

CENTER FOR MIND-BODY MEDICINE
COMPREHENSIVE CANCER CARE 2000

CONCURRENT: Most Promising Herbal Therapies

PRESENTERS: Ralph Moss, PhD and Mark Blumenthal

MODERATOR: Joseph Lamb, MD

COMMENTATOR: Fredi Kronenberg, PhD

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P R O C E E D I N G S

DR. LAMB: I'm an internist in Alexandria, Virginia, right here, with an integrative medicine practice, and I have the honor of moderating this session on most promising herbal therapies. We have Mark Blumenthal and Ralph Moss as speakers, and Fredi Kronenberg as our commentator.

I'd like to ask you to keep all of your questions until the end. We will have some time at the end for questions. But given the time, I want to let our speakers get through with their talks.

Additionally, there are evaluation forms on all of your seats, I think for this morning's plenary session as well as for this session. It helps the Center greatly if you turn them in. It helps them meet their requirements for continuing medical education evaluations, and it also helps them know what you want to hear about and meet your needs.

Our first speaker is Mark Blumenthal, the founder and executive director of the American Botanical Council, an independent, nonprofit group dedicated to disseminating accurate, reliable, and responsible information on herbs and medicinal plants.

He is the editor/publisher of HerbalGram, an international peer-reviewed quarterly journal. He is also an adjunct associate professor of medicinal chemistry at the University of Texas at Austin. He is the founding board member of the American Herbal Products Association.

Join me in welcoming Mark Blumenthal.

(Applause)

MR. BLUMENTHAL: Good morning. How is everybody? Welcome to the last of this conference marathon. I am in the herbal domain, and basically am in the herbal education domain. And I am basically not a cancer researcher.

I try to collect information that scientifically documents historical use on medicinal plants throughout history and their contemporary use. And consequently, a lot of the scientific documentation of herbs, at least those that are popular in the marketplace today, most of that is lacking, except for some salient examples that Dr. Moss will cover later.

So I would like just to share with you that this presentation specifically is not about herbs for cancer. I apologize if you are a physician, a therapist, or a cancer patient that is looking for specific data from this presentation.

I don't have that data because, for one thing, it is not the domain of our organization's focus and activity. And secondly, a lot of really solid scientific information is sorely lacking. And I think Dr. Moss can pinpoint those areas in which there is some reasonable or some documented science, and that is what his presentation is about. I am going to just present the herbal marketplace for a sense of perspective and for understanding.

Basically, when we talk about herbs, we are talking about plants that have numerous chemical compounds in them naturally that the plants probably developed, from an evolutionary or biology perspective at least, for their own defense since plants don't have a central nervous system, that it cannot fight or flight, so they have to develop alternative systems of defense, like thorns and stickers if they are faced with a predator like an herbivorous animal or insect, or they develop chemical defenses, and we see them in the colors and in many of the different noncolored materials in plants, that these chemicals actually help defend the plant to maintain its space because it cannot move around like animals do.

Now with the kind introduction that Dr. Lamb gave me, he didn't tell you that I come from a long line of herbalists, and I'm showing my family.

(Laughter)

MR. BLUMENTHAL: Yeah. However, you are laughing because we had an agripharacist in the crowd a couple of weeks ago, and he said, you can't fool me; they didn't have color photography back then.

(Laughter)

MR. BLUMENTHAL: And I told him it was black and white, and they colorized it. But the name Blumenthal originally was derived from neanderthal. And, basically -- as you can see, my uncle, Wolfgang Blumenthal, the great herbalist, is applying a poultice. And, obviously, the take-home message is herbs have been used since the very beginning of time with people evolving on this planet with plants.

People have used plants for food, fiber, shelter, color, fiber, fragrance, medicine, and for ritualistic purposes. We have used plants. We could not live without flowering plants, that even the advent of flowering plants 65 million years ago gave rise to and concentrated food sources like seeds, fruits, berries, and nuts, that allowed small rodents to evolve, and then eventually other primates and then humans.

If you believe in the theory of evolution -- in Texas, we have to be careful about that down there.

(Laughter)

MR. BLUMENTHAL: Since I'm from a foreign country. Anyway, going back to the ancient cultures, even the ones that we base our culture basically on, the Greek or Roman culture, they used herbs for medicines.

They did not go to HMOs or hospitals, fortunately or unfortunately. They went to the temples to learn how to heal and use their herbal medicines in a religious context often. And here is (unintelligible), the famous Greek herbalist, who was kind of a sensitive New Age doctor for his time because no matter how much the Roman soldiers were marching off to rape and pillage the next village, he would stop and take time and smell the flowers. So he is kind of a very

important -- if he is a California doctor, of course, you would see stop and take time and smoke the flowers.

Now, of course, every physician out here obviously knows about the great father of medicine, Hippocrates, who used herbs, and he was basically an environmental physician who believed in clean air, clean water, exercise, diet, resting, et cetera, and about 300 herbs that he used in his medical practice known collectively today by scholars as the Hippocratic Corpus, the body of Hippocrates' work.

Colchicum a Mediterranean herb from the autumn crocus, which was a poisonous corm or bulb, the source of colchicine, our anti-inflammatory drug for gout, is one of the herbs used by Hippocrates 2,500 years ago approximately. And many people believe that Hippocrates is dead, and I suggest that actually he is alive today, and history is cyclical and not linear. The evidence is fairly compelling, and we have evidence today that Hippocrates is extremely well.

(Laughter)

MR. BLUMENTHAL: Yeah. You know, you can see the evidence is fairly clear here. You'll notice that there are some frightening similarities here. You know, people talk about evidence-based medicine. This is strong evidence of the cyclical evolution of history.

In the monastic herb gardens they kept the herbal tradition alive from the Greek or Roman times by planting herbal medicines. And some of these, of course, came from India and from China. But most of them were western herbs from Mediterranean and Arabic use, et cetera. Of course, the modern pharmaceutical industry evolved from herbal medicine, much of it, and also from the use of mineral drugs, which we won't go through.

Here is a party where they are celebrating the advent of the modern pharmaceutical industry with the discovery of the isolation, the very first plant-derived drug from a medicinal plant. Here is the party where they are celebrating the discovery of morphine from opium poppies, and you can see them having a great time.

By the way, I'm acknowledging the Parke-Davis Pharmaceutical Company, whose series, "Great Moments in Medicine and Pharmacy," with a commission in the 1950s gave rise to some of these nice plates that I'm showing here with permission from Parke-Davis.

Well, the whole concept of herbal medicine and pharmaceutical drugs are tied together. The word "drug" itself really means, "to dry," from an old Dutch word, to dry. They dried plants to make medicines. The whole concept behind drug, like drought, is from a Dutch word droge, or drugge in Old English. So that is the whole idea.

Well, what happened? Well, back in the 1800s, 1900s, we got so involved with isolating active principles from plants and then eventually isolating them, purifying them, concentrating them to increase the pharmacological activity and the reliability, also thereby increasing their toxicity potentially, that we basically threw the plants away.

Twenty-five percent of our modern drugs are derived from medicinal plants, directly or indirectly, and some of them, another 25 percent or more, are patterned or modeled chemically from plant-derived compounds. So we could say at least over 50 percent of our drugs, directly or indirectly, are derived from plants.

But the difference between herbal medicine and plant-derived drugs in pharmacy is that herbal medicine uses the whole plant or the whole plant part and/or extract of essential oil, et cetera, in a polypharmacy, a chemical cocktail, as Jim Duke likes to call it, where the leaves, the flowers, the root, the bark, the berry, et cetera contain numerous chemicals. Some of them are dilute drugs in a very dilute form, but numerous chemicals operating either synergistically, in some cases antagonistically.

Of course, we have a big distinction now between herbs and drugs.

(Laughter)

MR. BLUMENTHAL: So a lot of these modern drugs that come from plants or synthetic drugs have sometimes intolerable side effects or tolerable side effects, as the case may be because we have risk benefit assessments for these drugs, and they go through FDA, and we say, okay, we'll tolerate these adverse side effects and risks so long as we know there is a recognized benefit.

The problem with herbs often is in most cases, in this country anyway, they don't go through the benefit or the risk/benefit assessment, so every time the media reports an adverse reaction to an herb that is reported somewhere in one case study or something or a couple of people, it is shown against a blank screen of no recognized benefit by the government.

Of course, that magnifies out of proportion and exaggerates the potential risks of these herbs, when in general, they are gentler than most pharmaceutical drugs and relatively safe. That is documented, of course, by good pharmacal vigilance systems in Europe.

Of course, a lot of people have decided to take the alternative route, so to speak, because of their concerns of the high costs of pharmaceutical drugs. Everybody is becoming an herbalist these days. You can buy a \$35 starter kit from a multilevel marketing company, and you are an herbalist already, and you are in business.

