctors developed by the Army – ICRF 187 and WR 2721 – and also vitamin A. But what is the data for this? Can we actually augment oncology care by changing nutritional factors and lifestyle factors? We know that during chemotherapy and radiation therapy, serum levels of antioxidants decrease as a result of lipid peroxidation. The fact that you're getting chemotherapy or radiation therapy will decrease antioxidants in your bloodstream. There are over 12 good references for that. We know that 40% of all cancer patients are malnourished, and many die of malnutrition and not the cancer.

We can see an increased response rate, which means a shrinkage of the tumor; we can see a decrease in side effects when nutrients are given with chemotherapy and radiation therapy. How do we know this? In over 51 references, cellular studies using vitamins C, A, K, E, D, B<sub>6</sub>, B<sub>12</sub> and carotene, selenium, cystine, in combination or as single agents, used with chemotherapy, tamoxifen, interferon, radiation or any of these combined will show these effects. In animal studies, over 53 references have been shown in the peer-reviewed literature. The same nutrients were used, except for a few. They were used as single agent, or in combination, with chemotherapy or radiation therapy.

In human studies, these are not new, either. There are almost 2,000 people studied in various human studies that show the same thing. We can increase the response rate – that is, shrink down the tumor quicker, decrease side effects – when nutrients are given with chemotherapy or radiation therapy. We also see in over eight human observational trials an increase in survivorship, which is very, very rare in any cancer care.

Now, how new is this information? This is very old stuff. In the 1970's this number of papers were published. These are cellular studies, animal studies, human studies. In the 1980's you can see it progressing, and in the 1990's those number of studies. This is not new, this has been around a long time, but there is lots of misinformation out there.

In fact, in a front-page article in *The New York Times* in October of '97, Jane Brody interviews Larry Norton, a doctor at Memorial Sloan-Kettering, and he says this: "Research at Memorial Sloan-Kettering shows large dose vitamin C could blunt the effects of chemotherapy in breast cancer cells." Nothing about cancer patients. This information has never been published. In over 200 peer-reviewed references, the exact opposite is the case, and not one reference in the medical literature shows otherwise. He also goes on to say that it is known that folic acid, which is a vitamin, negates the effects of methotrexate. This is absolutely wrong. It is not folic acid, but rather folinic acid, which is a cousin, a chemical analog to folic acid. Folic acid has absolutely no effect, and we published that information in *Lancet* not long ago. Folic acid has no effect at all on methotrexate. So misinformation abounds. Patients are told not to take chemotherapy with nutrients, not to use nutrients with radiation therapy, and it's all wrong. You can actually decrease side effects and increase the effectiveness of the chemotherapy.

This is a quick study we did and I'll end with this. We looked at over 425 consecutive patients who are all cancer patients. We asked them five questions. Do you take vitamins and

minerals? They almost all said yes. Did you take them before your cancer diagnosis? They said no. Did your doctor tell you not to take them with chemotherapy or radiation therapy? The majority said yes. After being told not to do so, did you do it? They said no. Now here's the kicker. Knowing that vitamins could help you, would you take them if your doctor said no? The patients said no. So the patient-doctor relationship is a very, very strong one. If the doctor is misinformed, misinformation gets translated directly to the patient. If you're undergoing chemotherapy or radiation therapy, vitamins and minerals will actually help you, not harm you at all. Thank you very much.

Dr. Davis: Thank you for that stimulating presentation. I'm sorry we didn't have more time. Let me now introduce Dr. Willis. Richard Willis is a professor in the Department of Human Ecology and Acting Director of Biomedical Research at the University of Texas at Austin. He is going to be talking with us about the effects of lovastatin, Coenzyme Q<sub>10</sub> and other aspects of his research underway now. Thank you.

Dr. Willis: My name is Richard Willis. I am Director of the Institute for Biomedical Research at the University of Texas at Austin and professor/head of nutritional sciences on campus within the Department of Human Ecology. I was asked to present information on breast cancer and Coenzyme Q. Most of this work was done by the former director, Karl Folkers, who passed away this past December, but I'll try to do Karl's work justice. First of all, I'll give you information about what CoQ is, what we know it does, some of the things that it's been used for in clinical medicine, in addition to cancer. I'll be echoing what Dr. Simone said about Coenzyme Q and whether or not it interferes with chemotherapy, then Dr. Folkers' work on

breast cancer, some possible ways it might be working, and then what we need to do to further this line of research.

I won't bore you with chemistry, but Coenzyme Q is a naturally-produced substance by virtually all cells in our body. It's found throughout biological systems. It varies in terms of the side chain – there's a little 10 out here on the side. Most mammals make CoQ<sub>10</sub>. It means that funny business in the bracket repeats 10 times. Walleyed pike, mice and rats make CoQ<sub>9</sub>. I don't know why the fish was in there, but he is, and plants make 9, 10, 8, 7; those are the forms that exist.

It was discovered in 1957, independently by two groups, one group in England. They found it in every biologic system they looked at, and named it Ubiquinone because it was the ubiquitous quinone. It was also discovered at the same time in Wisconsin by David Green and Fred Crane. They knew they had something important. They didn't know what it was. They sent it to Merck, Sharp and Dohme, to the laboratory run by my former director, my colleague Karl Folkers. He identified its structure, synthesized it and away we went in trying to find out more about this substance.

Early on, it was primarily studied in terms of its role in producing energy in the cell. It's involved in cellular organelles called mitochondria, and producing ATP, which is the currency of energy used by the cell for its various needs. Since it is a quinone, it is an antioxidant, it is lipid-soluble, and so it is the endogenous or self-produced lipid-soluble antioxidant in us and other mammals. Plants make some other lipid-soluble antioxidants, vitamin E being the one that most of us have heard about, that being for us the exogenous lipid-soluble antioxidant. In fact, vitamin E and CoQ work in concert with one another. CoQ because of its structure and its location in membranes also helps to stabilize membranes, and recently it's been discovered that

if we try to grow cells in the absence of serum, CoQ acts as a cell growth factor. Where that leads us it's a little too soon to say. But at any rate, in one system it does appear to be a promoter of cell growth.

Because initially it was isolated from beef heart, there was a lot of interest in the late 60's and early 1970's in looking at heart problems related to Coenzyme Q, and might there be some relationship? The Japanese took a leadership role in that work in studying congestive heart failure, or idiopathic cardiomyopathies. In the interest of time, to sort of speed that up, Coenzyme Q is now mainstream medicine in Japan and much of Europe, and beginning to enter cardiology in the United States and Canada and also in Britain.

It's also entering veterinary medicine as well as human medicine. There's been some work in the U.S., in Europe and in Japan, in looking at certain forms of periodontal disease, and there have been some reports in the literature of success. There's been a little bit of very preliminary work looking at Coenzyme Q and cancer. There are a number of other health problems where reports or case histories exist in the literature for CoQ, but certainly the data are at best a little thin on many of those diseases.

I get questions all the time about safety. I have a responsibility to the Food and Drug Administration to report on safety every year. We hold the IND, the Investigational New Drug permit, for Coenzyme Q, and part of my responsibility is to look for safety problems. Adverse effects are very rarely reported; certainly serious adverse effects are virtually unheard of, probably because the stuff isn't absorbed very well. At very large doses of 600 to 1,200 milligrams a day, some minor symptoms were reported two years ago by a group studying Huntington's disease. These consisted of headache, heartburn and fatigue. They were resolved by lowering the dose. A multicenter trial in Italy reported some patients – of 2,664 patients, 22

reported mild diarrhea, skin rash, and some heartburn, which again was resolved by lowering the dose. Doses in the trial were on the order of 600+ milligrams a day.

Japanese safety testing filed with the Japanese Food and Drug Administration shows that the LD 50, which is part of toxicology testing – what does it take for half of the animals to die? Lethal dose, 50%. They tested up to 4,000 milligrams per kilogram of body weight, which would be hundreds of thousands of milligrams for a human, and found that oral formulations produced no unusual symptoms to the rat other than the fact that their feces turned orange because CoQ is a very bright orange substance. Last month there was an international conference on CoQ in Boston. At that conference, one group reported on some toxicology work where they ran studies of groups of rats for 52 weeks at 1,200 milligrams per kilogram, and could find nothing of interest to the pathologists involved.

In our work at Texas, over 20 years I've never had anybody report anything except they don't like the fact that they have to pay for the stuff. It's expensive. Because of our work in Texas, lots of clinicians send us blood samples and we keep track of things. I'm an epidemiologist by training, which means I like to play with numbers. Some years ago we looked at a subset of blood samples that we had. We found that among cancer patients in this sample, that the mean (the average level) for CoQ wasn't any different from normals. We have thousands and thousands of data points on normal subjects. So we were ready to move on. There didn't seem to be anything there, but I started looking at that because often we pay too much attention to averages without looking at what the numbers and distributions really mean. What struck me was there were two patients in this group that had particularly high CoQ blood levels, higher than we'd expect to see in normal folks. When we looked at the distribution, we found that cancer patients, although on the average they had the same levels, their distribution

was such that they were at the low end of the scale more often than normal patients were, and substantially more often. This led us to begin to look at other things of interest relative to CoQ and cancer.

