Natural Defenses– Strengthening Your Immune System Against Modern Threats.

Dr. Paul Clayton

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Foreword

by Roger Clemens, DrPH

Immunonutrition is an emerging and dynamic arena that stands at the interface of food, medicine and health. Numerous consumer surveys indicate approximately 80% of respondents continue to seek information and food products that are evidence-based, and products that will deliver and improve personal "immune" health.

Strengthening Your Immune System is an immuno-nutrition primer prepared by an international expert in pharmaconutrition. This primer provides the casual reader with an interesting, yet practical perspective on the interplay of food components and their relationships that contribute to a "primed" immune system. This primer also provided the experienced scientist with cellular insights on immune functions and the compelling details on the role of specific types of beta-glucans pertinent to immune health.

The six-part primer nicely provides an overview on the immune system, perspectives on immune system development, aspects on factors that challenge our immune system, assessments of natural immune modulators, recommendations to protect the immune system, and answers to classic immune-health questions.

The careful dissection of the beta-glucan story that differentiates the ingredient from cereal grain and food yeast is particularly interesting. The self-guided tour of the immune system illustrates the working relationship of food yeast beta glucan and provides critical compelling evidence that this form of beta-glucan may have numerous applications in clinical settings and consumer environments.

From simple descriptions to complex explanations, this primer augments expert advice that a healthy lifestyle, including compliance with dietary recommendation and physical activity guidelines, may include less stress, adequate sleep, increased vitamin D and regular intake of yeast-derived beta glucan in an effort to strengthen your immune system.

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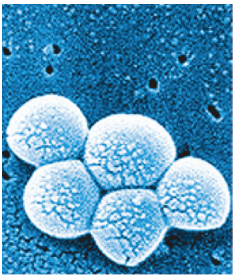
Introduction

Your immune system is your body's natural defence system, patrolling and defending your body 24 hours a day, every day of your life. It protects against invasion by bacteria, viruses, parasites and fungi and, on the relatively few occasions that these gain entry to the body, it fights the resulting infection. It is also one of the body's defences against cancer.

A weakened immune system, therefore, leaves your body vulnerable to disease. Many things can weaken the immune system, such as stress, a poor diet, lack of sleep, long-haul flights and crowded and uncomfortable travel conditions. Certain medications such as steroids weaken the immune system and many 'recreational' drugs have a similar effect.

The immune system is also depleted in the winter months when vitamin D levels fall, very inconveniently just when adverse weather conditions keep many at home, and in closer contact with others.

The dangers of inadequate immune function are very real. In the United States and in the United Kingdom, more people die each year from severe and systemic bacterial infections than from breast, colorectal and pancreatic cancer combined.



MRSA bacteria

Nor can we continue to rely on antibiotics to save us. The rise of 'super-bugs' like MRSA *(Methicillin-resistant Staphylococcus aureus)*, *C. difficile*, VRSA *(Vancomycin-resistant S. aureus)* and Multiple Drug Resistant Tuberculosis indicates that many antibiotics are losing their effectiveness, as antibiotic resistance continues to increase.

"More people die each year from severe and systemic bacterial infections than from breast, colorectal and pancreatic cancer combined."

Part 1

Your two immune systems

We talk of 'an' immune system, but in fact there are two distinct but inter-connected immune sub-systems; the innate immune system and the acquired immune system.

The **acquired immune system** is that part of the immune system with 'memory'. It is involved (positively) in immunisation, and (negatively) in allergy and auto-immunity. Once the acquired immune system has learned to recognise an enemy, after an initial infection or after a vaccination, it remembers the enemy's characteristics. On second exposure to the threat, the memory cells recognise it, and generate an immune response involving highly specific weapons such as anti-bodies. That's why it is highly unusual to catch measles or the same cold twice.

The acquired immune system is powerful, sophisticated and highly specific, but it is initially slow to respond and often insufficient to protect the host against the first onslaught of a virulent bacterium or virus.

It is only able to respond rapidly and at peak effectiveness if you have already encountered the threat previously.

Even small mutations in a virus—and some viruses, like the flu virus, mutate very rapidly—may be enough to 'fool' the immune system—one reason why it is only our second line of defence.

Our first line of defence, the **innate immune system,** is rather more basic. In evolutionary terms, it is much older than the more sophisticated and more recently acquired immune system. It is less specific; it can only recognise a limited number of compounds—around a dozen or so—that commonly occur on the surface of bacteria and yeasts. Its key cellular components are macrophages, neutrophils and Natural Killer (NK) cells.

Broadly, these 'front line defensive troops' constantly patrol the body and look out for anything that doesn't belong there. If macrophages and neutrophils spot a bacterium they swallow it and try to digest it. If NK cells recognise a virally infected cell they will kill it to prevent further viral replication, and if they encounter a cancer cell (and recognise it as cancerous) they will kill it to prevent tumour growth and spread. *(See illustration 1, page 5).*

All this makes the innate immune system very important indeed. Insects and other invertebrates—a group that constitutes the majority of animal species—rely solely on an innate immune system. They have no acquired immune system, and manage very well without one.

Another sign of the importance of the innate immune system is that while people born without a functional acquired immune system may live into their 30's, mutations that delete the innate immune system invariably cause death *in utero*.

As the numbers of antibiotic resistant bacteria in our environment continue to increase, and a flu pandemic approaches (see later), it makes good sense to ensure that your innate immune system is working as effectively as possible, and as effectively as it should be.

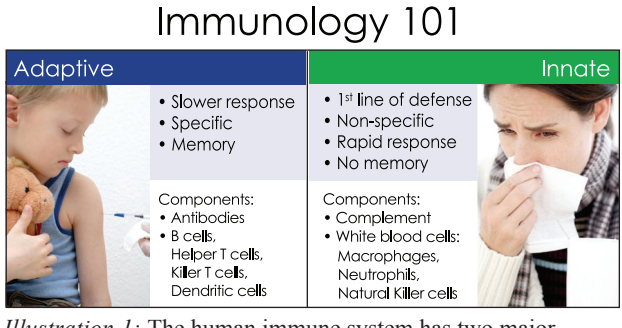


Illustration 1: The human immune system has two major subsystems: innate immunity and adaptive (acquired) immunity. Both must work together to clear the body of an infection.

Part 2

Why modern immune systems are less effective than they should be

An over sterile environment can reduce immune responsiveness

Despite, indeed ironically partly because of, modern medicine, your immune system may well be less strong than that of your recent ancestors—for three reasons.

1. We live in an unnaturally sterile environment!

Humans evolved in a dirty environment. We have been on the planet for hundreds of thousands of years but soap, antiseptics, disinfectants, canned and frozen foods have only been with us for a few generations, and antibiotics arrived less than a century ago.

