COVID-19: WHERE NEXT?

Now on the world stage, Covid-19 has passed the containment stage, and political and health care systems everywhere have moved directly to disease management. This was largely inevitable, given the viral attributes of high transmission rates and long incubation, and the common political tendency to normalcy bias.

Some nations have relied on contact tracing and lock-down to slow the increase in affected cases, essential in preventing hospital overload and – hopefully – in starving the virus of fresh victims. China appears to have done so fairly successfully, effectively militarizing their viral control effort in tandem with sophisticated online tracing and localization tools available via WeChat. South Korea has been able to achieve something similar, combining sophisticated tracing tools with a highly educated, motivated and relatively homogenous population who were willing to take appropriate actions such as self-isolation and, where necessary, self-reporting.

It remains to be seen if nations in Europe and North America will be able to follow suit. France has joined Italy in imposing a national lockdown; and Germany, Austria and Denmark have joined the Czech Republic, Hungary and Poland in closing their borders. The Czech Republic has also joined in the mass quarantine movement, sealing off some towns entirely.

The problem with lock-down, is that it is rarely completely effective, and infection may reappear once social conditions are normalized. Other nations have chosen a different path, with the UK in particular having decided to opt for herd immunity. The aim here is to trade larger numbers of initial cases with a longer-term reduction, achievable once 60% of more of the herd have been exposed and gained a degree of resistance to the virus. The problem with this approach, however, is that no one yet knows how many recovered individuals generate strong and/or permanent immunity. Initial reports indicate that after Covid-19 infection, immunity may not always be strong or long-lasting; and if these reports are representative, effective herd immunity may not be achievable. Viral mutation, as occurred with the 1918-19 influenza and may have already occurred with Covid-19, can also undermine the herd immunity strategy.

Both of the above options incur significant economic costs, due to disruption of supply chains and working patterns; and some believe that these may be so severe as to impact health statistics even more profoundly than the disease itself. There is a growing need, therefore, to shift resources to acute and to systemic disease treatments.

There will always be a place for symptomatic approaches (decongestants, iv drips, nasal washes and in severe cases ventilators and antibiotics/antifungals), but it is self-evident that more fundamental strategies are needed to protect our national health. Which brings us to the anti-virals, and the vaccines.

Initial promising reports of using combined antiretrovirals and neuraminidase-inhibitors continue to be investigated, and more recent reports on combinations of antiretrovirals and anti-malarials and/or remdesivir, are being evaluated. The anti-malarial hydroxychloroquine is increasingly being reported by scientists as a promising candidate for both prevention and treatment. Yet, data collection is at an early stage, and definitive efficacy remains to be proven. A number of vaccines are in prototype production and pre-clinical testing, with at least one vaccine already used in individual patients, but here again there is insufficient data at the time of writing to issue clinical guidelines or recommendations.

Going back to the basic epidemiology, it is known that 80-85% of infected individuals suffer only minor symptoms and do not require hospitalization. While size of inoculum may play a role here, the functionality of the innate immune system and the presence or absence of comorbidities appear to be the critical determining factors. In both of these factors nutritional status plays an absolutely crucial role, and this opens the possibility of using nutritional tools to increase the size of the group who experience only mild illness, and reduce the numbers requiring hospitalization to more manageable levels.

The disease progresses through a series of stages. It begins with a virusaemia lasting 7 to 9 days, which is associated with relatively nonspecific symptoms such as nasal discharge, sore throat and mild fever. In 80-85% of cases the disease does not progress beyond this point, because the innate immune system succeeds in overcoming the viral challenge. In approximately 15% of cases the innate immune system fails to contain the virus and the disease progresses to a mixed viral and bacterial pneumonia, and finally to a mixed viral and fungal pneumonia as the immune system breaks down and inflammation overwhelms the patient.

Food and food components have always played a preventive role in human health and such nutritional approaches can be manipulated to intercept and treat health conditions. Further botanical extracts have played a role in immune health across all traditional medical treatises. For instance, Cinchona gave us Chloroquine that is being considered with great interest in the management of the current COVID19 epidemic. Shikimic acid from Star Anise inspired the development of Tamiflu. Various elements of the innate immune system can be enhanced using such tools as the 1-3, 1-6 beta glucans to increase cellular competence, and iron and thiocyanates (co-factor and substrate respectively), to optimize the humoral component lactoperoxidase (LPO). Exogenous LPO may be an effective treatment on its own, and is just about to go into clinical trials. Palmitoyl ethanolamide (PEA) is another such constituent of food-based tool, due to its physiologically appropriate anti-inflammatory properties. PEA as a constituent of food had been studied in clinical trials to help manage symptoms of influenza and common cold thru' its physiological effects on metabolic and cellular homeostasis, and anti-inflammatory and immune-modulating properties. PEA was originally trialled against influenza in the 1970's, with 6 clinical studies showing a degree of prophylactic efficacy.[1,2,3] It is believed that PEA's immune-modulating and anti-inflammatory effects, mediated inter alia via the Ppar-alpha receptor, help to prevent excessive inflammatory responses and local tissue damage (via TNF-alpha, IL-1beta, ICAM-1, P-selectin and NF-kappaB), thus improving the likelihood of an initially successful innate immune reaction. As the immune system's nutritional requirements are so diverse, and as dysnutrition is so prevalent today, a nutritional approach would generally also include a comprehensive micro- and phytonutrient support program.

More research is currently being undertaken on PEA and Levagen+, its bioavailable form, to explore the potential of the product in other therapeutic segments based on the same mechanisms of action.[4,5]

The effectiveness of such programs are not yet proven, but they are supported by circumstantial evidence and unlike the pharmaceutical approaches, they have very wide therapeutic indices. This makes them eminently suitable for general usage, and for consideration as a mainstay of public health strategies going forwards.

Dr. Paul Clayton
Fellow, Institute of Food, Brain and Behavior, Oxford

References

1. Hesselink et. al. " Palmitoylethanolamide: A Natural Body-Own Anti-Inflammatory Agent, Effective and Safe against Influenza and Common Cold", International Journal of Inflammation Volume 2013, Article ID 151028. http://dx.doi.org/10.1155/2013/151028
2. Masek et. al., " Prophylactic efficacy of N-2-Hydroxyethyl Palmitamide (Impulsin) in acute respiratory tract infections", European Journal of Clinical Pharmacology, 7, 415-419 [1974]
3. Kahlich, R., et al. " Studies on prophylactic efficacy of N-2-hydroxyethyl Palmitamide (Impulsin) in acute respiratory infections. Serologically controlled field trials." Journal of hygiene, epidemiology, microbiology, and immunology 23.1 (1979): 11-24.
4. Steels, E., et. al. " A double-blind randomized placebo controlled study assessing safety, tolerability and efficacy of palmitoylethanolamide for symptoms of knee osteoarthritis", Inflammopharmacology. 2019 Jun;27(3):475-485.
5. Mallard, A., et. al. " The Effect of Orally Dosed Levagen+™ (palmitoylethanolamide) on Exercise Recovery in Healthy Males-A Double-Blind, Randomized, Placebo-Controlled Study", Nutrients. 2020 Feb 25;12(3).