UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

CORSO DI IGIENE

Scuola
di
Medicina

Principle of immunization

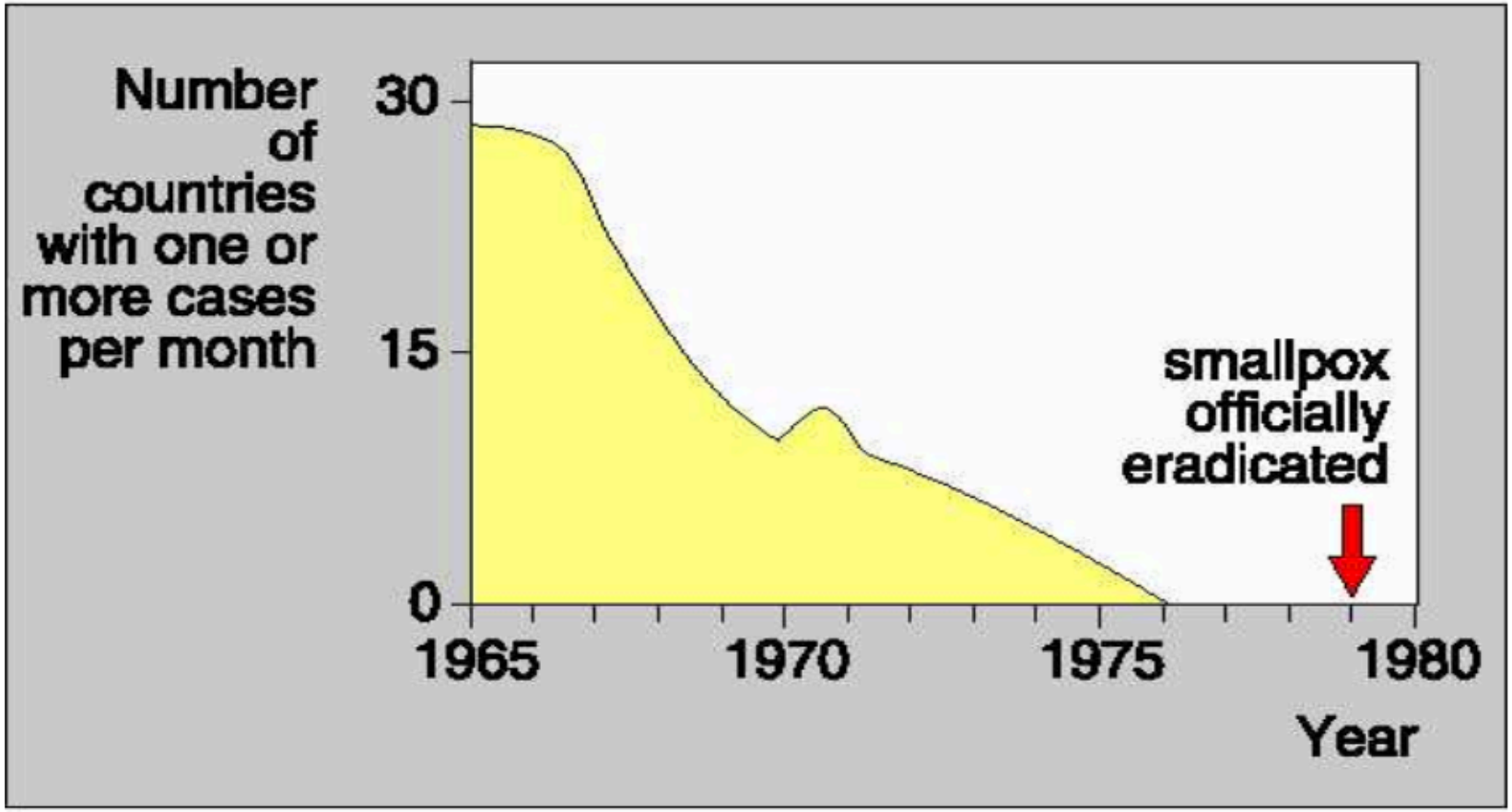
Vaccination is the most effective method for disease prevention

Table 1 | **Reduction of the number of vaccine-preventable diseases in the US**

Disease	Number of cases		
	Maximum	*1997*	*% change*
Diphtheria	206,939	4	99.99
Measles	894,134	138	99.98
Mumps	152,209	683	99.55
Pertussis (whooping cough)	265,269	6,564	97.52
Polio (paralytic)	21,269	0	100.00
Rubella	57,686	181	99.69
Congenital rubella syndrome	20,000*	5	99.98
Tetanus	1,560‡	50	96.79
Influenza (<5 years)	20,000*	165	99.18

Data taken from REF. 5. * estimated; ‡ mortality.

The case of the small-pox



The value of vaccines

Immunisation against infectious diseases has probably saved more lives than any other public health intervention, apart from the provision of clean water.

Bedford H, Elliman D. Concerns about immunisation. *BMJ : British Medical Journal*. 2000;320(7229):240-243.

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

Agenda

- The small-pox eradication
- Mechanism of immunization
- Passive immunization
- Active immunization
- Vaccination strategies
- Epidemiology of vaccinations

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

THE SMALL-POX ERADICATION

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

The history of small-pox vaccine

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

The history of small-pox vaccine

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

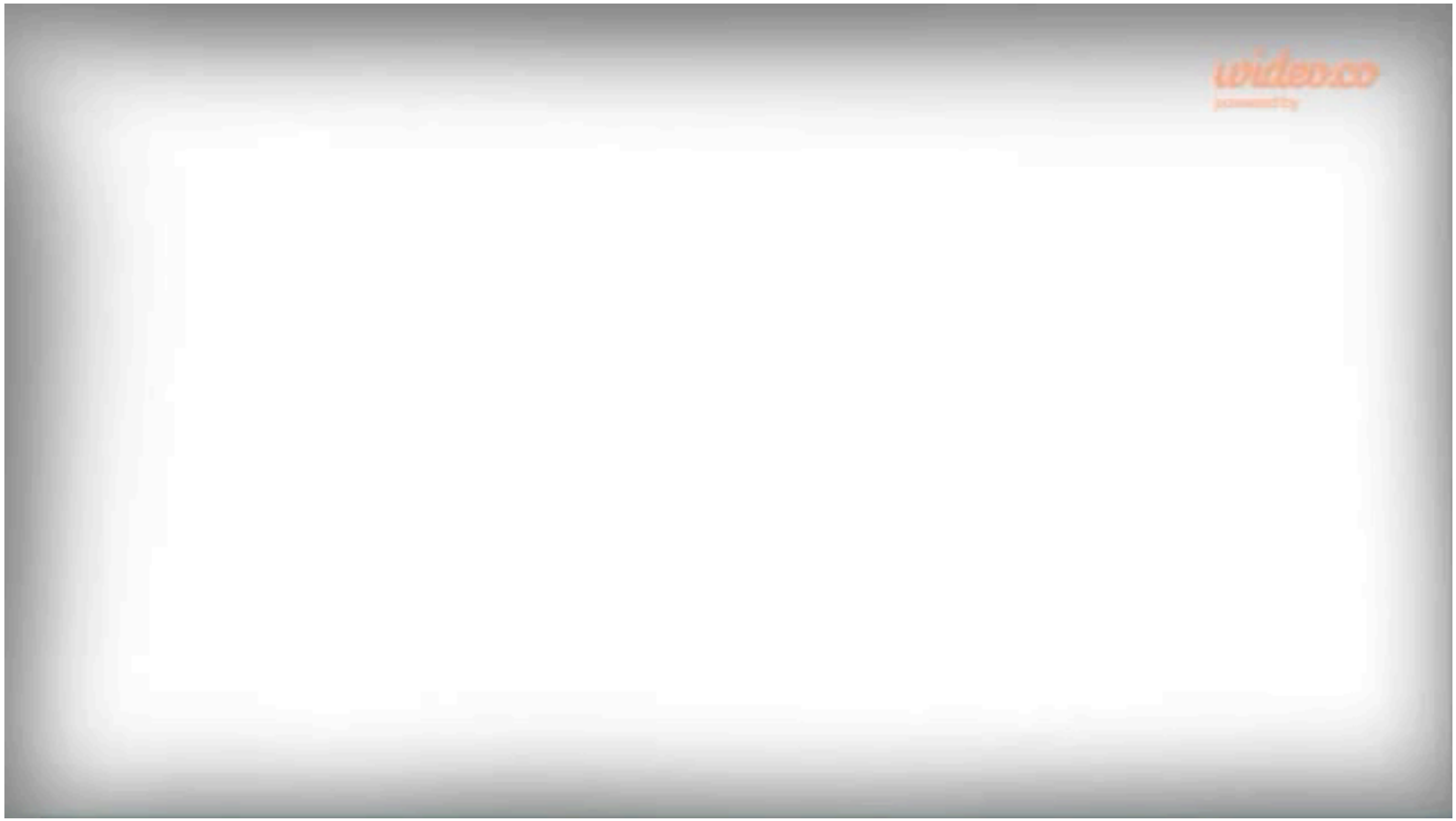
SCUOLA DI MEDICINA
CORSO DI IGIENE

The history of small-pox vaccine

Take home message of vaccine theory

- After a natural infection, our immunity system develops a **"memory"** that protects against new infections related to the same virus or bacterium
- The cowpox was an attenuated virus, that was not able to cause a natural infection, but could determine the memory against future infection

The small-pox eradication

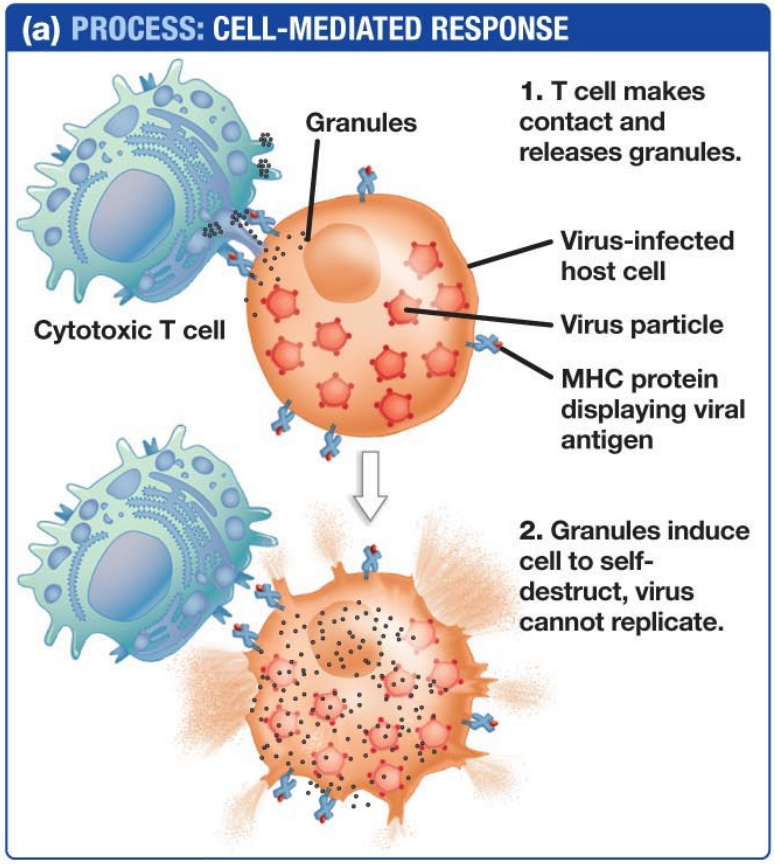


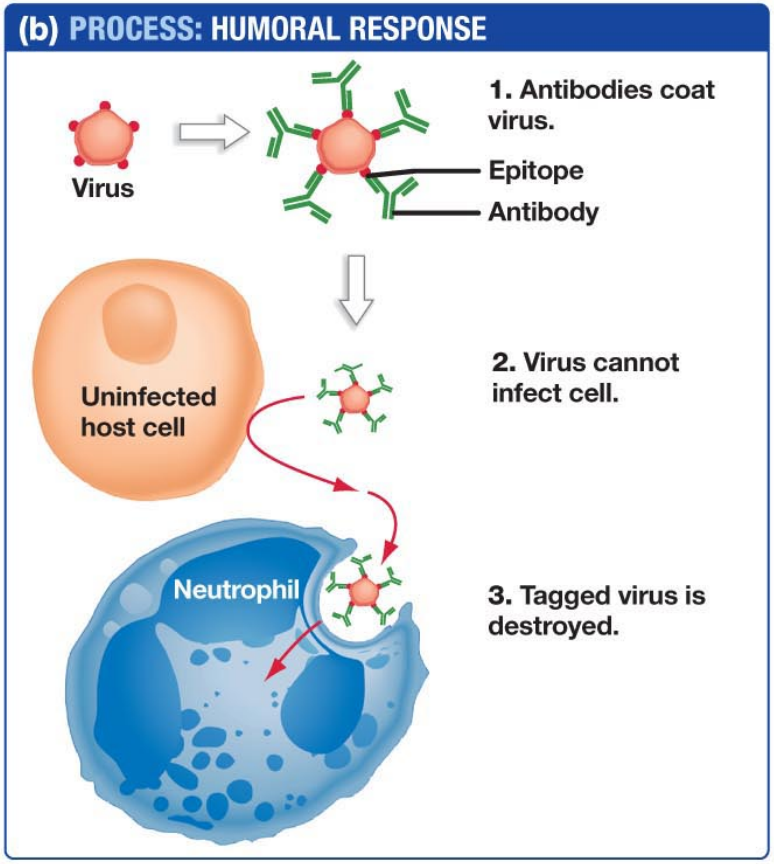
UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

MECHANISM OF IMMUNIZATION

The tools of the memory





Immunization

- Procedure by which the body is **prepared** to **fight against a specific disease**
- It is used to induce the immune resistance of the body to a specific disease
  - Passive Immunization
  - Active immunization

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

IMMUNIZATION

Passive immunization

Administration of serum or gamma-globulins from a person who is already immunized (e.g. who has been affected by the disease) to a non immune person

Passive immunization

Artificial

- Injection of previously prepared antibodies using serum from humans and animals
- Antibodies are able to protect against infectious disease few days after the injection (2-4 days) but for a limited time (e.g. 1-2 months)

Natural

- Antibodies are transferred from the mother to the child
  - During the pregnancy (IgG)
  - By breast milk (IgA)
- The natural passive immunization is crucial to protect infant in the first months against infectious diseases

