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HEALTHY MICROBIAL ORGANISMS

HMOs YOU CAN REALLY COUNT ON.

Few people realize that they carry within their gastrointestinal tract nearly 10^{14} (that's 100 trillion!) living bacteria, resulting in 10 times more bacterial cells than human cells in their bodies. It is clear that the proper understanding and management of these organisms within the gut is required to attain maximum health. We hope to review the micro-ecosystem known as the gastrointestinal tract and the use of natural probiotics and prebiotics for both health maintenance and therapeutic protocols.

The Gastrointestinal Ecosystem

The human gastrointestinal tract (GIT) extends from the mouth through the colon and allows for the ingestion, digestion, absorption and elimination of food, water, toxins, and waste materials. While the GIT is "inside" our bodies, it is in contact with the outside environment and is intended to maintain a controlled barrier to that environment like the skin. While the average person has about 2 m^2 of skin surface, the small intestines and colon alone have a calculated surface area of between 150-200 m^2, when the surfaces of the microvilli are considered. Considering the pH changing from the mouth (near neutral) to the stomach (pH 2.5- 3.5) and then gradually back toward neutrality through the rest of the gut, with the addition of enzymes, bile, varied levels of salts and liquids; there is ample opportunity to create hundreds of different microenviron-mental niches. At least 300 different species of bacteria, in 50 different genera, continually compete for these niches in the lower GIT of the average person (See Figure 1 for breakdown). For example, bacteria in the proximal colon have good supply of nutrients and grow at a fast rate, causing a drop in pH from the production of short-chain fatty acids (SCFA); while bacteria in the distal colon have lower nutrient availability and the pH is therefore near neutral. Different microorganisms prefer and thrive in these different environments. Many of them are beneficial and necessary to human health, while others are a potential source of disease.

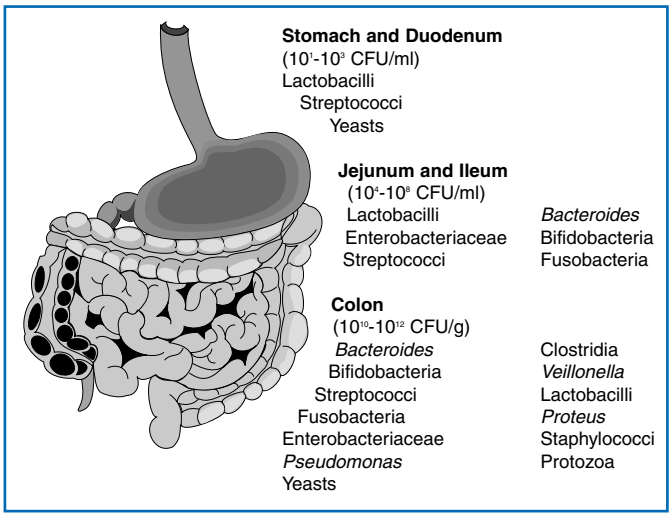

Fig. 1 Microbial colonization of the human gastro-intestinal tract.

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(continued from page 1)

As figure 1 shows, the most common microorganisms in the lower GIT includes a variety of bacteria such as Lactobacilli, Bifidobacteria, Bacteroides, Enterobacteriaceae, Pseudomonas, Streptococci, and Fusobacteria, as well as yeasts, protozoans, and possibly a few other parasitic organisms. With all these organisms competing for limited space and nutrients, a delicate balance must be maintained to ensure that the symbiotic relationship with the host (the patient) is a beneficial one and not a detrimental one. Often this balance is called "eubiosis", while the imbalanced situation is called "dysbiosis". Dysbiosis occurs when one or more types of organism (usually E. coli, Enterococci, yeast etc.) increases in cell growth and out-competes the growth of one or more of the beneficial strains (e.g. Lactobacilli or Bifidobacteria). The results of dysbiosis are seen in symptoms such as overproduction of gas, diarrhea, indigestion, nausea, chronic yeast problems, carcinogenesis, food allergies/ intolerance, B-vitamin deficiencies, as well as a number of other gastrointestinal complaints.