One thing that came up very quickly was, this is an antioxidant. We've heard already that other antioxidants have been tested and not shown to interfere. The work with Adriamycin which produces a cardiomyopathy of its own led obviously into CoQ because of the work in cardiomyopathy. There's been a great deal of work done, as well as with other antioxidants, to show that there is a cardioprotective effect. At this meeting last month in Boston, there was also a paper looking at a number of chemotherapeutic agents. They found that survival was much better in those folks who received chemotherapy plus CoQ. They also reported vitamin E as a separate group, which also had a good effect. A colleague in Houston has just done a good bit of cellular testing using the commonly used chemotherapeutic agents in breast cancer. He found that Coenzyme Q does not interfere with their ability to kill cancer cells, so that's good news for those of us who work with Q or worry about people who take Q.

At any rate, this work led to an open trial. We could argue about its design and also about its interpretations, but this in turn has made its way into the literature. It's generating an awful lot of interest in CoQ – perhaps a little more than the data themselves support. An open trial was conducted in Denmark using 32 patients with high-risk breast cancer. All patients according to Danish law (when a new therapy is being investigated) must receive appropriate normal therapy. The new therapy can only be an adjunct. They received surgery, radiation, chemotherapy, whatever was appropriate to their case. They received examinations every three months. The examination was appropriate to whatever stage they were in their problem. The study lasted 18 months. They were given a nutrient supplement containing a great many nutrient

antioxidants including Coenzyme Q, and blood was measured for those nutrients and for Coenzyme Q and other sorts of things.

Let me show you what the sample looked like. Very high in some of the antioxidant nutrients, not so high in others. In CoQ, about where we started when we first started studying congestive heart failure. We started at 30 and found we had to go to 100 or so before we got anywhere with congestive heart failure. After the first 12 months, blood levels of Coenzyme Q, beta carotene, vitamin E, vitamin B<sub>6</sub>, selenium, lymphocyte cell count and natural killer cell counts were all significantly increased as opposed to baseline. Other vitamins and minerals and the ratio of helper to suppressor cells were not different from baseline. No patient died during the first 18 months. Projections, expectation was that four of these patients would die. No patient lost weight. Uses of pain medication were reduced. Reported quality of life, using a quality of life instrument, was improved. They found no signs of progression of disease or spread of disease, no significant side effects. Six of the patients were reported by Lockwood, Folkers and Moesgaard to have shown some level of regression.

A second report was released two years later, where they continued the study. At 24 months they decided to increase the level of Coenzyme Q supplementation. The first patient was increased to 390 and the second one to 300. All the other aspects of the study changed. The reason for the change was based on experience in cardiology. In looking at blood level increases in cardiology, we like to see a certain level of increase. These two women did not increase to the level that would have been expected given the supplement, and so it was increased.

I've got a lot of these case reports, but I'm almost out of time, so I'll speed on through this. Basically we have a woman who had breast cancer, had surgery, had normal treatment, tumor was removed, tumor came back, tumor was removed again, and following the increase in

CoQ, which also followed the second surgery, the tumor was gone. As of last report, which was in 1995 – I'll explain that in a minute, we've lost these folks to follow-up – the tumor, to all apparent circumstances, had disappeared.

A third report came out – we're now to 1995 – three more of the original 32 cases had their levels moved from 90 milligrams a day to 390 milligrams a day, and in three more cases the tumors appeared to have regressed to the point that they were no longer palpable, no longer apparent on radiation, no longer apparent on echo scans, of liver, because one of them had some spread to liver. Those things occurred in time following this change in CoQ dosage. There were other things that were going on too – more surgery, more medication, more radiation. To say that it was purely the CoQ is pushing the data a little too far. However, in May, in Boston, two more groups – one in Italy, and one in Florida – reported increased survival. This is not frank regression or disappearance, but increased survival well beyond expected for a number of tumors, including breast cancer.

Where we stand today is at the suggestive point. There certainly appears to be something here. It may be purely an antioxidant, or something special to CoQ; but, certainly there's something worth looking at. Antioxidant is one of the possible roles. The reduced form of CoQ, if we put a hydrogen atom on each of those two double-bonded oxygens, if you by some bizarre reason remember those things, is the major endogenous, self-produced, lipid-soluble antioxidant. It's been shown to be the first antioxidant to disappear under oxidant stress. If we stress a cell, an animal, a membrane, CoQ disappears before vitamin E and the other sorts of things. It's been shown to participate in the regeneration of vitamin E in the membrane and the regeneration of vitamin C at the membrane surface. CoQ supplementation has been shown to protect tissues

from damage due to oxidative stress, drugs, and reperfusion injury following heart surgery.

We've got lots of information in terms of basic function.

There's also a lot of work that's been done looking at CoQ as a substance that may have an enhancing role in immune system function, in terms of white cells' ability to phagocytize microorganisms, to pick up carbon, which is a fairly routine test. Resistance in rodents to a variety of agents, including a leukemia virus that is peculiar to rodents, and actually some changes in immune system function in humans following CoQ supplementation. Better response to immunization.

We know that CoQ is required by the cells of the body for energy production and for antioxidant protection. It has been used and is used effectively in many parts of the world in the treatment of heart failure and periodontal disease. It has been shown to be low in the blood of some cancer patients. It does not interfere with the effectiveness of cancer chemotherapy. It protects the heart against Adriamycin. A few open trials and case reports suggest that CoQ supplementation may be useful as an adjunct therapy in some cancers. There are some mechanistic explanations for how this might work. There's work to be done. It doesn't mean to run out and buy stock in a CoQ company yet, but there is potential promise. Thank you.

Dr. Davis: Let me introduce Dr. Barnes, who has been working on soy. He'll be talking to us about his work, how soy can be used as a protective agent, and what the recent studies suggest.

Dr. Barnes: Thank you very much. I'm Steve Barnes. I'm from the University of Alabama at Birmingham. I'm a professor of pharmacology and toxicology and also in

biochemistry and molecular genetics. I got interested in soy and cancer about 15 years ago. I was doing work for the cancer center trying to determine women who would be most usefully treated with tamoxifen by looking at the estrogen receptors in the breast. I've always had an interest in estrogens, and a friend of mine got me into this by telling me about some work done on infertility in cheetahs. It may seem a little bit of a stretch to get into breast cancer, but the causative agent of the infertility in these cheetahs was soy. It started provoking some questions. If cheetahs become infertile on soy, surely humans will. And then I realized, no, of course humans are not infertile. The third of the world who eat large amounts of soy happens to be about the fastest-growing population. They have a real problem with too much fertility. Humans obviously are not infertile, but could they be affected by the soy?

At that time there was an increasing interest in trying to find a way to reduce the rates of a number of different chronic diseases that are characteristic of the U.S. and Western Europe, namely cancer and heart disease. When you look at the data from people from Southeast Asia, you find that they have the characteristics that we would like to have. There has to be a reason for it, and maybe as therapists we could look at the way things are going there.

We've talked about this type of data several times today. This is the death rate from breast cancer in the U.S. and Western Europe, and these are the figures for Southeast Asia. Changes are occurring in Southeast Asia as they move over to our types of diet. There were a lot of epidemiologic studies that suggested the consumption of soy was associated with a reduction in breast cancer risk. We've heard a lot about hypotheses today. The only way you can find out whether a hypothesis has real value is to test it.

We used an animal model of breast cancer, and it's one in which rats are given a carcinogen. They're given a large amount of it; they get a lot of tumors. These animals were

placed on different diets. Some animals were on what we might call a regular Western diet, but they actually had casein as their protein. This is a standard diet that's used by the NCI in evaluation of agents which may be anti-cancer. Other animals were on diets of isocaloric or isonitrogenous, in other words the same amount of nitrogen. The animals grew at the same rate, so we're not looking at any sort of starvation phenomena. You can see that the number of tumors that the animals on these diets got were much less than the ones on the casein diet. We were replacing the casein to varying degrees by powdered whole soybean. The whole soybean was a protective agent, at least in this model, and gave us the first clue that our hypothesis had some validity.

How are soybeans eaten? In the Orient they're eaten often as fermented products – miso or tempeh. They also convert them to soybean paste, particularly in Korea. My wife's Korean, so we have a lot of that. Soybeans are also converted to soy milk. There's very little cow's milk in China. Only the very old and the very, very young would have cow's milk. So most people drink soy milk. From soy milk, with a similar process you can make tofu, and if you've been to China or Japan you eat a lot of tofu. Tofu's appearing in this country. Even my local grocery store in Birmingham, Alabama has tofu, so the rest of you must see it. This is sort of the equivalent of cheese and milk in the Oriental environment.