Passive artificial immunization

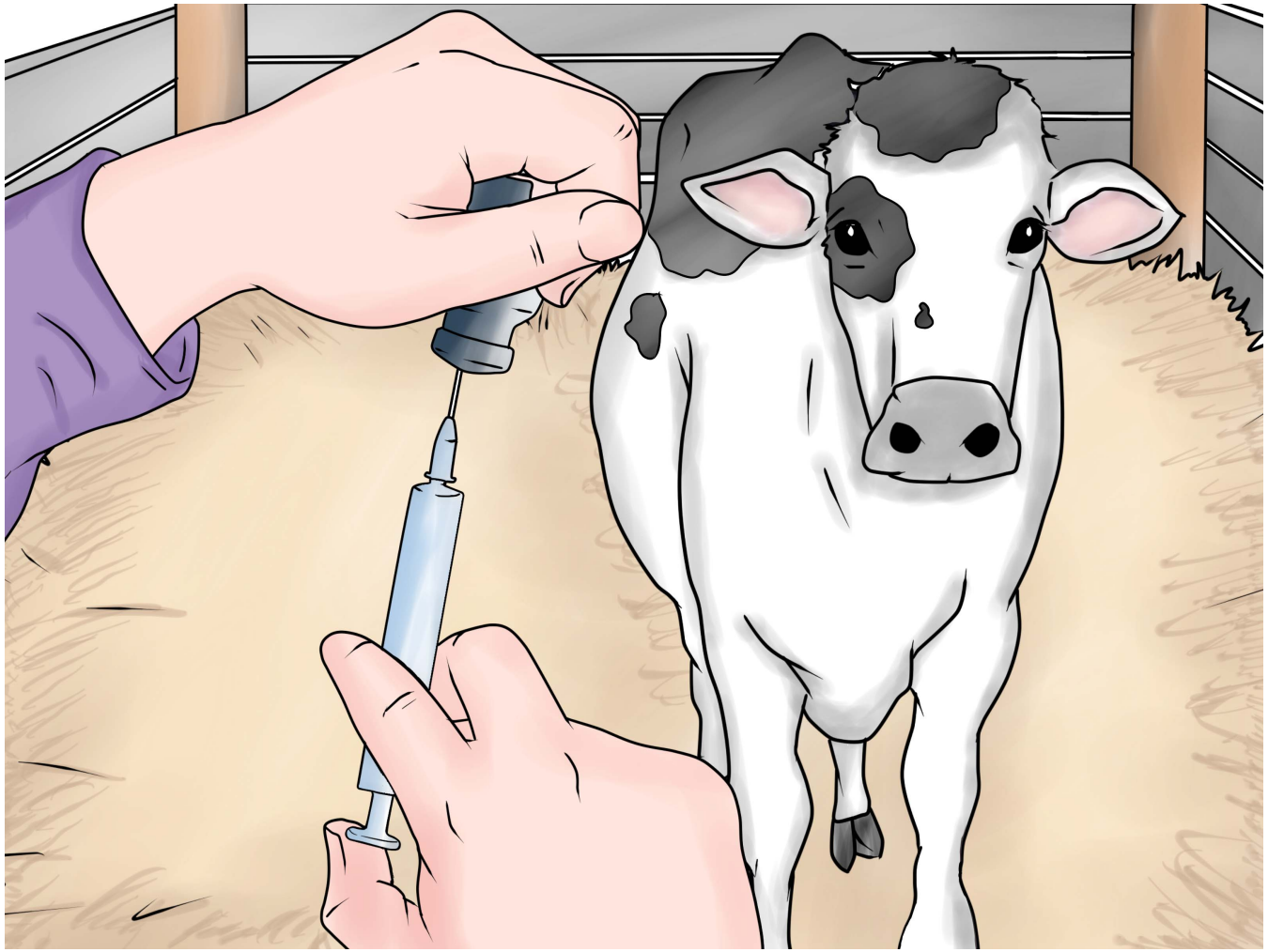
- **Heterologous serum**

derived by an animal, previously immunized with the antigen

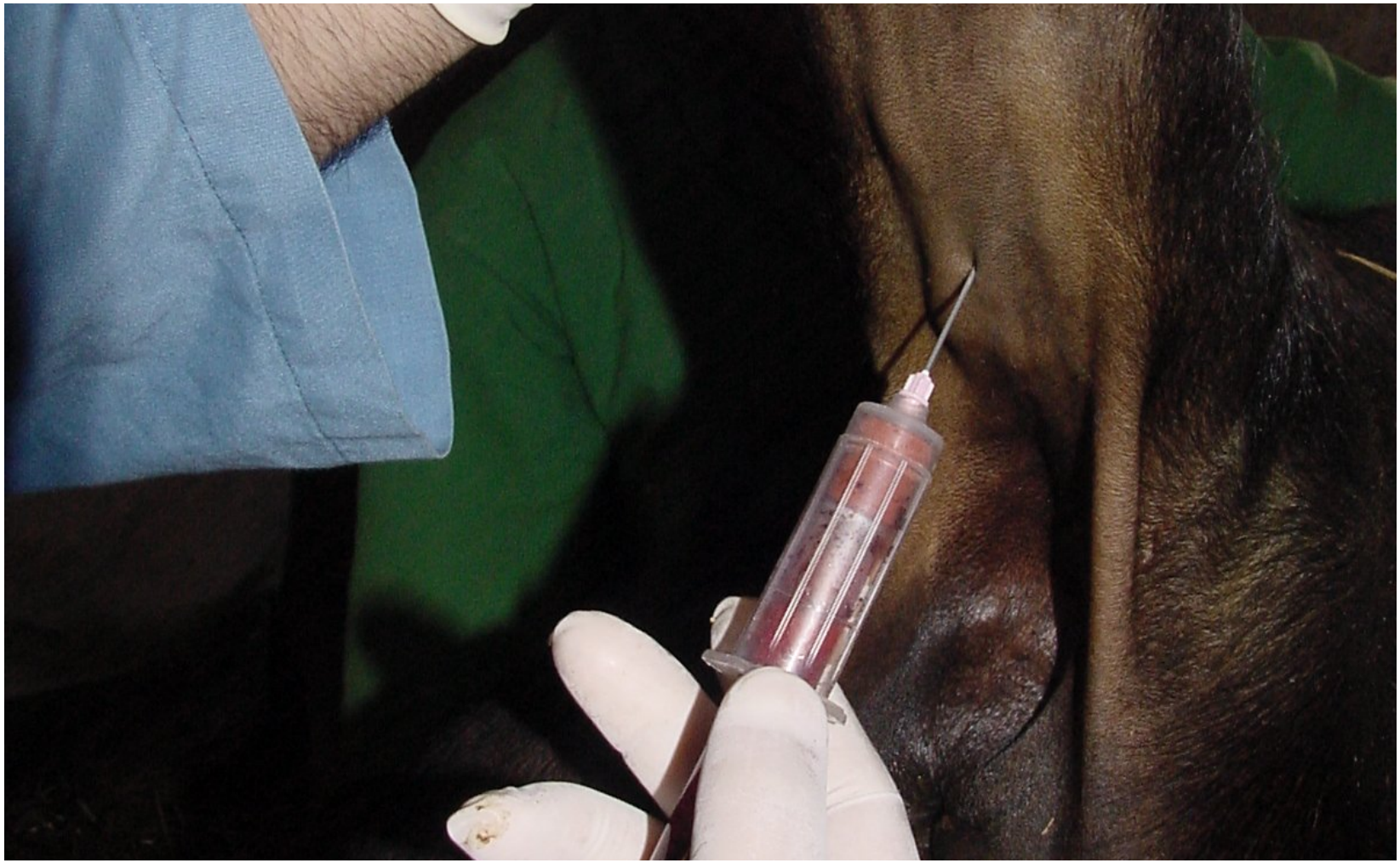
- **Prophylactic immunoglobulins**

derived from human serum of previously immunized persons

Heterologus serum



Heterologus serum



Heterologus serum

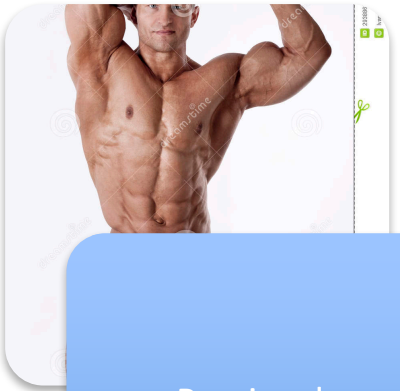
Heterologus serum

- Intra-muscolar or intravenous injection
- Rapid activity (2-3 days after the injection)
- Antibodies are cleaned in 2-3 weeks because the immunity response against animals proteins of serum
- Risk of adverse event:
  - Fever
  - Urticarial
  - Arthralgia
  - Anaphylaxis

Heterologus serum

- Anti-botulism anti-serum
- anti-ophidc serum (for viper venum)

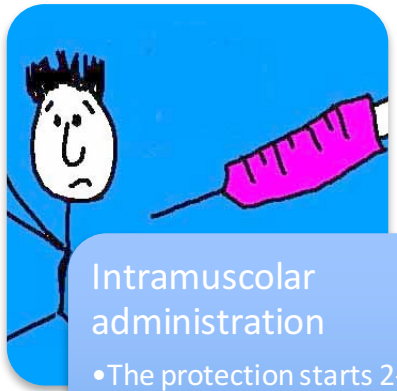
Prophylactic immunoglobulins



Previously immunized man

Blood sample

- withdrawn
- Cohn fraction



Intramuscolar administration

- The protection starts 2-4 days after the administration
- Immunized man remains protected for 4-6 weeks

Prophylactic immunoglobulins

- Adverse events:
  - dyspnea
  - nausea
  - Collapse

Prophylactic immunoglobulins

Subject recently exposed to the one virus

- Hepatis A
- Measles
- Rubella

Prophylactic specific immunoglobulins

- Derivated from sera of several subject recently immunized or recently affected by natural disease (high concentration of IgG)
  - Tetanus
  - Measles
  - Rubella
  - Hepatitis B
  - Varicella zoster

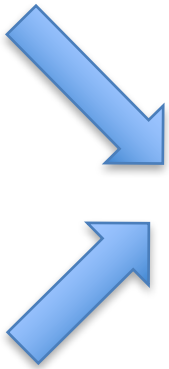
UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

ACTIVE IMMUNIZATION

Active immunity

- Following clinical infection
- Following subclinical infection
- Following vaccination



Natural immunity

The immune responses against infectious diseases

- **Prevention of infection**
  - virus or bacteria are inactivated at the inoculum, e.g. through mucosal tissues
  - Secretory IgA at the mucosal surface are involved in this activity
- **Prevention of disease**
  - virus or bacteria are eliminated after initial replication in the host
  - This mechanism is related to serum antibodies or CD4/CD8 Tcell responses

Vaccination

- Vaccination is a method of giving antigen to stimulate the immune response through active immunization
- A vaccine is an immuno-biological substance designed to produce specific protection against a given disease
- **A vaccine is "antigenic" but not "pathogenic"**

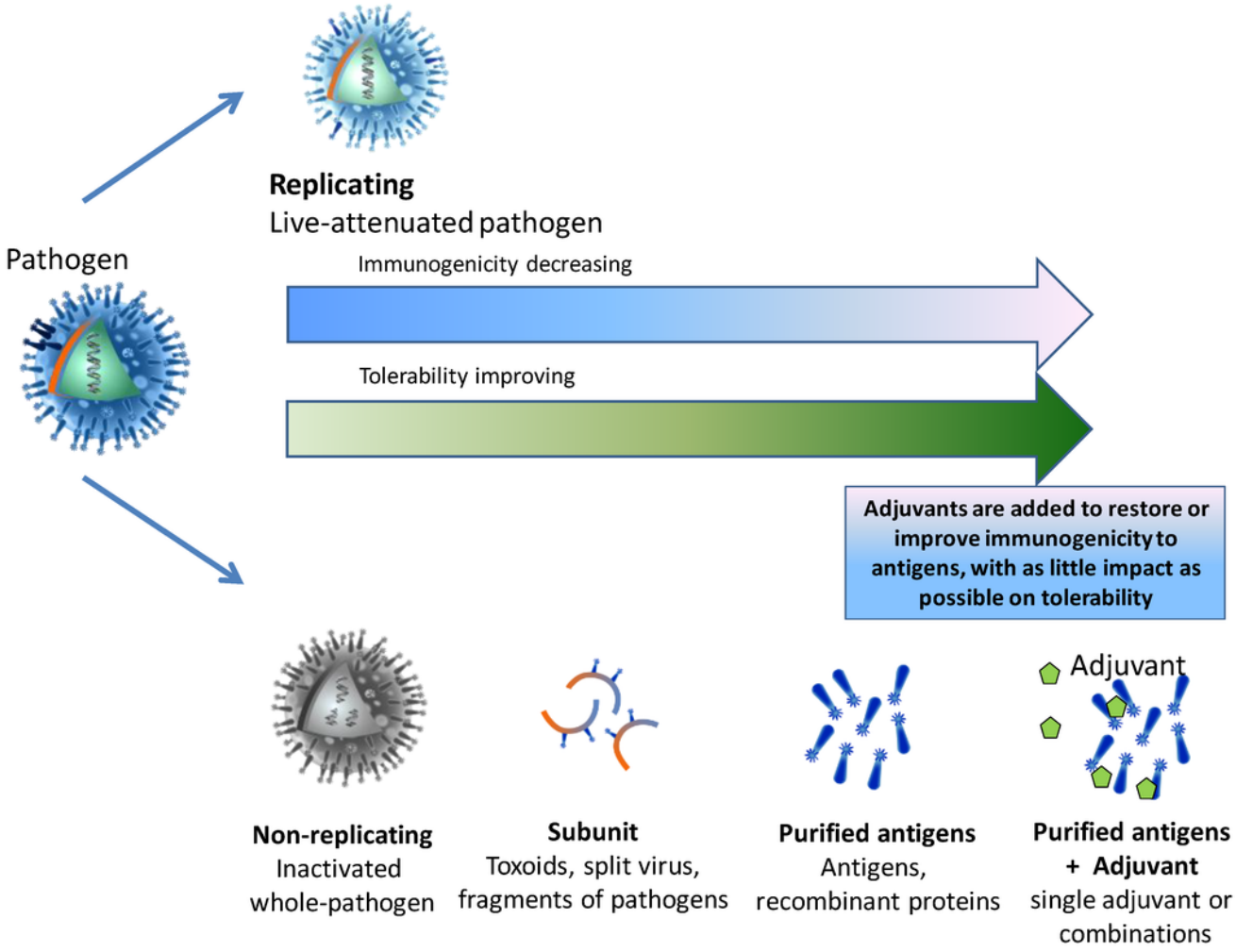
Vaccine ingredients

- Antigen
- Steril water
- Antibiotic (e.g. neomicin)
- Adjuvant
- Stabiliser (e.g. Thimerosal)

Types of antigens

- Live attenuated vaccines
- Inactivated vaccines
- Toxoids
- Polysaccharide and polypeptide (cellular fraction) vaccines
- Vaccines carried out by bio-molecular engineering

Types of antigens



Live attenuated vaccines

Virus

- Poliovirus Sabin
- Measles
- Rubella
- Mumps
- Varicella
- Zoster
- Yellow fever

Bacteria

- BCG
- Typhoid fever

Live attenuated vaccines

Live attenuated vaccines should not be administered to persons with suppressed immune response due to:

- Leukemia and lymphoma
- Other malignancies
- Receiving high doses of corticosteroids or antimetabolic agents
- Pregnancy

Inactivated vaccines

virus

- Oral poliovirus (Salk)
- Hepatitis A
- Rabies

bacteria

- Cholera
- Cellular pertussis (not yet used)
- Typhoid fever

Toxoids

- Vaccine against tetanus
- Vaccine against diphteria

Exotoxins are detoxified by the use of 0.4% phormol at 38°-40° C for 1 month

Vaccines contain adjuvant

Polysaccharide and polypeptide (cellular fraction) vaccines

virus

- plasma-derived Hepatitis B vaccine (not yet used)
- Vaccine against influenza

bacteria

- Acellular pertussis
- Haemphilus influenzae vaccine
- Meningococcal C vaccine
- Meningococcal ACYW135 vaccine
- Pneumococcal vaccine
- Typhoid Fever

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

The immunogenity of polysacharide vaccine is quite concerned….

Respir Med. 2011 Dec;105(12):1776-83. doi: 10.1016/j.rmed.2011.07.008. Epub 2011 Aug 4.

Pneumococcal vaccination in adults: does it really work?

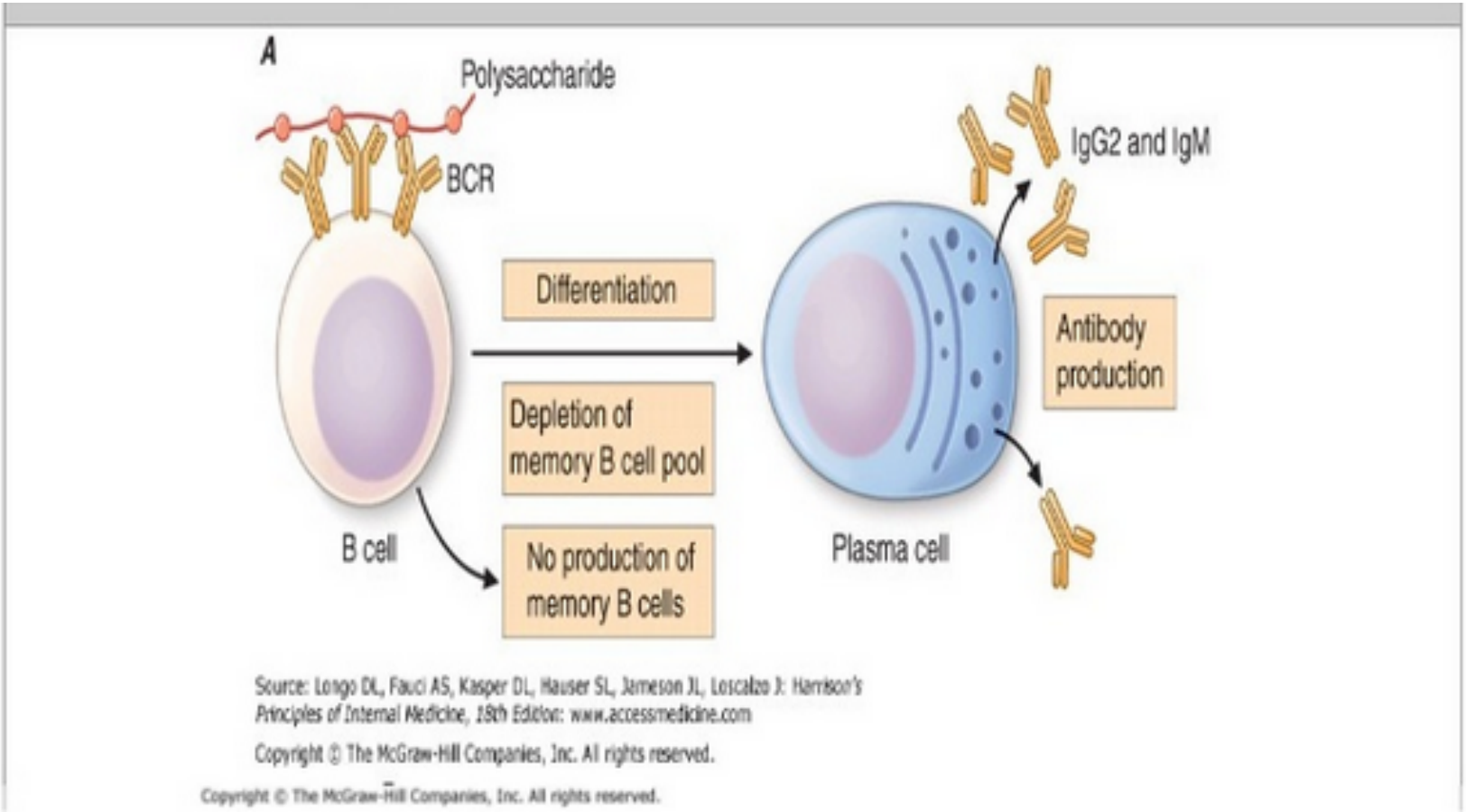
Pitsiou GG[1], Kioumis IP.

Author information

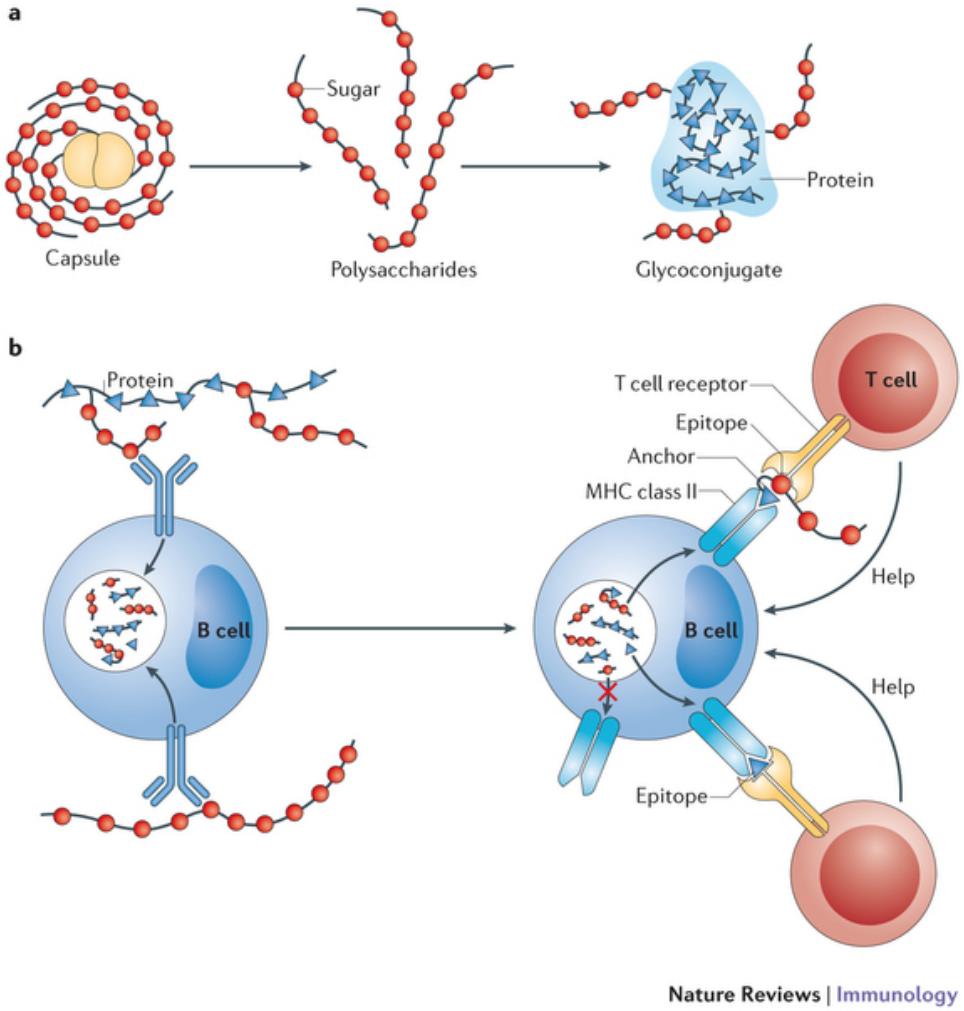
Abstract

The universal burden of pneumococcal disease is high. As pneumococcal capsular antigens induce serotype specific antibodies, both the available vaccines (polysaccharide and polysaccharide conjugated) are able to produce serological response. However, there is reasonable skepticism about the effectiveness and efficacy of the 23-valent polysaccharide vaccine, especially in the elderly and in immunocompromised adults. Results from numerous studies are conflicting but the more recent data suggest that polysaccharide vaccine raises inadequate protection against non-bacteremic pneumonia, while the benefit against invasive pneumococcal disease in high-risk population is uncertain. On the contrary, conjugate vaccine, -originally indicated only for infants and young children- appears to be highly effective but it does not cover the tremendous diversity of pneumococcal serotypes being able to cause disease in adults. Despite this, there is growing evidence that conjugate vaccines, due to their superior immunogenicity, could also be offered for adult vaccination, but still there are certain issues that warrant further investigation.