During most of our time on this planet, therefore, our environment was replete with bacterial and viral hazards, and our immune systems were constantly challenged. And as we had strong immune systems, which mostly worked very well, we survived and multiplied.

Those spots on the apple have an important immune function.

'Give me spots on my apples, but leave me the birds and the bees, please!'

(from Big Yellow Taxi by Joni Mitchell, 1970).

Indeed, recent studies have shown that the innate immune system adapts to facing constant challenges and responds to attack by up-regulating its state of readiness and effectiveness.

In particular, the innate immune system learned to recognise molecules called 1-3, 1-6 beta glucans, which are present in the cell walls of fungus, moulds and yeasts; and it responds to their presence by mounting a strong counter-attack. In an age before fungicides were routinely sprayed onto every food crop, almost everything we ate would have been contaminated with yeasts, fungi and moulds, and this was, paradoxically, one of the main factors keeping our innate immune systems at peak capacity.

This is why, when we still lived in caves, we were able to eat foods that, far from being kept in the sanitised conditions of today's food chain, were literally crawling with micro-organisms.

Joni was more right than she, or we, knew. The spots on our apples—and indeed, the traces of fungi, yeast and moulds that used to be on almost all our foods—are now known to be as important for our health as the apples themselves.

To make matters worse, recent changes in food technology have effectively removed the beta glucans from fermented products such as bread and beer.

In today's over-sanitised environment our immune systems have relatively little to contend with, leaving them less active and less able to neutralise new and unexpected threats. This explains why, when we travel to parts of the world where sanitation standards are lower than ours, we routinely fall victim to pathogens that locals have no problems with. Our vulnerability to 'Montezuma's revenge', 'Delhi belly' and many other travellers' ills is largely due to our under-strength immune systems.

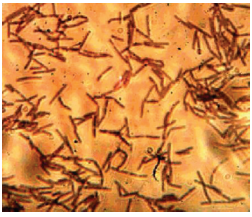
The absence of challenge in today's hygiene-obsessed world has also left our immune systems off-balance, and more prone to react to normally harmless substances such as pollen. This is thought to have contributed to the explosion that we have seen in the numbers of people with asthma and allergy.

This is the so-called 'hygiene hypothesis', and it probably explains why children who live on farms or with pets have a reduced risk of asthma and allergy. (Once allergy has been established, however, strict avoidance of such normally harmless things may sadly become necessary.)

The weakening of the innate immune system is also deeply implicated in the significantly increased incidence of cancer that has occurred in the last half century.

2. Antibiotics, over-prescription and the rise of the Super Bugs

Too many visits to the doctor end with a prescription for an antibiotic. That may be perfectly valid for a severe bacterial infection, but coughs and colds, for example, are usually caused by viruses, which cannot be treated with antibiotics. Nevertheless, nearly a half of children with common colds are treated with antibiotics *(Nyquist et al '98)*.



Because bacteria reproduce so quickly, they can become resistant to existing antibiotics before the next generation of antibiotics is developed.

Because children catch an average of three to eight colds each year, they may be given many courses of unnecessary antibiotics. And although doctors know that antibiotics will not help, they often find themselves pressurised to prescribe them, if only to reassure demanding parents that something—anything—is being done *(CDC '98)*.

In fact children with colds, ear infections, sinus infections, bronchitis and sore throats account for a staggering three quarters of all antibiotic prescriptions.

This is just one example of the over-use of antibiotics; a potentially dangerous and ultimately self-defeating activity, as antibiotic use inevitably induces anti-biotic resistance. Which is just another example of natural selection in action.

Bacteria have a shorter life cycle than ours, and DNA that is somewhat less stable, so they continually and rapidly produce variants on a genetic theme.

Take the case of a patient with a thriving bacterial infection. Impose an antibiotic on this unruly mass of micro-organisms and if the right antibiotic was chosen, the vast majority of the bacteria die; leaving a few that the patient's immune system, if all goes well, can finish off.

However, if the antibiotic is given improperly (for example at too low a dose, or too infrequently), or the course is not finished by the patient (a common problem), those bacteria which were slightly more resistant to the antibiotic survive in larger numbers. Among their descendants, those with the strongest resistance survive preferentially; and within a surprisingly short period of time, full-blown resistance can emerge.

Increasingly, however, the primary infection is caused by the resistant strains now prevalent in hospitals, and ever more often, in the community. The rising tide of 'superbugs' is a warning of bad times to come, and many people have become increasingly nervous about going to the hospital at all.

Leading bacteriologists now believe that the world may run out of effective antibiotics by 2010, with a gap of five years or more before new drugs can be developed such as the so-called 'Quorum Sensor Blockers'.

The warning that the age of infectious disease control is coming to an end was issued in early 2005 by one of the world's most influential scientists, Professor George Poste. Poste is Director of the Biodesign Institute at Arizona State University and an advisor to the U.S. president. "Frankly, most governments are asleep at the switch," he said in a recent interview, "even though we are facing a relentless increase in antibiotic resistance across all classes of drug."

Bacteria that have become resistant to previously effective antimicrobials include not only the well-known MRSA (*Methycillin-resistant S. aureus*), but also *pneumococci*, other *staphylococcus*, *C. difficile, enterococci, E. coli, Enterobacter,* and *Acinetobacter.*

3. 'Type B' Malnutrition

Health researchers are increasingly referring to 'Type B' malnutrition. This is not the sort of malnutrition associated with starving people in developing countries, but people in fully developed societies who have adequate calories—(often more than adequate!)—but an inadequate intake of vitamins, minerals and other vital nutrients. They suffer from multiple micronutrient depletion and the result is an impaired immune system.

An inadequate intake of vitamins, minerals and other vital nutrients cause people to suffer from micronutrient depletion and result in an impaired immune system.

If we examine the population at large we find that the average person, for example, has an intake of vitamin D and selenium that is only about HALF of the RDA *(Recommended Daily Amount)*. These are just two nutrients that are critical to the proper functioning of the immune system.

Moreover, the RDA was not established to give an optimum level of nutritional intake, but only enough to prevent deficiency. The optimum levels of many nutrients are almost certainly higher than the RDA's. This means that most people are likely to have intakes of many nutrients that are below the level needed for proper 'base line' support of the immune system.

Recent studies of hospital patients found that a staggering 60% were malnourished on admission *(Gallagher-Allred et al '96)*. In 30% to 40% of patients, the malnutrition was sufficiently severe to cause lymphopenia *(Bistrian et al '76, Naber et al '97)*, a condition in which numbers of white blood cells are significantly sub-normal.

