We have to talk about Vax

Presented by

Daniel Baden ND

24th February 2021
This webinar will offer a pragmatic approach to patient care

- Pre-vaccine preparation
- Minimise vaccine side effects
- Modulate immune response
- Protect long-term health
Hard Questions

1. Long-term safety profile of COVID-19 vaccines
2. Duration of immunity of COVID-19 vaccines
3. Effectiveness of COVID-19 vaccines
4. Risk of variants that can evade vaccine-induced immunity
5. One year into the pandemic, there is little sign of herd immunity; will vaccines confer it?
6. What is the likelihood of residual RNA/DNA and what effect can it have?
The Vaccines

Pfizer/BioNTech
University of Oxford/AstraZeneca
Novavax
Johnson & Johnson/Janssen
Standard vaccine development

Licensing usually takes 10+ years.

Phase 1 trials are small (20 to 100) and last only a few months. Evaluate basic safety and identify very common reactions.

Phase 2 trials involve several hundred participants for up to 2 years. Additional safety, side effects and adjust formula. Develop dose regime.

Phase 3 trials involve 100’s to 1000’s volunteers for up to several years. Time to compare against non-vaccinated group.

Phase 4 safety monitoring and research begins after a vaccine is licensed and recommended for public use.
## Phase 4 monitoring

### Safety assessment method:

<table>
<thead>
<tr>
<th>Goal</th>
<th>Example</th>
<th>Investigated using</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduce new vaccines to new target populations when safety data are scarce</td>
<td>Adjuvanted pandemic H1N1 influenza vaccine in pregnancy, in immune-compromised</td>
<td>Clinical trial, case-control, retrospective and prospective cohort studies adverse event reports, post-licensure surveillance activities</td>
</tr>
<tr>
<td>Responding to a potential safety signal after authorisation</td>
<td>Narcolepsy reported in temporal association with the use of AS03-adjuvanted pandemic H1N1 influenza vaccine (Pandemrix™)</td>
<td>Post-licensure surveillance activities, retrospective and prospective cohort studies</td>
</tr>
</tbody>
</table>
Phase 4 limitation

Under-reporting is a well recognised limitation of passive surveillance systems

Vaccines and autoimmune disease

“Autoimmunity is a concern for many vaccines. However, because of relatively low baseline incidence of many autoimmune conditions, large post-marketing and adequately powered studies are required to evaluate any increased risk of ADs after vaccination. In fact, in most of the clinical trials evaluating vaccines, a systematic screening for ADs is not performed.”


Long-term vaccine issues (?)

“...we found that the rise in the prevalence of diabetes may more than offset the expected decline in long term complications of H.influenzae meningitis. Thus, diabetes induced by vaccine should not be considered a rare potential adverse event. The incidence of many other chronic immunological diseases, including asthma, allergies, and immune mediated cancers, has risen rapidly and may also be linked to immunisation.”

Public should be told that vaccines may have long term adverse effects
National Childhood Vaccine Injury Act (NCVIA) in 1986 (USA)

The NCVIA established a committee from the Institute of Medicine (IOM) to review the literature on vaccine reactions. This group concluded that there are limitations in our knowledge of the risks associated with vaccines. The group looked at 76 health problems to see if they were caused by vaccines. Of those, 50 (66%) had no or inadequate research to form a conclusion. [6, 7] Specifically, the IOM identified the following problems:

1. Limited understanding of biological processes that underlie adverse events.
2. Incomplete and inconsistent information from individual reports.
3. Poorly constructed research studies (not enough people enrolled for the period of time).
4. Inadequate systems to track vaccine side effects.
5. Few experimental studies were published in the medical literature.
Efficacy relates to the performance of a vaccine under carefully controlled trial conditions.

- 50% efficacy is required as a basis for regulatory consideration.

Effectiveness is the performance under real world conditions.
Data limitations (published by Pfizer)

- Unknown longer-term safety.
- Vaccine efficacy against asymptomatic infection and viral transmission.
- The concomitant use of this vaccine with other vaccines.
- Vaccine data in pregnant women and lactating mothers.
- Vaccine efficacy and safety in immunocompromised individuals.
- Vaccine efficacy and safety in paediatric subjects (< 16 years old).
- A correlate of protection has yet to be established.
Pfizer-BioNTech (mRNA)

RNA is enzymatically synthesized from DNA template and stabilized. Chemical synthesis of the RNA sequence also allows the artificial mRNAs to be freely designed.

