
Targeted Nutrition in Health and Disease

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The use of food and nutrition in treating and preventing disease is certainly not new. But the Dietary Supplement Health and Education Act of 1994 created a new, and sometimes controversial, industry based on diet and health. Functional foods and nutraceuticals are foods or ingredients that are perceived by the consumer to be beneficial to health. The functional food industry has shown meteoric growth over the past several years, and is currently estimated at around \$18 billion in annual revenues. Growing acceptance of the role of nutrition in disease coupled with an expanding demographic provide strong fundamentals for continued growth of this industry.

However, major challenges remain. Early entrants to the nutraceuticals market relied heavily on advertising to gain market share, without strong evidence of product efficacy. Only in recent years, with the involvement of larger and more sophisticated companies, have science and proven efficacy brought broader support.

A GROWING MARKET

It is estimated that over 50% of the adult population now use some form of nutraceutical product for health reasons. Consumers report that the most common use of nutritional products is for cardiovascular health, general health concerns, and to promote a healthy lifestyle. Cold treatment, joint health, and energy-enhancement follow with a variety of other applications also gaining widespread use. Products such as coenzyme Q-10, carnatine, B vitamins, and antioxidants are promoted for cardiovascular benefit. Zinc has recently been introduced for cold treatment. Glucosamine and chondroitin are available for joint health, as are a variety of energy-enhancing supplements, some that work

and some that don't. There is growing evidence, as indicated by the recent report by the Harvard Medical School, that conjugated linoleic acid may play a role in slowing the progression of certain cancers, notably of the colon and prostate. All of this adds up to the fact that consumers are aware of the health benefits of certain nutrients, that they pay attention to scientific reports, and that they are prepared to follow the recommendations of health professionals with respect to nutritional support for disease management.

In the early years, the nutrition industry was built almost solely on marketing hype and short product lifecycles, reflecting lack of proven efficacy or scientific foundation. Bad press related to product safety led to regulatory and consumer pressure and the industry was forced to look hard at realignment. Now there is considerable emphasis on proven scientific findings, product safety, and the interaction of nutritional products with drugs and other therapeutic compounds. And so, while in the early going there was reliance on marketing to create the premise of health, a growing emphasis now is being placed on science to prove that premise.

A GROWING SCIENCE BASE

Many well founded factors support the growth of the nutritional/health industry. With regard to health, many factors contribute to a growing emphasis on nutrition at some cost to pharmaceuticals. Many nutraceuticals do indeed provide therapeutic or preventative benefits. And although these compounds typically are naturally occurring, their use can be patent-protected. Pharmaceuticals and nutraceuticals are tested clinically, and clinical results are published in respected peer-reviewed journals. Clinicians are beginning to see the value of nutritional products with proven efficacy, and a number of healthcare providers are recommending their use. At the same time, nutraceuticals and pharmaceuticals provide solid business opportunities. In some cases, in fact, nutraceuticals have advantages over pharmaceuticals as a business model. Because the compounds are not new and are typically naturally occurring, the route to market is generally shorter, faster, and more clearly defined. Safety issues are addressed by the FDA through food rather than drug evaluations, leading to safety affirmations as generally apply to foods. And the real advantage to industry is that mandatory generics are not required after compounds or compositions come off-patent. At the same time, however, third-party payers typically do not reimburse for nutritional products and patients are forced to bear the cost of their use.

BIOENERGY, INC., AND RIBOSE

So as an example of how nutritional products can be successfully employed in health, I will now shamelessly promote our company, Bioenergy, Inc. It was founded on the basis of enhancing lives by improving cardiovascular health and tissue function. John Folker, a University of Minnesota pediatric cardiovascular

surgeon, formed the company after completing studies of the effects of D-ribose on cardiac metabolism and heart function. D-ribose is a five-carbon sugar, or pentose, that occurs naturally in every living cell. The ribose that we use in our product manufacture is derived from corn sugar through a fermentation process. Ribose regulates the metabolic pathways used by the body to produce a class of compounds known as adenine nucleotides. The metabolic processes controlled by ribose are essential to existence. Energy production, formation of genetic material and compounds essential for cellular communication are all formed by pathways limited by ribose in tissues and in cells.

