Hyperimmune Eggs Capture Natural Immune Support

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Since the 1950s, immunology researchers have investigated the possible benefits to human health afforded by the intriguing physiologic state of hyperimmunity, which is achieved by the repeated immunization of laying hens or lactating cows against one or more antigens and more specifically against human pathogens.[1–7] The hyperimmunized hen or cow produces antibodies to the specific antigens (or pathogens) with which she has been vaccinated as well as a variety of low–molecular-weight cofactors that, in general, support and enhance the immune response. The hen concentrates the antibodies and immune cofactors into egg yolk for the sustenance and protection of the developing chick. The cow concentrates antibodies and cofactors in colostrum, which is the nutrient-rich lactation product that sustains a newborn calf.

Ordinarily, the egg yolk and colostrum of nonhyperimmunized hens and cows deliver high-density nutrition and confer general passive immunity to the developing chick or young calf, in the form of antibodies, to pathogens or other antigens in the mother's environment, and of less-specific, physiologically active cofactors that support and stimulate the immune function of the young animal. The movement of antibodies and immune cofactors from the hen's serum into the egg yolk, and from the egg yolk to the developing chick, corresponds to the transfer of immunoglobulin G across the mammalian placenta, to the developing fetus, and to the subsequent transfer of antibodies and immunoregulatory molecules through colostrum.[4,8]

Hyperimmunized hens and cows produce eggs and colostrum that provide concentrated sources of environmentally specific antibodies and immune-supporting cofactors that confer passive immunity on the chick, calf, or human being who consumes the eggs, colostrum, or milk. Hens and cows that are vaccinated with human pathogens produce antibodies that are specific to those human pathogens. A substantial body of research has demonstrated that human consumption of hyperimmune eggs or hyperimmune milk can protect against the specific organism(s) against which the hen or cow was vaccinated. [9–12] In addition, the immunoregulatory cofactors secreted into hyperimmune eggs and milk offer powerful and unexpected benefits to a number of different human structures and functions, including the circulatory and immune systems, the digestive tract, and the joints.[7,11–14]

The earliest research into hyperimmunity focused on transfer of passive immunity through bovine colostrum and milk. University of Minnesota (Minneapolis) researchers William E. Peterson, Ph.D., and Berry Campbell, Ph.D., published their seminal research in 1955,[3] and investigators subsequently published studies on the use of immune milk in the treatment of hayfever and rheumatoid arthritis and for disease prevention in humans and animals.[3,4,15,16]

During the 1980s and 1990s, university and industry researchers in the United States and New Zealand explored the immunoregulatory factors that are abundant in hyperimmune milk and eggs, noting that they had anti-inflammatory, antihypertensive, anticholesterolemic, and antibacterial properties.[11,13,16–33,*] These discoveries were protected by U.S. patents issued to companies that were conducting and sponsoring research, notably Stolle Research & Development Corp. (Cincinnati, Ohio),[34–43] Ophidian Pharmaceuticals (Madison, Wisconsin,[44,45] and ImmuCell Corp. (Portland, Maine).[46–48]

Twists in the Road to Commercialization

Regulatory uncertainties and the challenge of scaling up production impeded commercial development of products based on hyperimmune know-how until the mid-1990s. The U.S. regulatory category of "dietary supplement" did not exist until the passage of the 1994 Dietary Supplement Health Education Act (DSHEA),[49] which cleared the way for companies to make truthful claims about how a product makes an impact on normal human structure and healthy human function, without having to seek preapproval by the Food and Drug Administration (FDA).

Stolle has specialized in milk-based hyperimmune technologies, and has sold its milk products overseas, where the regulatory environment was more accommodating to the uncertain status of a natural, health-enhancing product that the FDA considered to be neither a food nor a drug.

ImmuCell has commercialized animal health products for dairy and beef producers, as it pursues a phase II human clinical trial of hyperimmune-

*Trentham, D. Morales, A., Gueraude-Arellano, M., Ahmad, T., Dynesius-Trentham, R., Fitzpatrick-McElligott, S., Daley, M., Dynesius-Trentham, R. Effect of immune egg in animals injected with type II collagen. (unpublished).