The question is, you know, how do you know who knows what? How do you become more aware of what is going on. We have this one, too, just for equal time, you know.

(Laughter)

MR. BLUMENTHAL: Let me prove I'm not a doctor. You can trust me at the natural healing meeting. There is somewhat of an antimicrobial bias in some parts of the population that have converted over to the herbal medicine field, especially some of the older people, part of a core value.

Of course, the baby boomers are pushing the saw palmetto for prostate and the (unintelligible) for menopause as baby boomers turn 50 and get more aware of their vulnerability and need to enhance their health for optimal levels and lifestyle.

Well, Time magazine is talking about the herbal boom. It is incredible how many people are using herbs. Let's look and see how many people are using herbs here. There are all kinds of herbs going on. But interestingly, if you take the statistics of the best-selling herbs in the market, ginkgo, St. John's wort, ginseng, garlic, echinacea, goldenseal, saw palmetto, kava, and then on to the next slide in a minute.

You'll see that in the mass market, in food, drug, and mass market retail stores, the best selling herbs correlate almost always with the herbs that are the most researched, especially in Germany and other parts of western Europe, where different regulatory systems and different cultural attitudes about herbs and more scientific approach to the documentation of the safety and the clinically derived or clinically documented benefits through clinical studies takes place.

So we have a very different system over there in Europe, which we'll talk about in a moment, which gives rise to a lot of our best-selling herbs because the documentation of the quality of the herb and of the activity in clinical studies almost always, except with -- increasing exceptions now because of doing more clinical studies over here, but we're lagging way behind them by 10 or 20 years in some cases. It is all coming from western Europe.

But there is a correlation that good research on herbs help stimulate the sales when that information gets back to the public and the public finds out that there is good data.

Then, of course, we have other ones here. The only one up here that really doesn't have any research on it was goldenseal. There haven't been any clinical studies on goldenseal in 70 or 80 years. It is part of our folk medicine, and people think it is good for colds and flu. No real good, solid evidence for that. There may be some clinical cases for it. But the (unintelligible) in the goldenseal is not orally absorbed anyway through the gut. So, basically, there is no good data to justify goldenseal.

Well, how many people are taking herbs? Forty-nine percent, according to a Prevention magazine survey in 1999. Ninety-two or 91 million Americans -- adults; these are adults -- 49 percent have admitted to using herbs at least once in the previous year. Twenty-four percent use herbs on a regular basis. Now these are American adults now.

Then, for what reasons? Well, the obvious ones that you already know, ensure good health, improve energy, improve memory, relax, lose anxiety, prevention of treatment of serious illness, which is something that I think physicians and health care professionals should be concerned about.

People are using herbs to treat or prevent serious illness, with or without the advice of their primary health care giver, often without the knowledge of their primary health care giver.

This shows in the red how many people are using on a -- these herbs are the top ones regularly. The yellow shows how people use them as occasionally as needed.

So this is an interesting survey. It has been published in HerbalGram No. 48 in our market section. Of course, the preference for natural, organic products is part of one of the drivers that is pushing this whole thing. People believe that there are fewer side effects, more effective, less expensive, and then gentler and milder, which is almost the same way of saying fewer side effects.

There is a perception out there, based on what is true, that herbs are gentler acting than pharmaceutical drugs, et cetera, et cetera. Of course, these are different reasons why people use herbs instead of an over the counter (OTC) or prescription drug, and basically the same kind of attitudes prevail, the preference of a natural.

There is this philosophy that natural is better, and many people, because of the environmental movement, the natural foods movement, et cetera, prefer the natural whenever possible. Of course, expense, safety concerns are also drives.

How they use herbal remedies, and this is interesting, 48 percent use herbs instead of an over-the-counter drug, which is consistent with the use of herbs often because people use them for treating minor, self-limiting, self-diagnosable illnesses.

But look at this: 36 percent say that they use herbs instead of an Rx drug, and 31 percent will use herbs with an Rx drug, alarming the pharmacists and physicians for potential herbal/drug interactions here; and 31 percent with OTCs.

We have 30 percent of the population saying that they use herbs with an OTC or prescription drug. I think that is interesting, and it certainly suggests the possibility of more reports in the future of herb/drug interactions, which is clearly a frontier of herbal epidemiology because we don't have all of the data in on that, and it is interesting.

There is another one. How long will people use herbs without any kind of observable benefit? That is two to three months up here, all right, 23 percent; 28 percent about one month. So people are relatively willing to allow these products to be ingested without noticing any effects.

In some cases, like taking garlic for lowering cholesterol, how do you notice that effect anyway? That has to be tested in a medical sense. You can't test your own cholesterol really. Blood pressure, yes, but cholesterol, no.

Well, I found the secret to happiness, says the guru, but the FDA won't let me release it. There is a growing perception in the population that the Food and Drug Administration actually limits the transmission of information about what these natural products can do. That was a major driving factor why 2 millions letters, phone calls, and faxes were sent to Congress back in the early '90s to support the Dietary Supplement Health and Education Act. People were concerned about how to use this one.

A large pizza with double cheese, please, to go. Why else?

(Laughter)

MR. BLUMENTHAL: Now everybody here gets that, I think. Anybody doesn't? Because the FDA doesn't get it because back in 1990, FDA actually banned the use of prunes in over-the-counter stimulant laxatives because their expert panel could find no new clinical studies to show that prunes worked safely and effectively as a stimulant laxative. So they said not enough data, category three. It has to be banned.

So prunes were banned in 1990 from the stimulant laxatives, even though obviously the population knows what is going on because in the funnies I've have got about eight prune cartoons. This is the best.

But I just keep collecting them because the kids even laugh about it in the cartoons. Everybody knows what is going on.

So what is going on here? The fact is that the over-the-counter drug system even, which we wouldn't expect herbs to fall into, doesn't even allow for an intelligent way for people to understand how to use these products.

So I'm basically going to go through some of the regulatory concerns because in Europe they have already dealt with this issue very compellingly. They have found ways to evaluate herbal medicines for modern therapeutic use according to the commission.

They use the system where physicians, pharmacists, and other pharmacologists and experts have been hired by the German health authorities, called the Commission E, to evaluate herbs, over 300 herbs, sold in pharmacies according to all of the available published literature on each herb, including but not necessarily requiring clinical studies, so long as the information shows that the herb is safe, and according to a doctrine of reasonable certainty, shows that the herb will probably produce some intended benefit.

They published their findings in the form of monographs, which are then published as package inserts so consumers, pharmacists, and physicians can actually open up their herbal product and find proper directions for use with government-approved use or uses, plural, so they know how to use these products responsibly and intelligently, often based on clinical studies published in Germany where they lead the world in the development of modern, western-controlled clinical studies because they have a regulatory system that already approves the herb, and the pharmaceutical companies will get a -- the natural pharmaceutical companies actually invest in clinical studies in order to use that for marketing purposes.

We have published that in the form of Commission E monographs in a book, and then we have taken many of the monographs and added more data, new clinical studies, and lots more references and color studies in this new book, called the Expanded Commission E Monograph. The first book came out in '98. This one just came out in 2000.

Quickly, I am going to run through some of the popular herbs to show which were the commission-approved, and then what some of the best-selling, best-prescribed brands are in Europe.

Now I am going to talk about some brands. I'm not here to recommend them. I'm not here to promote the brands. I don't work for an herb company; I'm nonprofit. But the brands are being acknowledged, and this is in your handout under B, somewhere in B, so you don't need to really write this down.

But I'm acknowledging, because one of the biggest questions I get from people all the time is, Mark, which brands do you recommend because we know black cohosh is good for menopause; we know about ginkgo for peripheral arterial occlusion, you know, for cognitive disorders, but which brand? We don't trust these products. Which ones do you trust?

I say, well, look at the clinical literature. Let's look at the clinical studies and see which proprietary products in Germany were used in those studies, and then which of these products were used. The leading brand in Germany for -- on clinical studies for black cohosh is called Remifemin®, imported under the same name. Of course, there may be other black cohosh products that are equally as effective or maybe even more effective.

The fact of the matter is they have not been documented as such in published clinical studies, although there are some clinical studies coming out in this country.

Camomile for upset stomach, by the way, when Peter Rabbit at all of those carrots in Farmer MacGregor's carrot patch and came home with an upset tummy, Mrs. Rabbit gave him chamomile tea, right? So this is what you call documentation in the literature that we have, really good.

(Laughter)

MR. BLUMENTHAL: Anyway, Chase Tree or Vitex agnus-castus used for PMS type complaints since Greco-Roman times. All of the research done by Commission E to review the material, almost all of the 34 clinical studies, 31 of those studies were all based on one product called Agnolyt® imported by Nature's Way as Femaprin®. Presumably other types of vitex products would work and be useful. But this is the one that is confirmed and documented in their clinical literature.

