Editorial

Covid-19 and dietary socioecology: Risk minimisation

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Pandemics have shaped humanity over and over again, but the coronavirus outbreak of 2019-2020 is in a world at the tipping point of catastrophic climate change. Its origins and distinction derive from over-population with inequity and an industrial revolution since the 17th century which has exploited fossil fuels as a globalised energy source, a period now described as the anthropocene. Asymptotic ecosystem loss and dysfunction, for people whose being is socioecological, makes ultimate survival tenuous. Microbial forms of life jump species when habitats are destroyed, or their host misused. Our innate immunity depends on our general health and fitness- social, mental, physical, and nutritional, in step with nature and its rhythms through walking in it, enjoying sunlight and sleep. Biodiversity and the associated benefit of food variety, after being breast-fed, is the key descriptor of a healthful, sustainable, accessible, and acceptable way of eating. How this pattern might contribute to our resilience in the face of a highly transmissible and biologically evasive virus is becoming clear. It may also be possible to compliment usefully preventive vaccination and therapeutic healthcare and rehabilitation through a greater understanding of our nutritional biology.

Key Words: innate immunity, food systems, phytonutrients, food biodiversity, nutritional biology, econutrition

A PANDEMIC

Pandemics are infectious scourges, with huge loss of life and socioeconomic transformation.[1,2] They have occurred infrequently in recorded history. One of the most devastating occurred at the end of World War I in 1918, attributed to influenza. The loss of life remains uncertain but was somewhere between 17 and 100 million lives when the world's population was about 1.8 billion.[3,4] In recent times, potentially devastating pandemics with viruses such as influenza, HIV-AIDS, spongiform encephalopathies, Nipah, Ebola, SARS, MERS (MERS-CoV) and Zika have been contained by swift and concerted local and international cooperation, notably with input from the WHO (World Health Organisation) and a trained public health workforce.[5] Ultimate containment has depended on source elimination, hygiene, anti-infective agents (eg antibiotics, antivirals) and/or vaccination, although the latter is not always achievable. The present ***coronavirus pandemic***, which commenced in late 2019, is unlike any of its predecessors. These include involvement in a record ***global population size of more than 7 billion***, an ageing demographic, and at least a third of whom impoverished or displaced with little ***access to health care***. The global workforce had become increasingly vulnerable given a dependence on ***economic systems*** involving trade complementarity, capital, materialism and cash flow, and inadequate ***community arrangements*** for livelihood and access to the Commons.[6,7] There were almost 6 million Covid-19 cases and some 350,000 deaths worldwide from January to May.[8] There is an ***uncertain infective trajectory and immune response***, and adverse health effects which are multisystem and complex. The ***ultimate aggregate health, economic and social impact*** of the coronavirus pandemic is unlikely to be less consequential than its antecedent pandemics, although the proportionate population affected and lost may be less (or varied) on account of more established and effective public health systems and health care.[9] However, the ranges of transmission, clinical manifestation and mortality rate ***impacts are wide***, with among the lowest in north-east Asia (Taiwan, Japan, South Korea, Vietnam) and the Pacific (New Zealand, Australia, Papua New Guinea and Fiji) and the highest in Europe (Italy and Spain), central Asia (Turkey), Russia, north (USA) and south (Brazil) America, and rates continuing to unfold in South Asia and Africa. As yet, data management and interpretative methodologies for such comparisons are inconsistent, especially in respect of what constitutes a case where asymptomatic, presymptomatic and symptomatic virus positive classi-

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fiers and aggregate descriptors are not settled; and cause of death may be presumptive against a background of co-morbidities.[10,11] ***Commonalities*** include disproportionately high rates among the socioeconomically disadvantaged, frail elders, and people with the chronic cardiometabolic disorders of hypertension and diabetes.[12,13] At the same time, youth and being a woman are relatively more protective than being an older male.[12]

COVID-19 BEGINNINGS: GEOGRAPHICS AND CRUISE SHIPS

Although it may never be known for certain where, coronavirus infection in humans is a zoonosis first recognised as an outbreak of a novel pneumonia in Wuhan, Hubei province, China, in December 2019.[14] Cases were soon found throughout China, in Europe, in the USA ,in Australia, New Zealand and elsewhere with estimated incubation times up to 14 days, reproduction numbers of 2-3 and mortality rates of about 2-3 %.[15-20]

