

Diabetes and Antioxidants C & E: Narratives of Risk

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Abstract

This thesis examines the precautionary principle regarding antioxidants C and E, especially their safety for diabetics. Antioxidants are a common food additive used to prolong shelf-life. Vitamins and minerals are necessary for human health, but at the same time questions of toxicology are raised when consumption levels increase. Currently, diabetic and antioxidant researchers debate the safety of antioxidants C and E for diabetics. Researchers have documented lower antioxidant efficient pathways in diabetics. Diabetic research has thoroughly shown that the disease is associated with oxidative damage. Although how doctors, patients, and healthcare practitioners should respond to the lower antioxidant efficient pathways is not clear. My focus question therefore is ‘what accounts for the varying perspectives on antioxidants incorporated into diets for diabetes patients?’ Some argue antioxidants increase the health outcomes and others believe increased consumption strains the antioxidant networks and elicit pro-oxidation. In diabetics research for example, controversies exist to whether antioxidants C and E reduce blood sugar and increase insulin sensitivity or if they increase complications for diabetics. Methods include literature review, expert interviews in antioxidant and diabetes research, as well as narrative analysis. Narrative studies grounds the data in the controversies of antioxidant C and E use, toxicology, future trends of antioxidant research, and the role of narrative to reach conclusions about antioxidants and food additives in general. I argue the precautionary principle applies to vitamin C and E for diabetics.

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The Globalization of the Food Network

For as long as humans have lived in cities, food traveled to support their populations, distinguishing place of consumption from the food or food product. In addition, preservatives allow food to travel farther distances and stay on shelves longer, defying the nature of time. Developed urban areas rely on food production grown and raised elsewhere, generally from developing nations. Cities cannot entirely feed themselves, especially when varied diets and foods out of season are sought after. Carolyn Steel asks the important question of how cities feed themselves, which is often an overlooked phenomenon (Steel 2009). Today, to eat local food is a mantra which urges consumers to eat food grown closer to home, for both the health benefits of fresher foods and to reduce one's carbon impact. In light of risk, locally produced food may reduce risks which transcend space because the consumer is much more likely to establish a relationship to the producer in close proximity and the food is likely to pass through fewer hands. Fewer hands in the production means more responsibility placed on each individual. In addition, local food productions tend to - though not always - have a lower energy impact per calories it contains (McWilliams 2007). The modern transportation system, including shipping or trucking food from one location to another, depends on fossil fuels. However, one must be aware that a city cannot feed itself completely within its city limits through community supported agriculture, urban gardens and the like. Food miles are here to stay in this increasingly globalizing world and therefore the human health aspect of food additives becomes increasingly important.

Since the majority of food travels, preserving the food through its journey is necessary. One way to reduce food spoilage, through prevention or delay of oxidation is to add antioxidants to food. Ascorbic Acid, commonly known as vitamin C and vitamin E are both antioxidants which are added to foods in order to react with unwanted oxygen. The result is an elongated

shelf-life and neutralized damaging substances known as free radicals in the body. The Food and Nutrition Board of the Institute of Medicine, proposes the following definition of antioxidants: “A dietary antioxidant is a substance in foods that significantly decreases the adverse effects of reactive oxygen species, reactive nitrogen species, or both on normal physiological function in humans” (1998). In this thesis, I specifically investigate the complimentary antioxidants C and E.

Chemically, antioxidants reduce the detrimental effects of free radicals. Oxygen in the atmosphere initiates reactions by either the loss of a hydrogen radical or the addition of a radical to a double bond (Desphande et al. 1996). Without antioxidants, a free radical or molecule with an unpaired electron reacts whenever possible. Therefore, free radicals are very unstable and continue a chain reaction forming lipid free radicals. Such a chain event will occur until two radicals bond to create a stable nonradical compound (Desphande et al. 1996). Vitamin C prevents loss of color and flavor in foods, especially used in meat, fruit drinks, and breakfast cereals while not altering the taste of the substance (Center for Science in the Public Interest 2014). Vitamin E in the form of alpha tocopherol is a nutritive antioxidant especially found in vegetable oils, commonly used to prevent oil rancidity. Vitamin E and C are complementary; vitamin E fights free radicals in lipids and vitamin C works in water solutions. In addition, vitamin E and C are uniquely interconnected because vitamin C has the ability to regenerate the active form of vitamin E. Vitamin C thus counteracts lipid oxidation because it converts the tocopherol radical to alpha tocopherol, allowing vitamin E to continue acting as an antioxidant. Such paired antioxidant pathways are known as an antioxidant system (Deshpande et al. 1996).

Marion Nestle, a writer, and a professor of nutrition, food studies and public health, believes part of the answer as to why so many foods are fortified lies in food companies’ desires to design “healthier” foods. Vitamin C and E are unique additives because they preserve food. At

the same time, antioxidants add necessary vitamins for human health. As more people spend an increasing portion of their budget on food prepared outside the home, improved nutritional quality was pushed as beneficial to the industry as well as the consumer's health (Nestle 2003). A new wave of fortification emerged in food additives as nutrient deficiencies became replaced by chronic diseases such as cancers, heart disease, arthritis, and diabetes. In 1994, The Dietary Supplement Health and Education Act prevented the US Food and Drug Administration (FDA) from enforcing nutritional supplementation in the United States. Thus, marketers could proclaim structure function claims or "how ingredients might alleviate deficiency, improve the structure or function of a part of the human body" (Nestle 2003, 225). Supplemental fortification is marketed to decrease chronic diseases and overall physical well-being in a single nutrient dietary vitamin or mineral. Supplementation of antioxidant vitamins is now a common additive, but these must be monitored by structural organizations to ensure their safety, like the US Food and Drug Administration (FDA). Vitamin E and C add nutrients in packaged foods, but that does not always mean they are safe for all populations. The increased consumption of these antioxidants may be safe for healthy individuals, but those with diseases may suffer consequences.