This indicates substantial immunosuppression, and a significantly increased risk of acquiring an infection while in hospital.

This is one reason why infection control in hospitals is so difficult; immunocompromised patients are being brought into an environment full of resistant bacteria—a situation rather like introducing petrol to flames.

Fortunately this kind of immunosuppression is easy to treat, and responds promptly to improved nutrition. Well-designed nutritional supplements have been shown to improve immune function in these patients, and to reduce the incidence of infections and other complications during and after their hospital treatment *(Daly et al '84, Andrassy et al '85, Fietkau '98)*.

Health Researchers now recognise two forms of malnutrition.

TYPE A
is characteristic of the poverty in some parts of the developing world.

TYPE B
is a Western problem and characterised by adequate calories-(sometimes more than adequate!)—but a diet that is depleted in many critical nutrients—especially those that support the immune system.

Hospital admissions are by definition unhealthy people, and the criticism has been raised that the findings of malnutrition in this group do not reflect the situation in the community. However, similar findings have been reported in the wider community. Sub-optimal immune function is now common in elderly *(Edington et al '99)* and in middle-aged subjects. As with the hospital patients, however, their impaired immune systems can be improved and brought back to normal with well designed supplement programmes; both the elderly *(Bogden'94, Meydani '97, Jain '02)* and middle-aged subjects respond positively to supplementation.

Part 3

The threats we face

Over-sterile environments and sub-optimum nutrition may have weakened our immune systems, but at the same time the threats have increased.

1. Crowded Transport

Millions of us have to commute on local transport systems that are overheated, over-crowded—and constitute ideal conditions for the transmission of bacteria and viruses.

One airline passenger can be importing more pathogens in one journey than there are humans on the planet.

Moreover, rapid global travel means that on any one day, a single passenger can contract a virus or bacterium on one continent and arrive in another before the first symptoms of illness emerge, thus avoiding early detection. And that passenger can be importing more pathogens than there are humans on the planet.

Which leads us to the forecast flu epidemic...

2. The Flu Scare.

Whether the current strain of swine flu virus (H1N1) becomes a serious threat or not, experts say that a flu pandemic will occur. At the end of 2004 the World Health Organization (WHO) issued a stark warning of the pending flu global epidemic. Said spokesperson Klaus Stohr of the WHO Global Influenza Programme, "There will be another pandemic. In the best case we expect billions to fall ill, with 2 to 7 million deaths—but it could be far worse."

Stohr and colleagues like him are convinced that there will be a global spread because history shows that flu pandemics occur every 30 years or so. After this time, the genetic makeup of a flu virus has changed so much that people have little or no immunity built up from previous strains.

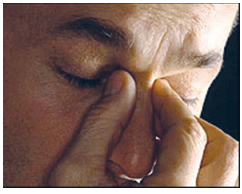
There were three pandemics in the 20th century, all spread worldwide within a year of being detected. The Spanish Flu in 1918-19 killed up to 50 million people. In the 1950s the Asian Flu pandemic killed a million, and in 1968 Hong Kong Flu killed another million or so. That was 41 years ago—so we're overdue for the next one.

"In the best case we expect billions to fall ill, with 2 to 7 million deaths – but it could be far worse."

Klaus Stohr WHO Global Influenza Programme

Antibiotics are no use in treating viral infections, and the right vaccines to protect us against the new strain of flu will take up to 6 months to produce in large amounts—which will be too late for many of us. Anti-viral drugs such as Tamiflu are not very effective, and in any case will only be available to about one in four of the population. And worryingly, but predictably, reports of Tamiflu-resistant flu viruses are beginning to appear.

3. Stress



Stress appears an unavoidable factor in modern life

Keeping stress under control is essential for a healthy immune system. In chronic or long term stress, our adrenal glands secrete a hormone known as cortisol. When cortisol output is high, the immune system is suppressed. It also secretes interleukin 6 (IL-6), which contributes to inflammation that can damage arteries and is thought to lead to heart disease.

Most surveys now show that a significant number of people report feeling stressed on a regular basis. That stress can come from many sources—work place pressure, the frustration of long commuting times, concern over the safety of children in particular and the family in general, and economic insecurity. And such stress can translate into a lowered immune status.

A stress-relieving activity of some sort is therefore definitely recommended, whether this is some form of physical activity or a more philosophical approach such as meditation.

4. Biological and radiation hazards

Exposure to radiation is another potent cause of immune-suppression, and contributes to the increased risk of infections after long-haul air travel. Unfortunately the risks of exposure to deliberate radiation—and even biological hazards—have increased in line with modern political tensions.

Summary

Investing in a strong immune system requires:

- ***a diet rich in fruits, grains and vegetables;***
- ***adequate sleep;***
- ***reasonable amounts of exercise;***
- ***Stress reduction, and;***
- ***Beta 1-3, 1-6 gluco polysaccharides Wellmune WGP®.***

The above analysis is not intended to be alarmist, but merely to make the case for each of us to do what is needed to invest in a strong immune status. Because, if the level of threat is increased and the defences are reduced, the risk of illness must increase.

The strategy should include a diet rich in fruits, vegetables and whole grains. It should include adequate sleep, reasonable amounts of exercise and stress reduction where appropriate. And it should also include an immuno-enhancer; beta 1-3,1-6 gluco polysaccharides or gluco polysaccharide for short.

Part 4

Nature's strongest immune-enhancer

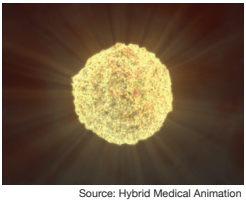
Of all the natural compounds known to activate the innate immune system, the best documented and most effective is gluco polysaccharide, derived from a proprietary strain of yeast. Indeed, when the Department of Defence of a major NATO member evaluated over 300 potential immuno-boosters, gluco polysaccharide had the highest score of all. This unique compound is part of a larger class of immune-enhancing carbohydrates called 1-3, 1-6 beta glucans, generally found in common baker's yeast *(Kernodle et al '98, Wakshull et al '99, Mansell et al '75, Hahn & Albersheim '78, Robertsen et al '94, Song & Hsieh '94).*

Beta glucans are complex molecules found in the cell walls of fungi and yeasts. These micro-organisms have always been a threat to animal species, and so the innate immune system long ago developed the ability to recognise beta glucan and react to them by mounting an immune response.

But it went further than that. As yeasts are so universal, the innate immune system became acclimatised to them, and dependent on them to function at peak effectiveness.

All innate immune cells possess CR3 receptors, which specifically recognise beta glucan; and are essential for full and effective innate immune function.