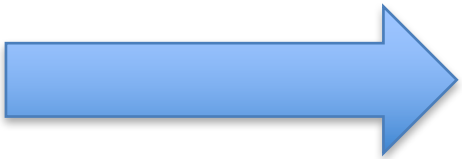
The immunogenity of polysacharide vaccine is quite concerned….



The immunogenity of polysaccharide vaccine is quite concerned….



From polysaccharide to conjugate vaccines



From polysacharide to conjugate vaccines

Vaccines carried out by bio-molecular engineering

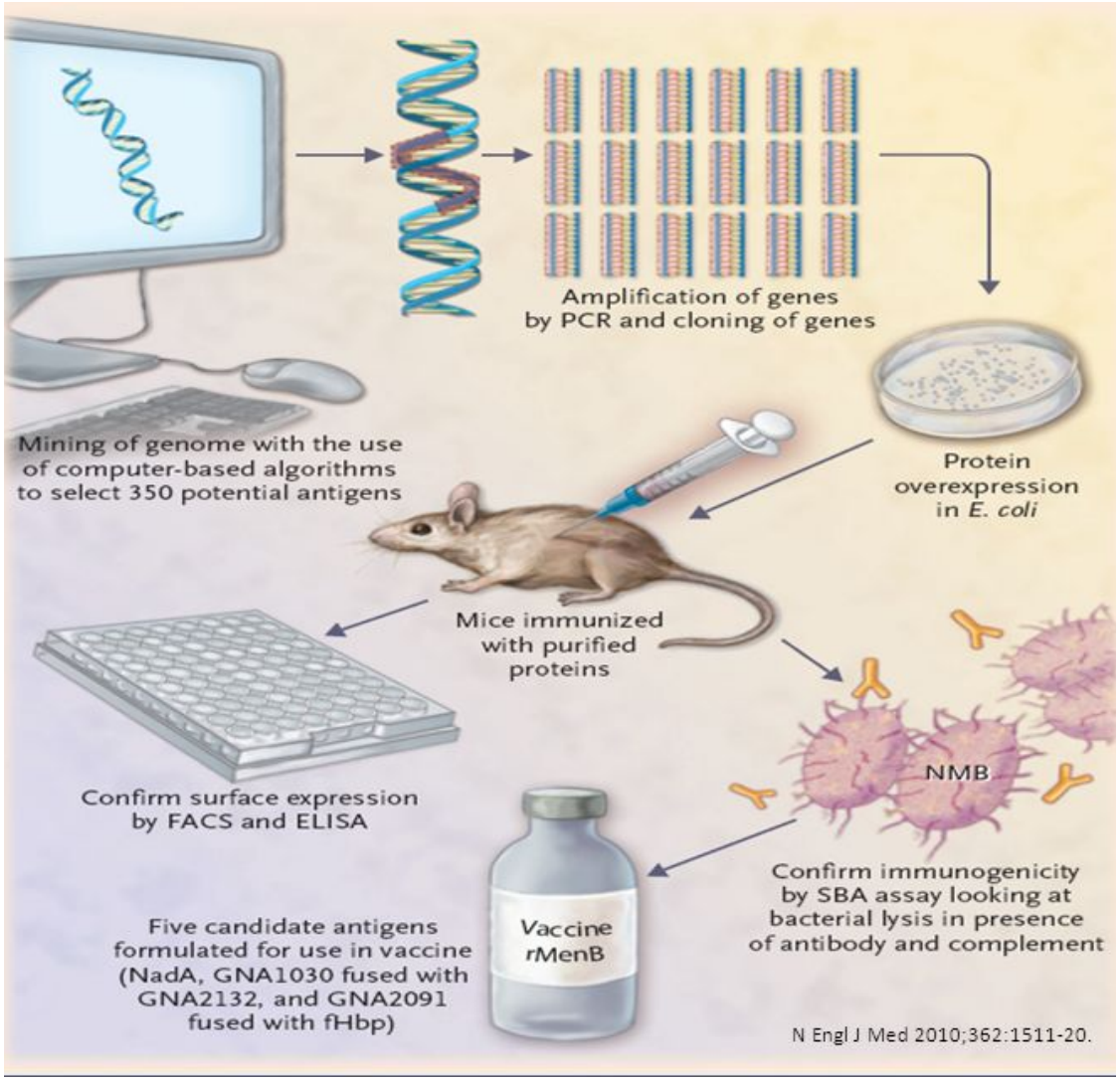
- Hepatitis B
- HPV

One or more genes of the virus are isolated and translated in a vector, to produce surface antigens or virus-like particles (VLP)

- Meningococcal B

Reverse vaccinology

Reverse vaccinology



Reverse vaccinology

Comparative immunogenicity of various types of vaccines

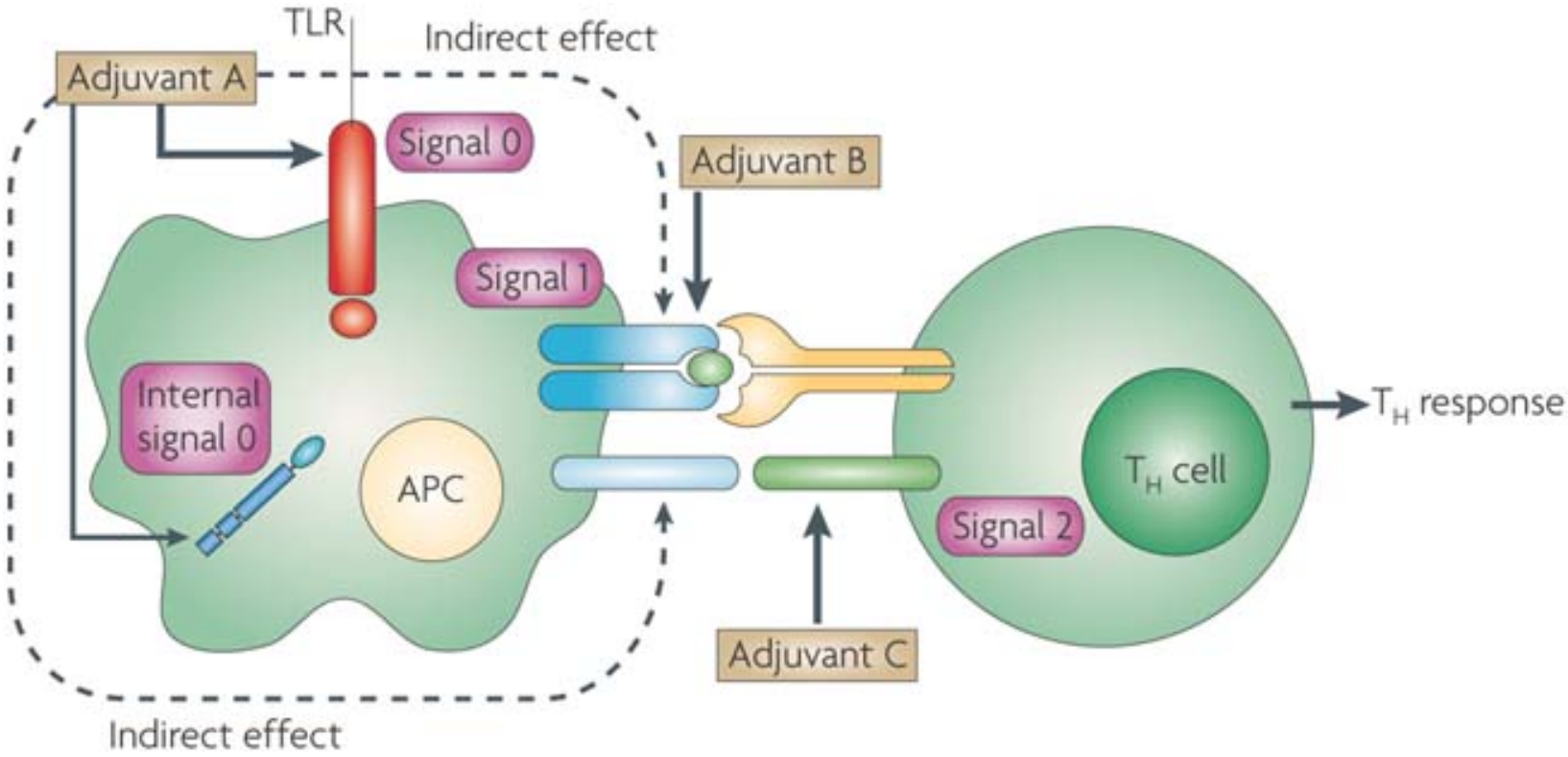
Vaccine	B cells/antibody	CD4+ T cells	CD8+ T cells
Live attenuated	+++	+++	+++
Whole inactivated	+++	++	+/-
Toxoids	+++	++	+/-
Polysaccharide	+	+/-	-
Polysaccharide-conjugate	+++	++	-

Adjuvants

ingredient of a vaccine that helps create a stronger immune response in the patient's body

- Aluminum (used since 1930)
- Monophosphoryl lipid A (used since 2009)
- AS04

Adjuvants



Nature Reviews | Microbiology

Vaccines containing adjuvants

- **Aluminum**
  - hepatitis A
  - hepatitis B
  - diphtheria-tetanus-pertussis (DTaP, Tdap)
  - Haemophilus influenzae b (Hib)
  - human papillomavirus (HPV)
  - Pneumococcus
- **emulsion adjuvants** (MF59® and AS03**)**
  - human papillomavirus
  - Influenza

Aluminum concerns

- alum is able to induce a **good antibody (Th2) response** but it has **little capacity to stimulate cellular (Th1) immune responses**
- Rarely, the use of alum could be related with sterile abscesses, eosinophilia and myofascitis

Petrovsky N, Aguilar JC, *Immunology and Cell Biology* (2004)

Aluminum concerns

Military Toxins, Autoimmune Disorders, The Gulf War Syndrome (GWS) and the Aluminum Adjuvant Vaccine Connection

By Dr. Gary G. Kohls
Global Research, March 09, 2016
Duty to Warn, Duluth Reader
Url of this article:
http://www.globalresearch.ca/military-toxins-autoimmune-disorders-the-gulf-war-syndrome-gws-and-the-aluminum-adjuvant-vaccine-connection/5513017

Gulf War Syndrome refers to the complex of symptoms that affects veterans of the 1990-1991 Gulf War at significantly excess rates. It is characterized by multiple diverse symptoms not explained by established medical diagnoses or standard laboratory tests, symptoms that typically include a combination of memory and concentration problems, persistent headache, unexplained fatigue, and widespread pain, and can also include chronic digestive difficulties, respiratory symptoms, and skin rashes.

…the biological effects of different combinations of pyridostigmine bromide (PB), multiple pesticides, low-level nerve agents, oil and dense smoke from burning wells, depleted uranium (DU) weaponry dust, fuel vapors, exhaust from tent heaters, Chemical Agent Resistant Coating (CARC) paint, airborne particulates, infectious agents, and receipt of multiple vaccines, experienced concurrently or over a brief time period, are unknown. Many have suggested that unknown and difficult-to-characterize effects may have been precipitated by an 'exposure cocktail' or 'toxic soup' effect during Gulf War deployment.

"Non-deployed veterans who reported getting vaccines…had significantly higher rates of symptoms in several domains (chronic somatic pain, neurological, and gastrointestinal problems) and a nearly four-fold higher rate of Gulf War illness than non-deployed veterans who did not receive vaccines. Veterans who served in theater, by comparison, had Gulf War illness symptoms at 11 times the rate of non-deployed veterans who did not receive vaccines."–

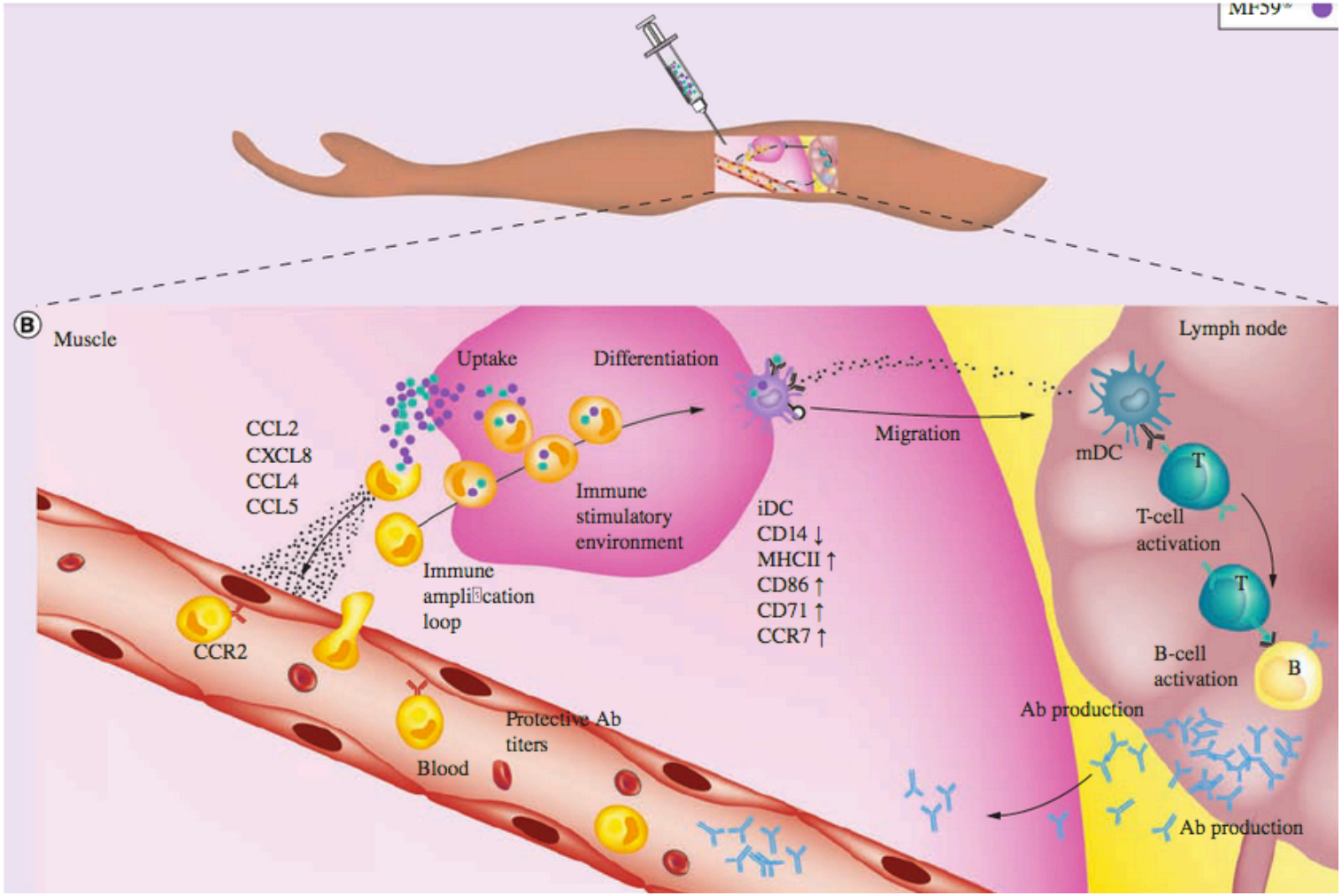
The above three quotes have been excerpted from the 465 page VA scientific document concerning the soldier victims of Gulf War I. There was very little mention of the now-well-known toxic effects of aluminum adjuvants in the document, which can be accessed at:

Safety of aluminum in vaccines

- In 2012, WHO reviewed several studies and data about the possible link between aluminum in vaccines and **neurological disease** or **autism spectrum disorders**
- thecomprehensive risk assessment further supports the clinical trial and epidemiological evidence of the **safety of aluminium in vaccines**