The Precautionary Principle

The precautionary principle is a common theory and framework which guides decision-making practices for numerous ecological and health policies, governments, and programs which aims to prevent harm and unforeseen damages associated with human action. The theory of the precautionary principle is necessary when toxicological studies and benefits of antioxidant consumption are inconclusive, particularly evident in the case of synthetic derivatives of vitamin C and E. The precautionary principle states that if an activity raises threats of harm or potential harm to either human health or a species and their habitat, precautionary measures should take

effect if scientific controversy exists (Hanekamp 2006). A certain level of risk is always present by non-human forces. Through modernization, humans are exposed to new manufactured risks (Beck 1992). A key element of the precautionary principle is time, or rather its timeliness: “to impose timely protective measures to prevent uncertain risks, that is, risks as to which there is little or no data on their probability and magnitude” (Hanekamp 2006). Guaranteeing safety to the public in scientific research becomes of utmost importance in this theory, and incorporates the lack of certainty.

However, there is always some level of uncertainty. The precautionary principle recognizes the limitations to science, and unavoidable nature of uncertainties. However, the theory is not against science, because it calls for more research. But at the same time the theory does not provide a clear answer to a health or biological problem (Pollan 2001). Uncertainties in science then lead to “ethically difficult policy decisions,” in which cost and benefits are incorporated (Proctor 1998). The precautionary principle consequently incorporates a long term horizon and less quantifiable risks usually ignored by other risk models (Pollan 2001). One question therefore is how uncertain experts in antioxidant research and healthcare professionals are about the scientific studies about this issue. And underlying my research is the question of the risk verses benefits of antioxidants and when one draws the line between consumption and avoidance of these vitamins.

Ulrich Beck, in his work *Risk Society: Toward a New Modernity* (1992) argues in today’s modern society, risks are not bound by time or space. Thus, risks easily transverse national boundaries and a majority of societies and demographics are exposed to hazards never before faced. In addition, the risk system focuses on scientist’s laboratory knowledge and not their application to society, questioning the truth of the findings. Unlike earlier societies, today no one

is considered liable or responsible for risks because products pass through an increasing number of handlers. Therefore no one person or group of people is considered responsible for a product. In order to reduce the appearance of lack of control in terms of risk, institutions are in place to ensure that dangers are minimal.

In the United States, the FDA and USDA are federal entities which regulate antioxidant content in food. Tocopherols in the vitamin E family and ascorbic acid have GRAS status, meaning the USDA considers these additives “generally recognized as safe,” which is commonly abbreviated to GRAS (Shahidi 2005). A food with GRAS status allows the additive that was used before the 1958 Food Additives Amendment to be exempt from testing because of “experience based on common use in food” (FDA 2014), or because of the scientific procedure. Substances with GRAS status do not require premarket testing or authorization for human consumption (Nestle 2003). The FDA describes this phenomena in general terms without specifics, stating that a GRAS “substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive” (FDA 2014). According to the Center for Science in the Public Interest (CSPI), they state that antioxidants C and E are additives that “the additive appears to be safe.”

In this thesis, I argue that the precautionary principle applies to the consumption of antioxidants C and E for diabetics. The increased consumption of vitamin C and E today does not automatically make a diet healthier, and potential benefits for diabetics are namely unknown - but benefits could be substantial with further research. At the same time, vitamin C and E raises questions of their potentially harmful effects for certain groups of people, specifically diabetics. Thus, the CSPI’s endorsement of the safety of vitamin C and E for most groups of people may

give a false sense of safety before benefits and risks are identified. In reality, uncertainty remains about vitamin C and E derivative toxicology and the effect to which they are beneficial. Such uncertainty is due to a variety of complex reasons. Therefore, questions still need to be explored in this field such as ‘what accounts for the varying perspectives on antioxidants incorporated into diets for diabetes patients?’

Antioxidants as Food Additives

Vitamin C and E are of the most important natural antioxidant groups that are highly effective at reducing free radical damage. Natural antioxidants mean they occur in plants, spices, lipids and amino acids. Due to the effectiveness of antioxidants, chemical synthesis of vitamin C and E has advanced to a successful commercial scale. Not only are synthetic versions created, but also derivatives of antioxidant molecules, which produce a substance that is not found in nature. The effectiveness of these synthetic substances has come into question by some. Antioxidants are most effective at very low levels, and at higher levels, antioxidants actually initiate free radical reactions, posing the same problems which they are intended to reduce. Consequently, as antioxidants are consumed in supplements and added to preserve foods at levels humans naturally would not consume, establishing an acceptable daily intake level becomes crucial for scientists and researchers.

The human body is always exposed to a certain amount of oxidation. For example, cellular respiration is necessary for human survival, yet requires oxidation to produce energy from food. Free radicals are also generated because of toxicological factors such as polluted air, nitrogen dioxide, cigarette smoke, smog and soot in urban air and automobile exhaust (Deshpande et al. 1996). In biological systems, pesticides, herbicides, and toxic waste produce

free radicals. Since oxidation is always present, a balance between oxidation and antioxidant availability is important to reduce the body's oxidative stress.

Regulation of Antioxidants

Food regulation in developed nations has existed for numerous decades. Toxicological studies aim to determine the safety of antioxidants and also determine Acceptable Daily Intakes (ADIs). In order to be a satisfactory food additive, an antioxidant must fulfill certain conditions. For example an antioxidant:

should be soluble in fats, it should not impart a foreign color, odor or flavor to the fat even on long storage; it should be effective for at least one year at a temperature of between 25-30 degrees Celsius; it should be stable to heat processing and protect the finished product, it should be easy to incorporate and it should be effective at low concentrations. (Pokorny et al. 2001)

Toxicological studies also test the carcinogenic properties of antioxidants and regulators state that there should not be any effect on the growth of an experimental animal in long term studies when given at a level 100 times higher than the proposed human consumption value (Pokorny et al 2001). However, such studies of individual antioxidants do not test how antioxidants will react in a product with other antioxidants, nor do these tests enable one to predict the function of pro-oxidants already in the food.

