
Conference Synthesis

Q&A

JEFFREY KAHN

WITH

MICHAEL D. FERNANDEZ, IRWIN L. GOLDMAN,
GREGORY JAFFE, AND CHARLES C. MUSCOPLAT

Phyllis Johnson (USDA, Beltsville, MD): I have a comment more than a question. An unstated assumption has underpinned much of our discussion: we know everything there is to know about people's nutritional requirements. In fact, we don't even know that for all nutrients for the population as a whole, much less in terms of understanding the genetic variability in what our individual requirements are, although the human genome and nutritional proteomics are going to lead us to a better understanding of that. The other thing that I think we have to be conscious of is that we also don't understand very well the interactions of nutrients in the diet. We don't consume nutrients in isolation, as a general rule. That's not how they come packaged in food. And our current approach in this first generation of functional foods—whether we create them through a food processing technique like fortification or through genetic enhancement—is based on our traditional reductionist approach of looking at one nutrient at a time. In fact, because we don't understand those interactions, if we drastically change the level of one nutrient in food, we may be creating interactions or eliminating interactions that we are not aware of.

Charles C. Muscoplat (University of Minnesota, Minneapolis-St. Paul, MN): When I think about looking at one nutrient at a time or whether or not we understand the human condition as far as nutrients go, I would reflect back on my presentation about drinking and heart disease. The questions are complicated. We have a new set of tools. When we look at people who are low converters for isozyme 3-alcohol dehydrogenase, they can benefit strongly

by having one to two drinks per day. Now we never thought of nutrients—if we look at wine as a nutrient—only for people with certain genotypes. Now if you are on the crop or horticulture side, you could breed varieties to produce micronutrients that are beneficial to people with a certain genotype. So, if we put those technologies on the table, we change the way we think about these things. And then perhaps in time we will study multiple nutrients simultaneously. Will aspirin become a nutrient to prevent heart disease or will Advil prevent Alzheimer's disease? Traditionally they are called medicines but taken life long will they be part of the required diet to treat or prevent chronic disease? I have a colleague at the University of Texas who believes that the future of treatment of diseases is prevention. So we could be at an era where all the definitions are changing as are the technologies. I think we wind up with stacked challenges. Not only do we have the ethical trust challenges that Jeff pointed out, but a whole set of new tools in the tool box that we are just experimenting with at the moment.

Kahn: There is a move to say, “Let us test your cytochromes and we will predict what are the best foods for you to eat or to avoid, or lifestyle changes to help you,” which speaks to the problem of over-promising. It's a complicated interaction between what's happening at a genetic level, and nutrition, lifestyle, and environment. All of those things are obviously going to play a role, and there is much that we don't understand. So I think its coming and Chuck is absolutely right—but the question is, what do we tell people in terms of what it means now?

Audience Member: When you have a specially prepared wine, and you ask a person of a specific genotype to use that wine for health, it sounds like wine is becoming a medicine. Can that particular wine be prescribed for that particular person?

Muscoplat: I would probably not want to suggest anything like that. I was mainly pointing out, as a provocative answer, that we have to think about things very differently. Research indicates that conjugated linoleic acids can delay the onset of type-2 diabetes. The best source of conjugated linoleic acids is milk from cows that are grazed on grass, as opposed to fed via silage. That causes a cascade of events back to the farm to a higher value for milk that contains conjugated linoleic acid. It would probably mean that the person who drinks that would have to have a family history of at risk for type-2 diabetes. Perhaps there is some weight control in the process. You can see the complexity escalate dramatically when it comes to making some of those decisions. Where does food become medicine, where does food become nutrition, and when does it taste good? Two hundred years ago, there was a point in time when that was probably true for vitamin C—if you didn't eat your limes, in the British Navy on

Admiral Nelson's ship, you got sick. Your commanding officer probably ordered you to eat those limes. If you recall, they had square plates on Admiral Nelson's ship, which is where "three square meals a day" comes from. So things don't always look the same, given the context of time. So the three square meals a day in the early 1800s looked a lot different from milk from grass-fed cows and the glass of red wine before you go to bed to deal with your diabetes and heart disease. So we just could be entering a new level of understanding, a new level of required dialogue among the players.

