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ARTIFICIAL IMMUNIZATION – II

**The 13th lecture for the 2nd-year students
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Immunization and its types I - revision

Immunization = the process leading to the development of immunity

Active immunization

natural: after infection

artificial: after vaccination

Passive immunization

natural: by the transfer of maternal antibodies through the placenta and by breast-feeding

artificial: after an injection of immunoglobulin (antiserum)

Immunization and its types II – revision

Immunization	natural	artificial
active	after infection	after vaccination
passive	by transfer of antibodies through placenta and during breast-feeding	after injecting antiserum (immuno- globulin)

Vaccination – revision

Vaccination = administration of microbial antigens in the form of vaccines with the objective to achieve immunity

Origin of the word **vaccine**:

from the Latin **vacca, cow**

Why cow? Because **Jenner** in 1796 discovered the vaccination against smallpox by means of **fluid from cowpox pustules**

Protective antigens – revision

There is no need to use whole microbes for the vaccination

It is better when the vaccine contains **only** so-called protective antigens

Protective antigens = such antigens, antibodies against which protect from infection

Examples of protective antigens:

diphtheric and tetanic **toxoids**

capsule antigens of pneumococci etc.

surface antigen of hepatitis B virus (HBsAg)

hemagglutinin and neuraminidase of influenza A virus

Types of vaccines – revision

- **Toxoids (anatoxins)**
- **Inactivated vaccines**
- **Chemovaccines**
- **Recombinant vaccines**
- **Attenuated (live) vaccines**

Toxoids (anatoxins) – revision

Toxoid (anatoxin) = bacterial toxin free from toxicity (e.g. by the action of formalin)

Its antigens must remain identical with the original toxin

Therefore antibody (antitoxin) developed against the toxoid can neutralize the original toxin

For better effect, the toxoid has been bound to the carrier called the adjuvant, e.g. $\text{Al}(\text{OH})_3$

Examples of toxoids:

- tetanic toxoid
- diphtheric toxoid
- staphylococcal toxoid

Inactivated vaccines I – revision

Bacterial v. (bacterins) – from carefully killed bacterial suspensions; in practice now only so-called:

- **autovaccines** – from strains directly cultured from a patient – for treatment of allergic states (e.g. asthma bronchiale)
- **stockvaccines** – prepared for stock also for other patients

Both types are successful for treatment of **staphylococcal furunculosis (boils)** and **vaginal candidosis**

Inactivated vaccines II – revision

Viral vaccines – from carefully killed virions:

- **influenza vaccine** (nowadays of the split-type from chemically disintegrated virions, with surface antigens from actually circulating strains)
- **Salk vaccine against poliomyelitis** – in advanced countries
- **antirabic vaccine**
- **vaccine against tick-borne encephalitis**
- **hepatitis A vaccine**

Chemovaccines I – revision

From isolated protective antigens:

Bacterial chemovaccines:

against **pertussis** (acellular mixture of 3 antigens – pertussis anatoxin, filamental hemagglutinin and outer membrane protein)

against **Q-fever**

Viral chemovaccines:

against **influenza** – **subunit vaccine** from isolated hemagglutinin and neuraminidase

Chemovaccines II – revision

Group of capsular polysaccharide vaccines:

against *Haemophilus influenzae* type b

against *Neisseria meningitidis* A and C

against pneumococcal infections (23valent)

against typhoid fever (from Vi antigen)

No cellular immunity follows (humoral only)
nor immunologic memory

For infants the polysaccharide vaccines
must be conjugated with a protein carrier

Recombinant vaccines – revision

Recombinant vaccines = chemovaccines
made from genetically modified microbes
with an inserted gene for the production
of appropriate protective antigen

against hepatitis B (from yeasts with the
gene for HBsAg production)

against papillomaviruses genotypes 6, 11,
16 and 18 (from yeasts with the gene for
the virus surface protein)

Attenuated vaccines – revision

Attenuated vaccines = live strains weakened
by culturing *in vitro*

Bacterial: BCG-vaccine from *M. bovis* –
against tuberculosis
vaccines against typhoid fever
and cholera