The US: FDA and USDA

The FDA and USDA, or United States Department of Agriculture, regulates antioxidant additives in food production and packaging in the United States. As noted before, vitamin C has GRAS status, and due to toxicological research, vitamin C has no usage limits. Consequently, it

is often added to foods externally. Vitamin C has been documented to be safe at supplementation levels of 600 mg/day. However, natural ascorbic acid can easily be destroyed in food processing, due to factors like heat, pH, and light (Shahidi 2005). Such fragility of vitamin C has driven manufactures to prefer chemical ascorbic acid (Pokorny et al. 2001). The USDA and FDA limit tocopherols to 0.03% or 300 parts per million in animal fats and 0.02% when in combination with butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate (PG), which are all synthetic antioxidants commonly added to foods. Alpha tocopherol consumption of 1000 mg/day is reported without risk, and up to 3200 mg/day supplementation is without consistent risk. In the US, some report that many men and women actually fail to receive the recommended consumption of vitamin E (Shahidi 2005).

The European Union

In European countries, antioxidant regulation is regulated by the European Economic Community or the EEC. Food additives are restricted by national order, meaning European countries must abide by national regulation and cannot authorize additional additives not already permitted in foods (Pokorny 2001). Additives, including antioxidants are only permitted in certain foods in addition to specific conditions of use. However, there are some differences in terms of utilization of antioxidants in various food products. Europe is a model for the system of national coordination. At the moment, efforts to maximize coordination in international regulation are in place. Regulation of antioxidants focuses on safety, but at the same time it aims to promote human health.

Toxicological Aspects

Vitamin C occurs widely in nature, and for healthy individuals, consumption is generally considered safe. Since vitamin C is water soluble, excess consumption leads to increased urinary oxalate levels. There is a chance that too much vitamin C could lead to kidney stones. However, some antioxidant researchers believe even with large daily intakes, the amount of oxalic acid formed is too little to cause harm. In rat models, high vitamin C consumption strains the liver and can lead to death. In humans, very high levels of vitamin C doses of 6000 mg/day can cause adverse effects of nausea, vomiting, headache, and fatigue (Desphande 1996).

To add another layer of uncertainty to antioxidant studies, the use of animal models does not “adequately recapitulate the effects of vitamin C deprivation and supplementation observed in humans” (Michels & Frei 2013). The reason is based on the genetically different synthesis capabilities in animals other than humans. For example, animals have the ability to produce ascorbic acid and thus the implications of such animal studies are limited in their conclusions for humans (Michels & Frei 2013). Differences like these illustrate the profound impact of evolutionary processes and remind us of the unique bimolecular pathways of mammals.

Vitamin E toxicological studies are even less conclusive than vitamin C studies because of the many families of vitamin E. The tocopherols include alpha, beta, gamma and delta. In addition, these four variances are also found in the tocotrienol family. Unlike vitamin C, which by definition is ascorbic acid and is chemically indistinguishable between a natural source and chemical synthesis, vitamin E is a much more complicated molecule. Molecules of vitamin E can be synthesized with different orientations of chemical bonds in the head and tail that cannot be found in nature (Michels 2015).

Both synthetic and natural forms of tocopherols are produced commercially, as well as mixed tocopherol molecules. Tocopherols as a family are used in food additives, but their absorption in the human body is not fully known. In addition, the acute toxicity of alpha tocopherol for example is not known. In humans, hypervitaminosis E, meaning high levels of vitamin E, can cause nausea, gastrointestinal problems, fatigue and impairment of blood coagulation (Desphande 1996). However, at normal doses, vitamin E is critical for eye and reproductive health as well as it inhibits some known carcinogens.

Antioxidants play a large role in the food additive world, and they are important in the global food network. The points above illustrate the complexity of antioxidant research for the general population, as well as the uncertainties around toxicological data for vitamin C and E. In order to reduce risk, these antioxidants are regulated by government entities as discussed earlier. Now the focus of this thesis will shift toward explaining the controversy specifically in terms of diabetics through interview narratives with experts in vitamin and diabetes researchers.

Antioxidants and Health Effects: How safe is vitamin C and E for diabetics?

The Current Understanding of Diabetes

For diabetes research, antioxidant studies are a controversial topic, with little conclusive evidence. Framing the diabetes and antioxidant debate is the effectiveness of antioxidants for healthy individuals. Scientists currently debate the value of vitamin C and E for healthy individuals, but once someone has a disease, the story becomes even more complicated, adding many more layers of complexity (Michels 2015). What guidelines hold true for a healthy population do not necessarily hold true for someone with a disease.

Diabetes Mellitus, commonly referred to as diabetes, is a chronic disease meaning it has no cure. The disease occurs when the pancreas' beta cells do not produce enough insulin or the

body is unable to use insulin effectively (WHO 2015). Insulin is a hormone which regulates blood sugar, and without insulin blood sugar rises and can cause significant damage to nerves and blood vessels. The overwhelmingly majority of diabetics are diagnosed with type II diabetes, accounting for over 90% of diabetics (WHO 2015). To make matters more pressing, rates of mainly type II diabetes continue to rise. Type II diabetes is commonly believed to be due to lifestyle factors and choices of foods and exercise, not a genetic inability to produce insulin as seen in type I diabetes. Barbara Corkey, a diabetes and nutrition researcher at the Boston University School of Medicine received the *2011 Banting Medal for Scientific Achievement Award*, the highest scientific award from the American Diabetes Association due to her proposed model of type II diabetes. She suggests that due to altered food, activity, and external factors, levels of insulin are induced. Insulin “superimposed on a susceptible genetic background, or basal hyperinsulinemia is the root cause of insulin resistance, obesity, and diabetes” (Corkey 2011). Corkey argues that new agents have entered our food supply without evaluation of causes of and for obesity or diabetes:

Many foods contain preservatives, emulsifiers, flavor enhancers, food coloring, and other fillers that have not been previously consumed in significant quantities. Virtually none of these nonfood compounds have been carefully assessed for a potential impact on obesity or diabetes. (Corkey 2011)

In her study, Corkey found an emulsifier mono-oleoylglycerol (MOG), artificial sweeteners saccharin, aspartame, and sucralose, and iron stimulate insulin secretion. Noteworthy is how common these items are to packaged foods as fillers and additives, which are being consumed at a higher rate. Today, the rise of diabetes seen increasingly among young children sparked the renaming of Adult Onset Diabetes to type II diabetes. Therefore, the role to understand

antioxidants in relation to oxidative stress, and the implications for this research is growing and is unfortunately applicable to a wider audience every day. Diabetes rates continue to skyrocket in both industrialized and non-industrialized nations.

