Vaccination and Vaccines: Active and Passive Immunization

Autumn is flu season and the perfect time for physicians to get vaccinated and take the opportunity to examine their vaccination certificate. This article outlines what you need to know about tetanus, diphtheria, and more, including how the vaccines differ in their nature and preparation? We vaccinate you with fresh knowledge.

Active Immunization

Active immunization involves the generation of acquired immunity by the application of antigens in the form of:

- Inactivated pathogens or their components (dead vaccine)
- Pathogens attenuated in their pathogenic effects (virulence) but still proliferative (live vaccines)

Active immunity is a process of exposing the body to an antigen in order to acquire a long-lasting or lifelong adaptive immune response that develops in the days or weeks after exposure.
Dead vaccines

Dead vaccines are weakly immunogenic, which is why multiple applications of the vaccine, as well as regular booster vaccinations, are necessary after successful basic immunization in order to achieve adequate vaccination protection. In addition, dead vaccines have few side effects. Undesirable accompanying reactions are mainly due to the addition of adjuvants. The advantage of dead vaccines is the production of antibodies from antigen related to the infection soon after exposure. Disadvantages include the need to administer several doses in order for a patient to acquire immunity.

Full vaccines

The simplest way of producing dead vaccines is via the cultivation of pathogens on specific culture media (bacteria) or within cell cultures or incubated chicken eggs (viruses), followed by physicochemical purification and inactivation by heat or formaldehyde. Full vaccines obtained in this way comprise all antigenic structures of the pathogen (e.g., human diploid cell (HDC) rabies vaccine, cholera).

Subunit vaccines

In contrast to full vaccines, subunit vaccines contain pathogen antigens that can be isolated from cultures by purification procedures or produced specifically using recombinant DNA technology (e.g., capsular polysaccharides of Haemophilus influenzae type B, pneumococci, meningococci, or typhoid). The main disadvantage of subunit vaccines is the likelihood of repeated local reactions at the site of injection.

Toxoid vaccines

Purified toxins, which are (formalin) inactivated for testing purposes (toxoids), are called toxoid vaccines. Examples are the vaccines against tetanus and diphtheria. They do not create immunity when small doses are administered, so large amounts and multiple doses of the vaccine are needed to ensure long-lasting immunity.

Conjugate vaccines

Polysaccharides produce a weak immunological response based on the T cell-independent activation of B cells. In order to ensure lasting immunity with the formation of IgG and immunological memory cells, vaccines have been developed that, through the coupling of polysaccharides to proteins, elicit T cell-dependent B cell activation (so-called conjugate vaccines). Conjugate vaccines are available against pneumococci (Prevenar), group C meningococci, and H. influenzae type b (Hib).

Adjuvants

Because of the low immunogenic potency of many dead vaccines (e.g., toxoid vaccines), active enhancers (e.g., aluminum hydroxide) are added to the purified excitatory antigens, which nonspecifically enhance the immune response. This is essentially achieved by a locally induced inflammatory reaction, which leads to an increased migration of macrophages and T and B lymphocytes to the site of the pathogen application.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Vaccine Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>Toxoid vaccine from deactivated diphtheria toxin, contains adjuvant</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Toxoid vaccine from deactivated tetanus toxin, contains adjuvant</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Acellular vaccine from different antigens</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Salk vaccine: Trivalent vaccine containing killed polioviruses from 3 different strains</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Genetically engineered vaccine containing the surface antigen (Hbsag)</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Inactivated viruses</td>
</tr>
<tr>
<td>Haemophilus influenzae Type b (Hib)</td>
<td>Conjugate vaccine containing purified capsular polysaccharides</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>Conjugate vaccine containing purified capsular polysaccharides</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>Conjugate vaccine against serotypes A and C, which contains purified capsular polysaccharides</td>
</tr>
<tr>
<td>Typhoid</td>
<td>Vaccine from purified capsular polysaccharides</td>
</tr>
<tr>
<td>Cholera</td>
<td>Full vaccine from killed pathogens for intravenous administration</td>
</tr>
<tr>
<td>FSME</td>
<td>Full vaccine from killed viruses</td>
</tr>
<tr>
<td>Rabies</td>
<td>Full vaccine from killed viruses</td>
</tr>
<tr>
<td>Influenza</td>
<td>Gap vaccines from purified antigens (haemagglutinin, neuraminidase)</td>
</tr>
</tbody>
</table>

**Live vaccines**

Live vaccines are **attenuated pathogens in their pathogenic effect** (virulence). Most live vaccine strains have been long known. Their pathogenicity loss is due to spontaneous mutations that have developed under the repeated passage of animal host organisms or suitable cell lines. Through recent advances in biotechnology, the production of genetically modified attenuated pathogens (e.g., the deletion of virulence genes) has become more possible.

The reproducibility of apathogenic pathogens in the vaccinated person leads to a pronounced immune reaction with the formation of long-lasting immunity. The prerequisite is a functioning immune system since the otherwise unbridled proliferation of the pathogen with the formation of possible vaccination complications can occur. It can trigger illness that is meant to prevent that illness if not attenuated sufficiently.

**Live vaccinations should therefore not be given to:**

- Patients with defects in humoral immunity (B cell defects)
- Patients with T cell defects
- Patients undergoing chemotherapy
- Immunocompromised patients undergoing immunosuppressive therapy (excluding local or low-dose cortisone therapy)
- Patients who have undergone bone marrow or stem cell transplantation (at least 2 years postinterventionally, with sufficient immune status)

Live vaccine is, however, recommended for patients with HIV, as long as there is no immunosuppression, as measured on the CD4+ cell count (see the [Robert Koch Institute’s website](https://www.rki.de)).