In the body, these compounds become deficient when there is insufficient oxygen supply. When under stress, hearts, skeletal muscles, blood cells, and other tissues lack the enzymes that are required to produce ribose. Therefore, giving ribose to these tissues speeds up the recovery process and improves function. Although other tissues—such as liver, adrenal cortex and mammary tissue—are active ribose producers, they are unable to transport the ribose that they produce to deficient tissues.

The use of ribose as a nutritional therapeutic is well founded in science. Our research has shown that its administration is effective in treating sick hearts, improving skeletal muscle metabolism, enhancing immune function, and preserving blood cells harvested for transfusion, all using the same metabolic pathways as a mechanism.

CORVALEN®

As a result of our research, last December we launched CORvalen® for treating patients with congestive heart failure and for those recovering from cardiac events such as surgery or heart attacks. This product is regulated by the FDA as a medical food and is distributed to patients by hospitals and other healthcare providers. The product works by increasing the energy in the heart and is effective in improving heart function in our targeted patient population. It enhances physical performance and quality of life.

We also provide ribose as a bulk ingredient for use in general health and nutrition. Sports-nutrition applications are expanding, and users report improved performance, reduced soreness and stiffness, and enhanced recovery from heavy exercise. Again, these effects are directly related to the biochemistry associated with ribose and stressed tissue. Many nutrients have been used in sports and energy products for years. However, recent concerns over the safety of several ingredients have caused the FDA to step up enforcement. As such, food and beverage manufacturers have been looking for effective ingredients with known and accepted safety profiles. Bioenergy ribose is included in many sports-energy and general-health products now on the market, because it has been affirmed safe. PepsiCo for example uses ribose as a drink supplement being sold as a sports-nutrition product. The distribution of ribose-containing products continues to expand.

The market opportunity for ribose is dramatic. As a heart supplement, we estimate the market potential to be in excess of \$3 billion. And as a sports- or general-use supplement, the market exceeds \$500 million. These numbers are given only as indications of the expansive potential of the nutrition market in health, and go a long way toward explaining why companies have invested so heavily in research and development in this industry.

Nutraceuticals are gaining wide market acceptance and many significant uses continue to be identified. There is a large and growing demographic now using nutraceuticals for health, and the market continues to expand. Physicians and other healthcare practitioners are gaining an understanding and approval of how nutrition products affect patient health. Historically, gaining acceptance by the medical community has been a significant challenge. But the redirected focus on research has forced open this door.

RESIDUAL RESISTANCE

Major challenges still exist, however. The industry has come kicking and screaming to the realization that science matters. But considerable resistance persists. Until this approach is universally adopted, there will continue to be grave concern that nutritional therapies are more hype than science. However, there are strong business reasons to continue the effort. It is incontrovertible that nutritional products founded in strong science can provide a meaningful contribution to health, laying the groundwork for solid business platforms and creating value for shareholders.

Genomics Education at the Mayo Clinic: A New Model for Data and Information

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I have been presented with a significant challenge, having been asked to discuss how genomics, specifically medical genomics, is being integrated into medical practice at the Mayo Clinic, a tertiary care, a highly scientific, and—if you are familiar with the people who are there—a very formal type of institution. I will explain the approach we are taking to provide some insight into:

- how an institution like the Mayo Clinic tries to assimilate new information that's important in diagnosis and treatment, but yet somewhat problematic for the physicians involved, and
- the possibility that there are overlapping areas of interest between nutraceuticals and the effects of diet on health, and genomics.

I believe that diet has very strong effects on health. I believe that it is also true that disease is almost exclusively determined by genes and abnormalities in genes. I don't think that these are contradictory positions, and I think that the challenge for conference attendees, and the challenge for those of us who are more classically interested researchers, is to find areas of overlap.

Sequencing of the human genome has had a profound impact in the medical community. The effects have been to focus attention on medical genomics, and it is clear that there are significant implications for clinical practice.

EVOLUTION OF MEDICAL GENOMICS

Major advances in medical genomics began in the late 1940s and the 50s with progress in genetics, and with genetic engineering in the 1970s. The human-genome project represented a major conceptual step forward, and when it was

completed, it was clear that there was tremendous potential for impact on the diagnosis and treatment of disease. This new information will gain entrance to medical practice through cardiomics and bioinformatics, and will assist in the diagnosis of disease, the identification of diseases in relation to genes, the identification of predisposition to disease, the identification of new therapeutics, and understanding of individual responses of particular patients to particular therapeutics.