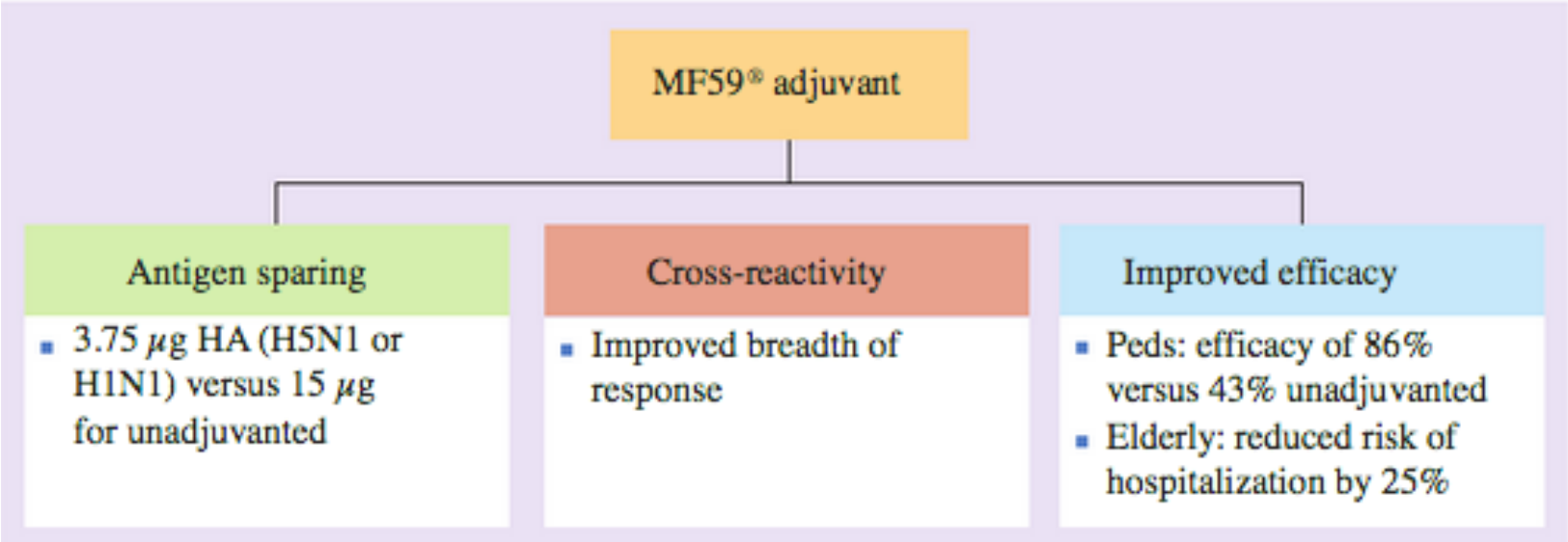
WHO, GACVS meeting, 6-7 June 2012

MF59



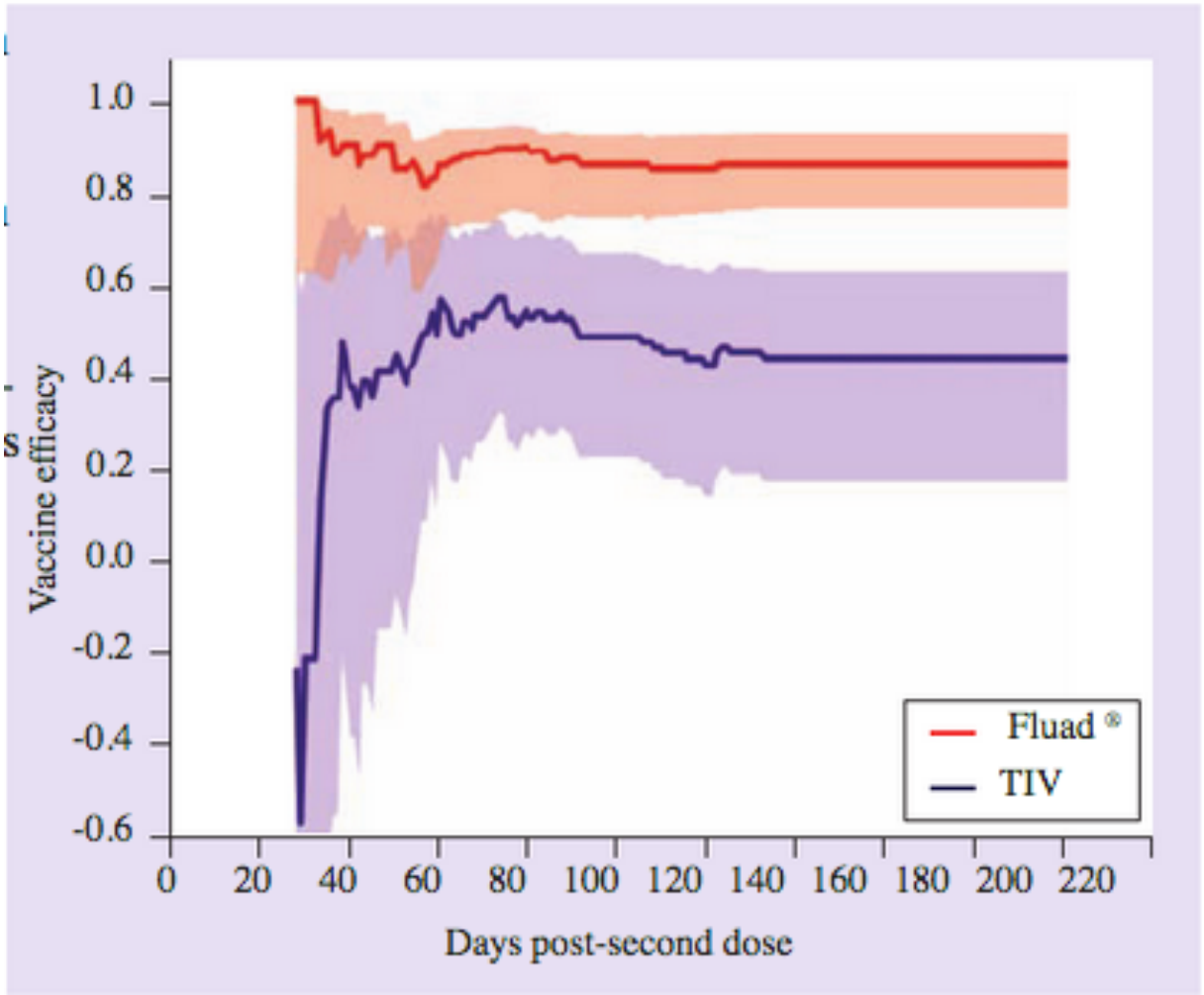
O'Hagan et al, Expert reviews of vaccine 2013

MF59



O'Hagan et al, Expert reviews of vaccine 2013

MF59



O'Hagan et al, Expert reviews of vaccine 2013

MF59 safety profile

- **150 million doses of MF59-adjuvanted vaccines distributed:**
  - Fluad®
  - licensed in 30 countries;
  - 60 million seasonal Fluad doses in the elderly;
  - Approximately 25 million H1N1 pandemic doses, including pregnant women and young children.
- Data available from approximately 120,000 subjects in clinical and observational studies.

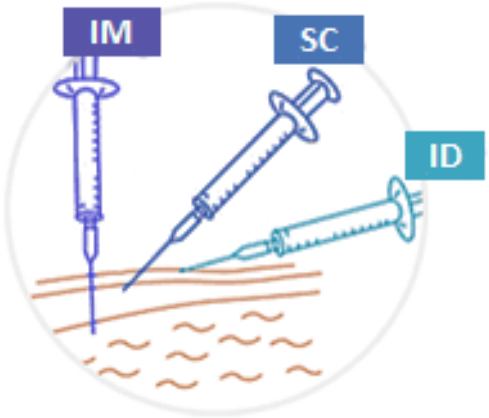
O'Hagan et al, Expert reviews of vaccine 2013

Stabiliser

- The most common stabiliser used for vaccine is Thimerosal, that contains **ethylmercury**
- Thimerosal prevents the growth of bacteria in vaccines.
- The human body eliminates thimerosal easily, than it is **safe** when used **in vaccines**.
- There are some **side effects** of thimerosal in vaccines
- **Scientific research does not show a connection between thimerosal and autism**.

Routes of administration

- **Oral**
  - OPV
  - Rotavirus
- **Intramuscular (IM)**
  - DTwP, DTaP, DT, Td, TT
  - Hepatitis B
  - IPV
  - Hib
  - PCV-7
- **Subcutaneous (SC)**
  - Measles
  - Yellow fever
- **Intradermal (ID)**
  - BCG

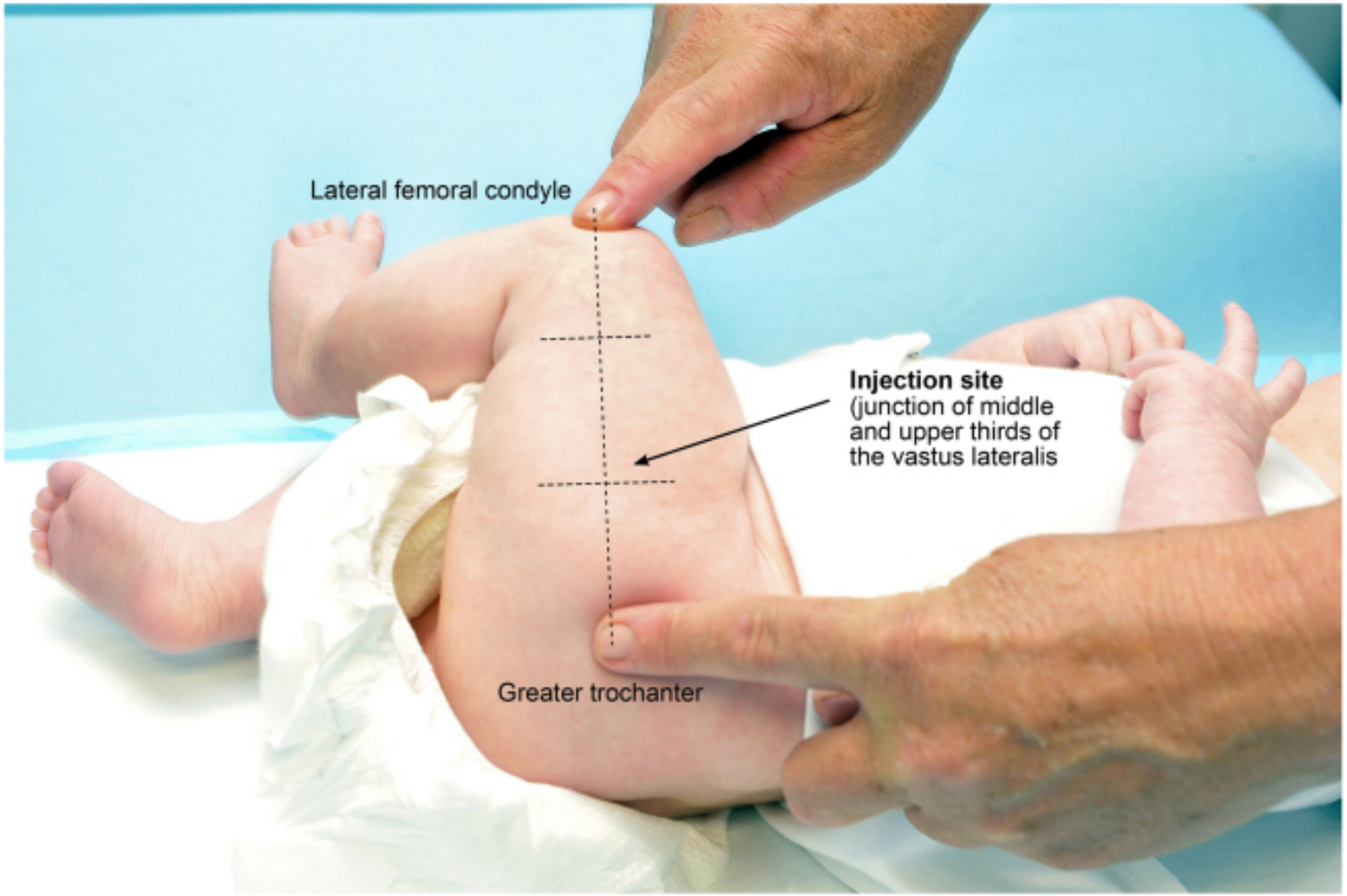


Manufacturers usually recommend the route of administration that limits best adverse reactions of the respective vaccine.

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

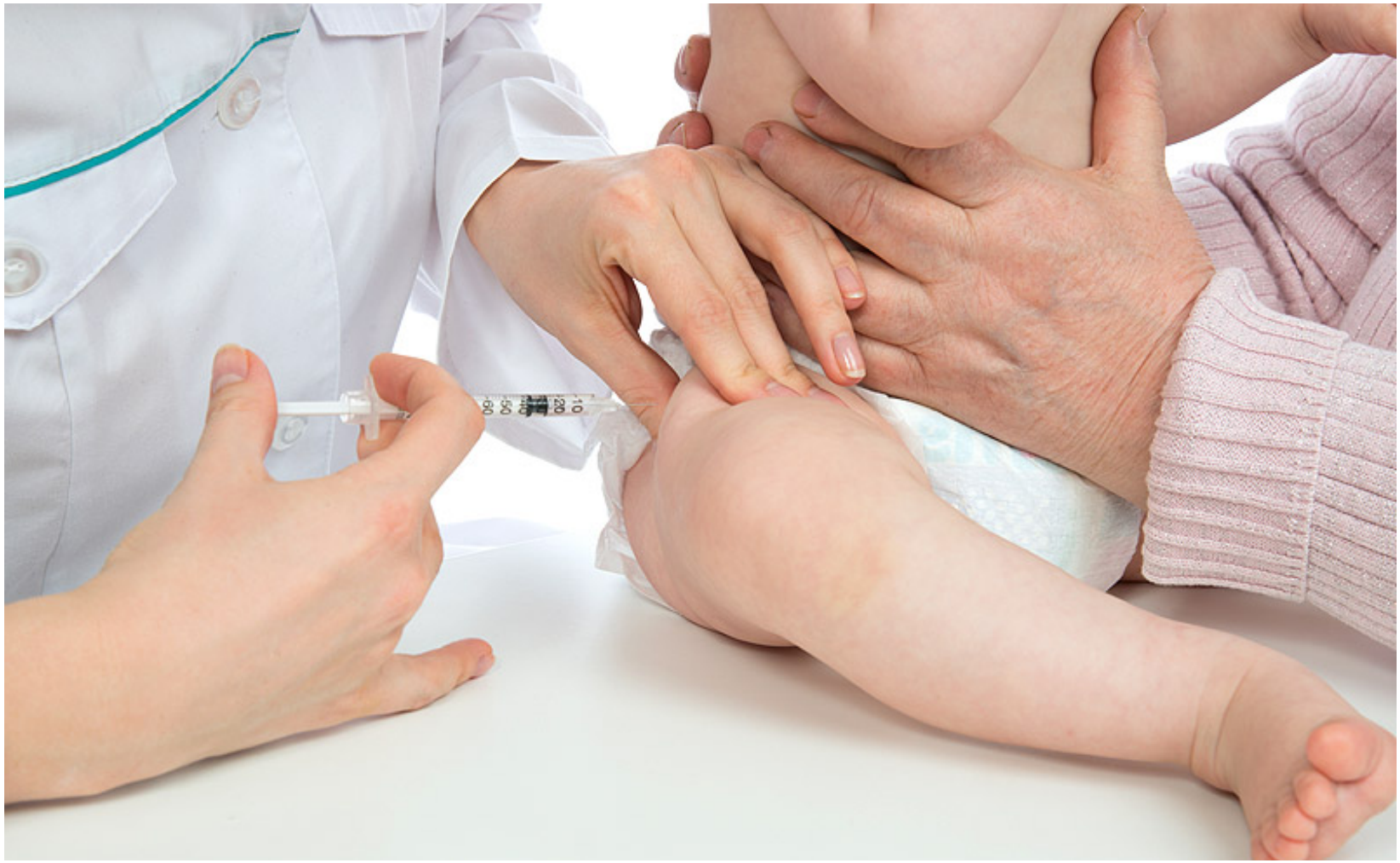
Intramuscolar administration infants



UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

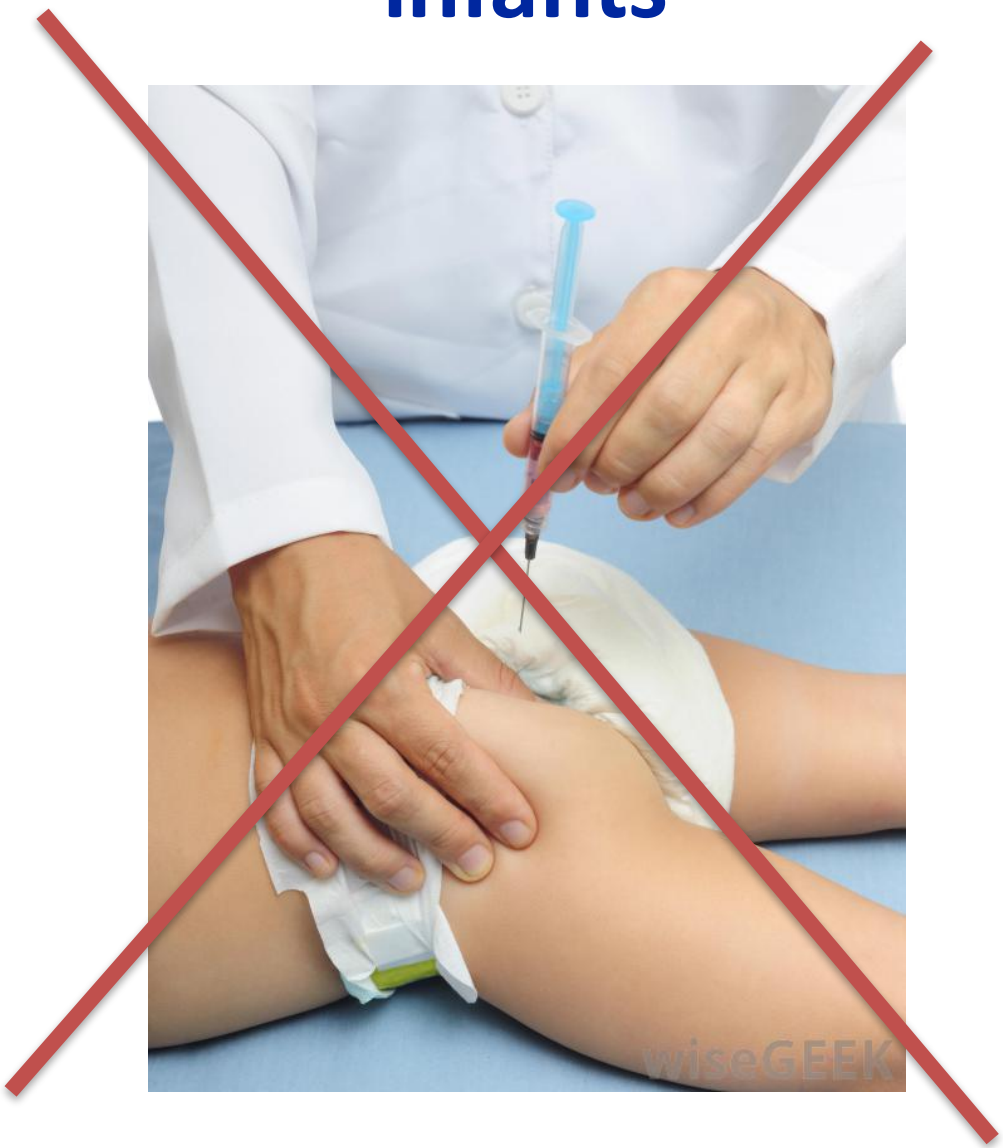
Intramuscolar administration infants



UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

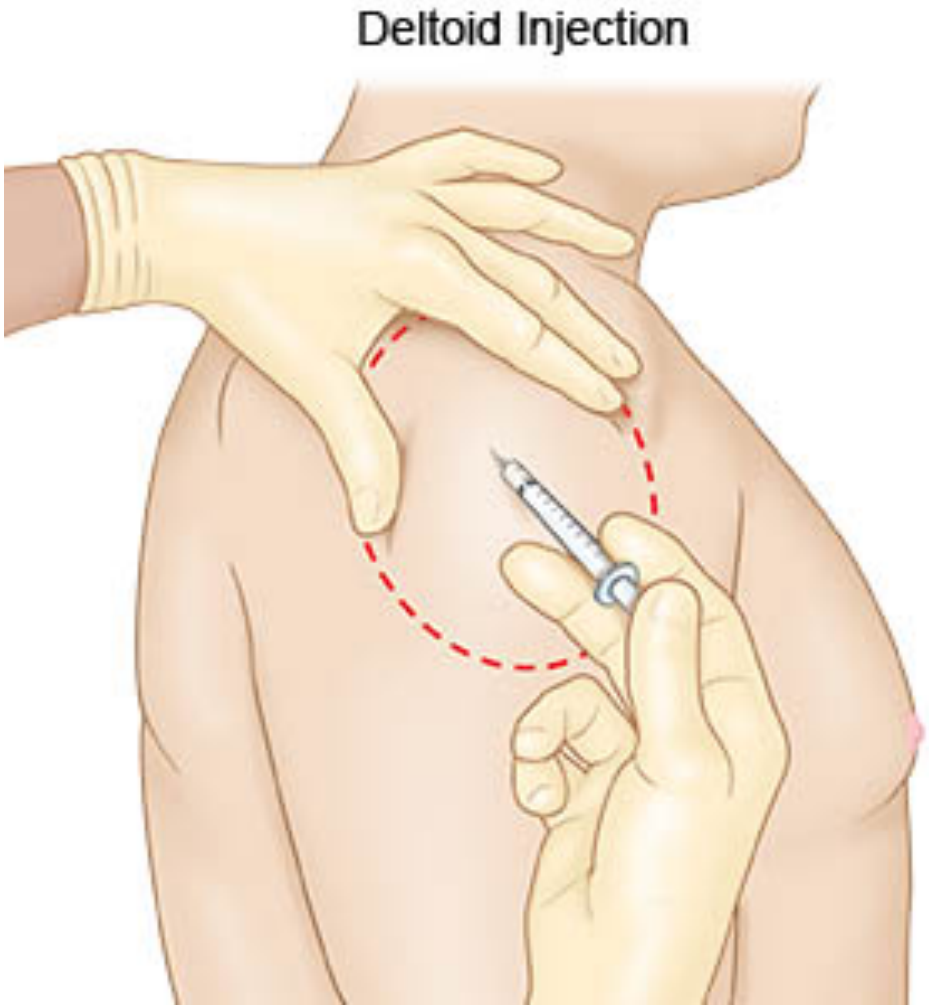
Intramuscolar administration infants



UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

Intramuscolar administration children and adults



JCN Journal of Clinical Nursing
International Perspectives on Healthcare Practice
Explore this journal >