Jerry Cohen (University of Minnesota, Minneapolis-St. Paul, MN): The basic premise of all of this is that we have a fixed diet of a known amount. I'm reminded of the story of a scientist years ago in my lab from Israel where they had figured out that persimmons would ripen without getting soft with ethylene. He was in charge of overseeing importation while he was in my lab so he would occasionally sneak away on the weekends. One weekend he got an urgent call that he had to fly to New York because a woman had intestinal blockage from having eaten Israeli persimmons treated with ethylene. She had eaten forty-seven at one sitting. It sounds humorous, but it wasn't. One of the things I would like you to consider, is that in deciding what's good for people we have to consider extremes of behavior as well as ideal behavior. This is certainly true when you seek to modify people's intake of food.

Muscoplat: That reminds me of the time when I was a young assistant professor in the College of Veterinary Medicine, someone brought a cat in, and the complaint was that the cat would not eat. It was gigantic. We asked the owner what he fed the cat: a whole chicken every day. There are extremes.

Anthony Shelton (Cornell University, Ithaca, NY): Steve Pueppke made a good point when he said that much of this is not a science-technology issue, but rather a social-science issue. I guess I would like to reframe that a little bit, although I agree with it. It's really a quality-of-life issue. When I hear the farmer say that agbiotech allows him to spend time with his family, I think that is an important thing that farmers have not been able to do. When I hear the health professionals ask, "Will it be healthful and prevent diseases?"—that's a quality-of-life issue. The consumer asks will it taste good, will it make me younger, will it make me thinner, make me look like I just came from Lake Wobegone? And the social scientist, Jeffrey Kahn said that quality of life involves a democratic process where people feel involved in the decision-making. I guess I think that that is a quality-of-life issue. As an ag scientist who works in biotechnology, I think of it in terms of quality-of-life for the environment too: will it enhance the environment? Can this science and technology improve the quality of life for each of us in our different forms, as a farmer, as a healthcare person, and as an agricultural scientist?

Kahn: If it all pulls in one direction, I don't think we have much to argue about. But the difficulty is when *you* think it is improving the quality of life from your particular perspective while others say it is degrading theirs. I'm an environmentalist, therefore what you think is an improvement in quality I see as degradation. Although we should not view this through only one lens, I think it's certainly a beneficial lens through which to view it. You might step back and say: from a public-health perspective, really all that matters is making sure that people have clean water to drink and that their sewage goes away from where they live—that's the big stuff, quality of life, and everything else is around the fringe and isn't saving lives. We attended to the really big stuff a hundred years ago, and all the rest is gravy. I don't share that view, but some might stand back from that perspective and say, we are really working on quality of life now. There's life saving, there is health improvement, there is quality of life improvement, but I don't think they are all the same thing.

Gary Gardner (University of Minnesota, Minneapolis-St. Paul, MN): One issue that has not been discussed very much has been the issue of dietary supplements. It seems to me if there is any topic where trust could be destroyed it's the potential for unethical behavior of people in the dietary supplement industry. I would especially like Mr. Jaffe to comment on the regulatory issues here, and what strategies we should use to bring science to bear in that industry.

Gregory Jaffe (Center for Science in the Public Interest, Washington, DC): I agree with you that dietary supplements are a problem, and that they aren't regulated in the way we think they should be. I'm not an expert on dietary-supplement issues, so I won't comment on specifics of how they should be regulated. There is a much greater potential for fraud, misrepresentation, and health concerns from some of the dietary supplements that are out there. We are pushing for stronger regulation of those, but I can't give you details.

