Clinical Clues / *Klinik İpuçları*

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How Long Should The Interval Be Between Vaccination and General Anesthesia/Surgery?

Aşılama ile Genel Anestezi/Cerrahi Arasındaki Süre Ne Kadar Olmalı?

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Question 1: *We have a patient who is being monitored for retinopathy of prematurity (ROP) and is due for their two month routine vaccinations. The ophthalmologist following the patient mentioned the possibility of ROP surgery under general anesthesia in a week. Should the vaccination be postponed?*

Question 2: *For any reason, should routine childhood vaccinations for infants who are scheduled for general anesthesia and surgery be postponed?*
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Introduction and general information: Vaccination is one of the most effective, economical, and successful health practices for protecting public health, especially during childhood. There is no internationally standardized approach regarding how long to wait between vaccination and anesthesia/surgical procedures. Routine childhood vaccinations can be administered almost monthly or bimonthly, especially during the first year of life when children are more susceptible to infections. Ensuring that vaccinations are not interrupted during this period of susceptibility to infections is one of the top priorities for health authorities. Therefore, it is very important that vaccinations, especially primary vaccinations, are administered on time and without interruption during the first 1-2 years of life. In subsequent years, more flexibility can be exercised regarding the timing of booster doses.

A similar question was answered seven years ago in the clinical tips section of the Journal of Pediatric Infectious Diseases (1). In light of recent evaluations and new developments, a reassessment has been made.

Based on the relevant question and answers, several clinical considerations are important when evaluating the relationship between vaccination and general anesthesia/surgery or examination under general anesthesia alone.

1. Is the anesthesia/surgical process adversely affected after vaccination?

2. Does vaccination before or after anesthesia/surgery affect the effectiveness of vaccination or lead to vaccine failure?

3. What should be the minimum and/or optimal interval between vaccination and anesthesia/surgery?

4. What should be the required interval between anesthesia/surgery and vaccination?

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To provide sound answers to these questions, it would be useful to discuss vaccine immunology, vaccine side effects, and whether anesthesia alone or anesthesia/surgery has immunosuppressive/immunomodulatory effects that could influence vaccine responses.

The formation of sufficient antibodies after vaccination occurs in a healthy child through the balanced functioning of T and B cells. Generally, after primary vaccination, antibodies begin to form after the seventh day and often peak around the first month (3-4 weeks). Subsequently, depending on antibody kinetics and the type and number of vaccines administered, a decline process occurs over months/years. After booster doses, antibody response formation is much faster due to the involvement of memory cells. Antibody responses begin to develop within days (usually 3-7 days) and rapidly reach peak levels (usually within 1-2 weeks). Antibody responses to live vaccines are generally higher than those to inactivated vaccines. Vaccine responses may be lower in immunocompromised patients (such as those with T and B cell deficiencies) and in those taking immunosuppressive drugs. Impairment of vaccine antibody responses is generally expected in cases of severe immunodeficiency (e.g., severe lymphopenia, CD4+ T cell count <15% or <200/mm^3, CD8+ <200/mm^3, or in the presence of severe functional impairment) (2). Live vaccines are vaccines that contain live attenuated microorganisms [such as oral polio vaccine (OPV), oral rotavirus vaccine, nasally administered live attenuated influenza vaccine, Bacillus Calmette-Guerin (BCG), measles-mumps-rubella (MMR), varicella vaccines] that mimic natural infection in the body but cause a much milder clinical course. Viral shedding may occur after live attenuated vaccine administration. This does generally not pose a risk to the patient or their close relatives/contacts. However, OPV vaccination is not recommended if there is a child with immunodeficiency in the family or hospitalized nearby. There is no such risk with the inactivated poliovirus vaccine. With the oral polio vaccine, fecal shedding lasts an average of 4-6 weeks (oral shedding is shorter; 1-2 weeks). After the oral rotavirus vaccine, fecal shedding generally lasts 7-14 days, and after the nasal live attenuated influenza vaccine, nasopharyngeal shedding generally lasts 3-7 days. These periods may vary/be prolonged depending on the age group, individual, or immunosuppression status. In addition, with repeated vaccine administration, shedding periods are generally shorter. After MMR and varicella vaccines, the risk of viral shedding and transmission to others is negligible for healthy children.