Review

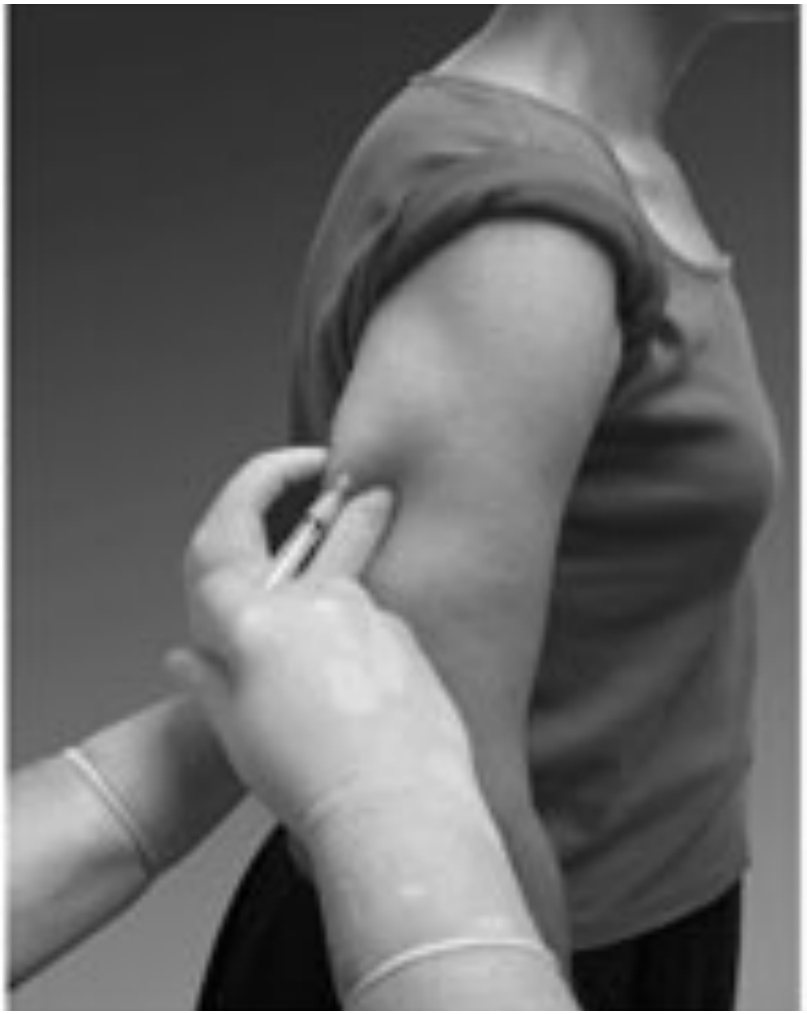
Aspirating during the intramuscular injection procedure: a systematic literature review

Helen Sisson MSc, RHV, RNT

Conclusions

In the paediatric vaccination setting, the practice of aspirating during the administration of an intramuscular injection is unnecessary and there is no clinical reason to suggest that these principles may not be applied when using the deltoid, ventrogluteal and vastus lateralis sites in other settings. Owing to its proximity to the gluteal artery, aspiration when using the dorsogluteal site is recommended. Nurses must be supported in all settings, by clear guidance which rejects traditional practice and facilitates evidence-based practice.

Subcutaneous administration

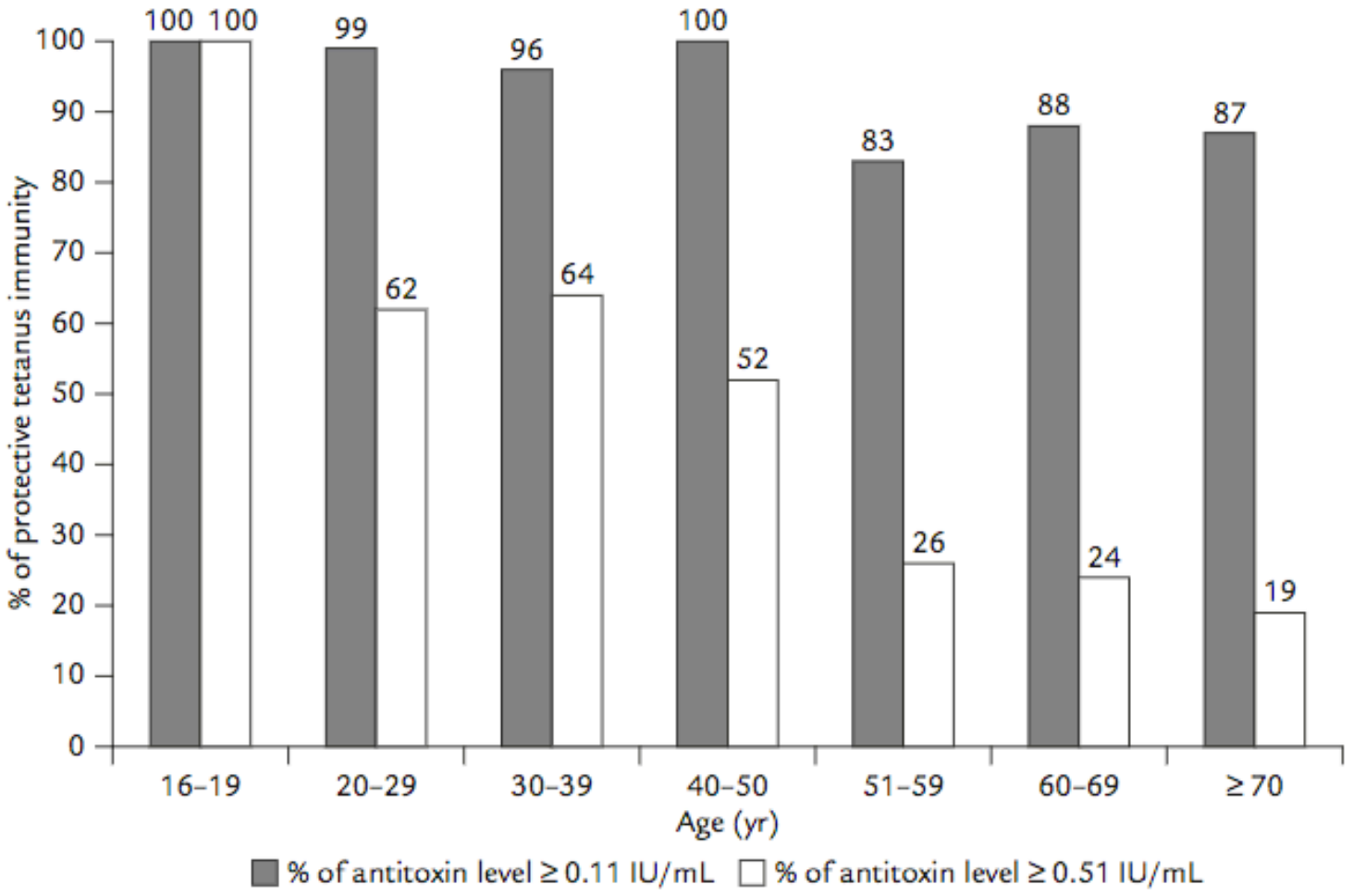


Intradermal administration

Scheme of immunization

- **Primary vaccination**
  - One dose
    - BCG
    - Hepatitis A
  - Multiple doses
    - Polio
    - Difteria, tetanus, pertussis
    - Hepatitis B
    - Measles, mumps, rubella
    - Varicella
- **Booster doses**
    - Difteria, tetanus, pertussis
    - Polio
    - Hepatitis A

Why a booster dose?



Wu CJ et al, J Formos Med Assoc. 2009

How long is the immunity related to the vaccine?

Period of protection	Vaccines
Some months	cholera
2 years	Typhoid fever (live attenuated)
3-5 years	DTaP, Polio
10 years	Yellow fever
>10 years (long life)	Hepatitis B, measles, mumps, rubella, varicella, pneumococcus, meningococcus

Indication for vaccine storage

- Vaccine are biological products and manufacturers must indicate the reccomendation for correct storage in the RCP
- The trasport of vaccine must respect the "**cold chain**", in particular for live-attenuated vaccine
- Uncorrect storage could cause vaccine primary failure

Polio and measles are the most sensitive vaccines to heat

Indication for vaccine storage

Indication for vaccine storage

Adverse events following immunization (AEFI)

Any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine

WHO

Key points about AEFIs

- There is **no such thing as a "perfect" vaccine** which protects everyone who receives it AND is entirely safe for everyone.
- Effective vaccines (i.e. vaccines inducing protective immunity) may produce some **undesirable side effects which are mostly mild and clear up quickly**.

WHO

Key points about AEFIs

- The majority of events thought to be related to the administration of a vaccine are actually not due to the vaccine itself - many are **simply coincidental events**, others (particularly in developing countries) are due to human, or programme, error.
- It is not possible to predict every individual who might have a mild or serious reaction to a vaccine, although there are a few contraindications to some vaccines. **By following contraindications the risk of serious adverse effects can be minimized.**

WHO

Classification of AEFI

- The inherent properties of the vaccine (**vaccine reaction**)
- An error in the immunisation process (**programme error**)
- Injection-related reactions arising from anxiety about or pain of the injection
- **Coincidental events**

Vaccine reaction

By type

- Local adverse reactions
- Systemic adverse reactions

By frequency

- Common, usually minor and self-limiting
- Rare and more serious

Local adverse reactions

- pain, swelling, redness at site of injection
- occur within a few hours of injection
- usually mild and self-limited

Systemic adverse reactions

- fever, malaise, headache
- Nonspecific
- may be unrelated to vaccine
- Urticaria
- anaphylaxis

Common vaccine reactions
MMR

Symptom or sign	Maximum difference in rate*		Peak frequency (days after vaccination)
	(%)	CI (95%)	
Local erythema (>2 cm)	0.8	0.1-1.4	2
Other local reaction	0.4	0-1.4	2
Mild fever (<38.5°C rectal)	2.7	0-6.1	10
Moderate fever (38.6-39.5°C)	2.9	1.6-4.3	9
High fever (>39.5°C)	1.4	0.7-2.1	10
Irritability	4.1	2.1-6.1	10

Rare vaccine reactions

- seizures
- thrombocytopaenia
- hypotonic hyporesponsive episodes
- persistent inconsolable screaming
- anaphylaxis

Although **encephalopathy** is included as a possible rare reaction to measles or DTP vaccine, there is **no difference in incidence between vaccinated and unvaccinated people**.

Anaphylaxis: emergency approach

- Call emergency service (118)
- Adrenaline:
  - 0.5 ml immediately by intramuscolar injection
  - 0.5 ml every 20 minutes if blood pressur is below 100 mmHg
- Antihistaminic drug by intramuscolar injection

Programme errors

- errors and accidents in vaccine preparation, handling, or administration
- the most common programme errors are **non-sterile injections** leading to bacterial or viral **infections**

Injection reaction

psychological reaction that spreads between individuals of the group, when a member suffers a reaction

- fainting (vasovagal reactions)
- Hyperventilation
- anxiety
- light-headedness
- dizziness
- tingling around the mouth and in the hands
- chest pain

Post marketing surveillance of vaccines

WHO strongly reccomends post marketing surveillance of vaccines because:

- Pre-licensure evaluation, based on clinical trial, is not able to observe long-time effects of vaccines
- In pre-licensure evaluation, some subgroups (e.g. females) could be excluded
- Uncommon and rare vaccine reactions may not be detected before vaccines are licensed

WHO, Vaccine safety basic

Vaccine safety: the need of accountability

- In recent years, in several industrialized countries the number of parents choosing to have **their children not vaccinated** is **increasing**
- The decrease of vaccination coverage is related to the activities of **antivaccination movements**
- Frequently, these movements **denounce** that national authorities do not carry out **postmarketing surveillance activities** about the incidence of adverse event following immunization

Tafuri S et al, Expert Review of Vaccine 2015

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

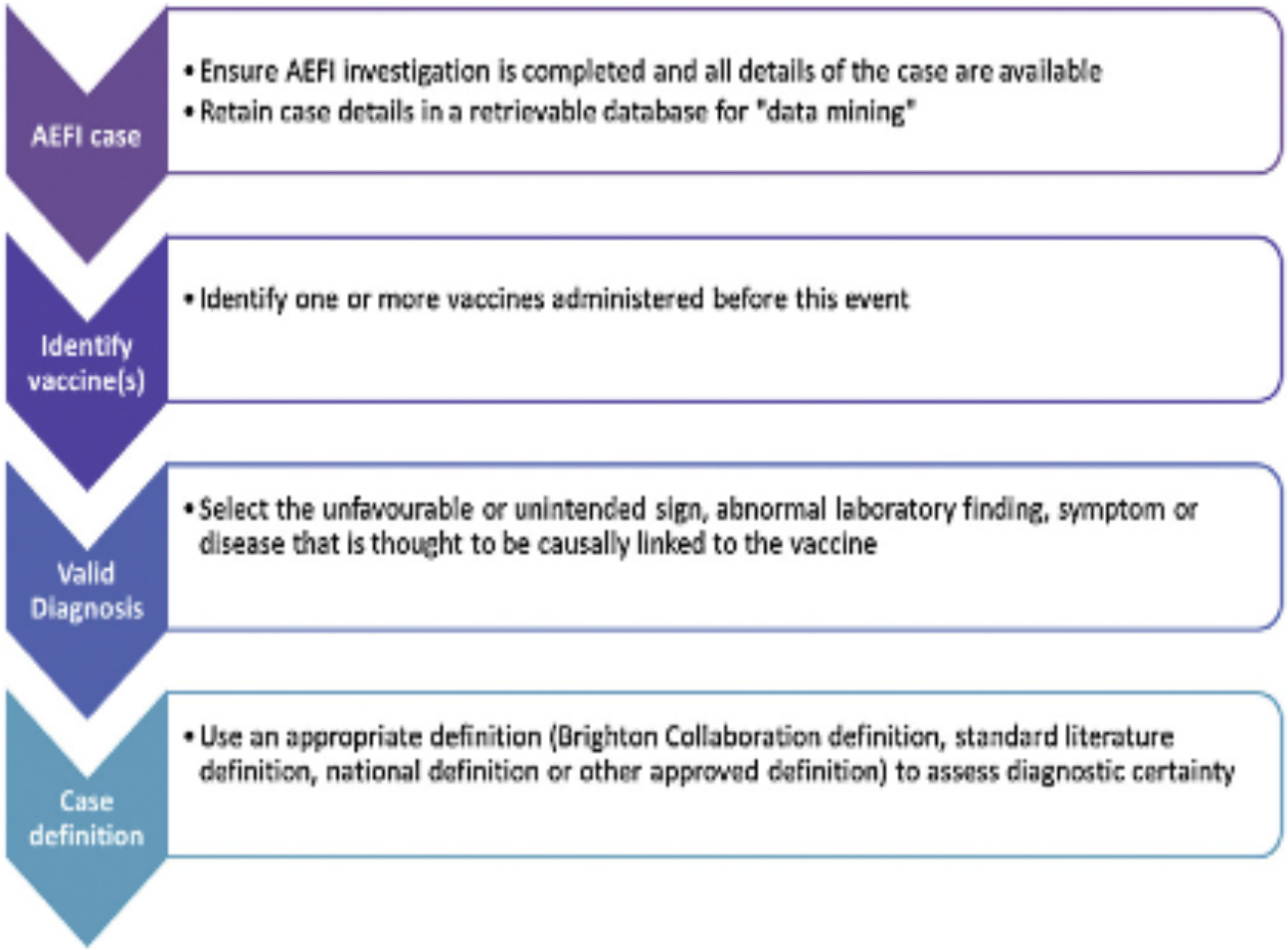
SCUOLA DI MEDICINA
CORSO DI IGIENE

Causality assessment of an adverse event following immunization (AEFI)

User manual for the revised WHO classification

World Health Organization

Causality assessment: eligibility



Causality assessment algorithm

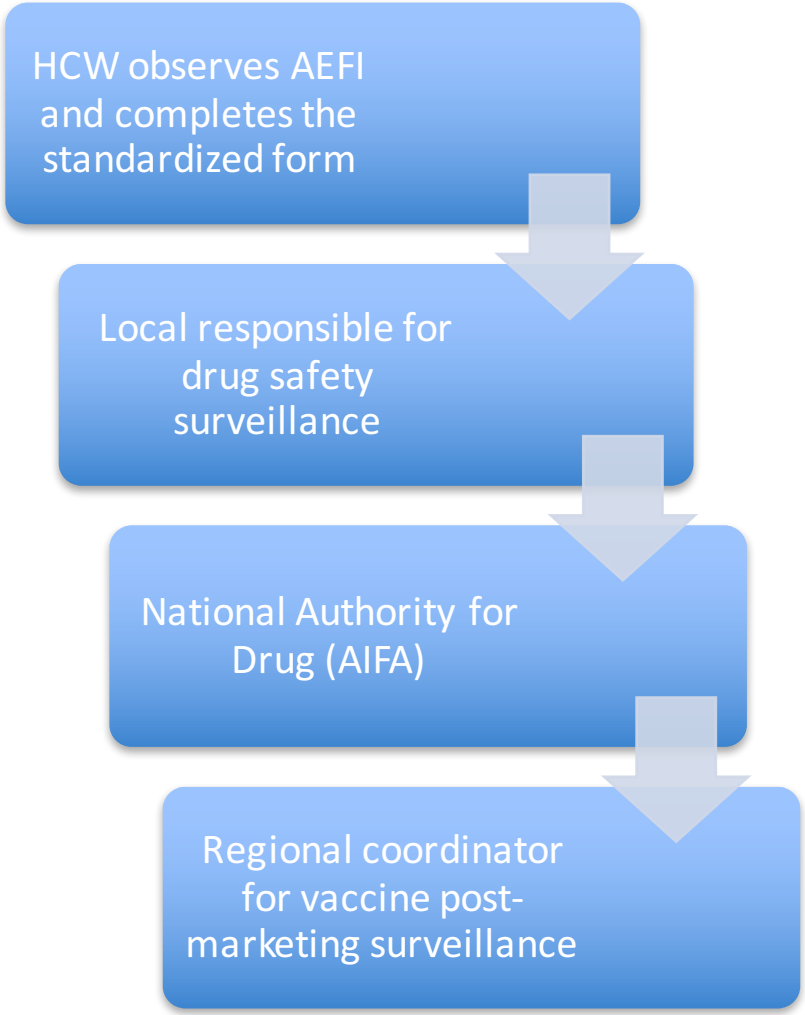
UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

