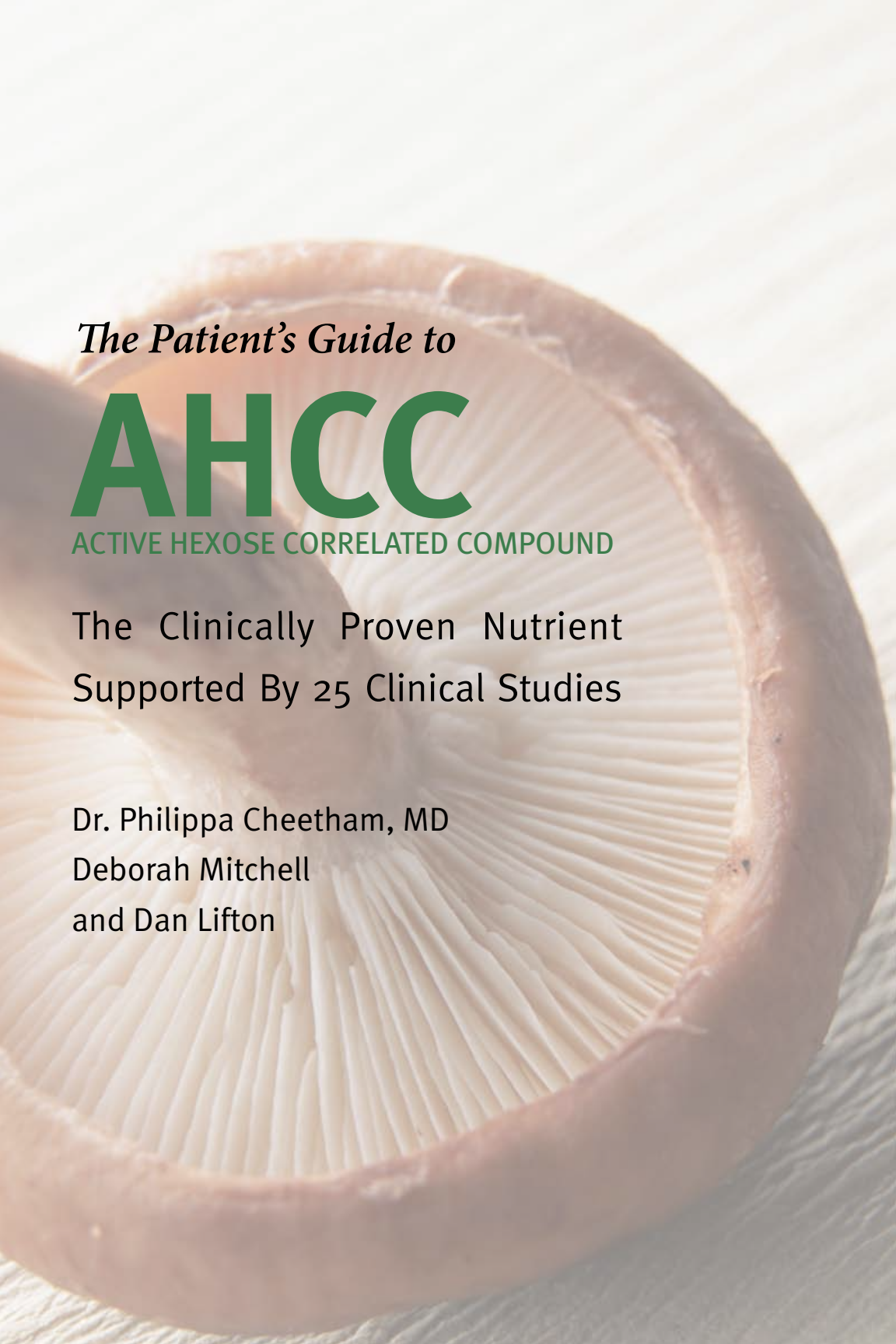

The Patient's Guide to

AHCC

ACTIVE HEXOSE CORRELATED COMPOUND

The Clinically Proven Nutrient Supported By 25 Clinical Studies

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INTRODUCTION

Active hexose correlated compound: the name may not be engaging or always easy to remember, but AHCC—as it is commonly known—is proving to be an exciting, innovative, effective—and memorable--nutritional supplement. More precisely, AHCC is not just a supplement; it is a functional food, and one that is, at its core, derived from healing mushrooms. Although mushrooms have long been recognized and honored by various cultures for their medicinal properties and there are numerous mushroom products on the market, AHCC is different from all the rest.

If you are thinking, "Yes, I've heard that line before" or "Just what we need, another supplement that claims to cure everything," we would have to agree with both of those sentiments. AHCC is different, but does it cure everything? No. Can taking it greatly enhance your health or the health of someone you care about? Most definitely.

This book shares what experts know about AHCC and individuals have experienced when using this functional food. Basically, scientists have discovered that this potent, versatile gift from Nature has impressive immune system enhancing abilities along with anti-inflammatory properties and other healing features. These characteristics are the core of what makes AHCC such an important product. We discuss these characteristics in more depth later in the book, but for now let's just say that strengthening and maintaining a strong immune system is instrumental not only for fighting infections like colds and flu, but also for protecting the body against and treating many serious and chronic diseases such as arthritis, heart disease, autoimmune diseases, and cancer because at their core, they may share one thing: they may be

controlled by, or otherwise intimately associated with, the immune system. Reducing inflammation is crucial because, although inflammation is the body's natural response to attack, it also is a key element in these same disorders, and more. Basically, where there's inflammation, there's a problem.

Therefore, having an effective, safe functional food supplement that can be called upon to help prevent, treat, or manage these and other health challenges is, to say the least, highly desirable.

Although AHCC has been studied extensively in both animals and humans for more than 20 years, scientists continue to learn more about it every day, with each new study presenting more insight and knowledge. It is not enough to say "We have done xx number of studies and AHCC it is a supplement you should take." We are on a journey of discovery, and what has been uncovered thus far has been promising and, in many cases, life-changing in small ways as well as big ones. You are invited to join us on this path of opportunity so you can discover how AHCC could make a positive difference in your life.

CHAPTER 1

AHCC: A MOST REMARKABLE MUSHROOM

Warning: if you were to look up AHCC in a book on mushrooms or fungi, you would not find it. AHCC is not a genus or species of mushroom but a unique compound extracted from the hybridization of several subspecies of mushrooms. Here is a brief rundown of the birth of AHCC.

Birth of a Remarkable Mushroom Product

First you take shiitake mushrooms, which have a rich history of healing powers. Add to the shiitake several hybrids from the Basidiomycete family of fungi. Rather than using the "fruiting body"—the familiar cap and stem part of the mushroom that is above ground—we are going to use only the mycelium (plural: mycelia), which are the hairlike root structures below the ground. The various mycelia are cultured in rice bran extract (which possesses antiviral and immune-system enhancing qualities of its own) until they form a colony.

This colony is then cultured for an additional 45 to 60 days. The resulting product undergoes a series of patented steps that involve cultivation, decomposition by enzymes, sterilization, concentration, and freeze-drying, all developed at the University of Tokyo Faculty of Pharmaceutical Sciences by Dr. Toshihiko Okamoto, along with researchers at Amino Up Chemical Co., Ltd. The end result of this carefully computer-monitored manufacturing process is the functional food supplement AHCC, a product with impressive and growing evidence of effectiveness and an impeccable safety profile (see more on safety in chapter 8).

One special part of the manufacturing process occurs when the enzymes break down the nutrients in the mycelia into a form that is better absorbed by the body. This fermentation process results in AHCC having a much lower molecular weight (5,000 daltons to be exact) when compared with other mushroom extracts, which average 100,000 daltons or higher. This low molecular weight is a unique feature of AHCC. A low molecular weight allows the compounds in AHCC to be utilized optimally by the body. In particular, the immune system's white blood cells have easy access to AHCC's constituents so they can use them to strengthen the body's defenses and fight tumors. So what are those nutrients?

AHCC: Much More Than a Fungus

The chemical composition of AHCC includes (approximately) carbohydrates (44%), fats (37.3%), proteins (7.2%), vitamins B1, B2, and B3 (niacin; 0.3% each), fiber, minerals (4.5%, sodium and potassium), and water (1.3%). Most of the carbohydrates are polysaccharides, complex carbohydrates formed by the bonding of various monosaccharides, which include sugars such as glucose and fructose. The "secret" of AHCC's activity in the body is found primarily in its carbohydrates; specifically the polysaccharides known as alpha-glucans and beta-glucans.

Excuse us if we get a bit technical here, but an explanation of alpha-glucans and beta-glucans can help you better understand why AHCC is much more than a fungus. First of all, polysaccharides are the active compounds in many healing foods and supplements made from mushrooms and plants. The primary polysaccharides in other mushroom-based health foods are beta-glucans. The words "alpha" and "beta" refer to the types of bonds each glucan has with sugar (glucose) molecules. [[FIGURE 1.6 COULD GO HERE]]

The main polysaccharide in AHCC is acetylated alpha-glucan (specifically, alpha-1,4-glucan) and, to a lesser extent, beta-glucans. The presence of acetylated alpha-glucan makes AHCC unique and especially effective. The word "acetylating" means adding an acetyl group (CH3CO-) to glucan. This occurs during the long culturing process that is part of the manufacturing of AHCC. Acetylated alpha-glucan has a molecular weight of 5,000 daltons while beta-glucans are much higher and thus more difficult for the body to digest and absorb. That does not mean the beta-glucans in AHCC are not helpful: they definitely have a positive impact on the immune system by stimulating the intestinal tract, a benefit that is sometimes referred to as "gut immunity."

The acetylated alpha-glucans, however, are the stars and the unique component of AHCC. They directly impact the immune system after they are digested and absorbed by the body. Various scientists have explored the activities and functions of alpha-glucans versus beta-glucans, including a team at the Cancer Research Unit of the Pathology Division of the Department of Medicine, Hokkaido University. They divided each component of AHCC into those with high molecular weight (e.g., beta-glucans) and low molecular weight (e.g., alpha-glucans) and studied their effect on cancer-bearing mice.

When the scientists examined the cancer cells in mice that received AHCC components of high molecular weight versus those of low molecular weight, they noted that certain immune system cells called interleukin-12 and tumor necrosis factor-alpha (beneficial immune cells that we discuss in detail in the next chapter) were induced, but induction of interleukin-12 was strongest when low molecular weight components were given. Experts also know that the low molecular weight polysaccharides of AHCC are mainly effective in improving the production abilities of immune system elements that have potent immune-stimulating actions. In other words, high-molecular weight beta-glucans are effective, but low-molecular weight alpha-glucans are superior.

"Radical" Ideas about Infections and Disease

What is a disease? If your doctor gives you a diagnosis of heart disease, you automatically assume you have a heart problem and your doctor treats your heart. Similarly, if you have benign prostatic hyperplasia, a disease characterized by an enlarged prostate gland, you have a problem with that specific gland and you are given a treatment plan for your prostate. This makes sense, right? Yes, and not necessarily.

Recently, experts within the conventional medical arena have been exploring the idea that some health conditions affect the entire body, even though they may appear to involve only the heart, lungs, prostate, or other organ or body part. This is a more holistic and encompassing perspective of disease and health, and introduces the idea that since the immune system is present throughout and affects the entire body, and thus can impact the activity of every organ and organ system, it makes sense to strengthen the immune system in order to fight, prevent, and/or treat a wide variety of health problems.

In fact, Katsuaki Uno, MD, a cancer researcher and oncologist who uses AHCC for his cancer patients, has pointed out that in order for cancer cells to develop into a tumor, they require a certain environment or "diseased condition," one that is the result of a deterioration of the immune system. He has stated that "cancer is an abnormality of immunity that brings about the onset of diseases—it's a disease of immunity."

This may be a radical idea for some people, but it is gaining a lot of attention and supporting evidence. Uno also explains that "these days many specialists have come to realize that abnormalities of immunity play a fundamental role in the deterioration of 'diseases of lifestyle,' conditions in which the system is overtaxed, such as arteriosclerosis and high blood pressure, into the onset of cerebral vascular disease, cardiovascular disease, diabetes, and other conditions."

In other words, if your immune system has been weakened and is struggling for any number of reasons ranging from stress to poor nutrition to exposure to environmental toxins, it provides a fertile environment for disease to take hold. And we are not talking about just an invasion of disease-causing bacteria and other microorganisms that can result in the common cold or flu or hepatitis, but chronic diseases not typically associated with infections, such as heart disease, diabetes, and arthritis.

So here is the other part of the "radical" idea: Scientists have found a possible con-

nection between microorganisms and chronic diseases not previously believed to be caused by infections. In fact, researchers have made a connection between microorganisms and arteriosclerosis, rheumatoid arthritis, polycystic ovary disease, some forms of cancer, multiple sclerosis, duodenal ulcers, diabetes, heart disease, Alzheimer's disease, various psychiatric disorders, and others.

Therefore, the concept of strengthening and supporting the immune system with a functional food supplement like AHCC is feasible because (as you will learn later in this book) research strongly indicates that AHCC has the ability to positively strengthen, enhance, or otherwise improve the immune system's response to elements that threaten to harm you, which is the key and gateway to physical and mental health.

Now, before we explore the immune system in detail and the intimate relationship between AHCC and components of the immune system, let's look at some special features of AHCC.