I just want to run through these quickly because we don't have a lot of time. Echinacea -- there are many different echinacea products in Europe from several different echinacea species, above and below ground parts, and three different species. So the chemistry of these various echinacea preparations is quite variable, which makes it very difficult to analyze all of the clinical studies because you don't have the same ingredient in each one. But echinacea has been shown to actually shorten the duration and severity of upper respiratory tract infection in colds and flu, but not prevent.

The clinical studies for prevention, three of them have been relatively negative on confirming statistically that it helps prevent, although the Commission E contraindicates echinacea for progressive systemic diseases of the immune system.

Even though there is no data to suggest that echinacea could compromise the immune system, the question for tuberculosis and collagenosis and MS, et cetera. This was based on theoretical concerns, no clinical documentation, because they were very concerned about the safety.

Very quickly, a bunch of clinical studies on echinacea -- I'll just run through these -- different kinds of preparations, impossible to meta-analyze, et cetera.

Here is one that everybody should know about, Hawthorne, because the commission has shown, based on eight clinical studies on two preparations, that it increases cardiac output, according to stage two of the New York Heart Association's functional classification for congestive heart failure. Very safe, no herb/drug interactions known that are negative, no adverse side effect, extremely safe material, hawthorne.

People should not be self-medicating for Hawthorne, however. But all of the Hawthorne data is based on two commercial preparations, four clinical studies apiece.

Horse Chestnut, seed extract -- I have got my 88 year old father on this material.

There have been 13 clinical studies meta-analyzed in the Archives of Dermatology published by AMA, for varicose veins and other swelling, edema in the lower legs, et cetera. The Horse Chestnut is extremely well tolerated, fairly safe, good clinical data on it.

This is an overview of the clinical studies, all 13 of them, showing that it reduces in a significant way leg volume, leg circumference, ankle circumference, et cetera, for people that have problems, especially with varicose veins and related conditions.

Garlic -- I mean, this is something that people are using, sometimes as a potential cancer prevention. There is a current study documenting the possibility that food taking garlic, onion, shallot, leeks, et cetera can reduce stomach cancer, published in '89 in the Journal of the National Cancer Institute.

Obviously, most people take garlic in the west for reduction of cholesterol. The last three studies published in this area do not support that but there is a body of studies from before that are very compelling. A four year study published in June '99 in the Journal Atherosclerosis showed that 900 milligrams of the German garlic preparation actually reduced significantly plaque buildup in atherosclerotic patients.

So that is very interesting. Of course, with all of this garlic information that we have, the Commission E did not find any documentation of the anti-vampiral activity of garlic.

So we know that these guys are being very rational because there is a very popular use of that in Europe. You can see that all of this, most of the research in Europe is based on a product called Kwai®, although the Japanese product is a very different preparation chemically and is used in some cases in some of the cancer studies that have been done on garlic. Again, anti-vampiral activity is noted here, but not approved by the government, et cetera. A lot of clinical studies on garlic, a lot of pharmacology on garlic. It is one of the most well- researched herbs in the world.

Then real quickly, we see ginkgo, over 120 clinical studies on ginkgo. It probably has more clinical studies, aside from ginseng, than any other in the world, extremely well tolerated for senile dementia, short-term memory loss, intermittent claudication, being able to walk further, and even tinnitus or ringing in the ear.

All of this data comes from two proprietary products. Almost all of the research comes from two products for ginkgo, and these are the overview of the ginkgo. Extremely well tolerated, and that's why it is the number one selling herb in the marketplace right now.

All of the research based on a product called Tebonin® in Germany, marketed under three different brands, which are in your handout here. And it is interesting that the breaking down of these clinical studies -- everybody is out there making claims for all kinds of ginkgo products, many of which have not been confirmed in clinical studies. But the clinical studies are very strong in this area here.

Kava for anxiety -- the leading clinical studies, eight of them on one product in Germany, not available in the United States.

Milk Thistle over 30 clinical studies or different open and controlled studies, almost all of them on one product, Legalon®, sold as Thisylin® in the United States for hepato protection, used for cirrhosis of the liver and hepatitis-A, some for hepatitis-C, not B.

Saw palmetto for prostate, for BPH, about three or four different leading brands in Europe and Italy, France and Germany, clinical studies. One Amway product just studied last summer was a positive clinical study. So we do have an American product.

And St. John's wort, almost all of the German research comes from one product, the product called Jarsin® (Li 160).

So the point is here that much of the research, and there is lots of it, deals with noncancer kind of conditions on these major herbs and are also based on leading products in Europe that are leaders in the marketplace, some of which may or may not be available in this country. Those that are are documented.

Then I have this chart here. This is the chart that is in your handout so I won't even go through it here, but showing all of the different brands of the herbs in Europe that are -- Germany especially -- that are the most prescribed and the most researched clinically, and in U.S. brand counterparts for your information so you know how to correlate them to your best benefit.

Before I close, I wanted to do just two things. One is about quality control. I know everybody is concerned about that. There is concerns about the variability of quality of product over here in the United States.

What we are doing at the American Botanical Council is testing over 500 -- we have tested over 500 commercial ginseng products in two university laboratories. We're publishing the results of this in HerbalGram No. 50 in November of this year. So it is the biggest test of any single herbal or natural product area ever conducted in history. It is over a million dollar study and other organizations are testing herbal products and dietary supplements.

This is a new organization here. Consumer Lab is posting studies, results of those studies, on the Web site. You may want to check consumerlab.com to see because about every month they put a new test on their Web site, consumerlab.com.

Finally, I'd like to invite you to come down to the rain forest with Jim Duke and myself to go visit some of the areas where plants that create pharmaceutical drugs grow. We're going in two weeks to South Africa for two weeks for CME and CE accredited workshops for physicians and pharmacists and nurses.

We also go to the Amazon every October and November. We're going down November 3rd, I think, this year, the Amazon, for a week to study some of the drugs that are derived from medicinal plants and how people use those plants.

This is our hotel we stayed -- the Two Seasons Hotel, rainy and dry. This is curare darts with a blow gun. They blow them at the monkeys and the sloths. Of course, they are neurotoxins. They get muscle relaxants. They fall out of the trees. This is where the drug (unintelligible) comes from.

Jim and I are on the board of directors of an organization called ACEER, the Amazon Center for Environmental Education and Research, where they have constructed a 400 yard long rainforest canopy walkway that is suspended on 80 trees, 12 stories in the air, where people can go and really be up in the canopy and see a whole different biota, different animals and plants than you see down on the forest floor. It is really amazing.

I know a lot of you have these secret dreams of wanting to go to the rainforest or some jungle and find an herb that will cure cancer, arthritis, or diabetes or whatever. I have always had that kind of dream myself, but I'm just an herbal cowboy from Austin, Texas, so I don't really have

the -- I was not trained in the field. But these are some of the -- this was done by Antonio Montero Pisco he's a shaman in the rainforest.

And, of course, I worked with this -- this is my shaman here, Jim Duke from the USDA, who is one of the world's leading experts on medicinal plants, a big fellow, about 300 pounds. You really want to be careful when you work with him because there is a major rule you have to learn when you work with a guy like Jim Duke, and that's pretty obvious.

(Laughter)

MR. BLUMENTHAL: In closing, I want to share that many people are talking about herbal medicines and using medicinal plants in modern therapy and/or for clinical -- for stuff -- self medication. The problem is getting sustainable supplies. And people are talking about rainforest plants and how sexy that is, and people decrying the destruction of the rainforest.

But at the same time, possibly a bigger problem and a bigger concern is the destruction of the cultures of the rainforest and the losses of people in these areas because when one of these old people dies, it is like a whole library burns down.

When they go, their knowledge and thousands of generations of their people's accumulated wisdom goes with them. And that is one of those challenges that we have at the American Botanical Council.

We're a nonprofit organization of 35 people in Austin, Texas. We're trying to develop information on traditional uses of herbs as well as modern documentation of the science of them. We're putting out C&E material on herbal medicines for pharmacists, physicians, nurses, and dieticians, and all kinds of other material for herbal stuff.

We have a magazine that is peer reviewed and doesn't take any advertising from the industry so we can maintain an independent editorial position, all kinds of public and professional, layperson information on herbs. And we have an extensive Web site that you can check out that has more information on herbs, 750 links to other herbal organizations and other sources of information, et cetera. And we do the best we can to provide you up-to-date information that is scientifically defined.

The herbal market is something that is growing very quickly. There is lots of confusion out there, and we're trying to bring some sense of relevance and understanding to that.

I thank you for your time and attention, and I appreciate being here today. Thank you.

(Applause)

DR. LAMB: Thank you very much. Our next speaker is Dr. Ralph Moss, an internationally known medical writer who has written 11 books and 3 film documentaries, mostly on the question of cancer research and treatment.