The Italian framework of post-marketing surveillance of AEFI

It is mandatory to notify every adverse event observed after the vaccines administration, severe or not, expected or not

Legislative Decree 219/2006



AEFI

Permanent contraindications to vaccination

- Severe allergic reaction to a vaccine component or following a prior dose
- Encephalopathy not due to another identifiable cause occurring within 7 days of pertussis vaccination
- Severe combined immunodeficiency (rotavirus vaccine)
- History of intussusception (rotavirus vaccine)

Contraindications and Precautions to Vaccination

Condition	Live	Inactivated
Allergy to component	C	C
Encephalopathy	-----	C
Pregnancy	C	V*
Immunosuppression	C	V
Severe illness	P	P
Recent blood product	P**	V

C=contraindication P=precaution
V=vaccinate if indicated

*except HPV. **MMR and varicella containing (except zoster vaccine) only

Vaccination of pregnant women

- Live vaccines should not be administered to women known to be pregnant
- In general inactivated vaccines may be administered to pregnant women for whom they are indicated
- HPV vaccine should be deferred during pregnancy

Vaccination of Immunosuppressed Persons

- Live vaccines should not be administered to severely immunosuppressed persons
- Persons with isolated B-cell deficiency may receive varicella vaccine
- Inactivated vaccines are safe to use in immunosuppressed persons but the response to the vaccine may be decreased

Invalid Contraindications to Vaccination

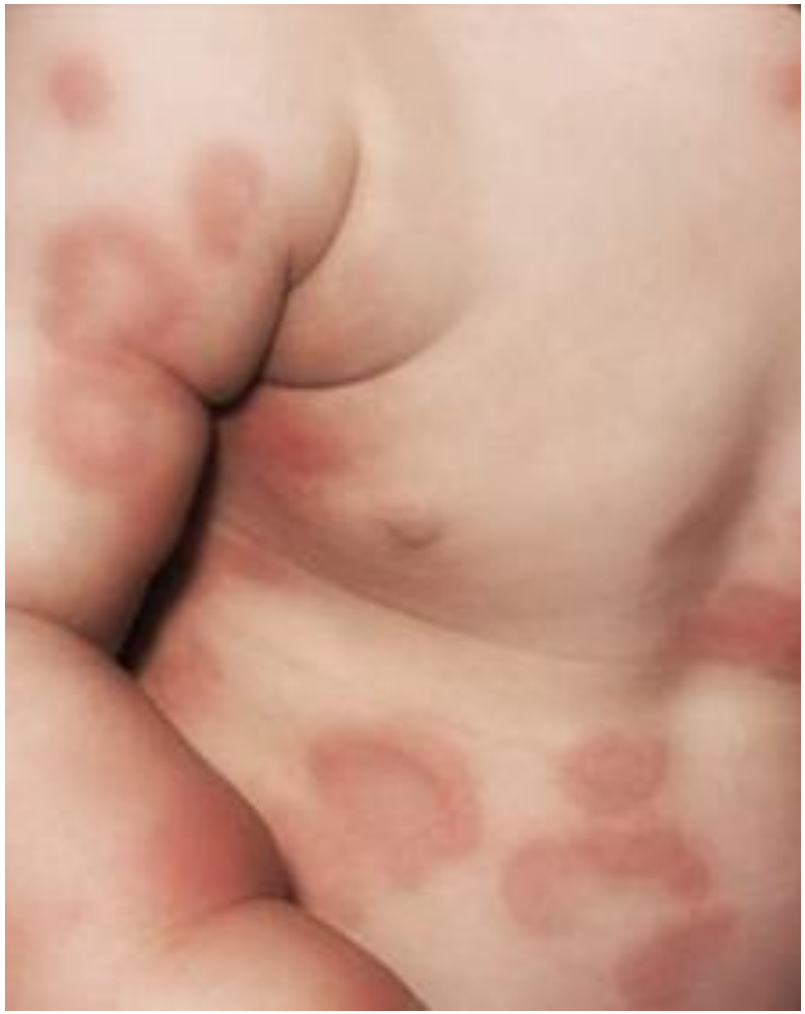
- Mild illness
- Antimicrobial therapy
- Disease exposure or convalescence
- Pregnant or immunosuppressed person in the household
- Breastfeeding
- Preterm birth
- Allergy to products not present in vaccine or allergy
- that is not anaphylactic
- Family history of adverse events
- Tuberculin skin testing
- Multiple vaccines

Pre-vaccination Screening Questions

- Is the child (or are you) sick today?

Pre-vaccination Screening Questions

- Does the child have **allergies** to medications, food, or any vaccine?
- Has the child had a **serious reaction to a vaccine** in the past?



Pre-vaccination Screening Questions

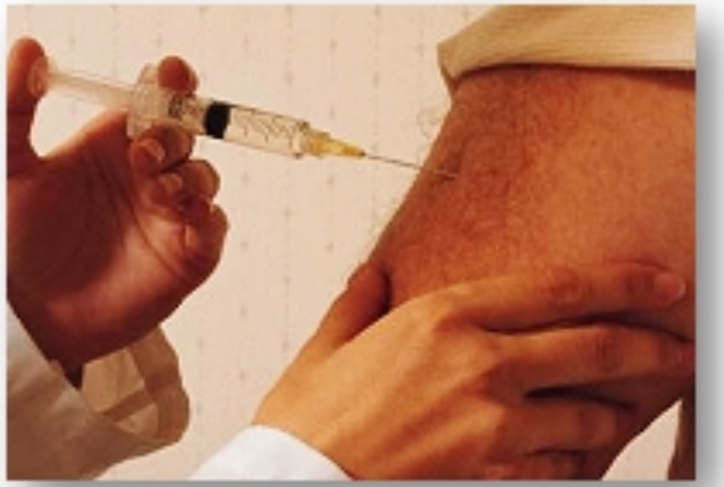
- Has the child had a **seizure**, brain or nerve problem?

Pre-vaccination Screening Questions

- Has the child had a health problem with **asthma, lung disease, heart disease, kidney disease, metabolic disease such as diabetes**, or a blood disorder?
- Does the child have cancer, leukemia, AIDS, or any other **immune system problem**?
- Has the child taken cortisone, prednisone, other **steroids, or anticancer drugs**, or had x-ray treatments in the past3 months?

Pre-vaccination Screening Questions

- Has the child received a transfusion of blood or blood products, or been given a medicine called immune (**gamma) globulin** in the past year?



Antibody and Measles- and Varicella-Containing Vaccines

Product Given First	Action
Vaccine	Wait 2 weeks before giving antibody
Antibody	Wait 3 months or longer before giving vaccine

Pre-vaccination Screening Questions

- Is the person **pregnant** or is there a chance she could become pregnant during the next month?

Pre-vaccination Screening Questions

- Has the child received **vaccinations in the past 4 weeks**?

Timing and Spacing of Vaccines

- **Inactivated vaccines** are generally not affected by **circulating antibody** to the antigen.
- **Live attenuated vaccines** may be affected by circulating antibody to the antigen
- **Patient who received a live attenuated vaccine are able to receive another vaccine after 4 weeks**

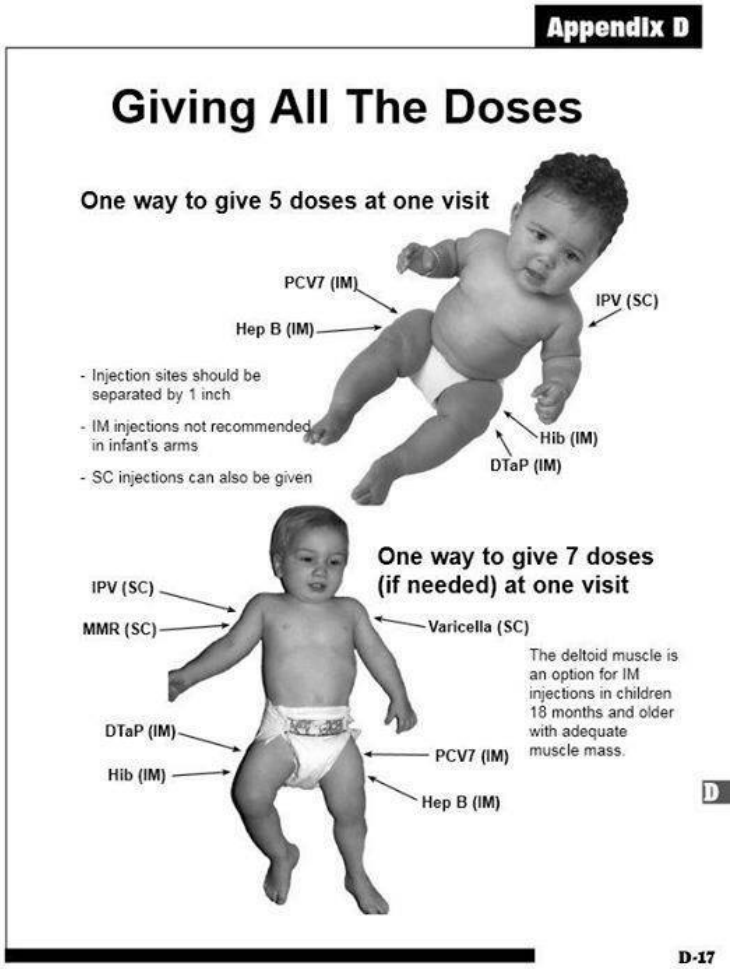
Timing and Spacing of Vaccines

- **All vaccines can be administered at the same visit as all other vaccines**
- Increasing the interval between doses of a multi-dose vaccine does not diminish the effectiveness of the vaccine.
- **Decreasing the interval** between doses of a multidose vaccine **may interfere with antibody response and protection**.

Simulatenous administration of vaccines

- Multicomponent vaccines:
  - MMR
  - MMRV
  - Hexavalent (DTaP-Hib-HBV-IPV)
  - DTaP
  - DT
- Simulatenous administration in different parts of the body

Simulatenous administration of vaccines



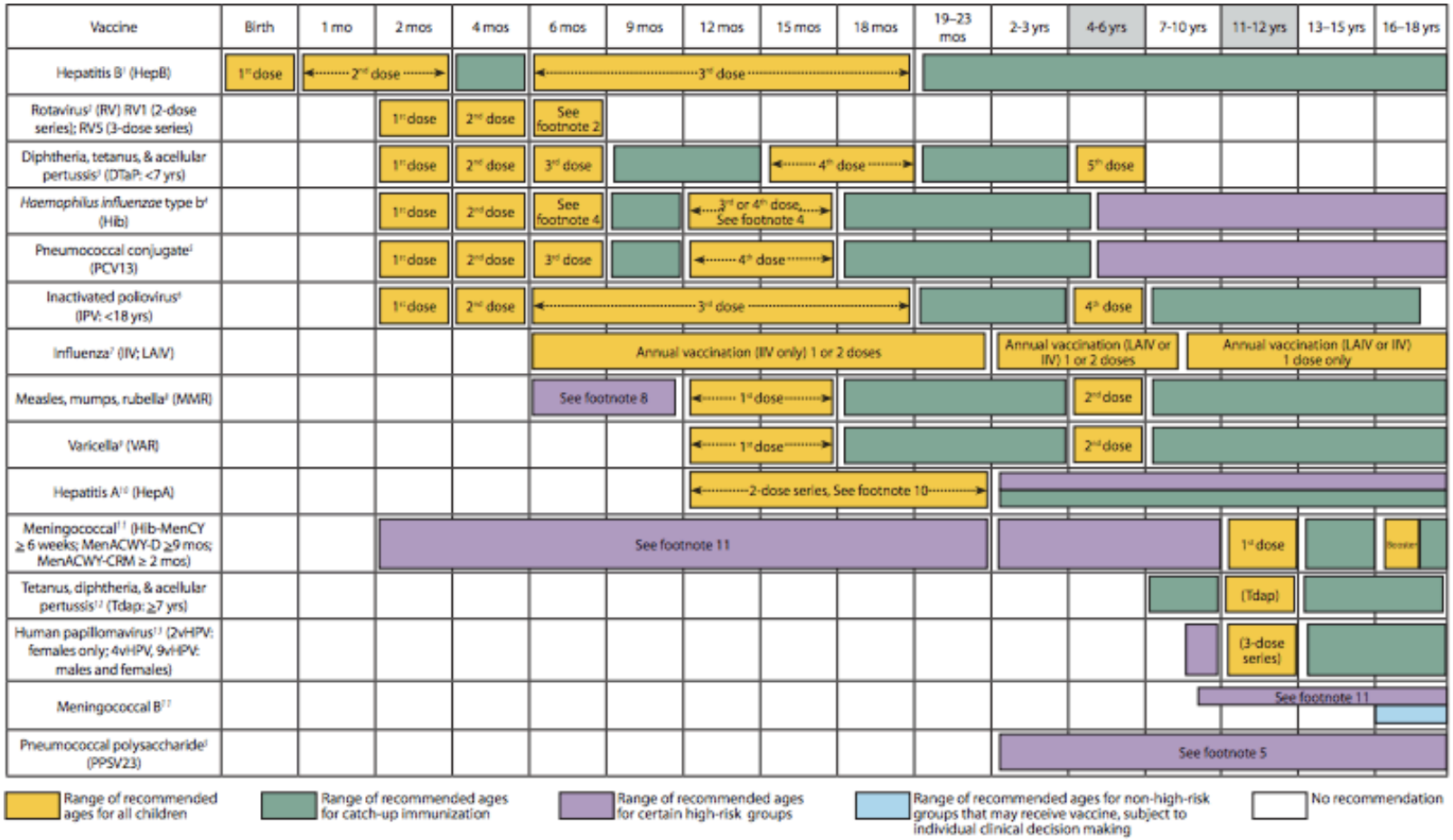
The advantages of simultaneous administration of vaccines

- Reduction of the number of visits
- Increase the compliance to vaccinations
- No significantly increase of reactogenicity
- No compromission of safety
- Some studies have shown that vaccine combination did not decrease immunogenity but it could increase the immune response

Extended Interval Between Doses

- Available studies of extended intervals have shown no significant difference in final titer
- It is not necessary to restart the series or add doses because of an extended interval between doses

Vaccination schedule



UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

VACCINATION STRATEGIES

Objectives of a vaccination program

- **Control**
- **Elimination**
  - **Infection**
  - **disease**
- **Eradication**

Control

- Reduction of incidence, prevalence, morbidity and mortality to locally accepted level.
- Control strategies often targeted high risk groups

Control strategies: influenza vaccination

Influenza vaccine is actively and free of charge offered to

- Old persons
- Children and adults affected by chronic condition

Who are at major risk of influenza complication

GOAL: reduction of morbidity and mortality in this group

Elimination of disease

Reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts; continued intervention measures are require

Elimination of infection

Reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent re-establishment of transmission are required

CERTIFICATE

WORLD HEALTH ORGANIZATION
EUROPEAN REGION

REGIONAL COMMISSION FOR THE CERTIFICATION OF POLIOMYELITIS ERADICATION

THE COMMISSION CONCLUDES, FROM EVIDENCE PROVIDED BY THE NATIONAL CERTIFICATION COMMITTEES OF THE 51 MEMBER STATES, THAT THE TRANSMISSION OF INDIGENOUS WILD POLIOVIRUS HAS BEEN INTERRUPTED IN ALL COUNTRIES OF THE REGION. THE COMMISSION ON THIS DAY DECLARES THE EUROPEAN REGION POLIOMYELITIS-FREE.

COPENHAGEN, 21 JUNE 1991

Eradication

Permanent reduction of the worldwide incidence of infection to zero.

Principal Indicators of Eradicability

- an **effective intervention** is available to interrupt transmission of the agent
- practical **diagnostic tools** with sufficient sensitivity and specificity are available to detect levels of infection that can lead to transmission
- **humans are essential for the life-cycle of the agent**, which has no other vertebrate reservoir and does not amplify in the environment.

