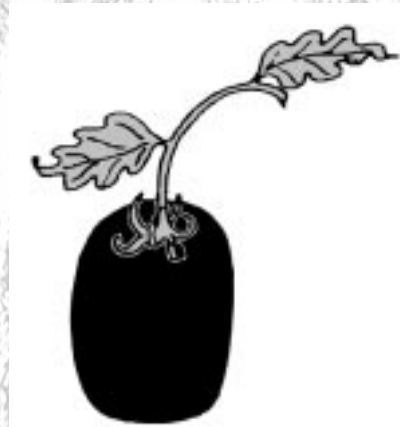


“Tomatoes and Health”

TRANSCRIPT OF TOMATO HEALTH PANEL
HOSTED BY THE
CALIFORNIA TOMATO GROWERS ASSOCIATION, INC.



February 6, 1997
Sacramento, California

CALIFORNIA TOMATO GROWERS ASSOCIATION

“Health & Tomatoes”

Biographies of Panelists

Mary N. Haan, MPH, DrPH

Director, Center for Aging and Health

UC Davis School of Medicine

Department of Epidemiology and Preventative Medicine

Dr. Mary Haan has worked in public health and medicine since 1969. She received her doctorate in epidemiology in 1986, and has been a faculty member of the School of Medicine at UC Davis since 1991. The Center for Aging and Health, which she has directed since 1992, is an interdisciplinary education and research unit, focusing on a broad array of health issues that affect older adults. Dr. Haan’s primary research is into the health of older women. Notably, she is the CoPI of the Women’s Health Initiative Vanguard Clinical Center at UCD. She is also conducting research into the role of diet in the prevention of breast cancer. She is widely published on topics related to adult health.

Kathleen M. Egan, Sc.D.

Harvard Medical School

Harvard School of Public Health

Department of Epidemiology, and Department of Ophthalmology

Dr. Egan is a graduate of the Harvard School of Public Health, having completed a doctorate degree in Epidemiology in May 1996. Dr. Egan’s primary research interest involves exploring the role of lifestyle, primarily diet, in the development of breast cancer. With expertise in Cancer Biology, Dr. Egan is also engaged in studies examining genetic aspects of breast cancer, including the role of family history, and the interactions of family history with established breast cancer risk factors. During the past six years, Dr. Egan has served as Project Director of a multicenter population-based case control study of breast cancer.

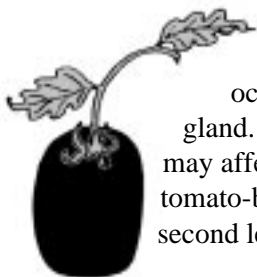
Dr. Edward Giovannucci

Harvard Medical School

Harvard School of Public Health

Dr. Giovannucci graduated from Harvard University in 1980, and receive a medical degree from the University of Pittsburgh School of Medicine in 1984. After completing his residency, he returned to Boston where he completed a doctoral degree in epidemiology from the Harvard School of Public Health in 1992. Currently, Dr. Giovannucci is in the Department of Nutrition at the Harvard School of Public Health and the Department of Medicine at the Harvard Medical School.

Over the past decade, Dr. Giovannucci’s work has included the study of how dietary factors and other “lifestyle” or “environmental” factors influence the occurrence of various cancers, particularly malignancies of the colon and prostate gland. His recent work has included a study of how tomato and tomato-based products may affect risk of prostate cancer. He and his colleagues found that high consumption of tomato-based products appear to protect against risk of developing prostate cancer, the second leading cause of cancer death in U.S. men.



CALIFORNIA TOMATO GROWERS ASSOCIATION

“Health & Tomatoes”

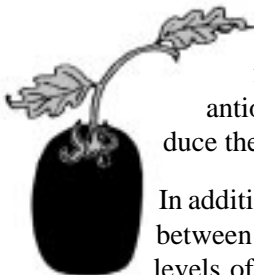
EXECUTIVE SUMMARY

Pizza, ketchup and canned tomatoes are all included in the recipe to fight cancer according to panel of leading researchers who met during the California Tomato Growers Association’s 50th annual meeting in early February. In the discussion, led by moderator Dr. Mary Haan of the U.C. Davis School of Medicine, Dr. Edward Giovannucci and Dr. Kathleen Egan, both of Harvard Medical School, labeled processing tomatoes as the richest food source of lycopene, a carotenoid thought to be especially powerful in fighting free radicals that may lead to some types of cancer.

Based on his research of male subjects who had five or more servings per week of processing tomato products, Dr. Giovannucci saw a 40 percent reduction in the incident of prostate cancer. Prostate cancer, Dr. Giovannucci says, is the number one cancer found in men and strikes over 200,000 men in the United States annually leading to 40,000 deaths.

“The bottom line is that there has been three studies to date that have looked at lycopene and prostate cancer, and all three studies show a benefit of lycopene or tomatoes,” said Giovannucci. All bodies produce off-balance molecules called free radicals, Dr. Haan explained. These molecules indiscriminately create chain reactions that produce more free radicals. All of this leads to damage to critical cells in our bodies, which accelerates the aging process. The process is called oxidation, and places humans at high risk for heart disease, makes us more vulnerable to cancers and is possibly linked to Alzheimer’s Disease, reported Haan, who heads the Center for Aging and Health at U.C. Davis.

Earlier research has found that fruits, vegetables and reduction of dietary fat intake can help prevent free radicals from doing harm. Many fruits and vegetables contain substances classified as antioxidants. Among these substances are vitamin C, vitamin E, vitamin A, retinal, keratin, gluten and lycopene. These antioxidants seize rampaging free radical oxygen molecules and convert them into harmless forms. Researchers feel that combinations of antioxidants may be the most effective way to reduce the risk of cancer and heart disease.



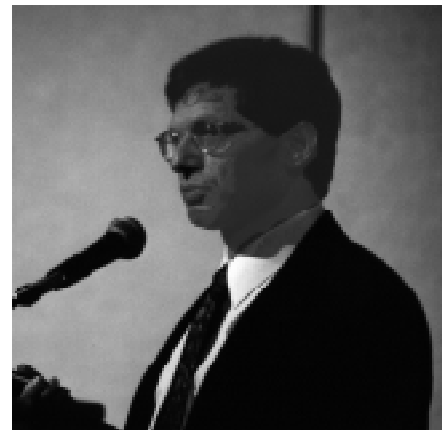
In addition to the widely reported research on the link between processed tomato consumption and reduced levels of prostate cancer, Dr. Haan says that studies



DR. MARY HAAN



DR. KATHLEEN EGAN



DR. EDWARD GIOVANNUCCI

have drawn similar parallels between a diet rich in tomato products and reduced levels of gastrointestinal cancers.