Then, very late in evolutionary terms, modern technology effectively sterilised our food chain and much of our environment. Levels of yeast and other fungi in our foods and in our immediate environment dropped away; and the lack of beta glucan left the innate immune system weaker and out of balance. This is the so-called 'Hygiene hypothesis' referred to previously.



Source: Hybrid Medical Animation

Illustration 2: Yeast gluco polysaccharide: nature's most effective immune system activator.

Adding beta glucan back into the diet restores the effectiveness of the innate immune system, with considerable health benefits. However, not all beta glucans are equal. Glucans are found in a variety of sources, including yeasts, moulds, fungi, cereal grains and bacteria. Each beta glucan type has a distinct molecular structure that translates into unique biological activity.

Research shows that yeast-derived beta glucans possess the greatest immune support characteristics; hardly surprising, as the innate immune system is set up to protect us against invasion by yeasts—and not mushrooms.

Interestingly, critical differences in the purity and sources of yeast beta glucans can result in wide changes in efficacy and safety. Impure glucans may be ineffective or trigger an allergic reaction.

Based on a large body peer-reviewed research published in scientific and medical journals, the most effective immune ingredient within the beta glucan genus is gluco polysaccharide, which is highly purified from a proprietary strain of yeast. *(See illustration 2).*

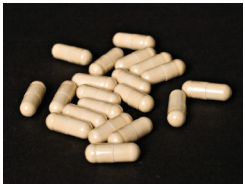


Illustration 3:
Wellmune WGP® capsules.

The following sequence explains how gluco polysaccharides prime the immune system to work at a higher level of activity. It is provided by Biothera, the leading researcher in this field and the manufacturer of patented gluco polysaccharides as ingredients for functional foods, beverages and supplements (Wellmune WGP® and WGP 3-6®), as well as retail immune supplement products (Immune Health Basics®). It was Biothera's compounds that were confirmed as so effective by the Department of Defence study mentioned above.

Biothera's Wellmune WGP® has been subjected to a significant number of clinical trials and has recently been chosen by the U.S. Government for trials in situations where the public may face radiation hazards, whether accidental or deliberate.

A biological guided missile—how beta 1-3,1-6 gluco polysaccharides work

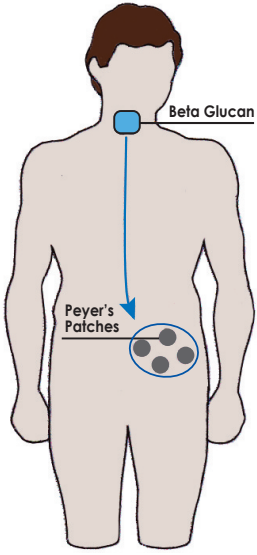


Figure 1

1. Once swallowed, gluco polysaccharide particles pass through the stomach into the small intestine where they are taken up by specialised regions called Peyer's Patches. *(See Figure 1).*

In the Peyer's Patches, the gluco polysaccharide molecules are encountered by circulating macrophages—immune cells whose function is to engulf and digest foreign invaders—whether bacterial, fungal or viral.

Macrophages have receptors which specifically recognise gluco polysaccharides *(Czop & Austen '85),* because they occur in the cell walls of many bacteria and fungi. This means that when you ingest beta glucans your innate immune system 'thinks', not unreasonably, that an enemy has arrived and it rises to the challenge.

This important first line of defence is now fully activated, and several well-conducted research papers have shown that resistance to infection is greatly enhanced *(Onderdonk et al '92, Kernodle et al '98, Vetvicka et al '02).*

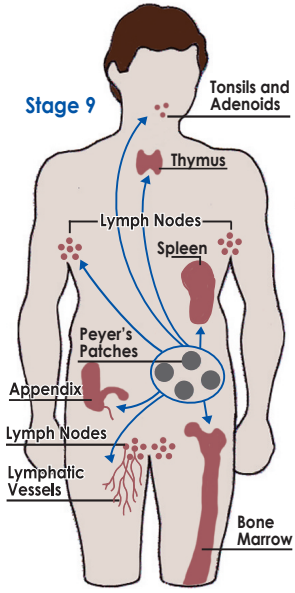


Figure 2

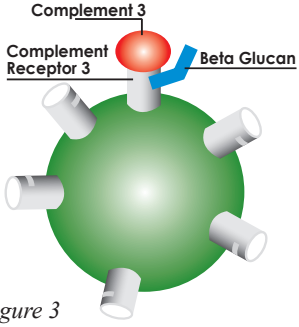


Figure 3

2. Specialised cells called M-Cells transport the glucan particles (containing the gluco polysaccharide active) to macrophages and these macrophages, in turn, convey the glucan particles to various regions of the immune system—such as lymph nodes, bone marrow and thymus. *(See Figure 2).*

3. The macrophages break down the gluco polysaccharides into smaller particles, and release them over a period of 24 to 36 hours. These active fragments bind or lock onto the surface of neutrophils, the most abundant immune cells in the body.

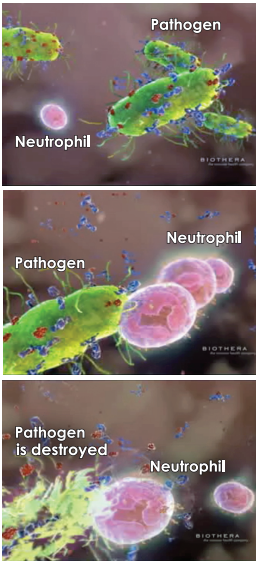
They lock on to a receptor called CR3—Complement Receptor 3. *(See Figure 3).*

The neutrophil is now activated or 'primed' and ready to react to foreign challenges or pathogens.

4. For a neutrophil to kill a pathogen or a cancer cell, the CR3 receptor (Complement Receptor 3) must be occupied by both complement—a blood protein—and beta glucan.

The CR3 receptor is occupied naturally by gluco polysaccharide found in the cell walls of fungus, moulds and yeasts. But there are other threats, including bacteria, viruses and cancer, where, in our over-sterile environment, gluco polysaccharide is not present in sufficient amounts.

Thus, by taking gluco polysaccharide, the neutrophils are provided with the missing element they need to trigger their natural killing mechanism.



Source: Hybrid Medical Animation

Figure 4

5. A fully primed neutrophil now migrates to the site of its target (whether virus, bacterium or cancer cell) through a process called chemotaxis.

The neutrophil then binds to the surface of this pathogen or cancer cell—and recognises it as 'non-self', i.e., foreign. It is now able to destroy that pathogen by releasing toxic chemicals. *(See Figure 4)*.

6. At the same time, other killer cells retain fragments of the pathogens that they have destroyed and 'present' them on their surface. These fragments—called antigens—send signals to other members of the immune system family, which become memory cells.