A clearer understanding of the potential prevalence, asymptomatic and presymptomatic status, transmission, morbidity, and fatality associated with coronavirus PCR (Polymerase Chain Reaction to detect SARS-CoV-2 RNA) positivity was opportunistically and unfortunately provided by outbreaks on US *cruise ships*. These were notably the *Diamond Princess on a return trip* from *Yokohama, Japan*, January 20th - February 3rd 2020 via Hong Kong on January 25th (one passenger was found to have boarded positive and left in HK); and the *Ruby Princess on a return trip from Sydney*, Australia (March 8th – 19th 2020). The passengers and crew on the *Diamond Princess* were quarantined at the Port of Yokohama for nearly 4 weeks and, by the end of quarantine, 712 COVID-19 cases had been diagnosed among 3800 passengers and crew. Some 104-throat swab PCR positive persons were isolated in the National Defense Army Central Hospital. The average age of affected individuals was 68 years, nationals came from 17 countries, and 48% had underlying disease of which hypertension was the most common. Crew members were mainly in their 30s and 50s, and passengers mainly in their 70s. The proportion of asymptomatic positive individuals was 31.7%, with 41.3% mildly and 26.9% severely ill. The most common symptoms were cough (41%), fever (33%), nasal discharge (24%), fatigue (21%), respiratory distress (18%), tachypnea (23%), headache (17%) and diarrhea (19%).[21] About two thirds of PCR positive passengers had CT scans. Abnormal shadows were observed in about half with what are now recognised as characteristic bilateral ground-glass opacities under the peripheral pleura, not seen on plain chest radiographs, and referred to as 'silent pneumonia'[22] (Figure 1). In about two-thirds of these, symptoms remained unchanged and, in the remaining third, worsened. When changing from silent to apparent pneumonia, cough or dyspnea were often exacerbated, SpO2 decreased in the elderly and tachypnea developed in the young. Symptom exacerbations usually occurred 7 to 10 days after onset and progressed relatively slowly. This was not always appreciated in the elderly, but presaged mortality. Fellow travelling family members and friends in the same cruise ship room, although asymptomatic, even PCR-negative, had bilateral peripheral ground glass-like shadows on CT scan. Some became positive after repeated PCR, while others remained negative throughout observation. The sensitivity of PCR was about 70%. Russell et al, adjusting for delay from confirmation to death, have estimated case and infection fatality ratios (CFR, IFR) for coronavirus disease (COVID-19) on the Diamond Princess ship as 2.6% and 1.3%), respectively. For China, they estimated CFR and IFR to be 1.2% and 0.6%, respectively.[10] Even though food was available on board the Diamond Princess, the development of lymphopenia,

Figure 1. Bilateral sub-pleural ground-glass opacities in Covid-19 evident on chest CT scan, but not on chest Xray (Japan, March 2020). Courtesy of Japan Self Defense Forces Central Hospital, Tokyo.

hypo-albuminemia and elevated hepatic enzymes among some passengers indicated a probable concurrence of Covid-19 with virally-related nutritional dysfunction.

Less information is available to date about the *Ruby Princess* passengers and crew, subject to criminal investigation for failure to divulge the case load aboard prior to disembarkation, but its March 19 arrival in Sydney was responsible for the largest single outbreak of COVID-19 in Australia, including 26 deaths.

GLOBAL HEALTH - ECOHEALTH DISORDERS

The understanding of the origins of the present coronavirus pandemic must acknowledge its rootedness in population density and ecological dysfunction. There is abundant evidence that crowding is conducive to microbial pathogen transmission; that public open space and natural landscapes encourage healthy outcomes; and that biodiversity is requisite for who we are.[23-25] Indeed, health status and trends have a complexity which is not intelligible or manageable unless they are considered as socio-ecological.[26]

We may be beguiled to think that because the intervals between global pandemics have been decades or even a century that the coronavirus event is a freakish event. But its pre-conditions of exponential global population growth, massive international travel, asymptotic ecosystem loss, exploitation and increased dysfunctionality, fossil fuel dependency and global warming have tipped planet habitability into an unprecedented health milieu. The present pandemic is a foretaste of more ecohealth disorder to come, and to be complex in its nutrition and health associations.[27,28]

