RESEARC BY NEW

Innovations in cancer, heart disease, and hypertension treatment aren't magic, but they almost seem like it.

Joanne Kaldy

A few years ago, diagnoses such as cancer were grim for elderly patients. At the very least, these illnesses often resulted in lost function or independence, hospitalizations and related complications, rehabilitation, and other problems. Thanks to new treatments and technology—some available now and others on the horizon—elderly patients can face a growing number of diseases with hope and optimism. These pharmacologic, research, and technical innovations aren't magic, but they may have a miraculous impact on how illnesses are treated and care is delivered.

Noninvasive cancer treatments, dietary supplements and nutritional guidelines, and other innovations are keeping elders healthier, happier, and more functional than ever before. Additionally, new vaccines planned for the near future are likely to treat or even prevent chronic diseases.

Cancer Treatment Innovations

In the past, cancer was frequently a death sentence for elderly patients. Even when they survived toxic or invasive treatments, they often were left weak and unable to attain their former quality of life. Now, some new treatments are available to manage the disease with a minimum of side effects and little if any time spent in the hospital.

Innovations in cancer treatments are important for the elderly. As Svetomir Markovic, MD, a researcher at the Mayo Clinic in Minnesota, notes, "One big issue for elderly patients with malignant disease is their number of comorbidities and their ability to with-

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HERS BUOYED DISCOVERIES

stand toxic treatments. So treatments with limited side-effect profiles—both drugs and agents such as vaccines—are key advances for this population."

One important contributor to evolving cancer treatments is the involvement of elderly patients in research regarding these products. "Many more elderly patients are participating in clinical trials than 10 years ago," Markovic says. "Clinicians often shied away from putting older people in trials because of fears of exposing them to toxic therapeutics. Now the treatments being studied are less toxic, and clinicians understand the need to know how these agents work in older patients."

Donald Braun, vice president of clinical research at The Cancer Treatment Centers of America, agrees. "Many of the treatments are being designed for people who will develop these diseases later in life. It is unconscionable to exclude these patients from clinical investigations. We need information about how these patients respond to treatment. There are very motivated people in this age group," he says.

Prevention is an important part of many promising treatments; that is, they are designed to inhibit the characteristics of malignant cells to prevent cancer cells from spreading or growing in the first place. "These products are by association less toxic because they don't target normal tissues surrounding the tumor," Markovic says.

One promising category of these drugs is the tyrosine kinase inhibitors. Sutent is one of the newer ones, recently approved to treat kidney cancer and gastrointestinal stromal tumors. One of the most popular drugs in this class is Gleevac (imatinib mesylate), used to treat chronic myelogenous leukemia and other malignancies. "These drugs offer low toxicity with better efficacy. They are especially appealing for patients with comorbid conditions," Markovic notes.

Other promising new drugs include:

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■ Avastin (bevacizumab), the first U.S. Food and Drug Administration-approved therapy to halt or slow the process by which new blood vessels develop and carry nutrients to a tumor. Used along with chemotherapy, this drug greatly enhances the chemo's ability to control the disease with some types of cancer.

■ Herceptin (trastuzumab), one of a series of drugs that interferes with growth factors identified in the blood. This drug is mainly used to treat breast cancer. It is important to note that the utility of this drug is limited, as only about 20 percent of women have receptors for the growth factors affected by Herceptin.

Elsewhere, aromatase inhibitors are hormone therapies used in the treatment of some women with breast cancer. They lower the amount of estrogen in post-menopausal women who have hormone-receptor-positive breast cancer.

Not surprisingly, breast cancer is the focus of much research. Currently, two targeted medications designed to treat an aggressive form of breast cancer are being tested in a large new study involving 8,000 participants worldwide. The Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization study will provide the first head-to-head comparison of trastuzumab and lapatinibin for the earliest, most treatable stages of breast cancer, according to the Natinoal Cancer Institute.