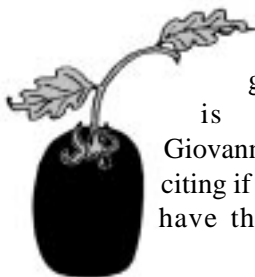
“A recent comparison of people living in Naples, Italy to those living in Gristle, England revealed that the Italians ate more tomatoes and tomato juice along with olive oil, and had about 40 percent lower levels of oxidation of lipids, which is a contributor to arteriosclerosis, hardening of the arteries, than the British group,” Dr. Haan said.

Her studies of breast cancer led Dr. Egan to give tomatoes greater attention as a possible preventative. “We’ve recently become interested in the question of whether the carotenoid, lycopene, may be a critical preventative for breast cancer, given that it’s the most potent antioxidant among carotenoids,” Dr. Egan announced. She claims that most lycopene in the diet comes from tomato sources. “At least one study does suggest a protective association for lycopene in human breast cancer,” Dr. Egan said. She says that she will address the question definitively in a large case control study of breast cancer involving 10,000 women.

“It will come as good news to many that french fries with ketchup and pizza with sauce several times a week may not be so bad after all,” Dr. Egan said.

The role of tomatoes in the diet was further emphasized by Dr. Giovannucci. “There are 14 different types of carotenoids that are important enough for us to mention,” he stated. “And the tomato is an important source of 8 of the 14.” Giovannucci explained that lycopene is readily absorbed into the body, in contrast to other such substances, and is the most concentrated antioxidant found in the prostate. “Lycopene

gets in the prostate, which is exciting,” said Giovannucci. “But it is more exciting if you think lycopene may have these beneficial effects



against cancer in terms of preventing free radical reactions.”

In his initial studies researching the affect of diet on prostate cancer, Dr. Giovannucci says three foods were readily associated with decreased risk of prostate cancer: Tomatoes, tomato sauce and pizza.

“We wanted to be cautious, as we waited another two years,” Dr. Giovannucci says, before he recreated the study. “Again, these same three foods, tomatoes, tomato sauce and pizza, were associated with lower risk of prostate cancer.” The test was conducted yet a third time with the same results.

“The relative risk (of developing prostate cancer) for consumption (of tomato sauce) of two to four servings per week was reduced by 24 percent,” Dr. Giovannucci told the audience. “And the men consuming five servings a week, had a 40 percent reduction in risk.”

“The strongest benefit we’ve seen [against cancer] was with tomato sauce and processed tomatoes,” said Giovannucci. “For some reason, it seems lycopene is absorbed better into the body through tomato sauce and other processed tomato products than fresh tomato products.

“In terms of overall health, the message should be for the American public to increase consumption of fruits and vegetables,” he said. “One caveat that I would like to add is that it’s important to have a variety of tomatoes or processed tomatoes (in that diet).”

Dr. Haan wrapped up the session by pointing out the opportunities open to the tomato industry. “I only hear good things about the tomato industry,” she said. “So I think you have a golden opportunity to support more research in this area and also to promote your product as a healthy and safe product.”

CALIFORNIA TOMATO GROWERS ASSOCIATION

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Transcript of Panel Discussion

February 6, 1997

DR. MARY HAAN:

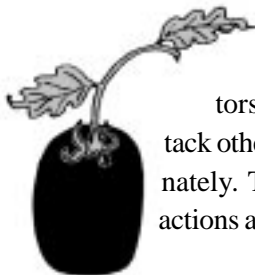
I'm particularly happy to be speaking to a group of tomato growers. I live in Solano County myself surrounded by tomatoes, and I understand that tomatoes are one of the largest legal cash groups in Solano County.

Tomatoes have come a long way since the Middle Ages when they were dubbed “love apples” and believed to be poisonous. Far from being viewed with suspicion, tomatoes are now believed to contribute to good health and to retard heart disease, cancer, dementia, and other degenerative diseases of aging.

I'd like to spend a few moments now explaining why tomatoes and other vegetables and fruits may help us to live longer, healthier lives. My colleagues will go into more depth about their research into the health benefits of tomatoes and other substances that are similar to those found in tomatoes.

All bodies produce what are called free radicals. These are not carryovers from the 1960's, but are, in fact, molecules that are off balance. They've lost an electron and

are out looking for a replacement. Free radicals are the bad actors of the body. They attack other molecules indiscriminately. They produce chain reactions and make more free radi-



cals. They break up other molecules and create cross-linkages between molecules that shouldn't exist. If they were human beings, they'd be arrested.

All of this leads to damage to critical cells in our bodies, and they accelerate the aging process. Indeed, this damage by free radicals may be one fundamental reason why we age, and the more free radicals we are exposed to, the faster we may age. This process is called oxidation. Oxidation puts us at high risk for heart disease and atherosclerosis and may also enhance damage to our genetic material and make us more vulnerable to cancer. Oxidated damage has also been linked to Alzheimer's Disease and other dementias.

Some of the things that we do to our bodies such as smoking, breathing in pollutants such as nitrous oxide, eating a fatty diet and not exercising, speed up the creation of free radicals. Is there any hope against the gang of free radicals? The hope in this case comes largely from three sources: vegetables, fruits, and reduction of dietary fat intake. Today we're going to be talking in depth about how my favorite vegetable, the tomato, may help to prevent disease. Dietary fat also affects health by producing oxidation or by influencing hormones that would lead to cancers and other health problems.

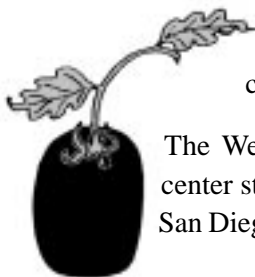
Many fruits and vegetables contain substances classified as antioxidants. These are the substances that combat oxidation. Although the major source of these is from our diets, our bodies also manufacture some of them in response to our diet. What are these and how can we get them? The list is long, but to name just a few: Vitamin C, Vitamin E, Vitamin A, retinal, keratin, lycopenes, and gluten.