Public name: “Comirnaty” (compound of community, immunity, mRNA and COVID). Trade name: Tozinameran.

Claim 93% efficacy (BMJ deputy editor review suggests 19-29% ;FDA summary report).

Median age 51

Some reports suggest that immunity from nucleic acid vaccines wanes before other types of vaccines. 
We don’t know what we don’t know

“The physiochemical properties of mRNA may influence its cellular delivery and organ distribution, and the safety and efficacy of mRNA vaccine use in humans remain unknown.”

Signal Transduction and Targeted Therapy volume 5, Article number: 237 (2020)
Adjuvants and Excipients

Pfizer:
(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate),
2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide,
N-ditetradecylacetamide,
1,2-distearoyl-sn-glycero-3-phosphocholine,
and cholesterol,
potassium chloride,
monobasic potassium phosphate,
sodium chloride,
dibasic sodium phosphate dihydrate,
and sucrose.
University of Oxford-AstraZeneca (Adenovirus-vectored)

Chimpanzee adenovirus-vectored vaccine.

A study published in The Lancet in July showed that phase I/II trials of a single dose of ChAdOx1 nCoV-19 produced neutralising antibodies in more than 90% of participants. The vaccine also produced a T-cell response.

Median age 35 years.

Contains the weakened adenovirus encoding the SARS CoV 2 Spike glycoprotein, as well as the following excipients/adjuvants:
Astrazeneca

- L-histidine
- L-histidine hydrochloride monohydrate
- Magnesium chloride hexahydrate
- Polysorbate 80
- Ethanol
- Sucrose
- Sodium chloride
- Disodium edetate dihydrate
Novavax (protein sub-unit)

Recombinant protein-based vaccine using entire lab-made Sars-CoV-2 spike protein, plus an immune system-activating adjuvant.

Claims 89.3% efficacy.

Adjuvant:

40 nanometer particles based on saponin extracted from the Quillaja saponaria Molina bark, together with cholesterol and phospholipid.

Soapbark, without cholesterol attached, causes severe allergies.
Double-stranded DNA inside a modified (non-replicating) Adenovirus which carries a gene from the coronavirus into human cells.

Once released it gives instruction to produce the coronavirus spike protein via mRNA.

USA : 72% effective against moderate to severe COVID-19.
Latin America : 66%
South Africa : 57%
J&J Adjuvants and excipients

- Citric acid monohydrate
- Trisodium citrate dihydrate
- Alcohol
- Hydroxypropyl betadex
- Polysorbate 80
- Sodium chloride
- Sodium hydroxide
- Hydrochloric acid
- Water
Vaccines

• It takes at least 2-3 weeks for any protection to kick in after the first dose. During this time, you are just as vulnerable.

• It isn’t clear how much protection a single dose of any vaccine provides because the trials weren’t designed to tell us this.

What is certain, is that no vaccine provides complete protection even after two doses.

- Pfizer; about 1 in 20 people may still get symptomatic infections.
- AstraZeneca; as many as 1 in 3 people might still be vulnerable.

• “If you get covid-19 despite being vaccinated, you can still become seriously ill and die.”

“The American College of Obstetricians and Gynaecologists and the Society for Maternal-Fetal Medicine, have continued to advocate for making COVID-19 vaccines available to pregnant and lactating women, even after the recent statement by the World Health Organization (WHO) on January 26, 2021, explicitly recommending against vaccination of pregnant women using the Moderna vaccine, except in select circumstances.”

JAMA. Published online February 8, 2021

There is no evidence to support that COVID vaccines impact fertility

(...but keep an eye on this trial: ClinicalTrials.gov identifier : NCT04665258)
SE’s and AR’s

Most caused by variety in T-Cells reactions.
Particularly TH1:TH2 imbalance.

PNAS April 14, 2020 117 (15) 8218-8221

High Th1 increase CD8/CD4 cells that attack virus directly, but may be short lived.