AHCC and Inflammation

Inflammation is a reaction of the immune system in response to trauma, infection, or irritation. Characteristic responses include a rush of white blood cells to the area involved, along with heat, swelling, pain, and dysfunction of the tissues or organs affected. Inflammation is the initial response that stimulates the immune system and a critical first step in the process of fighting an infection and healing damaged cells and tissues. However, when inflammation is chronic, which means the immune system is always in alert mode, it can lead to chronic conditions.

In recent years, scientists have discovered that inflammation plays a major role in a great number of chronic diseases. Included are allergic disorders, such as allergic asthma, atopic dermatitis, and pollen allergies; autoimmune disorders such as rheumatoid arthritis, lupus, and ulcerative colitis; and a number of other conditions you may not associate with inflammation, such as Alzheimer's disease, cancer, diabetes, heart disease, irritable bowel syndrome, obesity, Parkinson's disease, and more. This discovery has given scientists and clinicians a better understanding of these conditions as well as new ways to approach treatment. AHCC may be one of those treatments.

AHCC has anti-inflammatory properties, which makes it a potential candidate for addressing diseases characterized by inflammation. One very effective way to monitor the level of inflammation in the body is to measure the amount of a protein in the bloodstream called C-reactive protein, or CRP. When levels of CRP are high, this signals the presence of infections, certain cancers, inflammatory bowel disease, pancreatitis, cardiovascular disease, and other inflammatory conditions. Research has also shown that AHCC may reduce inflammation and the high levels of CRP.

AHCC may also increase levels of leptin, a hormone with anti-inflammatory properties. Dr. Satoru Yui of Teikyo University Department of Pharmacology has reported AHCC is capable of increasing levels of this anti-inflammatory agent. Leptin is also involved in weight control because it is instrumental in the metabolism of fat and in

regulating appetite. This suggests AHCC could be helpful in controlling weight.

Current conventional treatments for inflammation typically include medications such as steroids and nonsteroidal anti-inflammatory drugs (NSAIDs), which are associated with significant side effects, including gastrointestinal bleeding and nausea, while some NSAIDs even damage the immune system. AHCC could provide a safe, effective alternative, and they also could be used along with these drugs to enhance healing as well as have a positive impact on the underlying cause of the disease.

AHCC as Antioxidant

Oxidants are substances in food, the environment, and some medications—especially chemotherapy drugs--that increase the activity of oxygen in the body and result in a process called oxidation. Oxidation is the deterioration or aging of cells. Physical and emotional stress can also act as oxidants. Oxidants spawn the creation of free radicals, molecules that can damage cells, tissues, and organs.

Antioxidants fight oxidation and free radicals and the damage they can cause. AHCC has demonstrated antioxidant abilities against a number of oxidants, including various chemotherapy drugs and a potent oxidant called ferric nitrilotriacetate, and to induce enzymes that eliminate another powerful oxidant called superoxide dismutase (SOD).

AHCC has also been shown to alleviate the physical response to emotional stress. When the body is subjected to emotional stress, the balance between the immune and endocrine systems is disrupted, which can result in physical ailments and disease. An experiment conducted in rats by Professor Shigeru Matsuzaki of Dokkyo University School of Medicine revealed that administration of AHCC to rats subjected to confinement stress controlled the levels of elements known to rise under stressful conditions; namely, blood sugar and adrenalin. Thus AHCC can reduce stress and help maintain the balance between mind and body.

AHCC as Immunomodulator

An immunomodulator is a substance that changes, suppresses, or strengthens the immune system. Chemical examples include methotrexate and azathioprine, drugs that are often used to treat the immune response in people who have various cancers, psoriasis, or rheumatoid arthritis. Chemical immunomodulators, however, are a double-edged sword. While methotrexate can slow the growth of cancer cells and skin cells, for example, as well as suppress the immune system in rheumatoid arthritis patients, it can also damage bone marrow and reduce the number of red blood cells (also see chapter 5), along with damaging the liver.

AHCC presents a broader effect in that it has a normalizing function. That is, it can stimulate the immune system when there is an inhibited response, but it can also calm excessive immune reactions. An example of this dual ability can be seen in how AHCC affects cancer cells.

As you will learn in chapter 2 where the immune system is discussed in detail, AHCC

can stimulate production of a substance called tumor necrosis factor alpha (TNF-a). This substance promotes the breakdown of tumors, which makes it a good candidate for cancer treatment. TNF-a also has a pro-inflammatory effect, which is a problem in people who have arthritis. The good news is that AHCC has been shown that it can also stimulate the reduction of TNF-a in people who have rheumatoid arthritis. This is an example of AHCC's normalizing function, and it appears to be the result of AHCC's ability to strengthen the function of the immune system in the area of the body where it is most needed.

How AHCC is Studied

Since we have illustrated a relationship between infectious organisms and chronic disease and the immune system, it seems like a good time to mention how experts study AHCC. One of the challenges scientists face when researching ways to treat infectious diseases is that there are no ethical, reliable, or practical means to evaluate the human response to infectious agents. However, what they can and do perform are studies using animal models, which allow them to demonstrate the efficacy of AHCC. They also conduct human clinical trials, which allows them to show AHCC's ability to act on the many components of the immune system.

That is why you will notice that some of the studies discussed throughout this book have been done on mice. Mice are highly homologous with humans, and the strains of mice used in biomedical research have been genetically designed so scientists can accurately reproduce the same strains again and again. This helps ensure investigators are comparing "apples with apples," so to speak, when conducting research.

These mice have critical characteristics that make them ideal for drug testing as well as for research of a range of human diseases and conditions. In fact, scientists have developed strains of inbred mice to produce those with Alzheimer's disease, arthritis, lupus, ulcers, inflammatory bowel disease, diabetes, obesity, and a wide range of cancers, among other conditions.

Therefore, a combination of animal models, human clinical studies, and human case reports are the proving grounds for AHCC, and these are the grounds we will explore throughout this book.

Wrap-Up

AHCC is a most remarkable mushroom product, displaying anti-inflammatory, immune system enhancing, immunomodulation, and antioxidant properties. These characteristics make AHCC a likely candidate for a broad spectrum of health issues ranging from the common cold to cancer. Why? Because most of the ailments and diseases that affect people are intimately associated with the immune system. If you boost and strengthen immune functioning and immune response, then you can gain an upper hand in fighting these illnesses and diseases. And that's where AHCC enters the picture. The relationship between AHCC and the immune system is a complex and intimate one, and one that is explored in the next chapter.

CHAPTER 2
INTRODUCING YOUR IMMUNE SYSTEM

The immune system is something people tend to take for granted until they need it. The truth is, however, is that you always need it, even when you're feeling completely healthy. Your immune system is constantly "on," monitoring your body for any cinch in the armor: the presence of abnormal cells, renegade cell growth, and antigens: unwelcome bacteria, viruses, fungi, parasites, toxins, and other organisms that could trigger a health problem. However, the individual components of your immune system need to be "on" as well, primed to act when called upon. If one or more of those components are inadequate, then your health can suffer.

CC Image Courtesy of Vladimir Morozov via Flicker

Considering the critical role the immune system plays in your health, it's worth taking some time to understand it better. Knowing how your immune system functions, and especially the ways AHCC interacts with it, can help you better appreciate how AHCC can improve your health.

The immune system is the body's defense against infectious organisms and other unwelcome substances. Through a series of steps called the immune response, the immune system identifies, targets, and attacks these bacteria, viruses, and other antigens, that can cause disease.

Components of the Immune System

The immune system is a complex network that involves many different cells, tissues, and organs that have varying and often interconnected roles. (See list below). The main cells involved in immune system functioning are white blood cells, or leukocytes, of which there are two basic types: macrophages, which "eat up" abnormal cells and invading organisms; and lymphocytes, which destroy foreign substances, produce chemicals that act as messengers, or allow the body to remember and recognize previous

invaders so the body can destroy them.

The key transportation apparatus for the immune system is the lymphatic system, which is a combination of organs, nodes, and ducts that transport a watery clear fluid called lymph throughout the body. The lymphatic fluid performs several critical functions: it delivers nutrients and chemical messengers to the body's cells, and it interacts with the blood circulatory system to carry away waste materials from the cells.

The immune system also includes the spleen, tonsils, thymus gland, adenoids, and sections of the small intestine, all of which are composed of lymphoid tissue, where lymphocytes are formed. Other important players in the immune system are bone marrow and mucous membranes, which are found throughout the body as well. In fact, lymphatic tissue is found in every part of the body except the central nervous system. Therefore the heart, lungs, intestinal tract, liver, and skin also contain lymphatic tissue and thus are intimately connected to the immune system. When we say that AHCC has an impact on the entire immune system, it follows, then, that it has an impact on nearly all parts of the body.

Lymphocytes start out their lives in the bone marrow and either stay there and mature into B lymphocytes (B cells), or they migrate for the thymus gland, where they turn into T lymphocytes (T cells). The T cells and B cells have a close working relationship: B lymphocytes seek out invading organisms and send in forces to attack them, while T cells destroy the invaders once they have been identified.

Macrophages also arise from the bone marrow. These white blood cells ingest bacteria and other harmful organisms in a process called phagocytosis. Macrophages get some assistance from other white blood cells called neutrophils.

Here is a brief review of some of the players involved in immune function. Many of these factors work together in its effort to support and maintain an optimally functioning immune system. We will be referring to these various immune components a great deal throughout the book.

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- **Antigens:** Substances—bacteria, viruses, toxins, foreign blood cells—that when introduced into the body stimulate the production of an antibody, which can then neutralize the antigens.
- **T lymphocytes (T cells):** A type of white blood cells involved in various immune functions. There are several subtypes of T cells, including helper T cells, suppressor T cells, and cytotoxic T cells.
    - **Helper T cells** do not kill cancer cells or germs directly, but they release substances that help B cells and killer T cells work better. There are also 3 types of helper T cells, two of which we are concerned with: helper T1 (Th1), which are involved in cell-mediated immunity; and helper T2 (Th2), which are involved in humoral immunity
    - **Suppressor T cells** help make sure the immune system does not overreact (i.e., it suppresses) and attack other healthy parts of the body
    - **Cytotoxic T cells (killer T cells)** release substances that kill abnormal cells and invading organisms in the body
- **B lymphocytes (B cells):** B cells are produced in the bone marrow and mature into plasma cells. They are responsible for the production of antibodies, which are key in the fight against bacterial infections.
- **Dendritic cells (DCs):** White blood cells that process antigens (foreign materials) and present them to B and T cells. Thus DCs are the delivery boys of the immune system: although B cells and T cells are the mediators of immunity, their function is under the control of dendritic cells. This activity is especially important with respect to AHCC, because AHCC stimulates an increase in the number of DC cells.
- **Macrophages:** White blood cells that consume abnormal cells and invading organisms
- **Natural killer cells (NK):** A type of lymphocyte that performs a critical job in the immune system: they can detect and destroy tumor cells and microbes before they reproduce, which can protect you from chronic, degenerative diseases. NK cells work by latching onto a cancer cell or microbe and injecting a granule into its victim, which causes the cell or microbe to die. The activity of NK cells is an indication of the strength of the immune system and is also used to determine the prognosis of cancer and AIDS patients. When NK activity declines to zero, death occurs.
- **Lymphokine activated killer cells (LAK):** A type of white blood cell that has been stimulated to destroy tumor cells.
- **Neutrophils:** The most common type of white blood cell and the ones most responsible for immune response. Neutrophils are present in the bloodstream

until they are called to action at an infection site. After they ingest other cells, they die.

- **CD4:** These glycoproteins are found on the surface of T helper cells, macrophages, and dendritic cells. These "helper" cells initiate the body's response to outside invaders such as bacteria and viruses.
- **CD8**: These glycoproteins are mostly found on the surface of cytotoxic T cells, but also on natural killer cells and dendritic cells. They are involved in destroying cells that are infected with foreign microorganisms.
- **CD4/CD8 ratio:** Clinicians can use this ratio to determine how strong the immune system is and to help predict the risk of complications.
- **Cytokines**: Chemicals that act as messengers between cells to direct and enhance immune response. There are several types of cytokines:
  - **Interferon:** protects cells from viruses, destroys cancer tumors, and stimulates natural killer cells and macrophages
  - **Interleukin-2 (IL-2):** stimulates the growth and activity of T cells
  - **Interleukin-12 (IL-12):** stimulates natural killer cells and strengthens cellular immunity
  - **Transforming growth factor beta (TGF-b):** a protein that controls proliferation, cellular differentiation, and other cell functions. It has an important role in immunity and cancer, as cancerous cells increase their production of TGF-b.
  - **Tumor necrosis factor (TNF):** A cytokine that is involved in the inflammatory process and which is capable of killing tumor cells.
- **Lymph nodes:** Bean-shaped structures where lymphocytes often are first exposed to bacteria, viruses, and other antigens, which stimulates the lymphocytes to perform their functions. Lymph nodes, which form in clusters throughout the system, can become enlarged due to infection or a tumor.
- **Spleen:** An organ that processes lymphocytes that enter it from incoming blood
- **Tonsils and adenoids:** Structures that are composed of tissues similar to those in the lymph nodes. Together the tonsils and adenoids are part of a ring that encircles the back of the throat, and they are thought to help the body fight invading microorganisms.

Immune System: A Duet

The immune system has two main divisions, humoral immunity and cellular (cell-mediated) immunity, and these two divisions complement or play off of each other.

Humoral immunity is the part of immunity that is mediated by the secretion of antibodies produced by B lymphocytes and other processes that facilitate them, such as Th2 activation and the production of cytokines. These antibodies attach themselves to antigens, which marks them for destruction. Humoral immunity gets its name from the word "humours," a word that comes from ancient times and refers to substances that are found in bodily fluids.