Researchers have documented lower antioxidant efficient pathways in diabetics. Diabetic research has thoroughly shown that the disease is associated with oxidative damage (Rosen 2000). Many studies have documented this affect and the idea that diabetics have increased oxidative damage is not argued. Whether or not oxidative stress is a component in the genesis of diabetes is controversial, oxidative stress plays a role in complications due to diabetes and in the development of insulin resistance (Rosen 2000). The antioxidant network is an important component of diabetic investigation because as blood glucose levels rise, reactive species formation increases and a reductive imbalance occurs. Thus, the balance between oxidants and antioxidants is believed to be an important factor in maintaining health and proper function of the body, as well as protecting against diseases including diabetes, cancer, cardiovascular disease and many other chronic illnesses. The goal of this project is to understand how the research community and doctors can overcome boundaries in diabetes antioxidant research in order to establish a balanced and effective dose of antioxidants for patients, which will help maintain health while at the same time avoids pro-oxidation.

How doctors and patients should respond to increased oxidative damage in diabetics is currently debated. The possibility always exists that adding vitamin E and C to the diet will “add more fuel to the fire” by enhancing oxidative stress, since antioxidant vitamins do not always act as antioxidants (Michels 2015). On one side of the debate, the idea of supplementation to reduce the amount of oxidative damage persists and hopes to lesson damage to vasculature and cardiovascular risk (Neumiller 2015). Vitamin C added to the diet in the form of

supplementation is believed to reduce harmful oxidation due to high levels of blood sugar. Others believe high levels of vitamin C in the diet of diabetics actually increases risk of death from stroke and the risk of dying from coronary artery disease (Raloof 2005). Similarly, vitamin E research among diabetics is just as inconclusive. Vitamin E might temporarily enhance the body's sensitivity to its own insulin for type II diabetics. Increased insulin sensitivity is beneficial to a diabetic patient who suffers lack of sensitivity to insulin as body mass increases and the receptors of insulin malfunction. But vitamin E also could lead to a risk of blood sugar levels falling far too low. Others warn vitamin E can actually raise blood pressure in people with diabetes, posing problems of excessive bleeding, and possible increases in mortality (Neumiller 2014).

As a society, we are far from understanding all the physiological and mechanical mechanisms of antioxidants, especially vitamin E's influence on the body (Brigelius-Flohe 1999). Due to vitamin C and E's complementary nature, an investigation of these two antioxidants is an important factor in the antioxidant system. Furthermore, not only are antioxidants hardly understood, but how they interact with other food additives or other vitamins and minerals is almost impossible to know.

Methodology

In order to grasp the reasons for controversy in the field of antioxidant effectiveness and safety, I interviewed experts in the field. Five inquiries were sent out to possible interviewees, and three of those respondents were interviewed. The interviewees include a post-doctorate vitamin C researcher, a pharmacist and diabetes educator, and a practicing doctor and researcher of diabetes. Interviews were conducted over the phone and Skype and transcribed. Permission was granted from the interviewee to record the conversation in order to preserve the accuracy of

the respondent's wording. Once transcribed, the interview was analyzed using thematic analysis, a methodology often used in rhetoric and media studies. The interviews connect the field of diabetes and antioxidant pathways to theoretical understanding to the issue at hand. Riessman, a scholar of qualitative research, argues that thematic analysis is a valuable tool to make sense of data by connecting larger social structures or macro contexts with a personal narrative. She writes that power relations, hidden inequities, and historical contingencies become evident in this methodology (Riessman, 2008). Then, I discuss the types of narratives my respondents follow, and consider six commonly used narrative modes to connect the experts' interviews to a larger theoretical body of knowledge to understand how their story propels through time. To investigate the nature of the narrative allows one to infer how one views the future of antioxidant research as well. I consider the interviews narratives, as they are a story as to why each professional believes the antioxidant and diabetes controversy exists and where it stems from. At the same time, these narratives are partial truths; narratives include what each person believes to be important with the possibility of excluding other factors.

Humans inevitably tell narratives to explain events. William Cronon, a professor of history at Yale University argues in his work, "A place for stories: Nature, history, and narrative," that we connect the past in a meaningful way in order to make sense of history. He states:

When we describe human activities within an ecosystem, we seem always to tell stories about them... we configure the events of the past into causal sequences - stories - that order and simplify those events to give them new meanings. We do so because narrative is the chief literary form that tries to find meaning in an overwhelmingly crowded and disordered chronological reality. When we choose a plot to order our environmental

histories, we give them a unity that neither nature nor the past possesses so clearly.

(Cronon 1992, 1349)

Nature does not provide us with stories; humans craft a story with a beginning, middle and end. In doing so, one defines relevant voices while excluding others. The story thus moves “well beyond nature in to the intensely human realm of value” (Cronon 1992, 1349). Cronon also discusses two types of narratives which I too discuss later: progressive and declensionist narratives. These two narratives will help to illustrate the power of social constructions and human discourse.

The Contradictions in Diabetes Research

The lack of agreement in diabetes research is a complex topic with many reasons accounting for uncertainty. Early in conducting interviews, lack of agreement became clear in the numerous factors involved in the research. Marketing, study design, issues of funding, difficulties understanding the mechanisms of the disease of diabetes, and heterogeneity in the population all add layers of indecision as to whether or not antioxidants such as vitamin C and E are safe and effective for diabetes.

Alexander Michels Ph. D, a vitamin C research associate at the Linus Pauling Institute at Oregon State University in Corvallis, points to the influence of marketing in vitamin E and C on the public’s understanding of antioxidants. Dr. Michels suggests marketers are able to make claims about derivatives or chemically modified vitamin E and C supplements without backing up such health statements. For example, a derivative of vitamin C, Ester-C is thought to be better absorbed. Dr. Michels states how “that is marketing, and the data does not support those claims” and that “there is no evidence one way or another in most cases and so they use it as a marketing tactic” (2015). Furthermore, some marketers do not want the debate of vitamin C and E to be

completely resolved, because supplement companies will do more business in the uncertainty. He points out that “They actually obscure the answers a little bit because they do better business in the uncertainty. If everyone was certain vitamin C supplements work, there would be no market for the next vitamin C supplement” (Michels 2015). The supplement industries push their products, and thrive on formulating new products in the future. Though, one should be aware that the doses companies push may or may not be healthy, yet people still fall for marketing constantly. Dr. Michels’ view points to the power of the media and marketers to spin a story and influences the public’s beliefs about antioxidant derivatives.

