The Next Pandemic..

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"The next global flu pandemic is on our doorstep. Klaus Stohr of the WHO Global Influenza Programme recently stated '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'. In the UK, for example, the Department of Health predicts there could be as many as 750,000 deaths. Why are the experts so pessimistic?

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 immunity built up from previous strains becomes irrelevant; so that herd immunity, our main defence against pandemics, has become negligible.

There were three pandemics in the 20th century, and all spread worldwide within a year of being detected. The Spanish flu in 1918-19 killed up to 50 million people. In the 50's the Asian flu pandemic killed a mere million, and in '68 Hong Kong flu killed another million or so. That was 41 years ago – so we're due for the next one. Prime candidate is the swine flu now gathering momentum around the world, and which has already shown human-to-human transmission.

Antibiotics are no use in treating viral infections, and the right vaccines to protect us against the new strain of swine flu won't be ready until at least 6 months after the epidemic has started, which will be too late for many. Various EU member state governments have decided to purchase anti-viral treatments for, in some cases, as many as 1 in 4 of the population. Those decisions were based on two assumptions: firstly, that the emergency could be managed, and secondly that the anti-viral drugs will be reasonably effective. Both of these assumptions are very questionable. Our ability to deal with the fall-out of a contagious and highly lethal viral epidemic is, realistically, inadequate. And the efficacy of the anti-virals (which was never very high) is being seriously under-mined by the emergence of drug resistance.

Let us assume, however, that the anti-viral drugs are still at least partially effective when the time comes, and the emergency plans will actually work. One in four people deemed sufficiently important (army, police, medical personnel and the political classes) will be protected. What should the rest of us do?

The best defence against viral infection is to prep your innate immune system, which is the body's first line of defence against invasion by bacteria and viruses. Unlike the acquired (or adaptive) immune system, the innate immune system does not recognise every possible antigen. Instead, it is geared up to recognise and react to a small number of highly conserved molecules which are present in the cell walls of many pathogens; including LPS (gram negative bacteria), lipotechoic acids (gram positive bacteria), and 1-3, 1-6 beta glucans (bacteria and fungi).

Once stimulated, the innate immune response mounts both cellular and humoral responses. These involve:

1. Phagocytic cells. These include macrophages and related cell species such as Langerhans cells in the epidermis, Kupffer cells in the liver, microglia in the brain and osteoclasts in bone.
2. Cells that produce inflammatory mediators (mast cells, eosinophils and basophils)
3. Natural Killer cells
4. Mediator molecules such as complement proteins, acute phase proteins and cytokines. These include tumor necrosis factor (TNF), interleukins 1 and 6, hydrogen peroxide, and gamma interferon, all of which fight against invading pathogens.

Of all the natural compounds known to stimulate the innate immune system, the best documented and most effective are the 1-3, 1-6 beta glucans, generally derived from brewer's yeast (Kernodle et al '98, Wakshull et al '99). These molecules activate the innate immune system very strongly indeed; in humans and other mammals, and in birds, fish and even crustacea (Mansell et al '75, Hahn & Albersheim '78, Robertsen et al '94, Song & Hsieh '94). Macrophages have receptors which specifically recognise 1-3, 1-6 beta glucans (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).

The beta glucans' ability to activate macrophages has been extensively tested (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, '83, Leibovich & Danon '80, Lahnborg et al '82, Deluzio & Williams '83, Browder et al '83, Rasmussen & Seljelid '91, Tzianabos & Cisneros '96). Trials have shown the same substantial protective effects in human infections also (de Felipe '93, Babineau & Hackford '94, Barbineau & Marcello '94, Dellinger et al '99).

A glance at the references above shows that most of the key studies had already been completed by the mid – 90's, but the work was not thought to be commercial, and was not developed for clinical use. Antibiotics still ruled the roost, and were highly profitable for the drug companies, while brewer's yeast extracts were cheap and belonged to everybody. This meant that none of the drug companies was interested in investing in them.