FOOD SYSTEMS AND HEALTH

Our ability to cope with pathogenic organisms depends on our ***general health*** with its intricate systems in defence of our tissues or organs and their functions. In turn, these depend on our ***personal behaviours***, namely how well we are nourished by the foods and beverages we consume, how physically and mentally active and fit we are, the rest or sleep we get,[29] and whether we abuse ourselves with unhealthy products like tobacco or alcohol. A qualification to this claim is that strenuous exertion is followed by up to 3 days of suppressed immunity.[30] Regular physical activity which maintains muscle mass and reduces the risk of sarcopenic obesity minimises inflammatory disorder.[31] Yet ***the link between nutrition and the risk of infectious disease*** was not explicitly acknowledged until the work of Scrimshaw et al on infantile diarrhoea in meso-America and India in 1959.[32,33] It became clear that multiple food factors contributed to food borne illness and to immunity so that a food systems approach was necessary to reduce this over-riding global burden of a nutrition and infectious disease tandem.[33]

The proneness to infectious disease with ***undernutrition*** is not just a matter of energy and nutrient requirements, although formula feeds used in nutrition support endeavour to be nutritionally complete and can maintain life in the short to medium term. But this is not indicative of optimal nutrition, which requires a spectrum of food components, including phytonutrients, and a food structural matrix to enable bioactive factors to be delivered concordant with gut function and timely assimilation.[34] Even more, how pathogens interact with oropharyngeal, gut, respiratory, reproductive tract and cutaneous ***microbiomes*** will probably be critical.[35-37]

In the coronavirus pandemic we face a form of food insecurity generated by prevalent ***infectious disease and its impact on food systems and eating behaviour.*** The more accustomed food insecurity as a risk for infection is due to malnutrition and its consequent compromised immune status, which then may be mutually and spirally reinforcing. Food security is about availability, accessibility, acceptability, and safety.[38-40] With highly transmissible infection, people may not be able to produce, transport, process, store, distribute, cook and eat food to which they are accustomed or need.[24,41,42] In the case of coronavirus, loss of taste and smell are common, with likely effects on palatability and appetite, especially among elders and frail individuals, and will add to food insecurity.[43,44]

COEXISTENT CORONAVIRAL GENOMICS

Several steps are involved in Corona virus infection; attachment to the cell surface, entry into the cell, reverse transcription of viral RNA to host DNA, replication of viral protein and virus particles, spread of infection to other sensitive cells and viral shedding.

The coronavirus receptor is an ACE (angiotensin converting enzyme) on cells of the upper respiratory tract and beyond. It should be possible to mitigate infection here and control its onset.

Viral infectivity depends on interactions between components of the host cell plasma membrane and the virus envelope. Baglivo et al[45] found molecules able to reduce the infectivity of corona viruses by inhibiting viral lipid-dependent attachment to host cells.

Cleavage of the viral capsid and reverse transcription of RNA is host protease dependent.[46] Its viral tropism is related to virulence. Viral virulence can be affected by both the viral mutation and/or host susceptibility/resistance factors. Several mutated lineages have already been found for coronavirus to challenge whatever innate and acquired immunity we may have.

Some viral proteins can block interferon signal transduction to suppress the natural defense system in infected cells. Host RIG1 and mda-5 are candidates to recognize viral RNA and produce interferon to suppress viral proliferation.[47]

Degenerated or dead cells resulting from virus proliferation are phagocytised and antigen signals are delivered to lymphoid cells to produce specific immunity. This seems to take 10-14 days, a waiting period before acquired immunity to COVD-19 would be manifest and then a response which may not be sufficiently effective. Many viruses coexist with humans, such as herpes, HPV, and hepatitis C. This may yet happen with COVID-2019, when it may or may not attenuate, be more potent or simply coexist. Human genomic DNA contains as much as 8% of so-called endogenous viral elements, which are the signature of a long evolutionary process responsible for RNA-mediated immunity. The viral gene is transcribed into messenger RNA (mRNA), which moves to the ribosome outside the nucleus. At that time, microRNA (miRNA) would be the most important regulator in post-transcriptional regulation by binding to mRNA. miRNAs do not function singly but cooperate with other types of miRNAs to suppress gene expression of multiple

mRNAs.[48,49] The nutritional relevance of miRNAs as exosomes in foods is increasingly recognised, in transfer of this regulatory material from plant foods and from dairy to humans as examples.[49] This phenomenon may well be available for innate immunity enhancement.

