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REPORT

Integrative approaches to cancer, cardiovascular disease and diabetes treatment
ACAM Conference, Nashville 2001

by Ivy Greenwell

"Integrative" was a key word at the latest ACAM conference held in Nashville, Tennessee. ACAM stands for American College for the Advancement of Medicine. It is an organization dedicated to the promotion of a more physiologically based medicine, one that combines the best of mainstream and alternative therapies-hence the term "integrative." Through its conferences, ACAM tries to educate physicians in innovative approaches to prevention and treatment.

The recent conference included lectures on new breakthroughs in our knowledge of hypercoagulability and the role it plays in diabetes, cardiovascular disease, cancer and aging-related tissue atrophy. Keeping blood viscosity from rising as we age adds another important goal for anti-aging medicine.

As usual, there were also fascinating lectures on new treatments for heart disease and cancer, and question-and-answer workshops where a topic could be explored in depth.

New light on hypercoagulability in disease and aging

The most exciting lectures of this conference were devoted to the topic of hypercoagulability: the increased propensity of the blood to abnormal viscosity and the deposition of fibrin in the blood vessels. Hypercoagulability is a shift in haemostatic balance toward the dominance of pro-clotting factors. The typical result, however, is not the formation of a clot, which requires the cross-linking of fibrin caused by a burst of thrombin, but rather the deposition of fibrin (fibrinogen is the precursor of fibrin), obstructing blood flow and causing local ischemia, meaning deficient blood flow to certain areas.

When a trauma occurs, such as a severe infection, a car accident or severe emotional stress, most people eventually recover. But a minority go on to develop a chronic condition such as fibromyalgia.

When tissues don't receive sufficient blood, the cells are starved for oxygen and nutrients. Pain can result, as in headache or fibromyalgia. According to the speakers, David Berg, director of Hemex Laboratories and Carol Ann Ryser, M.D., a pediatrician, many chronic conditions such as attention deficit disorder, autism and schizophrenia, as well as multiple sclerosis, Parkinson's disease, irritable bowel, endocrine (hypothalamic-adrenal axis-related) sleep disorder, and the type of infertility that manifests itself in repeated miscarriages (fetal wastage syndrome), are all related to elevated blood viscosity and organ dysfunction caused by impeded, insufficient blood flow.

Dr. Ryser stated that in her clinical practice, every cancer patient she had tested turned out to suffer from hypercoagulability. It appears that cancer cells produce a protein that acts as a pro-coagulant. Research confirms that cancer patients have an increased incidence of blood clots, and that low-dose heparin can be a useful adjunct therapy in cancer, increasing survival. Diabetics and AIDS patients also appear to benefit from low-dose heparin, according to Ryser.

Hypercoagulability is part of the inflammatory response. It has not received the full attention it merits. We know that an excess tendency toward clotting is undesirable, and may indeed be fatal in the case of heart attacks and strokes. So far, however, not too much has been said about increased blood viscosity without actual clots, or about fibrin deposition inside blood vessels of individuals who suffer from chronic hypercoagulability.

When a trauma occurs, such as a severe infection, a car accident or severe emotional stress, most people eventually recover. But a minority go on to develop a chronic condition such as fibromyalgia. These individuals may be suffering from a genetic protein defect that makes them especially prone to develop hypercoagulability. High lipoprotein(a) also promotes hypercoagulability by blocking fibrinolysis. High homocysteine (over 10) is also associated with with hypercoagulability. High blood sugar and high triglycerides also promote elevated blood viscosity. Thromboxane, an eicosanoid derived through the metabolism of polyunsaturated fatty acids, is yet another factor promoting hypercoagulability. Altogether, the regulation of coagulation is quite complex, involving the balance of more than a dozen factors. It takes special tests to establish if a patient might be deficient in proteins C and S, for instance, or shows elevated fibrinogen.

Hypercoagulability can be easily detected through the use of the well-known "sed-rate" blood test. Sed rate of less than 5 indicates hypercoagulability. The difficulty comes in trying to find out the major factor(s) causing the condition. Thus the need for additional testing, so that the right factor (e.g., high lipoprotein(a) or high fibrinogen) can be targeted for treatment.