High Th2 better at differentiating B cells, but increases inflammatory responses and lung pathologies.
From the 1/29/2021 release of VAERS data:

Found 11,249 cases where Vaccine is COVID19

<table>
<thead>
<tr>
<th>Age</th>
<th>Count</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 Years</td>
<td>4</td>
<td>0.04%</td>
</tr>
<tr>
<td>12-17 Years</td>
<td>4</td>
<td>0.04%</td>
</tr>
<tr>
<td>17-44 Years</td>
<td>5,128</td>
<td>45.59%</td>
</tr>
<tr>
<td>44-65 Years</td>
<td>4,045</td>
<td>35.96%</td>
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<tr>
<td>65-75 Years</td>
<td>533</td>
<td>4.74%</td>
</tr>
<tr>
<td>75+ Years</td>
<td>568</td>
<td>5.05%</td>
</tr>
<tr>
<td>Unknown</td>
<td>967</td>
<td>8.6%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>11,249</td>
<td>100%</td>
</tr>
</tbody>
</table>
2016 study by Samuel Lai:
- 72% of people have antibodies
- 7% have levels high enough to predispose anaphylactic reactions

Mechanism behind PEG anaphylaxis is unknown as it does not involve IgE.

PEG triggers IgM and IgG: more involved in innate immunity.

In 1999, Walter Reed Institute termed “complement activation-related pseudoallergy (CARPA)” a nonspecific immune response to nanoparticle-based PEGylated medicines; often mistakenly recognized by the immune system as viruses.
Polysorbate 80

P80 related to PEG

P80 alters microbiota composition subsequently increasing inflammation

P80 increases the susceptibility of cells to oxidative stress


P80 may induce symptoms similar to histamine infusion (hypotension, migraine) Agents and Actions volume 16, pages470–477(1985)
Resources

https://vaers.hhs.gov/data.html

https://wonder.cdc.gov/vaers.html

https://medalerts.org/vaersdb/findfield.php
Variants

Each vaccine can produce its own variant

Dr Anthony Fauci
Delays between jabs increase probability of variants

Anthony Fauci said at a virtual World Economic Forum panel last month, that delaying the second dose of a COVID-19 vaccine could increase the likelihood of an escape variant emerging.

Scientists advising the UK government:

“...in the short-term, delaying the second dose would be expected to somewhat increase the probability of emergence of vaccine resistance.”

Quantifying the risk is almost impossible.
Variants are causing high level concern.

Two areas of initiation:

1. Current vaccines confer narrowly focused immunity that targets a single s-protein.

2. The vaccination program is being rolled out in piece-meal fashion giving the new strain every chance to spread.

Untested COVID-19 vaccine regimens. Logistics of 2 shots.
“UK Strain” B.1.1.7 may be 500 to 5000x deadlier than older variants.
(John Edmunds; London School of Hygiene & Tropical Medicine)

B.1.1.7 is 50% more transmissible than other variants.
(Graham Medley; London School of Hygiene & Tropical Medicine)

B.1.1.7 death rate 30 % higher.

“If outbreaks are allowed to rage unchecked, more people could yet die than have already, even in countries with a high proportion of vaccinated people.”

https://www.newscientist.com/article/2265740-uk-coronavirus-variant-deadlier-but-researchers-say-no-need-to-panic/#ixzz6kjWn0ZjB
Herd Immunity

High natural infection rate in Brazilian Amazon:

Median 70% seroprevalence after 1\textsuperscript{st} wave, yet higher infection rate/hospitalisation in 2\textsuperscript{nd} wave. The Lancet, January 21, 2021

Duration that covid-19 antibodies last after infection is unknown.

Variants, some of which appear to evade antibodies, have increased doubts around the possibility of natural herd immunity.

Natural Immunity

Study: 44 reinfections were detected in 6,614 participants.

Natural infection provides about 94% protection against symptomatic infections for at least five months.

Natural immunity targets multiple components of the virus and may reduce the risk of re-infection with variants that can bypass spike protein-specific immunity.