Eradication

POLIO GLOBAL ERADICATION INITIATIVE

Eradication

Universal mass vaccination

- Active and free offer of vaccine to a large number of persons, often targeted by age
- The age of offer is related to
  - Objectives of vaccination strategy
  - Immunological consideration
  - Epidemiology of the disease
  - Median age of infection
  - Practical/organizational questions

Hepatitis B strategy

- In 1991, Italian Government designed a strategy for Hepatitis B vaccination
- Since 1991 to 2003, vaccine has been actively and free of charge offered to
  - Newborns
  - 12 years old adolescents
- In 2004, all people born since 1979 to 2003 (24 cohorts of birth) have been vaccinated

Mandatory vaccination

- In **1853**, in UK **Vaccination Acts** was approved, that provided mandatory small-pox vaccination
- In the next years, several European countries established mandatory vaccination to reduce smallpox outbreaks

Why vaccination should be mandatory

- The mandatory policy guarantee high coverage rapidly achieved
- The vaccination is offered also to people with low-income or of low socio-economic level
- The mandatory policy was crucial in European countries after Second War

Mandatory vaccination in Italy

In Italy, 4 vaccinations are currently mandatory for new-borns

- Tetanus
- Diphteria
- Polio
- Hepatitis B

All other vaccination are strictly reccommended, but not mandatory

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

EPIDEMIOLOGY OF VACCINATIONS

Epidemic

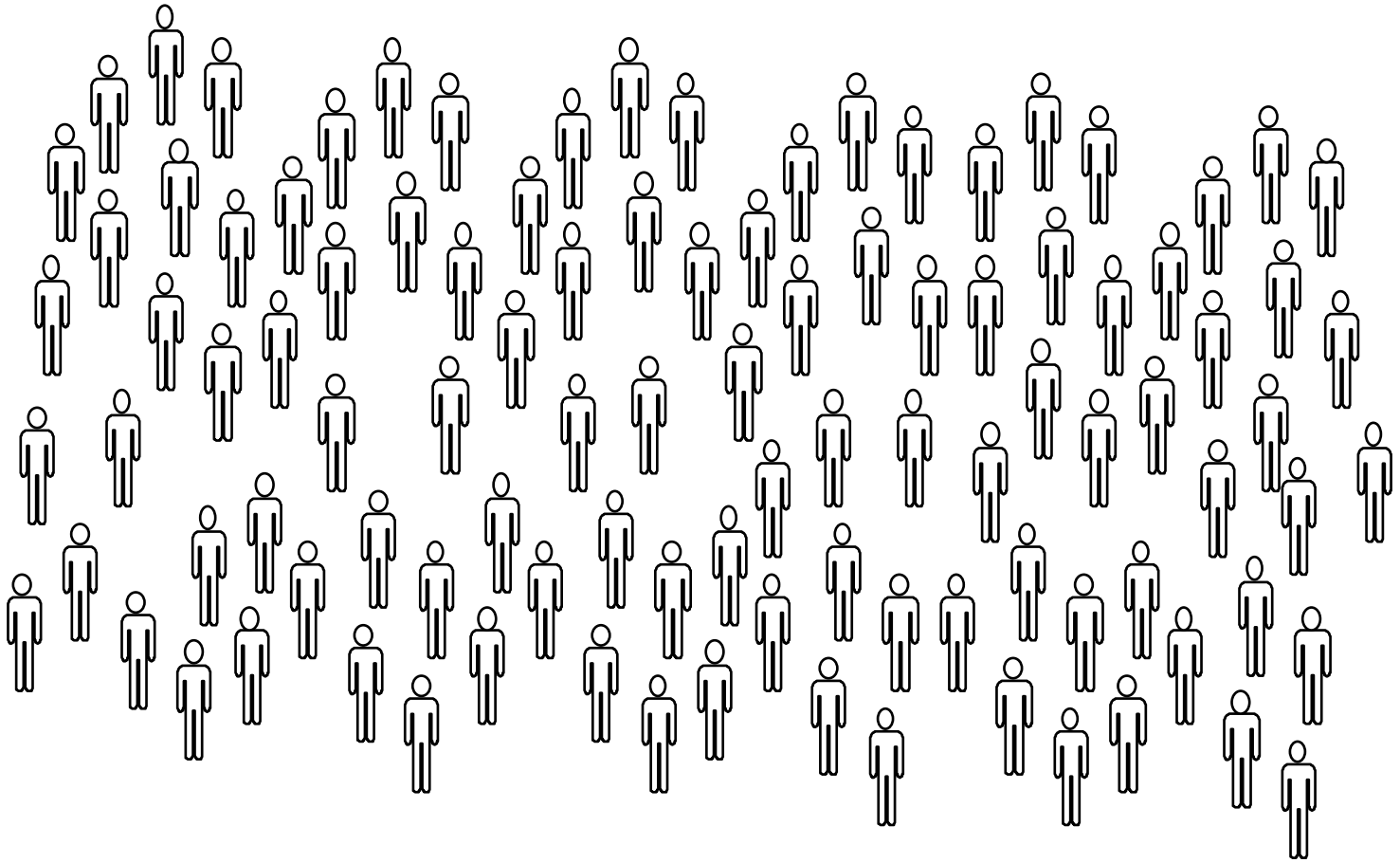
A widespread occurrence of an infectious disease in a community at a particular time

Oxford dictionairies

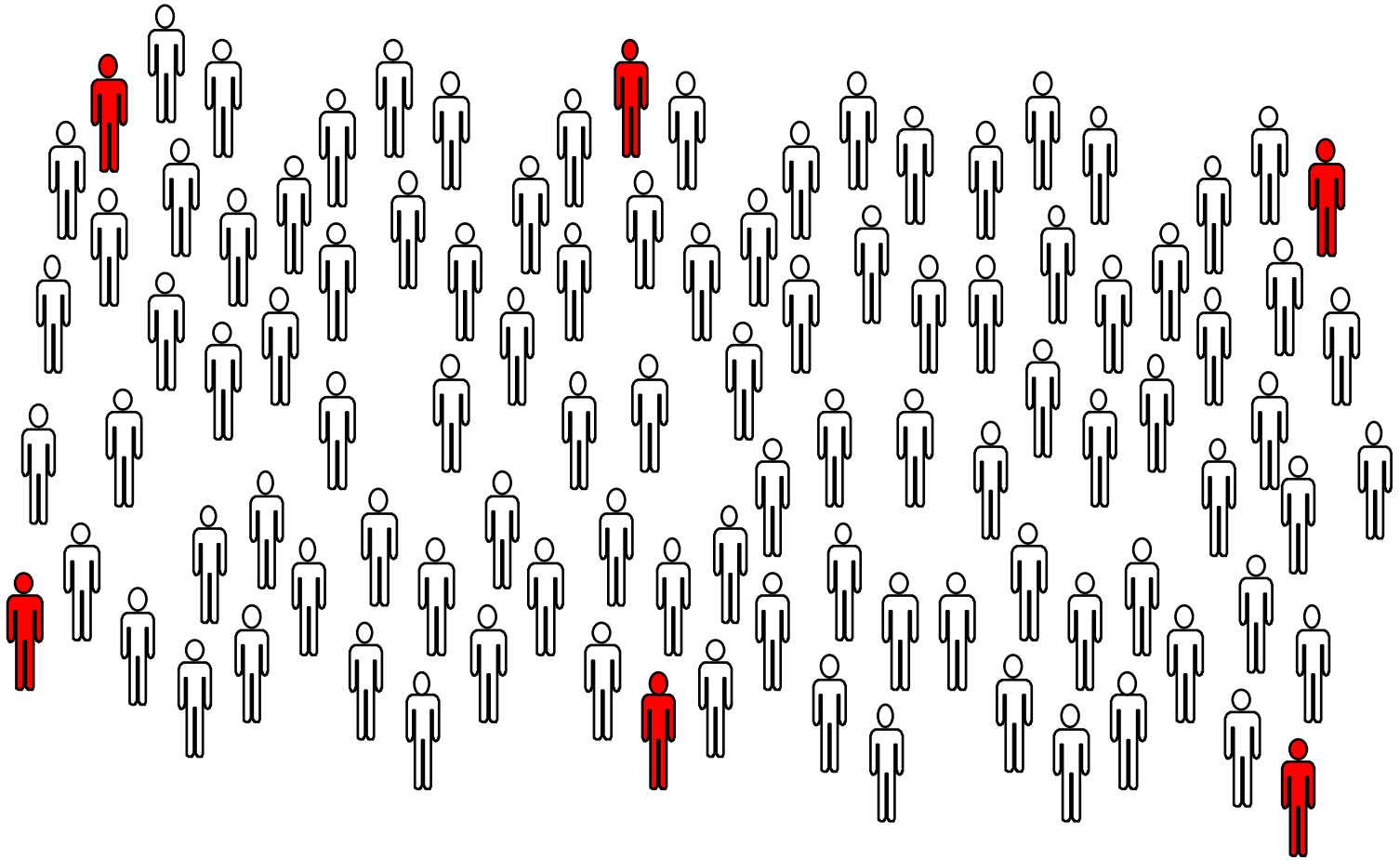
An increase, often sudden, in the number of cases of a disease above what is normally expected in that population in that area

