Chapter 7
Discussion

Overall, there are many studies assessing the vaccination of children with dysimmune disorders or after transplantation [1–12]. All published studies are very reassuring from a safety point of view and most vaccines appear to be safe in children on immunosuppressive treatment. They do not frequently cause serious adverse events and do not increase disease activity or induce rejection. However, there are only a few studies that have assessed vaccination with live vaccines in this patient population [7–43].

It appears to be safe to vaccinate children treated with low dose csDMARDs and GCs or after transplantation, including primary vaccination and booster doses of MMR and VZV, as there has been no report of severe adverse reactions, no cases of vaccine-derived viral infections, or no worsening of the disease activity or transplant rejection. In the setting of solid organ transplantation, a consensus of experts have dictated strict conditions enabling vaccination with MMR or VZV [12]. However, larger studies are necessary to define the exact conditions under which live vaccines can be given in children on high-dose DMARDs, bDMARDs and tsDMARDs, such as JAK inhibitors. In all cases, live vaccines should be considered on a case-by-case basis for children with higher immunosuppression. For these patients, it is important to have a

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systematic approach to assess vaccine status and to plan the vaccinations at a specific time of the disease.

Concerning immunogenicity, most immunosuppressive treatments at low dose induce a normal antibody response in the short term. However, immunogenicity of some vaccines under higher immunosuppression is less clear. Although all non-live vaccines can be given even under high immunosuppression, it is not always very clear how the child will respond to the vaccination. Therefore, when possible, it is important to assess the antibody response 1 month after vaccination as it might be necessary to give a supplementary dose of vaccine for some children [8].

Most studies have analysed the short-term responses post-vaccination in immunocompromised children. However, long-term protection depends on persisting antibody levels above the threshold of protection until we know if the immunological memory can act rapidly enough to induce protective antibody levels in case of infection. Of note, this threshold of protection has been only established in healthy children and may be different in immunocompromised children. Therefore, a correlate of protection needs to be defined for this specific population to ensure that long-term protection is maintained. Hence, it is very important to verify that children treated continuously with immunosuppressive treatment or suffering from various immunosuppressive conditions that can affect their response to vaccination maintain protective antibody in the long term. Indeed, it has been observed that specific antibodies wane more rapidly post-vaccination than in healthy children. The speed of decline of the specific antibodies post-immunization in immunocompromised children may depend on various parameters, such as the type and dose of immunosuppressive treatment, previous vaccinations, time since last vaccines, age, and the activity of the disease, but more studies are needed to define the exact factors that affect the rapidity of this decline. It is important to recommend how frequent the vaccine serology should be assessed in this population and how often vaccine booster doses should be given. For the moment, antibody persistence should be

assessed more systematically in all children on immunosuppressive treatments, especially those on bDMARDs, and against diseases for which the risk of exposure is continuous, such as pneumococci, influenza, tetanus, hepatitis B, VZV and measles. There is also a need to develop laboratory tests, which are more widely available to help monitoring long-term immunity to all vaccine-preventable diseases in high-risk children.

Assessment of immunity is largely restricted to antibody responses because of the difficulty measuring B and T- cell-specific responses outside of specialized laboratories. However, long-term protection is more complex than just measuring the level of neutralizing antibodies. The quality of antibody and B cells (function, repertoire) is also important. There are only few data on recall responses in immunocompromised children and no data on B cell memory functions. It is well-known that antibody levels can be under the protective threshold, although the individual may still be protected by the memory immunity, which can be re-activated very rapidly for some antigens, at least in healthy individuals. Studying the antibody and cellular immune responses in the short- and longer-term post-vaccination in this vulnerable population is crucial for the improved development of vaccine strategies (such as the use of new adjuvants or the use of DNA vaccines) to increase vaccine protection among these children.

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