

Vaccination in the line of fire

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Scene setting

Infectious diseases lay a heavy burden upon public health in many parts of the world. The toll they take in terms of human suffering, social hardship, and economic cost is huge and as a consequence, preventing and combating them are keys to the development of the most affected regions.

A number of these diseases are, fortunately, vaccine-preventable and the introduction of vaccination is one of the greatest achievements and most cost-effective interventions in public health that have ever been made. The health impact of current vaccination programmes is tremendous and perhaps only surpassed by the effect of measures to prevent poverty and to introduce clean water and well-functioning sanitation for all.¹

It is clear that vaccination programmes need to reconcile the interests of the community and those of the individual belonging to this community. While the interests of the community are expressed in terms of vaccine uptake and herd immunity, the determining parameters for the individual are in the first place vaccine efficacy and safety.²⁻⁴

Anti-vaccination ideas and movements bear the germ of endangering existing programmes.⁵ Organised anti-vaccination lobbies tend to extend their influence by all current means of communication and spread subjective and non-scientific information. The complexity of the subject is exploited by these groups, and anecdotal, dramatically looking pseudo-evidence is eagerly delivered. The lay public, if not properly guided and informed, is often confused. Being not familiar with a scientific approach, it is potentially susceptible to such influences.

Anti-vaccinationism

The value of vaccination is documented by enormous amounts of solid scientific evidence. It should therefore be easy, at first sight, to convince sensibly thinking laymen and professionals, and secure their support. This is unfortunately not always true. A vocal and active minority campaigns against vaccination by focusing on potential dangers and questionable personal experiences.

There is extreme diversity in background and motivation of individuals and groups adhering to anti-vaccination beliefs.⁶

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Some of them are worried parents or patients, whilst others are culturally, philosophically, or religiously inspired. Categories such as feelings of freedom and individualism, misinformation about risk, and overperception of risk all play a role.

Anti-vaccinationism is irrational and disregards solid judgements of the scientific community. This sometimes concretely leads to absurd situations. In a number of countries, including Belgium, Germany, and the United Kingdom (UK), 'measles parties' are organised where non-vaccinated children are deliberately exposed to children having measles, in the hope that they become infected too and acquire immunity in a 'natural' way. Part of the homoeopathic and anthroposophical schools propagate these dangerous views. They do not take into account that even in industrialised countries, measles remains a dangerous disease, potentially with debilitating consequences such as meningitis or bacterial superinfections.

Negative attitudes may also have other, more general roots arising from imbalances typical of modern societies. In the more affluent parts of the world there is a strong tendency towards growing self-sufficiency. The right of individual development and leisure ranks highly and is perhaps overstressed. Many lose their interest or even cultivate negative feelings, if not feelings of dread and hostility vis-à-vis science and technology. This in turn results in a distorted balance between the insight into scientific achievements as the basis of modern comforts and progress on the one hand and a sane attention for potential side effects on the other.⁷

An inclination to see associations and suppose causal relationships between observed or experienced events is an inherent characteristic of human nature. Evolutionary spoken it even makes part of a basic survival strategy. This type of intuition, however, easily deceives us. For a human being subject to irrational considerations it is virtually impossible to accept that misfortune can happen without a simple explanation. It becomes justifiable to designate an epidemic as a punishment or to blame vaccination for subsequent serious events. Here is a key role in store for science - more specifically for statistics and epidemiology - to present a rational perspective of the facts.⁸

The inauguration of immunisation safety surveillance systems as recommended by the World Health Organization (WHO) can only be applauded and encouraged. However, such initiatives may have a perverted side effect. Developing a monitoring system implies asking questions in the community. This might prompt governments to fear that people in turn might suspect that the true reason for making inquiries is a problem with the safety of vaccines, a problem that is kept away from the public. This suspicion might fuel anti-vaccination feelings.⁹

Some avenues remain largely unexplored by the anti-

vaccination movement, probably because they are deemed too scientific and hence difficult to sell to a broad public. For example, there is no doubt that the continuous impact of numerous species of pathogens on the human immune system helped in determining human immunological capacity. During millions of years, from the dawn of mankind or even before to the present, the steering evolutionary forces exerted by these organisms have made them 'co-responsible' for the current state of our defence mechanisms. Vaccinating people on a large scale affects or abruptly interrupts this process. Will this have negative consequences? We can only speculate about possible risks.¹⁰ It must be said that applying such arguments for the benefit of the anti-vaccination cause would not be an easy task, all the more so because an analogous reasoning is conceivable with reference to more health interventions.