National authorities, however, was taking careful note. Starting in the late '80's, they ran an exhaustive test programme to measure the immuno-protective effects of beta glucans and over 100 other immuno-stimulants, and as recently as 2004 reported that the beta glucans were the most effective of them all. Not only did they protect against infection with bacteria, viruses and fungi, they 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 US army began to stock-pile beta glucans. To this day Washington keeps significant amounts of beta glucans in readiness, to be issued as and when circumstances dictate. (To put this in context, all cases of 'bacterial warfare' reported in the US to date - such as the notorious 'anthrax by post' episode – were identified as being internal affairs!)

I personally think that these valuable compounds are too good to be left to the armed forces. I have put up a couple of kilos of purified beta glucans on the top kitchen shelf. When the time comes I will give them to my children, at a dose of 500 mg of beta glucans per day; armed with the knowledge that they are safe (Williams et al '88) and effective prophylactic agents. In trials with pigs, beta glucans reduce the harm done to the lungs after infection with swine flu virus, and reduce replication of the virus itself (Jung et al '04). As pigs and people have a good deal in common (metabolically and physiologically speaking), the pig model is very relevant to our own situation. When one looks at our governments' flu management strategies, George Orwell's porcine metaphors seem more appropriate than ever.

WHICH BETA GLUCAN?

It is no easy to ascertain which beta glucan preparation is most effective. Surprisingly, the actual amount of beta glucan per capsule is not critical; particle size is as or more important, with particles of around 100 k.daltons found to be the most effective immuno-stimulants. Another criterion is purity, generally expressed as a low protein and ash content. This will minimise the risk of an allergic reaction, a potential hazard in those rare individuals who have a genuine allergy to baker's yeast – as opposed to the much larger numbers who claim to be allergic! At this time, however, as none of the physical parameters has yet been validated as an appropriate proxy marker, it is probably best to rely on biological assays to measure quality. And as there are some very shoddy materials on the market, you may prefer to work with beta glucans from companies with a strong research background and an established track record.

Click here for an independent comparative review of commercial beta-glucan 1-3,1-6.

Two of the best are Glucasan made by a German company working in association with the University of Berlin who have done large scale studies using beta glucans to replace antibiotics as growth promoters; and Biothera, a US company who have also invested in research and quality control."

Details of Glucasan, distributed in the UK by Vitalize, can be found here: www.vitalizehealth.com or by phoning 0870 042 8423

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Flu Pandemic - the expert view

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Bird/Swine Flu - an alternative approach

Every adult has had more than a few colds and several bouts of flu over the years, but many people were very apprehensive about the last swine influenza pandemic even though the virus was relatively mild with mostly moderate symptoms.

Their real worry was what might happen if the virus mutated or combined with another virus making it very much more virulent and turning it into the killer flu that everyone has been worrying about, the one that could kill millions. In 1918 Spanish flu killed 50 million people.

Every year, seasonal flu causes an estimated fifty thousand deaths in the European Union; most people die from bacterial infections and secondary illnesses. The highly variable type A is the most virulent one among the influenza viruses. Based on the antibody response these pathogens can be subdivided into different sterotypes, e.g. H5N1 that causes avian flu, or H1N1 that caused Spanish flu in 1918, and the swine flu 2009. Owing to frequent variations in their genetic pattern, every year different strains prevail and, therefore, specially designed vaccines have to be manufactured.

Flu vaccination may help to avoid influenza. Antiviral medicines lessen flu symptoms, but they are usually only for individuals who could become seriously ill from flu. Side effects of antiviral drugs include nausea, vomiting, dizziness, and insomnia. In children much has recently been made of the fact they also cause nightmares. Although the H1N1 type causing the current influenza outbreak is of lower virulence, authorities nevertheless do fear the mortality rate could increase this winter and assess the pandemic as a potentially huge challenge for the health authorities. It has been announced that a vaccine against the swine flu virus should be available in the last quarter of this year. **But virus researchers worry about one thing above all; the formation of a new subtype combining two different strains of virus initiating a sudden antigenic shift. Such a rare but not unrealistic incident could thwart all efforts to contain the pandemic.**

Sober-minded contemporaries may wonder about alternative approaches to prevent flu carefully considering issues such as why so many individuals are not becoming ill in spite of contact with infected persons? The main reason might be that their immune defence copes effectively with the virus challenge. Until recently, immunity was seen as the process whereby extremely specific antibodies targeted the invading pathogen. However, it takes quite a long time before the acquired immune system produces the explicit antibody; though vaccination with innocent viruses may bridge that gap. One should nevertheless bear in mind that the overwhelming part of the antimicrobial defence still has to be done by the innate immune system. This arm of immunity was the poor cousin of biomedical research for a long time but recently many advances have been made in understanding host innate responses to microorganisms.