Next time the same pathogen is encountered, these newly programmed memory cells will recognise the virus and produce antibodies.

These antibodies stick to the surface of the pathogen and may destroy it, or prevent it from infecting healthy cells.

Size matters. The size of the gluco polysaccharide molecules may be important. There is some evidence that particles 2-6 microns in size may be most effective.

(See **www.drpaulclayton.com** for an animated explanation of the immune system.)

The evidence

Reduced Infection:

The beta glucans' ability to activate macrophages and prime neutrophils has been extensively tested (in over 800 studies) *(Rasmussen et al '85, '87, '89, '90, '91, '92);* and has been shown to protect animals such as mice against otherwise fatal infections. *(Williams & Deluzio '78, '79, '80, Leibovich & Danon '80, Lahnborg et al '82, Deluzio & Williams '83, Rasmussen & Seljelid '91, Tzianabos & Cisneros '96).*

In fact, in a pre-clinical trial conducted by Dr. Myra Patchen of Biothera, 90% of laboratory animals exposed to very high levels of *E. coli* survived when their innate immune systems were primed by gluco polysaccharide as opposed to 0% survival in the control group. *(See Illustration 4, page 28).*

Wellmune WGP® Increases Survival Against Deadly Bacteria

	% Survival		
	CONTROL	Wellmune (5 mg/kg)	p-value
Escherichia coli 1.0 X 108 CFU I.P.	0	90	<0.01
Staphylococcus aureus 1.0 X 108 CFU I.P.	0	80	<0.03

Patchen, Alpha Beta Technology

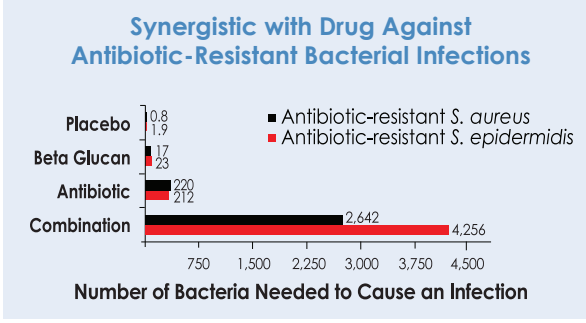
Illustration 4:
In this animal experiment, subjects were injected with a lethal dose of the gram-negative pathogen *Escherichia coli* or the gram-positive pathogen *Staphylococcus aureus*. In comparing the control group to animals treated with Wellmune WGP, there was significant enhancement in survival from 0 to 80 to 90 percent.

In a further test, 80% survived exposure to high levels of *Staphylococcus aureus* as opposed to 0% in the control group. And when gluco polysaccharides were administered in combination with antibiotics after exposure to bacteria, the number of bacteria needed to actually create infection was increased by up to 2,000 fold. *(See Illustration 5).*

A particularly impressive experiment was conducted by the Canadian Department of Defence. Mice were given a daily dose of gluco polysaccharides seven days before being exposed to a lethal dose of anthrax.

About half of the untreated control subjects died after seven days, whilst 100% of the gluco polysaccharides sample survived. In a further study over 80% survived (as opposed to 30%) even when the gluco polysaccharides were only taken after exposure to anthrax.

Studies on influenza showed a similar pattern. A high proportion of test rodents who received gluco polysaccharides prophylactically, (ie preventatively), seven days before exposure survived, and none of the untreated animals survived *(R Mandeville Biophage Pharma Inc.)*.



Kaiser and Kernodle. Antimicrob. Agents Chemother. 42: 2449-51, 1998

Illustration 5: Biothera gluco polysaccharide synergizes with antibiotics against methicillin-resistant bacterial strains.

Even more persuasively, gluco polysaccharides protect pigs. They reduce the harm done to the lungs after infection with swine flu virus, and reduce replication of the virus itself *(Jung et al i04)*. As pigs and people have a good deal in common (metabolically and physiologically speaking!), the pig model is very relevant to our own situation.

There are also clinical trials where gluco polysaccharides have been shown to reduce the risk of post-operative sepsis, and which are very much in line with the animal findings. *(de Felipe i93, Babineau & Hackford i94, Barbineau & Marcello i94, Dellinger et al i99)*.

Reduced Radiation effect:

Gluco polysaccharides have been shown to stimulate the regeneration of white blood cells after exposure to radiation, which of course happens to cancer patients undergoing radiation therapy. Less obviously it also happens to air travellers who are exposed to much higher levels of cosmic radiation than at sea level, as they are relatively unprotected by atmospheric shielding.

Laboratory studies have showed that when gluco polysaccharides are given at the same time as a normally lethal dose of radiation, over 50% of the sample survive in contrast to 100% mortality amongst mice who are not given gluco polysaccharides. The deaths were due to the fact that radiation normally sharply reduces white blood cell count and leaves the patient vulnerable to infection *(Patchen, ABTI) (University of Louisville 2005)*, the protective effects of the gluco polysaccharides were mediated by a more rapid return of normal white blood cell counts.

The U.S. army was taking careful note of this. Starting in the late '80's, the Armed Forces Radiobiology Research Institute ran an exhaustive test programme to measure the immuno-protective effects of beta glucans and as recently as 2004 reported that Biothera's WGP® 3-6 was most effective.

Not only did it protect against infection with bacteria, viruses and fungi, it also conferred protection against radiation injury *(Patchen et al '87, Patchen & McVittie '85).* Given that soldiers may at any time face an unpredictable range of biological weapons and even, in the worst case, radiation, the U.S. may begin to stock-pile gluco polysaccharides beta glucans—specifically WGP 3-6.

For most of us, however, travel, stress, superbugs and flu are a greater cause of concern; and in any case, these valuable compounds are too good to be left to the armed forces. As the age of antibiotics wanes and the threats advance, I have certainly made sure that I have a stock of gluco polysaccharides in my kitchen cupboard.

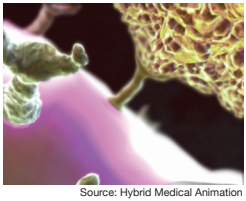
A role in cancer therapy

Cancer is the uncontrolled growth of cells. The immune system is only partially successful in fighting cancer, as cancer cells may not look very different to normal cells, and the immune system does not always recognize them as harmful. In fact it has been estimated that only 1 in 5 cancers triggers any sort of immune response at all.

It is only when the cancer cells become recognizably abnormal, that the immune system will attack them. Some of the work on cancer drugs is designed to 'paint' cancer cells with proteins to make them recognizable as foreign by the immune system.