Muscoplat: [audio lost]...legislation that created them. I saw specifically that it was intent on not regulate them. There are two or three requirements. One is that there is some nominal safety so long as the product is natural. We all know, as scientists, that there are many toxic things in the world that are natural. Mycotoxins are natural. There is nominal safety, usually 30 days of safety when we know that most people who take them, actually take them for longer than 30 days. So long as you are not making a claim, you can sell it as a dietary supplement. But many of the supplements are trying to make claims through media, other than what is on the bottle or in the store. The third issue is that, to my knowledge, there aren't any products sold as over-the-counter medications that can be taken more than 2 weeks without a doctor's advice. If you look at your antihistamine or Aleve® or Advil®, the label says that if symptoms persist more than 2 weeks please see your doctor. Well, many of the symptoms or

conditions that people take supplements for are present for longer than 2 weeks. So we have several cascading issues of what I think are conflicting philosophies. One is safety—it's okay to sell it so long as you don't say what it does, in the same medium as where the purchase is made. There is no restriction on time. So it's almost the antithesis of what we would imagine. Now many of us think that dietary supplements have some benefits, or could have, theoretically, if they were proven, if they were labeled and if they were taken according to some direction. There are also issues about assuring potency. To my knowledge, all pharmaceuticals in over-the-counter medications have a required shelf life: at the end of 4 years a minimum standard must apply. I don't believe that applies similarly for dietary supplements, largely because they are complex materials.

Irwin Goldman (University of Wisconsin, Madison, WI): I would say, too, in response to Gary, and to pick up what Chuck just said, there is confusion and that leads to misunderstanding and undermines trust. When people see a laxative on drugstore shelf, few have the sophistication to know whether or not it has gone through FDA, or whether it's a dietary supplement. And that is the problem. You pointed at all the regulatory differences, but I don't think people know which is which. That is problematic because they don't treat them as distinct entities.

Theodore Labuza (University of Minnesota, Minneapolis-St. Paul, MN): Jeff, in your slides, you talked about authenticating food. In fact, that system is in place. For a food to be put into the market place it either has to be generally regarded as safe (GRAS), which has a specific procedure for approval or, if it's a food additive, it has to go through toxicological testing, which in fact is more rigorous than for a drug. For drugs, we allow some risks. The Dietary Supplement Act, which Gary brought up and Chuck commented on, in fact is a system that has destroyed confidence in the Food and Drug Administration, which is bashed by the media. Yet, in fact, it was Congress who passed the law and tied the FDA's hands. One good example of what Chuck was talking about, is in 1997 the FDA proposed a regulation to require ma juang producers to put a warning label to consume it for only 2 weeks at a certain ingredient level. In fact that regulation has never been finalized because Congress won't let them do it. FDA knows that if they try, Senator Hatch will come down on them very hard. The system is out of whack.

Kahn: We do have that authentication, but the system is not working right now with dietary supplements or the whole concept of functional foods. If it's a functional in terms of health then it has to have a health claim. Barbara Schneeman has said that a number of times at this conference. And when people are looking at functional foods, it's much narrower than the typical health claims that we have on most products today. That is where we have to

get some trust in the system. Somebody in the regulatory system must educate the public and researchers. If we don't understand how new functional foods fit into the regulatory system, we may fail from the outset.

Muscoplat: I would guess that the large food-company representatives in the audience would say that their most valuable asset is their brand name, and they will do nothing that will put at risk the public trust in the brand name. When a product is changed, it is made more beneficial, and a lot of work goes into that to ensure the preservation of trust. The “improved” product has to actually deliver on the promise. It has to be approved and be validated and authenticated, all the way back through the system. On the dietary-supplement side, the leading brands of the vitamins now—I heard this last night on CNN—are many of the private-label brands and not the big brands. If brands have no value then other brands take them away or “no-brand name” takes them away.