These heroes of the body work in a wide variety of ways to protect our bodies against the invasion of free radicals. For

example, beta keratin molecules will seize a rampaging free radical oxygen molecule and convert it into a harmless form. Combinations of the antioxidants may be the most effective way to reduce risk from cancer and heart disease. Tomatoes contain high levels of lycopene, one of many antioxidants, and lower levels of other antioxidants including beta keratin.

Research is ongoing that examines the contributions of vegetable consumption and food consumption, intake of vitamin supplements and dietary fat reduction in relationship to the risk of heart disease, cancer, dementia and many other serious diseases of aging. Some research, which you will hear about today, is specifically focused on tomatoes or on lycopene and keratins.

Some of that research is happening right here in Sacramento. A great deal of my research is focused on the Women's Health Initiation, which is a national clinical trial involving 167,000 women nationwide. Here in Sacramento we have recruited nearly 4,000 women between the ages of 50 and 79, and approximately 1,400 of them at this time are involved in this study that is looking at the relationship between a diet that is high in fruits and vegetables and low in fat and its relationship in the prevention of both breast cancer and cardiovascular disease. This constitutes one of the largest major clinical trials that has ever specifically looked at dietary factors in breast cancer.



The Well Study, also a multi-center study, coordinated out of San Diego is a study that I'm in-

involved in that is looking at the question as to whether a diet high in fruits and vegetables and low in fat can help to prevent breast cancer from recurring in women who have already had it. So these two studies are extremely important. They look at whether we can prevent breast cancer and heart disease by changing our diet, and they also look

LYCOPENE

- most potent antioxidant among carotenoids*
- red pigment in fruits and vegetables*
- more than 90 percent of dietary lycopene comes from tomatoes*
- protective against prostate cancer*
- few data on the role of lycopenes in other 'oxidative stress' disorders*

at whether we can prevent mortality from breast cancer by changing our diet.

As Dr. Giovannucci will tell you in more detail, he has linked consumption of tomatoes and tomato sauce to a reduced risk of prostate cancer. You could consume tomatoes, tomato sauce, tomato juice and pizza and you may reduce your risk of prostate cancer by as much as 35 percent and have fun doing it.

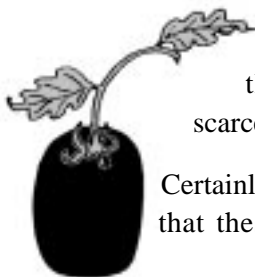
Just to put you in the picture a little bit, and I'm sure Dr. Giovannucci will go into more detail about this, prostate cancer is an extremely common problem in men. About 99 percent of men actually develop microscopic prostate cancer. Another 50 percent or so progress to macroscopic levels of disease and another 50 percent after that progress to clinically treatable prostate cancer, but only about 3 percent of men die from it. Nevertheless, it's a very large public health problem, and if tomatoes can be found to produce significant contribution to preventing the progres-

sion of this disease, that will be a very important contribution indeed.

Other studies have shown a reduced risk of various gastrointestinal cancers in people who eat tomatoes, especially with the intake of raw tomatoes, which may reduce your risk of esophageal, stomach and colon cancer by as much as 60 percent. It has also long been observed that Mediterranean people have lower levels of heart disease than people living in other parts of Europe and the United States. And a recent comparison of people living in Naples, Italy to those living in Gristle, England, revealed that the Italians ate more tomatoes and tomato juice along with olive oil and had about 40 percent lower levels of oxidation of lipids, which is a contributor to atherosclerosis, hardening of the arteries, than the British group.

In a more general way, the role of antioxidants such as Vitamin E, carotenoids, in the cardiovascular disease reduction continues to be extensively investigated, and the news is generally good. As we all know, dependency, dementia and memory loss is common in elderly people. However, the benefits of antioxidants in our diet for prevention of these problems have scarcely been examined.

Certainly the protective effects that these substances seem to



have on heart disease and stroke will extend to preventing memory loss and dementia that are a result of cardiovascular disease. It is the case that elderly people often become disabled and become dependent as they age, and Dr. Snowdon, who could not be here today, has conducted

this study on elderly nuns which showed a very strong relationship between high levels of Lycopene, which is again, found in tomatoes, and a reduced risk of dependency in older nuns.

Finally, Dr. Kathleen Egan will talk to us about her research into whether tomatoes, and more specifically, lycopene and other carotenoids can help to prevent breast cancer. The role of diet in the prevention of breast cancer is one of the most controversial areas in the world of science. The link between dietary intake of vegetables or fat in breast cancer has not been established. As I mentioned earlier, the Women's Health Initiative Clinical Trial is addressing this very question.

As you can see, there are many positive signs that tomatoes and other fruits and

vegetables can play a very important role in health, and I would now like to turn to the next panelist, Dr. Egan, to discuss her work with you in more detail. Thank you.

"It's believed that a diverse selection may be most effective in guarding against disease, and here tomatoes win out over all other good carotenoid sources. Nine distinct carotenoids have been identified in tomatoes compared to only two in broccoli and three in carrots, for example, and several are found in no other food source. Tomatoes are also the richest source of the carotenoid, lycopene, which new research shows may reduce cancer incidence."

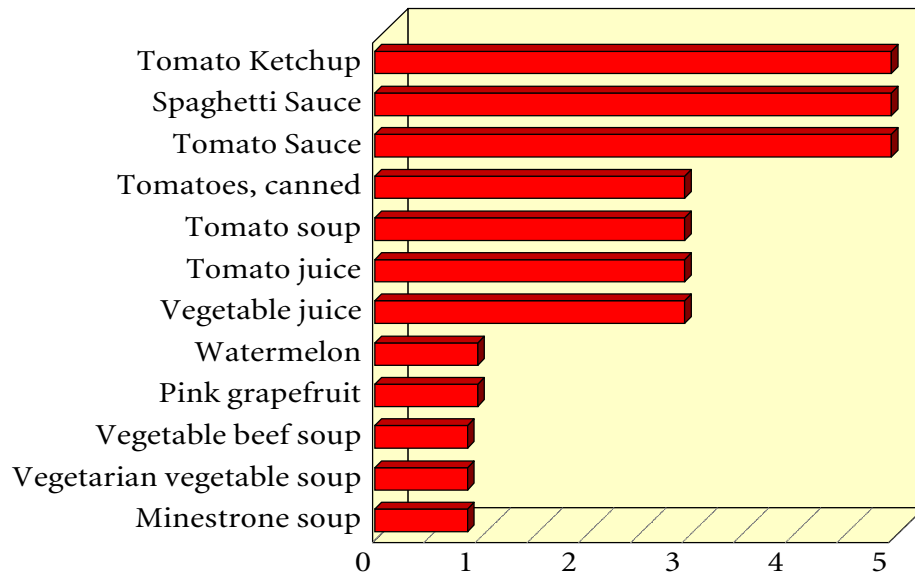
Dr. Egan

DR. KATHLEEN EGAN:

I'm going to spend the next ten minutes talking about some of the latest evidence supporting a protective influence of carotenoids found abundantly in tomatoes against certain eye diseases and cancer in general.