Virus infections have been singled out as particularly likely to provoke excess fibrin production. This fibrin accumulates in certain places, creating a "fibrin block" that impedes blood flow and deprives a certain area of the body of sufficient oxygen. Ryser said that she finds a history of two to six serious infections per every chronic fatigue patient. There is also suspicion that certain vaccines can act as precipitating agents for inflammation-induced hypercoagulability (e.g. anthrax vaccine contaminated with mycoplasma, a suspect in the Gulf War Syndrome).

Once hypercoagulability is understood, it comes as no surprise that low-dose heparin (a natural anticoagulant, one of several produced by our own body) dramatically improves blood flow and can quickly clear up conditions such as inflammatory bowel syndrome, or help certain women avoid repeated miscarriage.

One item of special interest was the new finding that glucosamine is a mild anticoagulant. Its unexpected benefit is the prevention of migraines in a percentage of cases, at a dose as low as 1,500 mg/day. Some patients need twice or more that dose, however. Using safe, mild, natural anticoagulants adds a useful new technique for migraine prevention.

Some conference participants expressed concern over the long-term safety of heparin administration. This matter requires further research. For milder cases, and for prevention, we have access to safe hypocoagulant agents such as fish oil, curcumin (turmeric extract), ginger and ginkgo.

Hypercoagulability, like inflammation in general, is one of the characteristics of aging. This

topic was addressed by Richard Kunin, M.D., founder and president of Society for Orthomolecular Health Medicine, and author of MegaNutrition. His thesis was that the emphasis on hypercoagulability represents a "paradigm shift" in our thinking about disease and aging. For instance, we can now make sense of the finding that cancer mortality drops dramatically if cancer patients are given heparin.

Giving insulin to a cancer patient induces more cancer cells to go into the division state, and thus renders them more susceptible to chemotherapy, which targets rapidly dividing cells. It has been found that cancer cells have six times more insulin receptors than normal tissue.

Our understanding of the aging process is also enhanced by the perception that impeded blood flow leads to local ischemia (oxygen deficiency), and this is turn translates into progressive tissue atrophy. Only fifteen seconds of ischemia turns off the mitochondria. This initiates an apoptosis (programmed cell death) cascade. The shrinking of our organs with age leads to ever-greater pathology. Loss of heart tissue eventually results in congestive heart failure. Loss of glandular tissue results in hormone deficiencies, loss of neural tissue brings on cognitive dysfunction and eventually senile dementia, loss of lung tissue leads to emphysema, and so on. This is the atrophy of aging that we see throughout the body. The new insight is that "ischemia is a silent cause of aging and degenerative disease."

In order to fight ischemia, we need to keep the blood from getting too viscous and sluggish, and platelets from clumping too readily. We now see that various micronutrients are not only antioxidants, but also anticoagulants. Their great advantage is safety. We know how to counteract various procoagulant factors: high homocysteine, for instance, can be remedied through the use of folic acid, B12 and B6; aspirin, curcumin, ginger and ginkgo inhibit platelet aggregation; curcumin is also known to lower fibrinogen.

High lipoprotein(a) responds to niacin (or inositol hexanicotinate), high doses of vitamin C, and the amino acids lysine and proline. Hormone replacement and exercise also help maintain a more youthful blood circulation. Enzymes such as bromelain and Wobenzym have been found to lower blood viscosity. Even massage is seen in a new light when we learn that it helps release tissue plasminogen activator (tPA) from the lining of blood vessels, thus promoting better circulation.

Once we understand the need to guard against local ischemia, we are better motivated and equipped to take the right countermeasures. Kunin cautioned, however, against accepting hypercoagulability as a primary cause of aging. In his view, hypercoagulability is secondary in importance to the aging-related dysfunction of the hypothalamic-adrenal axis (HPA). Hypothalamic-adrenal axis governs our neurohormonal response to stress. Oxidized adrenaline is a free radical, Kunin stated. "You're not neurotic; you're just living under enormous stress," he said. Ultimately, of course, stress, inflammation and hypercoagulability are inextricably linked. Stress reduction is an important measure we must take to reduce the pathologies of aging, including hypercoagulability.

Integrative cancer treatment

The first lecture on a new approach to cancer treatment was quite exciting from the point of view of theory. Steven Ayre, M.D., Medical Director of Contemporary Medicine Center in Chicago, presented the method he has used in his clinical practice for over 20 years. He calls it "insulin potentiation therapy." Developed by a Mexican physician, Donato Perez Garcia, in the 1930's, the therapy consists of administering insulin together with low-dose chemotherapy.