The commercially significant fact is that eggs contain higher levels of antibody per ounce than milk does.

milk–derived immunoglobulins raised against the human pathogen *Clostridium difficile.*[50]

GalaGen, Inc. (St. Paul, Minnesota), develops and markets bovine colostrum–based food ingredients, and commercializes them through joint ventures with food manufacturers. These ingredients are offered to promote wellness through the passive immunity conferred by colostrum, but GalaGen does not utilize hyperimmune methods to make its products. The passive immunity that nonhyperimmune colostrum provides to humans relates to antigens in the mother cow's environment, not to antigens or pathogens in the human environment.[51]

Ophidian Pharmaceuticals has pursued a conventional drug development path for hyperimmune egg–based polyclonal antibodies for treatment of human *C. difficile*–associated disease, which can be a costly and debilitating condition that is difficult to treat.[52]

Any company developing a food or dietary supplement based on hyperimmune principles faces the challenge of scaling production up to a commercially viable level. The two most widely available "producers" of hyperimmune foods or ingredients are lactating cows and laying hens. Although the earliest investigations of hyperimmunity focused on milk products, the commercially significant fact is that eggs contain higher levels of antibody per ounce than milk does.[11–14] This makes sense from the biologic perspective, as the egg represents the hen's only opportunity to pass nutrition and immune protection to a chick, whereas the lactating cow, like all mammals, takes weeks or months to transfer immune factors passively. The costs of raising hens and maintaining them in the hyperimmune state are substantially less than the corresponding costs of raising and maintaining lactating cows.

Hyperimmune Eggs Arrive

A Wilmington, Delaware–based company, DCV, Inc., has undertaken the first major commercialization of a hyperimmune dietary supplement. Building on hyperimmune egg patents acquired from Stolle, DCV has developed and started selling a dietary supplement that has seven structure-function claims, which are supported by a substantial—and growing—collection of published laboratory studies and clinical trials.

According to Örn Adalsteinsson, Ph.D., vice president of research and development of DCV and the creator of DCV's hyperimmune commercial products: "Egcel,™ consists of hyperimmune egg immunoglobulins and cofactors that are spray-dried and formulated into capsules of pure product, or a flavored vitamin-, mineral-, and nutrient-rich powder called BioChoice,® which is mixed with water, milk, or fruit juice, and consumed as a beverage."

DCV's packaging and supporting literature for the hyperimmune egg supplement make seven structure–function claims, such as are permissible under the DSHEA. The company's claims about hyperimmune egg supplementation are that it:

1. Balances and supports the immune system
2. Helps to maintain cardiovascular function and a healthy circulatory system
3. Helps to maintain digestive-tract health
4. Helps to modulate autoimmune responses of the body
5. Helps to maintain flexible and healthy joints
6. Helps to increase energy levels
7. Helps to enhance a sense of well-being.

Örn Adalsteinsson, Ph.D., DCV, Inc., Wilmington, Delaware.

The company bases these claims on laboratory and clinical research it has conducted or is presently doing, and on the original research upon which patents were based.

To date, DCV is the only company selling hyperimmune food products as dietary supplements in the United States. The company sells its proprietary spray-dried formulation as capsules and as a nutritionally enhanced beverage mix and has not announced plans to develop additional products in the near future. Because the product's egg yolk immunoglobulins

Thirteen patients with arthritis showed statistically significant improvement after 30 days and 60 days of consuming hyperimmune egg.

are not heat-stable, future formulations could include puddings and chilled or frozen desserts, but would not be likely to include baked goods.

Hyperimmune Egg Patents

DCV holds more than 100 worldwide patents on hyperimmune technologies and applications, most of them relating to the production and use of hyperimmune eggs. Many of the core patents were acquired from Stolle, the company that did the initial research and filed some of the earliest patents, but DCV has continued to expand and refine Stolle's original work. DCV's hyperimmune egg patents address the method of vaccinating hens in such a way that they produce eggs that are rich in immune cofactors that control cholesterol levels and lipid deposits and slow the development of arteriosclerotic lesions in individuals who eat the eggs. The choice and mix of bacterial antigens and the vaccination regimen are critical factors determining what immunoregulatory factors are emphasized in hyperimmune eggs. DCV's technical patents also address the purification of egg immunoglobulin and bioactive components of eggs.