NUTRITIONAL BIOLOGY AND IMMUNE FUNCTION

It is self-evident that, in all respects, biology or life itself must have nutritional dependence and consequence with its composite of elements and molecules derived from nature. In acknowledgement of its ecological connectedness in humans, it may be considered for its homoeostatic capacity, its energy dependence, its genetic inheritability, its microbiomic companionship, its acquisitive gut portal, its sensing abilities through touch, sight, sound, taste and smell, and its defence against foreign or injurious challenges by immunomodulation and inflammation.[50] While not functioning in isolation from the collective biology of which they are part, both immunomodulation through innate and acquired mechanisms and inflammation through metabolic and cellular pathways collaborate to arrest infection, to limit tissue damage and initiate repair. But before these potential insults present, they may be intercepted, mitigated or diverted elsewhere if the ecosystem of which we are part is sufficiently biodiverse and resilient; and if we are not vulnerable on account of atmospheric, water or food contamination and pollution, being physically or mentally unfit, or without livelihood and societal support. In other words, our ability to manage novel assaults on our biology requires our genetic and microbiomic make-up, our nutrient supply routes, our environmental surveillance systems and our defence and repair profile to be rooted in robust and sustainable systems. When a pandemic supervenes, the systems, with their ecological characteristics, checks, balances, and resilience have failed.

Broadly, the pathways to pandemics proceed from our natural (and unnatural) environment to our innate defense biology which, if inadequate, appeals to acquired mechanisms (including vaccination if in place), health care and therapeutics (if available). Where the infectious agent is novel, as with coronavirus (Covid-19), ***basic principles to reduce transmission*** through physical distancing and scrupulous hygiene are the mainstays of control.[5] ***Risk reduction*** is multifaceted along these pathways and its management depends on how benefit and cost are weighed against the risk at large and in accord with vulnerability. In the case of Covid-19, there have been ***many unknowns***, especially in relation to susceptibility, transmissibility, acquired immunity, immunisability, morbidity and mortality. Early estimates are that the infection is ***more likely in*** adults than children,[51,52] especially the aged, in men than women,[53] and where there is underlying hypertension, obesity or diabetes. In an unquarantined cruise ship community, it is estimated that about 20% may be virus positive and about 50% of these asymptomatic, few hospitalised with life-threatening illness, and fatality rates of between 2 and 8% depending, inter alia, on the denominator, location and health care system.[54-56] Quarantine of virus positive cases for the presumed maximum incubation time of 14 days markedly reduces transmissibility. The reproductive number (the number of new cases per affected individual in a naïve population) for a viral illness like Covid-19 should be <1.0 for its prevalence to decrease.[57,58] It is an illness acquired through aerosol or touching of face and eyes, with nasopharyngeal and upper airway viral replication, followed by respiratory passage and damage, enteric effects, and inflammation of the circulatory system leading to thrombotic disease and multisystem failure.[59] This includes the central nervous system with haemorrhagic encephalopathy,[60] stroke and adverse effects on cognition.[61-64] Indeed, the effects of coronavirus on the central, spinal and peripheral nervous system may occur earlier and be more extensive and consequential for disability-adjusted life expectancy (DALYS) than presently appreciated.[65] Loss of taste and smell may also have a central nervous system basis rather than or as well as one in the taste or olfactory receptors.[66,67] This cascade of tissue damage may culminate in a 'cytokine storm'.[68,69] Interruption of this often-rapid sequence all the way to respiratory support and intensive care has been a major clinical challenge with healthcare staff themselves at risk, especially where many are ill and resources stretched, locally and globally. What is not yet known is the recoverability from these potentially disabling complications of Covid-19, especially as the pathogenesis is unfamiliar territory.

Understandably, every effort has been made ***to stem the pandemic*** at the earliest stage through case identification, contact tracing and isolation. Until vaccination is available or antiviral agents effective and safe, the emphasis must be on reducing transmission and enhancing ***innate immunity***.[70] Where it is uncertain how durable acquired humoral (antibody) and cellular (T cell) immunity to coronavirus will be, strengthening viral innate immunity has much appeal; since to some extent it resides in mitochondrial capacity to activate interferon production, this may partly explain female advantage in the present pandemic.[71] The resilience of children despite exposure to the pandemic may reside in their relative lack of vascular pathology which may predispose to its dangerous inflammatory and thrombotic complications, the converse of those with established hypertension.[63] It remains to be seen to what extent this virus will remain as a permanent or recurrent feature of the international health landscape. From an evolutionary perspective, we have survived with viral symbionts becoming integral to us as in the case of mitochondria through endosymbiosis.[72] Viruses like varicella-zoster cause illness like chickenpox in childhood, become resident in our nervous system, and, when immunologically compromised in later life, cause herpes zoster,[73] referred to as shingles. The risk can now be reduced by a vaccine.[74] Advances in vaccine development technology provide some hope that covid-19 may be brought under control in a similar way.[75] A cautionary note of many with this exceptional virus is, however, that the immune-inflammatory response may itself may be part of its threat[76] that antibody responses so far monitored may not be protective and that prevention may be different by stage of virus positivity and illness, requiring a multivalent strategy.[77] Moreover, coronavirus is evolving with potentially greater transmissibility as in the D614G variant. This poses increased demands on our innate immunity, on vaccine development platforms, and on potential disease-modifying agents.[78]