The former assistant director of public affairs at Memorial Sloan-Kettering Cancer Center in New York, Dr. Moss has for more than 25 years independently evaluated the claims of various cancer treatments, conventional and nonconventional.

He currently directs the Moss Report, which are detailed, written reports on 175 varieties of cancer diagnoses. He also directs cancerdecisions.com and ralphmoss.com Web resources for cancer patients.

Join me in welcoming Dr. Moss.

(Applause)

DR. MOSS: Well, thank you, Dr. Lamb, and it is a pleasure to be here again.

Dr. Blumenthal is always a very difficult act to follow, and I'm going to sort of have to bring you back down to earth here, not that you are not on earth, Mark, but you just bring us up into the ethereal regions.

And by the way, let me put in an unsolicited plug for HerbalGram. It is really a magnificent magazine. We're happy to in our moral support to feature, a big color ad for HerbalGram on the back cover because we feel that it is something that every cancer patient should know about. And it is not only the information we get on herbs, but also the perspective, which has been so important for me in developing my own understanding about herbs.

I'm a medical writer, researcher, and I'm not an herbalist. My work focuses on finding effective cancer therapies for people. And I must admit from the start a certain amount of trepidation in giving this lecture because I understand that most people in the audience are dealing with cancer personally or else professionally.

So of course what we all want to know is the bottom line, what are the effective herbs for cancer, and how much should we take and so forth. And, you know, I am going to be a little evasive on that topic, or perhaps seem a little bit disappointing to some of you because I can't give a clear-cut answer to that question.

The best people in the field, such as Mark Blumenthal or Jim Duke, have all -- or John Boik who is also active, have all reached a similar conclusion, that for reasons that I will try to explain to you, we don't have a solid body of information that could lead us to firm conclusions at this time about what are effective herbal cancer therapies.

In fact, I was struck by one of Mark's comments, or his slides that showed that the best selling herbs generally correlate with the best documented herbs. In the cancer field, I would suggest this is exactly the opposite.

I think that the best selling items are precisely those that we know the least about. And this creates a very strange situation that I will get into because I think I know some of the reasons that that occurred.

Well, when we talk about the use of herbs in cancer, we are talking about a number of different things. One of them is the use of herbs as a primary treatment, in other words, as a cytotoxic or a cytostatic agent, something that could be used actually for cancer or to stop cancer.

I think all of us somewhere in the back of our neanderthal brains believe that there has to be some herb or combination of herbs out there that could stop this thing. So a lot of the activity and interest have been focused on these anticancer herbal formulas.

Other uses of herbs in cancer, though, could include modulated immune function, a pretty well-known and better documented area, counteracting the side effects of conventional treatment, which where even places like Memorial Sloan- Kettering are now getting into advising the use of herbs for functions like that, and for primary and secondary prevention, such as the garlic studies that Mark mentioned; and then the psychological benefit, either through the use of herbs that are psychotropic or else just simply the placebo effect that, you know, the patient feels that they do something, something probably harmless, and that could be a benefit to them.

But why is it that the recent herbs against cancer is such a controversial topic? You know, it is an historical question really. You have to understand that even in the 19th century, herbs started to be used by alternative doctors, what were called eclectic doctors, at that time.

The regular doctors, or the AMA, American Medical Association, more or less found itself in opposition to the claims being made by those alternative docs.

This sort of points ahead in the 1920s through the 1960s, and really on to the present day, around a herbal practitioner named Harry Hoxey. Harry Hoxey was from a small town in Illinois and was a coal miner. According to the story, his grandfather had seen a horse cure itself of cancer by eating certain herbs of the field. And he then developed this as a treatment.

There was an external -- a group of external remedies, and there was an internal treatment. And Hoxey was arrested more times for practicing medicine without a license than any other individual in history.

He traveled, he was chased really, from state to state, finally wound up in Texas, was confronted by Morris Fishbein, the editor of the Journal of the American Medical Association and in a very famous court case in the 1940s, he actually defeated Fishbein, who was convicted of slandering him in the pages of the AMA.

But the AMA had the last laugh, or the next to the last laugh, because they basically worked with the FDA, Food and Drug Administration, to have Hoxey shut down.

And this chain of clinics that Hoxey had built throughout the '40s and '50s was basically knocked out and put out of business by the FDA.

His nurse, Mildred Nelson, some years later went to Tijuana, Mexico and set up to buy a medical clinic, which was the first of the alternative clinics in Tijuana, Mexico. It is situated high up on a hilltop in Tijuana. And a lot of American patients continued, and still continue, to go there to get this combination of herbal therapy and also some of these external salves. And they do a few other things there as well. It is similar in some respects to some of the other Mexican clinics you may have heard about.

This is the current Hoxey internal formula: Licorice, red clover, cascara, burdock, barberry, poke and stallingia, and there are some other variants on this.

Hoxey, like most of these herbal cancer cures, if you want to call them that, was quite secretive about his formula, and it was only revealed by court order. And we're not really sure that he told the truth when he did reveal it.

But this is, I think, the truthful formula. And, you know, we would like this to work. I mean, Jim Duke has provided me with some of his information on red clover.

You may have seen my presentation two years ago where I showed that slide. And there are literally hundreds of compounds in red clover alone, many of which should have activity against cancer, and on many, many different ways. It is not just one mode of activity. It comes at the cancer from many directions.

Burdock just appeared over and over again as an anticancer agent. There are some Japanese data using what they call gobo, which is first -- second year burdock root. Burdock, by the way, is nothing but those annoying plants that grow up in your yard and attach burs to your dog's coat or to your coat.

Poke -- again, pokeweed is a very well known agent in science. It is used to force the differentiation or growth of cells. And it is kind of -- if it hadn't been, you know, invented by Hoxey's horse, you would think somebody would think of using it as a cancer therapy.

So, you know, I must say that until about the early 1990s, I was quite sure that the Hoxey formula was one of these depressed herbal cures for cancer and used to think about it in such terms. And then when I started to write Cancer Therapy, my book that came out in 1992, and then especially when I worked on Herbs Against Cancer, which is a more expanded discussion about all of these topics, I started to have my doubts because I realized that there really was no data to support the use of this.

When you try to chase down anecdotes, as with any cancer treatment, it is very difficult to pinpoint if there is any effect, pinpoint the effect of that particular treatment.

Mary Ann Richardson, who is at this meeting, now working for the National Center for Complementary and Alternative Medicine, but up until recently at the University of Texas, got the furthest of anybody in evaluating the Hoxey treatment.

Essentially, she looked at all of the patients who were treated in one three month period at the Hoxey clinic, and then she followed them for five years. And the results were rather disappointing, I would say.

There were some long-term survivors and there were some possible remissions, but there weren't very large in number. And some of those long-term survivors were early stage cancers, so you wouldn't normally include them in any kind of definitive studies.

So I don't think that the Texas study, while it didn't rule out the possibility of some benefit to the Hoxey treatment, it also certainly didn't point to any strong effect happening at this time. And my own visit to the Hoxey clinic, which took place shortly before Mildred Nelson died two years ago, was also, personally to me, very disappointing because again, they couldn't show me anything - any data that would be satisfying to me.

In fact, I found it to be extremely secretive. And having myself for the past -- you know, gone past the secretive stage and past the conspiratorial stage and now talking and wanting to cooperate with the government in doing evaluations.

You know, I found that they were sort of mired back in that old model that we had from back in the laetrile days of, you know, them versus us, and we're not really happy with the new development.

But this Hoxey controversy colored and in a way corrupted the whole atmosphere for the evaluation of alternative herbal treatments for cancer. They also used an escharotic or a burning paste type of formula. And you probably, if you surf the Internet, you know, you have probably come across this, and you wonder about this. This is a typical black salve formula that you find on the Net. And some of these formulas are probably pretty good.

One of the classic ingredients in the Hoxey external salve is arsenic trioxide. But arsenic trioxide is in fact, you could say, the oldest form of chemotherapy in the world for cancer. It is in the Edwin Smith papyrus dating from 3,000 B.C.

The Egyptians knew about it, knew about its effectiveness in cancer, used it as an external agent. It is still used in many of the -- you know, the escharotic salves and paste. And in fact, recently, as recent as two years ago, Memorial Sloan-Kettering issued a press release announcing a new discovery for cancer, in that case for leukemia. And, of course, the new discovery was arsenic, arsenic trioxide. So it is back now as a formula.

It is not exactly herbal, but one can't be too dogmatic in this area because botanical and chemical treatments often are mixed together, as even in the Hoxey formula they used a form of potassium iodide in that formula.

Again, many of these things you would like to have them be effective against cancer. Chaparral, there is some very intriguing anecdotal stories and even a little bit of laboratory work on chaparral. I think it was very poorly handled by the National Cancer Institute back in the '50s and '60s.