Supplement companies are also aware of their customer’s views, which influences the product purchased. The synthetic version of vitamin C is virtually indistinguishable from a natural source of vitamin C. The molecule is the virtually the same no matter the source of vitamin C. However, vitamin E is a more complicated molecule which when chemically synthesized can result in an alternation of the molecule, which is not found in nature. Thus, people extend the synthetic verses natural argument onto vitamin C, even though chemically speaking such an argument does not make sense for vitamin C (Michels 2015). Even though such information is misguided about the source of vitamin C, marketers still pay attention. “They don’t want their products to lose market share because they don’t have the right formulation,” especially in terms of the non-natural forms (Michels 2015). In general, the supplement industry continues to succeed on a lack of data. To add more confusion to the controversy, the majority of the public does not understand the differences of vitamin C and E derivatives on a case by case basis.

The experiment itself and the conditions of the study are also an important factor adding to uncertainty in the diabetes and antioxidant world. The lack of scientific agreement of

antioxidant effectiveness is rooted in a lack of conscientious in the criteria of antioxidant experiments. Dr. Michels claims:

Cell culture conditions greatly determine the outcome of a vitamin C experiment. This is an introduction of bias toward a particular conclusion before the experiment has officially begun. You set up your results before you start the test, which is a predisposition for a certain result, either a positive finding for vitamin C or a negative finding. (2015)

If more conclusions are to be drawn on antioxidants in diabetes management, the research community must define the studies better and pin-point criteria of relevance to their investigation. Questions of antioxidant supplement use are numerous, but “before we ask the question we need to set up the right criteria” (Michels 2015). Poorly designed studies are one thread of disputes in antioxidant research, and to move forward scientists need to have a clearer idea of these criteria. For example, such criteria could incorporate genetic variation of a population or polymorphisms. According to Dr. Michels we do have a sense of the criteria, but at the same time we know no study meets all the standards of a vigorous study. Part of the inclusive research is related to the little agreement among scientists of how antioxidant research should be done in order to yield meaningful results.

Not only are some studies flawed, but some findings in a study are also misinterpreted, or misinterpreted when the study is read by an individual. Dr. Robert Stanton, educator at Joslin Diabetes Center, the world’s largest diabetes research center in Boston, MA, discusses how another layer of confusion stems from misunderstood studies and the biological mechanism of humans. For example, antioxidant levels are often traditionally believed to be due to more or less oxidative stress. Dr. Stanton points out

But that does not take into account the changes in the antioxidant...so unless you think of it as a whole system you potentially misinterpret the findings. And that does happen quite often because you never thought about the other interpretation. (2015)

In addition, he discusses how NADPH, a compound required in the antioxidant network is necessary to promote a reducing cell surrounding and also resists oxidative stress. The main source of NADPH for the antioxidant system is glucose 6-phosphate dehydrogenase (G6PD). G6PD is often believed to be readily available, yet that is not always the case (Stanton 2015). Therefore, many studies may potentially misinterpret the findings simply because the whole biological system is not taken into account or because one never thought of another possible interpretation. Such a problem may stem from an absence of multiple disciplines and collaboration of backgrounds needed in order to understand an antioxidant study and its findings to the full extent.

Quantifying vitamin C and E intake also poses a difficult dilemma. Dr. Joshua Neumiller, a pharmacist and certified diabetes educator, as well as an associate professor of pharmacotherapy at Washington State University in Spokane, argues the difficulty to control consumption of vitamins during a study. As a pharmacist by training, he compares antioxidant research to drug trials. A problem in antioxidant research is controlling for non-study related vitamin intake. Dr. Neumiller discusses the dilemma in terms of vitamin C research:

A big issue in vitamin studies is how do you quantify how much vitamin C people are getting from their diet or other multivitamins they are taking or if they are drinking orange juice? I mean you name it; it is so hard to control their consumption of these products that you are trying to regulate in a placebo control environment. It is hard to

make a firm conclusion that was due to your intervention. The same is true for vitamin D, E, C, it is really hard to control versus a drug trial. (2015)

Quantification of vitamins in antioxidant research is an enormous limitation. As Dr. Neumiller states, in a drug trial, one can be sure the quantification of the drug is only consumed in the dose provided. Though, diet can largely affect antioxidant content, as sources of antioxidants are so varied and commonly consumed in various amounts by individuals.

How vitamin C and E is measured due to consumption and supplementation is also a predicament, as effects vary across individuals. Dr. Michels believes a common mistake in vitamin C and E antioxidant research is the assumption that a supplement was effective. For example, vitamin C can be measured in the bloodstream, but he questions how many studies test vitamin C blood levels instead of just assuming it has reached the bloodstream: “[researchers] give a supplement, and make the assumption that it is absorbed... but do they actually look?” (Michels 2015). For vitamin E, the issue is even more complicated because this antioxidant is fat soluble and stored in the body’s tissue. Michels explains, “The plasma levels are not actually reflective of an indicator of where it goes because vitamin E is fat soluble so it goes to your tissues and hangs out in the membrane. So how do you measure that? You can’t necessarily take the tissue” (2015). Such assumptions relate to the discussion earlier of a lack of consensus of what constitutes a robust study and the ability to misinterpret a study due to assumptions.

Vitamin C and E research in diabetic patients is a complicated topic with many different pockets of research. Dr. Neumiller further relates this issue in terms of three main areas of research in diabetes including cardiovascular events, blood sugar effects and prevention. These fields have overlap, but Dr. Neumiller suggests that “people look at it from different angles and

people can't add those studies together to make a meta-analysis to bolster your power to try to see an effect because they are looking at very different studies" (2015). Diabetes research incorporates a variety of areas of interest as mentioned above, yet it is important to understand how each area is connected to diabetes but also has a unique issue in and of itself. Dr. Stanton also echoes a similar concern, discussing how diabetes antioxidant research may have too large a target, or scientists may not be targeting the right mechanism. Thus, the correct antioxidant pathway may not be under investigation. For diabetes, Dr. Stanton believes efforts to target antioxidant inhibitors are increasing, but again, researchers are still in the midst of understanding the correct mechanism to target. The diabetes community must critically evaluate which studies are successful and then hone in to refine specific targets before anyone can move forward.