The study actually will compare four different regimens of targeted therapy administered over a 52-week period. Patients will be randomized to receive either trastuzumab or lapatinib alone, trastuzumab followed by lapatinib, or the two treatments in combination.

Pumping Up The Immune System

Researchers increasingly are looking at the use of monoclonal antibodies to treat cancer. These are made by injecting human cancer cells, or protein from cancer cells, into mice to strengthen their immune response to cancer. These antibodies can be used to treat cancer by strengthening the patient's immune system and to monitor disease progress. This represents an important advance because cancer patients—particularly the elderly—may have weakened immune systems.

Treatments that seek to improve immune response are key to this population, says Braun, because "immunological status of elderly is different than in younger patients, but it can be reprogrammed or reset with proper

treatments." Immune response generally degrades in the elderly, he adds, but immune response is subject to regulation with medications and nutritional support so these patients can have vigorous anti-tumor response.

"Patients—especially seniors—who have suppressed immune systems are more susceptible to infectious diseases and have a hard time healing wounds," Braun says. Therefore, he emphasizes that using nutritional support and dietary supplements that strengthen immune response and limiting medications that damage it is important for elderly patients, even if they don't have cancer. He suggests that long term care facility residents' attending physicians are best positioned to take the lead on this.

Research is changing the way clinicians think—or should think—about treating cancer in the elderly, says Braun. "It has become obvious in recent years that elderly patients who don't get full-dose therapy may be undertreated. We now know that patients with proper nutritional and other support can get full doses. With full support, of mind, body, and spirit, we can get elderly patients through full doses of therapy."

Vaccines For Victory Against Cancer

Strengthening the immune response also is important since many of the vaccines in development to treat cancer or prevent recurrence require healthy immune systems to be effective. "There is much emphasis on the development of vaccines for cancer, typically to treat low-level disease or address relapse," says Keith Knutson, a cancer researcher at the Mayo Clinic.

The use of vaccines to address relapse, particularly in elderly women with breast cancer or a history of the disease, is especially intriguing, Knutson says.

"We have fairly good treatments for primary tumors, but these women remain at high risk of relapse. If we could deliver a vaccine after chemo it would substantially reduce this risk," he notes.

"I'm enthusiastic about these vaccines," Knutson says. "We already have seen some tantalizing clinical trial results, and there are several ongoing studies. Ultimately, we would like to reduce relapse risk to zero, essentially stimulating the immune system to kill cells that are responsible for recurrence of the cancer. We're interested in cancer stem cells that aren't killed by chemo or removed with the tumors. This is a hot topic."

For cancers that have more familial and environmentally related causes, vaccines have to tell the body's immune system to specifically attack itself—but in a targeted fashion. "We need to identify ways to stimulate very targeted responses to cancer antigens. We are on the road to doing this, and I envision it happening within a decade," Knutson predicts.

> The CyberKnife concentrates higher-energy X-ray beams that focus directly on the tumor.

High Tech Targets Cancer

Cutting-edge cancer treatments that eliminate the need for risky surgery are gaining attention and respect. These are particularly useful for elderly patients who may have multiple comorbidities or who are just too weak for traditional surgery. One such option is the CyberKnife procedure, which involves the use of linear accelerators—devices that concentrate higher-energy X-ray beams that focus directly on the tumor. Unlike traditional radiation, this precise beam destroys the tumor while significantly limiting any damage to surrounding tissues and organs.

As Paul Chomiak, MD, medical director of the CyberKnife Center at Frederick Memorial Hospital in Maryland, explains, "The radiation beam is locked on the tumor, and we can deliver more energy to it without killing other cells. 'Collateral damage' is limited." Even if the patient coughs, sneezes, or moves in any way, the beam is programmed to stay on the tumor.

The noninvasive nature of the CyberKnife procedure is especially promising for elderly patients who aren't strong enough for surgery. Even those elderly who could survive surgery would be at increased risk of infection, pressure ulcers, and other complications during the several-week recuperation period that would follow.

