TITLE: The anti-vaccination debate and the microbiome

SUBTITLE: How paradigm-shifts in the life sciences create new challenges for the vaccination debate

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Vaccination is a public health intervention that depends on numbers: what matters is not just that individuals are immunized against particular pathogens, but that a certain percentage of the population is vaccinated in order to achieve so-called 'herd immunity'[1]. A high proportion of vaccinated people makes it more difficult for pathogens to spread among a host population. This helps to protect vulnerable individuals such as non-vaccinated newborns, the elderly or immunocompromised patients. As the percentage required for herd immunity is usually high – 80 to 95% of the population – a key focus of health policy is to make sure that a sufficient number of people get themselves and their children vaccinated.

However, an increasing number of people, particularly in the developed world, refuse vaccines both for themselves and for their children [2]. This worrisome trend puts the public health goal of herd immunity in jeopardy. A reduction in the uptake of the MMR vaccine, for instance, has been linked to an increase in measles cases in Europe, which reached a record high in 2018 (http://www.euro.who.int/en/media-centre/sections/press-releases/2018/measles-cases-hit-record-high-in-the-european-region).

SUBHEADER: The changing context of the anti-vaccination debate

The reasons why people refuse or delay vaccinations are manifold and complex. A key factor is the perception that vaccines could endanger human health. This worry has been a part of the debate for more than a century [3] but emerged with particular force after the publication of the fraudulent Wakefield paper in 1998 [4]. Another important factor behind vaccine hesitancy is an 'alternative' view of the human body and health [5]. Anti-vaccination advocates often refer to a holistic view of the body, emphasising co-existence, integration and harmony between humans and their environment. Such holistic views found little or no scientific support and were often in opposition to modern views of human biology. However, during the past 15 or

20 years, results from new research disciplines such as metagenomics have initiated a paradigm-shift in biology. Key to this shift have been new insights into the role and importance of microbes, which are now seen as an integral part of the human body rather than a mere component of its environment. This has led many scientists to adopt a different view of humans and their interactions with microorganisms, a change that has been noted and capitalised on by anti-vaccination advocates.

Here I want to show how this ongoing paradigm-shift in biology is already being incorporated into anti-vaccination arguments. This, I argue, creates a new context for the debate about vaccination that requires a concerted response from the scientific community. Anti-vaccination advocates have always argued against an enormous body of scientific evidence that disproves their views. While the new insights into the importance of the human microbiomes do not question the safety or importance of vaccines, they play into the hands of anti-vaccination activists who misuse the ongoing paradigm shift for their agenda: to challenge the safety of and the need for vaccines. The response required is therefore not just more data on the safety of vaccines, but a more fundamental debate about the human body, its microbiomes and their importance for human health.

SUBHEADER: The changing understanding of microbes and human health

Our understanding of the relation between microbes and human health has always been complex. The germ theory of disease, which became widely accepted in the late 19th century, painted a negative picture of microorganisms as outside agents that cause harm. Starting with the work of Henry Tissier and Elie Metchnikoff at the beginning of the 20th century, scientists began to emphasise that microbes are not necessarily bad for human health. Metchnikoff's work eventually led to the concept of 'probiotics', that is, the idea that some microbes are quite literally 'pro-life'. This narrative of 'good microbes' can also be found in the hygiene hypothesis proposed by David Strachan in 1989 [6] and, most importantly, in the more recent findings of metagenomics and microbiology. The latter are what I will focus on in the following.

During the past 15 years or so the life sciences have undergone radical changes, driven in part by technological developments that came out of the Human Genome Project (HGP). Importantly, this postgenomic revolution has not only played out on a methodological level but

also led researchers to a new understanding of the human body and its workings [7]. A key part of this postgenomic view is the insight that the microbiome is an integral element of the human body.

The term 'microbiome' was coined in 2001 by Joshua Lederberg and refers to the variety of microorganisms that are present in a particular environment – 'human gut microbiome', for instance, refers to the population of bacteria, archaea, fungi, viruses and protists that live in the human gut. Crucial to the development of microbiome research has been the emergence of a new postgenomic discipline called 'metagenomics'.

What is unique about metagenomics is that it does not focus on one particular organism as in traditional genomics, but that it uses next-generation sequencing technologies to analyse all the genomes present in an environmental sample, such as the human gut, skin, blood, but also ocean water or even air. Taking such a broad and inclusive approach has given researchers much insight into the abundance, diversity and dynamics of microbial populations in different environments and the vital roles microbes play in human health and development.