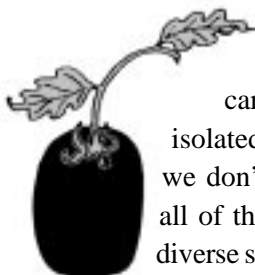
Lycopene in the American Diet

Milligrams in 1 oz.



As Dr. Haan mentioned, researchers are interested in dietary carotenoids based on experimental data and growing evidence from studies in human populations that these compounds protect against oxidated damage. Damage in target molecules by highly reactive particles called free radicals is thought to play a role in all major chronic diseases which plague mankind.

As tomato and processors you might be interested to know that tomatoes are a particularly rich source of carotenoids. A large number of nutritional



carotenoids have not been isolated to date in part because we don't know the function of all of them. It's believed that a diverse selection may be most ef-

fective in guarding against disease, and here tomatoes win out over all other good carotenoid sources. Nine distinct carotenoids have been identified in tomatoes compared to only two in broccoli and three in carrots, for example, and several are found in no other food source. Tomatoes are also the richest source of the carotenoid, lycopene, which new research shows may reduce cancer incidence.

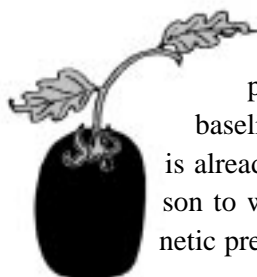
Carotenoids are thought to be potentially important players in the prevention of an eye disease known as age-related macular degeneration. Now, this is an obscure disease, but really shouldn't be, because it is the leading cause of irreversible blindness in the Western world. There's good news now though. Diets with high levels of certain carotenoids may prevent against this devastating disease.

This slide shows results from a recent study which compared the diets of 356 persons with AMD to 520 healthy controls. What these numbers tell you is that diets rich in various carotenoids, particularly lutein and zeaxanthin,

protect against the worst forms of AMD. Looking at the result for lutein and zeaxanthin to the far right, people in the highest, 20 percent of intake, had less than half the risk of disease compared to those in the lowest 20 percent, and the risk declined progressively with increasing dietary levels.

Now, carotenoids are pigmented molecules that give fruits and vegetables their color. An accumulating body of evidence suggests that multiple servings of these foods every day may also protect against many cancers. In fact, there's an impressive consistency among epidemiological studies, most of which shows substantial reductions in cancer mortality among persons consuming large quantities of the fruits and vegetables known to be good carotenoid sources.

My research at the Harvard Medical School focuses primarily on dietary determinants of breast cancer. Data from a large study we completed several years ago suggests that carotenoids in general can reduce the risk of breast cancer, particularly among women with a family history of the disease. Our data indicates that as much as 25 percent reduction in risk can



be achieved in these women, which is important because their baseline risk of breast cancer is already elevated in comparison to women without this genetic predisposition.

But we've recently become interested in the question of whether the carotenoid, lycopene, may be a critical preventative for breast cancer, given that it's the most potent antioxidant among carotenoids, and it has been shown by Dr. Giovannucci and his colleagues to reduce prostate cancer risk. Most lycopene in the diet comes from tomato sources.

Evidence from the laboratory is encouraging. In one study, lycopene was more effective than either alpha or beta keratin in controlling growth in human endometrial lung and breast cancer cell lines. The line on the bottom in every case corresponds to the curve for cell lines that were exposed to lycopene, and you can see the growth is cut almost to zero.

Breast Cancer Risk According to Carotenoid Consumption CBCS 1 ('89-'91)			
1000 IU/day	Family history of BRCA?		
	No	Yes	
<2	1.00	1.00	
2-3	0.98	0.79	
4-5	0.92	0.67	
6-8	0.89	0.76	
.8	0.77	0.73	
P for Trend =	0.01	0.02	

Advanced AMD According to Carotenoid Consumption EDCCS (1986-1990)				
356 subjects with exudative AMD / 520 controls				
Quintile	Beta Carotene	Lycopene	Lutein / Zeaxanthin	
1	1.00	1.00	1.00	
2	0.86	1.00	1.14	
3	0.86	0.70	0.84	
4	0.72	0.70	0.77	
5	0.59	1.16	0.43	
P for trend =	0.03	0.96	< .001	

In laboratory mice bred to have a high background incidence of mammary tumors, tumor incidence was substantially reduced in animals fed a diet high in lycopene compared to controls. In every case, at every age, the animals fed diets high in lycopene had a much lower incidence of mammary tumors.

Now, currently there's only very limited epidemiological data, but at least one study does suggest a protective association for lycopene in human breast cancer. So we plan to address the question definitively in a large case control study of breast cancer in which more than 5,000 women with invasive disease and 5,000 healthy controls were asked about their typical diets including consumption of

tomatoes. Analyses of data from that study are currently underway.

Now, it appears that despite all the evidence that a good diet prolongs life and prevents disease the message has not gotten out to many Americans. Data from the second national health and nutrition survey suggests that the majority of our citizens are not eating their vegetables against current recommendations by the USDA that five or more servings per day promote health. Therefore, it will come as good news to many that French fries with ketchup and pizza with sauce several times a week may not be so bad after all. Thank you.

DR. EDWARD GIOVANNUCCI:

We all know what a tomato is. Now, for the hard part, what's inside. These are a list of the various carotenoids, at least a chemical formula. Fortunately, I won't be quizzing you, but it's interesting to know that there is a variety of different chemicals in tomatoes and other fruits and vegetables.