Funding in the antioxidant world is also an important consideration of antioxidant research. Dr. Neumiller compares drug trials again to antioxidant research, pointing out that there is not one entity driving diabetes antioxidant research. He states:

I think we know what we need for a study to answer some of these questions, but in contrast to drug development where you have a drug company that is funding a study there is no good place to go for the amount of resources to perform a study. There is not an industry force driving the research, which I think is problematic. (Neumiller 2015)

Lack of funding is one possible piece of the controversy, linking back to the desire of disagreement in antioxidant research among marketers. The reduced funding affects the statistics of the power of a study. Compared to drug companies, Dr. Neumiller points out unequal opportunities for research prospects. In addition, studies in antioxidant research usually require long lengths of time in order to measure different outcomes in a diabetic population which

entails a large amount of resources. Most commonly, the smaller the sample size the less one can take away from those studies and apply it to diabetic populations. However Dr. Stanton takes a different view on the issue. He does state the difficulties in obtaining personal funding. But, he also points out the numerous studies which have been done and he thinks the study itself would have to incorporate a new variable or difference in order to obtain funding. He states:

I don't see people funding large vitamin E or C studies right now unless there was something very different, you know in combination with something else. Or realizing we should have given this dose all along, something scientific and realizing that is why we missed it. But short of that, people will sit there anecdotally arguing. (Stanton 2015)

The acknowledgement of funding is also an important element of such research. Funding in all other fields can influence a bias, but it is usually reduced or minimized with an acknowledgement of the source of funding. Dr. Stanton points out that one can interpret the study within the context of its researchers and funding sources. A dearth of funding, along with the lack of meaningful results in numerous studies has extenuated opportunities in antioxidant research, which means it has prolonged the controversy of antioxidant use for diabetic patients.

Variance in the population is another factor adding to the largely inconclusive evidence of antioxidant research. Dr. Neumiller describes the issue by saying:

There is a lot of heterogeneity in the population they enroll. There is lack of documentation of reserves for these vitamins so where they are deficient or not isn't really recorded and is hit or miss from study to study. (2015)

Genetic differences vary so widely throughout the population. Often times a study will therefore show no effect because of such inevitable differences, but also due to individual differences of

the vitamins stored in the body at the time of the study. Dr. Michels describes a similar phenomenon and points to a study which investigated vitamin E and people who had a haptoglobin polymorphism. These people have a genetic variation in the haptoglobin protein in the bloodstream which binds to iron. He explains:

And they found that when they gave vitamin E to those people who have the polymorphism, that they saw reduced risks of cardiovascular disease. Suggesting that under certain conditions, vitamin E supplementation could be helpful. If you look at the whole population regardless of their haptoglobin status, you saw no effect. Buried in the data is a group of people with a genetic polymorphism - and in those people vitamin E supplementation worked. (Michels 2015)

The size of a study is important, but in addition, the target of the nuance in the population greatly affects how meaningful the results in antioxidant research are. The example above shows the importance of building a study with a specific audience, or genetic variation in mind. This specific study shows the benefits antioxidant consumption in populations with haptoglobin polymorphism. Therefore, the study suggests antioxidants do have the potential to alleviate chronic conditions, under very specific conditions. To examine multiple factors at once in antioxidant research only complicates the argument further. In order to move forward, scientists, doctors, and researchers must acknowledge there is not one answer, but rather “go back to the basics and do it better if we really want to understand what is going on” (Michels 2015). Studies will require more specific investigations for particular populations, and precise inquiries to a particular diabetes stage, whether that is prevention, post-diagnosis, or cardiovascular complications. A one-size-fits-all approach is not the answer to diabetic research.

Experts show varying opinions on the future of antioxidant research. The prospects of antioxidants depend on whom one asks. Dr. Michels believes we are moving toward a time of more robust and targeted studies. However, the science world is not there yet, but we “have an idea what the criteria should be” (Michels 2015). A well designed study is one element, but as Dr. Michels points out, “whether or not we get a good answer is another question” (2015). How meaningful the results of a good study are in how they can affect and help the life of a diabetic patient is another question all together. Scientists may find meaningful results, though Dr. Michels points out:

Some evidence suggests that short-term effect of vitamin C supplements may make it easier on diabetics to regulate their blood sugar. But if you look ten years down the road are they [patients] faring better health wise because they took vitamin C supplements? That is still an unknown question. The success we have been having is little tiny studies that look at limited questions, but putting them all together in the big picture which becomes quite muddy. (2015)

Dr. Michels comments on the uncertainty not only around if antioxidants are beneficial for diabetics, but to what extent they have the ability to increase their quality of life and health in meaningful ways. These questions are currently not known or studied. The extent of other possible benefits requires much further investigation, and questions to what extent antioxidant supplementation affects quality of life.

In addition to the complications in diabetic antioxidant research discussed above, experts have different thoughts on how or if agreement regarding antioxidant use can be met in the future. Dr. Stanton believes the many possible uses of antioxidants will continue to limit the

agreement of scientists in the future. Antioxidants are not always antioxidants; they become pro-oxidants, the exact opposite of an antioxidant in great quantities. Dr. Stanton claims that “unless you can come up with a very targeted and specific mechanistic way to address this and a novel way of using it, I don’t see us reaching a consensus” (2015). Not only are antioxidants used in different ways in studies, people have an idea that vitamins are not bad or toxic and so they will continue to use them. The challenge therefore becomes trying to find an effective balance in a supplementation dose or consumption that does not harm the body and may provide health benefits. Dr. Stanton believes to get to a place where we know how to balance antioxidant consumption, the antioxidant world must shed itself from the fads of nutrition (2015). To some extent, oxidants are a part of life; they are necessary for energy metabolism for instance, and people usually take vitamin C and E without understanding what they wish to accomplish or fix in their body. The media may further this problem, and as Dr. Michels states, “It is kind of a doctor Oz thing, where someone recommends it and then everyone wants it without any evidence” (2015). Overall, once challenges are overcome, there seems to be a sense of hope to reach better knowledge of antioxidants as a therapy.