With CyberKnife, patients come to the center for one to five sessions that are 60 to 90 minutes long. They must lie still, but they can listen to music of their choosing, and staff monitor their comfort. Most patients can go back to their normal activities that same day.

As for side effects, they are minimal. "Some patients experience fatigue, and—depending on the tumor's location—some have pinpoint chest wall pain or problems swallowing," says Chomiak. Generally, however, patient satisfaction surveys have been positive and enthusiastic. One of Chomiak's elderly patients says that, without the treatment, his inoperable lung cancer likely would have disabled him in the short term and eventually caused his death. Instead, he is enjoying his life and has "all kinds of energy."

Patients who have inoperable tumors or who are poor candidates for surgery or other invasive therapies because of other health problems often are referred for a CyberKnife assessment. "I've been involved in this technology since 2003, and it allows me to offer options for patients who wouldn't be candidates for other treatments," Chomiak says.

For example, for a patient with early-stage lung cancer, the time-tested standard of care would be surgery in which physicians removed a portion of the lung, including the tumor. "This isn't feasible if the patient has other lung diseases or health problems. The best we could offer these patients would be something like chemotherapy, which is like killing a fly with a sledgehammer," Chomiak says.

Currently, Cyberknife Centers are using this procedure to treat tumors of the brain, spine, chest, liver, kidney, and prostate. There are only 122 Cyber Knife Centers worldwide, many of them in the United States.

The procedure is covered by Medicare, but some insurance companies still view it as experimental. However, studies to date have been promising—showing outcomes at least comparable to other treatments, and three larger trials are being planned. Eventually, this growing body of data could lead to increased insurance coverage for the procedure.

"We may reach a point where this becomes a standard of care, but only time and research will tell," says Chomiak.

The MammoSite procedure gives a better cosmetic result than standard therapy, and it has the same cure rate.

Homing In On The Target

Other technological innovations to treat cancer also focus on more precisely targeting the tumor. MammoSite is a procedure that lets doctors compress six and a half weeks of radiation for breast cancer into five days. "This gives a better cosmetic result than standard therapy, and it has the same cure rate," says Dan Cornell, MD, director of radiation oncology at the John Marsh Cancer Center in Hagerstown, Md.

Onboard imaging is another precise therapy that uses a higher dose of radiation and targets tumors more precisely. It involves placing "feducial markers," metallic seeds smaller than a grain of rice, near the tumor to keep the radiation beam targeted and increase its accuracy. "Otherwise, it's like going bird hunting with a deer rifle," he says.

Innovative treatments and new knowledge about cancer continue to come at a furious pace. "Cancer is a complicated issue. There is constant movement on all fronts. The answers could be close and come tomorrow or as far away as the next millennium," says Markovic.

New Blood Pressure Treatment

CYT006-Ang.Qb, a vaccine that blocks angiotensin II receptors, thereby relaxing blood vessels to lower blood pressure, could send a number of current blood pressure medications into obsolescence. In a recent study, the vaccine was well-tolerated and lowered blood pressure in hypertensive patients, according to the National Cancer Institute. Seventy-two patients with mild to moderate high blood pressure were randomly assigned to receive the vaccine at two different doses or placebo. The subjects' blood pressure was measured before the trial and 14 weeks after the trial began.

Researchers found that the subjects who received the higher dose of vaccine had an average drop in systolic blood pressure of 9 mmHg and a 4 mmHg drop in diastolic pressure. This decrease was even higher in the early morning, when subjects had an average 25 mmHg drop in systolic blood pressure and a 13 mmHg drop in diastolic pressure, compared with those who received placebo.

Only 10 subjects reported flu-like symptoms after injection. However, the researchers note that this reaction is common with many vaccines. Mild irritation at the injection site, also experienced by some subjects, also is a typical vaccine reaction.

An important advantage of the vaccine is that it would only require administration two or three times a year, as opposed to the rigorous daily regimens currently required of oral hypertension medications.