Cell-mediated immunity is an immune response that involves activation of various immune components we discussed, such as macrophages, natural killer cells, cytotoxic T lymphocytes, and various cytokines, all in response to invasion by antigens. In cell-mediated immunity, these and other immune cells release toxins to kill bacteria, viruses, and other antigens, or they attack the unwelcome organisms directly to kill them.

AHCC and Your Immune System

The Taoist philosopher Lao Tzu said "Health is the greatest possession," and to possess it, you need a strong immune system: If you keep your immune system operating at an optimal level, then you greatly increase your chances of avoiding and preventing infections, disease, and other health problems. In today's world, it can be difficult at times to protect your immune system from the assaults of microorganisms, stress, poor nutrition, lack of sleep, environmental toxins, medications, and other threats. Although the immune system is extremely resilient, it also takes work on your part to keep it operating optimally.

If your overall health is good and you don't have any pressing health problems, then you are ahead of the game. However, that does not mean you should let your guard down. "Health is not valued till sickness comes" is a grim reminder from the 17th-century British writer Thomas Fuller. If you already have one or more health conditions that are challenging you, supporting and protecting your immune system is even more critical.

AHCC is a functional food supplement that can help protect your immune system both when it is functioning well and when it is not. That is, is can protect you from getting sick as well as tackle the factors that cause you to be sick.

How AHCC Strengthens the Immune System

Numerous studies show that AHCC has the ability to promote and stimulate significant changes in the immune system. We explore the activities and functions of AHCC in more detail in subsequent chapters when we talk about how AHCC works with infections, cancer, gastrointestinal disorders, your liver, diabetes, and your heart. For now, here is a brief look at what research has shown about the impact AHCC has on some of the components of the immune system we have already mentioned.

- **Macrophages:** AHCC can significantly increase the number of macrophages, which in turn improves the ability of the immune system to function optimally. Because cellular immunity is initiated when macrophages and neutrophils are

activated, AHCC can play a major role in jump starting this process, especially in individuals with a compromised immune system. The activity of macrophages was demonstrated in a mouse model of breast cancer. Breast cancer was transplanted into two groups of mice, with one group also receiving an injection of AHCC. After one month, the tumor had shrunk in size by 60 percent in the AHCC-treated mice compared with the untreated mice. The presence of tumor necrosis factor-alpha (TNF-a) was confirmed in the AHCC-treated mice. TNF-a is mainly produced by macrophages, thus it was assumed that the cancer cells were acted on by a combination of factors: they were attacked by the macrophages and subsequently destroyed by the TNF-a.

- **Cytokines:** Both animal and human studies show that AHCC can increase the levels of cytokines, including tumor necrosis factor, interferon-gamma, and the interleukins 1 and 12 (IL-1, IL-12). In addition, AHCC can inhibit the activity of cytokines that suppress the immune system, such as TGF-b. In a study conducted by Dr. Katsuaki Uno of Comfort Hospital, 38 people with stage IV cancer were given 6 grams daily of AHCC. After four months of treatment, the levels of IL-12 approached the levels seen in healthy individuals in 90 percent of the patients, and a similar increase was seen in interferon-gamma levels, with a corresponding increase in the activity of killer T cells as these latter levels rose.
- **Natural killer cells:** Studies in people with cancer show that AHCC can elevate the activity level of NK cells by 200 to 300 percent. This ability to increase NK activity is critically important, because NK cells detect and fight abnormal cells, including cancer cells. The activity of NK cells also appears to have an additive effect on chemotherapy: patients undergoing chemotherapy have demonstrated an enhanced response to treatment when they take AHCC.
- **Dendritic cells:** A study published in Nutrition and Cancer reports that healthy individuals who took AHCC daily for one month had a significant increase in their DC levels compared with those who took a placebo.
- **T cells:** Numerous studies, including several conducted at Yale School of Medicine, have shown that AHCC increases the number and effectiveness of T cells, even as much as 200 percent.
- **T helper (Th) cells:** AHCC can improve the balance between Th1 and Th2 cells, which are involved in activating and directing other immune system cell functions, including activation and growth of cytotoxic lymphocytes and maximizing the activities of macrophages.

AHCC and Older Adults

Although AHCC can benefit immune function for people of all ages, we want to make a special mention here of how the supplement can benefit older adults, with examples from two studies. The gradual deterioration of the immune system that occurs with advancing age is called "immunosenescence." This type of immunodeficiency causes

the elderly to be more susceptible to infectious conditions ranging from the flu and the common cold to pneumonia, cancer, and other serious conditions.

In one study, AHCC was shown to stimulate T-cell function in adults aged 50 years and older. At Yale School of Medicine, Zhinan Yin, MD, a rheumatologist, and his colleagues evaluated the impact of AHCC on a group of 30 healthy adults. Each study participant had his or her cytokine production measured by the CD4+ and CD8+ cells before taking AHCC, after 30 days on AHCC, after 60 days, and again 30 days after they stopped treatment. (Remember, the CD4/CD8 ratio tells clinicians how strong the immune system is.)

The researchers observed significant and consistent increases in the CD4+ cells' production of both interferon-gamma and tumor necrosis factor-alpha, two key cytokines in the body's natural defenses against cancer-causing cells, within 4 weeks of AHCC supplementation. The increased production remained for the entire treatment period. At 30 days post-treatment, cytokine production by CD4+ had declined.

AHCC had a different effect on CD8+ cells. Although AHCC did not initiate much in the way of increased cytokine production after 30 and 60 days of supplementation, the researchers saw a significant increase in both cytokines 30 days after treatment stopped. These findings suggest that AHCC is effective both during treatment and after people stop taking it. Yin's study was also the first to show that AHCC could be beneficial in relieving immunosenescence, and thus could prove to be helpful in preventing the development of some conditions that affect older adults.

The second study we want to mention was a double-blind, randomized trial that included 21 healthy adults with an average age of 60. Each subject received placebo or 3 grams of AHCC daily for four weeks. The researchers collected blood samples both at the start of the study and at 4 weeks. The blood samples showed that subjects who took AHCC had significantly higher levels of total dendritic cells (DCs) and showed increased function of DC1s compared to baseline and to controls. These findings are significant because DCs are, in the words of the study's lead author, Naoyoshi Terakawa, MD, of Kansai Medical University, "critical for maintaining a healthy and balanced immune system."

Wrap-Up

The immune system is a complex network of many different cells, tissues, and organs designed to keep harmful invaders out or, when they do infiltrate, these components then take over to hunt down, attack, and destroy them. AHCC supports, strengthens, and enhances the immune system components so they can better perform the job they were designed to do.

CHAPTER 2

CHAPTER 3
COLDS, FLU, AND OTHER INFECTIONS

You would be hard-pressed to find someone who has not experienced an infectious disease. Have you had a cold recently? Then you had an infectious disease. The flu? Ditto. Not to mention pneumonia, urinary tract infections, fungal infections, and more. If you have a loved one who is a resident in a nursing home or other medical facility, you may worry about an outbreak of MRSA (methicillin-resistant Staphylococcus aureus) or other antibiotic-resistant infections. Cases of West Nile virus crop up each year in nearly every state in the nation, and the threat of avian (bird) flu still lingers. One of the best ways to protect yourself and your family against these and other infectious diseases is by strengthening your immune system with AHCC.

Fighting Infections

The standard approach to killing germs in the home and other environments, as well as in our bodies, has been "over kill"—overuse of antibacterial soaps, sprays, and other antibacterial products, and the over-prescribing of antibiotics. This zealous approach to fighting germs and preventing infections has, unfortunately, largely backfired because we now have to fight superbugs—bacteria that have become resistant to the antibiotics that were developed to attack and destroy them.

Given the ineffectiveness of antibiotics, not to mention the fact that they are associated with side effects and can make you susceptible to even more infections, many people are turning to natural alternatives. Among the more common nutritional and herbal supplements people take to enhance their immune system in an attempt to ward off or treat infections are vitamin C, echinacea, garlic, and ginseng, among others (see chapter 8). Generally these supplements have not been rigorously studied in response to infectious diseases, and results of the studies that have been done have provided mixed and often conflicting findings.

AHCC has been studied extensively and offers a way to prevent and treat infections from the frontline: building up, strengthening, and supporting the immune system by activating specific immune cells such as natural killer cells, among others, and enhancing their activities. That said, let's take a look at the more common infections shown to respond to AHCC and the studies that support the use of AHCC in preventing and fighting infectious diseases.

Cold and Flu

At the top of the infectious disease list are the common cold and the flu. The National Institute of Allergy and Infectious Diseases notes that people in the United States suffer 1 billion colds per year, according to some estimates. Children are usually the hardest hit, as they average 6 to 10 colds per year while adults usually get 2 to 4, with people older than 60 experiencing the fewest colds (but not the least number of other infections, which we will talk about later). However, while older adults may contract fewer colds, they often have a longer and more difficult time recovering from them.

According to the Centers for Disease Control and Prevention (CDC), up to 20 percent of Americans get the flu. While the flu certainly disrupts the lives of millions of people by making them feel too ill to go to work or school, for some people it is much more serious. The CDC reports that more than 200,000 people are hospitalized because of flu each year, and about 36,000 die. With the appearance of bird (avian) flu and swine flu (H1N1) in recent years, the word "flu" has taken on new, more dire meaning for many people, especially the very young, pregnant women, the elderly, and anyone whose immune system is already compromised.

The Studies

The need for a reliable, potent immune system enhancer to help ward off the common cold and flu is great, and studies have been done—and continue to be conducted—showing the efficacy of AHCC. One of the first studies in this arena was done at Drexel University in Philadelphia and reported in the Journal of Nutrition in 2006. Researchers used two groups of mice: one group was infected with influenza A (H1N1) flu only (control group) and the other group was administered AHCC (1 g/kg/body weight per day) for one week before they were infected with the flu, and throughout the course of infection.

The researchers found that the AHCC-treated mice had increased survival, decreased severity of symptoms, and a shorter recovery after they were infected than did the control mice. Specifically, use of AHCC reduced the death rate from 25 percent to 5 percent.

In addition, the investigators found that use of AHCC increased the activity of natural killer cells in the lungs one day after infection and in the spleen two days after infection. This rapid and increased activity means AHCC facilitated the clearance of the virus from the body. The AHCC-treated mice also maintained their body weight during the

infection when compared with controls, which is an indication the treated mice experienced less severe disease. The study's authors concluded that use of a dietary bioactive substance such as AHCC "may be one avenue for improving the immune response to primary flu infection."

In two other studies, researchers looked at the effectiveness of AHCC in mice that were infected with the H5N1 avian influenza virus, also known as the bird flu. In one study, published in the Japanese Journal of Complementary and Alternative Medicine, control mice were infected with the virus, while another group of mice was given AHCC daily for seven days before they were infected with 100 times the 50 percent lethal dose of H5N1 flu virus. All the control mice died by day 11 after they were infected, while 30 percent of the AHCC-treated mice were still alive 28 days post-infection.

In the second study, the scientists followed the same protocol, but this time they compared the effects of AHCC alone to H5N1 vaccination alone, as well as the combination of AHCC and the flu vaccine given together. In the mice that received the H5N1 vaccination only, approximately 80 percent survived the infection. However, 100 percent of the mice that received both the vaccination and AHCC survived.

When the results of these two studies of bird flu are considered together, we find that AHCC provides some protection against this virus, yet combining AHCC with the vaccine appears to be more effective.

The idea of combining AHCC with a flu vaccine was then tested in a small double-blind, placebo-controlled human trial. The 29 people in the study all received the flu vaccination, and then for two weeks after the vaccination, half took 3,000 mg AHCC daily while the other half took a placebo. Blood samples were taken from all participants on the day of vaccination and again two weeks later.

The post-vaccination blood samples of the people who took AHCC showed elevated levels of immune cells, including T cells (especially cytotoxic cells), and a type of natural killer cells that produce cytokines in response to the flu vaccine. This enhanced response was most evident in adults older than 60, who are at greater risk of complications due to flu. The results of this study led the authors to note that "This suggests that short-term AHCC supplementation may be a good therapeutic intervention to sustain, or increase, the immune response to influenza vaccination in healthy subjects."

Although no studies have yet been conducted to explore the impact of AHCC on the common cold, the ability of AHCC to promote the activity of natural killer cells shortly after infection, as demonstrated in the flu research, suggests it will prove beneficial. There is also convincing evidence suggested by the results of yet more studies of the activity of AHCC against other infectious diseases, as shown here.

West Nile Virus

Despite its name, the West Nile virus can affect people who do not live anywhere near the Nile. Basically, if there are mosquitoes where you live, there is a chance you could contract West Nile virus. In 2010, the Centers for Disease Control and Prevention not-

ed that approximately 1,000 cases of the virus had been reported to the agency, with 41 deaths. The three states reporting more than 100 cases each were Arizona, California, and New York.

About 1 in 150 people who are infected with West Nile virus develop severe illness, with symptoms that include high fever, headache, stupor, disorientation, coma, tremors, convulsions, numbness, and paralysis. Symptoms may last a few weeks and the neurological impact may be permanent. Up to 20 percent of infected individuals have milder symptoms—fever, headache, body aches, nausea, vomiting, and swollen glands or rash. These symptoms usually last for a few days, but even healthy people can be ill for several weeks. About 80 percent of people who are infected with West Nile virus don't display any symptoms.

