Vaccination and autoimmunity: reassessing evidence

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Abstract

The autoimmune risks of vaccines seem frequently overlooked. Whereas most available vaccinations are supposed to produce long-lasting immunity, the fact that they can also produce long-term detrimental immune effects seems to be ignored as evidenced by the short duration of safety studies during development. Likewise, whereas it seems natural to simply rely on surrogate markers, such as antibodies, to demonstrate vaccine efficacy, the levels of evidence required to acknowledge adverse effects is far higher. Reports to the Vaccine Adverse Event Reporting System (VAERS) are deemed more conclusive when reassuring than when suggesting significant toxicity. As a result of these blatant biases in clinical and/or epidemiological research, experts on autoimmunity and vaccine critics are limited to demonstrating *theoretical* mechanisms because evidence *in practice* is lacking.

Known as the bias of the *selective* assessment, this unbalance in the demonstration of the benefits as compared to the risks is the bête noire of *evidence-based medicine*. Therefore, when readjusted to the demonstrative level normally viewed as sufficient in clinical research in general and in vaccine science specifically, the corpus of data on the autoimmune hazards of vaccines appears certainly more impressive than generally recognized and calls for further research, for an overall reassessment of the benefit/risk ratio of vaccines including multiple vaccinations. Because vaccines are now aimed at preventing diseases which may be quite rare, the Hippocratic principle of prudence is more than ever a very topical issue.

Keywords: benefit/risk ratio, bias, evidence-based medicine (EBM), Hippocratic principle, vaccination

Competing interests: Dr Girard works as an independent consultant for pharmaceutical industry, including vaccine manufacturers and a number of their competitors. He received no funding for this paper.

1. Introduction

Although vaccine safety is obviously a major issue, its prime importance is often relegated to a secondary and unimportant role. A review of the medical literature reveals that more often than not, any legitimate question raised about the safety of any vaccine is likely to be ignored or interpreted as "myth", "fiction" or "misconceptions" [1-6].

A recent international conference held in Lausanne, Switzerland [6] may start to reverse this trend, help those scientists genuinely concerned with vaccine hazards regain their credibility, encourage others to come forth and put on the market genuinely safe vaccines, that will not need to be withdrawn following problematic post-marketing performances.

I will not speak in this debate as an immunologist, but as a specialist in drug research and as a medical expert witness with an extensive experience in criminal inquiries on drug scandals and data distortion. Thus, I would like to take the special issue of vaccines to illustrate the effects of quite general vices such as negligence, poor methodology, selective assessment, disregarding or rejection of data – and to suggest that, as a consequence, the autoimmune potential of vaccination could be greatly underestimated.

2. Negligence or carelessness

Several mechanisms can account for the autoimmune hazards of vaccines:

- An individual toxicity if a vaccine antigen mimics host antigens;
- A cumulative addition of the individual toxicities when several antigens are administered together;
- A potential interaction resulting when two vaccines administered together produce a reaction or a chain of reactions that neither would have induced independently.

Although theoretical, this multiple potential for autoimmune hazards should carry at its highest level the Hippocratic principle *first not to harm*. This should be all the more so since in developed countries most vaccines are administered to children and adults in perfect health, each of the exposed subjects has a tiny risk of developing a severe form of the infectious disease and the effectiveness of the vaccine is not assured.

Yet, strangely enough, caution is not always the rule with vaccination policy. In a country like France, and while epidemiological evidence is mainly lacking, up to 11 vaccinations (including one heptavalent pneumococcal vaccine) are recommended or mandated prior to the age of 1 year.

3. Data quality

The quality of the safety studies performed on vaccines is often questionable.

- They are usually of short duration in the range of days. Most safety studies during the development of Engerix B® (one product against hepatitis B) lasted 4 days as mentioned in the Physician Desk Reference (PDR). Yet, it is not easy to understand why products supposed to have beneficial effects in the long term could not also have detrimental effects within the same long term.
- Trials are usually carried out in developing countries, where reliable long term follow-up is most often not available.
- Even in developed countries, post-marketing surveillance depends mainly on systems such as the U.S. Vaccine Adverse Event Reporting System (VAERS) where almost every alert is discredited

doi: 10.1588/medver.2005.02.00072

on the basis that spontaneous reporting does not permit reliable assessment [7,8].

