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EDITORIAL

Humans as donors and producers of biological material: some ethical considerations on a thin red line

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FOREWORD

The donation of blood, organs, cells and tissues in accordance with the relevant regulations is an act of great generosity and altruism [1].

Human blood can be processed to produce plasma-derived medicines such as albumin, factor VIII and immmunoglobulin, which are precious therapeutic tools [2].

Human hepatitis B immunoglobulin (HBIg), for example, is used for both preventive and therapeutic purposes. It can be administered either intramuscularly or intravenously and is effective in a number of circumstances such as, in particular: for the prevention of post-surgery infections in liver transplant patients; as prophylaxis in persons exposed to the hepatitis B virus (HBV) either accidentally (through contact with infected blood) or through sexual contact; in paediatrics (in the treatment of children born to HbsAg-positive mothers and immunocompromised children) [3]. Several nations have put in place schemes to collect so-called "hyperimmune" plasma from donors [4]: this is obtained from healthy donors who have been vaccinated against HBV and are then given an additional booster in order to produce a high plasma antibody count. The resulting hyperimmune plasma is collected *via* plasmapheresis and is subsequently fractionated to obtain HBIg.

MEDICAL PROCEDURES NOT FOR THERAPEUTIC PURPOSES

The booster vaccination given to healthy donors is not intended to benefit the donor, but rather to obtain elevated levels of HBIg, a circumstance that raises a number of ethical considerations. It should be made clear immediately that the practice of giving donors substances to facilitate or improve the donation of biological materials is fairly common and should not surprise. It is normal for living donors of organs or parts of organs to receive various treatments, some of them potentially stressful, prior to undergoing surgery [5]. A booster dose of anti-HBV vaccine is nonetheless a different matter. With the exception of some countries in which organs are unfortunately traded, the donation of living organs is strictly regulated and any form of financial gain excluded. Plasma-derived products may, however, enter commercial networks [6] notwithstanding the fact that the donation of blood is generally unremunerated, in line with the recommendations of respected institutions [7, 8]. The existence in several countries of rewards for so-called "donors" is a complex issue that falls outside the scope of the present article, as do the merits of numerous other ethical considerations regarding the donation of biological material in general (voluntariness, non-remuneration, consent, use, etc.). These issues have all been addressed in various declarations [9], regulations, guidelines and other documents [10] as well as in an extensive body of specialised literature [11].

The present article aims only to propose a few considerations regarding the ethical aspects implied in additional vaccinations that are not given for the benefit of the donor but rather for the production of HBIg.

The implications can be analysed from two angles.

The first concerns the principles of reference: we must question the legitimacy of a medical procedure (a vaccination in this case) that is performed for the benefit not of the person on whom it is performed, but of another person.

The second angle (assuming that the procedure is held to be legitimate) concerns the practical requisites to ensure that the procedure is performed in accordance with the principles of medical ethics.

THE REFERENCE PRINCIPLES

The act of vaccinating an individual in order to induce the production of immunoglobulin for use not by that person but by others seems to be informed by a utilitarian view of ethics, in other words, the maximisation of the benefit.

To stretch a point slightly, we might suggest that it infringes the Kantian imperative ("Act in such a way that you treat humanity (…) as an end and never merely as a means to an end" [12]), since the individual is used as a means for the production of immunoglobulin to benefit other people.

One could go further and suggest that it even calls into question the traditional Hippocratic view of ethics focused on treatment: the vaccination in question is not

intended to benefit the person to whom it is given.

All these considerations, however, acquire a totally different prospective if we look at them from the point of view of a gift. If performed in compliance with the relevant regulations and guidelines, the donation of blood or of its components is a noble gesture of altruism: the donor accepts some discomfort for the good of other people [13].

Certain operating requirements should nonetheless be followed.

THE OPERATING REQUIREMENTS

For any medical procedure the foremost ethical requisite is scientificity: in other words, anything that is non-scientific is *ipso facto* non-ethical. Hence the need that every intervention comply with guidelines and similar documents.

The case in point, of a booster vaccination, is mentioned in the "Code of ethics for blood donation and transfusion" of the International Society of Blood Transfusion (ISBT): "Any procedures relating to the administration to a donor of any substance for increasing the concentration of specific blood components should be in compliance with internationally accepted standards" (Article 3) [14].

However, some procedures that are scientifically based and comply with guidelines may not necessarily be ethically acceptable: in the specific case in point three considerations are particularly important:

- *voluntariness and non-remuneration of donation*. According to the Council of Europe: "Donation is considered voluntary and non-remunerated if the person gives blood, plasma or cellular components of his/her own free will and receives no payment for it, either in the form of cash, or in kind which could be considered a substitute for money. This would include time off work other than that reasonably needed for the donation and travel. Small tokens, refreshments and reimbursements of direct travel costs are compatible with voluntary, non-remunerated donation" [15]. Voluntariness and non-remuneration are both particularly important in the present context, in which donation is for the preparation of plasma-derived products;
- *minimisation of risks*. Many respected institutions, including national [16] and international bioethics committees such as the European Group on Ethics in Science and New Technologies, underline the importance of protecting donors. According to the latter group: "The donor should be protected against to him or her unfavourable results of blood or plasma donation" [17]. The threshold of risk acceptability naturally depends on circumstances: for example, even serious risks that would not be acceptable in a research setting may be acceptable for a therapeutic procedure. Given that the medical procedure of vaccination is not, in the present case, given for therapeutic purposes to benefit the person receiving it, the so-called "minimal risk" level should not be passed. The level of minimal risk has been variously defined. According to the Additional Protocol [18] to the Convention on Human Rights and Biomedecine [19], risk is said to be "minimal" if it is expected to "result, at the most, in a very slight and temporary negative impact on the health of the person concerned", and the burden is said to be minimal if it is expected that "the discomfort will be, at the most, temporary and very slight for the person concerned" (Article 17). On this point Article 3 of the Council of Europe's Recommendation 95(14) establishes that: "All collection should be effected in such a manner that the donor's health is not harmed and that its therapeutic use in the form of cellular components or plasma derivatives involves minimal risks to the recipient" [15]. There are no reports in the literature of risks associated with a booster anti-HBV vaccination, nor are there any biological or clinical grounds to suppose that they may exist (apart from possible risks associated with any anti-HBV vaccination, which seem slight) [20]. Regardless of the magnitude of risks "Collection centres should have insurance cover for accidents arising in connection with blood/plasma/cell donation" as laid down in Article 18 of Recommendation 95(14) [15] as well as in other important documents;
- *information and consent*. Donors must be given appropriate information concerning the procedures, the intervals between donations and the number of donations envisaged, as well as concernng possible commercial consequences. For these reasons the case of plasmapheresis for the preparation of plasma-derived products differs from that of the donation of blood for transfusion: donors must be enabled properly to undersand the situation and the purposes of the donation.

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