In other words, I thought there were some more reasons for them to go forward with it. But again, one would be hard pressed to come up with any solid scientific evidence to support the use of the black salve. And in fact, I am very leary of them because I feel that in a way they would hark back to an earlier epoch in cancer, when surgery was out of the reach for a lot of poor people, and people had to apply these burning pastes to their faces or other parts of their body. This could be dangerous, and it is really not necessary in a lot of cases.

On the other hand, why shouldn't it be another tool that doctors use? It would take some skillful training in order to make that happen.

While the Hoxey controversy was raging in the United States, in Canada there was a very similar controversy taking place, another nonmedical -- in this case, she was a nurse practitioner named Rene Caise. Esiac is Caise spelled backwards. And it also was a secret formula, so we're not exactly sure that we have the actual components of this.

But Rene Caise also created a great controversy and got a little bit further than Hoxey did because she had more doctors on her side. And it almost was legalized in Ontario in Canada in the 1930s, but in the end was more or less stamped out, I guess you would say, or wasn't stamped out, but it was never made a legal remedy.

Caise died in her 90s back in 1978, '77 or '78, and she was a highly secretive person as well. She may or may not have given this formula to a number of people. This is what we think was in the formula.

Now this is supposedly a Ojibwa Indian, a traditional Ojibwa Indian remedy for cancer. It is impossible. Turkey rhubarb is an imported plant, an imported herb, that comes -- it is called

Turkey rhubarb; it really comes from China. It is a form of rhubarb that doesn't grow in Canada and probably couldn't be cultivated at the latitudes that she lived anyway. So that clearly was added in. Whatever else was authentically Indian in this, that was clearly added in.

Burdock -- interesting, isn't it, that it shows up again in two secret formulas at, you know, two ends of the continent. Slippery elm is probably added in for its traditional use for people, let's say, suffering with lung cancer as an emulsant, basically, to aid in expectoration. So I believe -- not much scientific backing, but I believe that the sheep sorrel is really the ingredient that was originally pointed out to her.

I know there was one herb that an Indian shaman pointed out to her. He took his walking stick and lifted up a plant as they were out for a walk one day and said, this is the cure for cancer. And the reason I believe this is if you go to Jonathan Hartwell's epic work, *Plants Used Against Cancer*.

Basically Jonathan Hartwell was a great researcher at the National Cancer Institute, and compiled all of the information about all of the letters that had been sent to the NCI about different cancer treatments, you'll see that in the 1920s, there was a rash of reports of sheep sorrel being used as a cancer treatment all throughout North America and say if anybody, were going to try to do a test. It would be very interesting to test the sheep sorrel.

There has been a lot of Esiac sold, and extremely little documentation. I mean, I would say virtually none, and not a very cooperative attitude either on the part of the main manufacturer of Esiac tea. They are cooperative in selling it, of course, but they are not terribly cooperative in doing the research.

Well, Mark told us about 25 percent of all drugs are still derived from herbs, and this is particularly true in the case of cancer. In particular, of course, you know about Taxol from a Pacific yew, camptothecin from the Chinese happy tree. But look at this one. It is etoposide and its related compound, teniposide.

These are semisynthetics which are ultimately derived from the May apple. It is a cute little plant. I grow it in my garden in Maine. It has actually an edible fruit, as long as you don't eat too much of it, the apple in May apple. But from that plant we get etoposide and teniposide, thanks to Jonathan Hartwell's work at the National Cancer Institute.

What I find particularly fascinating about this is that the eclectic physicians, like Scudder and Jones, Eli Jones, in the 19th century and early 20th century, included May apple in their anticancer formula. Of course, the AMA, which had nothing to use against cancer except surgery back in those days, derided this as the height of quackery, and yet they were using May apples.

So my conclusion is that in a sense, chemotherapy was discovered by the alternative community. These are cytotoxic agents. And it was being included in a formula that probably mitigated the side effects of the toxic effects of May apple, which was always known to be somewhat -- you know, you wouldn't want to eat a whole barrel of May apples. It was known from the 18th century that this could give you a tummy ache or something.

But it is an interesting sort of twist, isn't it, that we do have some idea that within alternative medicine, within these herbal formulas, there have been at times very effective agents, which in

a sense the alternative community beat the orthodox community to the punch on this one. And now, of course, it is being rediscovered and re-utilized.

Everybody wants to know, so what works? I can just give you some of my feeling about this. I think the best research of the cancer herbals is mistletoe. A fascinating story; Rudolf Steiner, the founder of anthroposophy, brought this into medicine, into cancer medicine, although it had been used in medicine for 2,000 years. It is an old Druid remedy.

You could read about this in my book and in many other sources. And I think there are some clinical trials by my friend Joseph Boyt (?) at the University of Cologne showing real benefit for cancer patients. It is not a cure, but it is something that works well with chemo and also improved quality of life.

Curoderm, from the particular species of solanum, related to the eggplant, has activity against skin cancers. It is quite remarkably similar to what Lane Labs is now selling as the cancer answer -- skin and -- what is it called, skin answer? Skin answer. Powdarco (?) and cat's claw -- powdarco, otherwise known as pahibo (?), is an old South American cancer remedy. It contains lapatrole (?). Lapatrole has been tested by NCI.

There is a small anticancer activity to it. It wasn't strong enough to convince them to go forward with any clinical trials, although some very reputedly good people have called for a reconsideration of this, and including Ellen Shlabowsky (?) at UCLA.

And cat's claw, there is a lot of data on its strong immuno modulation properties. The problem with the data, as with many of these things, is that it mainly emanates from one group, or people under their influence. So, you know, you would like to see confirmation of this by other places, other scientists.

Now a very interesting item is anvirzel, which is derived from the oleander. This is toxic. Again, don't go out and start chewing oleander leaves. It contains cardioglycosides similar to digitalis, which by the way, also probably has some profound anticancer activity.

Digitalis, we hope, will soon be subjected to a test in Trondheim, Norway, under Johann Hauks (?) there. And Ukraine, which is a mixture of a very old, you know, traditional anticancer herbal agent called Chelidonium majus or the greater celandine.

The cute little plant has a thick yellow sap, and it is used in traditional medicine, that's to say herbal folk medicine, according to the doctrine of signatures, that give that yellow sap as a way of, you know, of influencing the bile, the liver and the gall bladder.

In fact, we have doctors even at this meeting that I know who still use that, who give injections of Chelidonium majus in order to support the liver because they think it really works. Here, the sap of the Chelidonium majus is a burning paste. You don't want to get it on your hands. And so we think that throughout Eastern Europe in particular, it has been used traditionally for hundreds of years as a way of burning off growths.

So most cancer plants, by the way, just as a side note, traditional cancer plants relate to skin cancers or skin growths because, of course, before the discovery of histology in the 19th century, you know, people didn't have a clear idea of what cancer was. So the kind of cancer they were most familiar with was the external kind.

So I said it is a mixture. The other part of ukraine than Chelidonium is a drug, thiotepa, which was one of the first three alkylating agents in the world. It was the German contribution, if you will, to the first beginnings of chemotherapy.

So the real question in my mind is how much is the effect because there is an effect, an anticancer effect of ukraine. But how much of that effect is due to the herb? How much of it is due to the chemotherapy, and is there really a synergy? Is something new happening, or is this just very expensive thiotepa?

Then there are the ones that I think very little of, and maybe I'll offend some people in the audience. The Hilda Clark theories and the herbs connected to them, I think this is quite bogus.

Hilda Clark has a book called The Cure for All Cancers. It is selling wildly in a number of countries, especially Canada and Germany. And she basically claims that all cancer is caused by a particular parasite called Fasciolopsis buskii. And this parasite is actually extremely rare in North America, a little bit more common in third world countries where, incidentally, they have much less cancer. And I can go on all day about the flaws in Hilda Clark's argument.

But she is basically advocating the use of three herbs, including wormwood, as a treatment. Well, this might be beneficial to people if they are harboring parasites. I don't know what the effect of parasite infestation or infection is on people with cancer. It couldn't be good. I doubt if it is good. So to that extent, you know, it is probably okay for people to take these under medical supervision because there are some potential side effects to taking these things, too.

Avalos (?) I'll pass over. It was another one of the sort of exaggerated claim situations. Noni juice, it is like, you know, every second person in America is now a Noni salesman and, you know, America is one vast pyramid scheme of Noni juice practitioners. It is an amazing situation because there is extremely little data to support the effectiveness of Noni. Noni has some folk usage in the South Seas, maybe, maybe some slight connection with cancer, something like two or three animal experiments at the University of Hawaii involving a very small number of animals, where they did seem to show some anticancer activity, which you could say about, you know, 50 or 100 or 200 different herbs, by the way.

But on the basis of that, they formed this multibillion dollar business. And when I challenged them one time on the data, well, they said a number of humorous things.