"This vaccine would represent a profound breakthrough in treating hypertension in the elderly," says William Simonson, PharmD, a consultant pharmacist and past president of the

American Society of Consultant Pharmacists. "It would represent a dramatic cost saving. We also could avoid the morbidity and numerous side effects associated with traditional antihypertensive therapy," he adds.

Stem Cell Curiosity Continues

Interest in stem cell research to address a variety of diseases continues. Most recently, researchers reported that they were able to control diabetes in mice by harnessing human embryonic stem cells. This suggests the possibility of one day using embryonic cells to provide insulin-producing replacement cells to treat diabetes in humans.

Such an advance likely is years away, however, as there are some concerns that need to be addressed. For example, a small number of the mice in the study developed tumors, suggesting that the cells might not be characterized enough for use in people. Nonetheless, researchers already are experimenting with transplanting insulin-producing islet cells from cadavers for Type 1 diabetes patients. The early results are promising: Transplant recipients have not required daily insulin injections, at least temporarily.

The problem is that there are too few donors to provide cell replacement to more than a small percentage of diabetic patients. Embryonic stem cells, on the other hand, potentially could be turned into any type of cell in the body and could be a source of islet cells.

"Such treatments could represent an extraordinary new level of care—a groundbreaking paradigm shift that would revolutionize the way we view and treat diabetes," Simonson says. "The resultant reduction in blood glucose monitoring, insulin injections, and other interventions also would result in dramatic improvements in patient quality of life. At the same time, it would significantly reduce nursing time spent on diabetes care, but this is just icing on the cake," he says.

> We could avoid the numerous side effects associated with traditional antihypertensive therapy.

Researchers continue to learn about heart disease in the elderly. One recent study that has a lesson for long term care practitioners is the Action to Control Cardiovascular Risk in Diabetes (ACCORD), a large clinical study of adults with established Type 2 diabetes who are at especially high risk of cardiovascular disease. The study began enrolling participants in 2001 in 77 clinical sites across the United States and Canada. A total of 10,251 adults with Type 2 diabetes are participating. At enrollment, study participants were between 40 and 82 years old (with an average age of 62), had diabetes for an average of 10 years, and were at especially high risk for cardiovascular disease events.

Recently, the study's sponsor, the National Heart, Lung, and Blood Institute, stopped the intensive blood-sugar-lowering treatment in the study and transitioned participants in that group to the same goal as participants in the standard treatment group. The remaining two treatment questions in the study—blood pressure and lipid trials—will continue until June 2009 as originally planned.

This change was due to safety concerns following a thorough review of available data and recommendations by the study's Data and Safety Monitoring Board. Specifically, there was an unexpected increase in total deaths from any cause among participants who had been randomly assigned to the intensive blood sugar treatment group, compared with those assigned to the standard blood sugar treatment group. The data analyses showed that over an average of almost four years of treatment (ranging from about two to seven years), 257 participants in the intensive-treatment group died, compared with 203 within the standard treatment group—a difference of 54 deaths, or an excess of about three deaths per 1,000 participants treated for a year.

Lessons From ACCORD

The take-away message from this change for long term care clinicians, says Wilbert Aronow, MD, clinical professor of medicine in the Division of Cardiology and Pulmonology/Critical Care at Westchester Medical Center/New York Medical College, is that "we should stay with the current American Diabetes Association [ADA] recommendations of lowering hemoglobin A_{1c} to less than 7 percent. Intensive treatment caused more deaths than the ADA recommendations."

William Smucker, MD, CMD, adds, "The study did not support the hypothesis that cardiovascular death and disability from diabetes could be reduced by lowering Hemoglobin A_{1c} to below the ADA recommendations. This is particularly true in long term care, where a 'typical' resident with diabetes is a relatively poor candidate for aggressive glucose lowering." He adds, "Tight glycemic control also carries the risk of hypoglycemia, which is unpleasant at best, but potentially dangerous if prolonged and frequent."

Lastly, he notes, "The greatest reductions in cardiovascular risk for patients with diabetes mellitus come

from blood pressure control, aspirin, and lipid control."