There are many factors that influence whether an individual has enough "friendly" bacteria and whether the overall ecosystem of their GIT is in balance. Primary among them are host GIT factors (HCl, bile, enzyme secretions, peristaltic rate, mucus production etc.), microbial factors (adhesion, nutritional flexibility, half-life, dividing time etc.) and diet. Dysbiosis can be triggered by external factors such as the use of broad-spectrum antibiotics, radiation therapy, stress, drastic changes in altitude (air travel), dramatic changes in diet, or fasting. It is during these states of dysbiosis that live bacteria can be supplemented to the diet to bring the patient's GIT ecosystem back into balance.

The Use of Probiotics

The use of bacterial cultures in food goes back several thousand years. Fermented milk products such as yogurt, kefir, buttermilk, cheeses, and sour cream are well known, as are other fermented products like sour kraut. Fermenting acts to preserve as well as add flavor to foods. While traditions have attributed many health benefits to the use of these products, especially the fermented milk products, it was Metchnikoff, at the beginning of this century, who suggested that these bacteria in the GIT were important for health and longevity of humans (1). Since his statements, little interest was shown in the use of these bacteria outside the fermenting of food.

In the last quarter century, adding beneficial live bacteria to animal feed has been used to improve the health and production of various livestock. The interest in these bacteria, known as probiotics has grown in the past several decades from use in animals to use in humans, and from fermented milk products to capsule, tablet and powder form probiotic supplements. While definitions abound, a probiotic is essentially a living organism, which exerts a health benefit when ingested in the proper dose. The most common, and almost synonymous, are the class of lactic acid bacteria that reside in the GIT. A probiotic for our purposes then is a bacteria, that when ingested remains viable in the GIT long enough for its metabolic activity to benefit the host in some way prior to its death or removal. Lactobacillus acidophilus is the prototype probiotic.

Lactobacillus acidophilus:

Lactobacillus acidophilus (L. acidophilus) are facultative anaerobic bacteria. Under anaerobic conditions (like the gut) they ferment various carbohydrates to lactic acid. They occur naturally in humans and animals, residing primarily in the gastrointestinal tract, mouth, and vagina. They are added to fermented milk products such as kefir and yogurt for both taste and health properties; and are now used alone or in combination with other bacterial strains for their health promoting properties. The nomenclature of these probiotic species is quite complex and rapidly changing. Other strains in the Lactobacillus genus include L. casei, L. bulgaricus, and L. brevis to name only a few. Strains such as L. casei also include subspecies like L. casei rhamnosis (often just called L. rhamnosis) to confuse matters even more. While most of these strains share much in common, there are subtle differences in metabolism and genetics that make some strains more appropriate for certain individuals or conditions. We will discuss these as we go through the specific benefits of using oral probiotics.

Bifidobacteria:

Bifidobacteria are also normal inhabitants of the human GIT, and are capable of producing not only lactic acid but acetic acid as fermentation products. Since their discovery a century ago, Bifidobacteria have been classified numerous different ways until receiving their own genus. Popular Bifidobacteria strains include B. bifidum, B. longum, B. lactis, B. breve and B. infantis. The

fecal flora of breast fed infants is dominated by Bifidobacteria, while those of formula fed infants contains Bacteroides, Clostridia, Streptococci at similar levels with Bifidobacteria. The probiotic health benefits of these strains of bacteria make them an important class of organisms for human consumption.

Health benefits associated with probiotic use:

While there are multitudes of possible health benefits for ingesting live probiotic organisms, we will focus on balancing dysbiosis, therapeutic anti-microbial activity, immune enhancing activity, reduction of carcinogenesis, and control of cholesterol metabolism.