Michael Fernandez (Pew Initiative on Food and Biotechnology, Washington, DC): We have a system to deal with foods, to deal with drugs, and to deal with other types of products. But, when you blend those categories there are going to be challenges to that system. Issues about transparency and public confidence in that system are going to be very important. Where there are potential cracks or gaps in the system, then we need to do everything that we can to make sure that we fill those in. Because, as has been said, once public trust is lost it is very difficult to regain it.

Jaffe: I would agree that authentication is extremely important. I question whether we really have that with the current food-additive and GRAS process. For biotech foods there may be some authentication by the companies, but not necessarily by the FDA. With authentication comes transparency, with participation of the public and of an independent third party with no stake in the outcome. So, I question whether there really is authentication of foods in general, of biotech foods in particular, or of the other new foods that are coming on the market—mycoproteins, *etc.*—that may cause problems for people.

Audience member: To what extent should we allow the regulatory process that we endorse to be influenced by the extreme cases? Should we decide how these things should be regulated on the basis of the fact that every now and then people do stupid things and end up hurting themselves? This ties into how we should properly respond to, for instance, potentials of allergenicity, which affect only a minor portion of the public. To what extent should we as a whole share a burden in making sure that these people are protected as opposed to saying, well you have to protect yourself?

Jaffe: If you look at examples that exist already in regulatory systems, for example with pesticides, we don't examine the effects of the average level of pesticide eaten by the average person. We look at sensitive individuals—a child or an elderly person—and we then add a safety factor, 50-fold or 100-fold, partially because nothing is 100% safe and we are not expecting to prove safety to an absolute number. I would advocate that we do need to look at that. Maybe we don't look at the extreme of someone eating forty-seven persimmons, but we do need to take into account the range of population. It would be wrong to add risk for a small, but not miniscule, portion of the population.

Muscoplat: Recently an article in the *New England Journal of Medicine* focused on over-consumption of certain foods. They had pictures of individuals who ate 100 to 200 carrots per day and their skin color was exactly the same as that of a carrot. It is called carotenemia. Now how do you plan for something like that? Or the people who are elderly who have mild renal disease and like eating bananas and they elevate their serum potassium and become hyperkalemic. Or I think of the few tenths of a percent of the population who suffer from hemochromatosis and shouldn't eat iron. Dealing with the extremes is difficult. I would guess that most men over age 50 should not consume vitamins with iron because a high serum iron level in people my age and older means that they are at risk of a more-damaging heart attack. So, as we learn more, the issues get more complicated rather than less so, and I'm not sure how to deal with that.

Goldman: I don't know what the article said, but it has been my understanding that hypercarotenemia by itself has no inherent toxicity, even though the skin definitely changes color. What I found interesting about this was the debate about biotech and particularly golden rice. There is this idea that we can get vitamin A from a biotech product like rice, and there was a blurring on the part of the general public on vitamin-A nutrition and toxicity, which is very real, vs. carotenoid-based nutrition, which is not toxic. So just as a general comment: beta-carotene from a carrot, or from another natural product, is converted into vitamin A in the body by cleaving the carotenoid molecule, which is very safe even apparently at very, very high levels where your skin turns orange. Vitamin A as a supplement or as a vitamin can be very, very toxic and so there is an interesting interplay in the way people understand these things.

Muscoplat: I think the only known toxic source of vitamin A is polar bear liver.

Goldman: But vitamins, and particularly for pregnant women, is an issue that has been raised with respect to vitamin supplementation where you are taking it as vitamin A.

Kara Slaughter (University of Minnesota, Minneapolis-St. Paul, MN): I'm a student and have learned a lot from this conference. One of the messages that has had a big impact on me is the idea that consumers are not monolithic. When you talk about consumers you have to understand that they are as diverse—perhaps even more so—as opinions in the scientific community. Is it true that as consumers become more educated on the intricacies of what is genetic modification, what is biotech, do they become more receptive to those foods? My contention is that being well educated does not always mean being more receptive. Also, what is your opinion on the impact that these technologies will have on rural development?