Thus far, there are no vaccines or treatments to prevent or treat this virus. AHCC, however, has shown promise in the fight against this sometimes fatal disease.

For example, at Colorado State University, a team of scientists evaluated the ability of AHCC to enhance resistance when exposed to West Nile virus. They used a mouse model, with one group of mice administered 600 mg/kg of AHCC every other day for one week before they were infected with a lethal dose of West Nile virus. The mice were given AHCC on days 1 and 3 after they were infected as well. Mice in the control group received placebo and the deadly dose.

One month later, an analysis of the animals' blood showed that AHCC had increased the production of antibodies for West Nile virus in the treated mice. Overall, mice treated with AHCC had 19 percent less viral load than the control mice and were also twice as likely to have survived the lethal dose: 54 percent of treated mice were still alive compared with only 21 percent of the control mice. The authors, who published their work in the Journal of Nutrition, reported that "dietary supplementation with AHCC may be potentially immunotherapeutic for WNV-susceptible populations."

AHCC and "Superbug" Bacterial Infections

Although the use of antibiotics can be beneficial in some cases, overuse of these drugs has resulted in the emergence of antibiotic-resistant strains of bacteria, or "superbugs." This means that when clinicians are presented with patients who have a bacterial infection caused by microorganisms known to be resistant to the antibiotics that were once effective, they and their patients are faced with a treatment challenge that can, all too often, result in serious complications or even death. Pseudomonas aeruginosa infections, for example, which frequently occur in people who have a compromised immune system, cause death in half of those who develop this opportunistic infection. (An opportunistic infection is one that is caused by microorganisms that usually do not cause illness but do when the individual's immune system has been compromised and thus cannot fight off the infection.)

Along with P. aeruginosa, there are two other opportunistic infections that are important to understand and against which AHCC has been shown to be effective, MRSA and Klebsiella pneumonia.

Pseudomonas aeruginosa Infections

Pseudomonas aeruginosa is an opportunistic infection that often affects people who have a compromised immune system and rarely affects uncompromised tissues. However, P. aeruginosa is relentless when it does infect tissues, causing urinary tract infections, respiratory tract infections, dermatitis, ear infections, endocarditis, meningitis, brain abscesses, soft tissue infections, bone and joint infections, gastrointestinal infections, bacteremia, and various other systemic infections. Among people at high risk for P. aeruginosa infections are individuals who have AIDS, cancer, severe burns, or cystic fibrosis. Among patients who are hospitalized with these conditions, the fatality rate is about 50 percent.

Pseudomonas has a reputation for being resistant to antibiotics. Among the few that are effective against the bacteria are fluoroquinolones, gentamicin, and imipenem, yet they are not able to kill all strains. Perhaps the population hit the hardest with P. aeruginosa infections are cystic fibrosis patients, because nearly all of them eventually contract a strain that is so resistant to antibiotics that they cannot be treated successfully.

AHCC has proven effective against P. aeruginosa in a study conducted at Teikyo University School of Medicine in Japan. Researchers evaluated the effect of different doses of AHCC given by injection and orally to immune-compromised mice and found that the mushroom compound protected the mice form lethal infection with P. aeruginosa.

Specifically, the mice that received 500 mg/kg of AHCC by injection survived an average of 14 days after they were infected with P. aeruginosa compared with only 3 days among the control (untreated) mice. Oral AHCC provided a similar result, with 6 of the 8 mice treated with 1,000 mg/kg of AHCC surviving 14 days compared with only 3 days among the control mice.

MRSA

Another infection that has many people concerned is MRSA. This is a type of staph bacterial infection that is resistant to certain antibiotics called beta-lactams, which include methicillin, oxacillin, penicillin, and amoxicillin. Among the general population, most MRSA infections affect the skin. In health care settings such as nursing homes and hospitals, however, the infections are typically more severe or potentially life-threatening. The most recent figures from the Centers for Disease Control and Prevention on MRSA report about 94,360 people developed the infection in 2005, and that more than 18,000 people died.

The effectiveness of AHCC was tested in mice that were given both oral and injectable doses of the compound. Mice that were treated with AHCC survived significantly longer after receiving a lethal dose of MRSA than did mice that received placebo.

Klebsiella pneumonia Infections

Klebsiella pneumonia is among the most common gram-negative bacteria healthcare

providers encounter around the world. It is often found in hospitals, where it usually causes urinary tract infections, nosocomial pneumonia (pneumonia that develops as a result of treatment in a hospital or other healthcare setting), and intra-abdominal infections. People most at risk for developing a K. pneumonia infection include anyone who is using a ventilator or who has intravenous catheters, or patients who are on a prolonged course of antibiotics. Healthy individuals rarely get Klebsiella infections.

Several studies have looked at the impact of AHCC on resistance to infection with K. pneumonia, and the results have been promising. In one, published in the Journal of Applied Physiology, investigators chose a mouse model that is often used for spaceflight conditions (e.g., suspension) because these mice have a lower resistance to infection. The scientists administered AHCC to the mice one week before they were infected with K. pneumonia and were suspended, and throughout the 10-day suspension period as well. Mice that received AHCC had decreased mortality, longer survival, and an increased ability to clear the deadly bacteria from their bodies than did control mice that did not receive AHCC.

Another study evaluated how effective AHCC may be in preventing surgical wound infections caused by K. pneumonia in a mouse model. The 28 treated mice in the study were administered an oral dose of AHCC daily for eight days before and during the time they were infected with K. pneumonia. A control group of 28 mice received placebo and were also infected with the bacteria. The AHCC-treated mice survived longer than the control mice: 15 percent of control and 55 percent of treated mice were alive after 15 days. The AHCC-treated mice also cleared the infection much more effectively than did the control mice. This suggests to scientists that AHCC may be helpful in clearing bacteria in patients who are undergoing surgical procedures.

CC Image Courtesy of a.drian via Flicker

The most recent study of the effect of AHCC on K. pneumonia was published in the American Journal of Surgery. Here researchers found that AHCC-treated mice that were infected with the bacteria were able to clear the microorganisms entirely six days after they were infected. In addition, the investigators reported that levels

of important immune system cells—interleukin-12, interleukin-6, and tumor necrosis factor alpha—peaked earlier in the AHCC group than they did in the control group. These findings led them to conclude that AHCC appears to cause an early stimulation of the immune system, which leads to an effective clearance of the disease-causing bacteria and thus results in a more rapid recovery.

AHCC Fights Fungal Infections

Candida species of fungi represent the most common fungal pathogens that can affect humans. These fungi are highly opportunistic and are responsible for a number of infections that can range from mild to deadly. Women are often familiar with candidiasis, the fungal infection caused by Candida albicans, because it causes a highly irritating vaginal yeast infection. However, an overgrowth of C. albicans can also infect other parts of the body, most notably the mouth, digestive tract, and the bloodstream. When it reaches the blood, it can cause systemic infections that may cause organ failure and death.

Among the people at greatest risk of developing a Candida related infection are those whose immune systems are compromised by HIV/AIDS, diabetes, recent surgery, severe trauma, renal failure, or organ or bone marrow transplantation; anyone who is taking antibiotics or corticosteroids; or people undergoing chemotherapy, radiation therapy, hemodialysis, parenteral hyperalimentation, catheterization, or prolonged hospitalization.

Researchers at Teikyo University School of Medicine evaluated the use of AHCC in immune-compromised mice that were infected with Candida. One group of mice was administered 1,000 mg/kg of AHCC orally or 500 mg/kg of AHCC by injection for 4 days prior to their infection with Candida, while another group of mice did not receive AHCC. Within one week of becoming infected with Candida, all the control mice had died, while 80 percent of the mice injected with AHCC survived for 28 days. Oral AHCC also significantly extended survival time. When the investigators examined the mice's kidneys 3 days post-infection, they found that the animals treated with AHCC had 1 percent of the amount of yeast as the control mice.

Wrap-up

We have shown that AHCC has proven itself to be a powerful force against many different infections. Because the results of one study found that combining AHCC with a flu vaccine improved the outcome, studies are now underway to determine the role AHCC may play as a preventive during flu season, which has the potential to be a big factor in helping people of all ages from the complications of flu. Given these findings and AHCC's great safety record (see chapter 8), it makes sense to consider AHCC supplementation to enhance your immune system.

CHAPTER 3

CHAPTER 4
AHCC AND CANCER

The most aggressive and far-reaching studies involving the use of AHCC have been in the area of cancer. Since the 1990s, AHCC has been used as complementary therapy in cancer patients who are undergoing conventional therapy as an immune system booster and in the process, a way to help improve their quality of life. Because AHCC was developed and registered in Japan, the vast majority of the studies have been conducted there as well. By the end of the 1990s, AHCC was being used in about 700 medical institutions, most of which were in Japan, and AHCC was already accepted and used there as a food supplement for cancer because individual cases and study results suggested it was highly beneficial. In fact, AHCC became known as the "health food for cancer."

The good news is that the anticancer benefits of AHCC are being noticed and explored outside Japan, with studies in the United States at institutions such as Yale, Drexel University, and Colorado State University, among others. Although much research remains to be done regarding the potential of AHCC in the prevention and treatment of cancer, there is a promising body of literature already available, and we will review some of the work in this chapter. But first, let's look at the different types of cancer treatment and how AHCC differs from and fits into this scenario. Some of these studies discussed in this chapter have been published in journals; others have been presented at any of the International Symposium of the AHCC Research Association gatherings and/or are case reports.

Traditional Cancer Treatments

The three main conventional treatments approaches for cancer are chemotherapy, radiation therapy, and surgery. All of these treatments can have a positive effect on reducing cancer, yet they also have a dramatic, detrimental impact on the immune system and the body. A fourth, up-and-coming therapy is immunotherapy, which is the category into which AHCC falls. More about that later in this chapter.

Chemotherapy involves the use of drugs that are toxic to both cancer cells and to normal, healthy cells. This type of cell toxicity, called cytotoxicity, affects the cells when they are dividing, which cancer cells do excessively. However, because chemotherapy also impacts healthy cells, individuals who undergo chemotherapy also experience side effects related to the damage to these cells. The cells most affected are hair root,

blood, and gastrointestinal tract, because all of the cells also divide rapidly. This is why chemotherapy patients typically lose their hair, experience nausea and vomiting, and suffer with fatigue and increased susceptibility to infection due to damage to blood cell production. AHCC has a role to play here, as it can help alleviate symptoms associated with chemotherapy. (Read about the effect of AHCC on patients undergoing chemotherapy in chapter 5.)

Radiation therapy involves the use of high-energy radiation in the form of x-rays, gamma rays, and charged particles to shrink tumors and kill cancer cells. Radiation may be delivered via a machine outside the body (called external beam radiation) or from radioactive material implanted in the body (brachytherapy). Systemic radiation therapy uses radioactive substances that travel throughout the bloodstream to kill cancer cells. Radiation therapy kills cancer cells by destroying their DNA either directly or by creating free radicals within the cells that in turn damage the DNA. Unfortunately, radiation therapy also damages healthy cells, and in the process is responsible for a variety of side effects that depend on the area of the body treated, the dose given per day, the total dose, and other factors. Some of the side effects can include hair loss, urinary problems, skin irritation, fatigue, nausea, and vomiting. Although some symptoms disappear when treatment stops, others can continue or late side effects may develop after treatment has ended, such as damage to the bowels that result in bleeding and diarrhea, memory loss, infertility, and fibrosis.

In most cases, surgery for cancer involves removal of the tumor and some of the tissue that surrounds it. Lymph nodes are also extracted in some cases. Surgery is a major traumatic event and so has a negative impact on the immune system. Side effects associated with surgery depend mostly on the size and location of the tumor and the type of surgery performed.

Cancer Stages and Categories

Cancer Stages

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Staging refers to the severity of cancer based on the extent of the original (primary) tumor and whether it has spread (metastasized) in the body. Clinicians depend on cancer staging to help them develop the most appropriate treatment for a patient, to help estimate a patient's prognosis, and to determine whether patients are eligible for specific clinical trials. Because cancer staging utilizes standard terminology, it also allows healthcare providers and researchers to be "on the same page" in most cases when they exchange information and compare research findings.

That said, there are differences within the staging system for the different types of cancer. For example, the criteria to assign the label "stage II" to a case of bladder cancer

differs somewhat from a designation of stage II for a case of colon cancer. In addition, the prognosis for a given cancer stage depends on what kind of cancer is involved, so a stage II lung cancer has a different prognosis from a stage II cervical cancer. To help assign a cancer stage to a specific case of cancer, several elements are considered, including the site of the primary tumor, tumor size, number of tumors, involvement of the lymph nodes (spread of the cancer into lymph nodes), cell type, tumor grade, and the presence or absence of metastasis.

Here is a basic outline of the stages of cancer.

Stage 0: Carcinoma in situ—the cancer cells are present only in the layer in which they developed

Stages I-III: The higher the number, the more extensive the disease--larger tumor sizes and/or spread of the cancer beyond the organ in which it first developed to nearby lymph nodes and/or organs near the primary tumor

Stage IV: The cancer has metastasized (spread to other organs and/or parts of the body)

As you might expect, identifying cancer stages is more complex than this, and overall staging is further divided with classification such as IIa and IIIb. Depending on the type of cancer, the difference in prognosis between a stage IIIa and stage IIIb may be very significant. Therefore, patients need to get a thorough explanation from their healthcare providers about the stage of cancer that pertains to them. Another factor that goes along with staging is tumor grade. Tumor grade is a system used to classify cancer cells in terms of how abnormal they appear under a microscope and how quickly the tumor is expected to grow and spread. The factors used to determine tumor grade is different for each type of cancer.