One of them was to cite to me how much money they are making, really. And the other one was they said to me, well, we are not interested in having a story done about us at this time. I said, I don't understand. I mean, you know, I am not asking you for anything. I'm just going to write the story whether you are interested or not. And they said, you mean you don't want any money to write it? I said, of course not. They said, well, that is a first. It is the first time we have ever been contacted by a writer in this field who didn't want to be paid for writing a laudatory piece about us.

So this is very strange, you know. I mean, there is a lot of hucksterism and stuff in this field. It goes back to the history that I told you about. And it has been very hard to penetrate to the core of this issue and trying to see what is useful and what is not.

I don't want to leave on a negative note. I do believe in my heart that there is something of real value here. But I do kind of play up the negative aspects, the lack of data, as a challenge to the

world and especially to the people who make the claims because I feel that, you know, they have to comply with the same rules of evidence that everybody else does.

So while I remain hopeful there will be something of benefit, I also think, you know, we have to sort of hold their feet to the fire to make them come up with the evidence to support the use of these herbs.

Well, I thank you very much.

(Applause)

DR. LAMB: We have now heard from our two speakers, and we will now be hearing from our commentator.

Dr. Fredi Kronenberg is an associate professor of clinical physiology and is director of the Rosenthal Center for Complementary and Alternative Medicine at the College of Physicians and Surgeons at Columbia University. Dr. Kroneneberg received her BS from Cornell University in neurobiology and behavior and her doctorate from Stanford University in physiology and behavior.

Her current research involves alternative treatments for menopausal problems, and she is conducting a multiethnic, multilingual national survey on alternative medicine used by women.

Dr. Kroneneberg is the director and principal investigator of the Center for Complementary and Alternative Medicine Research on Aging in Women's Health. In 1997, she was among those who received the American Health for Women award, Ten Heroes in Women's Health.

Please join me in welcoming Dr. Kroneneberg.

DR. KRONENEGERG: Thank you very much. What I wanted to do is make some comments that extend and take some of the comments that Mark and Ralph made a little bit further and provide additional information and things for you to think about in order to place some of this information in context and think about where we go from here.

Both Ralph and Mark mentioned and kept alluding to the fact that there are very few studies or little data in many of these areas. And this is obviously a problem, and it is a frustration for all of us who want to know answers right now.

I think there are a number of things to think about in the area of clinical trials. First of all, obviously, there has not been a lot of money, particularly in this country, up until recently in this area.

Now, of course, there is increasing, almost an exponential rise in funding. The Office of Internal Medicine started 6, 7 years ago with a \$2 million budget, and now we are up to a \$70 million budget. And more and more we have private foundations and groups funding this work. But there has been relatively little money, especially compared to the money that pharmaceutical companies put into clinical research in this area.

But there are additional problems that arise in this arena that are not necessarily the same problems that you have in drug research. And one is when you are doing animal controlled trials, in this area a lot of times people don't really want to be randomized.

They know that they either want the alternative approach or they don't. So this is a problem that we have in this kind of research trying to get people to be willing to be randomized. (Unintelligible) had this problem in the study that they were doing. People either knew they wanted what he did or they knew that they didn't.

So these are some of the issues that we'll confront in terms of thinking about other approaches, other ways of getting scientific data that may involve some creative thinking in terms of how we do this and how we get people to be willing to be involved in some of this research.

Now the Commission E that Mark spoke about has a lot of information on studies that have been evaluated in Germany based on research, often data provided confidentially by companies, so that it wasn't indicated how some of these results and conclusions were obtained. Sometimes the information is there, and you don't exactly know why.

For example, Mark talked about black cohosh. Black cohosh in the Commission E says that you can take black cohosh for six months. It doesn't say that after six months it is known to be harmful or the reasons behind it.

It turns out the reason why the six months are used is that there have been no trials that have been longer than six months to demonstrate whether this is safe. So we don't know that it is unsafe, but we also don't know that it is safe, and therefore the six months caution there.

A number of studies are underway. Black cohosh in particular is a topic that has been studied for 50 years in Germany. There has been many legal studies. The studies, of course, have gotten better over time and over those 50 years, there is really only four good randomized controlled trials. But the weight of the evidence, in terms of menopausal symptoms, is beneficial.

The questions that are still remaining in people's minds are is this herbal alternative to hormone therapy safe for women with breast cancer, women at risk for cancer.

We don't know the answers to that yet. The company who manufactures the primary product sold in Germany in the United States would like us to think this is safe, but really the data aren't there. The data aren't there to show that there is endometrial protection by taking these alternative hormone therapies.

Mark mentioned about people wanting natural hormones, people thinking that natural is better. In the cases of these herbal hormonal alternatives, it is not clear whether it is better for people who are told that they shouldn't be taking estrogen because these maybe estrogenic, but they may be operating by totally different mechanisms, so that they may have the benefit of being protective against some of the menopausal symptoms, and yet they may not be causing cancer. But we don't know this. The data are really preliminary in terms of the cancer and anticancer effects.

One of the things that was discussed throughout this conference, it talked about particularly the difference between herbs and whole herb substances and the chemicals in drugs, which are, you know, similar molecular entities that the NIH and the FDA are used to dealing with.

When you deal with herbs, either single herbs or mixed herbs, of course, you have hundreds of compounds there and how do we sort out what is important?

The issue of quality control that was mentioned. I don't think anybody would think otherwise than that we should have product that are what they say they are on the label. But the issue of standardization, I think, has created a lot of confusion in the mind of the public, in particular where products are stated; some products on the label are stated to be standardized to a particular compound.

In many cases, and I would say most cases right now, we don't know which compound or groups of compounds together are responsible for the activity of any particular herbal remedy. So when something says that St. John's wort is standardized to hypericin, that is a market compound that tells you that it is in fact St. John's wort in the bottle. But we know that that is probably not the main active ingredient in St. John's wort.

So people are a little bit confused when you have the Boston Globe publishing an article evaluating seven St. John's wort products for their activity. And if they are looking for hypericin maybe that is not the important thing to look at.

If they are looking at biological activity based on that, what does that mean if we don't even know that that is important.

So these are just things that one should keep in mind. And I think I -- one of the other things that has been particularly disturbing to me is to see on the market now not only herbal companies producing these various products, but a lot of the large pharmaceutical companies.

If you go into drugstores now, producing all kinds of herbal products. Now in these cases, I'm sure that what they say on the label is in fact in the bottle. But if you look at some of these bottles, as I go in pretty regularly to the stores and try to see what the newest products are because they are coming out almost weekly, you can pick up now herbs for women. You can pick up these multiherbal formulas. There are whole ranges of herbs in them.

I think what these companies have done is put in this bottle every herb ever mentioned in the same sentence as the word "woman."

You look at these products, and you see that in cases like black cohosh, where there have been clinical trials done, and you do know a baseline dose that is recommended and it seems to be effective, if you look at these bottles, the doses are some fraction of doses of these three or four or five different herbs.

So I'm sure that while these products have the herbs in them, I'm sure that the companies, since they don't have to, did not put the money into the studies to say does this mixture -- if you have a third of A and a third of B and a third of C, do they add up together to give you biological activity?

I'm sure that these studies have not been done. So people think, oh, black cohosh; it must be effective, and now black cohosh plus soy. This is great. But we don't know that these things act either synergistically or maybe antagonistically to work together. I think these are important questions that need to be asked.

Now over the last six months, I have been actually more concerned to see the doses escalating in these products from what have been the studied doses to now much higher doses. I think that we're doing an experiment here that has not been done scientifically. In this culture, we think if a little of it is good, more is better. And having these huge doses is of somewhat concern to me.

You also have issues of new uses of traditional formulas, of course. Particularly our traditional Chinese medicine has been used historically in a lot of cases to boost immune system, for wellness, to maintain health.

Now we are expanding these uses and we're extending them beyond that which they are initially intended, taking these things and saying well, maybe they could be used to treat cancer, to treat heart disease, to treat some of these more clinical illnesses. And they weren't necessarily used for that purpose initially, even though some of the herbs in them may have these kinds of activities.

So I think we need to look at traditional uses and what we're doing to these formulas currently.

When I came in Friday night, I happened to turn on the television. I don't know if any of you saw 20/20 on Friday night. But they had a whole session on soy, and it was the untold soy story; all of the downsides of soy that you haven't been told about because, as you know, soy has been marketed like crazy for the past year or so or more.

I think that certainly there has been a lot of research showing its benefits for cholesterol lowering and in vitro work on anticancer effects. And I think that a lot of these substances, when they are used as whole foods by certain populations for years, we are now taking this epidemiological data and taking it and jumping a whole other step to say, okay, we can use this for treatment, used acutely in people who have never taken this and have the same effect.

I think with topics such as soy, we don't know, for example, whether that is the main thing in the Asian diet that is protective against breast and prostate cancer. Maybe it is the seaweed in the diet. We know that there is an estrogenic effect from seaweed. Maybe there are other factors. These associations were made.