Thus, when an immunologist addresses the issue of the autoimmune complications of vaccines, he starts with a long list of potential mechanisms but quite often is obliged to conclude that no trustworthy evidence is available. To be sure, lack of evidence is an expected result of such a poor surveillance system; but if reliable assessment of vaccines hazards is out of reach, it still remains to be re-assessed whether it is consistent with our Hippocratic principles to expose so many people in perfect health to such products.

Just as disturbing is the fact that the reliability of vaccine surveillance seems to fluctuate according to the trend of its results: very poor when suggesting a toxicity, quite satisfactory when no hazard is detected[1].

- After an analysis of the VAERS database suggested that cerebellar ataxia, autism, mental retardation and permanent brain damage were significantly increased following MMR vaccination [9], the UK Medicines and Healthcare Products Authority (MHRA) issued a statement dismissing the findings on the basis that "the authors failed to consider the limitations and biases inherent in VAERS data (…)"[2].
- About the same time, others published a re-assuring study on vaccines safety which therefore concluded that VAERS is not only important for detecting vaccine-associated adverse events, but it also serves to "reassure the general public concerning the safety of a new vaccine, as in the safety assessments of varicella vaccine and hepatitis A [10]." Interestingly this robust optimism on the reliability of the database did not attract any comment from the regulatory authorities about "the limitation and biases inherent…"

4. Selective assessment

In contrast with physics or chemistry data, drug research data is "soft" [11]: its significance often requires an interpretation. However, interpretation does not mean *selective* assessment of available evidence (as illustrated by the preceding examples). On the contrary, our main requirement to claim a minimum of scientific validity should be a strict, I should say an obsessive regularity in giving the same weight to data of the same reliability. For example, the concern should not be to assess whether severe toxicity is "certain" when the efficacy of vaccines is never certain.

When it comes to vaccines, where no assessment can be more than statistical, our only concern should be to ascertain that the level of evidence for any toxic effect is the same, lower or higher than the level of evidence normally considered as "sufficient" to take medical or regulatory measures.

Let's consider one example. Tolcapone (Tasmar®) is a drug that was licensed for use in some severe forms of Parkinson's disease. In September 1998, further to a safety alert, all international reports of liver injury were reviewed by the European Agency for the Evaluation of Medicinal Products (EMEA). At the time, in an indication where severely disabled patients may have been willing to accept a high level of risk in the hope of even a modest benefit, a total of ten serious cases worldwide, generally of questionable causality and of which only 3 were published, was sufficient to justify drug withdrawal [12]: it would be interesting to compare this level of "significance" with that requested by governmental agencies to admit that there might be a problem with, for example, sudden infant death syndrome, for which hundreds or even thousands of cases have been reported following vaccination... [8,13].[3]

So, let us take as a unit of measure the level of evidence normally deemed as "sufficient" even for drugs aimed at curing even severe diseases. **My point is to show that with such a natural unit of measure, evidence of toxicity for some vaccines is already far higher than usually claimed by experts or agencies.**

Consider, amongst others, the case of hepatitis B vaccine (HBV). It has been repeated that no significant problem was ever reported outside France and that the French problem was an artefact due to media coverage.

This is not true.

Besides the overwhelming predominance of reports about adverse events following hepatitis B vaccination, it is clear (Table 1) that this predominance was evident and blatant as compared to other vaccines of far larger exposure—before any media coverage which began in 1996. When one compares the reaction of governmental agencies to the many HBV problems to those resulting from only three publications on tolcapone (above), the bias is immediately noticeable: by the end of 1994, when dozens of publications were already available and many problems had been publicised, the French Minister of Health launched a national universal campaign of hepatitis B vaccination. Ten years later, universal vaccination in other countries remains an issue [14,15].

The data of the French health system (Fig. 1) reveal a clear increase in neurological and autoimmune complications after the mass campaign (red arrow) was launched. As differences in the absolute frequencies render maintaining a vivid representation difficult, it may be useful to examine the evolution of multiple sclerosis (MS) as compared to the number of vaccine units sold (Fig. 2).[4]

[1] Exactly the converse of what should be expected on purely methodological grounds: reporting represent an alert for the least, whereas non-reporting leaves completely open the issue of an undetected toxicity (as illustrated by a number of examples in the history of pharmacy).

[2] Statement from the Medicines and Healthcare Products Regulatory Agency (MHRA): study on safety of MMR vaccine by Geier and Geier—conclusions are not justified. Internet-Document, page (2 pages), May 22, 2003.