Cancer Categories

Cancer is also classified by category, a system that allows clinicians and researchers to use a uniform system when describing cancer and exchanging information. Those categories are:

In situ: Abnormal cells are found only in the layer of cells in which they developed

Localized: Cancer cells are present only in the organ in which they first appeared, with no evidence of spread

Regional: Cancer has spread beyond the primary site to nearby lymph nodes or organs and tissues

Distant: Cancer has spread from the primary site to distant organs or distant lymph nodes

Unknown: There is not enough information to identify the stage of cancer

Immunotherapy, BRMs, and AHCC

Conventional medicine has recently added another cancer treatment modality to the mix: immunotherapy. Immunotherapy is a nontoxic method of cancer treatment that utilizes certain parts of the immune system to fight cancer or to reduce the side effects that are associated with treatment. These goals can be accomplished by stimulating the body's immune system to work harder or smarter, or by taking synthetic immune system proteins or other components, known collectively as biological response modifiers (BRMs). Although immunotherapy is sometimes used alone to treat cancer, in most cases it is combined with chemotherapy or radiation therapy to enhance its effects.

In conventional medicine, some antibodies, cytokines, vaccines, and other immune system substances are synthesized in the lab to be used in cancer treatment. These BRMs change how the body's immune defenses interact with cancer cells in an attempt to enhance or restore the body's ability to fight the disease.

Does this sound familiar? If so, then you probably already know that AHCC is a biological response modifier. In fact, in Japan AHCC is widely considered to be the strongest known immune system strengthening BRM, and it is often used alongside conventional cancer treatments. A goal is to have AHCC accepted by medical professionals around the world as a BRM for cancer patients.

When clinicians are able to halt the development of cancer using immunotherapy, a "truce" has been established between the cancer and the immune system. The cancer is dormant, and as long as the patient can maintain this state of truce, it is possible to postpone future treatment.

Here are two examples of studies that explored the impact AHCC can have on the immune system of cancer patients.

E**xample One:** The study was conducted at the Seoul Internal Medicine Clinic, Cancer Diagnostic Center by Dr. Jang Seok Won and included 12 cancer patients: 4 with stomach cancer, 3 with colorectal cancer, 2 with lung cancer, and one each with breast cancer, ovarian cancer, or melanoma. Won evaluated the effect of AHCC on a variety of components, including lymphocytes and natural killer cells, as well as various blood elements. All the patients received 3 to 6 grams of AHCC daily for three months in addition to their conventional treatment of radiotherapy or chemotherapy, and they were then followed up at three, six, and nine months.

Overall, Won noted the following:

- There was no significant change in white blood cells count, hemoglobin, and other blood factors that would indicate a worsening of immune function, even though the patients were undergoing radiation or chemotherapy. This finding suggests AHCC can be helpful in preventing depression of bone marrow from cancer treatment.
- There was a slight increase or no change in peripheral blood lymphocytes. This was a positive sign, as lymphocyte levels tend to decrease as cancer progresses.
- The percentage of natural killer cells, which are important for eliminating tumor cells, increased by 21 percent after 3 months and was still at 20 percent six months after treatment.

Overall, AHCC appeared to be a safe and effective BRM for these cancer patients and may be helpful in preventing bone marrow depression associated with chemotherapy.

Example Two: The effects of AHCC were examined in 11 patients who had advanced cancer: three patients each with prostate, breast, or ovarian cancer, and two who had multiple myeloma. All the patients were treated with conventional therapies. In addition, all were administered 3 grams daily of AHCC. After two weeks, the researchers observed a 2.5-fold increase in the level of natural killer cell activity in 9 of the 11 patients, and the increased activity was maintained at a high level over time. They also observed a decline in PSA (prostate specific antigen) in the three prostate cancer patients. (PSA is an indicator of malignancy in prostate cancer.) Two of the three breast cancer patients showed a significant decline in the level of CA125, which is an antigen and a marker for this type of cancer. The rapid decrease in CA125 occurred after taking AHCC for one month and continued to decline until it reached normal values 3 to 4 months after treatment with AHCC.

The study's authors, who published their findings in the International Journal of Immunotherapy, also examined the impact of AHCC on tumor cell growth in two different tumor cell lines: K562 (a leukemia cell line) and Raji (a Burkett cell lymphoma). They found that AHCC suppressed the growth of both cell lines, with a higher concentration of AHCC (1 mg/mL) providing the most effect when compared with a lower one. Overall, 1 mg/mL concentration of AHCC resulted in a 21 percent reduction in the leukemia-like cell line and a 43 percent decline in the lymphoma cell line.

Although the study populations in the above two studies were small, their findings suggest AHCC offers some potent anticancer activity and thus has a place in the treatment of patients who have cancer.

AHCC and Immune Surveillance

A healthy immune system performs a function called immune surveillance, in which it uncovers the presence of cancer cells and tumors throughout the body. This surveillance function is critical because cancer cells have an ability to hide, thus avoiding detection by the immune system. Restoring immune surveillance means that tumor cells can be "unmasked," which then allows the immune system to once again detect and destroy them.

White blood cells and the interferon they release are necessary for the immune system to "sniff out" and unmask cancer cells and tumors, and so researchers set out to determine how AHCC may be helpful in this effort. Researchers at Yale University and Amino Up Chemical Company explored the effect of AHCC on immune surveillance by administering the supplement to test animals. AHCC significantly delayed the formation of melanoma and reduced tumor size. Specifically, AHCC significantly increased levels of tumor-antigen-specific immune cells and their ability to produce gamma interferon, and also increased the numbers of natural killer cells. The authors of the study concluded that their results demonstrated that AHCC can enhance tumor immune surveillance through regulating both humoral and cell-mediated responses.

AHCC's Other Anticancer Activities

While traditional cancer treatments destroy both cancerous and healthy cells, AHCC focuses solely on the latter. That is, rather than kill cancer cells directly, AHCC strengthens and stimulates the healthy immune cells—lymphocytes, natural killer cells, macrophages, and other immune compounds--whose job is to attack and/or destroy cancer cells. AHCC also improves the body's inherent immunity. All around, AHCC can be a powerful healing force for people who have cancer.

Scores of research studies and individual case reports have illustrated the benefits associated with AHCC in patients who have cancer. Because AHCC strengthens the function of the immune system, it can be appropriate for addressing cancer that affects any part of the body. A review of the available research shows that more than 100,000 cancer patients with different types of cancer have been treated with AHCC. Results indicate that the supplement has been effective in people who have breast, colon, kidney, liver, lung, ovarian, pancreatic, stomach, testicular, and tongue cancers. It appears AHCC truly can have an impact on cancer cells wherever they are in the body.

Overall, 60 percent of cancer patients have reportedly derived some benefit from the supplement. Some individuals have had a reduction in tumor mass while in others the tumor stopped growing, the cancer stopped spreading to other parts of the body (metastasis), survival time increased and, in most cases they experienced an improvement in their quality of life. For some patients, AHCC has reportedly been effective enough

to induce remission from their disease.

It is important to emphasize that AHCC is used in addition to conventional cancer treatment; that is, AHCC does not replace chemotherapy, radiation therapy, and/or surgery, or even other immunotherapies. Doctors in Japan typically use AHCC along with mainstream cancer treatments, and it is gradually gaining acceptance in other countries throughout Asia and the United States.

AHCC and Survival from Cancer

Some studies have examined the effect of AHCC on cancer survival, including patients who are in advanced stages of the disease. For example, a total of 195 patients who were in the last stages of various cancers (e.g., gastric, colon, liver, pancreatic, lung, breast, and ovarian) were given 6 grams of AHCC daily for six months. The patients also took other immune stimulants. The investigators monitored levels of various immune system components during the study period, including natural killer cells and Th 1 cytokine production (e.g., interferon-gamma, interleukin-12). The scientists observed a significant increase in natural killer cell activity and in the production of interferon-gamma and interleukin-12, all of which support optimal immune system functioning.

Dr. Katsuaki Uno, managing director of Comfort Hospital and the head of the study, reported that 114 people experienced a partial or complete recovery after starting AHCC treatment. Forty percent (81 patients) experienced no change or had progression of their disease.

Although researchers often cite the immune-stimulating properties of AHCC as the reason for their helping to prolong survival from cancer, AHCC's anti-inflammatory and antistress properties have also been studied for this purpose. In the studies discussed in the following sections, you will see examples of how AHCC is associated with an improvement in quality of life and survival in cancer patients, including those with final stage or advanced disease.

AHCC and Cancer Studies

In addition to the results of other cancer studies we have already covered, there are several others that have focused on one specific type of cancer and reported on the impact of AHCC in the treatment of these patients. Therefore the following cancer studies are examples of the types of research that has been done in cancer patients who included AHCC as part of their regimen for liver, gastrointestinal, and breast cancer.

Liver Cancer and AHCC

Many of the cancer studies and case reports done so far have involved the use of AHCC in patients who have liver cancer. According to the World Health Organization, liver cancer is the fourth leading cause of death due to cancer (following behind lung, stomach, and colorectal cancers) in the world. The American Cancer Society reported that an estimated 24,120 adults in the United States would be diagnosed with primary liver cancer in 2010, and that nearly 19,000 people would die of the disease. Liver cancer is

the fifth most common cause of cancer death among men in the United States, and the ninth most common among women.

Given these statistics, one would expect a poor five-year relative survival rate associated with liver cancer, and it is: at about 10 percent when all stages of liver cancer are considered (i.e., localized, regional, and metastatic). One reason for this low survival rate is that most patients who have liver cancer also have other liver problems such as cirrhosis (scarring of the liver), which can be fatal. In patients who have small, resectable tumors and who do not have other liver problems, however, five-year survival can be more than 50 percent.

Generally, however, survival is poor, and this is why any improvement in survival associated with the use of AHCC in liver cancer patients is especially noteworthy. Even though liver resection is the most effective treatment for liver cancer, many patients are diagnosed in the late stages of the disease, when surgery would not be effective. At that point, the most commonly used treatment option is chemotherapy. However, some clinicians are also turning to biological response modifiers, and that is where AHCC can enter the picture. Two examples of AHCC's impact on liver cancer patients and survival are illustrated here.

Example One: The Journal of Hepatology published the results of a prospective study that covered a time span of nearly a decade, from February 1, 1992 to December 31, 2001. A total of 269 patients who had hepatocellular carcinoma were evaluated in the study. Hepatocellular carcinoma is the most common type of liver cancer, and it is usually caused by cirrhosis, which can be the result of alcohol abuse, certain autoimmune diseases of the liver, hepatitis B or C, excess iron in the body (hemochromatosis), or diseases that cause long-term inflammation of the liver.

All of the patients underwent resection of the liver tumor, which is a surgical procedure to remove the affected portion of the liver. AHCC supplementation was assigned to 113 patients after surgery. The investigators noted a significantly higher overall survival rate (14%) among patients who took AHCC when compared with the control patients. In addition, the recurrence of cancer was significantly lower (49%) among the AHCC patients compared with controls (67%).

The mechanisms responsible for the benefits observed in the patients who took AHCC were not explored in this study. Therefore, while the authors note that AHCC intake improved liver function, reduced recurrence of liver cancer after resection, and prolonged five-year survival, further research is necessary to both confirm their findings and identify the reasons behind them.

Example Two: A subsequent study was conducted in Thailand and included 44 patients with advanced liver cancer and unresectable tumors. All of the patients randomly were assigned to receive either AHCC (6 grams daily) or placebo until the end of their lives.

The investigators examined the patients' clinical parameters monthly or as specified to determine quality of life and various blood, biochemical, and immunological param-

eters, such as gamma interferon and interleukin-12 levels. Magnetic resonance imaging was performed on patients who survived longer than one year.

By week 6 of the study period, five (50%) of the patients in the placebo group had died, while all the patients in the AHCC group were alive. The follow-up period ranged from 6 weeks to 24 months in the AHCC group and from 2 weeks to 3.5 months in the control group. Overall, the median survival time was 3.5 months in the AHCC-treated patients and 1.5 months in the control patients. The investigators also noted that the percentage of lymphocytes did not decline as rapidly after AHCC treatment when compared with controls. This suggested that AHCC provided some immune system benefits for these patients in their final months. Plasma levels of interleukin-12 showed a slight increase in the AHCC treated patients, but it was not significant. The authors noted that their findings suggest AHCC helps to prolong the lives of patients who have advanced liver cancer. As in the previous study, the authors did not explore the mechanisms responsible for these benefits.

Gastrointestinal Cancers

Cancers of the gastrointestinal system include esophageal cancer, stomach cancer (also known as gastric cancer), colorectal cancer, and anal cancer. According to the National Cancer Institute, approximately 142,570 people were diagnosed with colorectal cancer in 2010 in the United States. Estimates for other gastrointestinal cancers include 21,000 people diagnosed with stomach cancer, 5,260 with anal cancer, and 16,640 with esophageal cancer.

Dr. Yusai Kawaguchi of the Kansai Medical University Department of Surgery treated two groups of cancer patients with AHCC. One group included 132 individuals with stomach cancer who took AHCC following their surgeries. Patients who had stages I-III cancer were given 3 grams daily of AHCC while those who had stage IV cancer took 6 grams per day. Patients who had stages II-IV also were taking low-dose chemotherapy.