Viral: Sabin vaccine against poliomyelitis
vaccine against morbilli
mumps
rubella

Mixed vaccines – revision

Mixed vaccines are nowadays used most frequently

Examples:

Hexavalent vaccine against 1) diphtheria, 2) tetanus, 3) whooping cough, 4) hepatitis B, 5) invasive infections by *Haemophilus influenzae* type b (conjugated) and 6) polio (inactivated)

Trivalent attenuated vaccine against 1) morbilli, 2) rubella and 3) mumps

Different kinds of vaccination

– revision

In most countries following kinds of vaccination are recognized:

- a) Regular**
- b) Special**
- c) Extraordinary**
- d) At injuries and accidents, at not healing wounds and before some therapeutic interventions**
- e) Before travelling abroad**
- f) On request**

a) Regular vaccination – revision

= vaccination of every person of certain age, or of persons in higher risk of infection other than during work

It includes regular vaccination against:

- Diphtheria, tetanus, whooping cough, invasive disease caused by *Haemophilus influenzae* type b, infectious infantile paralysis (poliomyelitis) and viral hepatitis B
- Morbilli, rubella and mumps
- Viral hepatitis B (e.g. of dialyzed persons a.o.)
- Influenza and pneumococcal infections (e.g. persons in hospitals and old people's homes)
- Tbc as so called selective primovaccination of children from families where tbc occurs

b) Special vaccination – revision

= vaccination of persons in the higher risk of infection during pursuance of a profession

It includes special vaccination against:

- **Viral hepatitis B** (e.g. in laboratories with the biologic materials, in surgical departments, students of health professions)
- **Viral hepatitides A and B** (new members of rescue service system)
- **Rabies** (employees of respective institutions)
- **Influenza** (workers in old people's homes etc.)

c) Extraordinary vaccination – revision

= vaccination in extraordinary situations

It includes extraordinary vaccination at:

- **Imminent outbreaks of e.g.**
influenza
hepatitis A
meningococcus meningitis
- **Threat of an terrorist attack and things
like that**

d) Vaccination at injuries etc. – revision

**= Vaccination at injuries and accidents,
with not healing wounds and before
some therapeutic interventions like
surgery on rectum or large intestine**

It includes vaccination

- **against tetanus**
- **against rabies**

e) Vaccination before travelling abroad – revision

**Compulsory vaccination (according to the
place of stay abroad)**

**against yellow fever and
meningococcal meningitis, possibly
revaccination against tetanus,
poliomyelitis and
diphtheria**

**Recommended vaccination against typhoid
fever, cholera, Japanese encephalitis B,
viral hepatitides A and B and rabies**

f) Vaccination on request – revision

**Vaccination on request = voluntary vaccination
(paid one)**

**Against influenza (except specified groups of
persons)**

tick-borne encephalitis

**papillomaviruses (except regular
vaccination of 13-years old girls)**

meningococci (except in outbreaks)

rotaviruses

**hepatitis A (except special vaccination of
rescuers)**

chickenpox

Contraindication of vaccination – revision

Vaccination = stress, but not so great as some
“would-be experts” try to scare the people

During the first week after it the **resistance against
infection decreases**

Because of this the vaccination is sometimes
contraindicated but only relatively

As a rule following persons are not vaccinated:
sick

suspect from infection

reconvalescent

substantially debilitated

Caution is advisable in pregnancy

in allergic states

Aim of vaccination – revision

Aim of vaccination is

- **not only the protection of an individual**
- **but above all the protection of the whole population against transmission of infections**

Only the high number (at least 95 %) of vaccinated persons

- **prevents the transmission of agents of infection on non-immune individuals and**
- **therefore lowers the morbidity and mortality of the infection in question**

...