In this country we make a lot of soy flour, because soybeans are a big commodity issue. It's used to make vegetable oil, and most of you have cooked with vegetable oil. What's left afterwards is ground up, and it makes a product called soy flour. It's very similar to wheat flour, and can be used in an approximately equivalent manner. From the soy flour they can get rid of the carbohydrate component and make other products – the isolates, and the concentrates. The concentrates you sometimes see in the no-fat milk, the powdered milk – that's made from a soy

concentrate. The isolates go into all sorts of things, particularly into sports drinks. If you've ever been in a GNC store and bought one of those protein supplement drinks, it's made with the isolated soy protein, which is about 90% protein.

The question was, what is it in soy that's causing this anti-cancer effect? If you review the literature, there's a large amount of data showing soy inhibiting other types of cancers – intestinal cancer as well as breast cancer. I presented this work at a meeting in 1990 at which the director of the NCI was present. It was at Daytona Beach, Florida. We were actually there for work, not a holiday. He was very intrigued by this and immediately convened a workshop in Washington, where a number of us got together and talked about our thoughts on this matter. What could be coming from the soybean which was anti-cancer? There were a variety of compounds, including the isoflavones, but also protease inhibitors, which seem to have profound effects on intestinal cancer and esophageal cancer; phytic acid, which often is looked upon negatively, but some people say that inositol is very effective against colon cancer; saponins and phenolic acids. All of these have been studied to various degrees. It is possible that we should look at them more as a comprehensive group than as separated, isolated components as is done in traditional investigative research.

The phytoestrogens. This is genistein, an isoflavone that's found in the soybean and pretty much nowhere else in the American diet. You won't find isoflavones in other foods. Obviously it's quite similar in structure to estradiol. This is the main physiologic estrogen, has a phenolic group here, and it has an oxygen atom as you can see at this positioning over here. And a very similar sort of pattern for genistein. Not surprising that genistein has estrogenic properties. It's very weak compared to estradiol, but it's still an estrogen. And this is the structure of tamoxifen – you've all heard about tamoxifen. This is anti-estrogen, but it has that

same sort of structure – the phenolic ring, and it actually gets hydroxylated, so again you have the same sort of structure. So you'd expect these compounds to have similar properties.

Could genistein itself have any effect on breast cancer? I managed to encourage one of my colleagues, Coral Lamartiniere, to get into this. He was a toxicologist. He was actually out there looking for toxic reactions. He wasn't looking for prevention. He came into this very cynically. He did an experiment where he exposed the animals to genistein on the first few days of life, and that was the only genistein they were exposed to. He also did an experiment where he gave the genistein just prior to puberty starting, and that was the only genistein those animals were exposed to. As you can see, as the experiment went on, the animals that had this brief exposure to genistein had a substantial reduction in the number of cancers that were seen. This suggests that early life exposure to these compounds is very important for determining cancer risk. It makes a lot of sense, and I'll expand on that in just a second.

What's going on, particularly in the breast, during development? Well, it's a cell explosion. Somebody said earlier today that radiation as a cause of cancer is most effective during the puberty period. It's because cells are dividing at that time. When cells divide and the DNA gets damaged (unless it gets repaired), it carries a genetic error into all the daughter cells, and it's sustained for the rest of life. This is a very crucial period of sensitivity to the start of cancer. Women's cancer starts during puberty. These are the growing cells. They're sort of exploding. Every cell is dividing and splitting off and going on. Eventually that cell growth stops, and what stops it is pregnancy.

We think of estrogens often as being negative components, but they're very positive. Obviously women have estrogens for a reason. They're not toxins to a woman. They're very helpful in many respects. That very high level of estrogen that occurs during pregnancy carries

out process of differentiation. It causes the cells to quit dividing and move over to becoming a more specialized cell type – a cell type that no longer divides, a cell type that can't be damaged by carcinogens of any kind because the cell doesn't divide any more. If you could influence this process, if you could shift the population of cells at this time from a dividing cell type into a more differentiated cell type, you're going to reduce the risk of cancer. We think that's what's going on.

We could say soy and genistein alone, neonatally or prepubertally, prevents breast cancer. Genistein actually changes the proportion of proliferating cells susceptible to carcinogens. I haven't shown you that data, but it's about to be published. Early life exposure to a weak estrogen may provide protection that's otherwise offered by a full estrogen, 17-beta estradiol, that occurs during pregnancy. It may be possible to simulate that. We know that when women from Japan and China come to the U.S., their children will get increased cancer, but to a large extent the women themselves don't, so long as they come here as adults. If they come here as children, they're going to pick up the same rate as an American woman. It's obviously an early life event that's really important for preventing cancer through these sorts of methods.

Now what about baby boomers? Obviously this audience is more in the category of people who are in the baby boom situation. Can soy affect that? Remember, we've only talked about one component of the soy so far. This is work that came from the University of Chicago several years ago. In this case they gave the animals a carcinogen, and waited until the first tumor appeared. They resected the tumor surgically, and put the animals on different diets, to see (by changing the diet after the appearance of that first tumor) if you could affect the rate at which the next tumor appeared. For women who have breast cancer, there is a distinct risk, having removed the tumor in the first breast, that a second tumor will appear in the other breast.

This is analagous. Rats have six mammaries, so they get a lot of tumors. The animals on the soy diet, otherwise isocaloric, had much less tumors. In these animals, this is a soy protein isolate that was protective in preventing the appearance of that second and third cancer.

Other data that seem to suggest in humans that the same thing may be going on appeared in the *Lancet* last October. A group in Australia took women who had breast cancer, and they tried to age-match them and match them for socioeconomic status, with a group of women who didn't have breast cancer. They then collected a 24-hour urine from each of these women. They analyzed them for the phytoestrogen content of the urine, and then graded it into four groups – lowest, mid 1, mid 2, and highest levels of phytoestrogen output. They looked to see how the two groups, the cancer patients and the non-cancer patients, distribute among these four new groups.

They found the following. The patients who had the lowest phytoestrogen output had the highest risk of breast cancer. As you went down to more and more urinary phytoestrogen being excreted, the cancer rate was falling in each group. It was significantly associated with an isoflavone, equol, and with a lignan, such as comes from flax, another phytoestrogen, was found in these patients. The amount of soy or flax they ate in these studies wasn't that high. It was about eight to ten grams a day, which is relatively small. This is the structure of these particular compounds. This is a lignan, and you can see it has similar structure to the genistein.

Now how can all this be? We worry about estrogens, but how can estrogens be protective? There's a lot of data out there that is very confusing. When people started using tamoxifen, a so-called anti-estrogen, we found that it protected bone. This was the reverse of what was expected. When they started tamoxifen trials, they thought there would be all sorts of problem side effects. This turned out not to be the case.

We understand a lot better, but only in the last year or two, a group at the Karolinska Institute found another receptor in the body. We call it the estrogen receptor beta. It's on a totally different chromosome. It is particularly expressed in bone, which explains how estrogens can be effective in bone, even though there's very little estrogen receptor that's measurable in bone. It's also found in the bladder. Women respond very well to estrogens if they have urinary incontinence following menopause. We have a second receptor that we have to build into the equation. It turns out that genistein particularly binds to this receptor, the beta receptor, ten times better than it binds to the alpha receptor. The beta receptor is hardly found in the breast at all, which explains why genistein is not having much of an estrogenic effect that we can see in the breast. It's very helpful in that respect. Genistein and soy both protect against osteoporosis.

I'll leave with this last area. There is a search for what I call the mythical estrogen, or you might call it designer estrogen. Designer estrogens should have good effects on the bone, good effects on cognitive function, because this is a problem postmenopausally, and very good effects on the cardiovascular system. Cardiovascular disease goes up fivefold in women once they go through menopause. Although you might worry about trying to get rid of estrogens to reduce the risk of cancer, you're going to increase the risk of heart disease.

Heart disease is far more likely than cancer is. Women lose the protective effect they have prior to menopause, over men. It's gone once they've got through menopause. So they're going to die of a heart attack. You need estrogens, but you want an estrogen that doesn't affect the breast, and you want an estrogen that doesn't affect the uterus. That's what the search is on for. You may have heard about raloxifene. It's a synthetic estrogen that's supposed to work in the bone very well and not be uterotrophic.

In Japan, for women who are on this high soy intake, is uterine cancer raised? No it isn't, it's almost absent. People on a soy diet have extremely low uterine cancer rates, and not high uterine cancer rates, which you might worry about if you were on a tamoxifen study. Bear in mind the heart disease. We can talk about that more later. I'll stop for now. Thank you.

Dr. Davis: I'd like to introduce Dr. David Blask, who is an MD, PhD, and who is a senior research scientist at the Mary Imogene Bassett Hospital and the Basset Research Institute. He's a prolific writer who has done pioneering work and has published more than 150 research articles with his collaborators. He will be talking today about some of the very interesting results obtained using melatonin. While Dr. Blask is waiting for assistance with slides, we'll take a question here about soy from Dr. Simone and the other presentations on soy. Is soy useful with patients who already have breast cancer, especially those who already have metastasis?