The company's patents also describe methods of using hyperimmune eggs and milk products to prevent or minimize damage to the gastrointestinal tract that is often caused by long-term use of nonsteroidal anti-inflammatory drugs.

Comparison of Hyperimmune Eggs to Supermarket Eggs

Hyperimmune eggs and supermarket eggs have the same protein (including immunoglobulin), fat, and cholesterol contents. They differ principally in two ways: (1) The exact types of immunoglobulins (antibodies) that make up the eggs's respective proteins differ; and (2) the hyperimmune egg contains higher levels of more active immunoregulatory factors than the supermarket egg.

Most supermarket eggs come from hens that have been vaccinated one time, at birth, against avian (in this case, chicken) diseases. Hyperimmune eggs are produced by hens that have undergone repeated vaccinations against many human diseases. DCV's proprietary method of producing hyperimmune eggs calls for the repeated immunization of laying hens with a patented vaccines containing at least 24 inactivated enteric pathogens that infect human beings. These include, but are not limited to, *Shigella dysenteriae, Staphylococcus epidermidis* and *simulans, Escherichia coli, Salmonella enteritidis* and *typhimurium, Pseudomonas aeruginosa, Klebsiella pneumoniae, Haemophilis influenzae,* and at least 6 species of Streptococcus. DCV notes, in its technical information on the eggs, that the hens laying the eggs, and not the eggs themselves, are injected with vaccines and that the vaccines are made of inactivated pathogens. The hen produces immunoglobulin antibodies against microbes that are of special concern to human health and concentrates those antibodies in the eggs she lays. When eaten by a human, these eggs transfer passive immunity to the pathogens in the vaccine.

After an appropriate time subsequent to vaccination of the hen, her eggs are collected and processed under good manufacturing practices, in a U.S. Department of Agriculture–inspected facility. The eggs are washed and broken, and the yolks and egg whites are spray-dried under mild conditions to produce a fine protein powder that is rich in egg antibodies and active immunoregulatory factors.

An expert panel has reviewed information on hyperimmune eggs and milk products, in general, and for DCV's hyperimmune eggs, in particular, and has affirmed that they are Generally Recognized as Safe (GRAS), under FDA regulations.

Hyperimmune eggs, like conventional supermarket eggs, should not be eaten by individuals with known egg intolerance or egg allergies.

Human Clinical Trials

DCV has entered its hyperimmune egg supplements into four human clinical trials, three of which are complete. The studies investigated the effects of hyperimmune egg product supplementation in three distinct patient populations, demonstrating the benefits of this approach for patients with arthritis, patients with wasting syndrome, and individuals whose elevated serum cholesterol levels place these patients at risk for cardiovascular disease. Collectively, the studies open the door to future investigations of and applications for this powerful form of natural nutritional support.

Thirteen patients with osteoarthritis, rheumatoid arthritis, or psoriatic arthritis showed statistically significant improvement ($P<0.05$) in physician mean global assessment scores after 30 days and 60 days of consuming the hyperimmune egg supplement beverage.[22] Patients with osteoarthritis achieved statistically significant ($P<0.05$) improvement over baseline scores at 30 days and at 60 days from the start of the program.

Hyperimmune egg supplementation may beneficially modify the regulation of serum lipoprotein levels and thus reduce the possibility of cardiovascular disease.

A second randomized, double-blind placebo-controlled study of supplementation with hyperimmune egg for maintenance of healthy and flexible joints has been underway since July of 1998.[31–33] D. Trentham and R. Dynesius-Trentham of Harvard Medical School, Beth Israel Deaconess Medical Center, in Boston, Massachusetts, are recruiting a total of 63 patients with rheumatoid arthritis and randomly providing them with a daily dietary supplement drink with, and without, hyperimmune egg. Study participants consume one of the supplements daily for 3 months and make regularly scheduled visits to the principal investigator. After 3 months, each participant receives the hyperimmune egg–containing supplement, and visits with the principal investigator continue. At the end of the second 3-month period, the participant and investigator find out whether the original supplement did or did not contain hyperimmune egg.