When gluco polysaccharides are present– together with Complement—on the CR3 receptor sites of neutrophils—that neutrophil cell is primed and, once it recognises the cancer cell as non-self, is far more likely to attack it effectively. *(See Illustration 6.)*

In this way, pharmaceutical-grade gluco polysaccharides enhance the effect of cancer drugs, specifically the monoclonal antibody therapy drugs such as Herceptin. Indeed this is a prime objective of Biothera's research which is currently showing encouraging results.



Source: Hybrid Medical Animation

Illustration 6: Neutrophils, the most abundant immune cell in the body, have special receptors called CR3 that bind to gluco polysaccharide. Once primed with gluco polysaccharide, neutrophils are able to recognize and kill cancer cells that are marked with antibody and complement.

Just why I conclude that the 1-3, 1-6 gluco polysaccharides are so important is clear from this summary table of some of the research results that I have quoted above. The studies were all animal studies, but the mechanism of action is sufficiently similar in humans for the conclusions to be clear.

Exposure to:	Survival rate with gluco polysaccharide	Survival rate control group
E. Coli	90%	0%
Staphylococcus aureus	80%	0%
Anthrax	100%	47%
Influenza	50%	0%
Radiation	55%	0%

Life-long exposure to immuno-primers clearly extends life.

Brousseau & Miller '05

Safety

Beta glucan and gluco polysaccharide are supplements—and the safety of any supplement is a priority.

Perhaps because they have always been in our environment, beta glucans are non-toxic *(Williams et al '88, Acute Oral Toxicity Study '90)*. This was accepted by the U.S. FDA. (However only gluco polysaccharide from Biothera is designated as GRAS (Generally Recognised As Safe) under FDA regulations.) European regulatory authorities have permitted the sale of beta glucan-enriched soup and beer in Germany. Since beta glucan are natural supplements derived from food (baker's yeast), they are safe for adults and children.

Some nutritional therapists still maintain that the chronic use of so-called immuno-stimulants such as Echinacea is potentially harmful, but this is based on a fundamental misunderstanding of these compounds' mode of action. The idea that chronic immuno-priming could be harmful (as opposed to the natural state of affairs) was squashed by a recent report that clearly showed that life-long exposure to immuno-primers actually extended life *(Brousseau & Miller '05)*.

This is hardly surprising. As stated before, we evolved in a dirty environment, before soaps, antiseptics and modern food processing were developed, with high background levels of yeast and fungal contamination.

Our innate immune systems are designed to cope with constant priming, and depend on it to function properly.

It is important to note that pure beta glucans do not trigger allergic symptoms because they have little effect on the acquired (or 'learned') immune system, which is involved in those types of problems *(Washburn et al '96)*. Indeed, by tricking the acquired immune system into 'thinking' that there is an ongoing infection, the acquired immune system changes in a way which makes it more effective against pathogens, and less likely to develop allergy symptoms.

Transplant patients, however, should only use beta glucans cautiously and under medical guidance, or not at all. As the beta glucans can enhance general immune function, they could theoretically increase the risk of graft rejection.

Our innate immune systems are designed to cope with constant priming, and depend on it to function properly.

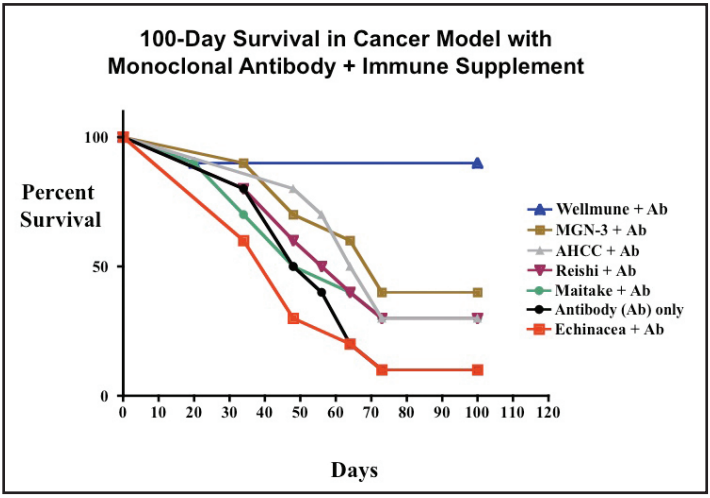
Alternative Sources

Beta glucans occur in several plants with a history of medicinal use such as aloe vera, Echinacea and fungi such as the Shitake mushrooms. However, these glucans have a different structure to those in yeast, and are not as effective in occupying the critical CR3 receptor. That is why they are not as good or as consistent immuno-primers as the beta glucan or gluco polysaccharides derived from yeast *(Goldman '88)*.

Indeed a recent animal study at the James Brown Cancer Center showed Echinacea to have only a very minor effect on immune function when combined with monoclonal antibody cancer therapy. (Specifically 100 day survival rate was 10% with Echinacea as a supplement and over 90% with Wellmune WGP®.) *(See Illustration #7, page 38)*.

These factors, together with the considerably larger database supporting the yeast-derived gluco polysaccharides, make them the agents of choice.

Wellmune WGP® is far superior to other immune supplements



Therapeutic potential of various β-glucan sources in conjunction with anti-tumor monoclonal antibody in cancer therapy. Cancer Biology & Therapy 8:3, 216-223; 1 February 2009.

Illustration #7:

Researchers at the James Graham Brown Cancer Center, located at the University of Louisville, measured the ability of leading immune supplements to enhance the immune response. For this purpose, a preclinical cancer model was selected in which animals were treated with a monoclonal antibody that targeted the tumor. Although no nutritional supplement is intended to treat or cure any disease, researchers wanted to determine whether the supplements would complement the drug therapy by fortifying the immune response.

Supplement doses were based on information provided by the manufacturer of each product. Only 10% of the animals treated with the monoclonal antibody survived 100 days. However, 90% of the animals that also received Wellmune WGP® survived 100 days, compared with 40% for those given MGN-3 and 30% for those whose diets were supplemented with Maitake or AHCC. Only 10% of animals treated with Echinacea survived 100 days, the same percent as those that were treated with the monoclonal antibody alone.

Part 5

The Acquired Immune System

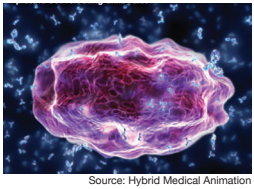
This is also called the Adaptive Immune System because, after a first exposure to a pathogen it 'adapts' itself so that it can destroy the same germ the next time it encounters it. Its 'heroes' are lymphocytes (white blood cells) called B cells and T cells.

Both B and T cells are made in the bone marrow. B cells grow in the marrow but T cells move out and mature in the Thymus (hence T cells). When mature, both cells travel via the blood stream to the lymphoid tissues—the lymph node, spleen, tonsils, adenoids, Peyer's Patches, appendix etc. Some of these cells are relatively sedentary while others travel from site to site.

