

# **Markers of autoimmunity after hepatitis B vaccination**

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**Abstract - Recent publications in this journal have highlighted the unusual potential of hepatitis B vaccines to produce markers of auto-immunity such as anti-phospholipids antibodies. Put together with an impressive corpus of convergent data, these papers contribute to the biological basis for how hepatitis B vaccines, with a high degree of certainty, can induce autoimmune reactions, some of them quite severe.**

According to Bogdanos et al (1), "the question of a connection between vaccination [against hepatitis B] and autoimmune disorders is surrounded by controversy". In 25 years of professional life devoted to the study of drug hazards, I have rarely seen an issue clearer than that related to the potential of hepatitis B vaccine to induce auto-immune diseases.

In a job where no assessment can be more than statistical, experts' concern is not to quibble about whether causality is, or not, "demonstrated-with-certainty": it is simply to appreciate if the level of evidence for such or such toxicity is the same, less or higher than the level of evidence normally considered by professionals as "sufficient" to take medical or regulatory measures (2). And there can be no doubt that, in the

case of hepatitis B vaccine which generated hundreds of published case reports and *thousands* of spontaneous reports (for not to speak about a number epidemiological inquiries), this level is far higher than that normally required to take severe measures of restriction or even withdrawal. Illusions that the contrary is true are fuelled by the stubborn refusal of regulatory authorities to publish alarming studies (3), and to give free access to their database even to authoritative researchers (4). They are fostered also by "Reviews" which challenge the most elementary principles of evidence-based medicine as exemplified by a recent paper supposed to discriminate between "consequence or coincidence" regarding "the significance of autoimmune manifestations after viral vaccines" (5): accepted in Feb 2005, this paper completely *ignores* the results of Hernan et al which, for the main, were available as early as one and half year before (6), but it persists in quoting those of Zipp et al (7) in spite of their gross inconsistencies (see their Table 2, where an unfortunate misprint – uncorrected to my knowledge – allows the authors to halve the clear increase of multiple sclerosis in teenagers and young vaccinated adults) which led the French Agency (yet one of the fiercest promoter of the vaccination) to assess that they should be "discarded" (Communiqué of Feb, 2000). Likewise, Schattner's paper goes on using the assessments of the WHO or like organisations at the same level of evidence as independent investigations, without any consideration for the obvious fact that those experts, some of them more or less sponsored by manufacturers and who have passionately promoted hepatitis B vaccination in spite of long-standing safety concern (8) are of problematic reliability as soon as the issue is now to assess with a minimum of neutrality the health catastrophes induced by this irresponsible

promotion: to be sure, “controversy” may be long-lasting when based on such an evidence...

Having been commissioned as a medical expert witness by French Courts or lawyers in dozens of litigations related to hepatitis B vaccine, I have spent thousands of hours on this subject, and had access to a heap of confidential documents which confirmed me – amongst others (9;10) – in the idea that hepatitis B vaccination is characterized by the *number*, the *variety* and the *severity* of its hazards (3). Although most of my conclusions are still confidential or even secret by Court Order, the beautiful investigations by Martinuc Porobic et al (11) and by Bogdanos et al (1) reveals convincing perspectives on the molecular mechanisms of autoimmune reactions induced by hepatitis B vaccine. They add to an impressive spectrum of convergent data including long-standing warnings about the auto-immune potential of a vaccine targeted against hepatitis B virus (8;12), crosschecking showing significant similarities between viral genome and myelin basic protein while making the quite credible hypothesis that the manufacturing process could leave minute amounts of HBV polymerase protein as a contaminant (13;14), community between hepatitis B components and auto-antibodies produced in patients developing immune diseases just after vaccination (15;16). Of course, this massive body of evidence towards *biological plausibility* strongly reinforces the reach and significance of an unusual corpus of case reports (see (3) for a more complete bibliography) as well as of epidemiological data (9;10;17-22). It is also in line with anecdotic evidence taken from a association of victims suggesting that amongst people developing multiple sclerosis after hepatitis B vaccination, HLA distribution is strikingly atypical (Le Houezec, personal communication) with a high frequency of DR15 or DQ6 subtypes.

Martinuc Porobic et al's results (11) are also crucial to understand how evidence of auto-immune toxicity due to hepatitis B vaccine may be *reversed* to deny this toxicity and to harbour "controversy" beyond any rational assessment. The preliminary experiment by Poirriez (16) was related to a 11-year old girl<sup>1</sup> who developed symptoms of a severe (and, unfortunately, irreversible) transverse myelitis 2 months after a hepatitis B booster injection: high titres of antinuclear antibodies were found, which proved to be absorbed by various concentrations of vaccine, strongly suggesting antigenic community between vaccine components and auto-antibodies produced by the patient, in spite of the limitations of this experiment performed in only one subject and in uneasy circumstances. Yet, this case was previously subjected to another publication (23) in which the development of other stigma of autoimmunity after vaccination – *such as anti-phospholipid antibodies* (11) – was interpreted as a clue of an underlying auto-immune disease called "neurolupus" – a very rare, if existing, entity – in order to minimize and even to deny the causal role of the vaccine. Having been recently in charge of a new report on this case, I was able to check that this young girl had not any clue of "lupus" except anti-nuclear and anti-phospholipid antibodies: yet, Poirriez (16) demonstrated the striking community between these anti-nuclear antibodies and vaccine antigens, whereas it is now clear from Martinuc Porobic et al (11) that hepatitis B vaccine has also a strong potential to induce the development of anti-phospholipid antibodies.

This paradoxical assessment of causality – excluding the role of hepatitis B vaccine on the basis of auto-immune markers after vaccination – is not at all exceptional in my experience of medical expert witness. Latest piece of a very consistent corpus of

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<sup>1</sup> The paper mistakenly reads 12-year.

data, Martinuc Porobic et al's results (11) give convincing evidence of biological plausibility and strongly support the view that, far from excluding a causal role of the vaccine, biological markers of auto-immunity in a subject complaining of post-vaccine hazards may represent an important clue to retain this vaccine as *the* trigger of auto-immune disorders.

*Declaration of interest: Marc Girard works as an independent consultant for pharmaceutical industry, including vaccine manufacturers and a number of their competitors. There was no grant support for this paper.*

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