General anesthesia can be administered as a combination of intravenous and inhaled anesthetics (balanced anesthesia) or as total intravenous anesthesia. Anesthesia methods are safe practices for both children and adults (3). However, both general anesthesia and surgery can affect the immune system. In this context, if performed recently, there may be a theoretical possibility of affecting immune responses to vaccination. However, no studies providing evidence-based data on vaccination responses and/or interactions with anesthesia/surgery in humans have been found in the literature. In vitro and in vivo studies, mostly conducted in adults, have examined the effects of anesthesia and surgery on the immune system. Some studies have observed a tendency toward lymphopenia, characterized by an absolute decrease in T and B cells, following surgical procedures performed under general anesthesia in children. This trend has been detected to a much lesser extent in newborns (3-5). Other studies have shown that the immunomodulatory adverse effects of anesthesia/surgery on lymphocyte counts and populations (such as a decrease in number and function) return to preoperative baseline levels (normal) within hours and days (3,5-7). In pediatric studies, unlike in adults, neutrophil function was not affected by inhalation anesthesia (3,8). Each anesthetic agent can suppress the immune system through different mechanisms and pathways. These effects on the immune system are primarily on the innate immune system, with only a small portion having the potential to affect humoral responses. Table 1 shows the general

Table 1. Effects of anesthetic agents on immune response (9)

Anesthetic Agent	Effect on Immune Response
Volatile anesthetics	Inhibits lymphocyte proliferation and neutrophil activity, reduces NK cell number and proinflammatory cytokine levels
Propofol	Inhibits neutrophils, monocytes, and macrophages; increases the infiltration of NK cells and assistant T cells in the tissue
Midazolam	Inhibits proinflammatory response triggered by lipopolysaccharides in macrophages
Nitrous oxide	Inhibits monocyte activity
Ketamine	Disrupts intrinsic immunity in animal models; reduces NK cell number and activity
Fentanyl	Inhibits NK cell activity
Morphine	Inhibits neutrophil, monocyte, macrophage and lymphocyte functions; suppresses NK cell function, alters the differentiation of T-assistance lymphocytes
Local anesthetics	Reduces surgical stress response by blocking the sympathetic nervous system in regional and neuraxial anesthesia applications, and thus there is no immunosuppressive effect

effects of anesthesia on the immune response (9). In general, all studies conducted on this subject have shown that immune functions, such as lymphoproliferative responses, are reversible and return to normal preoperative levels within two days. The effects of anesthesia and surgery on the immune system are often considered together (3). The effects of anesthesia on the immune system have been evaluated primarily in in vivo and in vitro studies. These studies, which are observational, involve a small number of patients, and evaluate indirect effects, have not included clinical evaluations (including the effects of anesthesia/surgery on post-vaccination antibodies). Based on an evaluation of the current literature, it has been suggested that the immunomodulatory changes in these laboratory values associated with anesthesia/surgery do not lead to clinically significant outcomes, such as increased risk of infection or vaccine failure (3,9-12).

The perioperative period (anesthesia and surgery) can affect immune responses. In this context, the surgical operation itself may exhibit immunosuppressive properties. Surgical stress can primarily lead to an increase in catecholamine and cortisol levels in response to stress. This effect is expected to be greater in major surgical operations. Furthermore, the stress and anxiety associated with surgery, particularly in some patients, may also contribute to an increase in these stress hormones. These hormones may exert immunomodulatory effects, suppressing macrophage and T cell activity and antibody production (9).

Vaccine side effects can be systemic or local. Systemic side effects, such as fever and fatigue, can sometimes be confused with signs of infection. Side effects of inactivated vaccines usually appear within the first few days. However, after the measles vaccine, which is a live vaccine, side effects such as fever may appear 7-10 days later. The incidence of vaccine-related side effects may vary depending on the type of vaccine and the dose administered. High fever (≥39 °C) associated with vaccines is much less common. Immune thrombocytopenic purpura as a complication after the MMR vaccine is extremely rare (<1/32000) and can be seen up to six weeks after vaccination (3,12). However, due to its very low probability and the fact that no adverse anesthesia/surgical outcomes have been reported, it can be considered negligible. Similarly, there is no evidence or literature suggesting an increase in anesthesia/surgical post-operative complications in humans associated with MMR and other live vaccines (9,11). The OPV vaccine should not be administered to children undergoing surgery in clinics where immunocompromised patients are hospitalized.