Dysbiosis and related conditions:

As previously stated, dysbiosis is an unbalanced condition in the GIT, resulting in fewer than normal "friendly" bacteria and an over abundance of potentially harmful bacteria, yeast, or parasites. This unbalanced condition is often the result of broad-spectrum antibiotic use, radiation therapy or exposure, stress (GIT pH changes), dramatic changes in altitude (air travel), ingestion of different organisms (food poisoning or local adjustments to water supply etc.), or changes in diet. The use of broad-spectrum antibiotic like amoxacillin is often associated with gastrointestinal complaints due to the drastic alteration of GIT microflora. When patients were given concomitant doses of Lactobacillus acidophilus, they had a significant decrease in gastrointestinal complaints and accompanying yeast infections (2). In the event that such antibiotic treatment is warranted (although many would say this should be a rare event), a probiotic supplement providing 5-10 billion organisms/day should be added to the regimen during, and the weeks following, antibiotic treatment.

Gastrointestinal dysbiosis may also be involved in conditions such as Crohn's disease and various food allergies. Patients with active Crohn's disease have a reduced β–D-galactosidase activity (a measure of bacterial enzymatic activity), compared to healthy controls (3). These numbers correlated significantly and directly to a decreased number of Bifidobacteria in these patients. Increasing Bifidobacteria, either by direct supplementation or by the use of prebiotic bifidogenic supplements (see section on prebiotics), may improve the symptoms associated with Crohn's disease, irritable bowel syndrome and related conditions like food allergies. A Lactobacillus strain of bacteria reduced symptoms in infants associated with atopic dermatitis (eczema) caused by allergies to cow's milk (4). The researchers conducting this study concluded that these bacteria might promote endogenous barrier mechanisms and alleviate intestinal inflammation, both of which would help patients with food allergies. Dairy allergies/intolerance may be particularly addressed with lactic acid bacteria, as lactose is easily digested by these organisms.

A well studied strain of Lactobacillus casei (rhamnosus) bacteria called strain GG has been used in the prevention and treatment of diarrhea, primarily in children. In one study, 100 children with diarrhea were followed and some received probiotic treatment. Of these children, 61 were positive for rotavirus and 39 were negative (5). Interestingly, the duration of diarrhea episodes among probiotic treated individuals was reduced from 6 days to 3 days, regardless of rotavirus status. Furthermore, six days after the onset of probiotic treatment, only 4 of 31 children were still positive for rotavirus in the stool (compared to 25 of 30 in the control group). This same strain was used in a preliminary study evaluating the prophylactic use of probiotics in diarrhea episodes of undernourished Peruvian children (6). Their results suggest that episodes of diarrhea can be reduced, especially in non-breast fed toddlers with the prophylactic use of probiotics, in this case added to gelatin.

Another major cause of dysbiosis is the exposure to radiation, intentionally or accidentally. An extreme example would be a case of 5 individuals accidentally exposed to unshielded radioactive Cesium (gamma irradiation). The viable bacteria count decreased dramatically in all individuals and shifted away from the anaerobes (Lactobacillus and Bifidobacteria) and toward Enterobacter, Klebsiella, Serratia and Staphylococci. Three patients were given oral doses of Bifidobacterium longum for 30 days. The patients receiving B. longum moved away from dysbiosis and the fecal flora normalized in 2-3 weeks, while the control individuals developed multiple antibiotic resistant strains of facultative and obligate anaerobes (7). While this may be an extreme case of radiation sickness, similar events

occur when a patient undergoes radiation therapy, especially in the abdominal area. Probiotic supplementation would be warranted before, during, and after such treatment (8).