Jaffe: Regarding consumers and education—consumers don't know a lot about genetic engineering and biotech foods. The education level is very low as we have heard in the last couple days, and that can only improve. When it does improve, you will find some people who will embrace it. As you said, consumers are not of one type, so you will also find that some will still question it. But I think everyone will feel that the process has become more transparent and more open and they will feel more comfortable with having those foods on the shelf even if they do not choose them for themselves for whatever reason—they think it is not helpful for the environment and so forth—but the education process will be beneficial overall.

Kahn: I'm not sure that it is education so much as it is getting used to having it around. We have a lot of experience on the medical side with this, what people technically term the “yuck” factor. Heart transplant is a good example: “What, do you mean we're going to take a beating heart out of one person's chest and put it into another person?” It was viewed very skeptically at the outset, but now we can't find enough hearts to transplant into the people who want them. There are people who study the way that technologies are viewed and adopted and it doesn't track necessarily with education. It's not the same as food, but there are useful parallels. It takes time for a new technology to find acceptance.

Goldman: To comment on your first question again: to some extent agriculture is a tremendous disruption of our environment, but it's one of the most important such disruptions that we have been able to create. Over time, as technology has crept into agriculture, there has been resistance and then there has been, as Jeff just mentioned, acceptance. But we see people drawing lines in the sand—even after education—about adopting certain technologies. I'm not convinced that with the information being available and even well understood, people won't still draw their lines in the sand and say, “Here's where I'm willing to accept it and here's where I'm not.” Food is a very sensitive issue for a whole variety of reasons that we have discussed. So I agree that the information has to be out there, but I think we will see people more willing to say no.

Muscoplat: Rural development is a complex topic and many forces have operated on the rural American scene for the last 150 years. Some of these technologies and potentials will have some effect on some individuals. To contend that it will have a major reversal on rural-development trends would be misleading. Other, vastly greater forces are at work: the recent Farm Bill, the aging population. Successful rural development will have many sources of activity, this being but one—it will benefit some, but, my fear is, not many.

Audience member: There is a lot of information on labels and on packages. There is a lot of food and nutrition information you can get from magazines, but what would be the best, most trustworthy, easily accessible information source on nutrition and diet that you would recommend? I'd like to go to a Website and type in what I've eaten over the past day or so and find out whether I've gotten too much of something or not enough of something and I might mend my ways.

Kahn: Does anybody on the panel have any thoughts? Otherwise maybe we will refer to our experts in the audience.

Pam Vanzyl-York (Minnesota Department of Health, St. Paul, MN): I would like to respond. Over the last year we have been improving our Website to provide credible information and to lead consumers to other similar sources. A variety of credible sources of information exist through universities, through many of the extension sites, through many of the other public-health outlets, and through other federal agencies. But consumers need guidance as to how to get there and how to evaluate that information. Another point that I want to make: I have heard numerous times over the last couple of days that changing behavior doesn't work and educating consumers doesn't work, particularly you, Dr. Khan, today. In fact, we have put virtually no resources into consumer education and behavior-change programs in this country. Coca-Cola spends more on one brand than the entire budget for the national five-a-day program. What do you think we are going to do about some of these resource issues in the future, and how are the actions that you outlined going to come about?

Kahn: You are right—we need to ask that question. Resources are always strapped, obviously. A problem of silence, I guess. You come from a department of health. How do people like you talk to people who come from industry and academia? How do we get people in the same room to have this conversation? That is part of the goal of the inter-disciplinary piece. But, how do you push that so that the right people are around the table to ask that question—not so that you look at each other and shrug, but where there are checkbooks to actually make things happen? I am hopeful that there are ways to do that.

Fernandez: I want to make a shameless plug for my organization's website, which actually does not provide the nutrition information that you are looking for, but which we hope is a reliable source of information on agricultural biotechnology: www.pewagbiotech.org.