Dr. Simone: I did not present the soy information, but that's a key question I was going to ask Dr. Barnes. Should a patient with breast cancer be on soy at all?

Dr. Davis: I'm sorry, Dr. Simone. I thought you had mentioned soy products as part of your diet.

Dr. Simone: I did, briefly, but I didn't expand on it. Soy has not been studied properly in postmenopausal women without cancer or breast cancer patients who have estrogen receptors or not. I don't think that's ever been studied in a human model at all. People shouldn't be on an estrogen-like compound in either of those instances.

Dr. Barnes: Well, that study obviously has to be done in order to make any recommendations. That is underway at the University of California, Los Angeles. David Heber who was on Dateline the other night is carrying out that study. It's in women who have had previous breast cancer, but it's not focused on postmenopausal women.

Participant: Are they using genistein or soy products?

Dr. Barnes: They're using soy products. You should not be using genistein at very high concentrations. I wouldn't want to take 40 times the dose of aspirin a day because I know what would happen, and aspirin, remember, is a natural substance.

Dr. Davis: Let's have Dr. Blask begin now. Thank you.

Dr. Blask: Thank you very much. My name is Dave Blask. I'm from the Mary Imogene Bassett Hospital Research Institute in beautiful Cooperstown, New York, at the southern end of Otsego Lake in upstate New York.

I've been working for about 20 years now on the pineal gland and particularly the hormone melatonin in relationship to cancer, particularly breast cancer. I'd like to discuss with you today the work that we've done in the laboratory. It has extended to some clinical trials in Europe suggesting that the hormone melatonin produced in the pineal gland may be a promising agent in combination with tamoxifen to enhance tamoxifen's effect on breast cancer. I'll show you some evidence that may suggest that melatonin may reverse tamoxifen resistance. I'm going

to take you through our laboratory bench studies to the bedside. Along the way I'll take you on a little tour through the pineal gland and how melatonin is produced, what it does. Then, I'll take you through our laboratory studies and some of the published clinical studies. All the studies that I'm going to show you are published in the scientific peer-reviewed literature unless indicated otherwise.

This is a prototypical breast cancer cell, actually an estrogen receptor positive (ER+) breast cancer cell. It illustrates the fact that breast cancer cells are literally bombarded with growth factor signals that stimulate the growth of these cells. You've already heard about estrogen being a very prominent stimulator of cell growth. We think that melatonin may be a direct inhibitory signal, a naturally occurring substance produced by the body, produced by the brain, that may serve to counteract some of these growth-stimulatory signal effects. One of the mainline treatments for breast cancer is tamoxifen, which has been mentioned already by Dr. Barnes. About 50 to 60% of all breast cancers are ER+ -- and ER+ breast cancers are the most responsive to tamoxifen.

However, 40% of ER+ breast cancers don't respond to tamoxifen. About 10% of estrogen receptor negative (ER-) do respond to tamoxifen. The current thought is that tamoxifen somehow blocks the action of estrogen at the level of its receptor. The tamoxifen story (in terms of its mechanism of action) is turning out to be much more complicated than we had originally anticipated. Although it's an excellent drug as drugs go, a problem with tamoxifen is either *de novo* or acquired resistance. Eventually all women who are on tamoxifen will become resistant to it. This is where melatonin comes into this story.

This slide shows you that the pineal gland may have a very important interaction through melatonin on the growth of breast cancer through a variety of levels, including influences on the

brain, influencing hormones produced by the brain, as well as a direct effect of melatonin itself on breast cancer, which we believe is its primary mode of action. The pineal gland is located in the geographic center of the brain. Everyone has a pineal gland, and virtually all vertebrate species have pineal glands, and they produce melatonin. One of melatonin's main functions is to act as part of a very complex biological clock system, in terms of biological timing of physiological and probably pathophysiological processes. Influencing this biological clock system is the light/dark cycle.

As you'll see in a moment, melatonin is produced during darkness. Light or darkness through the eyes influences the pineal gland to produce this hormone melatonin through a very complex set of nerve pathways that eventually impinge upon the pineal gland, again in the center of the brain. This shows you that during the nighttime we produce a melatonin signal. These are individuals and their nighttime melatonin signal. If you introduce light during the darkness, light will shut off the ability of the pineal gland to produce melatonin. This has important implications for some of the tumor studies that I'm going to talk about. Light suppresses melatonin production.

The nighttime production of melatonin declines with age. By the time you're around 80 years old, you're barely producing any melatonin during the night. There is age-related decline. How long melatonin is elevated during the night literally tells all the organs and cells of the body that it's dark. Obviously our liver doesn't have eyes. Through the nighttime melatonin signal all the cells of the body know that it is dark, or when melatonin is very low, know that it is light. The pineal gland, through the melatonin signal, is a clock. If you live in extremes of latitude like the northeast or the northwest, for example, during the long nights of winter the duration of the melatonin signal becomes longer. During the spring and summer the signal becomes shorter.

The melatonin signal is also part of a calendar system involving the pineal gland. The pineal gland is both a clock and a calendar.

What's the relationship with breast cancer? A study done back in the early 80's demonstrated that the nighttime melatonin signal in women with ER+ breast cancer was severely blunted as compared with normal healthy age-matched women, as well as women with ER- breast cancer. This suggested that there must be some important relationship between breast cancer and the melatonin rhythm. Another group of German colleagues demonstrated that in breast cancer this nighttime signal was blunted. The degree of the blunting of that nighttime surge correlated with the size of the tumor. The larger the tumor, the bigger the decrease in the nighttime rise in melatonin, again suggesting an important relationship.

In our own studies, using a carcinogen called NMU, we injected animals with either a placebo or a vehicle or melatonin, 250 micrograms per day. We injected it in the afternoon, a few hours before lights off. This is very, very important. I'll tell you why in a second. Here's tumor growth, breast cancer growth, in the animals receiving the vehicle. Here's tumor growth in the animals receiving the afternoon melatonin injections. If we inject melatonin, the same dose, during the morning a few hours after the lights go on in the animal room, there's no effect of melatonin. There is a time of day sensitivity to the anticancer effect of melatonin in this model. If we remove the pineal glands from animals, you can see that removing that normal melatonin signal that these animals experience during the night allows their tumors to grow or develop in much greater manner. It enhances tumor development. If we put animals on constant light, which also knocks out the melatonin signal, we see a very similar effect. The endogenous melatonin signal, as well as exogenous melatonin, can inhibit cancer growth in this mode.

When we look at the growth of human breast cancer cells, particularly ER+ breast cancer cells in the petri dish, if we expose these cells to melatonin for seven days, and we expose them to concentrations of melatonin that are present in the blood during the nighttime – these are physiological – you can see that, compared to control cells without melatonin, the growth is inhibited quite substantially. There is a direct effect of melatonin on human breast cancer cell growth *in vitro*, or in the petri dish. To emphasize that estrogen is important, and that there's a relationship between estrogen, the estrogen receptor, and the ability of melatonin to inhibit cancer growth, let's look at the next couple of slides. This shows the ability of estrogen (a physiological amount) to stimulate breast cancer growth, again in a petri dish.

Here's the effect of melatonin compared to the control cells, by itself an inhibitory effect. If we combine melatonin with estradiol you can see that melatonin inhibits estradiol's ability to stimulate the growth of those cells, so it has an anti-estrogen effect. But I must emphasize that the mechanism is very different from tamoxifen. We see a similar effect when we again go back to that carcinogen model, where we inject the animals with a carcinogen. This represents estrogen-stimulated growth of these tumors. If we combine melatonin at several different doses with estradiol, you can see that estradiol completely blocks this stimulation with estrogen in these animals. In fact it's as effective as tamoxifen in this particular study.

There is an anti-estrogen effect of melatonin in these models. We did an experiment where we were trying to figure out some of the mechanisms by which melatonin interacts with the estrogen receptor. We treated cells with either estrogen or tamoxifen or combinations of these agents as well as melatonin. We found when we initially treated cells with tamoxifen, and stuck in estrogen a couple of days later, that we could partially reverse the effects of tamoxifen. Tamoxifen by itself had an inhibitory effect. Melatonin by itself had an inhibitory effect. We

found that estrogen treatment reversed the effects of melatonin. What we noticed was very interesting was that when we combined tamoxifen with melatonin in the presence of estradiol, we got a greater inhibitory effect than either of the two alone. There seemed to be an enhancing effect of the combination of tamoxifen and melatonin. Melatonin sensitized breast cancer cells to the actions of tamoxifen.

In the next experiment, we took cells and just exposed them to three different doses of tamoxifen. This dose is equivalent to what is used clinically to treat breast cancer. This again is in the petri dish. We pretreated another group of cells with melatonin at a physiological level for 24 hours and then we washed out the melatonin and exposed those melatonin pretreated cells to the tamoxifen. Here's the inhibition of breast cancer cell growth in cells that were not pretreated with melatonin. Tamoxifen has a very substantial inhibitory effect. But look at the effect of tamoxifen in those cells that were pretreated with melatonin. Melatonin enhanced the effects of tamoxifen in inhibiting cell growth. This suggested to us that melatonin does sensitize breast cancer cells to the inhibitory effects of tamoxifen and that these two agents might be used in some combination to the advantage of the patient eventually.