Revisiting the Precautionary Principle

The experts I interviewed all echoed the importance of the precautionary principle in the wake of minimal knowledge of antioxidant effects. Dr. Michels, Dr. Neumiller and Dr. Stanton all discussed the value of caution when asked about the precautionary principle; however the way in which they urged caution differed. Dr. Michels suggests “unless it is tested, you can’t say anything about it. We will have no data on a vitamin C derivative or mixture until someone performs a study on that particular formulation. Until the safety and efficacy studies are performed, we [the Linus Pauling Institute at Oregon State University] can’t recommend it”

(2015). He relates caution to testing, or the lack of testing which results in his cautious stance. Dr. Neumiller discusses the importance of the dose in safety of antioxidant consumption in comparison to drug models. He states:

Precaution is definitely warranted with these products the whole issue is the ‘poison is in the dose.’ We talk about in pharmacy that people.... they perceive these as safe because they are vitamins and natural and the like. But potentially anything you take can be too much. The literature on vitamin E and C and cardiovascular disease could be potentially a dose related issue. (2015)

The view of vitamin C and E as ‘natural’ may lend people to believe they are safe. However, natural and safe are not always equitable. Larger quantities of a substance always have the possibility to cause harm, and antioxidants are no different. In addition, Dr. Stanton states how he does not believe more of a supplement is better unless further research strongly suggests otherwise: “And I generally advise people not to take super high doses; I think there is a lot of evidence that shows a lot of something is not better than a little of something” (2015). Like Dr. Neumiller, Dr. Stanton points out the importance of the amount of substance one consumes. Furthermore, Dr. Stanton already incorporates the precautionary principle through his advice to not take high levels of antioxidants in order to ensure safe consumption levels and reduce oxidative stress. Overall, experts in diabetes and antioxidant research and clinical practice agree the precautionary principle is a necessary and valuable standpoint in the contemporary antioxidant debate for diabetics in the contemporary era. Without additional targeted research, patients may do more harm than good for their body especially if supplements are taken in too high a dose, which is a problem if a patient believes a produce being natural automatically means that it is safe.

The precautionary principle should not halt action. What the theory teaches humankind is necessary collaboration of many disciplines in order to unite scientific knowledge. Currently, some areas of studies in antioxidant research are under-appreciated, like genetics for instance. For example, Dr. Michels discussed above the importance of integrating genetics into antioxidant research through the haptoglobin polymorphism case. Antioxidant research must acknowledge the multi-faceted, complex nature of the problem and should consult a variety of expertise. Multi-disciplinary research is one solution to move toward understanding the controversy of antioxidant consumption for diabetics. Merging expertise also increases individual care and attention.

The precautionary principle has the ability to guide individualized medicine. Currently the answer to this dilemma is not clear and therefore the precautionary principle applies to this debate. However research may soon have the ability to suggest consumption levels based on individual profiles based on individual genetics, proteins, metabolites, and lifestyle and diet. Dr. Stanton exemplifies this point:

Using high or low dose you are using now is not justifiable, maybe in the future we will know better from biology or individualized medicine that will allow us to say you should take ten times the recommended dose ... That kind of balance, that will come (2015).

A valuable next step for diabetes research is to target specific differences in the population. Patient care will thus drastically benefit from individualized medicine, accounting for differences in medical profiles.

Due to the rarity of complete knowledge, the precautionary principle is therefore a tool in risk assessment. Currently, recommended intakes of antioxidants C and E for diabetic patients

are unknown. The best practitioners can do is to recommend the use of common sense and abide by the precautionary principle, unless further research suggests otherwise. The conversation of type I and II diabetes research relates to and is embedded in the safety of other additives and food products. We vote with our fork, and our food choices make a difference as well as portray our ethical beliefs. When we eat a meal, we support and send a message to what we believe is safe for our body.

Other contemporary health and science issues debated can also be viewed through a precautionary principle lens. For example, the use and incorporation of new molecules, chemical elements, pesticides, or bio-engineered organisms for instance all pose risks in conjunction with potential benefits. The introduction of these new, and possibly potentially harmful substances and technologies have long term consequences for the health of the public, numerous species and ecological habitats. Specifically, Genetically Modified Organisms, or more commonly referred to today as GMOs are a controversial subject. Genetically modified organisms incorporate genetic engineered organisms and the incorporation of select genes with specific traits from one organism to another. GMOs are argued to both increase crop yields and express desirable traits in organisms and also increase resistance in pests and diseases and introduce unforeseen consequences. Like the antioxidant and diabetes controversy, the precautionary principle applies to the GMO debate as well.

However, one must be aware of the tradeoffs inherent with the precautionary principle, specifically that beneficial technologies may not be implemented alongside a cautionary stance. In addition, the precautionary principle may not apply to situations and dilemmas which require timely action and attention, like climate change for instance. Climate change for example may be a case in which the precautionary principle does not apply as fully because of the nature of the

impeding problem and lack of time to implement policy. A certain amount of precaution is warranted, but in a time sensitive manner the precautionary principle may delay policy necessary for urgent matters. The precautionary principle guides humanity when risks can be avoided, or when risks and benefits are both unknown, but it must also be acknowledge how it does not fit all ecological and health dilemmas at hand.

Narrative Types and Future Trends

Each of the three narratives from the experts in antioxidants embodies a different narrative type, which opens a window into the individual and group subjective. The way a narrative is ordered allows one to see the personal interactions as well as the cultural institutions which shape the story. Thus how a certain story is told should be understood with its content in mind as well (Holloway 2005). Such an analysis of narrative types allows one to think beyond the data into how society and culture influence and construct the reality we tell. Kenneth Gergen in his work *Realities and relationships: Soundings in social construction* proposes three narrative types: regressive, stable, and progressive (2009). Regressive narratives show deterioration and decline through time. Stability narratives represent a steady plot and do not change over time. Finally, progressive narratives advance in plot (Holloway 2005). Arthur Frank, a sociology professor and writer of narratives, illness, especially regarding illness and medicine, discusses three other common modes of narrative. First, the quest narrative transcends hope, embraces novelty and the unknown, and is open to change. Second, chaos narratives lack plot, struggle to put a narrative into words and is characterized by a sense of hopelessness. Third, restitution narratives are at essence a narrative of confidence, and health to restore the body to its original condition (Frank 2013). Each body tells a unique story, and the ability to recognize a type of

narrative allows closer attention to the story and the problem faced. Oftentimes, narrative types are combined and mixed. Therefore, general types of narratives are able to aid the listener to better understand their story (Frank 2013).