The media grabs it way before the data are substantive to back it up and takes it to another extreme.

I think there is also concern when you take now out the active ingredients like genistein or dazine(?) and concentrate them and give them to people and say, take this regularly. Well, that is not what has been done historically in this culture, where it looks like it has been beneficial.

There is work coming out; it should be published in the next couple of months, looking at Asian populations who have been consuming soy through puberty. Maybe it is important to have taken this during the period of breast development that is protective. We don't know these things, and these are things that we need to look at.

But I think we need to be careful about taking new uses and concentrated amounts of things that have not been used that way but yet we're basing our use on a traditional experience.

And I think two other points. And one is that when you are reading research studies, I think even though there are quite a number of research studies on herbs, thousands of research studies in fact around the world on herbs, and if you look at the ones particularly that are in the English language, either in the United States now or in Europe, it is really difficult in many cases to be able to repeat that study because when you are reading these studies, you need to make sure that they indicate what the substance is, what its Latin name is, what its source was.

And in many cases, they don't indicate any of that. They don't indicate a dose. They say five capsules were taken, and you have no idea how much were in those capsules. You have no idea of where that product came from.

So I think you need to pay attention to these things in reading research studies. And unfortunately, a lot of the cases in the literature, when there are case reports of adverse effects of botanicals, it is often because of misidentification of products and contamination of products. Someone may issue a clarification later on in the literature, but you don't often see that. And this is now in the literature forever, and it is very difficult to get these things out of both scientific and public knowledge when it was a mistake in the first place. So these are things we have to pay attention to.

I think one last point is that there are, as I said, many studies that have been done, not all that have been up to the rigors of what we would like to see in science, but certainly a lot of research that one can look at for trends and indications and interesting possibilities and these data are not always available in Medline.

Medline doesn't indicate many of the journals. Many of them are not in English. They are in Chinese and Japanese, in German. Almost all of the cohash literature is in German.

We have to have them all translated because we are beginning a long-term study now on black cohosh for both the side effects in menopause and trying to look at the safety data.

You have to dig into this other literature and there are databases around the world that exist that you can dig out and find what is going on in these areas.

We have a project where we are working so far with seven countries to try to create some kind of cohesive database so that people will be able to go in, search in these different databases in different languages that will be sort of transparent to you and will be able to get you to all these different places.

This is a consortium that we have begun a few years ago and hopefully will bring to fruition in the next year or so. And I think that even though there is a lot of confusion today, we don't have the answers we want, I think it is an exciting time.

There is more and more research being done. There are more people looking at these questions. There is increasing, although not anywhere near adequate, funding being done.

I think that if we can just be a little cautious and not be ready to jump on the latest media claim and rather look more deeply into it, I think there are lots of possibilities.

We don't have all of the answers yet. It is not what we all want. But I think it is a really promising and exciting time. Thank you.

(Applause)

DR. LAMB: Thank you. We have about -- why don't you join us at this table? We have 15 minutes for questions, and we are going to end promptly at 12:15. I am going to ask people who have questions to ask to come up here and get in line, which is probably the easiest way, and that way the speakers will be able to hear you. The speakers will repeat the question for the benefit of the audience.

I would also like to ask you as you leave the room to please leave your evaluations.

AUDIENCE MEMBER: I have a twofold question. My first part is one, you stated that there was a 120 studies ———. Why in all of this well-earned that cancer is getting, why are they spending \$17 million in the ——— program when there is already 120 studies of it out. That's one part.

The second part is with all of these studies ———. As a consumer and a researcher, I would like to say that, you know, for example, mistletoe shows great promise as a ———. It has been well studied in Germany. Why isn't it more widely used in this country? A researcher like me ——— it is probably a money thing, a drug company ——— money thing. There is no money in for the research. There is no ——— to gain for national ——— so nobody researches it.

MR. BLUMENTHAL: I'll take the second question first because it deals with cancer directly. Why is not mistletoe, if it has been researched in Germany and used over there, why is it not more widely used over here? What is holding it up, and why isn't it employed or researched and approved over here?

The mistletoe extract, as I understand, is a homeopathic preparation. There are ones made. Weleda. It is called Iscadore®. It is available, I think, in vials that are subcutaneously injected.

So it is not a dietary supplement. It is available to the practitioner only, as a homeopathic drug. And in that sense, it kind of skirts, if you will allow me to use that term in a nonperjorative manner, the normal FDA/NDA process because it is being sold as a homeopathic drug, which is approved by the Homeopathic Drug Pharmacopedia of the United States, which is written in the law in grandfathering homeopathic products in 1938.

Consequently, there has never really been a due diligence as a drug, and its acceptance is one of basically education and word of mouth, but it is not official with the FDA.

It is basically just out there, as I understand it. Ralph may have a different perspective.

The thing about ginkgo, yes, there are 120 clinical studies on ginkgo for a variety of different clinical endpoints. Why are we spending I think \$15 million on an NIH study? You said 17; I believe it was 15. But whatever, it is a lot of money.

Over here I think what they want to do is -- there has only been one ginkgo study published in the United States, which was a German product studied over here, published by LeBars (?) et al. in JAMA in October '97 for the early stages of Alzheimer's dementia, which was shown positive.

I think what is happening is that NIH wants to do another study of large scale that has been -- that meets all of the potential objections that people might have as far as control and design to ensure that there is good data on a multicenter, large scale, long- term study so that there could be definitive data that can be reliably accepted in this country because there is a bias, like it or not, about foreign research in the United States, even though, ironically, most people -- some are old enough to remember this in this room -- in the '50s and '40s and earlier that were premed would have to study Latin and German in order to be able to understand the medical literature if you wanted to go med school.

It is interesting that we have such a difficulty accepting some of this German research when in fact that was a precondition of med school just a few years ago.

DR. KRONENEKBERG: And just a further comment on your statement about nothing to be gained by studying natural products, I don't quite understand this actually because -- and then the issue of companies putting in thousands or millions of dollars into a search, and then, of course, anybody can take this product and make another product and use that claim, if often made.

I think in this case the companies are not required to do research. They don't have to put hundreds of millions of dollars, but maybe just millions of dollars or in some cases even less into some of these studies.

It seems to me, and I'm not a marketing person, that if you have a study and you have a clinical trial, and you have good results, and it is published in the New England Journal of Medicine, that would do a lot more than the ads in all of these popular magazines because you have your practitioners getting that data.

I think that these studies can be done with less than exorbitant amounts of money, and I think they should be done. And I think responsible companies, even though they don't have to do it, should want to be doing it.

DR. LAMB: Your question, please.

DR. MCKEE: Actually, I would like to raise an issue and propose an idea. And the issue is, I think, well-known. I would be hard to -- I'm Dwight McKee. I'm a medical oncologist, and I have been active in nutritional and body/mind areas for 12 years before I became a medical oncologist.

But the thing I want to raise is that I attended the pre-IND meeting for anvirzel, the oleander extract that you referred to with Bob Newman from M.D. Anderson, in whose pharmacology lab a tremendous amount of research was done with chromatography and fingerprinting.

It was very clear that the mind-set at the FDA is very uncomfortable in dealing with a botanical extract that contains hundreds of compounds, many of which aren't known. And without the extensive work that Bob had done in being able to verify within plus or minus 5 percent that one lot was the same as the other, it would have never stood a prayer of getting an IND. And even so, it took a year.

Now take a compound like PC-SPES, which is, in my mind, clearly an active drug in herbal combination in prostate cancer that contains I think eight herbs, some of which are 6,000 to 1 extracts.

That would blow the FDA out of the water if they tried to go through that process. Clearly, we need another mechanism. The FDA would have to hire the botanical medicine experts, all of who are 60 and up, who are probably not going to move to Bethesda, to have the expertise to deal with this issue.

I wonder, since Jim Duke came out of the USDA, if Tom Harkin or somebody might introduce legislation to propose that the USDA regulate botanical medicines as a food because they have more of a tradition there. And I'm interested in your ideas about that.

MR. BLUMENTHAL: That's a great idea that has been actually promulgated previously by the people, especially during the conversations going on about who should handle herbal medicines outside of FDA, if anybody, Office of Dietary Supplements, somebody at NIH or even the USDA, which is a totally different organization entirely. And it has been floated.

I don't know that it is really a politically viable idea at this time, although it is certainly a sexy one according to a lot of people who see the longstanding bias at the FDA against many of these natural products as an incumbent or as an impediment against being able to move forward in a way that is consistent with the health care needs of the American population in the 21st century.

This dietary supplement issue that came up in the passage of this law was clearly an outgrowth of this resistance of FDA, although there has been some change at the FDA. They have opened up a lot more, and they have reduced some of the preclinical toxicology requirements for some of these natural products since they are already in the marketplace being used by people anyway as a precondition for INDs and stuff. But there is still some resistance there.