Arguments used by anti-vaccinationists

Opposition against vaccination has deep historical roots and causes. At present, the most prominent arguments brought forward by the anti-vaccination movement^{11,12} can be subdivided in a number of groups.

The *first* one appeals on philosophical and political pondering and comprises the following: 1) vaccination recommendations are extraordinarily influential and represent totalitarian intrusions upon personal liberty and democracy, for the benefit of pharmaceutical companies, researchers, physicians, and public health bureaucrats; and 2) failure of the immune system following vaccination is covered up.

In the *second* group of arguments the consequences of the disease are minimised, pretending that 1) the disease is not serious; and 2) the disease is uncommon.

Vaccines and vaccination programmes are virulently attacked with the aid of a *third* type of arguments: 1) vaccines contain dangerous living organisms and very significant amounts of highly toxic substances; 2) vaccines interfere with the natural process of getting childhood diseases and hence cause adverse health outcomes; 3) immunity after vaccination is temporary, while protection after the disease is lifelong; and 4) vaccination is unreliable and ineffective as a protective disease-preventing measure.

In addition, several national and international bodies have published a list of the most common arguments, misconceptions, and myths handled by the anti-vaccination movement, together with advice on how to take the edge off them.^{13,14} The list comprises the following opinions: 1) Diseases had already begun to disappear before vaccines were introduced, because of better hygiene and sanitation; 2) The majority of people who get an infectious disease have been vaccinated; 3) There are 'hot lots' of vaccines that have been associated with more adverse events and deaths than others - parents should find the numbers of these lots and not allow their children to receive the corresponding vaccines; 4) Vaccines cause many harmful side effects, disorders - say, multiple sclerosis (MS) or autism - and even death, not to mention possible long-term effects we do not even know about; 5) Vaccine-preventable diseases have virtually been eliminated in the country we are living in, so there is no need for my child to be vaccinated; and 6) Giving a child multiple vaccinations for different diseases at the same time increases

the risk of harmful side effects and can overload the immune system.

Finally, health-related and general arguments state that: 1) a healthy lifestyle, including personal hygiene and diet, ensures natural immunity and does prevent disease; and 2) other methods of disease prevention, such as homoeopathy, are superior alternatives to immunisation. The latter argument is in keeping with the naturopathic belief, which is rooted in pre-20th-century vitalism and asserts that biological processes do not conform to universal physical and chemical principles. Naturopaths describe a 'healing power of nature,' which is compromised by modern medicine. Both naturopaths and homoeopaths are practitioners of so-called complementary and alternative medicine (CAM), a current with rising popularity.¹⁵ Some of them reject the value of vaccines and are affiliated with the anti-vaccination movement.¹⁶

Risks associated with vaccination

Real risks

Local symptoms at the injection site of a vaccine are not uncommon. They include minor pain, redness, and swelling. The most often described systemic symptoms following vaccination are slight headache, fever, fatigue, and gastrointestinal complaints. Also true complications are known for which a causal relationship with the administration of specific vaccines has been established (eg. Guillain-Barré syndrome) or for which epidemiological analysis favours acceptance of such a relationship. Severe events leading to permanent damage or death, however, are rare or very rare. Real risks related to vaccines rightfully draw the attention of the scientific community, the media, and the public.^{3,17,18}

Scares

There is a lot of literature available on the scares that cause or caused controversy.¹⁷ A number of unsubstantiated rumours regarding vaccines have circulated during recent years.^{5,19} Some prominent examples are: a) Allegations that hepatitis B vaccination is responsible for the onset or relapse of MS or other neurological disorders were refuted by several studies showing no evidence of a causal link.^{20,22} b) Thiomersal, used as a preservative in vaccines, has been under fire because of an alleged link with acute lymphoblastic leukaemia (ALL), but most of the studies conducted did not support this idea.²³ c) It is likewise improbable that the doses of methyl mercury - the active component of thiomersal - that are present in vaccines are adequate to induce neurological adverse events in infants, children, or adults.²⁴ d) Based on the observation of a number of macrophagic myofasciitis (MMF) patients in France who had received aluminium-adsorbed hepatitis B vaccine, claims were brought up that the aluminium component would be the cause of the general systemic complaints these patients were suffering from. There is currently no solid evidence for such a link.^{25,26} e) Although it cannot be excluded that vaccination is able to trigger a pre-existing autoimmune disease in genetically susceptible individuals, an association between a specific vaccine and autoimmune pathology was demonstrated only in rare cases.²⁷