A second group consisted of 113 patients with colon cancer. Individuals with stage I-II cancer were given 3 grams of AHCC daily while those with stages III-IV took 6 grams daily. Low-dose chemotherapy was administered to patients with stages II-IV.

When the investigators compared the five-year cumulative survival rates from their two study groups with those of other institutions where AHCC was not administered, they found that in patients with stomach cancer, survival rates were superior in patients with stage I to stage IIIA cancers. (Stage III stomach cancer can be classified as IIIA and IIIB, and stage IIIA has a better prognosis than does stage IIIB cancer.) Among colon cancer patients with stage II and stage IIIA cancer in the study, five-year cumulative survival rates were superior to those at other institutions where AHCC was not given.

Kawaguchi and his team noted that overall, use of AHCC in patients with stomach cancer and colon cancer resulted in an improvement in cumulative survival rates in some stages of cancer. These findings suggest AHCC can be beneficial as a complementary

treatment for patients who have these types of cancer.

Other Cancers

In addition to all the studies we have mentioned already, there are many other individual case reports from different doctors and their experiences with patients who had pancreatic, brain, ovarian, lung, stomach, breast, and other cancers and whom they treated with AHCC along with conventional treatment. Virtually without exception, the patients treated by these doctors seemed to benefit in some way from their treatment with AHCC, with an improvement in quality of life and/or pain relief being the most common advantages of taking AHCC. In some cases, patients reportedly defied their cancer and lived on for years after doctors had given up hope and beyond when conventional medicine said they would pass on.

It is important to remember, however, that AHCC is not a cure for cancer, and that its place is alongside conventional treatment for cancer, as a potent immunotherapy that may provide patients with a stronger immune system and a better quality of life.

Wrap-Up

AHCC is frequently administered to patients who have cancer to strengthen, enhance, and boost the immune system response, which often have the effect of improving quality of life and improving survival rates. There have been reports of patients with advanced cancer whose disease appeared to vanish after they began treatment with AHCC as a complement to conventional therapy. Any definitive relationship between use of AHCC and the disappearance of cancer in any given patient has not been determined.

CHAPTER 5
AHCC AND CHEMOTHERAPY

More than half of the people who are diagnosed with cancer undergo chemotherapy at some point. This means tens of millions of children and adults are treated each year with drugs designed to kill cancer cells, but these drugs also destroy healthy cells and as a result cause some significant side effects, as we noted in chapter 4. Some cancer cells grow slowly while others grow rapidly, therefore clinicians need to select different chemotherapy drugs designed to target the specific growth patterns of a person's cancer cells. Whether the drugs taken are designed to attack cancer cells that grow slowly or rapidly, medication-related complications are often a result.

Of the common side effects associated with chemotherapy—nausea and vomiting, hair loss, fatigue, impaired liver function, loss of appetite, and low levels of white blood cells, red blood cells, and platelets, one that has the potential to be very serious is neutropenia, or low white blood cell levels. White blood cells fight infections, and if patients' levels drop too low, they may need to stop chemotherapy for a while. This action not only places patients at an increased risk for serious infections that could be life-threatening, but it also interrupts their cancer treatment.

Impaired liver function also can be dangerous and infrequently can result in liver failure. Low platelet levels (thrombocytopenia) could result in clotting problems (e.g., easy or excessive bruising, excessive bleeding when cut, bloody nose or gums, blood in the urine), while low red blood cells levels often cause anemia, characterized by fatigue, dizziness, and shortness of breath.

Given the great number of cancer patients who undergo chemotherapy each year and the disruptive and sometimes debilitating side effects it can cause, it is important that these individuals have effective options available to them to help alleviate and hope-

fully eliminate these adverse effects and enhance their quality of life. AHCC supplementation has demonstrated an ability to help chemotherapy patients improve their lives in some of the ways we discuss here.

Hair Loss

Losing one's hair because of chemotherapy is not a life-threatening side effect, but it can be very life-altering and emotionally devastating. Both men and women report that hair loss is one of the side effects they most fear after they are diagnosed with cancer. Not everyone who undergoes chemotherapy loses their hair, because it depends on the type and dose of drug used. However, hair root cells grow rapidly, and if you have a rapidly growing cancer, chances are you can expect to lose hair, and not just from your scalp. Chemotherapy can cause eyebrow, armpit, pubic, eyelash, and other body hair to fall out.

The good news is that in most cases, hair loss from chemotherapy is temporary: hair tends to regrow three to 10 months after treatment ends. The other good news is that AHCC may help reduce hair loss.

For example, scientists evaluated the effect of AHCC on hair loss caused by a single dose of the chemotherapy drug cytosine arabinoside (Ara-C). Rats used in the study were administered either 500 mg/kg per day of AHCC for seven consecutive days plus a single dose of Ara-C or a single dose of Ara-C. Results of the study, which were published in Cancer Epidemiology in 2009, showed that 5 of 7 rats treated with Ara-C alone had severe hair loss and 2 had moderate hair loss. Four of the nine rats that received both Ara-C and AHCC, however, experienced no hair loss, two had moderate and one had severe hair loss.

Nausea and Vomiting

According to the American Cancer Society, nausea and vomiting are among the most feared side effects of chemotherapy. Even though these symptoms are not considered life-threatening, they can significantly disrupt the lives of those who experience them, making it very difficult or impossible for them to work, care for their children, and perform normal, everyday functions.

Although the prevalence and severity of nausea and vomiting associated with chemotherapy have been somewhat alleviated by the introduction of new drugs to treat these symptoms, these drugs are not for everyone. Some patients do not want to take additional drugs along with their chemotherapy. In addition, anti-nausea drugs are not always effective and they also have side effects of their own, which can add to the discomfort cancer patients experience. Nausea and vomiting can be so severe for some cancer patients that they choose to stop their chemotherapy.

Clinical studies and case reports show that AHCC can improve patients' quality of life regarding nausea and vomiting. In one small study, for example, Dr. G.H. Ahn of Ok-Cherm Hospital in South Korea prescribed AHCC for 8 months to 12 patients who had stage III-IV cancer. Over the treatment period Dr. Ahn noted any changes in nausea,

vomiting, and pain experienced by the patients and found an improvement in all three symptoms, which results in a better quality of life for these patients.

Impaired Liver and Spleen Function

In the same study that explored the effect of AHCC on hair loss in rats exposed to a chemotherapy drug, researchers also evaluated the impact of AHCC on modulating liver damage. To accomplish this, they administered a single dose of 6-mercaptopurine (6-MP) plus methotrexate (MTX), two antimetabolite, cancer-fighting drugs, to two groups of rats: one group received the drugs only, and a second group received AHCC for 28 days plus a single dose of 6-MP plus MTX.

The researchers then measured the levels of two liver enzymes that are used to determine the degree of liver function: SGOT (serum glutamic aminotransferase, also called aspartate transaminase) and SGPT (serum pyruvate aminotransferase, also called alanine aminotransferase). The higher the levels of these enzymes, the greater the damage and destruction to liver tissue. The scientists found that rats given AHCC had normal levels of SGOT and SGPT while the untreated rats had large increases in these enzyme levels.

In addition, the rats treated with AHCC along with 6-MP and MTX demonstrated significantly increased body weight and levels of leukocytes and red blood cells. All these factors together indicated that AHCC significantly reduced the side effects associated with the chemotherapy drugs.

The spleen is an organ that people don't hear much about, but it plays an important role in immune function. This fist-sized organ is part of the lymphatic system, contains white blood cells that fight infections, and destroys damaged and old cells. Although it is true that people can live without a spleen, the body loses some of its ability to fight infections if the spleen is removed because of disease or damage.

A team of scientists investigated the impact of AHCC on the spleen after it was subjected to chemotherapy. The researchers used the chemotherapy drug cyclophosphamide, which typically causes the spleen to shrink in size by 50 percent. In mouse models, the researchers noted that the spleens in mice given cyclophosphamide plus AHCC did not shrink as much as they did in mice not treated with AHCC. The AHCC-treated mice also had a lower rate of infection than mice not treated with AHCC.

Myelosuppression

Chemotherapy can both destroy white blood cells as well as damage bone marrow function, a condition also known as myelosuppression. Bone marrow is the spongy tissue, located inside some large bones, that houses stem cells. These stem cells transform themselves into white and red blood cells and platelets. When chemotherapy damages bone marrow, the production and levels of these critical immune system substances decline. The result is that patients become highly susceptible to infections, and they may also develop anemia, which exacerbates their lowered resistance. Overall, myelosuppression is a very serious and life-threatening state.

Several studies have shown that AHCC can have a positive effect on myelosuppression and improve the white blood cell levels in response to chemotherapy. In South Korea, Dr. G.H. Ahn of Ok-Cherm Hospital administered 6 grams daily of AHCC to 12 patients who had stage III-IV cancer (two patients each had breast, ovarian, stomach, lung, uterine, and lung cancers) and who were undergoing chemotherapy. Over a period of seven months, levels of white blood cells rose from below 6,000 to nearly 8,000.

In animal studies, scientists have observed a reduction in damage to bone marrow when AHCC was administered. In one such study, published in Cancer Epidemiology, two chemotherapy drugs (cyclophosphamide and 5-fluorouracil) were given to four groups of mice: one group each received one of the drugs, one group received AHCC plus cyclophosphamide, and one group received AHCC plus 5-fluorouracil. The red blood cell count remained close to normal in the two groups of mice that were treated with AHCC, but it declined in the two groups that received the chemotherapy drugs only. A study in rats given chemotherapy also demonstrated that oral intake of AHCC protected the animals against a loss of red blood cell production.

Similar results were observed in another mouse study reported in AHCC: Research and Commentary that used four groups of mice. Two groups were injected with chemotherapy drugs (5-fluorouracil and cyclophosphamide, methotrexate and 6-mercaptopurine) alone, and the other two received the drugs plus AHCC. Mice that received AHCC had a normal weight and normal levels of red blood cells, while the mice not treated with AHCC expressed a decline in both of these factors. Although the AHCC-treated mice showed some decline in white blood cell counts, it was not as significant as the decline observed in the drug-only groups.

In a study published in the Journal of Experimental Therapeutics & Oncology, scientists evaluated the impact of AHCC in groups of mice that were treated with a variety of chemotherapy regimens, including paclitaxel alone or some combination of paclitaxel, 5-fluorouracil, cisplatin, irinotecan, doxorubicin, and/or cyclophosphamide. They found that the myelosuppressive effects of chemotherapy were generally alleviated in mice that also received AHCC, and that both liver and kidney toxicity related to chemotherapy were significantly improved by AHCC.

The ability of AHCC to mitigate myelosuppression and to enhance immune cell activity and function are critically important benefits for individuals who experience a decline in white blood cell levels as a result of chemotherapy, as well as a potential way to reduce the risks associated with this life-threatening complication.

Loss of Appetite

Along with nausea and vomiting, chemotherapy can cause cancer patients to experience changes in taste. These factors often add up to a loss of appetite and poor nutritional intake. Because cancer patients already have a compromised immune system, a poor or inadequate diet can result in weight loss, a breakdown in muscle, increased susceptibility to infection, and an overall poorer quality of life.

AHCC has been used by thousands of cancer patients, and many report an improvement in loss of appetite when taking the supplement while undergoing chemotherapy. When their appetite is restored, patients are better able to maintain or regain lost weight, improve their nutritional intake, and support their immune system.

Is AHCC Safe to Use with Chemotherapy?

The answer is, with one caveat, yes. In fact, AHCC is reported to enhance and strengthen the therapeutic effects of the anticancer agent cisplatin, and perhaps others as well. The caveat relates to the results of a study conducted at The University of Texas MD Anderson Cancer Center in Houston and published in the Journal of the Society for Integrative Oncology. Researchers found that AHCC may be involved in a drug-drug interaction when used with chemotherapy agents that are metabolized via a specific pathway called CYP450 2D6. This includes drugs such as doxorubicin and ondansetron. Specifically, use of AHCC with these drugs reduces their effectiveness. The authors concluded that "the overall data suggest that AHCC would be safe to administer with most other chemotherapy agents that are not metabolized via the CYP450 2D6 pathway."

Wrap-Up

The take-home message here is that AHCC has demonstrated the ability to improve the quality of life of patients who are plagued with side effects associated with chemotherapy. This is no small achievement, as people with cancer often feel like they are losing control of their health and their lives. Making the functional food AHCC a part of their treatment plan can provide them with a safe, natural way to improve the quality of their lives while they battle cancer.

CHAPTER 6
OTHER CHRONIC DISEASES

The ability of AHCC to have a positive impact on immune cells and immune response throughout the body opens the door for its use in treating many health challenges. Research into the numerous possibilities is ongoing, and thus far scientists have documented promising results, which we share with you in this chapter.

Diabetes

Diabetes is a formidable opponent, and the statistics on the prevalence, future projections, and complications regarding type 2 diabetes are alarming. The latest available figures from the American Diabetes Association show that 23.6 million children and adults in the United States—nearly 8 percent of the population—have diabetes. An additional 57 million have pre-diabetes, which means they are very likely to develop the full-blown disease within a few years. Each year, 1.6 million new cases of diabetes are diagnosed in people aged 20 years and older. In 2010, the Centers for Disease Control and Prevention forecast that as many as one in three people (33%) in the United States could have diabetes by 2050, more than triple the current number.