As Dr. Egan mentioned, tomatoes are a particularly good source of



a lot of different carotenoids. There are about 14 different of these chemicals that are absorbed in appreciable amounts in the body. There are actually about 600 or more carotenoids in nature, but given our dietary sources and the foods that we eat, there are only about 14 that are important enough for us in terms of what we eat. And the tomato is an important source of 8 of the 14. As was mentioned earlier carrots, which we always associate with beta keratin, is really a source of beta keratin and a few other carotenoids, but it has almost essentially no lycopene, which seems to be an important carotinoid. So tomatoes are a very good source of carotenoids.

"...a very interesting finding in that there were three foods that were associated with decreased risk of prostate cancer. These were tomatoes, tomato sauce and pizza, and these were all independently statistically significant related to reduced risk of prostate cancer."
-Dr. Giovannucci

Now, as this slide demonstrates -- these are various carotenoids of these chemicals in tomatoes, and the first one is lycopene. But as you can see, tomatoes also has some other carotenoids which may have some benefit. My talk will focus on lycopene because that is a particularly important carotinoid in crunching these free radicals.

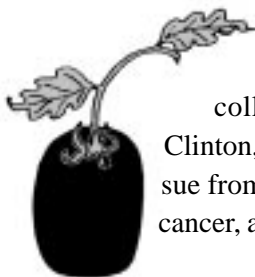
Probably what happened many billions of years ago is that plants developed these chemicals to protect them against sunlight, and the lycopene seems to be probably the best,

Relative Risk (RR) of Prostate Cancer Adjusted for Age and Total Energy, Excluding Stage A1 and 95% Confidence Intervals (CI) Among 47,894 Members of the HPFS (1986 to Jan. 31, 1992)						
	Q1	Q2	Q3	Q4	Q5	P trend
a-carotene						
RR	1.00	1.05	1.09	1.07	1.09	0.77
B-carotene						
RR	1.00	1.24	0.96	0.99	1.05	0.70
B-cryptoxanthin						
RR	1.00	0.97	1.14	0.99	0.94	0.76
Lycopene						
RR	1.00	0.90	0.94	0.89	0.79	0.04
Lutein						
RR	1.00	1.01	1.01	0.96	1.10	0.34

or at least among the best, of these compounds. It's like our bodies. We don't get the same damage from sunlight that tomatoes are exposed to every day, but we do have a lot of chemical reactions that have similar oxidated reactions, chemical reactions to free radicals. It seems perhaps gratuitous that lycopene may help us in terms of quenching these bad reactions.

So now I'll talk a little bit about prostate cancer. These are a list of cancer rates in men in 1994 and top on the list is prostate cancer. Prostate cancer is by far the number one cancer in men, followed by lung cancer. The slightly good news about prostate cancer is that not all the cancers are deadly. In fact, probably about 20 percent that are diagnosed may be deadly. There are 200,000 cases diagnosed every year, but 40,000 men die of the disease. So while a lot of the cancers are not that malignant, still 40,000 men in the United States every year is a very high number, and there's effectively no good treatment for prostate cancer once it has spread.

So it seems that the best thing that you can do is prevent the disease. Early detection is good, but even that's questionable. Given that treatment is probably many years away, if not decades, it seems that all we can hope for now is to prevent the disease, and I think perhaps that's where diet may have a role as I will talk about carotenoids and the prostate.



In a study done by a colleague of mine, Steve Clinton, in Boston, he got tissue from men who had prostate cancer, and this is actually look-

Multivariate Analysis of Current Use of Tomatoes as Related to Prostrate Cancer Risk in Male Adventists '(1976-82)

Food Frequency	RR(95% CI)	Two-tailed P Value
< 1 x/week	1.00	
1-4 x/week	.64 (.42-.97)	0.02
> 5 x/week	.60 (.37-.97)	0.02

ing at the normal prostate tissue to see if these carotenoids actually get into the tissue. This brings up somewhat of an interesting point.

The beneficial effects of grapes and how a compound in grapes is good for cancer made the news recently. I don't mean to offend anyone who might be in the grape industry,

but that compound actually is not well absorbed into the body. So even though this study was very exciting and should be followed through, I don't think that really can explain much in terms of what we know now about cancer.

"This shows that the more tomato sauce you eat, the lower your risk goes. And those men consuming five servings a week actually have the lowest risk of prostate cancer. They had a 40 percent reduction in risk."
-Dr. Giovannucci

Lycopene, in contrast, is found in very high quantities in the body. So we seem to absorb lycopene, and, in fact, in the prostate. On average lycopene is the most concentrated carotenoid in the prostate. This is exciting if you think lycopene may have these beneficial effects against cancer in terms of preventing

free radical reactions.

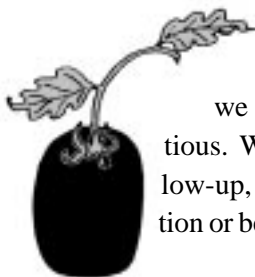
We conducted a study testing a hypothesis in human population. We have detailed dietary information on 52,000 men, and, as shown in the diagram, we collect dietary information every four years. The study began in 1986, and we collected diet information again in 1990 and again in 1994. So this is an ongoing study, but one of the points of the study is to look at what men were eating in 1986, for example, to see if their diet is related to various cancers and other diseases, and one of my interests was looking at

prostate cancer. I also looked at prostate cancer and the various carotenoids in risk of prostate cancer.

This slide shows a lot of potential beneficial compounds in many fruits and vegetables. I certainly agree with the statement that a diet high in fruits and vegetables offers many potential benefits in terms of health. Perhaps, some benefits are very specific to certain diseases. Perhaps, Vitamin C is beneficial to some disease and another compound for another disease.

For prostate cancer we did a very simple analysis just correlating intake of all these fruits and vegetables to a risk of prostate cancer. As you can see in that long list, there is no association with most of the fruits and vegetables. So high intake, for example, of bananas didn't increase or decrease your risk of prostate. There was no association. Now, if you look at the bottom, where it says "reduced risk", we have at first glance a very interesting finding in that there were three foods that were associated with decreased risk of prostate cancer. These were tomatoes, tomato sauce and pizza, and these were all independently statistically significant related to reduced risk of prostate cancer.