In the meantime, the focus must be on hygiene and on enhancement of the innate immunity evident in the major-

ity of the population who do not succumb when exposed, or have minimal or manageable symptoms, and reducing transmission from any who are carriers of live virus, whether symptomatic or not. Resistance to Covid-19 should be enhanceable by personal behaviours as outlined above, including dietary pattern.

PREVENTIVE AND THERAPEUTIC NUTRITION IN THE COVID-19 PANDEMIC

Nutritional approaches to reduction of the transmission and burden of Covid-19 in the community may vary from how and with whom we obtain, prepare , and eat our food, our encounter with the virus, whether it gains a foothold, which organs or systems it reaches , their resilience and damage suffered, and recoverability. Since we lack most of the specific answers to these questions at present, we must draw on the general principles of how nutritional status contributes to our immunity, inflammatory and repair processes. This means identifying dietary patterns and foods which optimise nutritionally related immune function, with the least risk, maximum benefit, affordability, and sustainability. We can expect that where greater protection for vulnerable patients or clinical benefit, and risk more acceptable, foods, and specific food components might be deployed, and combined with pharmacotherapy. For example, if food components like caseopeptides, as ACE inhibitors, were found to block coronavirus entry into naso-respiratory cells, these might be given with a dosage and schedule unrelated to a more physiological food intake i.e. therapeutically.[79,80]

Food systems

Although coronavirus has not been considered a food-borne illness, a number of illnesses, especially enteric, are attributable to food-borne viruses, sometimes zoonotic .The present pandemic is instructive of a wider canvas of future unprecedented and novel viral pandemics, their protean manifestations, recognition, prevention and management.[81] Most challenging is where the pandemic might not be acute, but asymptomatic and oncogenic with delayed presentation. Indeed, as yet, we do not know what the long-term effects of coronavirus will be, but we do know that immunoinflammatory disorders predispose to neoplastic disease.

More immediate with coronavirus is that isolation and loss of workforce are imposing constraints on the entire food system from agriculture and food production to transport, storage, processing and preparation, retailing, shopping, and eating out. Each has potential health consequences.[82-86]

Biodiverse food pattern

Humans are omnivorous, even if a plant or aquatic food orientation confers biological and environmental advantage.[40,87-90] More biodiverse diets are associated with better overall as well as arterial health (with or without diabetes) and disease specific survival, especially among older people, including pneumonia.[91-94] They are advanced by the UN System as an indicator of household food security.[95-97] They are relevant in a range of food socio-cultural settings. Eponymous dietary patterns like Mediterranean,[98-100] Lyon[101] or DASH[102] (directed at hypertension) are relatively greater in biodiversity than their reference diets. By their nature, they are more likely to capture the wide spectrum of food physical (matrix) and chemical (nutrient and other bioactive food component) characteristics required for optimal health while decreasing potentially adverse food effects and toxicities through dilution and competitive offsets.[23] Conceptually minor dietary contributors like ***culinary herbs and spices*** often have potent bioactive profiles and offer palatability and acceptability, enhancing the healthfulness and immunoinflammatory properties of food biodiversity. To have the settings and health outcomes that they do, biodiverse diets are likely to be associated with innate immunoinflammatory robustness, a high degree of safety, cost-effectiveness and utility in Covid-19 prevention and disease-modification (cost,[99,103] DV mortality[104]). They are now fundamental to international and local Food Based Dietary Guidelines (FBDGs).[86,90,105]

FBDGs inevitably provide adequate energy and macronutrient (protein, carbohydrate, dietary fibre, fat, water) intakes and from a variety of sources which subserves our omnivorous biology with enough of its essential components like essential amino acids and fatty acids. Nevertheless, illness like covid-19 and the socioenvironmental factors which have facilitated its advent may increase the risk of energy and essential nutrient deficiencies at-large. Recovery requires attention to these risks. In the report of Fei Zhou et al. on the clinical course and risk factors for mortality among covid-19 patients in Wuhan, complications and survivorship were associated with indications that poor immune capacity linked to malnutrition reflected in hypo-albuminemia and lymphopenia.[106] Not surprisingly, nutrition support must not be overlooked in covid-19 as in other critical care situations.