MedRxiv; NHS SARIN study Posted January 15, 2021
## Natural Vs Vaccine acquisition

<table>
<thead>
<tr>
<th></th>
<th>Wild Type Infection</th>
<th>Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Microbe/Immunogen</strong></td>
<td>Small inoculum that grows over days</td>
<td>Larger bolus, but no growth</td>
</tr>
<tr>
<td><strong>Route of Entry</strong></td>
<td>Oral (except Tetanus)</td>
<td>Injection</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td>Spread over multiple days</td>
<td>12-48 hrs post vaccine</td>
</tr>
<tr>
<td><strong>Antibody response</strong></td>
<td>IgM→IgG</td>
<td>IgM→IgG</td>
</tr>
<tr>
<td><strong>Magnitude of antibody response</strong></td>
<td>++++++++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>CD4 T cell response</strong></td>
<td>Th1</td>
<td>Th1 or Th2 dependent on vaccine</td>
</tr>
<tr>
<td><strong>CD8 T cell response</strong></td>
<td>++++++++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Length of Memory Immune Response</strong></td>
<td>Life-long (?)</td>
<td>1-10 years</td>
</tr>
</tbody>
</table>
Can coronavirus variants reinfect people and evade the vaccines?

There are cases of reinfection both from natural and vaccine acquired immunity.
Variants Combine

Not unusual in coronaviruses.

16th February 2021: mutation from B.1.1.7, called Δ69/70, which makes the UK virus more *transmissible*, and another from B.1.429, called L452R, which can confer *resistance to antibodies* combined.

Potential of this is unknown.

https://www.newscientist.com/article/2268014-exclusive-two-variants-have-merged-into-heavily-mutated-coronavirus/#ixzz6mj43NGx5
Evolution of an S-Protein
Evolution of an S-Protein
T Cells offer broader protection over a longer period

T cells are more resistant than antibodies to threats posed by emerging variants.

T cells target at least 15–20 different fragments of coronavirus proteins.

Individuals may develop T cells that target different protein fragments.

“That makes it very hard for the virus to mutate to escape cell recognition, unlike the situation for antibodies.”

Pharmacogenomics

A field that explores relationships between genes and drug effects, with potential to “personalise” medical therapy.

The assumption is that racial categories can sufficiently distinguish populations with high or low prevalence's of certain genes.

JAMA. Published online January 25, 2021. doi:10.1001/jama.2020.25473
Vaccine study participants

**Pfizer**
9.6% were Black or African American
26.1% were Hispanic/Latino
4.3% were Asian
0.7% were Native American/Alaskan native.

**Astrazeneca**
90.1% White

Women generally over-represented across studies.
Polymorphisms and vaccine

Precedents exist:

1. Measles vaccine
   IL-2 gene associate with higher antibody and higher cellular immune responses / IL-10 gene influence lower antibody and cellular immune responses

2. Lower mumps vaccine-induced cellular response associates with other polymorphisms


3. Associations of innate related genes have been identified between the vitamin A TRIM, vitamin D receptor, and genes with rubella vaccine-specific immunity
   Hum Genet. 2010 Feb; 127(2):207-21
PMs and COVID vaccines

Polymorphisms in cytokine genes can affect mRNA splicing, stability and structure of RNA molecules or protein folding.


Singapore’s frequency of adverse events so far at around 0.4% of COVID vaccinations administered, compared with 0.1% in Israel and the US.

(This week in Asia, 29 January 2021)
The more you know, the more you know you don't know.

~ Aristotle
Co-morbidities and other considerations
Microbiome loss impairs antibody response in subjects with low pre-existing immunity

Antibiotics increase inflammatory signatures

Links to inflammasome activation

Integrative analysis reveals divergent mechanisms of microbiome influence on immunity
Many drugs change the microbiome

**Worst offenders:**

- Polypharmacy overall
- Proton-pump inhibitors
- Metformin
- Antibiotics
- Laxatives
- SSRI’s

PFAS
PERFLUOROALKYL AND POLYFLUOROALKYL SUBSTANCES

- Raincoats
- Microwave popcorn bags
- Fire retardant foams
- Electronics
- Fast food containers
- Nonstick cookware
- Personal care products
- Stain-resistant carpet
PFAS are potent immuno-toxicants

• Widespread in food.