Anti-microbial Activity:

Lactic acid bacteria have the ability to prevent the growth of specific microbes that have pathogenic potential. They accomplish these functions by both passive and active mechanisms. Passive mechanisms would include physically competing for attachment sites, nutrient competition, and pH modification. Several strains of Bifidobacteria were shown to adhere to Caco-2 cells (enterocyte-like human colon carcinoma cell line used for *in vitro* intestinal simulation) and HT29-MTX cells (a human mucus-secreting cell line). While bound, they prevented the binding of pathogenic strains of E. coli, Salmonella typhimurium, and Yersinia strains (9). This same research group found similar results with strains of Lactobacillus acidophilus (10). This inhibition is most likely due to a physical blocking of the receptors to which these other pathogenic strains would attach, often called steric hindrance (11). In this manner, we can see how probiotic strains can be used prophylacticly, because this competition favors the friendly bacteria more if they adhere prior to the pathogenic strains. It may be the prior adhesion of Bifidobacteria bifidum that protects and treats against rotavirus adhesion and accompanying diarrhea episodes (16,17).

Several strains of Lactobacilli are now known to inhibit the growth of other bacteria simply by producing organic acids and reducing the micro-environmental pH. Organic acids from Lactobacillus acidophilus and L. rhamnosus were shown to inhibit the growth of Helicobacter pylori (a major cause of intestinal ulcers), in a dose dependent manner (12). Similarly, supernatant from L. rhamnosus GG cultures inhibited the adhesion of Salmonella to Caco-2 cells via a pH effect (13). Within the GIT, these passive pH and steric hindrances to pathogenic bacterial growth and adhesion allows the other host Lactobacillus and Bifidobacteria strains to adhere, grow and bring many of the other health benefits associated with probiotics.

More than just passive hindrances, many probiotic strains have active anti-microbial activity. In 1992 a group from Argentina described the inhibitory effect of Lactobacilli on the growth of a pathogenic bacteria, Shigella sonnei. They determined that it was not a pH effect, but was something released by these bacteria into the media (14). This group also determined that the survival of mice given Shigella sonnei could be improved from 60% to 100% if they were fed a live mixture of L. casei and L. acidophilus in fermented milk prior to Shigella exposure (15). A group from France has demonstrated that Lactobacillus acidophilus secretes antibacterial substances that are active against pathogens such as Staphylococcus aureus, Listeria monocytogenes, Salmonella typhimurium, S. flexneri, Klebsiella pneumoniae, Pseudomonas aeruginosa and Enterobacter cloacae (18,19). This antibacterial activity was not observed to inhibit normal gut flora such as Lactobacillus or Bifidobacterial strains. Several strains of Bifidobacteria have also been found to have broad-spectrum anti-microbial secretions that inhibit pathogenic bacteria in genera such as Salmonella, Listeria, Capylobacter, Shigella, as well as Vibrio cholerae (the etiological agent for cholera) (20). Bifidobacteria species have also been shown to secrete a proteinaceous factor that inhibits the binding of pathogenic strains of E. coli (21), adding to their anti-microbial effects.

The use of Lactobacillus acidophilus containing fermented milk products has been shown to reduce the incidence and duration of vaginal and colon Candida (yeast) infections (22). While the mechanism is probably somewhat complex, it most likely includes both passive and active anti-microbial activities, as well as a variety of immunological mechanisms (23).

Immune-Enhancing Properties:

Many of the health benefits associated with lactic acid bacteria and probiotic supplementation are derived from increased immunological activity. This would be expected because of the close association between the gastrointestinal tract and the immune system. For example, several strains of Lactobacilli were shown to enhance the serum and intestinal IgA response to rotavirus induced gastroenteritis in children (24). In another study involving 25 elderly patients, oral doses of Bifidobacterium bifidum and L. acidophilus were shown to significantly increase B cell frequency in peripheral blood and reduce colonic inflammatory infiltration compared with placebo controls (25). Bifidobacterium bifidum supplementation increased phagocytosis of E. coli, a general measure of increased immune response (26,27). Other cellular and humoral responses to Lactobacillus strain ingestion have been associated with reduced

type II collagen induced arthritis in mice (28). More research is needed in these areas to determine how these lactic acid bacteria effect various aspects of the immune system. It is clear, however, that reduced levels of these microflora are compromising for the hosts immune system, setting off a cascade of detrimental effects. Oral probiotic therapy would be warranted in cases of chronic as well as acute immune system suppression.