When we saw this association, we didn't want to jump the gun. An association was seen in 1988, but we wanted to be very cautious. We conducted more follow-up, and again this association or benefit was there in 1990.



Again, we wanted to be extra cautious, and we waited another two years, and again these same three foods: tomatoes, tomato sauce and pizza, were associated with lower risk of prostate cancer.

"It seems that the potential benefit of tomatoes was even considerably stronger with more aggressive cancers. So not only do you get less cancers, you get less aggressive cancers. You have an even more dramatic reduction in mortality. So there's like a 40 percent reduction in overall risk, but perhaps a 50 to 60 percent reduction in mortality from prostate cancer."

-Dr. Giovannucci

act same associations uphold.

This slide shows tomatoes, tomato sauce, and pizza, and the relative risk for consumption of two to four servings per week. What this actually shows is the men who were consuming tomato sauce two to four times per week had a relative risk of .66. That's a 34 percent reduction in risk of prostate cancer. That was highly statistically significant.

For those consuming canned tomatoes two to four per times per week, there was a 26 percent reduction in risk. And men who consumed the same amount of pizza saw a 15 percent reduction of risk. These were all statistically significant. This shows that the more tomato sauce you eat, the lower your risk goes. And those men consuming five servings a week actually have the lowest risk of prostate cancer. They had a 40 percent reduction in risk.

So at that point we felt that this can't just be chance. There's something. These three foods that are high in lycopene and perhaps other carotenoids have been associated with a lower risk of prostate cancer. In a sense, three consecutive studies -- supported our findings, and that's when we published the study you probably heard about last year. We are continuing our study, and, in fact, we see a stronger association with even more follow-up. The initial study went up to 1994. Now, we have follow-up to 1996, and, again, the ex-

In fact, what was even more interesting to us was -- as I mentioned earlier, prostate cancer comes in different forms. Some of them are quite benign, but a certain percentage are quite aggressive, and cause mortality relatively quickly. It seems that the potential benefit of tomatoes was even considerably stronger with more aggressive cancers. So not only do you get less cancers, you get less aggressive cancers. You have an even more dramatic reduction in mortality. So there's like a 40 percent reduction in overall risk, but perhaps a 50 to 60 percent reduction in mortality from prostate cancer.

Now, in these studies, even though we tried to be as careful as we could, we actually statistically controlled for many other factors. What that means is that we're looking to see that perhaps the people who eat tomatoes were exercising more or doing something else that was beneficial, but to the best that we can tell, this benefit seemed very specific for tomatoes and not something else in the tomato consumer's lifestyle that was accounting for this benefit.

Another bit of interesting evidence is that a few other studies, smaller studies, demonstrated the same asso-



ciation. This is a similar study and again you can see the relative risks for consumption. The bottom line is that men consuming the high levels of tomatoes (I think it was like

four times a week or more) had a relative risk of .60, which means a 40 percent reduction. That is very consistent with our study about a 40 percent reduction of risk and high consumption.

Another study that actually collected blood samples from over 10,000 men, followed the men over time. They looked at various levels of these carotenoids in the blood that was collected years earlier, and the men who had the high levels of lycopene had the lowest risk of prostate cancer. They had about a 70 percent reduction in risk of prostate cancer.

So the bottom line is that there have been three stud-

ies to date that have looked at the connection between lycopene between and reduced risk of prostate cancer. All three studies show a benefit of lycopene or tomatoes. They are almost indistinguishable. We have other studies ongoing to look at this in more detail. The preliminary results

"For some reason it seems that the lycopene is absorbed better into the body in tomato sauce or processed tomatoes than in the fresh tomato, which is quite interesting. You hear sometimes negative things about processing foods but, in this particular case, it seems that processing may actually have a benefit in making lycopene more easily absorbed into the body."

-Dr. Giovannucci

Age and Energy Adjusted Relative Risk (RR) of Prostate Cancer by Intake of Primary Contributions of Lycopene in the HPFS

No. of Servings:	0	1-3/mo	1/wk	2-4/wk	P for trend
Tomato Sauce					
No. of Cases	209.00	313.00	158.00	65.00	
RR	1.00	0.85	0.77	0.66	0.00
Tomatoes					
No. Of Cases	148.00	161.00	300.00	155.00	
RR	1.00	0.90	0.91	0.74	0.03
Pizza					
No. of Cases	396.00	287.00	60.00	11.00	
RR	1.00	0.94	0.76	0.85	0.05

Relative Risk of Prostate Cancer by Intake of Tomato Sauce, Tomatoes, Tomato Juice and Pizza

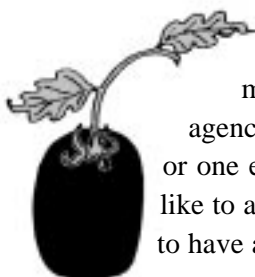
Servings per week	<1.5	1.5-4	4.1-7	7.1-10	>10	P-trend
PY	41,802	95,674	70,202	32,202	15,834	
Total Cases	168.00	293.00	176.00	102.00	34.00	
RR	1.00	0.92	0.78	0.85	0.65	
(95% CI)					0.44-0.95	0.01
Stage C/D	53.00	115.00	61.00	34.00	8.00	
RR	1.00	1.15	0.86	0.88	0.47	
(95% CI)					0.22-1	0.03
Stage D	26.00	55.00	34.00	18.00	2.00	
RR	1.00	1.11	0.96	0.94	0.24	
(95% CI)					0.06-1.02	0.12

look quite promising in confirming this association with tomatoes.

And just a final point I'd like to make is that the strongest benefit that we saw was with tomato sauce, processed tomatoes. For some reason it seems that the lycopene is absorbed better into the body in tomato sauce or processed tomatoes than in the fresh tomato which is quite interesting. You hear sometimes negative things about processing foods, but in this particular case it seems that processing may actually have a benefit in making lycopene more easily absorbed into the body.

QUESTIONS

DR. GIOVANNUCCI: I will say that in terms of overall health, the message should be for the American public to increase consumption of fruits and vegetables, and that's a wide recommendation made by many agencies. But the one caveat or one extra point that I would like to add is that it's important to have a variety, and tomatoes,



or processed tomatoes, should definitely be part of that equation.