**Examples of live vaccines**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles, mumps, rubella, varicella</td>
<td>Attenuated viruses</td>
</tr>
<tr>
<td>Typhoid</td>
<td>Attenuated bacteria; taken orally (typhoral)</td>
</tr>
<tr>
<td>Cholera</td>
<td>Attenuated bacteria; taken orally</td>
</tr>
</tbody>
</table>
Passive Immunization

Passive immunization involves the administration of immunoglobulins to rapidly build up a sufficiently high humoral immunity. Unlike inactive immunization, no immunological reaction or permanent immunity are generated by the vaccine.

Rather, passive immunization serves as a prophylaxis against an infection after pathogen exposure (postexposition prophylaxis), whereby, if possible, simultaneous vaccination with active vaccine (e.g., tetanus prophylaxis in unvaccinated injured persons) should be carried out. This will induce immediate immune response within hours or days. It can also help give immunity to patients who don’t respond to immunization.

The antibodies used in passive immunization are taken from human (homologous antibodies) or animal (heterologous antibodies) donors:

- **Homologous immunoglobulin preparations** mainly contain IgG. Depending on how they are produced, standard immunoglobulins (from a pool of different donors) and hyper-immunoglobulins (from the plasma of donors with high Ak titres) are distinguished. Their average half-life is 21 days.

- **Heterologous antibodies** consist of animal proteins and can cause sensitization reactions, whose frame represents the serum disease. The formation of circulating immune complexes can lead to fever, urticaria, arthritides, conjunctivitis, and proteinuria. In addition, allergic reactions have been noted. For this reason, heterologous antisera should be administered exclusively intramuscularly.

### Human immunoglobulins for passive immunization

<table>
<thead>
<tr>
<th>Disease</th>
<th>Immunoglobulin</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Human standard immunoglobulin</td>
<td>Immunodeficiency in children</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Human standard immunoglobulin</td>
<td>Contact with an infected person</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Human hyperimmune globulin</td>
<td>Pathogen inoculation by needle stick injuries, if there is insufficient Hbs titer (&lt;10 IU / l), postnatal in newborn infants of infected mothers</td>
</tr>
<tr>
<td>Varicella-zoster</td>
<td>Human hyperimmune globulin</td>
<td>Protection of the unborn child in case of infection during pregnancy; Immunocompromised persons after exposure</td>
</tr>
</tbody>
</table>
Rubella | Human hyperimmune globulin | Unvaccinated pregnant women who were exposed to pathogens

Rh- intolerance (anti-D-prophylaxis) | Human hyperimmune globulin | Postpartal (until 72h) with rhesus negative mother at the birth of a rhesus-positive child

Tetanus | Human hyperimmune globulin | Missing/unknown vaccination protection in case of injuries, simultaneous with active immunization

CMV | Human hyperimmune globulin | Immune compromised patients

Rabies | Human hyperimmune globulin | After bite injuries by infected animals

Diphtheria | Animal antitoxin | Especially diphtheria

Botulism | Animal antitoxin | Especially botulism

Passive immunization has some drawbacks, including the fact that the immunity developed lasts for a short period of time and therefore does not provide long-term immunity.

Both active and passive immunity can work together; for example, rabies antibodies generate an immediate response to the rabies virus, and rabies vaccine elicits long-lasting immunity.

**Side Effects of Preventive Vaccinations**

Regardless of the vaccine used, as a result of immunological responses to the vaccine, unpleasant but harmless vaccination reactions can occur. These typically develop within the first 3 days after vaccination. Frequently occurring complaints include local inflammatory reactions (redness, swelling, pain) in the area of the stitch channel.

**More rarely, there is:**
- Fever
- Muscle and joint pain
- Fatigue
- Flu-like symptoms

A diminished form of the disease (e.g., vaccination measles, arthralgia after rubella vaccination) is also possible after the administration of live vaccines.

**Vaccination complications**

Vaccine complications are vaccine-specific side effects that go beyond the normal, expected vaccination reactions. Their probability of occurrence is very low; data are often based on individual case reports. However, physicians must inform their patients of these complications before vaccination begins.

Complications include:
- Anaphylactic reactions (reported with various vaccines)
- Neuritis, neuropathy (diphtheria, tetanus)
- Fever cramps in infants (DPT combination vaccination, measles, mumps, meningococci, pertussis, pneumococcal conjugate vaccine, rubella)
- Guillain-Barré syndrome (FSME, H. influenzae type b, tetanus)
- Encephalitis (TBE, measles)
- Meningitis (mumps)
- Cramps (*H. influenzae* type b)
- Arthritids (measles, mumps, rubella (MMR), rubella)
- Thrombocytopenia (pneumococcal polysaccharide vaccine, MMR-V, MMR, MM, influenza, TDaP)

**Egg protein allergy**

Because some vaccines are in incubated chicken eggs (e.g., measles, mumps, influenza, yellow fever), traces of egg protein can be present within the vaccines. However, these are usually so marginal as a result of the purification process that there is no concern about administration in patients with an egg protein allergy. According to the Standing Committee on Vaccination (STIKO) recommendations (2007), this contraindication only applies to influenza and yellow fever vaccination.

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