We took this one step further and took another animal model. We took a nude mouse, which is devoid of an immune system. It allows us to transplant human cancer cells into the mouse and grow solid human tumors. What we did in this model was inject animals either with a vehicle, with a very low dose of melatonin (which would not inhibit tumor growth), with a very low dose of tamoxifen (which wouldn't have very much of an inhibitory effect alone on tumor growth), or the combination of the two. Melatonin itself had virtually no inhibitory effect at this low dose. The low dose of tamoxifen by itself had a modest inhibitory effect compared to control animals. However, when we used the two in combination, we saw what appears to be a

synergistic effect. We interpret this as an enhancing effect of melatonin on tamoxifen action. This is an unpublished study, by the way.

I'm going to finish up by showing you the results of two clinical trials that were done in 1995 and published in *The British Journal of Cancer* by an Italian group. These are small clinical trials. You could argue that they're not very well done. One is randomized, but they're not double-blind and placebo-controlled trials. They take what we've done in the laboratory the next step and are very provocative. They took 14 patients that were either ER+ or ER- and had metastatic breast cancer, and they had been treated with tamoxifen. Ten had stable disease in response to tamoxifen, and then they developed resistance. The remaining four patients were refractory to tamoxifen right out of the gate.

All of these patients became refractory to tamoxifen, they had resistance. They took these patients off of tamoxifen for about a month, and then started them on melatonin, giving them oral melatonin in the evening, at 8 o'clock. They were giving the tamoxifen, 20 milligrams, at noon. They gave the melatonin alone for a week and then started them back on tamoxifen. You can see that this combination of melatonin with tamoxifen resulted in stable disease in 57% or eight of the patients. A partial response, or partial regression was achieved in four of the patients, and progressive disease in two of the patients. Ten of the 14 patients survived a median duration of 14 months. This suggests that melatonin somehow resensitized their tumors to tamoxifen. This goes along with our laboratory data.

I'll share just one more clinical study to finish up. The same group did a randomized study. This was not double-blind or necessarily placebo-controlled. They took ER- patients, a total of 40 of them, and put half of them on melatonin and tamoxifen in combination, and the other half on tamoxifen only. They found that apparently with tamoxifen alone, the one-year

survival was 37%; however in combination with tamoxifen, melatonin seemed to produce a larger one-year survival.

There appears to be some data, from the bench to the bedside, indicating that melatonin may be, in combination with tamoxifen, a new alternative therapy for the treatment of breast cancer. Obviously this has to be investigated much more thoroughly, but it suggests that melatonin may reduce the toxicity while enhancing the efficacy of tamoxifen, and may be helpful in solving some of the problems of acquired tamoxifen resistance. Thank you very much.

Dr. Davis: Next we have Dr. Penny George. She'll be talking about her own experience both as a person with breast cancer as well as a clinical psychologist.

Dr. George: I'm going to change the rhythm here, because this is a very different kind of talk. I've been asked to share the perspective of a patient who was trying to make an integrated healing plan and bring complementary therapies along with the traditional protocols into treatment. This is just one patient's perspective, an "N of one." Yet it's pretty clear to me from being with a number of you that I am part of an invisible mainstream of patients who are doing this.

By way of background, my healing journey began in February of 1996, when a routine mammogram revealed that I had an invasive breast cancer. I was treated at the Virginia Piper Cancer Institute in Minneapolis, where I elected to have a mastectomy followed by chemotherapy, and now I'm on tamoxifen.

Coming at a point in my life when I have never felt healthier, the idea of my having breast cancer was a blow to some of my most fundamental beliefs about myself. I felt betrayed by my body, deeply exposed, vulnerable – anybody in this room identify with those feelings? I also felt more out of control than I ever had before. While I was confident that I was receiving the best conventional medical care available, I knew that I had to do something to take charge of my life. If disease is what happens to you, illness is what you make of it. I gradually found I had resources I hadn't believed I would have.

In spite of my good prognosis – my oncologist said that I am a stage two on his five-point scale, so he uses a slightly different scale. It's a late stage one cancer – I realized that it wouldn't be helpful to me to think in terms of curing this disease. I am not in control of my biology. If I don't die of this, I surely will of something else. What did make sense to me (and what still does make sense to me) is to use this illness as an opportunity to heal my life, so that when I do die, I will have lived fully and become as whole as it is within my capacity to be. A byproduct is that in succeeding at that, I will have achieved a very high quality of life, and that has physiological correlates.

I believe that true healing is about wholeness. It cannot be separated from its spiritual foundation, nor exist apart from the complex web of human relationships with which we love and suffer and grow. I have been powerfully supported by the love and care of my family and friends. My family are all here supporting me. My husband Bill in the back of the room has learned what it means to be a support person in a situation where he can't take control in his CEO-like way and make things come out right. Having lost his mother and a fiancée to cancer, he was up against his own growing edges with this. We had to struggle for a while. His approach to this was to tell me all the positive things about my situation, and my response to that

was to tell him all the negative things. We got into quite a dance for a while that wasn't very productive. I finally realized that all I really wanted from him was an acknowledgment that he was as scared as I was.

My spiritual foundation, and the sense of community that I have, has played a large role in my healing. I'm in a women's spirituality group that's in its 25<sup>th</sup> year, and my husband and I are in a couples spiritual growth group that's been going on for almost that long. During the first years of my recovery, I convinced Bill to join with me in changing churches, changing denominations even, so that I could be in a more nourishing environment. I feel so fulfilled by these relationships and our common quest for inner growth that I haven't felt the need to join a cancer support group. Wherever one can find it, true healing does not exist apart from community.

In those early weeks (as I absorbed the reality and magnitude of what a cancer diagnosis implies), I now see that I was preparing to use this crisis as a means of transforming myself in every dimension of my life: body, mind, heart, and spirit. Because I sensed that Western medicine lacked the holistic framework I needed, I was forced to look further afield for ways to heal myself.

Over the past two years I have done the obvious things to help heal myself, like continuing to exercise, and continuing to meditate, but to really meditate – I sat a lot but I didn't meditate – improving my diet, cutting down on alcohol consumption and taking certain nutritional supplements. I now have to add another. Pretty soon I won't be able to leave the house – I'll just be taking pills all day. These things I see as being so mainstream that they ought to be covered with every patient by every physician.

There's a real need for clear, concise and credible information about nutrition. I consulted a dietician in Minneapolis, who is head of a local branch of a study investigating the possibility that very low-fat diets will prevent recurrence of cancer. She was very generous. She was very competent. She was also very conservative and she was saying that she felt 500 milligrams of vitamin C was the maximum I should take. I just wasn't looking for that kind of answer. I've been forced to go to books, but in this area in particular I really feel like I'm stumbling in the dark.

I've tried some far-out things on my path toward healing, like attending a weekend workshop on shamanism, and doing energy work. I've done Qi Gong. I did find benefit in the energy work. I scheduled it after the first two chemotherapy treatments when I basically was not particularly functional. I decided to do this, and from then on I scheduled an energy treatment for the day I had chemotherapy, and I was able to go back to work on those days. I don't think it's all in my mind. The notion of releasing energy blocks within the body, according to a system of chakras, or meridians, or whatever it might be, makes a lot of sense. It just seems like these are alternative ways of looking at how the body functions that are different from, but not necessarily less than, the biomechanical model that we've grown up with.

I'd like to tell you some of the other things that I have found helpful in my healing. One of the most important, both in terms of helping me to absorb the magnitude of what was happening and helping me heal my life, was psychotherapy. Within the safety, support and intimacy of the therapeutic relationship, I have been able to look at the possibility of my death without being overwhelmed. I have spent a good deal of time reflecting on the personal meaning imbedded in my illness, how to make it a constructive presence in my life, rather than a fearful

preoccupation. I have learned to grieve past and present losses, and to experience rather than to rationalize painful truths about my life.

I will never know if there are psychological antecedents to my cancer, but I do find compelling Candace Pert's and Robert Ader's research that documents the debilitating effects of prolonged stress on the immune system function. I had lived for years with a very high level of stress and self-criticism. Psychotherapy should be considered a complementary form of healing for all those who can make use of it, and not just for those who have a diagnosable psychological disorder.

I have come to understand the powerful magic in human touch. Massage therapy is another complementary approach that has been immensely helpful in my healing. It took me awhile to find a massage therapist whose style and personality were a good fit with mine, but now that I have, I count on releasing stress and soothing my mind and body on a regular basis.

After chemotherapy ended my ovarian function and the hot flashes began, a combination of acupuncture and an herbal preparation called Remifemin that contains black cohosh were helpful in relieving my symptoms. I only went to an acupuncturist maybe six times and only took those dietary pills for a few months, but I got my system back in balance and have had no further problems. I've also tried to take some soy products, and that may or not be a good thing to do and it may or may not have helped.