For example, the recommendations to increase fruits and vegetables to at least five servings a day -- if you eat five apples a day, you follow the recommendation, and five apples a day is fine, but you won't get many carotenoids, especially lycopene and other compounds.

So I think the key -- I don't like to want to just focus on tomatoes, but, I believe, it's an important part of a healthy diet, and I think the evidence is becoming quite clear that that's the case.

DR. HAAN: Let me follow-up with another question to you, Dr. Egan. Is there any study now that shows that a diet high in carotenoids and especially lycopene can prevent the progression of breast cancer once a person already has it?

DR. EGAN: That's a really interesting question, and it's one that my colleagues and I at Harvard School of Public Health hope one day to be able to address. We are actually thinking of forming a cohort of breast cancer survivors from whom we collect dietary data and follow those same women forward in time to determine whether any aspect of diet may determine survival with breast cancer. But to my knowledge there is no study at the moment which addresses that question directly.

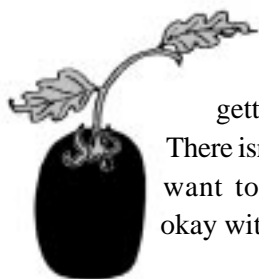
DR. HAAN: Let me ask one last question. What should the tomato industry be doing to promote these research

findings to consumers, if anything? Now, are we ready to go out there and promote tomatoes as a sort of prescription for any part of a healthy diet or is it too early to say?

DR. GIOVANNUCCI: Well, again, I would say that at this point the evidence is quite promising. In the scientific community we are taught to be quite restrained and conservative in terms of making widespread recommendations, but I think the evidence is quite strong. If you look at the overall diet, a diet that's high in fruits and vegetables is quite beneficial. That's been proven by hundreds of studies, and I think the evidence in the last few years regarding tomatoes is relatively new, but it seems that study after study is beginning to show this, and Dr. Hahn mentioned earlier there are other cancers where it may be a benefit to tomatoes.

So there certainly doesn't seem to be much harm in eating the products and they're quite tasty, and the evidence is getting pretty good that tomatoes may have some extra benefit in terms of cancer and other diseases.

I think a point that I'd like to make is that people, sometimes in the press, and sometimes even in the research community, jump on one study and say well, this study shows this, and this is the end all. But what we try to do is to look at the evidence that's accumulating, and after literally hundreds of studies have tended to show something, then at



that point we'll make a recommendation. I think the evidence is getting strong for tomatoes. There isn't much harm. So if you want to recommend it, that's okay with me.

AUDIENCE MEMBER: Basically is it better for health to eat processed tomatoes or fresh tomatoes?

DR. GIOVANNUCCI: Well, our study showed that the processed tomatoes were more strongly beneficial for prostate cancer. In another study that we did we found that the

"Another point is that to absorb lycopene you need some oil, a little bit of fat, and it seems that making spaghetti sauce, cooking it in some olive oil, is the ideal way to absorb lycopene."

-Dr. Giovannucci

tomato sauce was by far the strongest predictor of lycopene in the blood. And, in fact, tomato juice did not predict lycopene in the blood. In other words, the men drinking fair amounts of tomato juice did not have an increase of lycopene in the blood. It probably has to do with something in the processing, perhaps in the cooking of tomatoes, that's important.

Another point is that to absorb lycopene you need some oil, a little bit of fat, and it seems that making spaghetti sauce, cooking it in some ol-

ive oil, is the ideal way to absorb lycopene. So I think the processing and the cooking in an oil medium is probably the best way to absorb lycopene. But I also will say that I think there needs to be more specific studies in this area. This is a very new theory of research.

AUDIENCE MEMBER: What portion constitutes a serving?

DR. HAAN: Generally, that will be about a half cup. I don't know specifically with respect to tomato paste, but if you're looking at, say, consumption of raw tomatoes, about half a cup constitutes one serving.

MALE AUDIENCE MEMBER: Is there a difference in the potential health benefits of tomato juice that is made from reconstituted tomato paste versus that tomato juice which is made directly from raw tomatoes?

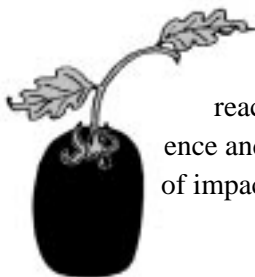
DR. GIOVANNUCCI: I think it's a very good question, and I think probably people up until a few years ago were not concerned about these questions. I mean, people didn't

really care how much lycopene you were absorbing from tomato juice or tomato sauce. Actually ever since our study came out, there are many people in the industry that have asked similar questions. I think that if there is a potential role for research that some of you people could support it would be looking at some of these issues. I think that would be important work to supplement our studies. I'm interested primarily in looking at the association with prostate cancer, and all these questions are very important, but we can't do everything. We don't have the money to do everything.

AUDIENCE MEMBER: At what point does the research community translate their finding into action by trying to influence government feeding programs or any recommendations to change the few programs that are available?

DR. EGAN: Generally that process takes years in terms of putting into, say, a nutritional labeling statement or availability under FDA of any health claim. I don't personally know of any particular process regarding tomatoes about that at the moment.

AUDIENCE MEMBER: It seems to me that the wine industry is riding the wave of the red wine-French Paradox phenomenon with far less conclusive studies than your studies. Why aren't your findings as broadly publicized and reaching as large an audience and making the same kind of impact?



DR. HAAN: First of all, it's more fun to drink red wine. And they must have a better PR firm. That would be my prediction. Actually, I am quite serious. I think that if the tomato industry were to take the evidence that now exists and try to translate that message to the consumer that it

"You (tomato growers) do not have any negative publicity or any negative findings that I'm aware of about the potential bad health effects of tomatoes. I only hear good things about tomatoes. So I think you have a golden opportunity to support more research in this area and also to promote your product as a healthy and probably safe product."
-Dr. Haan

would have a similar impact, although you might not be able to make quite the same claims that the alcohol industry has made. And I would say that at the moment the evidence that drinking red wine truly reduces the risk of cardiovascular disease is still quite an unanswered question although it's enjoyable to test the question.

DR. EGAN: I just would like to add to that wine has the baggage that alcohol probably does increase breast cancer incidence, and, of course, there's a segment of

the population prone to abuse. And this is a problem that you people won't have selling your product.