Bioactive food components and their food sources which may reduce viral invasion and replication

The most critical site of action required is the portal of virus entry. Since that appears to be the ACE2 receptor, the possibility that known blockers[77] might check coronavirus invasion has attracted much interest given that they are used as antihypertensive agents and that people with hypertension are at greater risk of Covid-19.[79,80,107] Such bioactives are also found in <u>*dairy products*</u> as peptides derived from casein and whey proteins.[79,80] and in <u>*culinary herbs.*</u>[108,109] Nutritional epidemiological studies and clinical trials of them in at-risk individuals would be justifiable, along with other food products. It is always safer, and often more effective and accessible to consider the food, rather than an isolate. Food alternatives can be sought, and cultural preferences addressed. The gender difference in susceptibility to Covid-19 in favour of women may be partly related to the difference in androgen-dependent ACE2, which may have implications for men's dietary preferences in a pandemic.

A different approach depends on the cooperativity of the gut microbiome as a producer of short chain fatty acids (SCFA) including <u>*butyrate*</u> during the fermentation of dietary fibre and resistant starch in the large intestine.[110] It is known that this is a substrate for colonocytes and reduces the risk of large bowel cancer. But, in the gut lining, and systemically after absorption butyrate has antiviral properties, reducing viral replication.[111-113] This is best studied for influenza,[114,115] but has potential for Covid-19.[116] Foods which could be useful promoters of butyrate nutrition include <u>*wholegrain cereals like oats, barley,*</u>

millet, rice and wheat and legumes.[117-125] Brown (unpolished) rice, known as *genmai* in Japan, favours a gut microbiome with highly prevalent Fermicutes and a low prevalence of Fusobacterium and is associated with relatively abundant butyrate production attributed to several pathways.[126] The phytonutrient profile of *genmai* includes feruloylated oligosaccharides, γ-oryzanol and GABA which collectively may enable this microbiomic profile and function. A focus on microbiomic characteristics that have an immunoregulatory role may be useful in coronavirus protective diets.[127] Kenya Honda has found that there are rare, low-abundance components of the human microbiome with potential as broadly effective biotherapeutics. Brown rice eaters have most of these, and the difference between brown and white rice eaters by microbiota profile is in high butyrate production. In particular, Faecalibacterium prausnitzii may favour butyrate production, and *Blautia wexlerae* intestinal immunity.[126] This may contribute to possible differences in susceptibility to Covid-19 where rice rather than wheat is a staple (Figure 2, 3).[128] The differences between ultimate apparent grain and health outcomes on a country basis may have to do with how they are processed and consumed; wheat, for example, may be an ingredient in highly refined as opposed to whole grain alternatives. The positive relationship seen for COVID-19 prevalences in G20 countries and Spain and wheat consumption may partly reflect the increased usage of refined flour and extruded products with economic development typified by ultra-processed foods.[129] Oats are especially anti-inflammatory on account of their avenanthramides content, and other of these foods are also generally anti-inflammatory, an added advantage with infectious disease; reduce vulnerabilities like obesity, diabetes, and hypertension; and improve overall survival.

Legumes and wholegrain foods are also sources of *phytosterols*, lipids[45] which compete with the animal sterol, cholesterol, in humans. They can interfere with the attachment of coronavirus to cells, effectively increasing innate immunity of a specific kind. It is of related interest, and in support of this finding, that *statins*, which are commonly used in the treatment of hypercholesterolaemia, originally found in nature as fungal metabolites, may also reduce the risk of Covid-19 through interaction with its main protease and other pleiotropic effects.[130-132]

Conferring immunoinflammatory advantage, both innate and acquired.

Examples of foods which are phytonutrient-dense from throughout the edible plant kingdom have been provided for reduction of viral ingress. Less certain in their mechanisms in disease progression, but potentially worth emphasis for nutritional security in the background diet are several foodstuff components and matrices, integral to the food rather than as isolates. For consideration would be:

1. *nuts* for their arginine-rich proteinsand nutrient density[133]
2. *berries* and purplish root vegetables for their anthocyanins and nutrient density[134]
3. *fermented dairy* as in soft cheeses for vitamin K-2 and
4. *fermented soy* (natto, miso, tempeh) for vitamin-K-2 which is essential for vasculoprotective proteins, blood vessel inflammation and thrombosis being a major contributor to morbidity and mortality in Covid-19[135-141]