This research is driving a transformation in our understanding of microbes and human health as it not only shows that microbes can be good for us but that they are an integral part of the human body. Microbes are no longer treated as outside agents that can either benefit or harm humans. They are now seen as part of the system that maintains normal development, gut function or immune responses. This means that the previously well-defined boundary between 'human' and 'non-human' – or self and non-self – which still guided the earlier work on probiotics and the hygiene hypothesis, is disappearing.

Importantly, this new picture of the human body is not only more integrated but also more inclusive. Earlier work on probiotics usually focused on bacteria, gut bacteria in particular. With the rise of metagenomics and microbiome research, the range of microbes that are considered to be relevant for human health has quickly broadened to also include fungi or viruses as potential players in many physiological processes.

By way of example, scientists in Ken Cadwell's laboratory at New York University found that norovirus infection does not just have the well-known disruptive effects on the digestive system but can, like bacteria, restore normal gut morphology and T-cell repertoire in germ-free mice

[8]. Their results suggest that some viral infections could help to maintain a functioning immune system. A similar view is also expressed by the 'imprint' theory, according to which chronic viral infections generate an immunological imprint that helps shape and maintain a normal immune response [9].

SUBHEADER: How microbiome research is being taken up in the anti-vaccination debate

Unsurprisingly, microbiome research has already found its way into the campaigns of antivaccination activists, in particular on blogs or websites that push anti-vaccine messages under the guise of 'health information'. A good example is the above-mentioned research on norovirus infection in mice, which led one author of an anti-vaccine website to claim that "we may need viruses more than vaccines" [https://wakeup-world.com/2014/11/30/why-we-may-need-viruses-more-than-vaccines/]. The author ignores that there is no similar data on potential beneficial effects of norovirus in humans and goes on to question whether "the present-day globally orchestrated vaccine program really [improves] health" or whether "it [belies] a hubris that shirks the scientific evidence in favor of exerting control over the human body for economic and socio-political gains?"

Another article on a similar website discusses a broad range of findings in viromics and concludes that "vaccinations may deprive the body of favorable immune-modulating effects of some viral infections. Contrary to the dualistic view of Western medicine, most viruses are neither innately good nor bad" [http://www.greenmedinfo.com/blog/profound-implications-virome-human-health-and-autoimmunity]. While the second part of this statement is, at least in part, in line with contemporary research – if we ignore the subtle switch from 'some' to 'most' – the first part clearly has no support from research. Polio, diphtheria, measles or viral encephalitis have no positive immune-modulating effects on the human body and no scientist claims that these microbes might be good for health. Hence vaccines against them will protect the human body and not deprive it of beneficial agents.

There are many more examples where new findings from microbiome research are used by anti-vaccination activists to question the need for and safety of vaccination efforts. It is clear that the overall conclusions of these articles are not supported by current research. But the crucial point is probably not so much whether these arguments can withstand fact-checking

and evidence. What matters is the way in which they play on and misuse recent developments

in the life sciences to attack public health policies and the very idea of vaccination itself.

SUBHEADER: Where do we go from here?

It is of course impossible to completely avoid the misuse of data and evidence by anti-vaccine

websites and activists. Sentences can always be taken out of context. Important qualifiers like

'some' can be replaced with 'most'. Findings can be generalized far beyond what the original

research actually shows. Moreover, a fast-moving research field, such as research on the human

microbiome, creates a lot of new hypotheses that need further testing, a situation that makes it

easy for people to distort and misuse new data. But even if it is not possible to stop such misuse,

it is certainly possible to make it much harder.

To counter the propaganda by anti-vaccine activists, the research and public health

communities have to adjust their communication. Arguing that vaccines are safe and the most

efficient public health intervention to combat infectious diseases is no longer just a question of

providing more data on the safety of specific vaccines. It has to expand to discuss a broader

view of human biology, the body's microbiomes and their role in health and disease to reassert

that while not all bugs are bad, some are and vaccines help to protect us against these.

It also means that communication efforts to convince the public have to come from a larger

group of scientists than just those working in epidemiology, immunology or health policy. It

also should include, for instance, scholars from philosophy, where the question of biological

individuality has gained significant attention in recent years [10]. Overall, and even beyond the

anti-vaccination propaganda, there is a greater need for a concerted effort to confront

misinformation and to openly discuss the new insights and theories from the postgenomic life

sciences.

[Conflict of Interest: The author declares that he has no conflict of interest.]

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