Carcinogenesis protection:

There has been much research in the past decade investigating the role of lactic acid bacteria and the prevention and treatment of various cancers. Ten years ago, researchers from The Netherlands showed a correlation between increased consumption of fermented milk products with decreased incidence of breast cancer (29). Since then, most of the studies have focused on colon, liver, and bladder cancer. Researchers at the University of Tokyo have reported that oral administration of Lactobacillus casei preparation was effective for preventing recurrence of superficial bladder cancer in two separate double-blind placebo controlled trials (30, 31). The mechanism is most likely related to reducing the amount of ingested carcinogens that find their way to the urine. Individuals fed Lactobacillus casei for 3 weeks had an average of 47% lower urinary mutagenicity (32).

It is known that the ingestion of various foods, especially cooked meats, contain carcinogenic heterocyclic amines. Eight different strains of lactic acid bacteria were shown to have the ability to bind to 4 types of heterocyclic mutagens produced by cooked food (33). This likely explains much of the front-line carcinogenesis protection in the colon as well as the rest of the body. When researchers attempted to induce carcinogenesis with IQ (2-amino-3-methylimidazo[4,5-f]quinoline) in rats, they found that oral Bifidobacterium longum cultures reduced the incidence (% of animals with tumors) in the colon by 100% and in the liver by 80%(34). Multiplicity (tumors/rat) was also significantly reduced in colon, liver and small intestines of male rats. In female rats fed B. longum, mammary tumor incidence was reduced to half and mammary tumor multiplicity was significantly ($p<0.05$) reduced. B. longum has also been shown to suppress azoxymethane-induce colon carcinogenesis, as well as decrease colonic mucosal cell proliferation, tumor ornithine decarboxylase activity, and ras p21 activities (35). All of these activities make B. longum, and similarly other Bifidobacterial strains, important in the protection against carcinogenesis, especially colon cancer. In fact one author concludes: "oral administration of probiotic B. longum exerts strong antitumor activity" (37). Other groups have confirmed these reports (38,39,40). Likewise, similar studies have shown that lactobacilli strains may also have some of these same anticarcinogenic properties (36).

Other benefits:

While this review could continue to define many other benefits associated with GIT lactic acid bacteria and the use of probiotics, only a few more will be mentioned. Many strains of lactic acid bacteria are able to deconjugate bile acids resulting in coprecipitation of cholesterol (41). It is this activity, along with the ability to promote excretion of dietary cholesterol in the feces and a possible inhibition of the enzyme HMG-CoA reductase, that have lead many people to consider probiotic organisms hypocholesterolemic (42). Another major benefit of lactic acid bacteria is the production of short chain fatty acids (SCFA). The colon mucosa is dependent on SCFAs for energy (40-50% of its total energy requirements) and these are produced by the colonic microflora (43). Bowel transit times are regulated by keeping a balanced microflora. And many vitamins (vitamin K and B complex primarily) are supplied to us by a healthy and balanced GIT microflora.

Prebiotics:

A prebiotic is a nondigestable food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon (46). Of the few natural ingredients that meet this definition, Fructooligosacharides (FOS) are by far the best studied and most widely used. FOS is derived from the partial enzymatic hydrolysis of inulin, usually derived from chicory roots. Naturally occurring FOS is found in garlic, onions and Jerusalem artichokes. One of the major benefits of FOS (or other prebiotics) is that it will increase the Bifidobacteria and Lactobacillus strains that have already adapted to that host. It is a way to specifically increase the good bacteria in each patient, without knowing the details of their GIT microenvironment.

FOS has been used to specifically increase the numbers of lactic acid bacteria, especially Bifidobacteria populations in human (46,49) as well as in vitro studies (47). Many of the benefits

described for probiotic use have been found with the use of FOS. Specifically, FOS ingestion reduced the signs of initial colon carcinogenesis in rats (48).