[3] The exaggeration of the European authorities in precautionary measures in this instance was further confirmed by the fact that the withdrawal was lifted some years later (http://www.emea.eu.int/humandocs/PDFs/EPAR/tasmar/034397en8a.pdf); in Autumn 2005, the drug was re-introduced on the market.

[4] One may note that even considered alone, this graph (which concern dozens of millions of vaccinated subjects) is an impressive denial of Sadovnick and Schefele's paper which concluded that the vaccine was safe as no change in the frequency of neurological complications was observed after a program of vaccination was implemented [19]: although this paper was only based upon a tiny population (less than 300 000 students) and paid no attention to the real exposure (implementation of a program may not alter vaccinations practices), it is classically included amongst the hard arguments of every experts panel or "consensus" conference contending that there is no significant hazard with HBV.

doi: 10.1588/medver.2005.02.00072

Table 1. Published case reports on various vaccine hazards in REACTIONS database

Vaccine	Number of case reports	
	prior to 1995	1983-2004
Hepatitis B (HBV)	42	102
Measles or MMR	20	40
Tetanus or DTP	13	27
Haemophilus influenzae type b (Hib)	4	7
Polio or DTP	3	3

But returning to the original graph (Fig. 1) reveals another interesting trend, namely the time lag of about 1 year between the increase in MS and the subsequent increase in unspecified "neuro-muscular disorders" which was not evident prior to 1996. In fact the first increase had an important impact on media coverage and from then on, because of the stubborn denials of health agencies as well as of experts, it became scientifically "incorrect" to make a formal diagnosis of MS in a person exposed to hepatitis B vaccine: this reluctance is clearly illustrated by the time lag and the subsequent dramatic increase. The addition of both curves (Fig. 3) gives a clearer picture of the effects of the mass campaign on the prevalence of severe neuromuscular diseases. It should be pointed out that this dramatic evolution, affecting thousands of citizens who were in perfect health prior to their exposure, only represents the more *severe* cases.

The clear evidence graphically demonstrated in these exhibits were completely ignored by the regulatory agencies as well as by "experts" panels until I made them public starting in 2002. Those willing to go on ignoring the health catastrophe that was caused in France by hepatitis B vaccination have contended ever since then that the data – if not "myth" or "fiction" – simply corresponded to artefacts related to better diagnosis of multiple sclerosis and to the recent wider availability of therapy using interferon.

Obviously, evidence supporting these claims is weak:

- Due to the abovementioned climate of scientific correctness, enormous time and energy were spent to narrow the criteria for the diagnosis of MS. This resulted in a significant increase of unspecified "severe neuromuscular disorders" (the second curve) which, as clinical experience confirmed, included genuine cases of multiple sclerosis MS which for one (generally lame) reason or another were not labeled as such. This general tendency was facilitated by the fact that often drug-induced diseases are generally *atypical* and a little different from the "classical" illness. In this particular case, it is striking that quite often, the lesions in the white substance as detected on MRI examination are unusually tiny and modest when compared to those normally seen in non-iatrogenic instances of MS. In addition, and for unexplained reasons, the size of these tiny lesions is often disproportionate to their clinical expression, which may be severe so that in most cases, this perplexing disproportion between small anatomical lesions and significant symptomatic expression, far from being interpreted as an interesting clue towards exogenous etiology, was on the contrary an easy pretext to evoke a non-neurological disorder such as hysteria or cardio-vascular disorders, etc. Although such a context of reluctance to make a diagnosis of MS should have automatically led to a *decrease* in observed MS cases, the opposite occurred and newly diagnosed cases of MS increased significantly as clearly demonstrated in the attached graphs: in other words, increase in neuromuscular disorders occurred in spite of repeated efforts to reduce the number of newly diagnosed post-vaccinal MS.

- It is also evident from the figures supplied by the manufacturers that significant increases in the sales of interferon did not begin prior to 1997, a full two years after the impressive increase shown in Figure 2.

5. Data rejection or dissimulation

The unprecedented potential of HBV to induce MS is also evident from a number of additional clues [16,17], such as the alarming epidemics of *paediatric* MS. The French regulatory authorities have kept unpublished the existence of a cohort of about 800 children who developed MS, some as young as of 2 years old. Similarly disturbing studies revealing a significant increase in lupus erythematosus (LE) and Graves' disease post hepatitis B vaccination are still unpublished [16] and it is likely that they will remain so.