CDC

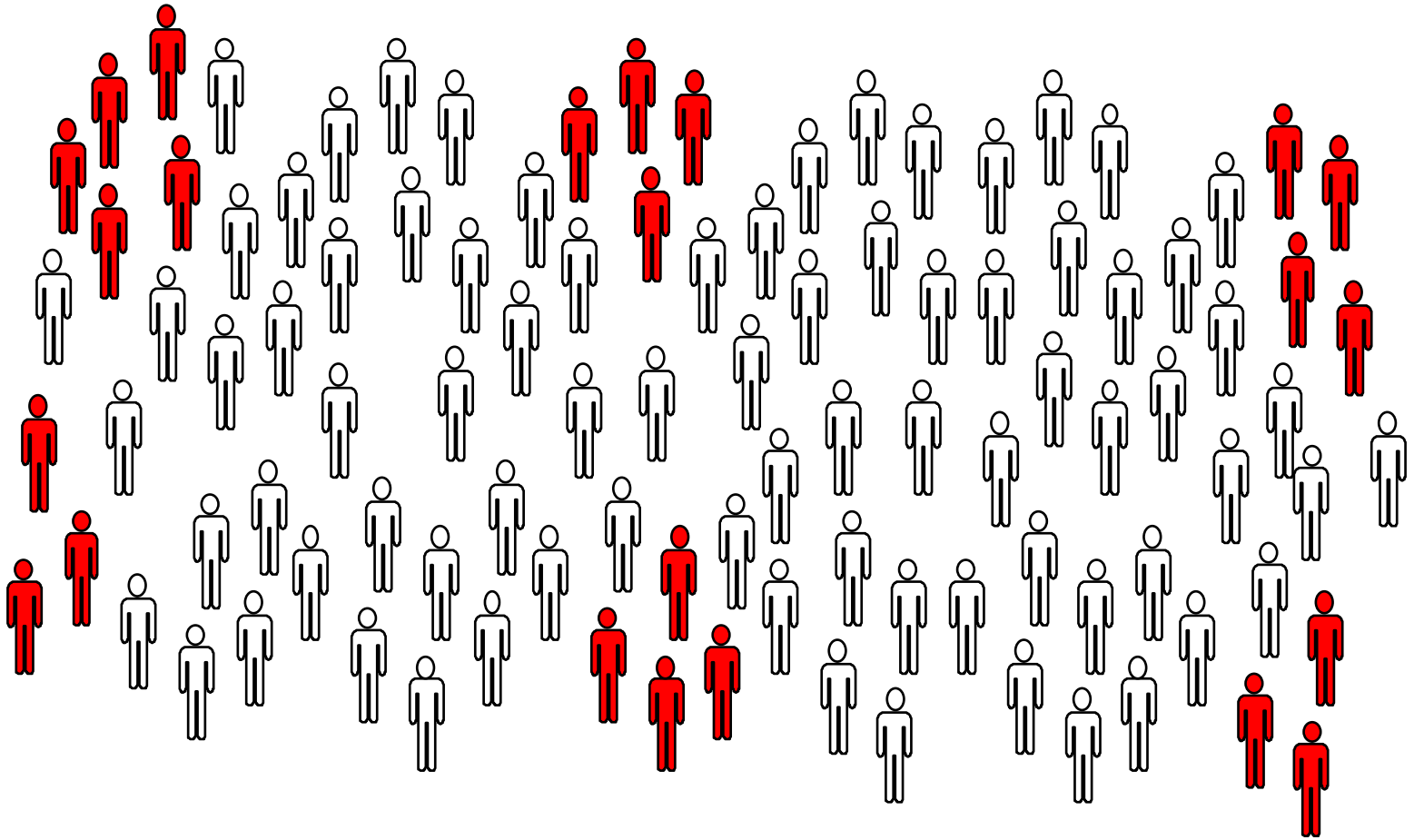
Epidemic



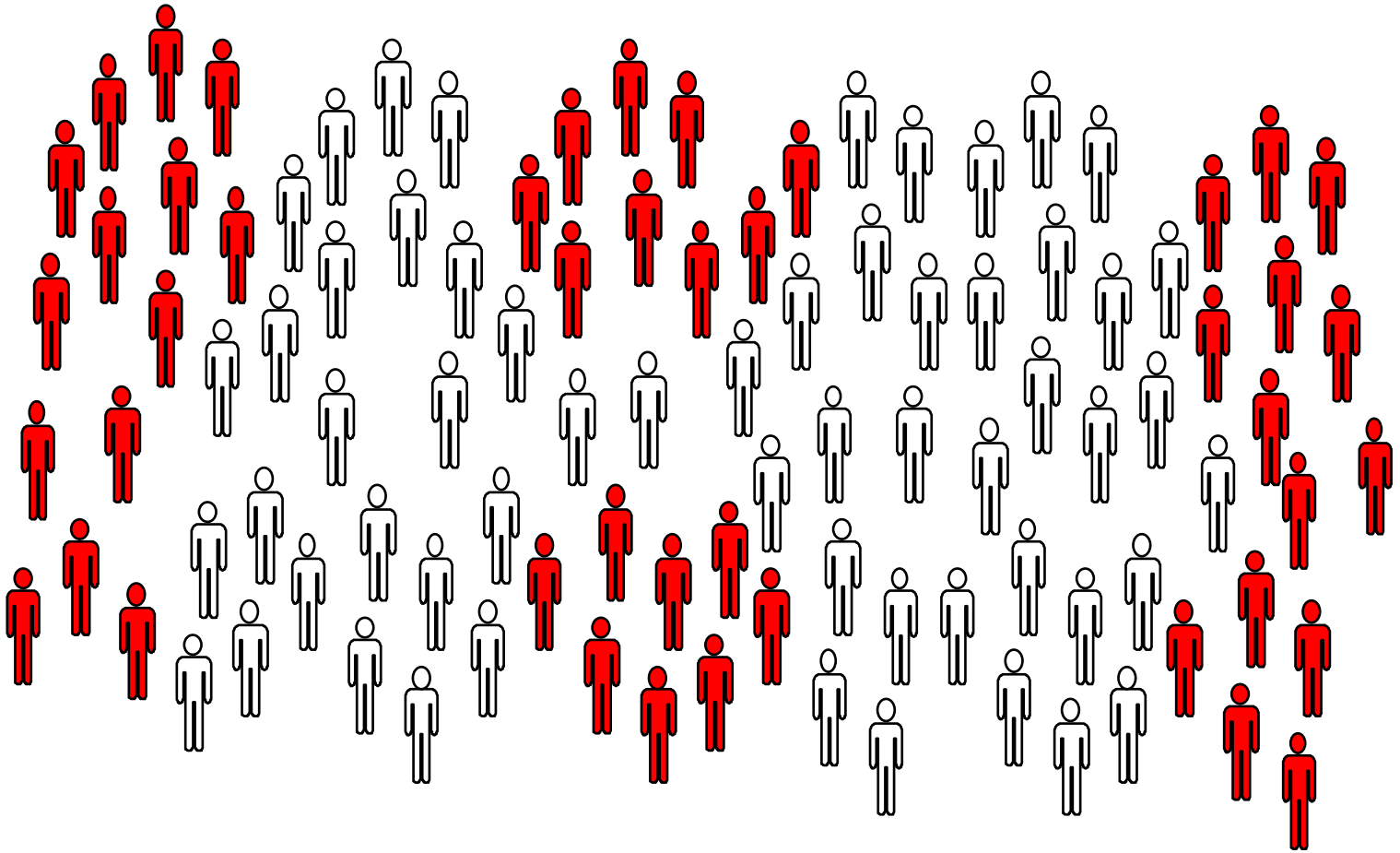
Epidemic



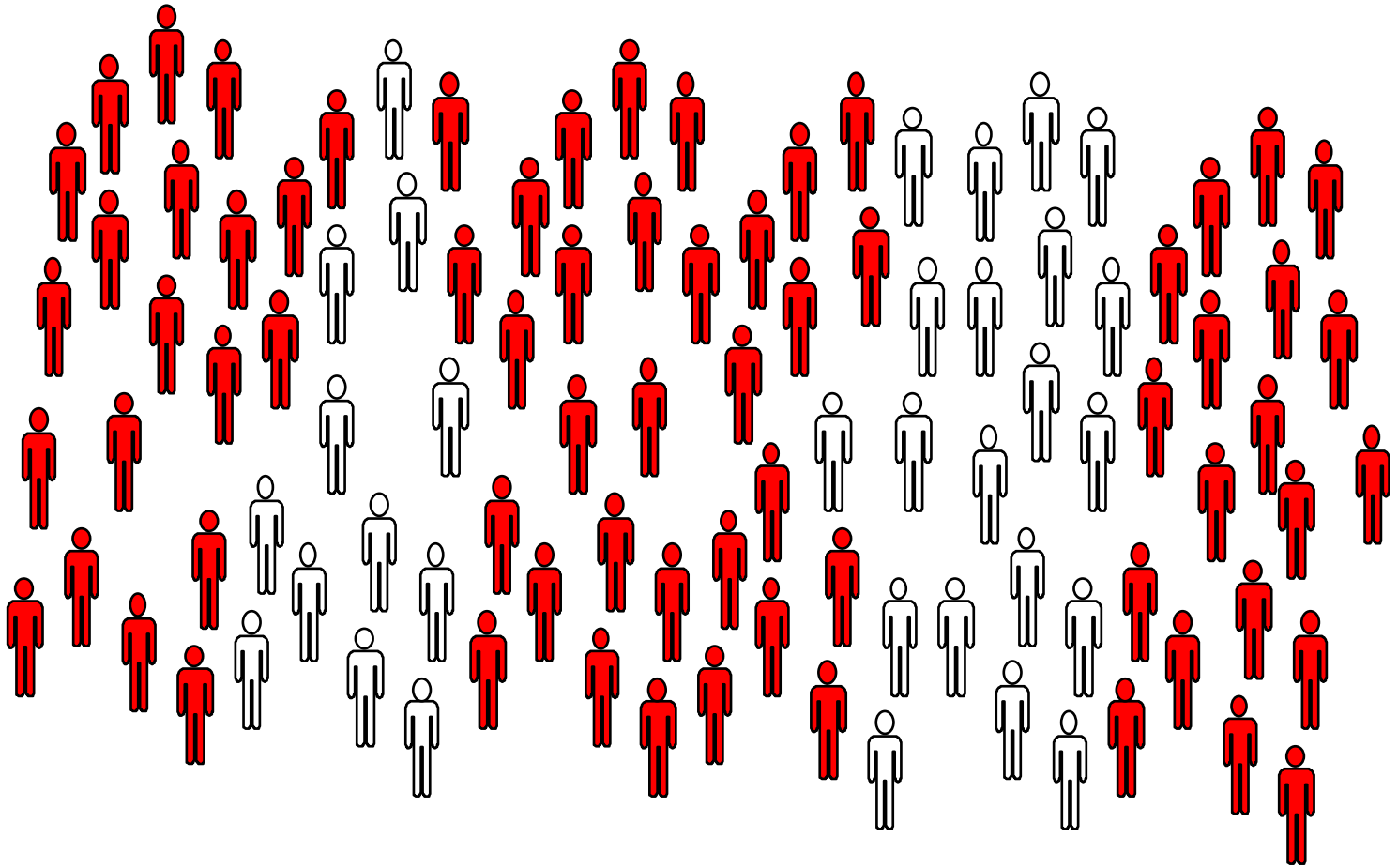
Epidemic



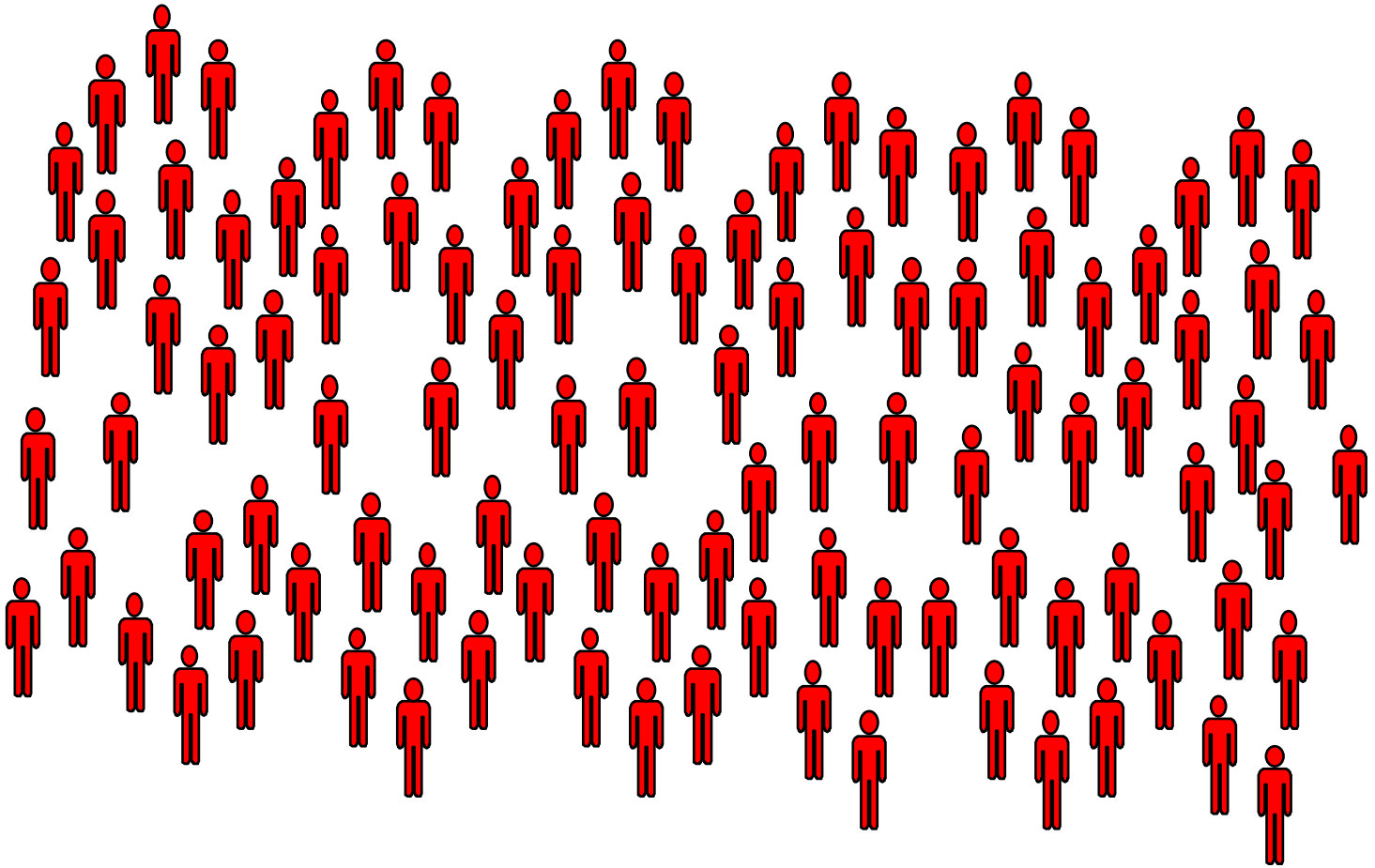
Epidemic



Epidemic



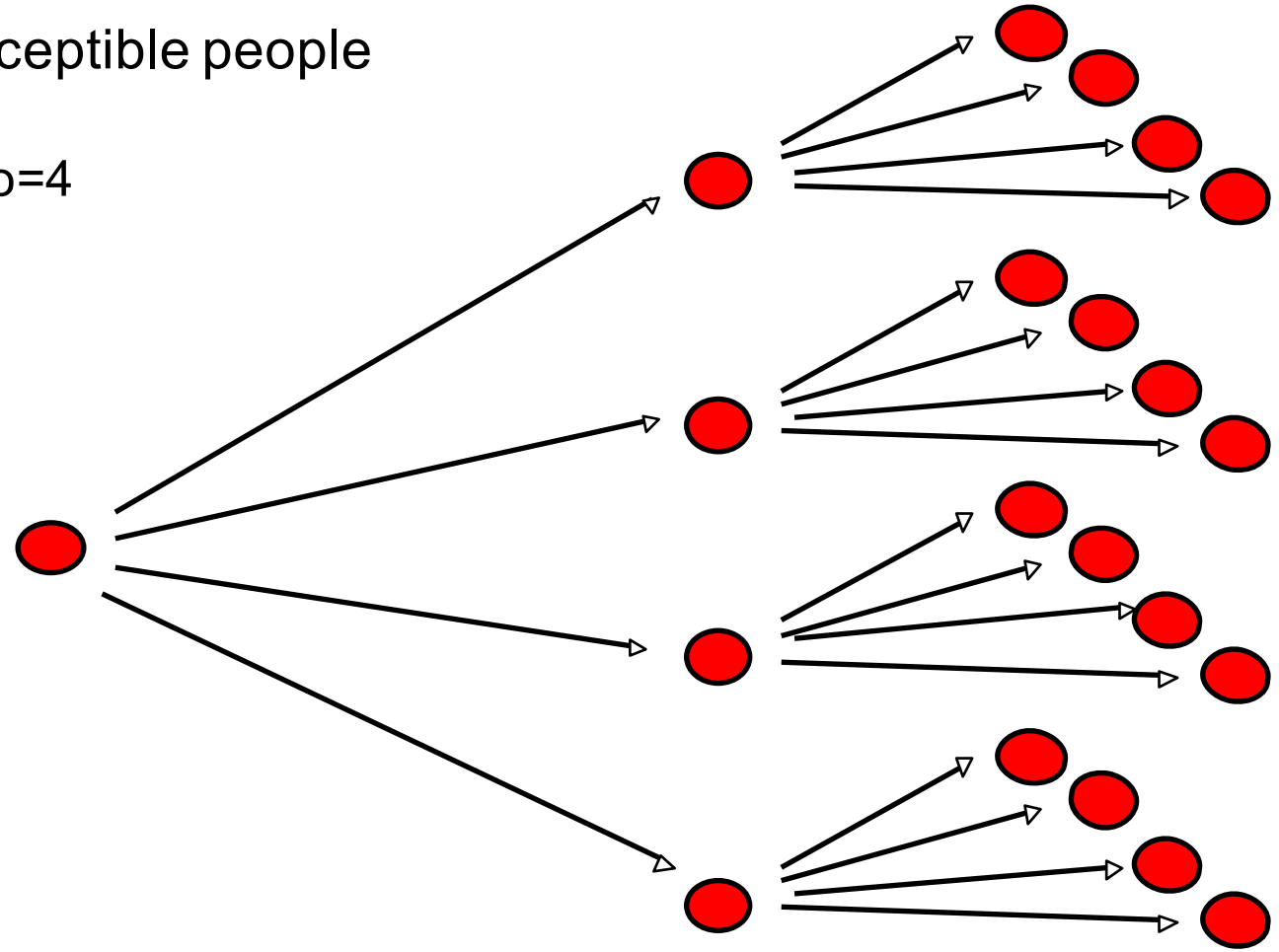
Epidemic



Epidemic

Susceptible people

Ro=4



= susceptible person who begin infected

= immune person

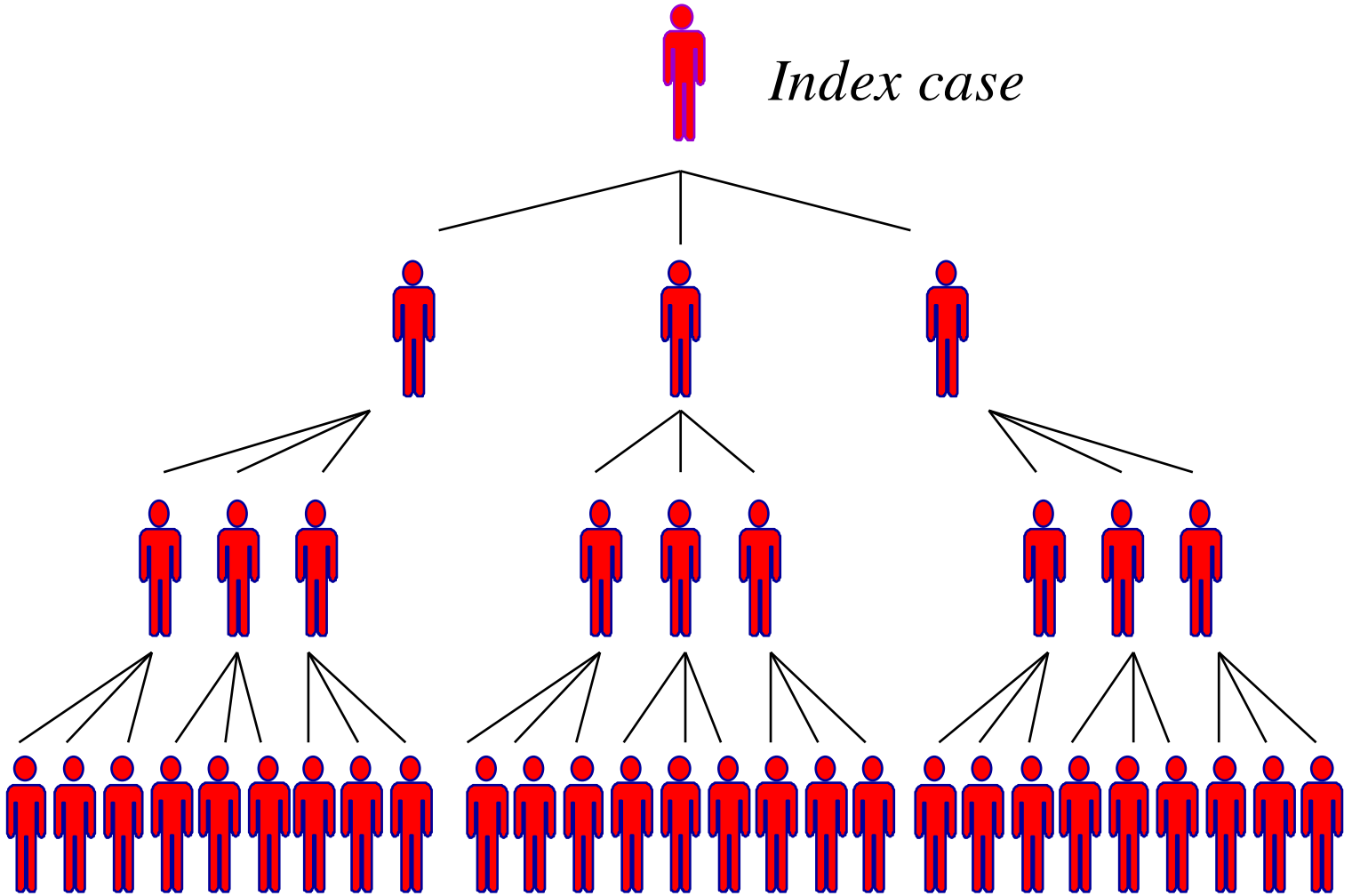
Population immunity or herd immunity

When a critical portion of a community is immunized against a contagious disease, most members of the community are protected against that disease because there is little opportunity for an outbreak

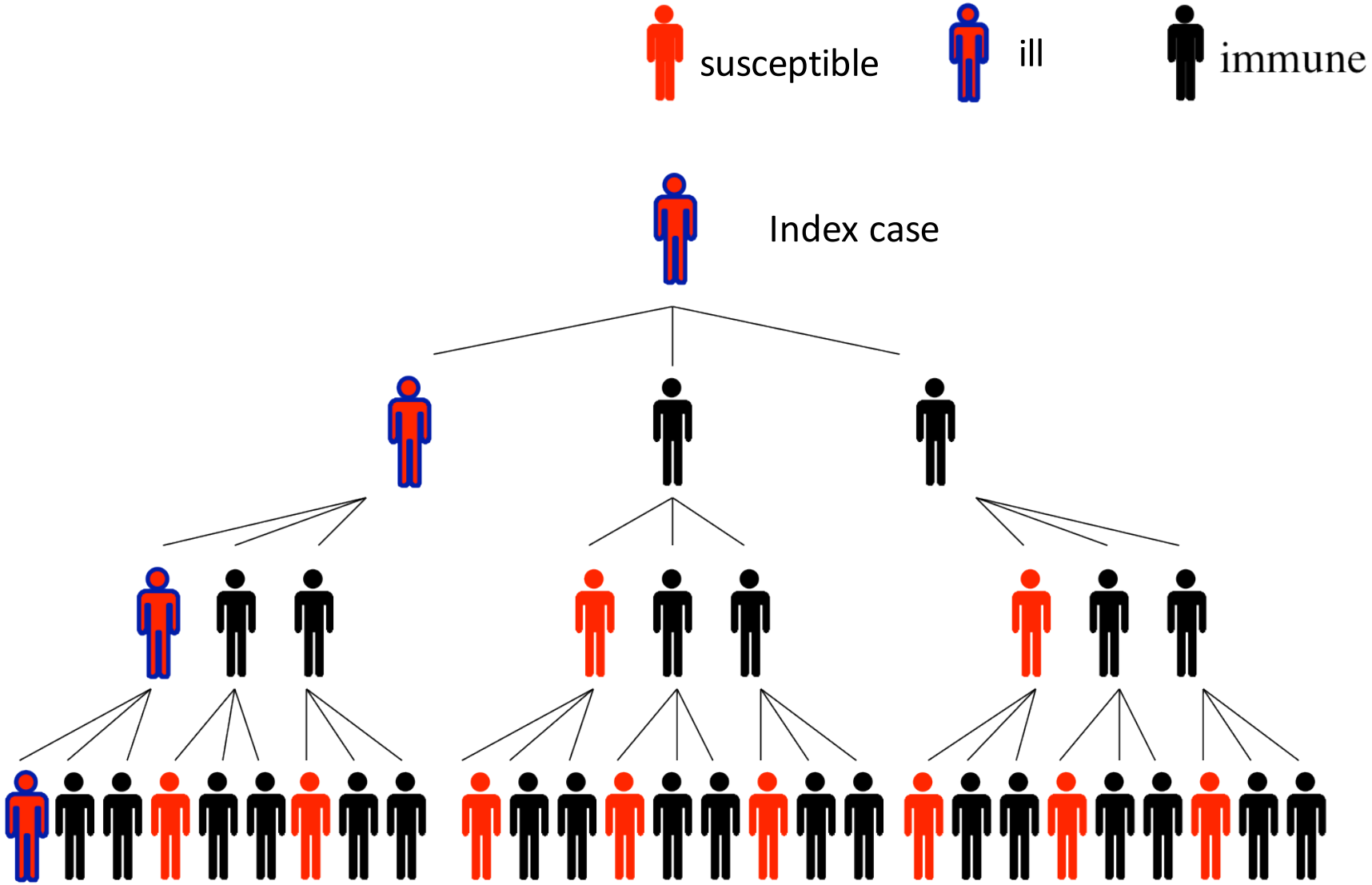
Herd or immunity

Epidemic

susceptible ill



Herd immunity



Basic reproduction number

The basic reproduction number, R0, is defined as the **expected number of secondary cases** produced by a single (typical) infection in a **completely susceptible population**

Basic reproduction number

$$R0 = \tau \cdot c^{-} \cdot d$$

T= infection/contact

C= contact/time

D= time/infection

R0 and infectious diseases circulation

R0	Epidemiology burden
<1	Elimination/interruption of circulation
1	Endemic circulation
>1	epidemic

Anderson and May: Infectious Diseases of Humans, 1991

RE: effective reproduction number

average number of secondary cases per infectious case in a population made up of both susceptible and non-susceptible hosts

$$RE = R0x$$

X= fraction of the host population that is susceptible

Condition of eradication

The goal of eradication is achieved when

$$RE<1$$

If RE= R0X

Then

$$RE<1 \text{ if } R0X<1$$

Vaccination coverage to achieve eradication goal

$R0X<1 = R0(1-p)<1$

$P>1-(1/R0)$

P=Vaccination coverage

Vaccination coverage to achieve the goal of measles eradication

- Measles R0=16
- P>1-1(1/16)

P>1-(1/16)

P>93,75

Immunization coverage

Number of people of the target cohort who received the established doses of vaccine

---

Population of target group

Coverage must be calculated after the end of vaccination activity

Immunization coverage
Hexavalent vaccine

- Hexavalent vaccine is currently offered in 3 doses (at 3, 5 and 11 months of age)
- We usually calculate the coverage per birth cohort

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

Immunization coverage
Hexavalent vaccine

Coverage of 2013 birth cohort was

Number of people born in 2013 who received 3 doses of Hexavalent vaccine

---

People born in 2013

We will be able to calculate the coverage after 31 December 2014

Immunization coverage
MMR vaccine

- First dose of MMR vaccine is currently offered at 12 months of age
- Coverage of 2013 birth cohort was

Number of people born in 2013 who received 1 doses of MMR vaccine

---

People born in 2013

We will be able to calculate the coverage after 31 December 2014

Immunization coverage
Men C vaccine

- First dose of MMR vaccine is currently offered at 12-15 months of age
- Coverage of 2013 birth cohort was

Number of people born in 2013 who received 1 doses of Men C vaccine

---

People born in 2013

We will be able to calculate the coverage after 31 March 2014

Vaccine efficacy

- reduction in disease incidence in a vaccinated group compared to an unvaccinated group under optimal conditions
- It is often calculated in pre-marketing studies, such as RCT

UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

SCUOLA DI MEDICINA
CORSO DI IGIENE

Vaccine effectiveness

- ability of vaccine to prevent outcomes of interest in the “real world”
- Vaccine effectiveness could be different than vaccine efficacy because of:
  - RCTs have less stringent eligibility
  - RCTs Clinically relevant treatment selection and followup duration
  - RCTs have not adequate sample size to detect clinically relevant differences

Vaccine effectiveness calculation in cohoort study

$$\frac{ARU - ARI}{ARU}$$

ARU= Attack rate among unimmunized people

ARI= Attack rate among immunized people

Vaccine effectiveness calculation by screening methods

Vaccine Effectiveness

$$= 1 - \frac{\left(\frac{\textit{Number of cases that are vaccinated}}{\textit{Number of total population that is vaccinated}}\right)}{\left(\frac{\textit{Number of cases that are unvaccinated}}{\textit{Number of total population that is unvaccinated}}\right)} \times 100\%$$

$$= 1 - \frac{\left(\frac{\textit{Proportion cases vaccinated} \times n}{\textit{Proportion total population vaccinated} \times N}\right)}{\left(\frac{(1 - \textit{Proportion cases vaccinated}) \times n}{(1 - \textit{Proportion total population vaccinated}) \times N}\right)} \times 100\%$$

$$= 1 - \frac{\left(\frac{\textit{Proportion cases vaccinated}}{\textit{Proportion total population vaccinated}}\right)}{\left(\frac{1 - \textit{Proportion cases vaccinated}}{1 - \textit{Proportion total population vaccinated}}\right)} \times 100\%$$

$$= \left(\frac{\textit{Proportion cases vaccinated}}{1 - \textit{Proportion cases vaccinated}}\right) \times \left(\frac{1 - \textit{Proportion total population vaccinated}}{\textit{Proportion total population vaccinated}}\right) \times 100\%$$

Vaccine effectiveness

- If no cases among immunized people were detected, VE=100%
- The surveillance of vaccination failure (cases among immunized people) is crucial to calculate vaccine effectiveness
- The VE could decrease if the attack rate among immunized people increase