Administering Probiotics and Prebiotics:

No doubt many health care professionals using complementary therapies will already have used probiotics in the form of fermented milk products or capsule/tablet dosing. Now that we have discussed the benefits of a healthy gastrointestinal microflora population, let us look at what defines a good probiotic and how it should be administered.

Viability is extremely important. One of the ultimate requirements of a probiotic is that it consists of living organisms. None of the benefits described previously are valid if the organisms are dead prior to ingestion. Most commercially available strains are grown in large cultures and then quick-frozen or lyophilized for addition to probiotic products. While there are some variations in the survivability of different strains to freeze-drying, the viability of each can be measured after such processes. This viability is measured in colony forming units per gram (cfu/g). For instance, 5 million cfu/g means that in each gram of product 5 million bacteria are capable of forming a colony (a result of active cell division). There may be more than 5 million cells per gram but only 5 million viable organisms. Typically, probiotics deliver 500 million to 10 billion viable organisms (measured at time of manufacturing) per capsule or tablet.

Product viability is reduced dramatically by three things: air, moisture and heat. In the manufacturing of a probiotic, care must be taken to minimize exposure to these factors. Ideally the probiotic will be sealed under nitrogen and kept frozen until it is thawed for encapsulation (encapsulation generates less heat and usually requires less processing time than tableting). Once encapsulated, the product should be immediately bottled with a desiccant to minimize exposure to air and moisture. At this stage, most lyophilized bacteria are fairly stable, even at room temperature, for up to a year. Keeping them cooler longer, and refrigerating them after they are opened will prolong their viability (desiccants should always be kept with product until completed). Purchasing product in one month or at most two months supply eliminates most shelf-life concerns. Some manufacturers are able to keep their inventories very current, which increases product viability for the ultimate consumer. Unlike viable bacterial strains, prebiotics like FOS are extremely stable in most conditions, and are not significantly affected by heat, air, and moisture.

Gastrointestinal survivability and colonization is the next concern. Ingested bacteria must survive the low pH of the stomach, bile salts, and a myriad of digestive enzymes before finding a place to adhere along the mucosal lining. While this is a legitimate concern, this can usually be overcome quite easily by increasing the number of viable bacteria ingested. That is, if 10 billion organisms are ingested and only 10% survive the upper GIT, 1 billion organisms are still available to transiently colonize the colon (per day!). Several in vitro methods are being developed to test strain resistance to gastric juices, enzymes, and bile salts (44) and the ability to colonize the human gut (45). Probiotic products are best ingested away from meals, when stomach acids, bile, and digestive enzymes are not at their peak. While some feel that enteric coated capsules or tablets will overcome such problems, the increased processing time (increasing exposure to heat, air, and moisture) and cost nullifies most of these advantages.

Formulation of probiotics and prebiotics as synbiotics may be an excellent supplemental approach. Each individual has a unique GIT microenvironment and microflora to inhabit it. It is important that a probiotic product supports and stabilizes this environment, without itself creating an artificial microfloral environment. For instance, it is not the intent of a probiotic to replace the Lactobacillus or Bifidobacteria that have adapted to the individual with supplemented strains. These supplemented strains should be thought of as temporary residents that help the permanent residents by keeping harmful bacteria in check and modifying pH to improve lactic acid bacterial growth. Using a prebiotic like FOS with viable bacterial strains (called synbiotics) is an ideal way to do this (50). High levels of viable strains (10-20 billion cfus/day in divided doses) may be warranted in cases of radiation sickness, high dose antibiotic use and severe dysbiosis or candidiasis. Supplemental and prophylactic doses would usually be less than 10 billion cfu/day. FOS is often included in the capsule or tablet with the probiotic strains and would usually range from 50-200 mg/capsule. FOS is often used in gram amounts as a single ingredient, usually supplied as a powder in jars or packets.

While there are many beneficial strains, there is no magic strain for all individuals. Excellent strains would include Lactobacillus acidophilus, L. casei, L. rhamnosis, L. GG, Bifidobacterium bifidum, B. longum, and B. lactis. Choosing a probiotic that has high amounts of 3-5 of each of these or similar strains, along with FOS, will generally be applicable to most patients and most situations.