Insulin is a potent mitogen: it makes cells proliferate. Thus, giving insulin to a cancer patient induces more cancer cells to go into the division state, and thus renders them more susceptible to chemotherapy, which targets rapidly dividing cells. It has been found that cancer cells have six times more insulin receptors than normal tissue. Exogenous insulin thus transforms chemotherapy into the equivalent of a "smart bomb." Because the effective dose of chemotherapy is much lower thanks to the affinity of cancer cells for the extra insulin, side effects are relatively minor.

The difficulty of this technique lies in the proper administration of insulin. Obviously, the patient's glucose levels need to be closely monitored. The other problem is that, as always, there are some patients who do not respond. All agree, however, that the theory behind this therapy sounds plausible, and controlled research would be of great value. Once chemotherapy ends, insulin therapy should stop. Some cancer patients undergo insulin suppression therapy because they don't want to stimulate the propagation of residual cancer cells.

Another speaker was Friedrich Douwes, M.D., Director of St. George Hospital (Klinik St. Georg) in Bad Aibling, Germany. His approach stresses hyperthermia and electrotherapy, but includes conventional treatments as well. Psychotherapy is also available to the patients. Cancer is seen as a complex all-body disease, not just as a tumor that needs to be destroyed. Another principle is that treatment needs to be individualized.

Obese smokers tend to be abdominally obese. Interestingly, 90% of all diabetic amputations (loss of a foot or limb due to diabetes-induced gangrene) are among smokers.

Perhaps the greatest success story of the St. George Hospital is the use of local hyperthermia for prostate cancer, using a catheter with heating electrodes. The heat treatment is combined with a short-time androgen blockade. St. George Hospital boasts of 100% five-year survival for its prostate cancer patients. Local hyperthermia has also turned out to be very effective for brain cancer. Pancreatic cancer patients, on the other hand, aren't so lucky; even with combination of hyperthermia and chemotherapy, the median survival is 21 months-an improvement on mainstream outcome, to be sure, since most pancreatic cancer patients treated with chemotherapy alone die within six months.

Douwes also presented dramatic slides showing the progress of electrotherapy in a patient with breast cancer. Electrotherapy, also called galvanotherapy, is simply the use of electricity to destroy the tumor tissue. It has been found effective also for head and neck cancers. In many cases, electrotherapy makes surgery and radiation unnecessary, according to Douwes.

Isaac Eliaz, M.D., a holistic physician in private practice in Northern California, concentrated on integrative treatment for prostate cancer. He uses androgen-blocking drugs (chiefly Casodex), but also employs a wide array of supplements. Chief among them is modified citrus pectin, shown to inhibit metastasis. Another important supplement is fermented soy protein, tested by Eliaz in an experimental study. The bacterial fermentation process apparently dramatically increases soy protein's anti-cancer activity, as shown by the dramatic inhibition in the rise of patients' PSA in the fermented soy group compared to placebo. Eliaz emphasized that this is not a matter of increased genistein content, but more likely of other compounds found in soy protein. Eliaz found no correlation between serum genistein and the PSA response.

Eliaz individualizes each patient's program. Some of the supplements that he recommends include green tea extract, curcumin and D3, among others.

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Eliaz also expressed the view that surgical removal of the prostate may be undesirable, not only because of the frequent unpleasant side effects, but, more importantly, because the main tumor produces anti-angiogenetic compounds-chemicals that inhibit the growth of new blood vessels in distant tumors. He is more comfortable with the use of radiation, since radiation has been shown to increase the levels of endostatin.

The final speaker on cancer treatments was Rigdon Lentz, M.D., director of the Nashville Apheresis Center. Apheresis is blood filtration similar to dialysis. It can selectively remove certain proteins from the serum. Dr. Lentz focused on the use of aphoresis as therapy for melanoma.

Melanoma responds poorly to chemotherapy, interferon and other mainstream treatments. On the other hand, tumor necrosis factor alpha (TNF alpha), a cytokine produced by macrophages, kills melanoma completely. When a molecule of tumor necrosis factor alpha attaches to the cell membrane, it causes tremendous oxidative stress; the cell dies in seconds.