It is now generally accepted that macrophages and other white blood cells constitute the backbone of our innate immune system. Just like gate keepers they accumulate in the epithelia of nasopharynx (nasal cavities), mouth, intestine and other mucous surfaces – the main entry ports of viruses, bacteria, fungi, and parasites. These cells are armed with germ-line encoded proteins to recognize a set of surface structures on pathogens, engulf, kill and destroy the invader. In that way the

overwhelming majority of potential infections are arrested in epithelial and superficial connective tissues long before antibodies and antigen specific killer cells have had time enough to come to the rescue.

Occasionally, the immune system may become unbalanced, overwhelmed and/or respond incorrectly. Allergy, asthma, arthritis pain, chronic fatigue, diabetes, cancer, and frequently recurring infections are related to impaired immunity or inappropriate reactivity. A wide range of factors may restrict immune defence: old age, poor diet, exhaustive life style, mental or physical stress, sudden change in personal life, grief, exposure to UV irradiation, and possible insufficient exposure to microbial products that exercise the innate immune system in a natural manner. Furthermore the immune system of infants and school children may have not be fully developed.

Studies in many laboratories have begun to elucidate the network of surface receptors on immune cells and signalling mediator molecules. On this basis it has become possible to design ways using ummuno-modulators to up-regulate or down-regulate specific facets of the host response to infectious agents. This approach allows the host to better cope itself with invading microorganisms. **Viruses and other pathogens are not able to develop any resistance to such immuno-modulators**.

Numerous reports document the ability of certain sugar polymers to non-specifically activate cellular and humoral components of the host immune system. During evolution, the immune system has “learned” to recognize surface beta-glucans as alien to the members of the animal kingdom and to allot a microbial as a potential pathogen that is implemented with such a molecular assembly. **Beta-glucan – or exactly beta (1,3),(1,6)-D-glucan - primes the host immune system through a mechanism similar to that of an infection by a pathogen.**

This occurs as a primary constituent in the cell wall of fungi and bacteria. Beta-glucan molecules apparently have a structural function in forming a fibrous scaffold of the cell wall of bakers yeast and are responsible for its rigidity and cell shape. Disintegration of yeast cells by autolysis and skilful fractional purification of the cell wall have been shown to be a sufficiently gentle procedure to create products that have a very high immuno-modulatory effect. Detailed studies elucidated a pattern recognition mechanism for the beta-glucan interaction with the receptor complex on macrophages. Harsh procedures to yield highly purified beta-glucan may disorganize the supramolecular assemblage of the polyglucoside-glycoprotein-network. In experimental assays on neutrophils highly purified samples have proven lower biological activity.

As yeast has virtually disappeared from today’s diet since it has been replaced with chemical surrogates in the baking of bread and cakes and beer brewing, **a daily intake of about ½ a gram of beta-glucan can help prevent flu virus infection and puts our innate immune system on highest alert to cope with any subsequent infection such as pneumonia**. As soon as a vaccine against flu is available continuous regular administration of beta-glucan is recommended. Veterinarians investigating the antibody titre (using special testing dilutions) against the swine flu virus in vaccinated pigs confirmed much better results when the animals were fed beta-glucan brands derived from yeast.

If used in combination with anti-viral drugs, where the mode of action is very different, each component amplifies the efficacy of the other. Furthermore, no adverse effects, reactions or toxicities were reported by any healthy or ill individuals involved in studies. Both in the US and Germany beta-glucan 1-3, 1-6 has been consumed as a food supplement in large quantities for years.

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