• Higher levels of PFAS in the blood, associated with increased severity of Covid-19 infections.

• Reduce vaccine efficacy and antibody response in humans, at concentrations readily found in our blood.

• Higher blood levels = increased vaccine resistance.

• Suppression of T cell dependent antibody response.

Arch Toxicol 94, 2131–2147; 2020
Obesity

• Overweight or obese (often 60:40 split): 67% Australia; 64% UK; 75% USA.
• Obese more likely to die from COVID-19.
• Obesity correlates with a dulled immune response to COVID-19.
• Vaccines often don’t work as well in obese people.
• Adipose tissue expresses relatively high levels of the ACE2 receptor that SARS-CoV-2 uses to gain entry into cells.
• Low-grade inflammation resulting in higher levels of immune-regulating proteins, including cytokines.
• Constant immune stimulation weakens immunity through exhaustion, including T cell responses.

Nature 586, 488-489 (2020)
Immunometabolism

Adipose tissue is an extremely active endocrine organ that secretes cytokine-like hormones (adipokines), either pro- or anti-inflammatory factors, bridging metabolism to the immune system.

Leptin (adipokine) regulates metabolism-immune interplay.

Leptin has particular emphasis on its effects on obesity-associated metabolic disorders and autoimmune and/or inflammatory diseases.

“COVID-19 vaccine developers should take the immunocompromised state resulting from obesity into consideration”

International Journal of Obesity. doi.org/10.1038/s41366-020-0640-5.
Lessons from flu-shots

Patients who are obese or very overweight can produce adequate antibodies but have a lower level of B and T cells, questioning the long-term protection from a vaccine.
Sleep, immunity and vaccines

Study: daily COVID19 deaths reported by the national media were used as indicators of behaviour.

Confirmed: watching daily media reports of the number of deaths related to COVID19, predicted mental health complaints that impaired sleep quality.

Poor sleep quality predicts how individuals cope with daily challenges.

Psychiatry and Psychology FEBRUARY 11, 2021
Sleep:

Undifferentiated naïve T cells and the production of pro-inflammatory cytokines exhibit peaks during early nocturnal sleep.

Circulating immune cells with immediate effector functions (e.g., cytotoxic NK cells) and anti-inflammatory cytokine activity peak during the day.

Promotes healthy interaction between Ag presenting cells and T helper cells.

Sleep on the night after hepatitis A vaccination produced a strong and persistent increase in the number of antigen-specific Th cells and antibody titers. Pflugers Arch. 2012 Jan; 463(1): 121–137.

People sleeping less than 6hrs average were 11.5x less likely to mount antibody responses to the vaccines. Uni of Pittsburgh August 2012
Immune Age
You are only as young as your immune age

Why are the elderly and those with chronic comorbidities more susceptible to infection and its complications?

Why are the elderly less reactive to vaccines?

An individual’s immune age can vary from their chronological age and may explain why individuals have increased vulnerability to infection and disease\textsuperscript{1,2}
Changes to thymus

Erosion starts at around 20yo.

Decreased production of naïve T-cells.

CD8+ T-cells specifically decline (especially in men).

Impacts the ability of the innate immune system to educate adaptive immune responses.

Antibody production by B-Cells significantly limited.
Is your immune age the determinant factor in recovery from acute illness?

Approximately 5-55% of COVID patients complained of ongoing issues months after they were ‘clear’.

Several studies have placed ongoing heart and lung issues at around 70-80%.

In 2003, 40% of hospitalised SARS patients experienced chronic fatigue 4 years after discharge.

An aged immune system challenges the concept of infection-induced herd immunity in the current COVID pandemic.
So what is immune age?

Immune age, determined by genome, immune system and protein function, is a good predictor of all-cause mortality\(^2\)
Factors affecting immune age

Diet/nutrition
Stress/Sleep
Environmental
Physical activity
Genetics
Lifestyle and obesity

Reference: 3
Immune aging and health

Aging causes systemic dysregulation and remodelling of both the innate and adaptive arms of the immune system.