I also have had difficulty seeing myself into the future. That's always been an issue. I couldn't project out into the future and picture myself. I don't like the idea of getting old and infirm in the first place, and then when the cancer diagnosis came along it reinforced a pessimistic view. Hypnotherapy, which is a kind of focused attention in a state of deep relaxation, I have found very helpful. It's similar to guided meditation in that the patient's own

unconscious is invited to offer up images in response to a particular scenario. One session I found particularly helpful was an interactive guided imagery in which the hypnotherapist elicited specific details of what my life was going to be like ten years in the future.

What I pictured was significant, both in terms of what it revealed about how I might like my life to be different in the future, and also in increasing my awareness that at some level I do have a desire to live to be old. I believe that hypnotherapy or guided imagery is a powerful vehicle for amplifying the body's natural ability to heal, particularly in patients with active imaginations. In working with my own clients I have always found that if a person can't imagine something new happening in their life, a career, or a different, better relationship, it's much less likely to happen. Although willing oneself to live is no guarantee of longevity, a deep-seated belief that one is not going to live, or does not deserve to live, is not an auspicious indicator.

In my healing journey I have touched on other healing arts, from homeopathy to biofeedback to aromatherapy. I have just begun looking at Ayurvedic medicine. I have neither the time nor the interest in continuing with all of them, but I am glad to have been able to sample some of what's out there and to make some determination about what seems to work for me, largely trusting my intuition to guide me. Now, two years out, I see that I have in fact healed, in body, mind and spirit. There's still more growth in me, but if I died tomorrow, I could be satisfied to have achieved the wholeness that I sought. I realize that I've now entered into a maintenance mode. With major medical breakthroughs possibly on the horizon, one of my challenges is to continue the hard work of disciplining myself to live a healthy lifestyle. I don't find this easy in our harried, hurried culture of excesses.

Watching other people in their healing journeys, I have come to recognize and appreciate how individual and varied are the ways in which people heal themselves. What works for one person may not work for another's healing. What appeals to one may spark no interest in, or may even threaten another. There is no single protocol for how holistic breast cancer healing should take place. Women shouldn't be made to feel guilty if all they want to do is just get back into their lives.

I have found my own path, but as a psychologist I was well equipped to identify and make use of alternative sources of help, as well as to pay for them. Many women would be at a disadvantage in this regard. Recognizing this, the Virginia Piper Cancer Institute developed within its Breast Center a program called Life Choices in Healing. It exposes women to a wide variety of complementary healing avenues. They have hired a Healing Coach, whose role is to help women, once the basic conventional treatment decisions have been implemented, to assess their whole-person needs and to create their own personal healing program, drawing on resources within the hospital and within their own communities.

Working with the assistance of an information coordinator, who happens to be sitting in the third row, the coach helps the patient determine what complementary approaches she may wish to explore. The coach's other role is to interface with the physician team, to facilitate communication and support for the healing plan the patient creates. The end result is that by bridging the worlds of allopathic and complementary therapies, the Healing Coach helps empower the patient to be responsible for her own healing.

As complementary therapies are increasingly shown to be effective in the treatment of chronic illness, more and more medical centers are bringing the practitioners of these healing arts into the medical arena. This does not necessarily mean they are being embraced by

physicians, let alone treated as peers. We are still some distance from the collaborative integrated medicine the 21<sup>st</sup> century needs. One day I believe that we will no longer see such tension among the different approaches to healing, and the needs of the patient for a full complement of treatments in an integrated fashion will prevail. Already some insurance companies are seeing the value in these approaches. In Minnesota for example, Medica, the insurance arm of Allina Health System, has expressed enthusiasm for Life Choices in Healing and its intention to authorize payment for these services without prior authorization.

The new paradigm in medicine that many people think is rapidly emerging is one in which healing is going to be seen in a much broader context. In the next millennium, I envision practitioners from a wide variety of healing arts working collaboratively in partnership with their patients. They will contribute to the shared goal of not just restoring the patients to pre-illness levels of functioning, but rather to fuller and healthier lives. In the future I envision physicians being trained in a radically new way, starting with selecting medical students for their potential for dealing with patients as whole beings.

I picture a world of healing in which hierarchy and professional arrogance are no longer rewarded, a world in which expensive Western treatment approaches are not seen as the gold standard, and everything else compared to those approaches based solely on the results of double-blind crossover random studies. Our increasing awareness of the power of the mind-body connection should make us all realize that we need to take a fresh look at how we assess effectiveness in healing.

In conclusion, my experience over the past two difficult but rewarding years has convinced me that, while Western medicine has much to offer in the treatment of breast cancer, much more can and should be offered patients by helping them to take more responsibility for

their own healing. An integrated approach should be used, facilitated by enlightened physicians and medical institutions who understand the value – and I firmly believe, cost-effectiveness – of a collaborative, integrative approach. Thank you.

Dr. Davis: Thank you so much. It really puts things in perspective for us, and I appreciate the graciousness with which you made them. It's a reminder of what we're trying to do and what we need to focus on.

I'm pleased to introduce Dr. Alison Estabrook. Some of our panelists may have to leave, unfortunately, to catch airplanes, so you'll have to excuse them. I've asked that we keep our discussion pretty focused and we will try to get to as many of the questions as possible. I'm delighted that Dr. Estabrook is here. She is a renowned breast cancer doctor – a legend in her time – has received many awards, was profiled in a book, and is also one of the leading doctors in New York. Dr. Estabrook.

Dr. Estabrook. Thank you. I was asked to be the commentator for this session. I'm going to comment very briefly and then we'll get to your questions. I enjoyed all the presentations, and I'm here really as a student. I use a lot of alternative medicines and therapies in my practice, but I am not a holistic doctor. I refer people to alternative medicines. We try to check out who we're sending people to and what kind of therapies, and I'm very interested in this whole subject.

Dr. Simone's presentation was very good. I'm sorry it had to be so quick. His main points about nutritional supplements and the use of vitamins in chemotherapy, or during chemotherapy, and during radiation are very important. We were taught that these things should

not be used, and that's totally not true. It makes women feel better and it does protect normal cells, so the use of vitamins and diet and nutrients and maintaining an ideal weight is very important to remember. His other point about the ten steps to a better lifestyle seems like it's common sense, but we have to remind ourselves about these things constantly.

As Dr. George also mentioned, this is a very stressful life. When you're trying to make an extremely important decision about chemotherapy, surgery, radiation, in a very stressful time of your life when you have breast cancer diagnosis, it's a good idea to try to step back. You need to reduce your stress levels, and try to follow some of the things that Dr. George mentioned.

Dr. Willis' discussion of Coenzyme Q<sub>10</sub> was very good and we need to look into this more. The studies can't be anecdotal studies. We really have to look into the value of CoQ.

Dr. Barnes' presentation about soy is very, very important. As he mentioned there's been a discovery of a new estrogen receptor – estrogen receptor beta, which is found in many organs of the body, but not in breast. Soy is very good. What he presented explains to us some of the things we've been dealing with all this time – why Asian women have a lower incidence of breast cancer than women that live in Western societies. Was it really the soy in their diet, was it really low animal fat, what is it exactly? Now we see that it's through soy and this estrogen receptor beta that's actually lowering their risk of breast cancer and their development of breast cancer.

Soy is also very important for hot flashes. Someone had a question about the use of soy in postmenopausal women. Soy has been studied in petri dishes. It's been studied in patients. It's been studied in many ways. I don't see any down side to using soy in postmenopausal women for the treatment of hot flashes or for any other reason. Scientifically there's no reason

not to use soy. A lot of postmenopausal women who have had breast cancer and cannot take estrogens are now using soy and finding great relief from hot flashes. I don't see any medical reason for not using it.

Dr. Blask's presentation about melatonin was wonderful. It seems to sensitize cells to tamoxifen. It inhibits breast cancer cell growth, so should I start using this on Monday? It's available. Should people start using it? I don't think we should start using it right away. We need controlled studies to see what is the quantitation of the decrease in breast cancer cell growth. A lot of this stuff is available, it's out there. It's confusing when we're trying to decide what is the actual quantity of the impact from melatonin and soy and all these other things if people are using it and not reporting it to doctors. It would be nice to have a dialogue with patients and be able to report all these things.

All the things that Dr. George mentioned in her talk are extremely important. The goal of this conference is to increase quality of life. What she mentioned does increase the quality of life, and she said if she died tomorrow she feels she's had a full life. She's gone through this two-year journey and has had a full life. That's extremely important from the doctor point of view. We really need to know if what she's doing and what everyone presented here actually increases overall survival. That's very important, and I hope we'll be able to address these issues in the next few years. Thank you very much.

Dr. Davis: I'm serving as a counter, sorter and computer to try to farm out the questions to my colleagues. I'll ask Dr. Simone to begin. He received a lot of questions about the nutrition recommendations. I know there's a lot of interest, a lot of commitment in these questions.