There are a lot of people that actually agree with you and like your idea. There is quite a bit of regulation. We have a new article coming out in HerbalGram No. 49 that is written by Bill Soler (?) from the Consumer Products Health Care Products Association, which is the nonprescription drug association, documenting the various laws and regulations that are in place right now for herbs and other dietary supplement.

The reason why people think there is no regulation here is, number one, they are regulated differently from drugs, and so they think that means no regulation, which is not the case, because they are not required to go through FDA approval to get in the market. But there are considerable regulations, which have been selectively unenforced by the agency.

If the FDA would just enforce what is on the books right now, you would see a lot more activity, and a lot of these variable products which are sometimes mislabeled would be cleaned up.

DR. KRONENBERG: In terms of the IND, I think that there are, even though most of the FDA is uninformed, there are selective patches of knowledge there and support there. We had our ten Chinese herb formula approved for an IND, and there were some people there who even helped me translate the Chinese. And so there are some people there who understand these things.

We are about to go in with another herbal product. I don't anticipate problems, but there are selective people there are understanding, knowledgeable, and helpful, and a lot of others who need to be educated.

So I think that there are possibilities, and it is slow and tedious, but it is not unhelpful.

AUDIENCE MEMBER: Your folks didn't come to my meeting, so I'm glad to hear they exist.

AUDIENCE MEMBER: Do any of you have any knowledge or opinion about something called MGN-3 that is coming out of Japan?

DR. MOSS: MGN-3, the original product is AHCC, which is a kind of mixture. It is an enzymatically modified form of shiitake mushrooms and rice bran. And there is a considerable amount of information in Japan on this, most of it untranslated.

I know at least popular books have been written about it. It is enormously popular in Japan. And then Lane Labs is marketing it in this country, marketing a product called MGN-3, which may or may not be identical to AHCC.

I kind of believe it is identical because Dr. Gonium (?), who did the American clinical work on this, a very small, uncontrolled clinical trial at Drew University in Los Angeles, originally published his paper about AHCC and now that paper is cited in support of MGN-3, so I would have to conclude they are almost identical.

We know, of course, that mushrooms are highly effective immunostimulants. And the biggest selling anticancer agents in the world, as far as I understand -- maybe now tamoxafin has overtaken them, but PSK and lentinin in Japan are used for almost every cancer patient and, of course, with some effectiveness in terms of building up the immune system.

So I think, you know, a small amount of clinical data, a general background of effectiveness from mushroom products, pretty high probability that it is a good product, but highly priced, very highly priced.

In fact, now there is another product called Immpower. Their representatives have been at this meeting. I-m-m-p-o-w-e-r. And that is AHCC, and it is a fraction of the cost of the MGN-3.

AUDIENCE MEMBER: _____

DR. MOSS: Yes, right.

AUDIENCE MEMBER: The FTC has gone after MGN- 3 has a --

DR. MOSS: Yes.

AUDIENCE MEMBER: _____.

DR. MOSS: Right. Along with I think other Lane Lab products.

AUDIENCE MEMBER: _____

DR. MOSS: Yeah. You'll see the ads for MGN- 3, "This is the magic bullet." You'll see full page, color ads in almost all of the alternative journals, which, of course, is pretty ridiculous, you know.

There is no magic bullet, and that certainly isn't it. But that doesn't mean that it has no value to it and that is one of the tragedies of this field.

It is paradigmatic of the tragedy of this field that for whatever reasons, cultural or economic, people who have an herbal treatment for cancer feel that they have to hype it as the cure, the magic bullet, you know, and then the government reacts against that with repression and you are caught up in another one of these laetrile battles instead of having some sort of reasonable agreement that this useful and deserves further study. This has been our history.

AUDIENCE MEMBER: Does either of our speakers have any information about the efficacy of some of the Chinese herb preparations, SPES and PC-SPES for cancer?

DR. MOSS: Well, I should have mentioned at the beginning -- the question is do I have any information about the efficacy about SPES and PC-SPES, two preparations that were brought from China and refined by Sophie Chen, who also is at this meeting. And, yes, there is some data on this, more published data about PC-SPES.

SPES means hope in Latin, and PC for prostate cancer -- two papers at the American Society for Clinical Oncology this year and a couple of other peer reviewed articles in the previous couple of years, which demonstrate a very interesting thing, which is that the mixture, it is a mixture of eight herbs, has an effect on both hormone-responsive and also on hormone refractory, or androgen-insensitive prostate cancer.

This may be the first agent, I don't know of any other, that actually can dramatically lower prostate-specific antigen in hormone refractory patients, as well as in hormone-sensitive patients.

Now there was confusion, is some confusion, over this because there is no doubt that one of the actions of PC-SPES is as a hormonal or anti-androgen agent. And in fact, it is pretty similar to DES in some respects.

Of course, DES would be a tiny fraction of the cost. And in fact, it is interesting that this controversy over PC-SPES has reenergized the use of anti-androgens or estrogens in the treatment of prostate cancer, which of course goes back to the days of Huggins (?) in the early 1940s, really first chemical treatment for prostate cancer.

So it is definitely that, okay? But what got lost in some of the early papers was the fact that in addition to that, there is that other aspect, maybe another herb in the mixture that has an effect on the hormone refractory patient. And that would be extremely valuable, and it would be worthwhile knowing and doing. And Sophie, who, you know, may even be in the audience -- I don't know. But, you know, she is working on this.

She is at the New York Medical College, and she is aware also of the extreme problems, production problems, that occur in making this highly concentrated product in China, although now PC-SPES is a viable product in the marketplace.

But the future of SPES, I would say, is much more in doubt, although it is, as many of you know, the herbal mixture that Bill Fair is using to treat his own cancer, and based on some good scientific testing. His case -- I don't think I am giving away any confidences here.

So, you know, I think this is an example of what can be done when the traditional herbal world meets up with good science. And that is the kind of exciting results that I am looking for with all of these things.

There are many, many herbal treatments that could, if people took the care and the time and they had an ethical presentation, could be used in treating cancer.

DR. LAMB: We have time for one more question. Dr. Gordon was just poking his head in and saying we need to finish. So one more question, please.

AUDIENCE MEMBER: Do any of you have any information about the plant red bloodroot? I believe that is the one that Andrew Weil tells the story of ——— skin cancer.

DR. MOSS: Bloodroot is one of these very traditional escharotics. It is probably the -- I didn't mention it, but, you know, one of the really common plants used to apply topically to cancer. It goes back to the 19th century.

There was actually a whole big controversy in England over the use of bloodroot, and it was also part of the original Moe (?) microsurgery formula. Moe used zinc chloride and bloodroot to fix tumors and then shave them. And Moe's microsurgery is the most effective treatment there is for skin cancers, about 99 percent effective.

So, you know, it probably has some activity to it. But it is not terribly well-researched in the modern age.

MR. BLUMENTHAL: Bloodroot is a Native American plant, first of all, and I think it may have been in some of the Hoxey escharotics. And I think that was even shown by Hoxey, when he -- when Hoxey was fighting with Morris Fishbine of the AMA in their contentious battle.

I think ultimately I think Fishbine acknowledged that the bloodroot and other ingredient escharotics was effective for topical cancers, which was an interesting issue, since they were so vehemently opposed to Hoxey. But they never tested the internal treatment.

By the way, the Hoxey stuff -- I believe you forgot to mention that -- is coming out in a book, this whole story, in Kenny Ausubel's new book, which just came out this month, called *When Healing Becomes a Crime*, the whole story of Hoxey that Ralph was talking about earlier.

But bloodroot has also been used, by the way, recently in the last decade as an ingredient, sanguinarine. The primary alkaloid in bloodroot has been used in a tooth preparation or oral preparation called Viadent for gingivitis, I believe it was, and there was some controversy about that. But that has been purchased by Colgate from a company called Vipond (?) in Colorado.

So they are now using bloodroot in toothpaste and mouthwashes for some of its effects.

But the escharotic was apparently useful. And there is an article -- there is a book by a woman - - I forgot her name. Naiman, I think her name --

AUDIENCE MEMBER: Ingrid Naiman.

MR. BLUMENTHAL: Ingrid Naiman. It is about escharotics and bloodroot and other kinds of topical cancer cures. I forgot the name of the book, but it is Ingrid Naiman, N-a-m-a-n or something like that.

AUDIENCE MEMBER: N-a-i-m-a-n.

MR. BLUMENTHAL: N-a-i-m-a-n. Anybody else?

DR. LAMB: I'm sorry. The closing ceremony is a very special ceremony, and we would like everyone to attend.

We have minimal time for individual questions, minimal time because I know the speakers would like to attend as well. So please join us for the closing ceremony.

(Whereupon, the PROCEEDINGS were adjourned.)

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