There are thousands of different B and T cells, each created to recognize one particular antigen—the little piece of pathogen displayed on the surface of a phagocyte. The antigens in turn stimulate the release of chemical messengers called cytokines which tell B and T cells to ramp up their attack on the foreign virus or bacteria.

They do this by multiplying into a whole army of cloned cells, some of which become memory cells that ensure your immune system remembers each pathogen in future. (This is why you will generally not catch the same infection more than once).

Much of the time you are unaware of all this drama acting out in your body. At other times swelling, heat and inflammation tell you that B and T cells are multiplying in the area of infection.



Source: Hybrid Medical Animation

Illustration #8:
B Cells releasing antibodies.

Vaccines stimulate the Acquired Immune System and give you immunity in the same way as a 'real' bacterial or viral attack. By inoculating you with a pathogen that has been inactivated, your B cells are stimulated to produce antibodies as if the attack were real—and in this way they create the memory of that yet-to-be encountered threat. *(See illustration #8).*

The process of vaccination was first developed by Edward Jenner in the late 18th Century when he noticed that milk maids—who were exposed to cow pox—rarely contracted the closely-related small pox. (The word vaccination comes from vacca, the Latin for cow.)

There are vaccines for very many of the contagious diseases, but in the case of flu they are only effective against a specific strain.

This means that if the flu virus mutates (as it does from year to year) the previous vaccine will be ineffective—hence the importance of the latest version, and the non-specific defense conferred by the Innate Immune System.

Flu is not just a bad cold—some 7,000 people die of it each year in the UK. The real worry is that a virulent strain (which the Bird flu might become) could kill a hundred times as many.

Allergic Reactions

Allergies are disorders where the immune system over-reacts to a normally harmless antigen like pollen. That can typically cause a runny nose or sneezing, since many allergies are inhalation-related, but in extreme cases the reaction can be anaphylactic shock—for example to peanuts.

An allergic reaction is essentially a cascade of interlinked cell-to-cell communications. Initially an allergen will bind to an IgE antibody which in turn binds to a type of immune cell called a mast cell, triggering it to release compounds called histamines. It is histamines that cause the symptoms of swelling, itching, runny eyes, etc. These symptoms cause more inflammatory cells to mass at the site, a vicious circle that can damage tissue and lead to chronic illness like asthma.

Treatments include anti-histamines, decongestants and anti-inflammatory agents, and an anti-IgE drug called Omalizumab.

Occasionally the immune system will turn on the body it is supposed to protect, resulting in an auto-immune disease. It does this when T cells and B cells—which normally ignore the body's own cells—malfunction and begin to attack the cells as if they were foreign. This is the case with diseases like lupus, Type 1 diabetes and rheumatoid arthritis.

Since women are three times more likely to suffer from auto-immune disease, it is thought that hormones may play a role. Genes are a factor in some cases, and bacteria, viruses and exposure to certain toxic substances may also be involved.

Today's drugs designed to treat auto-immune disease are generally aimed at reducing inflammation. However, some of these suppress the overall immune response, and may be associated with an increased risk of certain types of infection. (See **http://www.drpaulclayton.com/scripts/index.aspx** for a full and illustrated account of a natural and safe approach to arthritis issues).

An allergic reaction is essentially a cascade of interlinked cell-to-cell communications.

Part 6

Eight ways to protect your family from viral and bacterial threats

1. A diet rich in fruits and vegetables

A large body of evidence indicates that the 'Neo-Mediterranean diet', which contains high levels of flavonoids, anti-oxidants and anti-inflammatory ingredients, not only lowers the risk of heart disease and cancer, but also supports good immune function. This diet is high in fruits and vegetables, wholegrain, beans and other legumes, olive oil, nuts and seeds, garlic, oily fish and a moderate intake of red wine.

2. Adequate sleep

Getting enough sleep is essential for health generally. Lack of sleep is perceived by the body as a form of stress—and stress reduces the immune response.

3. Baseline nutritional support

I recommend that anyone over the age of 45 take a comprehensive daily nutritional supplement.

It should include not just optimum—as opposed to merely adequate levels—of the classical vitamins and minerals, but also flavonoids and carotenoids (derived from fruits and vegetables), Omega 3 fatty acids, limonoids and many other micro and phytonutrients.

I have consulted on the design of a supplement called NutriShield **(www.uni-vite.com/nutrishield)**, which meets my criteria for comprehensiveness.

There is evidence that it is particularly important to ensure you have optimum levels of two specific micro-nutrients that are too low in the average diet and which are important for a strongly functioning immune system.

Vitamin D – up to 4,000 IUs per day

In the European and U.S. temperate zones, most people are depleted in vitamin D for most of the year—with the exception, perhaps, of the summer months. This is not bad enough to cause rickets, but it has been identified as a key contributory factor to the common problems of osteoporosis and osteopenia.

More recently, vitamin D depletion has been shown to reduce the effectiveness of the innate immune system. A gene called Vitamin D3-Upregulated Protein 1 (VDUP1) plays a crucial role in directing stem cells to diversify into natural killer cells, one of the key elements in the innate immune system.

Flu epidemics are most likely to occur in the winter months, when vitamin D levels are at their lowest. (Canell et al 08)

One of their functions is to eliminate virus-infected cells. If you are low in vitamin D fewer NK-cells are formed, and your innate immune defences against viruses become impaired. As the other function of NK-cells is to kill tumour cells, D-depletion probably increases our risk of cancer also.
(http://www.news-medical.net/?id=8080)

Adequate vitamin D is extremely important and leading experts in this area now state that as much as 4000 IUs a day (the amount you make in your own body by walking around in the sun without a shirt on for an hour or so) is the safe and effective dose. I absolutely agree—but you should note that the current RDA for vitamin D is only 200 IUs (with the US advising 400 IUs for the over 50's) and the current UK official upper safe limit is only 1,000 IUs. However, there is active current discussion about increasing this upper safe limit and it is already assessed as 2,000 IUs in the USA.

Selenium – at least 150 mcg a day

Selenium deficiency allows invading viruses to mutate and remain for a longer period in the host *(Beck et al '95, Beck et al '03).*

Researchers at the University of North Carolina in Chapel Hill compared mice that received a selenium-deficient diet with non-deficient animals, all of which were exposed to the human influenza virus.

The deficient mice had more severe cases of the flu that lasted for a longer period of time than the non-deficient mice.

Selenium depletion is prevalent in large parts of the world, including the UK *(Rayman '97)*. Accordingly, here is another dietary factor contributing to an increased risk of infection.