Dr. Simone: The literature supports a number of issues. The question was which vitamins and minerals should one take in general, but specifically during chemotherapy or radiation therapy? Remember we talked about the antioxidants as being good. I did not show you my hypothesis as to why it probably does not interfere with chemotherapy or radiation therapy, but I could do that later.

Let's go over what I think is appropriate based on the literature, animal studies, and importantly some human studies, intervention studies. Intervention studies are important, because intervention studies say, if I give this thing to a patient, what will happen? When you look at the antioxidant levels, beta carotene should be in the 20 milligram range; vitamin A about 5000 international units a day; vitamin D 400 international units a day; vitamin E 400 international units a day; vitamin C anywhere from 350 to several thousand milligrams a day, depending on what other issues are going on; folic acid, 400 micrograms a day; the B vitamin generally in the 10 to 20 milligram range, except for vitamin B<sub>12</sub>, which should be at the 100% RDA which is 18 micrograms; biotin, 150 micrograms – important distinction, milligrams, micrograms; pantothenic acid, again a B vitamin, in the 20 milligram range; iodine – actually there's a relationship between low iodine and risk of breast cancer – 150 micrograms a day; copper, another antioxidant, 3 milligrams a day; zinc, 15 milligrams a day; selenium, 200 micrograms a day; chromium, 125 micrograms a day.

What these numbers can't tell you is it's important to know the right word. Every multiple vitamin today has the right words, like One-a-Day has beta carotene. It's also important to have the correct dose. Equally important is the correct chemical form. Oil-based softgels generally have a shortened life of activity. If you're taking vitamin E or beta carotene in a little

football or a little softgel, that's probably the short-lived version of that nutrient. Fourthly, you need to know the correct ratio of one to another. For instance, if you take too much E you actually wipe out beta carotene. Four factors go into making an excellent formulation – the correct name (the word), the correct dose, the correct chemical form and the correct ratio of one to another. Thank you.

Dr. Davis: It's not going to be possible for anyone here to fully digest all of that very valuable information. Some is available in your book.

Dr. Simone: Yes. I'll be available if you want after everyone breaks up. I'll stick around.

Dr. Davis: That would be appreciated by many people. There were a number of other questions. I passed them to the panelists. Dr. Willis, do you want to address some of the ones you were given?

Dr. Willis: First of all, if I don't get to your question or you think of a question later you can write me at the Institute for Biomedical Research, University of Texas at Austin, Austin, Texas 78712. I respond to every letter I get, every phone call I get, so I'll get to you. It may take a while, but I'll get to you. The telephone number is (512) 471-7174.

Most of the questions had to do with either doses or how one ought to go about supplementation. People are quite variable in terms of their absorption, or at least in terms of the ability of what they take to influence blood levels. There are a great many different kinds of

products. People get little or no instruction. The important thing is to remember that this is a lipid-soluble compound. If you're on a lettuce and lemon juice sort of diet, you're not going to absorb very much CoQ, no matter how much you swallow. Absorption is poor under the best of conditions, but it should be taken along with food, and that food doesn't need to be high fat, but it doesn't need to be zero fat. A glass of orange juice won't do it. In cardiology they sometimes talk about taking it with a little peanut butter, something of that nature. There's also some question about dosages. In a recent prostate cancer trial that is yet to be published, we found that to get reliable blood levels and then see clinical responses we needed to be in the 400 to 600 milligram per day range, again with food. That is about double what we've had to look at in terms of cardiology. In cardiology between 200 and 300 milligrams get us to the blood levels we want.

I also have a question related to, do humans make CoQ<sub>10</sub>? Yes we do. If we didn't, we would be dead. What about CoQ<sub>9</sub>? CoQ<sub>9</sub> will function as far as we know. There is some question as to whether all of the functions are interchangeable. We don't know the correct answer to that in humans. We know in rats – remember I said that rats make CoQ<sub>9</sub> – CoQ<sub>10</sub> substitutes for some of the functions but not all of the functions in rats, so there may be a species specificity to what we need. We do know that for some roles 7, 8, 9, and 10 are all functional.

Dr. Davis: Let me point out two things out that are relevant to every single presentation here. There has got to be a fundamental change in who pays for these materials. With the evidence that we see on the efficacy of some of these agents, there ought to be controlled clinical trials underway where people could receive these materials. Coenzyme Q<sub>10</sub> is extremely expensive. I calculated on the back of an envelope. The dosage you talked about as the

therapeutic dose would cost more than \$100 a month, even at the Price Club, and you can get it at the Price Club.

And the second issue – it may be time to rethink what it means to do clinical trials in this context. Forty percent of the women on the Women’s National Health Trial for testing estrogen are in fact using some form of complementary medicine. Forty percent, and we don’t get good data on it. The possibility of getting good data out of these trials is getting less and less because of this. It’s time to call for a summit of clinical researchers to come up with a new methodology. It’s going to be increasingly difficult to get people into clinical trials given the kind of results that we have, and some of us can’t wait. That’s the sad truth of it. I’d like to ask Dr. Barnes to comment on this question since he got lots of very interesting questions on this point.

Participant: Could I just ask one question that’s pertinent? What is a naturally occurring plant or food that has Coenzyme Q<sub>10</sub> in it?

Dr. Davis: Is there any naturally occurring Coenzyme Q<sub>10</sub>? That was one of the questions.

Dr. Willis: Virtually any animal food that you eat, spinach, most of the dark green leafy things – but the amounts of CoQ in food are tiny. A couple of milligrams a day in the average diet, maybe two, maybe up to ten.

Dr. Barnes: Can I comment too about the conference? I come as an outsider to the conference. I hate to criticize, everyone having been so nice to me for the last 20 years whilst

I've lived here, but I always thought that medicine was practiced exactly as you're asking for. It was a real shock when I got here and I found out it wasn't. American medicine is practiced too much on the basis of money, and not on the basis of commitment. It was a real shock when I arrived here. So all the things I've heard today I thought were obvious. I didn't think they needed anything special, because to me it's always been that way. You should care about your patient. I'm in a university setting which may be a little bit different, but the physicians I've met here, for the large part, don't like seeing patients. It wastes their time. I'm sure you've all felt that. Anyway, I'll answer some of your questions very quickly.

Somebody asked about level 2 allergy to soy. You can't take soy if you have that degree of allergy. However, I've been here in Washington all week, talking about the plant genome initiative. The soy industry and many other aspects of U.S. agriculture are going to start changing the genetics of plants that we grow to improve the way they grow and to get rid of things like allergens. The allergen is due to a protein, and a particular sequence in that protein, so we can go back to the soybean and take that sequence out. In 10 or 15 years maybe that will be possible, but not now.

Somebody asked, is soy a natural tamoxifen? I think I said that about 10 or 12 years ago. I'm actually coming back to the fact that it is a closer relative to tamoxifen than I thought maybe five years ago. People are beginning to understand the mechanisms of how genistein works in cells, which includes antioxidants. We have a whole series of new metabolites of genistein that we're detecting which reveal its antioxidant activity.

Dr. Davis: And they bind to the beta receptor?

Dr. Barnes: We don't know what these metabolites do yet, whether they have pharmacologic action or physiologic action. That will be fascinating to find out. I have a student working on that topic.

Dr. Davis: Again it's the genistein, not the soy?

Dr. Barnes: It's the genistein, yes. Now remember, the epidemiologic data are strongest for soy and not for genistein. I chose to work on genistein because that was my interest and because the way NCI funds studies is very directional. They will not allow you to work on a matrix. They want you to work on a substance. In fact this audience, despite its wanting to embrace this mind-body medicine concept, still thinks in terms of compounds. I've watched your faces, the reactions to various compounds that are being talked about. You still think therapeutically. You do not think in a comprehensive way. You would take times of anything that's been mentioned here in the hope that it might work rather than actually embrace the culture that seems to be lowering cancer rates.

I said at a meeting in New Orleans last year that we approach medicine from a totally Catholic manner. We ignore everything until we get into trouble, and then we go into the confessional and we want to get relieved of our dreadful ways. The 21<sup>st</sup> century will change that. Medicine is going to be preventive. We've not going to be treating patients. We're going to be treating people, before they ever get that disease. That's the difference. It's coming, and it's not far away.

The ability to look at your genes and find out what's wrong with you – when somebody presents with a cancer, we'll be able to look at every one of the known target sites that are

thought to be oncogenic to see what your cancer actually is. Up to now you're just said to have breast cancer. Breast cancer is just a name for a huge number of different forms. Each person has a different type of cancer, and therefore requires a different treatment. We're going to find that out. That's part of the bigger picture that's coming.

Panelist: Go to the trophoblastic conference tomorrow and you'd get a different view of it.