The complications associated with diabetes are often debilitating and deadly. Adults with diabetes have heart disease death rates that are 2 to 4 times higher than adults without diabetes, and the same higher risk applies to stroke as well. Diabetes is the leading cause of new cases of blindness among adults, and it is also the main cause of kidney failure. About 75 percent of adults with diabetes have blood pressure greater than or equal to 130/80 mmHg or take prescription medication for hypertension, and between 60 and 70 percent of people with diabetes have nervous system damage (neuropathy).

Research indicates that both inflammation and oxidative stress (a state in which there is an excess amount of free radicals and/or an insufficient level of antioxidants to fight them) are involved in type 2 diabetes. In addition, inflammation appears to hinder the body's ability to properly utilize insulin as well as contribute to the breakdown in the cells that produce insulin in the pancreas. AHCC has anti-inflammatory properties, and so scientists explored its use in animal models of diabetes.

In a study conducted at Dokkyo University School of Medicine, Dr. Koji Wakame used rats with diabetes induced with the drug streptozotocin. One group of rats were pretreated with AHCC for one week before they were given streptozotocin while a second

group of rats did not receive AHCC. The untreated rats lost weight and their fur, increased their intake of water, had markers associated with a stressed liver, and demonstrated a decline in insulin levels accompanied by a rise in blood sugar levels—all signs of diabetes.

The AHCC-treated rats did not lose their fur, gained a slight amount of weight, had no increase in water intake, had normal liver markers, and maintained normal insulin and blood sugar levels. Upon microscopic examination, Wakame observed a decline in the number of insulin-producing cells in the pancreas in the untreated rats and only a slight decline in the AHCC-treated rats. Wakame concluded that AHCC may have a significant effect in preventing the onset of diabetes by protecting the insulin-producing cells.

In another study, presented at the 12th International Symposium of the AHCC Research Association in 2004, researchers at Osaka University also used rats with diabetes induced by streptozotocin. They reported that AHCC suppressed the onset of diabetes and delayed the development of complications.

Dr. M. Iwamoto of Nobuyama Medical Corporation conducted a study that involved 13 diabetic patients. All the individuals took AHCC for more than six months and experienced significant declines in both average blood glucose levels and glycohemoglobin. This latter factor is measured in a test called the glycohemoglobin A1c. The glycohemoglobin A1c level is important because, unlike a blood glucose level which is a "snap shot" of how well a person is controlling his or her diabetes, it provides clinicians with a reliable indication of how well the diabetes has been controlled over the last 2 to 3 months.

Two patients from Dr. Iwamoto's study can serve as examples of what is possible with AHCC in diabetes. He reported that when AHCC is taken by a patient who has a blood sugar level of 250 mg/dL (normal is 70 to 110) and a glycohemoglobin A1c level of 9.1 percent, the blood sugar level can return to normal after six months' treatment with AHCC, and the glycohemoglobin A1c can decline to 6.8 percent. In a patient whose glycohemoglobin A1c declined to 6 percent after taking AHCC for one month, the blood sugar level decreased to a normal value after two months of AHCC. In the latter patient, glycohemoglobin A1c levels remained normal and a problem with paralysis of the left leg associated with diabetic neuropathy improved.

Liver Diseases

In chapter 3 we noted that AHCC may help prevent liver damage in cancer patients who are receiving chemotherapy. Other reports suggest AHCC may be helpful in treating serious liver diseases, such as acute liver failure and hepatitis. Acute liver failure is an uncommon but serious condition that has a high mortality rate. "Hepatitis" means inflammation of the liver, and it also refers to a group of viruses that affect the organ. The most common types are hepatitis A, B, and C. According to the Centers for Disease Control and Prevention, an estimated 4.4 million Americans are living with chronic hepatitis, although most of them are not aware they are infected. Approximately 80,000

new infections occur each year in the United States.

Some studies of AHCC in liver disease have demonstrated promising results. For example, a mouse study was conducted to identify the effect of AHCC on liver damage. A group of mice were given AHCC in advance of being treated with carbon tetrachloride, which is known to cause liver damage and in animal studies has been shown to increase the risk of liver cancer. The scientists discovered that AHCC prevented a decline in the enzyme glutathione S-transferase (GST), which is involved in detoxification. Therefore, AHCC was able to reduce the amount of liver damage associated with carbon tetrachloride. In addition, when the scientists studied liver cells from the mice under a microscope, they found that cell destruction had been prevented. Overall, the researchers concluded that AHCC prevented damage to the liver associated with the oxidation caused by a toxin such as carbon tetrachloride.

Acute liver failure, which includes both fulminant liver failure and subfulminant liver failure (or late-onset liver failure) is an uncommon condition in which the liver undergoes rapid deterioration in a previously health individual. The condition usually affects young people and has a high mortality rate ranging from 60 to 80 percent. Scientists explored the effect of AHCC in an animal model of acute liver failure.

In the experiment, which was conducted by Professor Masatoshi Yamazaki of Teikyo University's Department of Pharmacy, two groups of mice were administered lipopolysaccharides (LPS) and galactosamine to induce acute liver failure: one group was pretreated with AHCC and the other group was not. Thirty percent (3 out of 10) mice that did not receive AHCC died within 24 hours of receiving LPS and galactosamine while none of the AHCC-treated mice died. Thus AHCC protected the mice against drug-induced liver failure.

Experts have also looked at possible benefits of AHCC in hepatitis patients. In some cases of hepatitis and liver cancer, there are reports of an improvement in the loss of platelets, a decrease or elimination of the viral load (the concentration of virus in the blood), and cessation of the deterioration of liver function.

An example of how AHCC may help patients with hepatitis can be seen in a case study of a thirty-two-year-old man who had chronic hepatitis B. After he began taking 3 grams of AHCC daily, he experienced a decline in the HBe antigen value (which indicates the amount of hepatitis B virus) and his Hbe antibody value increased (the antibody that helps eliminate the hepatitis B virus). Although the patient's platelet count decreased even after he started taking AHCC, it did not continue to decline. Eventually, elimination of the hepatitis B virus was confirmed.

People who have hepatitis C also reportedly respond to AHCC. Hepatitis C is a chronic viral infection that is characterized by elevated levels of liver enzymes, high viral loads, inflammation, and scarring of the liver. Untreated hepatitis C can result in cirrhosis and liver cancer.

Healthcare professionals, especially in Asia, have reported on case studies in which 3 to 6 grams of AHCC daily have successfully reduced liver enzyme levels and viral

loads in hepatitis C patients. There are reports that numerous patients have achieved a decline in viral load of more than 80 percent after taking AHCC for six months, and that some reach the normal viral load range after taking AHCC for seven to 12 months. Controlled studies are still needed to verify these findings.

Cardiovascular Disease

Cardiovascular diseases are the leading cause of death in the United States. According to the latest available figures from the American Heart Association, more than 81 million people in the United States has some form of cardiovascular disease (e.g., hypertension, coronary heart disease, stroke, heart failure), and approximately 34 percent of all deaths are attributed to the disease.

AHCC possesses a few qualities that may help in the prevention of cardiovascular disease. One is via its anti-inflammatory properties, as scientists have identified inflammation as playing a key role in cardiovascular disease. As we discussed in chapter 1, C-reaction protein (CRP) levels are an indication of the amount of inflammation in the body, and blood levels of CRP are a sign of increased risk of stroke, heart attack, and other cardiovascular conditions. AHCC has demonstrated an ability to reduce CRP levels.

Another way AHCC may benefit the cardiovascular system is through its ability to increase the production of nitric oxide. Nitric oxide is a chemical produced in the inner lining of the blood vessels (endothelium) when enzymes convert the amino acid arginine and oxygen through a series of steps.

Nitric oxide is important to heart health because it relaxes the smooth muscle in blood vessels, which improves the flow of blood. It may also widen blood vessels and arteries, which in turn can reduce the amount of pressure exerted onto the vessel walls by the blood. Nitric oxide's antioxidant properties can reduce the buildup of plaque in the arteries by lowering cholesterol and calming inflammation that causes plaque to accumulate.

One challenge presented by nitric oxide is that while high levels in the blood seem to reduce the risk of cardiovascular disease, there are few dietary or lifestyle factors that can impact nitric oxide production. AHCC may be able to address that challenge.

Other Conditions

Given the many positive results AHCC has shown in the host of studies regarding enhancement of immune function, it appears there is evidence that AHCC may be beneficial in the treatment of many other ailments and diseases, although clinical studies specifically for this purpose have not yet been conducted.

- Given AHCC's anti-inflammatory properties, for example, it seems likely it could help individuals who suffer with arthritis. Dr. Mitsuaki Iwamoto of the Enzankai Medical Corporation reports that patients with rheumatoid arthritis who have taken AHCC continuously experience an improvement in their symptoms. This

may be the result of AHCC's ability to stimulate the reduction in the levels of TNF-alpha and a substance called calprotectin, both of which have pro-inflammatory properties. Calprotectin is found in large amounts in the synovial fluid around the joints in patients who have rheumatoid arthritis.

- In a mouse model of ALS (amyotrophic lateral sclerosis), a progressive disease that affects the muscles and eventually results in death, scientists tested the possible benefits of AHCC in treating this autoimmune disease. In mice with laboratory-induced ALS, the administration of AHCC significantly enhanced grip strength and survival. This finding was presented at the 12th International Symposium of the AHCC Research Association.
- Colitis is a type of inflammatory bowel disease characterized by inflammation of the colon. Investigators in Spain induced the disease using hapten in two groups of rats. In one group, however, the animals were pre-treated with AHCC. The rats pre-treated with AHCC showed significantly lower levels of pro-inflammatory cytokines compared with the untreated rats.
- According to anecdotal reports regarding patients with HIV, AHCC is reported to maintain T cell counts and even increase them in some cases. This is critically important in people who have HIV, which attacks T cells. Dr. Daniel Rubin, a naturopathic physician board certified in naturopathic oncology, reportedly has prescribed AHCC for AIDS patients and confirmed an increase in B-lymphocytes and CD8+.
- Reports regarding AIDs patients claim AHCC has increased T cell counts after just one month of treatment, accompanied by an increase in the activity of natural killer cells, which typically are weakened in people who have HIV.
- People suffering with glaucoma have noted a reduction in intraocular pressure
- AHCC has been associated with lowering blood pressure in people with hypertension
- Individuals with chronic fatigue syndrome have reported an improvement in fatigue after taking AHCC. Dr. Dan Kenner, PhD, Lac, recommends 3 grams of AHCC daily for at least six weeks for treatment of chronic fatigue syndrome

Wrap-Up

Despite more than two decades of research, the full scope of benefits people can reap from AHCC has hardly been realized. Significant inroads into its impact on diabetes, cardiovascular disease, liver diseases, and other chronic illnesses have already been made. Because AHCC can impact the body's immunity at a very basic level, the possibilities appear to be quite substantial.

CHAPTER 7
USING AHCC

Now that you have read about the research surrounding the use of AHCC and the various beneficial effects it can have on the immune system, you are probably wondering how to use AHCC—how much to take and who can use it—as well as any side effects, its safety record, and if it can be taken with other medications. All these questions and more are covered in this chapter.

Taking AHCC

AHCC is manufactured by only one company, Amino Up Chemical Company, and is available as fine granules, soft granules in capsules and as a liquid. AHCC is meant to be taken orally only, never by injection.

If you are in good health and want to take AHCC as a preventive measure and/or to maintain your health, then 1 to 3 grams daily is suggested. This can be taken as two to six 500-mg capsules. If you are undergoing treatment for cancer (chemotherapy, radiation therapy, surgery), then 3 to 6 grams daily is recommended while cancer treatment is ongoing. This dosage can be reduced to 3 grams daily once treatment has ended to help prevent recurrence of cancer. In either case, it is best to take AHCC in divided doses three times a day (e.g., 1 to 2 grams three times daily).

Children can take AHCC as well, but you should reduce the dosage by up to 50 percent because of lower body weight. For elderly patients, the dose should be moderated to match their physical condition and introduced gradually since they may have a hypersensitive digestive system. AHCC can be mixed with yogurt or honey to make it easier to take.

Although AHCC has no reported side effects when taken in appropriate amounts or when taken with conventional medications or supplements, you should consult your healthcare provider before taking AHCC yourself or giving it to a child or other adult, especially if you or the other individuals are taking any prescription or over-the-counter medications or supplements.

Quality and Safety

AHCC is manufactured by only one company and under a strict, proprietary production method and culturing system. The manufacturing methods prevent contamination from foreign microorganisms and facilitate a stable culturing environment for the

entire process. To help ensure culture conditions (e.g., temperature, stirring, etc.) are always properly controlled, computer monitoring is utilized.

Generally, health foods derived from mushrooms are natural products, which means the components may differ depending on the producer and how the products are manufactured. When AHCC is produced, however, the chemical constituents and the quality are consistently maintained through attention to every detail of the manufacturing process and the latest technology.

Since the first days when AHCC was developed in 1983, safety studies have been conducted according to standards equivalent to the Good Manufacturing Practices (GMPs), standards for clinical research protocols on the safety of medicines. GMP provides standards for toxicity tests in animal testing. Along with general toxicity tests, standards for special toxicity tests, such as reproduction/generation tests, carcinogenesis tests, and others have also been developed. Despite the use of doses in excess of those estimated to be fatal in animals, AHCC has not demonstrated any toxicity.

In 1994, the AHCC Research Association was established. This Association consists of professionals from medical institutions and universities who are working to prove AHCC's medical reliability. Thus far, volumes of reports on basic research and studies related to clinical and safety issues have been produced. Dozens of studies have been published in journals, while scores of case reports have been documented. Although much work remains to be done, the results thus far have been very promising, and thousands of patients have benefitted from taking AHCC.