More significant to long term care than ACCORD, says Aronow, are the results of a recent study on the treatment of hypertension in the elderly, reported in the *New England Journal of Medicine*. Authors N.S. Beckett *et al.* randomly assigned 3,845 patients from Europe, China, Australasia, and Tunisia 80 years old or older with a sustained systolic blood pressure of 160 mmHg or more to receive either the diuretic indapamide or placebo. The angiotensin-converting enzyme inhibitor perindopril or placebo was added if necessary to achieve the target blood pressure of 150/80 mmHg.

Not only was there a reduction in the rate of fatal and nonfatal strokes in the treatment group, but there was a reduction in the rate of death from cardiovascular causes and fewer serious adverse events. This reinforces the benefit of treating hypertension in stroke prevention.

Nutrition News

There is much confusion and debate about how, when, and even if various vitamins, dietary supplements, and so-called nutraceuticals are beneficial in elderly patients. However, there is growing interest in this area, particularly as boomers age and seek more options for disease prevention and treatment. A broad discussion of this topic would fill a book. However, here is a summary of some recent and significant data about these products and the elderly.

■ Co-Enzyme Q10 (CoQ10) is a nutritional supplement used to improve and maintain heart health. In fact, researchers have found that, in most cases of heart disease, there was an associated deficiency of CoQ10, while healthy hearts had an ample amount. To date, over 20 double-blind studies have shown CoQ10 supplementation to improve heart function by increasing the energy production in the heart muscle and acting as an antioxidant.

While the body manufactures some of its own CoQ10, research has demonstrated that supplementation has significant benefits. CoQ10 is being studied as possibly having a positive impact on Parkinson's disease (PD), as PD patients have been shown to have low CoQ10 levels. Without this, the cells of the basal ganglia become very susceptible to damage by circulating toxins, according to researcher M.F. Beal, as reported in the *Annals of the New York Academy of Science*. By improving the function of mitochondria, which produce energy in the cells, CoQ10 also helps provide the brain cells the energy needed to function properly.

One study involved patients with the three primary features of PD—tremor, stiffness, and slowed movement. After being divided into four groups, three received different doses of CoQ10, while the fourth received placebo. The group receiving the largest dose (1,200 mg/day) displayed slightly less decline in mental function, motor function, and the ability to perform activities of daily living than the other groups, according to researcher C.W. Schults *et al.* in the *Archives of Neurology*.

■ A few supplements show some evidence of being efficacious in the treatment of dementia. While some studies have shown a benefit of Ginkgo biloba in treating dementia, others have shown no difference between Ginko biloba and placebo in these patients, according to researchers E. Ernst and M.H. Pittler in the journal *Clinical Drug Investigation*. Nonetheless, both the British and German Pharmacopoeias list dementia as an indication for Ginkgo biloba extract.

■ Other supplements such as B12 and -7, curcumin-8, -9, -10,- and -11, aloe vera, and ashwagandha-12 are being studied for their effects on cognition and memory loss. Methylsulfonylmethane has properties that inhibit cholinesterase. While there are no large randomized controlled trials of these supplements, they are used by patients and alternative medicine specialists. No studies have found these supplements to have side effect profiles or interfere with drug actions.

■ At least one study has shown that rice bran lowered blood glucose by up to 30 percent in a small group of patients with Type 1 or 2 diabetes in a pilot study. Researchers say that one out of four people with diabetes in the 57-subject study was able to reduce daily insulin injection or medication dosages after adding stabilized rice bran to their diets for just two months, said researcher A. Qureshi in the *Journal of Nutritional Biochemistry*.

"We need more studies to determine the precise impact of herbal and nutraceuticals in the elderly, but there is enough evidence out there to suggest that some of these products are useful in this population," says Jacqueline Vance, RNC, director of clinical affairs at the American Medical Directors Association.