Conclusion:

Oral administration of Lactic acid bacteria in the Lactobacillus and Bifidobacteria genera are well tolerated and have been used safely in over 140 clinical trials (over 7500 subjects) for more than 25 years with no adverse effects (51). Few therapeutic ingredients can claim that kind of track record. We hope that this discussion of lactic acid bacteria and probiotic therapy will increase the options health care professionals have in helping their patients maintain the best health possible.

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In my opinion

"Scientists have uncovered a new worry about some of the most popular herbal remedies: the possibility that they could cause infertility, or genetically damage sperm."....or have they? This was the lead sentence in an AP news article written by Lauran Neergaard (AP medical writer), released on March 26, 1999. Many of the readers of this publication have no doubt heard, seen, or have been asked directly about this so-called "Herbal-infertility link". Let us probe this issue to see what can be uncovered.

First, the research data itself (published in Fertility and Sterility, March) is of little value in interpreting anything related to human consumption. The experiment involved the soaking of hamster eggs (with the outer zona pellucida removed) in solutions containing either St. John's wort, ginkgo, echinacea, or saw palmetto products. They then added human sperm cells to see if they could penetrate the eggs (a measure of sperm and egg cell competence). They found that St. John's wort, and to a lesser extent, echinacea and ginkgo were able to prevent sperm from penetrating these eggs. They also reported sperm DNA damage after being soaked in St. John's wort for seven days. The authors conclude that the data suggests that these herbs "at high concentrations damage reproductive cells". The AP article goes one step further and "suggests that the side effects of some of the popular herbs—St. John's wort, echinacea and ginkgo—could include blocking conception."

We agree with Varro Tyler (Purdue University professor emeritus in Pharmacognosy) that this study is "seriously flawed". He points out that the products were never tested to determine the exact concentration of the herb used, nor is it even known whether any of these components would ever get to the reproductive cells when taken orally. Dr. Alan Penzias (a reproductive endocrinologist at Harvard Medical School and Boston InVitro Fertilization) is quoted by ABCnews as saying "You can't draw any conclusion from it all, the number of eggs they studied were very few. I've never seen a basic science study that has used so few. And they did not repeat their test several times to see whether they got the same results." He stated that diluted grapefruit juice would kill these eggs, but you couldn't conclude that drinking grapefruit juice causes infertility.

The author of the study, Richard Ondrizek, is quoted in the April issue of Nutrition Outlook as being "flabbergasted" that this in vitro study was being reported as evidence that these herbs could cause infertility in humans. "There is absolutely no parallel between this study and humans. The results of this study were never intended to be equated to human use" says Ondrizek. This didn't seem to be the response from Alan DeCherney, the editor of Fertility and Sterility, who said "This is a very important study that could provide important information to patients suffering from infertility. The growing popularity of these herbal products means we must examine all their possible side effects". Quite enigmatic, at best.

We would like to raise a few questions for our readers to ponder. How is it these authors chose four of the most popular herbs off the shelves of health food stores to do this research, and then were flabbergasted and said these data were never intended to be equated to human use? How could the editors and reviewers overlook the implications of this study, and not require the authors to explore the relevance of this study to anything remotely useful? And how did this insignificant, flawed, and certainly preliminary study find such willing ears in the news media? We may not ever get to the bottom of these questions, but you can be sure this is not the last of such studies.

What will ring in the ears of the public are the final sentences of the AP article: "What's most important about this study is it illustrates something that gets lost in the discussion of herbal preparations," [Dr. Eric] Widra [of Georgetown University] said, "Despite an apparent high degree of willingness among people to try these things, there's very little science to back up their safety." Could it be that the purpose of this study, and its 'naively' vague conclusions, was to allow blanket statements like these to be spread far and wide? I am sure no one would financially gain if that happened.....