What stops tumor necrosis factor apha from working, according to Lentz, is being bound to a decoy receptor produced by the tumor. "Cancer patients make plenty of tumor necrosis factor alpha, but it goes to the wrong receptors," Lentz stated. Fortunately, these receptors (the soluble tumor necrosis factor alpha receptors shed into circulation by the tumor tissue) can be filtered out. Lentz concentrated on melanoma cases, but stated that the treatment works also for breast cancer and ovarian cancer, colon cancer, soft-tissue sarcoma and non-small cell lung cancer.

Integrative diabetes treatment

Claude Lardinois, M.D., an endocrinologist at the University of Nevada and medical director of the Nevada Diabetes Association, gave a provocative lecture on Syndrome X and type II diabetes. Syndrome X is also known as the "deadly quartet," consisting of dyslipidemia (elevated serum lipids), insulin resistance (and the high insulin levels that go with it), obesity and high blood pressure. Hypercoagulability is also associated with this syndrome, which perhaps should be called the "deadly quintet." But Dr. Lardinois has come up with a new label that accurately pins down the two chief causes of Syndrome X. It is the "deadly duet of hyperactive fork and hypoactive foot, or the foot and fork disease." In other words, it is a disease brought about by the consumption of excess calories combined with lack of exercise. Hence, the best treatment is the hypoactive fork (calorie restricted, low-glycemic diet and weight loss) combined with hyperactive foot (regular exercise).

Make no mistake about it: while Dr. Lardinois' renaming of Syndrome X and diabetes as the "foot and fork disease: hypoactive foot, hyperactive fork," sounds humorous, it is extremely useful. Rather than simply describing symptoms, it shifts attention to the causes of these pathologies.

We are currently experiencing an explosive epidemic of type II diabetes. African-Americans and Hispanics have especially high rates of diabetes. The label "adult-onset diabetes" has become dubious, since 75% of diabetes now diagnosed among children is type II, once seen mainly only after the age of forty-five. Type II diabetics produce plenty of their own insulin, at least in the earlier stages of the disease. However, insulin is a hormone that downregulates its own receptor. Thus, the higher the insulin levels, the less sensitive the receptors, until severe insulin resistance develops, and glucose remains in circulation rather than entering the tissues. Excess glucose is toxic. This "glucotoxicity" results in accelerated aging and a number of disabling diabetes-related conditions, including heart disease, neuropathy (damage to the nerve cells), kidney disease (nephropathy) and kidney failure, and retinopathy that may lead to blindness.

An effective treatment should address the causes of diabetes (the "deadly duet," leading to insulin resistance), and not just try to ameliorate the symptoms. Metformin, which increases insulin sensitivity, is very useful, and has become the number one drug for the treatment of type II diabetes. Lardinois referred to metformin as a "powerhouse drug." It's interesting that metformin was developed from guanidine, the active component of such botanical folk remedies against diabetes as French lilac and goat rue.

Simply giving patients insulin can be counterproductive. "Doctors make patients even more insulin-resistant by giving them too much insulin," the speaker cautioned.

Dr. Lardinois stated that diabetes has become the number three killer in this country. The reason that this fact is not widely known is that the death certificate tends to list "heart attack" as the immediate cause. Hence the public still doesn't understand the danger that lies in the consumption of a diet high in refined carbohydrates and low in fiber and omega-3 fats (fish oil, flax oil, walnuts) and lack of sufficient exercise. Smoking constitutes another serious risk for diabetes, since it increases insulin resistance. Those who smoke more than 25 cigarettes a day have double the risk of diabetes.

Surprisingly, alcohol consumption decreases insulin resistance, but it may do so through a peculiar mechanism. Alcohol appears to impair the function of beta cells, which leads to less insulin release. Lower insulin levels are then reflected in more sensitive insulin receptors. Both glucose and insulin levels are lower in moderate drinkers than non-drinkers. Lardinois warned, however, that the beneficial effect of alcohol is seen in individuals with body mass index (BMI) over 22 (the average American has a BMI of 26). A thin person (BMI < 22) who drinks too much is at an increased risk of alcohol-dependent diabetes, related to pancreas damage.

The best predictor of diabetes is the body mass index (BMI), and also the type of obesity (being apple-shaped or abdominally obese correlates with diabetes risk, rather than being pear-shaped, with most fat on thighs and buttocks). Obese smokers tend to be abdominally obese. Interestingly, 90% of all diabetic amputations (loss of a foot or limb due to diabetes-induced gangrene) are among smokers. Even smokers who do not develop full-blown diabetes show lower HDL cholesterol, higher triglycerides, greater insulin resistance and higher blood pressure; basically, smoking causes Syndrome X.