Prevention, prophylaxis and therapy of infections – I

Prevention of infection = avoiding an infection in the future

As the specific prevention of infection serves the vaccination

Prevention, prophylaxis and therapy of infections – II

Prophylaxis of infection = avoiding an imminently threatening infection

For the prophylaxis, **passive immunization** is usually used

Only rarely for the prophylaxis the **vaccination** is used (e.g. rabies) or the **re-vaccination** (e.g. tetanus)

Prevention, prophylaxis and therapy of infections – III

Therapy of infection

For the therapy the **passive immunization** is used (of course apart from antibiotics); very rarely active immunization by means of autovaccines

Immunization and its types

Immunization	natural	artificial
active	after infection	after vaccination
passive	by transfer of antibodies through placenta and during breast-feeding	after injecting antiserum (immunoglobulin)

Artificial passive immunization

= application of antibodies in the form of antisera or globulins

Formerly: complete animal sera

Present-day preparations for passive immunization:

- animal (heterogenous) sera and globulins (purified and enzymatically split)
- human (homologous) immunoglobulins
 - normal
 - specific

Animal sera and globulins – I

Disadvantages:

They are very antigenic

- body tries quickly to get rid of them
- therefore the protection lasts few weeks only

Complications (even after the first application):

- *Serum disease*
- *Anaphylactic shock* (applying adrenalin and corticoids is essential)

Animal sera and globulins – II

Examples:

Antirabic serum (antigen used for its production = for the immunization of animals = inactivated rabies virus)

Globulin against

botulismus (antigens used for its production = botulotoxins A, B, E)

gas gangrene (antigens used for its production = α -toxins of *Clostr. perfringens*, *Cl. novyi* and *Cl. septicum*)

viper toxins (antigens used for its production = toxins of some European vipers, e.g. *Vipera ammodytes* or *V. berus*)

Human immunoglobulins

Two kinds of human (homologous) immunoglobulin:

- Normal immunoglobulin
- Specific immunoglobulins

Use:

- For the prophylaxis and therapy of some infections
- As a substitution of antibodies in some types of immunodeficiencies

Normal immunoglobulin

Normal immunoglobulin (formerly called normal gammaglobulin)

Origin: from the mix of plasmas from at least 1000 healthy donors → hence it contains antibodies against all common infections

Examples of the use:

- For the prophylaxis of hepatitis A in contacts with the ill
- At the defects of antibody production
- During therapy of serious infections (special intravenous preparations)

Specific immunoglobulins

Origin: from the plasma of actively immunized donors:

- Human **tetanic** immunoglobulin for the prophylaxis of tetanus
- Immune **antistaphylococcal** plasma
- Ig with high titre of antibody against HBsAg for the prophylaxis of **viral hepatitis B**
- Ig for the prophylaxis and therapy of **chickenpox and zoster**
- Ig for the prophylaxis and therapy of **cytomegalovirus infections**
- Ig for the prophylaxis of **tick-borne encephalitis**
- Ig for the prophylaxis of **rabies**
- monoclonal Ab against **RSV** (in premature newborns)

Nonspecific build-up of immunity

Replacement of missing factors: normal Ig, fresh plasma, transfer-factor from lymphocytes

Immunomodulators: components of common urinary and respiratory bacterial pathogens – e.g. peroral autovaccines, stockvaccines and a vast number of commercial preparations

Probiotics: live non-pathogenic strains of microbes reportedly able to re-establish normal mucosal microflora – e.g. strains of *E. coli*, *Lactobacillus acidophilus*, *Saccharomyces boulardii*

Interferon: for the treatment of hepatitis B and C and some malignancies

Recommended reading material

Paul de Kruif: Microbe Hunters

Paul de Kruif: Men against Death

Axel Munthe: The Story of San Michele

Sinclair Lewis: Arrowsmith

André Maurois: La vie de Sir Alexander Fleming

Hans Zinsser: Rats, Lice, and History

Michael Crichton: Andromeda Strain

Albert Camus: Peste

Victor Heisser: An American Doctor Odyssey

Richard Preston: The Hot Zone

Mika Waltari: The Egyptian

Richard Gordon: Doctor in the House

Richard Gordon: Doctor at Large

Please mail me other suggestions at:

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Thank you for your attention