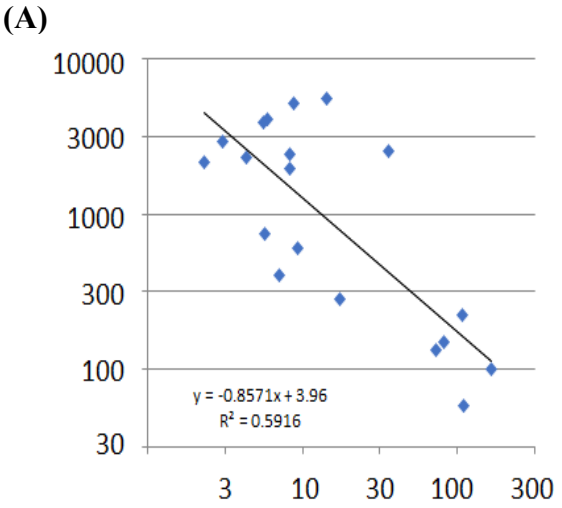

Figure 2A. Rice consumption per capita and COVID-19 patients by country as at June 6th 2020.
Y-axis; Number of COVID-19 patients/million, X-axis; rice consumption/capita kg/year.[128]

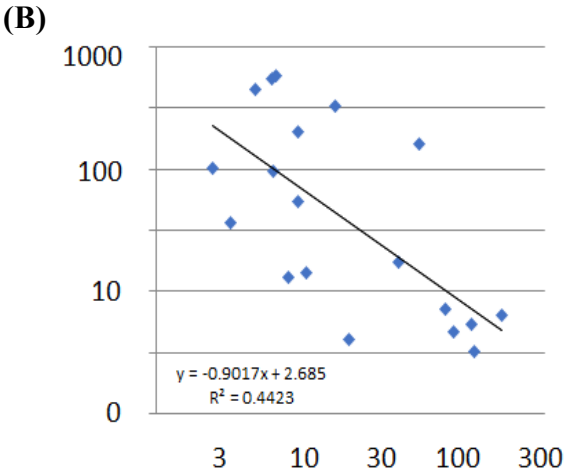

Figure 2B. Number of deaths per one million population and rice consumption per capita as at June 6th 2020.
Y-axis; number of COVID-19 deaths/million, X-axis; rice consumption/capita kg/year. [128]

5. *green leafy and yellow vegetables and tomatoes for a spectrum of carotenoids, other phytonutrients and micronutrients,* which collectively modulate the immune system and inflammation[142-147]
6. *fruits* A variety of intact fruits is preferable to juice, the latter, but not the former, presenting problems for glycaemic control.[147-153] Potassium rich bananas, along with fruits and vegetables in general, are a convenient and good source of potassium to improve the potassium; sodium ratio and keep down blood pressure, along with their nutrient density
7. *fish* for n-3 fatty acids, vitamin D. Just how vitamin D is involved in the susceptibility and management of Covid-19 remains controversial.[154-156]
8. *yeast, wheat germ, Vegemite, whole grains, occasional liver*, small serves of various meats for niacin (vitamin B-3 and other micronutrients) with potential to minimise pulmonary damage.[77] Yeasts are sources of beta-glucans which have immunomodulatory properties which favour innate and adaptive immunity.[157] Gliadin (gluten) and grain proteins may have adverse,

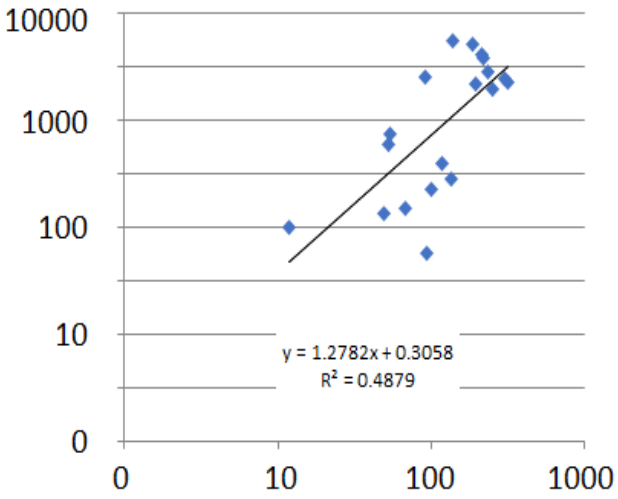

Figure 3. Wheat consumption by country and number of COVID-19 patients as at June 6th 2020. Y-axis; Number of COVID-19 patients/million, X-axis; wheat consumption/capita kg/year. [128]

sometimes allergic, effects on the gut and not be of net immunoinflammatory advantage. But nutrient -dense items based on wheat germ or yeast are of potential nutritional security value.[158]