It has been suggested that the possible theoretical suppression of the immune system by anesthesia does not lead to an increased risk of infection, that possible/theoretical immune suppression after anesthesia or surgery does not lead to vaccine failure in practice, that avoiding vaccination before or after anesthesia does not lead to a decrease or increase in post-op complications, and that it probably has no significant effect on the development of post-op complications such as fever complications compared to the baseline risk level in unvaccinated individuals (13). Likewise, vaccination is not thought to lead to results that would affect treatment, follow-up, or prognosis (10,13). There is no evidence in humans of failure in routine pre- and post-operative vaccination due to any short-term immunosuppression associated with anesthesia (9). However, vaccine complications and surgical complications may sometimes overlap. Vaccine side effects for inactivated vaccines (diphtheria, pertussis, tetanus, Hib, hepatitis B, hepatitis A) are generally seen within the first 24-48 hours. When the meningococcal B (4CMenB) vaccine is administered simultaneously with the four-component (ACYW) conjugate meningococcal vaccine, a fever reaction is relatively more common within the first 48 hours, and routine post-vaccination paracetamol is recommended for this. However, the likelihood of fever occurring after 48 hours being related to the vaccine is lower. If fever does occur, it is appropriate to investigate other causes of fever. With live vaccines such as MMR, the duration of fever can extend up to three weeks, and sometimes a mild rash may accompany the fever (11). However, it has been shown that vaccine-related side effects such as fever occur at rates similar to or slightly higher than the baseline rates in unvaccinated children (9,11,13). In vaccines such as live attenuated influenza vaccine, rotavirus vaccine, varicella vaccine, and oral polio vaccine, the duration of vaccine-related fever may be shorter. In addition, fever reactions associated with these vaccines are less common. A fever reaction associated with BCG vaccination is generally not expected. Careful clinical (including careful history) and laboratory evaluation is generally helpful in distinguishing between fever due to vaccination and fever due to anesthesia/surgical post-operative complications.

Opportunistic vaccination during anesthesia/surgical procedures; Anesthesia/surgical procedures may present an opportunity (opportunistic vaccination) to complete missing vaccinations in certain situations (particularly in cases of vaccine anxiety and behavioral issues before/after vaccination, resulting in incomplete vaccination) (9,11,14). In such cases, vaccination can be administered during or immediately after anesthesia/surgery. The Centers for Disease Control and Prevention (CDC) recommends that every effort be made to ensure that necessary missing vaccinations are not delayed during hospital stays, including anesthesia/surgery, or upon discharge (10).

In the healthcare system, anesthesia and surgery must be planned and scheduled according to each hospital's characteristics and working conditions to ensure the efficient use of operating rooms and surgical staff. Postponing a previously planned and scheduled surgical operation due to vaccination (when there are routine vaccination or emergency vaccination indications such as rabies or tetanus) can lead to imbalances and additional burdens in the healthcare system and may pose additional health risks for the patient scheduled for surgery.

Different countries around the world may have different views on anesthesia/surgery and vaccination practices. The Australian vaccination handbook states that there is no evidence of adverse effects of anesthesia/surgery in children who have been vaccinated recently or in the past. However, systemic side effects of vaccination, such as fever and malaise, may be confused with post-operative side effects. Patients in a specific risk group can receive their routine vaccinations as recommended, or they can be given electively during surgery/anesthesia (15). This guide also notes that some countries' guidelines state that if elective surgery/anesthesia is to be postponed after vaccination, one week after inactivated vaccines and three weeks after live viral vaccines may be waited, and that routine vaccinations can be given one week after surgery (15).

In the UK, the routine vaccination schedule, especially for infants, should not be delayed due to elective surgical procedures, and emergency surgery should not be postponed due to vaccination (recently administered). After inactivated vaccines, major elective surgery can be performed 48 hours later (this timeframe is appropriate to distinguish between surgical complications and side effects), and there is no need to delay elective surgery after live viral vaccines, but fever at the time of elective surgery should be monitored. To distinguish between surgical complications and side effects, there is no need to delay elective surgical procedures after live viral vaccines, but vaccine side effects such as fever at the time of elective surgery should be considered in the pre-operative assessment. It is stated that vaccines can be administered without time restrictions once the child has recovered and is feeling well after elective surgery (11).

The CDC Advisory Committee on Immunization Practices states that vaccines can be administered before surgery or as soon as possible after surgery, once the patient's condition is stable (3,9,10). According to the CDC's latest recommendation (2024 recommendations reviewed in July 2025), vaccination before or after surgery is not considered a contraindication for a child hospitalized. However, the presence of certain factors (as in general vaccination practice; high fever, unstable general condition, potential for vaccine-surgical complications/side effects, etc.) is considered a precaution (10).