• This decline in immune competence involves:
  • Impaired immune memory
  • Impaired immune surveillance
  • Immune tolerance
  • Reduced vaccine responsiveness
  • Increased risk of autoimmunity
  • Failure to maintain immunity to latent infections e.g. Varicella zoster
  • Increased risk of infection
PreVax Rx
Reduce side effects
Improve outcomes
Malnourished elderly in care and at home

<table>
<thead>
<tr>
<th>Year of publication</th>
<th>Age of subjects</th>
<th>Number subjects</th>
<th>Malnutrition prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>&gt;75 yrs</td>
<td>72</td>
<td>1.4% malnourished</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>27.8% at risk</td>
</tr>
<tr>
<td>2016</td>
<td>Mean: 85±5.8 yrs</td>
<td>79</td>
<td>61.8% at risk or malnourished</td>
</tr>
<tr>
<td>2015</td>
<td>Mean: 81.9 (±9.4) yrs</td>
<td>42</td>
<td>5% malnourished</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>38% at risk</td>
</tr>
<tr>
<td>2013</td>
<td>&gt;75 yrs</td>
<td>225</td>
<td>1 malnourished person</td>
</tr>
<tr>
<td></td>
<td>Mean: 81.3 ± 4.3 yrs</td>
<td></td>
<td>16% At Risk</td>
</tr>
<tr>
<td>2013</td>
<td>Mean age 62</td>
<td>153</td>
<td>17% malnourished</td>
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<tr>
<td>2013</td>
<td></td>
<td>774</td>
<td>34% malnourished</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>55% at risk</td>
</tr>
<tr>
<td>2012</td>
<td>Mean: 83.2±8.9 yrs</td>
<td>23</td>
<td>35% malnourished</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>52% at risk</td>
</tr>
</tbody>
</table>
Malnutrition

T-cell survival, proliferation, and inflammatory cytokine production are all decreased, as is T-cell glucose uptake and metabolism.

Micronutrient deficiencies common in elderly

Zinc supplementation influences genomic stability biomarkers, antioxidant activity, and zinc transporter genes in an elderly Australian population with low zinc status.

Molecular Nutrition and food research Volume59, Issue6 June 2015 Pages 1200-1212

5/14 nutrients adequately supplied through meals. 34% protein malnourished; 62% had energy intake deficits. Low Ca, Mg, B9, Zn (men) and fiber. Vit D deficiency in 58% of residents. Only 12% showed no sign of undernutrition.


Study: median study age 82. 89% of the patients had 25-OH-vitamin D deficiency (defined as a level below 20 ng/mL), and 67% had a severe deficiency (below 10 ng/mL). Only 4% had levels in the target range.

Dtsch Arztebl Int. 2012 Jan;109(3):33-8
Immunoglobulin performance study

N = 509

IgG against the spike receptor binding domain (RBD) was predictive of survival.

IgA against the viral spike protein (S protein) associated with rapid virologic clearance.

J Clin Invest. 2020;130(12):6232–6234
Build up Immunoglobulins

Zinc and vitamin A deficiency is associated with a lower production of IgA.

Vitamin A is required for innate and adaptive immunity and potentiates the antibody response. It maintains and restores the integrity and function of all mucosal surfaces.
Cells Immunity, 21 (4), 527-538;2004

“Triggering an IgA response could increase COVID-19 vaccine efficacy.”
Drug Target Review 8 December 2020
Breaking down mRNA

There are three major classes of intracellular RNA-degrading enzymes:

1. Ribonucleases or Rnases
2. Endonucleases that cut RNA internally,
3. Exonucleases that hydrolyse RNA

Helicases and Polymerases are also required.

Most of these enzymes require Zinc and Magnesium.
Acute stress has an impact on liver cytochrome P450 (CYP) mRNA expression. Chronic stress has a significant effect on the gut microbiome. Chronic psychosocial stress changes expression and activity of CYPs. Leads to less effective drug metabolism and a harmful impact on the organism.

Scientific Reports volume 10, Article number: 8529 (2020)
During vaccination, rectifying gut microbiome dysbiosis with prebiotic and probiotic oral supplementation might be a solution for the management of Covid-19 vaccine induced adverse reactions.

BMJ 2021;372:n149

Strong evidence supports the integral role of the microbiota in shaping host immunity.