Investigators conducted a 26-week long, double-blind placebo-controlled study of the effect of hyperimmune egg protein supplementation on elevated cholesterol levels and cardiovascular risk among a group of 47 students at the Sergeants Major Academy, in Fort Bliss, Texas.[23–25] The 44 men and 3 women, ages 35 to 55 years old, had left a more physically strenuous active duty for a period of more sendentary classroom study and had elevated serum total cholesterol levels of 180–290 mg/dL. Study participants were randomly assigned to three treatment groups: the 15 individuals in Group 1 served as the controls and received no dietary supplement drink at all; 17 people in group 2 were given a placebo supplement drink that contained nutrients but no hyperimmune egg; and 14 people in Group 3 received a nutrient drink supplement that contained hyperimmune egg. All study participants followed a regimen of strenuous exercise and dietary education addressing reduction of fat and cholesterol intake. By the end of the trial, the total cholesterol levels of individuals in the control and placebo groups had increased, whereas these levels of the group that consumed the hyperimmune egg supplement showed no significant changes. An accepted biomarker for elevated risk of cardiovascular disease, the ratio of total cholesterol to high-density lipoproteins and apo-lipoprotein (Apo) B levels, were increased in the control and placebo groups, but did not change significantly in the group consuming hyperimmune egg. Triglyceride and Apo AI values remained essentially unchanged in all three groups. The investigators suggested that hyperimmune egg supplementation may beneficially modify the regulation of serum lipoprotein levels and thus reduce the possibility of cardiovascular disease.

An unpublished human trial evaluated the effect of hyperimmune egg supplementation on weight gain and weight maintenance in 17 men, ages 18–50 years

Leo Galland, M.D., Foundation for Integrated Medicine.

About DCV

DCV, Inc., is a diversified company with specialized experience in specialty chemicals, food, health, and nutrition. The company has developed four principal U.S. and international market areas: BioNutrition and Life Sciences, Food Ingredients, Animal Health and Nutrition, and Specialty Products.

Legacy USA, Inc., is the marketing arm for several of DCV's human nutritional and dietary supplement products, including its Egcel™ and BioChoice™ hyperimmune egg formulations.

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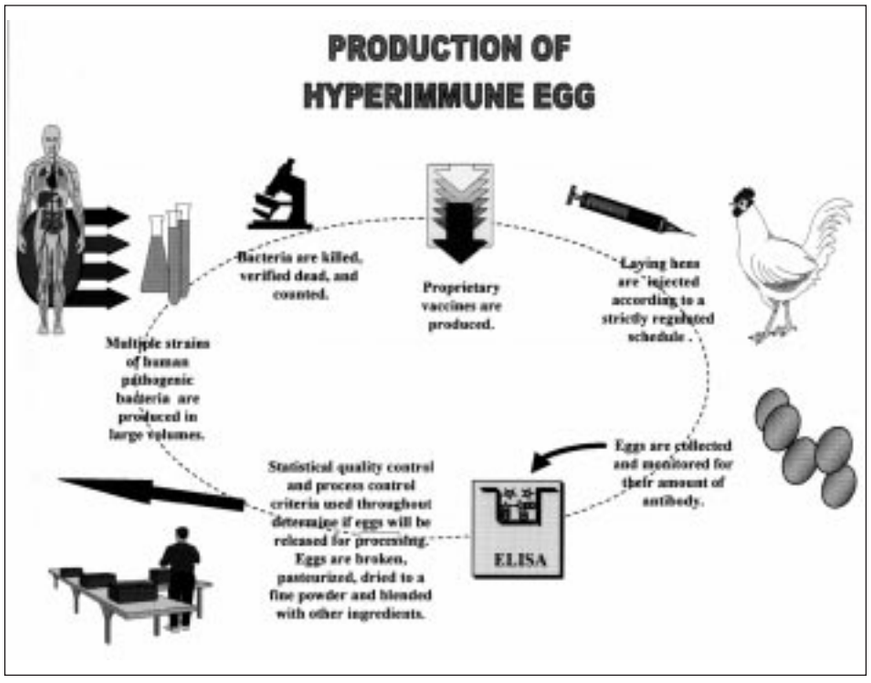
Information is provided because this product is not easy to find. The author has no vested or other interest in DCV or any of its related arms.

The supplements have been especially beneficial to patients with recurrent bacterial infections.



Production of the hyperimmune egg. Drawing provided courtesy of DCV with permission to print.