"One definite plus is that these products include natural ingredients and don't contribute additional toxics or chemicals to the body," adds Jonathan Musher, MD, CMD, a Maryland-based physician. There is a movement by a growing number of practitioners to embrace these products to treat specific conditions documented in the literature." He notes, "We likely will see more studies in this area in the coming years."

Like most Americans, facility residents don't necessarily get enough vitamins and minerals from daily food intake. "Supplements don't substitute for foods such as fruits, vegetables, and whole grains, but they are beneficial in conjunction with a healthy diet," says Annette Dickinson, former president of the Council for Responsible Nutrition in Washington, D.C.

Dickinson suggests that long term care facilities consider using dietary supplements to help make sure their residents get the nutritional values they need. "Almost everyone could benefit from a good daily multivitamin with minerals," she notes. This is particularly true of elderly people, as "surveys show that they are even more likely than others to fall short in nutrients."

Vitamin D supplementation can be especially important for elderly long term care residents.

The Value Of The Sun

The benefits of calcium supplementation in the elderly have been well documented, but lately attention has turned to vitamin D. "The current recommendation is that people over age 70 should have 600 units of vitamin D daily," Dickinson says. "Vitamin D supplementation can be especially important for elderly long term care residents, especially those who don't get much sun exposure."

This brings up an additional controversy, she says. "Dermatologists advise against sun exposure, although this has always been an important source of vitamin D. The medical community has not done us a favor by failing to reach an agreement about the amount of sun exposure that is safe and beneficial," says Dickinson.

"In recent years, the emphasis has been on fear of sun and the heavy use of sun blockers. We want to avoid both ends of the spectrum, but there needs to be a way to ensure residents get vitamin D from other sources if they don't get sun exposure."

This is an important issue, as there is reason to believe that nursing facility residents aren't getting enough vitamin D even with supplementation. Two recent studies showed that half or more of nursing facility residents receiving substantial vitamin D supplements are deficient in the nutrient. Authors of both suggest that residents generally should receive twice the dose of vitamin D recommended for healthy seniors. A 14-epi analog of dihydroxyvitamin D—a prescription preparation that mimics the vitamin D the body produces—may be useful or necessary for some residents, particularly those with osteoporosis.

The influx of vitamin waters on the market can create some misconceptions about nutrition. "You can't assume that drinking one of these waters is enough. It certainly isn't a substitute for supplements," Dickinson notes. "It also is important to realize that some of these products have sugar, caffeine, and other ingredients that patients shouldn't have." These may be appropriate for patients who can't swallow pills, but she suggests looking at options like chewable vitamins.

One new dietary recommendation is for people over age 50 to get vitamin B12 from supplements or a fortified food source. "The synthetic form is easier to absorb, and it might be easier to use in an institutional setting," says Dickinson. However, she notes that as many companies have begun to add folates to food such as cereals and breads to ensure adequate intake of folic acid, some are beginning to add B12 as well. So, increasingly, food may be a plentiful source of this vitamin.

While many consumers have jumped on the antioxidant bandwagon, Dickinson suggests that this enthusiasm may be a little premature. "Many disease prevention studies with antioxidants aren't showing as positive a result as hoped for. However, it is still important to consider antioxidants for mental function and to protect against infectious diseases," she says. "There is more awareness than ever in the medical community about the importance of nutrition and dietary supplements."

Treatments Improve Quality Of Life

"We need to treat the patient, not the disease," says Braun. "This message needs to come across, especially for those clinicians caring for the frail elderly. Assessments need to be global in nature, and we need to consider all of the patient's needs—physical, emotional, and spiritual." This growing move toward patient-centered care is evident in many of the new and evolving treatments addressed here. The trend is toward less invasive procedures that can be done on an outpatient basis and treatments with minimal complications and side effects.

All of this suggests a future in which seniors will have more options than ever to treat their illnesses and access to care that will seem like nothing short of a miracle. ■

For More Information

■ To read about the "Action to Control Cardiovascular Risk in Diabetes" study, go to www.accordtrial.org.