There are other forms of data dissimulation. Figure 4 shows the corrected proof of a paper which was accepted and had already received a digital object identifier (DOI). After repeated requests about failure to access it in "author's gateway," I received a one sentence explanation from the editor of the journal:

Dear Dr. Girard,

On the basis of the advice I have received I have decided not to go ahead with your publication.
Signed, Emeritus Professor of Science and Engineering Ethics (…)

This should be a matter of concern for every scientist that an unidentified "advice" is sufficient to justify the rejection of a paper at this step of the publication process. This should be all the more so since, apparently, the editor responsible for this unusual shift in publication rules claims to be in charge of teaching scientific ethics…

doi: 10.1588/medver.2005.02.00072

6. Conclusion

Many other examples of poor methodology, selective assessment or dissimulation of data could be given. This suggests that research and development on vaccines are still **at the zero-level of evidence-based medicine** (EBM) [18].

As assessed with the same units of measure used with other drugs, some vaccines and specifically the hepatitis B vaccine have **an unacceptable benefit/risk ratio**, especially in countries where the diseases they claim to control are not endemic.

For obvious reasons of profit, the threats to the scientific and medical ethics of our job have reached a worrying level: it is **the personal responsibility of each** of us to resist – and to support those who are the most under pressure.

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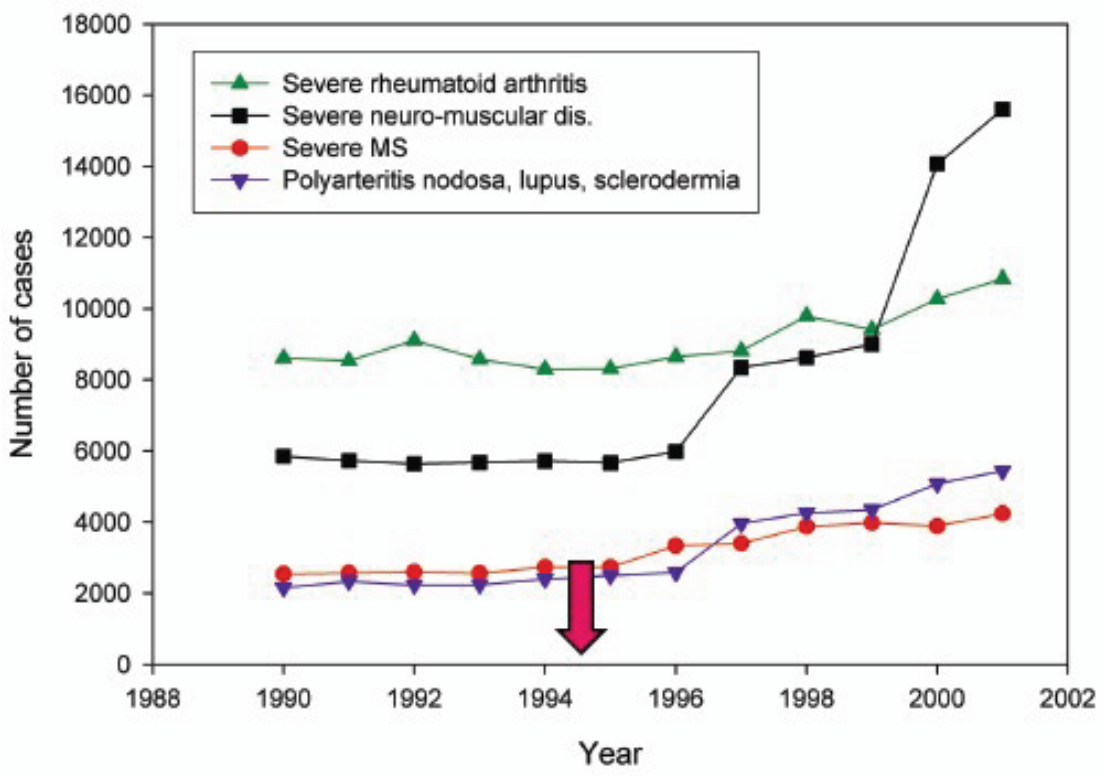
Figure 1. Data of health insurance system, France



doi: 10.1588/medver.2005.02.00072