Taking AHCC with Other Medications

Research has shown, including evaluations done at the University of Texas MD Anderson Cancer Center in Houston that AHCC can be taken along with most conventional medications without initiating any drug-supplement interactions. This includes chemotherapy drugs and supportive therapies, such as antidepressants and anti-nausea medications, as well as insulin and over-the-counter drugs, but with one minor exception. AHCC can induce an enzyme called CYP450 2D6, which is involved in certain metabolic processes. If AHCC is taken with drugs such as doxorubicin or ondansetron, which are substrates of this enzyme, it may decrease the activity of these drugs. Therefore, consult your physician before using AHCC if you are using any medications, both prescription and over-the-counter, as well as any supplements.

Natural Ways to Enhance Your Immune System

Although AHCC is proving itself to be an excellent way to enhance and strengthen the immune system, it is unreasonable to expect that taking AHCC is all you need to do to protect yourself against illness and disease. Numerous lifestyle habits and other factors are also essential for achieving and maintaining an optimally functioning immune system. Those factors include the following:

- **Regular exercise.** Studies show that participating in regular, moderate exercise, like 30 minutes of brisk walking or bicycling 4 to 5 times a week, boosts the immune system by raising the level of infection-fighting leukocytes. Inactivity can weaken the immune system indirectly by contributing to obesity, poor sleep, and other problems that can increase your risk of disease.
- **Maintaining a healthy weight.** Being overweight or obese increases your risk of developing heart disease, cancer, diabetes, and other serious conditions. An excessive number of fat cells can trigger the release of pro-inflammatory chemicals that can result in chronic inflammation that leads to tissue damage and disease. Animal studies have shown that being overweight or obese causes a reduction in the number of antibodies the body produces after receiving vaccinations.
- **Manage stress.** Short-term stress may actually help your immune system operate better because in response to stress, the body produces cortisol, the "fight or flight" hormone that helps resolve the stressful situation. Chronic stress, however, can be damaging to the immune system, as the steady release of stress hormones cortisol and adrenaline suppresses the system's ability to ward off infections and disease. Epidemiological research into health psychology suggests there is a high risk of cancer in people who experience high levels of emotional stress. To help manage stress, choose management techniques that work best for you, be it exercise, meditation, aromatherapy, psychological counseling, yoga, dancing, deep breathing, laughter, or visualization, among others. All of these methods have been studied to varying degrees regarding their ability to help individuals reduce and manage stress.
- **Follow a nutritious diet.** A diet that focuses on antioxidant-rich foods such as fresh fruits and vegetables, whole grains, and legumes supports the immune system. Antioxidants neutralize the cell-damaging molecules called free radicals, which can cause and contribute to cancer and other diseases. Other immune-supporting foods include fresh garlic, turmeric, and mushrooms. A nutritious diet also means minimizing or avoiding sugars and unhealthy fats, such as saturated and trans fats. For example, consuming 75 to 100 grams of a sugar solution daily, which is equal to two 12-ounce soft drinks, can suppress the body's ability to respond to immune system challenges. Table sugar, fructose, glucose, and honey can all cause white blood cells to lose 50 percent of their ability to digest bacteria.
- **Stay socially connected.** Building and maintaining strong relationships and

social networks is critical for both physical and emotional health. Studies show that people who feel they have a good social network have a stronger immune system than people who feel alone.

- **Get adequate sleep.** Fatigue feeds illness: when you have not been getting enough sleep, you are more likely to develop an infection. Insomnia can cause a rise in cortisol levels, which in turn can lead to inflammation. Adults should get 7 to 8 hours of sleep per night for good health.
- **Avoid environmental toxins**. This can be a tough one, given the many ways people are exposed to chemicals and pollutants in air, water, food, soil, and everyday consumer products. A good start: avoid food additives, use natural cleaning products in your home and on the job, use natural pest control products in your garden, avoid secondhand smoke, use filtered water, buy organic foods when possible, avoid dry cleaning, and wash your hands with soap and water often.

CHAPTER 8
Q & A

Q: *Is AHCC only for people who are sick, or can someone who is generally healthy take it to boost their immune system?*

A: AHCC's potent antioxidant properties may provide the immune system boost so many people need in today's high-powered, overly stressed world. For individuals who are generally in good health and who want to support and maintain their immune system, 1 to 3 grams of AHCC per day is typically sufficient and recommended as an "insurance policy" against unexpected and unwelcome bacteria, viruses, environmental toxins, and other assaults to the immune system.

Q: *Can AHCC be used instead of conventional cancer treatments?*

A: AHCC is not a cure for cancer, and therefore anyone who has cancer should take advantage of the many conventional treatment options for cancer. However, AHCC is suggested as a complementary treatment for anyone who is preparing to undergo conventional cancer treatment, as well as patients who are currently in treatment and for those who have completed treatment. AHCC can offer immune system enhancing benefits to individuals in each of these circumstances.

Q: *If AHCC is made from mushrooms, why can't I just eat mushrooms and get the same benefits?*

A: Although whole mushrooms do possess many beneficial nutrients, AHCC is the product of special processing and culturing of selected mushrooms to produce a functional food that has a unique constituent called acetylated alpha-glucan. Alpha-glucan has a low molecular weight that makes it easy for the body to digest and absorb. These unique components also have a powerful immune-stimulating action not found in ordinary mushrooms, nor in other mushroom products.

Q: *Does immunity (cell-mediated immunity) improve in everyone who takes AHCC?*

A: Although the studies conducted thus far have shown that use of AHCC can result in an improvement in immunity for many patients and for healthy individuals as well, not everyone responds in the same way or to the same degree. Therefore, there is no guarantee AHCC will strengthen your immune system. The immune system is a complex network, and a compromised immune system is especially so. Strengthening and supporting one's immune system defenses is a job that requires many helpers, and AHCC is just one of them, albeit a potent one.

Q: *Besides AHCC, are there other natural immune system boosters?*

A: Although there are many other nutritional and herbal supplements that are used to boost the immune system, AHCC has probably undergone more intensive research than all of them. However, others to consider include astragalus, echinacea, flavonoids (plant compounds such as quercetin and catechins [found in green tea]), garlic, goldenseal, maitake (a Chinese mushroom), probiotics (beneficial bacteria), reishi (another Chinese mushroom), vitamins C, D, and E, and zinc. Before taking these and any other supplements, consult a knowledgeable healthcare professional.

Q: *Can AHCC be used in companion animals, such as dogs and cats?*

A: For many people, dogs and cats are considered members of the family, and when these animals develop serious health conditions such as cancer, some individuals turn to veterinary specialists who can offer them a variety of treatment options to improve their pet's quality of life and to treat symptoms. Numerous reports of the use of AHCC in dogs and cats have been recorded. Assistant professor Masato Kuwahara of Nihon University's Department of Veterinary Radiation Research and a colleague evaluated the use of AHCC and shark cartilage on breast cancer tumors in dogs. This combination was used because AHCC is an immune system stimulator, and shark cartilage is an angiogenesis inhibitor (prevents the formation of new blood vessels that feed tumors, thus starving them). A total of 62 dogs that had breast cancer were given these two supplements twice daily for more than 60 days. The combination had an antitumor effect in 29 dogs and improved quality of life in 45. Progression of the tumor was stopped in 24 dogs.

In addition to this study, there are other reports of individual cases in which veterinarians have used either AHCC plus shark cartilage or AHCC alone in dogs with breast and other cancers. There are also reports that AHCC is effective against age-related diseases, such as cataracts.

Suggested doses for animals are as follows:

- Large dogs: 2 to 3 grams daily
- Medium-sized dogs: 1 to 2 grams daily
- Small dogs: 0.5 to 1 gram daily
- Cats: 0.5 to 1 gram daily

Q: *Where can I get more information about AHCC?*

A: The AHCC Research Association has a website (http://www.ahccresearch.com/) that provides information about the functional food, including research articles, presented studies, and general information about AHCC.

END NOTES

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GLOSSARY

Acetylating: Adding an acetyl group to a molecule. An acetyl group is composed of several organic compounds, including the neurotransmitter acetylcholine, acetyl-CoA, acetylcysteine, acetaminophen, and aspirin (acetylsalicylic acid). In the case of AHCC, the acetyl group is added to glucan.

Antibody: A protein on the surface of B cells that is released into the bloodstream or lymph in response to stimulation by an antigen, such as a bacterium or virus, and that then neutralizes the antigen.

Antigen: Any substance that is capable of initiating a specific immune response, typically the production of an antibody. Antigens can be bacteria, viruses, fungi, toxins, or other substance that is foreign to the body.

Antioxidants: Molecules that interact with free radicals and stop the chain reaction of damage these radicals can cause. Commonly known antioxidants include vitamins A, C, D, and E, beta-carotene, the minerals selenium and zinc, and many phytonutrients such as catechins and carotenoids.

Apoptosis: A normal part of the life cycle of the cell in which the cell is programmed to die or "commit suicide." When treating cancer, one goal is to use an approach or substance that induces apoptosis of cancer cells so they die rather than continue to reproduce excessively.

Biological response modifiers (BRMs): Substances that stimulate or restore the ability of the immune system to fight infections and improve its functioning. They may be found in small amounts in the body and can be made synthetically as well. AHCC is a biological response modifier.

Brachytherapy: Also known as seed implantation, brachytherapy is a type of radiation therapy in which radioactive "seeds" are placed inside the cancerous tissue in a way that allows them to attack the cancer cells.

Cell-mediated immunity: Sometimes referred to as Th1 immunity, it activates T cells, such as natural killer cells and macrophages, that attack and destroy antigens.

Chemotherapy: Cancer treatment that involves the use of drugs designed to stop

the growth and reproduction of cancer cells by destroying them. In the process, chemotherapy also kills healthy cells. There are dozens of different chemotherapy drugs, with specific drugs prescribed for specific types of cancer. A few of the commonly used chemotherapy drugs include cisplatin, cyclophosphamide, doxorubicin, 5-fluorouracil, methotrexate, paclitaxel, and 6-mercaptopurine.

C-reactive protein (CRP): A protein that is produced by the liver, found in the bloodstream, and whose level rises with increasing inflammation in the body. AHCC's anti-inflammatory properties can be measured by monitoring its effect on CRP.

Cytokines: Chemical messengers that are secreted by immune cells that signal the type of response to antigens by the immune system. Some of the many different cytokines include interferons, interleukins, and tumor necrosis factor, among others.

Cytotoxicity: The ability to produce a toxic (destructive or killing) effect on cells.

Free radicals: Atoms or groups of atoms that have an unpaired number of electrons in their outer shell, and which are formed when oxygen interacts with them. Free radicals are highly reactive and can initiate a chain reaction of cell and tissue damage, including damage to DNA and cell membranes that can result in symptoms, disease, aging, and death.

Humoral immunity: Also referred to as Th2 immunity, this immune response uses antibodies produced in the B cells to identify antigens that trigger an immune response.

Immune response: How the body recognizes and defends itself against the invasion of bacteria, viruses, fungi, and other substances that appear to be foreign and harmful to the body

Immunomodulator: A substance—natural or synthetic--that has the ability to change, suppress, or strengthen the immune system.

Immunosenescence: The gradual decline in the integrity of the immune system that occurs as a result of aging. Age-related immunodeficiency makes individuals more susceptible to infectious conditions, including serious diseases.

Interleukins: A type of cytokines that are mainly produced by and act on white blood cells (leukocytes) to signal the type of action required by the immune system.

Leptin: A hormone that has anti-inflammatory properties, and that also is involved in fat metabolism and appetite regulation.

Macrophages: A type of white blood cells that "gobble up" and digest cellular debris and disease-causing organisms.

Myelosuppression: A condition in which the bone marrow activity is decreased,

which results in a reduction in the production of red blood cells, white blood cells, and platelets. Myelosuppression is a side effect of chemotherapy and radiation therapy.

Neutropenia: A blood disorder in which there is an abnormally low number of a critical type of white blood cell called a neutrophil. Neutrophils are a primary defense against infections because they destroy bacteria in the blood. Individuals who have neutropenia are at increased risk of contracting a bacterial infection.

Oxidation: The aging and deterioration of cells due to an increase in the activity of oxygen in the body.

Oxidative stress: A situation in which the body is unable to control damage to cells, tissues, and organs caused by free radical activity because there is an inadequate amount of antioxidants available. To counteract oxidative stress, the body produces antioxidants, and its ability to produce those antioxidants is controlled by genetic makeup and influenced by environmental factors, including diet, lifestyle habits, and other factors.

Phagocytosis: A cellular process by which cell membranes "eat" (phago) cells (kytos). In the immune system, phagocytosis is a major mechanism used to remove pathogens and cell waste, such as bacteria, dead tissue cells, and mineral particles.

Polysaccharides: Complex carbohydrates, including starches, cellulose, and glycogen, that are stored in the liver and metabolized (broken down) into blood sugar and released into the bloodstream as needed. The polysaccharides that make up the main ingredients of AHCC include beta-glucan and acetylated alpha-glucan.

SOD: The abbreviation for superoxide dismutase, which is an enzyme and powerful antioxidant that is involved in detoxifying activities. SOD removes excessive active oxygen from the body and neutralizes the effects of oxidative stress.

Tumor necrosis factor: A cytokine that is involved in the inflammatory process and which is capable of attacking and destroying cancer cells.

Viral load: A way to measure the severity of a viral infection by counting the amount of virus in the blood or other bodily fluids.