The American Academy of Pediatrics (AAP) states that vaccination close to anesthesia/surgery is not contraindicated. It supports vaccination during hospitalization or upon discharge, provided the patient's general vaccination conditions are suitable, due to anesthesia/surgery. However, during the perioperative period, if blood or blood products are administered, MMR and varicella vaccines are delayed for a certain period (e.g., up to 11 months in the case of high-dose IVIG administration) due to the interaction between antibodies in blood or blood products and live vaccines (9,16). The AAP recommends that in cases of emergency splenectomy, if inactive vaccines such as pneumococcal vaccine have not been administered previously (at least two weeks before splenectomy), these vaccines should be administered as soon as the patient's condition stabilizes after emergent splenectomy (2,17). Previous recommendations from the AAP were to administer vaccines at least two weeks after emergency splenectomy (16,18). However, the latest recommendations have been updated to administer indicated vaccines as soon as the patient's condition is stable, without waiting two weeks (2,16-18). The American Academy of Family Physicians does not make any additional recommendations regarding anesthesia and surgery in its preoperative assessment recommendations for children (2023) (19).

The Turkish Society of Anesthesia and Resuscitation did not evaluate the relationship between vaccination and anesthesia/surgical procedures in its recommendations for preoperative assessment in pediatric patients (2025) (20).

In conclusion; If the above general information is summarized and interpreted within the scope of the question, our general recommendations (in line with the latest recommendations of the American Academy of Pediatrics, CDC, and the UK Good Vaccination Practice) are as follows (2,10,11,15,21):

1. The immunomodulatory/immunosuppressive effects of anesthesia/surgery are short-term (usually a few days), and there is no data indicating that they clinically affect vaccine immune responses and vaccine antibody levels. In this context, it cannot be said that vaccine responses will be adversely affected by anesthesia/surgery. In examinations under general anesthesia, such as ROP screening in premature infants, the risk can be said to be even lower than that associated with additional surgical procedures.

2. The immunological processes induced by the vaccine do not adversely affect the anesthesia and/or surgical process, but systemic side effects related to the vaccine may be confused with the patient's preoperative infection findings or postoperative complications. Therefore, considering the periods when this risk is highest, it is appropriate to perform elective surgery 48 hours after inactivated vaccines and,

especially, three weeks after live vaccines such as MMR. However, in risky situations such as a measles outbreak or contact between a non-immune child/infant and a measles patient, it is appropriate to administer the measles or MMR vaccines without waiting for this period, based on expert advice.

3. Vaccination after anesthesia and surgery can be performed when the patient is clinically well; in the hospital, upon discharge, or after discharge. If there will be no significant delay in the vaccination schedule, a one-week waiting period after anesthesia/surgery may be appropriate. However, it should be noted that this waiting recommendation is not based on scientific evidence. If there will be a delay/gap in the vaccination schedule, the vaccine can be administered while the patient is hospitalized or upon discharge, provided the patient's condition is stable. However, in cases where blood and blood products are administered due to surgical operations, it is appropriate to administer MMR and varicella vaccines after a recommended period (up to 11 months) so that the vaccine antibody response is not affected.

4. In emergency situations (such as traumatic wounds, animal bites, or other emergency surgical procedures), there are no restrictions on administering vaccines after surgery or administering vaccines before surgical procedures. In such cases, rabies, tetanus (such as diphtheria-tetanus or diphtheria-pertussis-tetanus vaccines), and, if indicated, passive immunization such as hyperimmune globulin should be administered immediately, depending on the indication. In such cases, the distinction between vaccination and anesthesia/surgical complications should be made through careful clinical (including history) and laboratory evaluation. A similar approach may also be applicable for outbreaks or high-risk exposure situations that warrant urgent vaccination.

5. In some cases (such as serious vaccine phobia or delays in the vaccination schedule due to vaccine-related behavioral changes), anesthesia/surgery may create an opportunity for opportunistic vaccination.

6. Deficiencies in routine vaccination can lead to more risky outcomes at the individual and community levels. Therefore, all necessary measures should be taken to ensure that the routine vaccination schedule is not disrupted, and delays in the vaccination schedule should not be permitted, especially for simple procedures.

In conclusion, the short answers to the questions asked can be summarized as follows:

1. There is no need to postpone routine vaccinations for ROP examinations; it is recommended that vaccinations be administered on time. If possible, the ROP examination may be postponed for two days after routine vaccination.

2. Routine infant vaccinations should not be postponed in children who will undergo elective general anesthesia/surgery for any reason. To avoid confusion with complications such as fever after vaccination, elective surgery can be performed two days after inactive vaccination, and three weeks after live vaccines such as MMR and varicella.

3. In emergency situations, anesthesia/surgery after vaccination, or vaccination after anesthesia/surgery, can be performed without any time interval.

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