In a hypothesis launched in a 1998 study,²⁸ it was suggested that the measles-mumps-rubella (MMR) vaccine might be responsible for a number of cases of gastrointestinal disease and developmental regression disorders such as autism. Most of the subsequently conducted studies did not support this possibility and a number of the authors of the original study later on retracted their supposition.²⁹ Based on careful examination of all available data, the renowned Institute of Medicine (IOM) rejected a causal relationship.³⁰

In general, it is worth mentioning that even if all allegations regarding severe adverse events following immunisation (AEFIs) were proved to be true, they would amount to very few cases, resulting in small calculated odds ratios and a benefit-risk balance that would remain crushingly positive in favour of vaccination.

Many millions of doses of vaccine are administered annually worldwide. It is therefore most probable that temporal and merely coincidental associations between vaccine administration and adverse events will occur regularly. Unfamiliarity with a scientific approach causes misinterpretation of such associations and leads in a number of cases to an unjustified impression of causality. It is the role of postmarketing surveillance systems to detect adverse events at an early stage and respond adequately in order to curtail the potential negative impact on vaccination programmes.

Risks associated with non-vaccination

There is no doubt that dangerous infectious diseases do return when immunisation programmes are halted, as illustrated by the following example. In the first decades of the twentieth century, diphtheria was still one of the most common killers of children in many industrialised countries. The introduction of vaccination programmes resulted first in a dramatic decline in its incidence and later on in its virtual elimination. In eastern Europe, however, many thousands of people died from the consequences of diphtheria after a disruption of the national programmes in the 1990s.

Anti-vaccination campaigns do have consequences, which are manifested in a dip or a decline in vaccination coverage curves.³¹ It is important to see the mechanisms causing such situations. Whereas a former major concern among health officials in Europe and the United States of America (USA) was to increase vaccination coverage among the poor and the underserved, part of this concern has now shifted towards a segment of the educated population, among whom vaccine refusal has become more probable.³²

Rejecting vaccination does not only leave the concerned individual unprotected. If it happens on a larger scale, it has also serious repercussions at the community level and therefore goes beyond individual rights and responsibilities.

The principle of herd immunity is based on the simple assumption that a community as a whole is better protected when more people are immunised. The exact coverage needed to reach herd immunity depends on the infectivity of the pathogen and the geographical proximity of clusters of unvaccinated individuals. If coverage is sufficiently high, persons who are not vaccinated benefit from vaccination accepted by others. This type of piggybacking, provoked by anti-vaccination ideas or not, endangers the health of others

and eventually compromises the whole community. Opting out of the social contract to be vaccinated is regarded as a bioethical challenge by some and as sheer unfairness or at least as a cynical attitude by others. Legal exemptions to mandatory childhood vaccination on philosophical and religious grounds are however provided for in some countries, such as the USA.^{33,34}

Certain religious communities are especially vulnerable to the consequences of non-vaccination. Between September 1 2004 and February 25 2005, 128 serologically confirmed cases of rubella were notified in the Netherlands, which represents a very significant increase compared with the annual average in the years 2000-2003. Several of the infected women were pregnant in their first trimester and as a consequence prone to give birth to a child with congenital rubella syndrome (CRS), which potentially results in heart disease, deafness, and blindness. None of the patients had been vaccinated and in the majority of cases (118/128), it was their choice not to receive the vaccine based on religious motives.^{35,36}

In contrast with the generally high uptake of MMR vaccine in the Netherlands (96% for the first dose), there is low vaccination coverage in a number of sociogeographical areas with a high proportion of religious inhabitants. Some of them refuse vaccination because they believe that higher forces decide in health matters and experience prevention of disease as interference with divine providence. Disease outbreak in this specific community is not unusual. During the last decade there were, besides another rubella epidemic, also outbreaks of poliomyelitis and measles. In several of these cases, the disease spread to other countries, especially Canada, because of the historical and social links, and frequent travelling between orthodox religious communities in both countries. Comparable cases have also been recorded in other countries.³⁵⁻³⁷