9. *eggs, as the beginning of life, are a rich and comprehensive source of essential nutrients*; they are a convenient and generally accessible and affordable food item; with consumption of one egg a day ,their cholesterol content manageable for most people without concern for any adverse effect on blood lipids and , if free range , with hens eating seeds, insects and worms, they have as much n-3 fatty acid as an average serve of fish which, along with their vitamin D and vitamin K-2 content, makes them a relatively immunoprotective food. Eggs are also a good source of the orange coloured carotenoid lutein, depending on what they feed, important in vision and brain function
10. *herbs and spices like turmeric, Lamiaceae like mint and basil* for which there is evidence of multiple health benefits are likely to be protective[108,109,159,160]
11. *Tea* as a source of quercetin (as are *apples and allium vegetables* like onions, among other plant foods)[161,162]

Mouth, gum and dental hygiene

Optimising nasopharyngeal and gut microbiomics should improve the barrier to respiratory viruses like coronavirus. The synergy of microbiomes and viromes in the oropharyngeal and upper respiratory tracts, and their nutritionally-dependent metabolomics will contribute to innate immunity at initial coronavirus exposure[163-167]

Disease-modifying

With a greater understanding of organ and system loss of function and damage with Covid-19, dietary and other modalities to reduce those risks will be enlisted. Currently, the emphases and possibilities for attention are the nasal and upper airway passages where viral replication and damage to the senses of taste and smell occur, the lower respiratory tract and lungs, the blood vessels, and the central nervous system. A biodiverse diet with plant food orientation which includes fish and is nutrient and phytonutrient dense, enough sunlight to complement dietary vitamin D, and physical activity to maintain adequate energy throughput without risk of obesity, and interaction with nature, are the basics.

Social role of food

The awkward part of the strategy is that food confers health partly through its social role, and this needs maintenance in ways that minimise physical, but not social contact. There is a gender difference in this respect since men are more at risk through eating alone than are women.[93]

We have yet to learn what the long-term effects of covid-19 will be and will almost certainly involve rehabilitation and ongoing care for many. But the distillation of relevant dietary practice and policy outlined has characteristics conducive to healthy longevity, sustainability, and intergenerational well-being.[25]

NUTRITIONAL ETHICS AND EQUITY

Pandemics disproportionately affect the socioeconomically disadvantaged who have little room for discretional spending and tend to sacrifice more nutritious food and redistribute it within the family as a matter of short term survival, with mothers and children, and elders, the most vulnerable.[167] Fruits and vegetables may be sidelined in favour of more satiating staples with greater health risks in general and for infectious disease.[169-171] Policy-makers and budget holders have difficulty dealing with the inequities and ethical dilemmas.[38,97,168,171,172]

THE FUTURE

With a major and continuing decline in human ecological protectedness, increased exposure to atmospheric and aquatic contaminants, and adverse personal behaviours compromising innate immunity, pandemics with zoonotic viruses like Covid-19 may become more likely. Their sources will be more difficult to control with global warming, their management more demanding of healthcare systems, vulnerability more problematic on account of concomitant so-called chronic disease and social inequity, and livelihood supply chains more insecure. The nexus between food and health security will be

more evident and requiring of extensive intersectoral governance.[42]

CONCLUSIONS

To minimise the risks of infection with coronavirus, hygiene, keeping a distance, and innate immunity (sleep, physical and mental activity, and dietary pattern) will be the principal preventive and management tools for a long time to come. Antivirals and disease modifying agents will become invaluable. Given that acquired immunity after coronavirus infection is not adequately represented by the antibody and cellular responses, that they have limited tenure, and that the inflammatory response is itself part of the multisystem disease, effective, safe and enduring vaccination may be difficult to achieve. The social role of food and its maintenance with physical rather than social distancing is a tricky goal worthy of effort, with health and economic relevance. More fundamentally, the coronavirus pandemic is one of others to come, together with the wider and growing consequences of ecosystem loss and dysfunction. The likely concurrence of pandemics with climate change and natural disasters which will also affect food and health security is in urgent need of mitigation.[173]

AUTHOR DISCLOSURES

The authors have no conflict of interest relevant to this publication.

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