Dr. Barnes: I'm sure I would. There were some comments about whether soy should be taken postmenopausally. That's a reaction to the possibility that these compounds have estrogenic action. Remember the Orientals of course are eating it postmenopausally. That's the simplest answer to what is a difficult question. However, it is being tested. If Dr. Heber can finish his studies at UCLA, we should have a much better picture in a couple of years.

Panelist: Well it's more than just soy. It's a lifestyle that the Japanese observe, and that confers protection, not just soy.

Dr. Barnes: I quite agree, and that was my point. You have to embrace the whole story and not just selected parts.

Dr. Davis: I would be remiss if I did not point out that unfortunately all over Asia today the rates of breast cancer are increasing as McDonald's is making inroads. Lifestyles are

changing, and they are consuming more animal fat and less phytoestrogens, and less fiber and less lignans.

Panelist: And lifestyle has changed as well – smoking, alcohol . . .

Dr. Barnes: Television has changed everything. We were talking yesterday amongst the soy group – in Japan you can now get tofu French fries. So they try and get around it that way. But the young have seen McDonald's. The young see television. They're convinced that this is the way to go. If we want to prevent cancer – and some of you I know feel about this very personally, because cancer's very close, and I've had it in my family too, so I've been there – the answer is prevention, and prevention starts with your children.

Dr. Davis: Thank you Dr. Barnes: Now I've asked Dr. Blask to please address the many questions he received. If you would like to reach Dr. Barnes, his e-mail address is [stephen.barnes@ccc.uab.edu](mailto:stephen.barnes@ccc.uab.edu).

Dr. Blask: First of all, I want to thank the Center for Mind-Body Medicine for inviting me. It was a pleasure to speak in front of this group. What I tried to do is group the questions and comments under a few themes, with more or less success.

The questions I got the most had to do with the dose of melatonin and whether you should take it if you are on tamoxifen, if you have ER- breast cancer, or as a preventive. I can't give you a good answer to any of those questions. I never recommend to anybody to take melatonin, because we just don't know enough about it in relationship to cancer. I showed you

some very encouraging laboratory work. There are a couple of clinical studies that hint at some promise, but this is not enough. This is really scratching the surface.

Although I'm convinced that melatonin has anticancer effects, particularly with respect to breast cancer, it's not going to live or die based on my opinion and my work. Others need to work in this area. With respect to the dose, the dose that was used in the clinical studies I showed you was 20 milligrams a day orally. I'm not recommending that you do that.

Dr. Davis: Twenty milligrams? That was in the rodents.

Dr. Blask: No. Twenty milligrams in the clinical studies.

Dr. Regelson: There has been one study of birth control which looked at toxicity over a period of time at a dose of 75 milligrams.

Dr. Blask: Right. I was going to get to that, Bill. The other important piece is that the timing of melatonin is very important. This is based on animal studies that may apply to human studies. The time of day that you take melatonin may be very critical. In the Lissoni studies that 20 milligrams of melatonin was taken around 8 o'clock in the evening before bedtime. We don't know about the long-term toxicity of melatonin. That's the argument that's frequently made against using melatonin. It's widely available in health food stores. It's sold as a nutritional supplement, but it is in fact a hormone. It also has potent antioxidant effects.

The study that Dr. Regelson just mentioned was a study in which melatonin was combined with a progestin as a new birth control formulation and administered to women over a

period of four or five years. They used as much as 75 milligrams of melatonin with no apparent long-term toxicity. This is probably the best long-term study that's out there. The unfortunate thing is there aren't other long-term studies with melatonin administration to humans. There are a lot of studies indicating that, in the short run, melatonin is virtually without toxicity. Its main toxic effect is that it makes you sleepy. That's what a lot of people use it for and there's a lot of research on melatonin in relationship to sleep.

I apologize if I sound like I'm hedging on some of this stuff, but I feel like I would be irresponsible if I didn't tell you exactly what I just told you. Melatonin as a preventative? It may be. There are some animal studies in breast cancer that suggest that melatonin could serve as a preventive agent. We're working on some of this ourselves in my own laboratory with resected breast cancer and liver cancer as well. Are any studies underway with using melatonin as a single agent, by itself clinically? No. There are no clinical trials with respect to melatonin in cancer in the United States at all.

Participant: There was one at the University of California involving melanoma.

Dr. Blask: Well, yes.

Dr. Davis: There's a report here of an adverse reaction. Was that excess sleepiness? Agitation? Dreams?

Dr. Blask: Some people have the opposite reaction to melatonin than the one that you hear about. They become hyposomnic. It makes them stay awake. I don't know what the

percentage of people who experience that are but it's a relatively small percentage. It brings to the fore the idea that everyone has a different response to anything. What you say about melatonin – well, I responded differently – you could take any drug that's available or any hormone that's available and make the same argument. So yes, it can actually cause problems for people in terms of sleep. If you were trying to use it for that and you had that reaction, I would not take it. Some people report nightmares, some people report vivid nice dreams, some people have reported some gastric upset, but this is a minority of cases. By the way, there's no LD 50 for melatonin. It's never been reached. Gram quantities have been fed to animals.

Dr. Davis: Lethal Dose 50 is the dose that it takes to kill half of the animals. We don't know the long-term effects of melatonin, either beneficial or harmful.

Dr. Blask: For those of you whose questions I was not able to address, I'd be glad to talk with you after the session.

Dr. Davis: Thank you very much. I want to thank all the panelists for their willingness to do that. This is an issue of great urgency to many people in this room, and we all appreciate that. Let me ask Dr. George to respond to one question and then I'll give Dr. Estabrook the opportunity to wrap it up.

Dr. George: The herbal formulation that I referred to in my talk is called Remifemin. It's used I think quite a lot in Germany. It's \$25 for roughly a month's supply and you're not

supposed to take it for more than six months. That's what I've been told. That's the one that contains black cohosh.

Dr. Estabrook: A lot of my patients use that too, and they respond to it very well. It's for hot flashes. There are three questions here. One is about an antimalignant antibody screen test, a blood test which supposedly discovers breast cancers (actually it's for all cancers) 18 months before they appear on either mammography or other types of scans. I've looked at these papers. This is unreliable so far. It would be very nice to have this test but so far it's unreliable. In other words, it's negative when people actually have cancer, and it's high when people don't have cancer. Yes, it's AMAS, done by the doctors Samuel and Elaine Bogoch.

There's a question about natural progesterones. Some women who are on hormone replacement therapy get depressed on progesterone. They feel bloated and they have some depressive symptoms, and natural progesterone is supposed to be better than the synthetic progesterones. A lot of pharmacies can draw that up. There's also a women's pharmacy I think in Wisconsin that can supply it. It does have some advantages over other synthetic progesterones.

Participant: (Comment about progesterones.)

Dr. Estabrook: So there is no natural progesterone? Because they claim to do this at this women's pharmacy.

Participant: (Comment about progesterones.)

Dr. Davis: We're not going to be able to resolve this right now. Why don't we let Dr. Estabrook complete her comments. Sir, if you want to identify yourself and if people want to talk with you afterwards – your name? You'll be available to talk with people about this?

Participant: There's no such thing as a natural progesterone.

Dr. Estabrook: It was the difference between medroxyprogesterone versus a progesterone that's closer to the progesterone that's made in women's bodies. I think there's a slight difference maybe in the synthetic compound.

Dr. Davis: There are reports of clinical differences in your experience with patients' response to these?

Dr. Estabrook: Yes, just like there are with estrogen replacement. Women have different reactions to different types of estrogen – Premarin versus other estrogens – Ogen and the other estrogens. The last question is a very good one. As a young mother and survivor of breast cancer, what can we tell our young daughters? What can we do for them to live well and not live in fear? This is a very big question and it involves I think a lot of issues.

The children of women who had breast cancer are terrified that they're going to get breast cancer themselves. I wanted to say something that Devra said this morning – only 5-10% of breast cancers are inherited. Most are mutations that go on from living – they're not inherited mutations. If you're worried about your children getting breast cancer if you've had breast

cancer, they probably will not develop breast cancer. They have to be looked at carefully at a certain age, and that age is usually 25 and older, not when they're very young. Some of the panelists addressed these things about what to do for young children. You should consider using soy, soy milk. Dr. Simone's healthier lifestyles exercise has been shown to decrease the risk of breast cancer. There are definitely healthy lifestyle things that we can do with our children.

Dr. Davis: Let me add one word from my talk from this morning, and those slides that I presented. Some of them are available on our web site, [wri.org](http://wri.org).

Many of the risk factors that have been identified for breast cancer are things that you cannot change, like your family history, or what you ate 30 years ago, or whether or not you had children before age 20. We are trying to focus attention on modifiable risk factors, what you can change, the things that society can change. Among the modifiable risk factors are aspects of the environment that can alter your body's own production of hormones. These do not explain all of breast cancer, but they are matters that we can all do something about – the private sector can do something about and the public can do something about.

Now I'd like to close, because this is Shabat for many of us, with a prayer that was told to me by a breast cancer veteran. Yesterday is the past. Tomorrow's the future. Today is a gift. That's why they call it the present. Shabat Shalom.