Discussion

It is an established fact that anti-vaccination sentiments and lobbies do exist; ignoring their existence or influence would not be wise. Yet, willingness to accept and appreciate vaccination as a beneficial intervention overwhelmingly remains the norm and all surveys conducted in this domain show that feelings leading to rejection are present in a small, albeit clamorous minority.³⁸

Epidemiology has its own, more or less specific limitations. For instance, it is virtually impossible to prove that something does not exist. Proving the nature of a relationship between observed events to be causal is feasible, while showing with absolute certainty that there is no such relationship cannot be done. This principle is perfectly acceptable for a scientist, but may be hard to sell to a layman without risking misunderstandings and ambiguity. Thus, trying to prove that an adverse event will never occur is impossible and this all the more holds true for events that may occur in a distant future.³⁴ If this message is not brought carefully and explained with patience, mistrust can grow. In specific cases, among other examples an alleged link between thiomersal-containing vaccines and autism, it is considered wise to state that there is a predominance of evidence that does not corroborate a causal link and that the scientific world has nonetheless been looking very hard to find such a link.³⁹ To serve this purpose scientists should be

encouraged to publish the results of 'negative' studies.^{40,41} This attitude is in line with the rules of good communication and at the same time in accordance with Popper's basic principle implying that science should actively look for 'falsifications'.

Irrational reflexes subsist since ancient times or reappear in a modern shape. A present-day example is the turning-up theory of 'intelligent design', an adapted version of creationism: nature is so remarkably complex that it is inconceivable it was brought about without the intervention of God. The Darwinistic principles of natural selection are discarded - each species was created as such. The most disturbing aspect is the organised way in which such scientifically unsound ideas are propagated - this corresponds to the methods used by sections of the anti-vaccine movement.

Anti-vaccine sentiments are by far not always based on pronounced opinions inspired by organisations, or religious or philosophical concepts. Sincere personal worries about vaccine safety do exist and should be handled with respect. Also less emotionally charged attitudes prevail. 1) 'Omission bias' is a remarkable phenomenon observed with parents not being ill-disposed towards the benefits of having their children vaccinated, but still being reluctant to take the ultimate decision. It is well known in human psychology and interpreted as a preference for inactive rather than active options, even if inactivity leads to a situation that is worse or more risky than the alternative. 2) A somehow related category is *status quo* or 'bandwagoning'. People take a decision to vaccinate or not, simply because their environment or community does or does not, and because they wish not to disrupt this *status quo*. Other heuristics that affect decisions on vaccination include 3) 'ambiguity aversion' - reluctance to take decisions when the likelihood of an event is unknown; and 4) the already mentioned 'freeloading/free-riding/piggybacking' - taking advantage of herd immunity materialised by others. On the positive side, an attitude more or less opposite to the latter category is 'altruism,' based on the wish to contribute to herd immunity.^{42,43}

It is not unusual that misinterpretation of statistical results occurs, even without specific intentions.⁴⁴ Statistics often gets across as a discipline almost impervious to laymen. A straightforward application of sometimes simple rules does indeed not suffice: only correct interpretation of the results leads to better insight. Interpretation unfortunately remains the bigger problem, and this counts also for many scholars. This situation is easy to exploit by the anti-vaccination movement. Even if the odds ratio of, for example, the relationship between hepatitis B vaccination and the onset or triggering of MS would equal 2 - which is by no means a realistic estimation - the benefit-risk balance would still be extremely positive in favour of vaccination. The numbers in such examples are however prone to false interpretation. Also assumed bona fide researchers walk into the trap of improper use of statistical/epidemiological methods.

Good communication about vaccine efficacy and safety will not totally annihilate anti-vaccination sentiments, but remains a key factor in the process of countering them. Evidence-based information resulting from reliable investigations⁴⁵ should rapidly be transmitted to both healthcare workers and the public in a language

comprehensible for all. Delays in communication potentially lead to misunderstandings and false impressions, and ultimately to a negative impact on vaccination programmes. Creation of a positive environment for immunisation¹⁷ by applying a proactive communication strategy on the other hand facilitates the task of decision makers and contributes to avoiding crises.

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