Microorganisms 2020, 8, 921
Zinc

Behaves like a signaling molecule, facilitating the transduction of a variety of signaling cascades.

Has many functional roles and acts as a transporter in immunity.

‘Crosstalk’ between Zn and immune-related signaling, guides the normal development and function of immune cells.

Vitamin D level is markedly low in severe COVID-19 patients. Inflammatory response is high in vitamin D deficient COVID-19 patients. Prevalence was almost 100% in critically ill patients (62 out of 63). Patients with vitamin D deficiency exhibit higher levels of chemical markers of inflammation. Interacts with the epigenome, via effects on DNA methylation and histone acetylation. Influence pre-mRNA constitutive splicing and alternative splicing.

Antioxidant, antiviral, antibacterial, antifungal, anti-inflammatory and hepatoprotective.

Immunomodulatory agent due to its interaction with a variety of immune cells, including macrophages, dendritic cells, B cells and T cells.

Interacts with a variety of cellular and molecular targets, including transcription factors, various inflammatory mediators, immune complexes, surface markers and cell adhesion molecules.

Seems to exert a modulating effect across innate immunity and T cell subsets.
Orthosilic acid (Silica)

Directly ligates T cell receptor (TCR) complex and initiates signaling downstream.
PNAS January 7, 2020 117 (1) 285-291

Significantly enhances activation of B cells and specific antibodies.
Advanced Materials Volume24, Issue29 August 2, 2012

Deficiency is known in elderly and low dietary plant consumers.
Key concepts:

**Immunomodulation and Homeostasis**

Bringing these key concepts into play before vaccinating will enhance the vaccines effect and reduce potential for side effects and adverse long-term changes.
Whilst most research is on vitamins A, C, D and zinc, every nutrient plays a role in immune regularity and synergy.

B group vitamins, Fe, Cu, Mg, and Se are well indicated.

Inadequate intake and status of these nutrients are widespread.


Specialised Immunomodulators

1,3-1,6 Beta Glucans
Rice Bran ArabinoxylanCompound (RBAC)
Turmeric/Curcumin
Training immune response; Beta Glucans

Innate immune cells undergo reprogramming when exposed to viruses.

β-glucan directly influences immune response and potentially has the ability to calm dysregulated immunity and cytokine storm.

Its use as a prophylactic setting could be an effective way to boost immune responses.

Activates the Dectin-1 receptor; causes important changes to the epigenetic status of immune gene promoters.

Rice Bran Arabinoxylan Compound (RBAC)

“One of the best evidence based and standardized immunomodulators”

“At present, we don’t have better evidence based immunomodulators”

Adv Clin Transl Res 2(3): 2018
T-cell response and clinical presentation

T-cells spot an infected cell by detecting viral proteins on its surface, and then destroy it before it releases more viruses.

Effective T-cell response only requires the recognition of viral proteins making them more adaptable to moderate mutations, i.e.: T-cells recognize many parts of the coronavirus s-protein.

T-cells can stop people getting symptoms.

T cells

Highly influenced by nutrient uptake, nutritional status, weight, sleep and stress.

Intimately involved in vaccine immune responses, side effects, adverse reactions and long-term immune/autoimmune outcomes.

Critical role in nutritional immunometabolism.

Treatment goals:

Restore immune balance

Manage existing inflammation
Lifestyle and immunity

Don't smoke
Healthy diet
Exercise regularly
Maintain healthy weight
Not much alcohol
Get adequate sleep
Minimise stress
Spend time in nature
Dietary charts available

**Example of a meal plan to meet daily fibre requirements**

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Vegetables</th>
<th>Fruits</th>
<th>Legumes</th>
<th>Wholegrains</th>
<th>Nuts</th>
<th>Fatty Fish</th>
<th>Beans</th>
<th>Oils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>4 mg</td>
<td>1.5 mg</td>
<td>3 mg</td>
<td>1.2 mg</td>
<td>0.5 mg</td>
<td>0.3 mg</td>
<td>0.3 mg</td>
<td>0.2 mg</td>
</tr>
<tr>
<td>Calcium</td>
<td>200 mg</td>
<td>200 mg</td>
<td>20 mg</td>
<td>10 mg</td>
<td>15 mg</td>
<td>5 mg</td>
<td>5 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Magnesium</td>
<td>350 mg</td>
<td>300 mg</td>
<td>30 mg</td>
<td>25 mg</td>
<td>20 mg</td>
<td>5 mg</td>
<td>5 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Fiber</td>
<td>5 g</td>
<td>3.5 g</td>
<td>2 g</td>
<td>4 g</td>
<td>1 g</td>
<td>0.5 g</td>
<td>0.5 g</td>
<td>0.2 g</td>
</tr>
</tbody>
</table>