A low-glycemic diet that is high in fiber and in healthy fats (with special attention to fish oil) is the cornerstone of holistic treatment of diabetes. "Low-glycemic" means that the diet doesn't increase blood sugar to the degree that typical American diet does, due to heavy reliance on white bread, sugary breakfast cereals, and other highly processed carbohydrates. Because omega-3 fats lead to a profound reduction in insulin resistance, diabetics would do well to eat fish daily.

Omega-3 fatty acids are known to enhance the utilization of fat for energy, thus helping prevent obesity. Long-term supplementation with omega-3 fatty acids has been shown to lower blood pressure and serum lipids.

To point out the importance of low-glycemic diet, Lardinois cited the example of traditional Eskimos, whose typical diet consisted of 45% fat (much of it omega-3), 40% protein and only 5% carbohydrates. Diabetes and cardiovascular disease were unknown. And yet Lardinois hesitated to recommend the Atkins diet. In his opinion, calorie restriction was more important than the actual composition of the diet. Exercise plays a major role both in the prevention and treatment of diabetes. A patient can achieve a 50 to 60 points drop in blood glucose with exercise alone. Skeletal muscles have a unique ability to take up glucose without the need for insulin. The process is regulated by glucose transporters (GLUT-4). Regular exercise induces a greater expression of glucose transporters (GLUT-4), thus lowering blood sugar and improving insulin sensitivity.

If blood sugar is extremely high (over 250), however, no exercise is permitted. "First, get blood glucose down to 125-then any treatment is effective because glucotoxicity is down," the speaker stated. Giving insulin can be the lesser evil, since glucotoxicity is more harmful than the bad effects of high insulin. By the way, the speaker stressed that in a normal person, insulin is a beneficial hormone; for instance, it increases nitric oxide production. Insulin is atherogenic only when there is insulin resistance, which leads to the pancreas secreting too much insulin. Chronically high levels of insulin are particularly dangerous. When insulin resistance develops, nitric oxide production goes down and coagulation increases, paving the way for a heart attack.

When it comes to supplements, Lardinois cautioned that chromium and vanadium do not seem to work for everyone. He was in favor of magnesium. "I strongly feel that all my patients should be on magnesium," he stated, adding, however, that "we don't really know the dose." Testing for magnesium levels is not reliable. We have more knowledge about lipoic acid, especially helpful for neuropathy, and CoQ10, essential for energy production. Likewise, conjugated linoleic acid (CLA) has been shown to be beneficial. Antioxidants such as vitamin E and vitamin C also appear to help.

The overall message is that the patient needs to be "in the driver's seat," taking responsibility for his/her diet, exercise and supplements. Furthermore, the implications go beyond those officially diagnosed with diabetes. As we age, our insulin levels typically increase, and insulin sensitivity decreases. "It's not that people eat more as they get older; it's that they become less active," Lardinois explained. Keeping insulin low should be one of the primary goals of any anti-aging program. Fortunately, there is no mystery about how to accomplish this goal: stay away from processed, refined carbohydrates, get daily exercise and take supplements that support healthy metabolism, including fish oil, CLA, CoQ10 and lipoic acid.

Cardiac care

This year's Denham Harman Lecture was delivered by Gerald Lemole, M.D., Chief of cardiac surgery at Christina Care Hospital in Newark, Delaware. This innovative surgeon explained how he uses supplements both before and after heart surgery.

Before discussing supplements, however, Dr. Lemole stated that he was one of the pioneer surgeons who participated in the first heart transplants. A lot of the early patients didn't live very long after the transplant. It turned out that the surgeons used to sever thoracic lymphatic vessels. Impeded lymphatic circulation (and thus waste clearance) led to "galloping atherosclerosis." Lemole concluded that lymphatic clearance was a very important factor in cardiovascular health, and increasing lymphatic function was vital to the cardiac patients' recovery.

Fortunately, it is relatively easy to promote lymph clearance. First, deep breathing is vital to thoracic lymph circulation. Massage and exercise also promote good lymphatic function. Finally, flavonoids (phenolic compounds found in red wine, tea, chocolate,

berries, citrus and other fruit and many vegetables) also enhance lymphatic clearance. The speaker emphasized that vegetables do not have their previous content of nutrients, due to nutrient depletion in the soil and factors such as long storage; animal food likewise is not as nutritious as in the past. In addition, many drugs cause micronutrient deficiencies. Supplements have become a necessity.