The key then is that using the new medical-genomics information is going to transform diagnosis, therapy, and treatment, and approaches to predisposition to disease in practices such as we have at the Mayo Clinic.

We have always known that some diseases are genetic, or have a genetic component. Since the early '90s, there has been an exponential increase in the identification of diseases that have a strong genetic contribution. There has been, as another example, quite a bit of interest in pharmacogenomics, where it has been determined that specific genes or specific polymorphisms in genes will determine the response of a particular individual to a drug. Why, for example, will one person take aspirin and have success in treating their arthritic pain, while another patient will not? The most likely answer is that differences in the genes that those patients have determine those variable responses.

Along with these opportunities, however, there are challenges and, indeed, problems. The potential exists for a loss of patient privacy and confidentiality of medical information, which is of concern to all physicians in all institutions. There is also the potential for a loss of control on the part of the patient over their medical care. Some would argue that this is already occurring. The potential is certainly there for this to get worse. Discrimination on the basis of genetics and on the basis of finances is, of course, real. Expectations are going to change from the physician perspective in a way that is unpredictable, and, unfortunately, as it always has been in the past, more-technical medical care will be associated with much higher costs.

MAYO'S MISSION

These changes and opportunities are reflected in our mission statement, "The Mayo Clinic prides itself in its ability to elucidate the goals that it has," and one of the current major goals is to include genomics in the integrated practice of medicine. The difficulty is that for the majority of physicians there is very little understanding of genetics, little understanding of its principals, little understanding of the practice, and little understanding of the tests. And so the challenge for the individual physician, for the clinic, and for the medical community at large, is to develop paradigms and opportunities to educate physicians in practice about the new opportunities, and also the new responsibilities and problems.

The guiding principal at our institution is that all physicians, not just medical geneticists as a subspecialty, but all physicians can participate in this

process. But without a strong knowledge base, to achieve that goal is going to require a significant educational effort. To achieve this educational effort a Genomics Education Steering Committee was formed with three goals and charges:

- to transmit information to all physicians of the clinic,
- to transmit to the clinicians the significance and importance of this information, and
- to develop an educational plan to maintain the standards of education and the standards of care.

The group, of which I am a member, has initiated efforts in several areas. There has been provision of resources, primarily on a Web-site. There have been educational activities, including seminars. There is also coordination of research activities at the clinic, which is being done in consultation with the communications department.

One of the first things that we did as a committee was assay the level of knowledge and the level of comfort of our physicians with genomic tests and with ethical, legal, and social issues, termed “elsi.” Interestingly, a high number of the physicians were not at all comfortable. As a corollary, a high number of physicians expressed strong desire for educational materials, reinforcing our initial concept of both a strong need for education and also a very good opportunity for education.

There has been significant activity in continuing education. We have organized a large number of lectures and several symposiums, videos are available to physicians and we are coordinating activities with allied health staff. We will continue these activities to bring new genomics information to our clinicians. We have given a major introductory course on medical genomics, in which a large number of people from the committee participated. We are planning a major continuing educational course; Alan Bradley, the director of one of the major genome-sequencing centers in the world, the Wellcome Sanger Center in the UK, will be our keynote speaker.

We have also put together as a second area of activity, a group of interested faculty members who are supporting the effort as liaisons between our committee and the different departments and committees. Clearly there is a need for information that is specific for particular physicians’ practices or the practice of a particular group or division. And, by identifying interested individuals in each group, we hope to facilitate the educational process.

We have put together a web site, which, unfortunately, is not yet available outside the clinic. We are working diligently to construct something that will be transportable and will be usable by physicians other than those at the clinic. As the director of this process, I have to say that this is an incredibly time-consuming and resource-consuming activity, and it will be some time before we will be fully operational.

THE CHALLENGE

In conclusion, the Mayo Clinic is engaged in what I think is reasonably termed an aggressive effort to prepare the staff and the allied healthcare for changes in medicine, with genomics and medical genomics becoming a central part of the therapies that we will offer. To reach this goal, to effect this education, we are expending effort as I've described, we are identifying key staff developing web sites and supporting material for those individuals.

This is a little different from the interests of most of those attending this conference, but I would stress the need for integration of the new genomics information, new nutraceuticals information and foods-for-health information towards a more comprehensive understanding of health and of disease. That's a challenge for all of us.