Dr. Michels' narrative represents a combination of progression and regression in his narrative. He first brings up the notion that researchers are moving to a time when we understand the most effective way to conduct an antioxidant study, stating "I think we are moving toward that... but there are physician's practitioners in other fields that do not understand the nuances of vitamin research and antioxidant research" (Michels 2015). The use of the words "we are moving" are of special importance because they show progression toward a time when studies follow certain criteria. Later, he even uses the word progress: "as we have progressed we have realized there is no one size fits all protocol for everything." However, before the antioxidant researcher moves forward, Dr. Michels dwells on the fact that first movement backwards is required "to go back to the basics and do it better if we really want to understand what is going on" (2015). Dr. Michels' narrative exemplifies hope for the future of antioxidant research, but at the same time acknowledges that progress requires regression first to achieve successful results.

Dr. Neumiller's narrative demonstrates periods of stability with a small element of progress. He outlines numerous challenges to antioxidant and diabetes research. When I asked about the future of the scientific world, he responded "I think scientifically it is well known what the rigor and size of a study is needed" (Neumiller 2015). Interestingly, he believes we understand how to do a good study, but that we have not yet. He discusses the lack of an industry pushing an antioxidant research forward which he believes is problematic, and thus seems to indicate a lack of progress. Numerous barriers are evident even though "there has been hope for a long time that supplementation would decrease the amount of oxidative damage" (Neumiller

2015). Overall, studies are small and therefore lack power needed to make robust conclusions. He discusses a hope which exists but has not significantly moved the scientific community forward in antioxidant therapies for diabetics.

Dr. Stanton's narrative also illustrates a stability narrative, but he also presented a quest thread to his interview. He states how unless we find a new way to study antioxidants "people will sit there anecdotally arguing" in a static position (Stanton 2015). However, he does bring up a valuable meaning to the story. In the antioxidant controversy stems the idea of individualized medicine. Dr. Stanton points out "we are all trying to get to is the point where we have individualized medicine for each of us" (2015). Quest narratives confront the uncertainty and use it for a great good, to triumph medicine. Patient advocacy embodies a quest story which allows for a change and improvement in one's life.

The ability to understand the different narrative threads in the experts I interviewed connects their beliefs to larger narratives, and their understanding of the past and future of antioxidants. At the same time, new meanings and patterns emerge. Stories are never completely our own, we take bits and pieces and mold them, calling them "ours" even though they are gathered from others (Frank 2013). Narratives depend on certain structures as people make sense of an experience through narrative. Narratives are a technique to assemble our understanding on an issue or event and recommends how someone will act based on expectations and assumptions (Holloway 2005). At the same time, narratives are based on how the storyteller understands the world. In this case, the doctors I interviewed told a narrative to how they understand the antioxidant controversy, especially in relation to diabetes patients. Depending on their approach and connection of points, their story implies how cautious one should be through their different narratives.

The Stories We Tell

Part of the confusion of the safety of antioxidants and other food additives may also stem from how one narrates the story of not only antioxidants, but other food additives. We do not make food choices, or narrate a story in solitude. Humans continually interact and share beliefs and values. How one attributes meaning to their story affects the conclusion of the story, and the conclusion is implied based on the value intertwined in the story. Cronon (1992) explains in an example of two different stories about the same historical event:

Both narrate the same broad series of events with an essentially similar cast of characters, they tell two entirely different stories. In both texts, the story is inextricably bound to its conclusion, and the historical analysis derives much of its force from the upward or downward sweep of the plot. (1348)

Therefore, narratives embody a form which leads up to a goal, and ultimately a moral. Humans draw on their own sense of right and wrong, or values, to answer questions, conflicts and interactions. We tell stories because they are fundamentally engrained in our culture and also because some believe stories are the way in which we organize our experience (Cronon 1992). No matter the reason, stories are here to stay, and are a cohesive way to organize thoughts. Stories illustrate how we understand the world. The degree of concern of food additives and preservatives therefore is grounded in how a story is shaped and the extent to which one relays the risks or benefits of food additives.

How successful a story is in convincing its audience depends on the structure and appeal to the listeners. Some desire a depth which allows for increased explanation and causation of events, others breadth with only the most relevant details, while still some prefer many different

voices (Cronon 1992). What constitutes a good story depends on many factors and the audience's judgment of aesthetics. The listeners then interpret the meaning of the story based on their own values. Scholars and community members, or anyone who has a stake in the story, also participates in the story and "will also judge the fairness and truth of what we say" (Cronon 1992: 1373). Our stories are interactive, they change through time incorporating critiques and interaction, and they impact our understanding of the making and the workings of the world and nature. Narratives have the ability to shape our understanding and suggest the safety of not only food additives, but other potential risks to listeners as well. Thus the way in which we tell stories affects the conclusion and embeds actions with a sense of morality.

Conclusion

The precautionary principle relates to the debate over vitamin C and E for diabetics due to impending threats as well as benefits for patients. Consumption of antioxidants C and E have the potential to increase wellbeing because of their ability to reduce harmful oxidation and high levels of blood sugar that the diabetes population experiences, as well as enhance the body's sensitivity to insulin. However, antioxidants C and E also can raise blood pressure, lead to excessive bleeding, and possibly increase mortality, stroke, and coronary artery disease in diabetics. Unless future targeted studies for diabetics or mechanisms of genes, proteins, or metabolites suggest otherwise, increased consumption beyond levels necessary for bodily function exposes humans to otherwise avoidable risks. To abide by the precautionary principle for diabetes and antioxidant controversy is currently a rational choice.

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