Optimum nutrition is particularly important to keep immune function strong in the older population, who tend to have poorer nutrition, less effective immune systems and a higher risk of infection.

Since Type B malnutrition is very common in older people, it is logical to ensure that they receive supplements that have a direct impact on the health of the immune system.

From this report it is obvious that I consider that gluco polysaccharides are an important element in any immune-enhancing programme.

4. Gluco polysaccharide—250 mg a day

A gluco polysaccharide supplement can be taken by anyone as a daily supplement in periods of extra stress or threat. It is logical to take them on a daily basis as the life cycle of neutrophils, the key effector cells of the innate immune system, is some 2 days or less.

This applies especially to people who are at immediate risk of infectious diseases, taking immuno-suppressant medication or experiencing slow and incomplete healing.

People about to enter hospital, and long distance air travelers are also prime candidates.

I would also consider taking a gluco polysaccharide supplement at the first sign of a cold or sore throat and during the main winter months—especially for people regularly traveling on crowded transport.

The 'preventative' daily dose is around 2 mg per kilo of body weight—or about 250 mg of purified gluco polysaccharides a day.

Wellmune WGP® 3-6 gluco polysaccharides produced by Biothera, whose research is quoted above, is patented and available in the UK in the brand ImmunoShield®, and in numerous products in the U.S.

5. Pre and probiotics

There are hundreds of different types of bacteria in your digestive tract. There is evidence that some of these—the so-called probiotic species—have a positive effect on immune health. Prebiotic fibers such as inulin stimulate the production of probiotic bacteria.

6. Exercise

Exercise is an effective immune booster and important for health generally. Being unfit is as dangerous as smoking 20 cigarettes a day! A program of regular, moderate exercise relieves stress and makes it easier for you to sleep at night.

Excessive or intense, sustained exercise by elite athletes, however, may reduce immune response.

7. Other precautions

Cold and flu viruses are transmitted through the air—via coughing and sneezing—and through surface contact, such as door handles. It therefore makes sense to wash your hands regularly with soap and water and to avoid touching your eyes, nose or mouth.

Food preparation is another area where sensible precautions can avoid problems with food poisoning. Rinse all meat and fish under running water before cooking, wash your hands each time a new raw food is touched, and never cut cooked and raw meats on the same board.

8. A healthy lifestyle

In addition to the above, stop smoking if you haven't already done so, maintain a healthy weight, control blood pressure and drink alcohol in moderation—two glasses of red wine per day seems about right. Children and the over 50's should get a flu shot. Regular medical check-ups are also important.

Part 7

Your questions answered

Does being cold make you sick?

Most experts agree cold and flu infection is more prevalent in the winter because cold weather means we spend more time indoors in closer contact with other people—not because of the cold itself. Prolonged cold exposure may, in some circumstances, reduce immune functions. Another reason we get these infections in winter is because falling vitamin D levels depress certain aspects of immune function.

Can beta glucan or gluco polysaccharide trigger a yeast allergy?

Many people have concerns about yeast because they have been told by well-meaning therapists to avoid brewer's or baker's yeast as it somehow increases the risk of Candida infections. Others believe, rightly or wrongly, that they are allergic to it.

These concerns are misplaced. The Candida story was popularised by untrained therapists who mistakenly believed that brewer's yeast and Candida were related species—whereas in fact they are totally unrelated.

Although allergy to yeast can occur, purified gluco polysaccharide preparations are free of yeast cells, and yeast protein; and they are hypo-allergenic.

Why is infection often accompanied by fever?

A higher body temperature helps speed up the workings of cells, resulting in a faster immune response. In addition, some germs do not reproduce well at higher temperatures.

Why can antibiotics be counter-productive?

Your skin is part of your first line of defence. It is a barrier to pathogens and slightly acidic, which is hostile to many microbes. On the other hand, both your skin and gut are teeming with bacteria that are necessary for health. So anti-bacterial soaps and vaginal douches can upset the balance of bacterial flora.

Similarly, antibiotics can knock out both the bad and the good intestinal flora—which can leave 'a vacancy' for bad bacteria to move in and flourish. In these circumstances, prebiotics that encourage the body to make its own probiotics, ('friendly bacteria'), may contribute to health.

When should I give children antibiotics?

Broadly, children with sore throats should not be given antibiotics UNLESS lab tests show a strep or other bacterial infection. Bronchitis or non-specific coughs rarely warrant antibiotics, UNLESS the symptoms last more than 10 days, and a particular bacterium is suspected; and in cases where there is an underlying lung disease such as cystic fibrosis (but not asthma).

Antibiotics should not be given for the common cold, even when there is a nasal discharge (this is fairly normal); and whereas short courses of antibiotics should be given for acute middle ear infections (otitis media), they are not indicated for otitis media with effusion. (This is a subtle but vital distinction which the doctor makes when he/she first sees the child).

If an antibiotic is going to do the job properly it must be taken for the duration of the recommended course. Antibiotics don't work right away. Most children take a couple of days to start to feel better, yet some parents assume that the drugs aren't working and stop after the first dose. Others stop once the child has started to improve, and do not finish the course.

These last strategies greatly increase the risk of resistance developing; as does the not uncommon practice of re-using antibiotics that may have been lying around at home from a previous bout, or even belonged to someone else. The problems of drug resistance cannot be left to the specialist infection control teams; we all have a responsibility to ensure antibiotics are used properly, and we all have an important role to play if we want to be able to continue to rely on antibiotics when we really need them.

Are oat beta glucans similar to yeast derived beta glucans?

Despite their name, yeast-derived and oat-derived beta glucans are quite different. Oat beta glucans have been shown to help lower cholesterol as part of a overall healthy diet. They have a different structure, and are technically 1-3, 1-4 beta glucans

whereas the yeast compounds are 1-3, 1-6 beta glucans.

Which beta glucan is most effective?

Comparative studies have shown that the 1-3, 1-6 beta glucans derived from brewers or bakers yeast, Saccharomyces cerevisiae, are the most effective at priming and normalising immune function. However, not all products derived from bakers yeast and brewers yeast are the same. There are significant differences between different strains of this yeast, because the different yeast strains have slightly differently configured beta glucans. These differences in both purity and configuration can lead to major differences in how effectively the product enhances immune function. These are large molecules, and they must fit the CR3 receptor as accurately as possible to generate the most effective immune response. After a long period of experimentation Biothera uses a proprietary strain that has been developed for maximum effectiveness and they use this strain consistently in their clinical trials and in their products. Other less technically advanced companies have attempted to use Biothera data to support their products, but this is highly misleading as their products are not identical, and often not even standardised.

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