Hyperimmune Eggs in Clinical Practice

In an unpublished statement, dated January 14, 2000, to Örn Adalsteinsson, Ph.D., Leo Galland. M.D., wrote: "It seems likely that the nutraceutical effects of [the hyperimmune egg supplement] are derived from its content of antibodies and immune-modulating peptides. In patients with immune deficiencies, these appear to stimulate immune response, decreasing the frequency of new infections. In CFS [chronic fatigue syndrome], on the other hand, the immune system appears to be stuck in a hyper-stimulated state. Most people with [CFS] feel as if they have the flu and it never leaves them. I believe that [the hyperimmune egg supplement] helps these patients by 'unsticking' the immune response, allowing it to ease back to normal, freeing it from the overactive condition."

old, whose weights were less than 90 percent of their ideal weight.[†] All of the subjects had been diagnosed with one or more AIDS (acquired immune deficiency syndrome)–defining conditions and were suffering from wasting syndrome, which is characterized by progressive weight loss, weakness, fever and diarrhea. After 1 and 2 months on a daily serving of the dietary supplement, from 50 percent to 70 percent of the patients experienced weight gains ranging from 0.5 kg to 4 kg, or maintained their initial weights. Monthly visits to the physician during the study resulted in detailed evaluation of each participant. Physicians' evaluations and patients' self-assessments concurred on the beneficial effects of hyperimmune egg supplementation for improving physical functioning and a global sense of well-being.

Bringing Hyperimmune Eggs into Clinical Practice

Darryl M. See, M.D., a physician in the division of infectious diseases, department of medicine, University of California, Irvine, in a 1998 review of complementary therapies in arthritis, examined the possible multiple roles of "immune food products"—eggs and milk, in particular—in correcting some of the immune dysfunctions that have been identified as possible causes of some forms of arthritis.[14] He observes that passive immunity, conveyed by food items, delivers beneficial antibodies directly to the human gut, which is a major point of

[†]Unpublished communication from Leo Galland, M.D., To Örn Adalsteinsson, dated January 14, 2000.

The anti-inflammatory properties of hyperimmune foods may promote general health in ways that are as yet poorly understood.

entry to the body for numerous pathogenic organisms. He speculates that the hyperimmune food's delivery of antibodies to human pathogens may reduce exposure to gut pathogens and lighten the body's immunologic activation, thereby reducing the likelihood of the immune overactivity that has been associated with some forms or arthritis. He speculates, additionally, that the anti-inflammatory properties of hyperimmune foods may promote general health in ways that are as yet poorly understood.

Leo Galland, M.D., director of the Foundation for Integrated Medicine in New York City, and a specialist in hard-to-diagnose conditions such as chronic fatigue syndrome (CFS) and recurrent infections, has found that hyperimmune egg supplements provide an invaluable resource for patients whose conditions do not respond to the first round of immune-function restorative measures that he recommends. He has found the supplements to be extremely helpful in reversing or reducing a wide range of health problems and notes that the supplements have been especially beneficial to patients with recurrent bacterial infections, particularly those of the respiratory tract. Patients with CFS have experienced improvement after taking the hyperimmune egg supplement, as did one patient with congenital immunoglobulin A deficiency. Dr. Galland suggests that hyperimmune eggs are more appropriately regarded as powerful biologic response modifiers and not simply as a nutritional supplement. He observes that the anti-inflammatory actions of the supplement are characteristic of active immune response modifiers and not of passive immune agents. (Dr. Galland's comments about hyperimmune egg supplements are reproduced in the box entitled Hyperimmune Eggs in Clinical Practice.)

As clinical experience with hyperimmune egg supplementation continues to grow and as basic research into hyperimmune products (principally eggs, milk, and its derivatives) expands the understanding of their physiologic actions, it is to be expected that additional applications for these promising healing foods will emerge. It is not difficult to envision dozens of scenarios in which a natural, gentle, immune-supportive dietary supplement could have important applications. Patients with cancer whose immune function has been compromised by chemotherapy or radiation therapy could benefit, as could anyone whose immune response has been disrupted by illness or therapy. The hyperimmune egg's boost to the immune system could help to protect individuals who are exposed to physically or emotionally stressful living environments. Hospital employees and people whose daily occupations expose them to many different people at close quarters stand to benefit from the hyperimmune egg's healing potential. □

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50. Web site at www.immucell.com
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