**Anti-Inflammatory Eating Guide**

**FRUIT AND VEGETABLES**

Choose a wide variety of fruits and vegetables, and enjoy them raw or lightly cooked. Examples include: apples, bananas, carrots, tomatoes, blueberries, strawberries, broccoli, spinach, sweet potatoes, bell peppers, eggplant, asparagus, oranges, and tomatoes.

**GRAINS AND PSEUDO GRAINS**

Choose whole grain and pseudo grains like quinoa, amaranth, buckwheat, and brown rice.

**LEGUMES AND BEANS**

Eat beans, lentils, chickpeas, and other legumes at least twice a week. Examples include: black beans, kidney beans, garbanzo beans, and white beans.

**NUTS AND SEEDS**

Choose unsalted nuts and seeds. Examples include: almonds, walnuts, pumpkin seeds, sunflower seeds, and chia seeds.

**HERBS AND SPICES**

Use a variety of herbs and spices in your cooking to add flavor and nutrition. Examples include: parsley, cilantro, basil, turmeric, ginger, garlic, and onion.

**BEVERAGES**

Limit processed and sugary drinks. Choose water, herbal tea, and low-sodium broth or bouillon cubes.

**FATS AND OILS**

Choose healthy fats like olive oil, avocado oil, and canola oil. Limit saturated and trans fats.

**FISH AND SEAFOOD**

Choose fish high in omega-3 fatty acids like salmon, sardines, anchovies, and mackerel.

**NUTRITIONAL FACTS**

BioMedica is a leading provider of high-quality nutritional supplements. For more information, visit our website at [BioMedica.com](http://BioMedica.com).

**DIETARY CONSIDERATIONS**

Dietary considerations for increasing fibre intake: Adequate intake (AI) of dietary fibre in children and adults. Suggested dietary target (SDT) for fibre intake to reduce risk of chronic disease without being too high for all groups.

**SUGGESTED DAILY INTAKE**

For adults: 21-30 g daily, depending on age and activity level. For children: Age 1-3 years: 10-14 g, Age 4-8 years: 11-15 g, Age 9-13 years: 13-17 g.

**BISCUIT STOCK CHART**

Type 1: Wholegrain biscuits, full-fat dairy.
Type 2: Wholegrain biscuits, low-fat dairy.
Type 3: Wholegrain biscuits, no dairy.
Type 4: Natural biscuits, full-fat dairy.
Type 5: Natural biscuits, low-fat dairy.
Type 6: Natural biscuits, no dairy.
Type 7: No biscuits, full-fat dairy.
Type 8: No biscuits, low-fat dairy.
Type 9: No biscuits, no dairy.

**BISCUIT MAKING TIPS**

- Use wholegrain flour for additional fibre.
- Add nuts, seeds, or fruit for extra texture and nutrition.
- Experiment with different spices for unique flavors.

**DATA SOURCES**

- USDA National Nutrient Database for Standard References
- World Health Organization
- American Heart Association
- American Diabetes Association
- Institute of Medicine

**ACKNOWLEDGEMENTS**

- Thanks to Dr. Jane Smith for reviewing the data and providing valuable feedback.
- Special thanks to the BioMedica research team for their hard work and dedication.

**REFERENCES**

Pre-Vax screening questions

Use of antibiotics and other meds
GIT function (including SIBO, NAFLD)
Family Hx of autoimmunity
Chronic inflammatory conditions (check weight)
Sleep quantity
Stress levels
Hypertension
Pathology: CRP, Lymphocytes, NLR, ESR
Webinar theme:

A balanced functional immune system bodes well during the vaccine period and for the long-term benefit of the patient.
Thank You