DR. GIOVANNUCCI: I agree with the premise of the question that there has been a real proliferation (of information about the health benefits of wine). I have to roll my eyes every time I hear something -- specifically about red wine, because I'm not sure -- there's very little evidence at all that there's anything specific to red wine beyond the alcohol benefit.

DR. HAAN: Before you all rush out and order a bottle of Johnny Walker Red, I'd like to mention that the evidence on cardiovascular disease and alcohol consumption shows that the reduced risk is really only for people who are moderate drinkers.

You (tomato growers) do not have any negative publicity or any negative findings that I'm aware of about the potential bad health effects of tomatoes. I only hear good things about tomatoes. So I think you have a golden opportunity to support more research in this area and also to promote your product as a healthy and probably safe product.

AUDIENCE MEMBER: How do we as an industry support research in this area without it being self-serving?

DR. HAAN: Generally, and I'm sure that Dr. Giovannucci or Dr. Egan could add to this, but generally what happens is that researchers at a University will receive funds. So believe me it happens that private industry gives money for research in the University and that the agreement will generally specify that the industry can control the conduct of the research, and, of course, any re-

searcher is concerned about those issues. However, I believe that, especially at UC Davis, there's a great deal of private industry support particularly for research in the food industry, and I would characterize that research in general as being above board, well done, and ethical.

DR. GIOVANNUCCI: Getting back to an earlier questions about absorption of lycopene and different products. I think that type of research is important, but it's less likely to occur. If the industry supports that kind of research, I think that it will add a lot of knowledge. Knowing if lycopene can be well absorbed without having the potential for bias and the studies correlating the lycopene directly with a disease. I wouldn't want to say that lycopene prevents prostate cancer sponsored by the California Tomato Growers, but you support studies looking at some of these issues in terms of absorption of a specific product and absorption of lycopene. I think that research will be very beneficial.



CALIFORNIA TOMATO GROWERS ASSOCIATION

“Health & Tomatoes”

References and Resources

Dr. Gay R. Beecher
USDA/ARS/BHNC/FCL
Building 161, Room 202
Beltsville, Maryland 20705
Phone: 301-504-9161

*Additional Resource**

Steven K. Clinton
Dana-Farber Cancer Institute
Boston, Massachusetts
Phone: 617-632-3000

Studying how reduced prostate cancer may be related to consumption of tomato-based foods

Dr. Leonard Cohen
American Health Foundation
1 Dana Road
Valhalla, New York 10595
Phone: 914-592-2600

*Additional resource.***

Dr. Kathleen Egan, Sc.D.
Harvard Medical School
Harvard School of Public Health
Department of Epidemiology, and
Department Ophthalmology

Work on the effect of tomatoes and lycopene as a preventative to breast cancer.

John W. Erdman, Jr.
Director, Division of Nutritional Sciences
University of Illinois
449 Bevier Hall
905 S. Goodwin
Urbana, Illinois 61801
(217) 333-2527

Studying the dietary factors which affect how lycopene is absorbed into the system, transported and stored.



Dr. Jean G. Ford
Harlem Hospital Center
Division of Pulmonary Medicine
506 Malcolm X Boulevard, MLK 12-106
New York, New York 10037
Phone: 212-939-1459
Fax : 212-939-1456

Study of 92 patients with lung cancer and 103 cancer-free controls found that low plasma level of lycopene is associated with increased risk of lung cancer.

Dr. Edward Giovannucci, M.D., Sc.D.
Harvard Medical School
Harvard School of Public Health
655 Huntington Avenue
Boston, Massachusetts 02115
Phone: 617-432-4648
Fax: 617-432-2435

Cancer and the effect of lycopene on the prevention of prostate cancer and other cancers.

Dr. Myron D. Gross
Division of Epidemiology
13000 S. 2nd Street, Suite 300
University of Minnesota
Minneapolis, Minnesota 55455
(612-624-5417)

Has worked with Dr. David A. Snowden with the elderly to find high levels of lycopene in the blood correspond to ability maintain self-care while low levels correspond with inability to maintain self-care.

Dr. Mary Haan
Director, Center for Aging and Health
UC Davis School of Medicine
Department of Epidemiology and Preventive Medicine
Phone: 916-752-3967
Fax: 916-752-4474

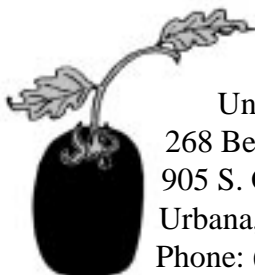
Doing research related to breast cancer and diet. Specifically with carotenoids.

Dr. Joseph Hotchkiss
Department of Food Chemistry and Toxicology
Cornell University
Ithaca, New York
607-255-7912

*Additional resource?****

Elizabeth Johnson
USDA Human Nutrition Research Center on Aging
Tufts University
711 Washington
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Boston, Massachusetts 02111
(617) 556-3133

*Additional resource.******



Barbara P. Klein, Ph.D.
Department of Food Sciences and Human Nutrition
University of Illinois
268 Bevier Hall
905 S. Goodwin Avenue
Urbana, Illinois 61801
Phone: (217) 333-1325

Has studied the effects of canning on the carotenes in vegetables and found that they are just as available in canned as fresh vegetables. In some cases they appear to be more available as the result of processing.

Steven J. Schwartz
Department of Food Science
& Technology
Ohio State University
144 Howlett
Columbus, Ohio 43210
614-292-2934

Has studied the influence of processing on the lycopene in tomato tomatoes, the chemistry of lycopene and the physiological aspects of

Dr. David Snowden
Sanders-Brown Center on Aging
Department of Preventative Medicine
University of Kentucky
Phone: 606-257-1527
Fax: 606-323-2866

Lead researcher on study of the elderly indicating high levels of lycopene in the blood correspond to ability maintain self-care while low levels correspond with inability to maintain self-care.

**Dr. Beecher participated in the San Diego conference and is referred to as a research chemist in the article by Jane Brody.*

***Dr. Cohen is with the American Health Foundation which co-sponsored the San Diego conference. He was referred to us by Dr. Steven Clinton who said he does "animal research" in the field.*

****Dr. Hotchkiss' name comes to us from your original list. We have not been able to contact him to verify whether or not he actually does research in this area*

*****Dr.(?) Johnson.'s name was given to us by Dr. Steven Clinton with no description as to the nature of her research. Given the source, she is undoubtedly active in the field.*





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