Lemole uses supplements both before and after surgery. A novel supplement that has turned out to be very helpful is ribose, a pentose sugar involved in energy production. Supplementing patients with ribose, both pre- and post-op, increases their ATP levels (ATP is our "energy molecule"). This helps prevent post-surgery heart failure due to a drop in energy production. The recommended dose is 1 gram for healthy individuals, and 5 grams or more for cardiac patients, 20 grams being the uppermost dose. Ribose has gained some popularity with athletes, but the public is still largely unaware of the benefits of this new supplement.

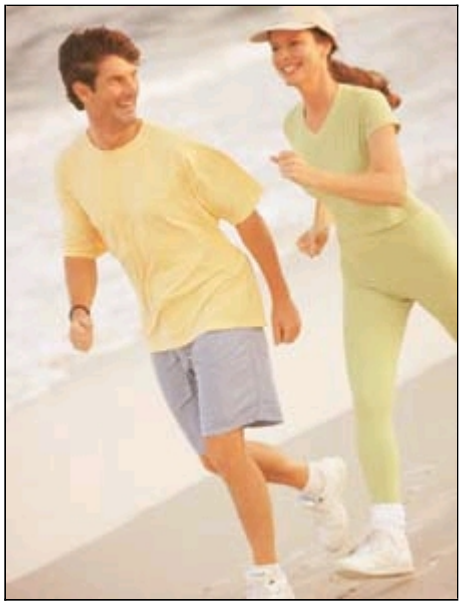
Besides ribose, pre-operative loading includes CoQ10, carnitine and adenine (one of the building blocks of nucleic acids, as well as a part of nicotinamide adenine dinucleotide [NAD], a coenzyme involved in energy production). Together with ribose, these supplements help the heart muscle produce the energy it needs for its contractions.

In addition, Lemole uses such supplements as magnesium, arginine, N-acetyl-cysteine, flavonoids, omega-3 fatty acids, B vitamins, vitamins C and A (to increase fibrinolysis, and thus make the patient less prone to clotting) and vitamin E (which acts as a vasodilator, among its many benefits).

Supplements are not a substitute for a diet change. Lemole pointed out that processed food constituted only 10% of the American diet in 1940; today it is a shocking 90%. A return to unprocessed, fiber-rich food is needed, together with a shift from meat consumption to much more fish consumption. Rather than speak of a low-fat diet, physicians should promote the "good-fat diet," high in omega-3 fatty acids.

Exercise is also a necessity for cardiac patients. Lemole recommends a brisk two-mile walk every day. In addition, the patient can benefit from massage and deep breathing.

Finally, noting the strong connection between depression and heart disease, Lemole urged physicians to become aware of the need for stress reduction and positive emotions in cardiac patients. Through positive self-talk, affirmations and setting positive goals, the patient can learn to become more optimistic. Quality self-help books such as Victor Frankl's Man's Search for Meaning can become an important recovery tool. Meditation and yoga also have proven cardiovascular benefits.



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With the use of this "tripod approach" of exercise, stress reduction and diet combined with supplements, hospital re-admissions could be dramatically reduced.

Conclusion

The ACAM conference in Nashville confirmed the need to fight inflammation and hypercoagulabity as we grow older, pointing to the hitherto relatively neglected idea: adequate blood flow of the immense importance if we are to prevent the ravages of local ischemia and the tissue atrophy that follows. Aging-related tissue atrophy is a universal biomarker of decline, yet until now we have not really regarded sluggish, viscous blood and circulation impeded by fibrin deposits as a major causal factor in local ischemia and tissue atrophy.

One technique for improving circulation is exercise, and the need for exercise came up again and again in terms of diabetes and cardiovascular disease prevention and treatment. Keeping overall calories and the insulin levels low is another requirement for longevity. Finally, it became apparent that certain supplements kept being mentioned over and over. This was especially true of omega-3 fatty acids and curcumin (turmeric extract) as both an anti-cancer agent and a fibrinogen reducer, and thus an anticoagulant.

Aging still seems like an immensely complex biological jigsaw puzzle. Finally, however, more and more pieces are beginning to fall into place. Conferences such as that of the ACAM are helping keep physicians aware of these advances.

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