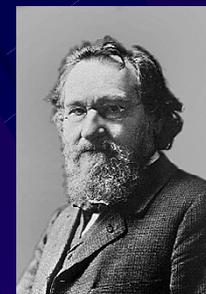


I.I.Mechnikov Research Institute of Vaccines and Sera RAMS



# Modulation of Innate Immunity to Protect Against Biological Weapon Threat

**Vitaly Zverev**

## I.I. Mechnikov Research Institute for Vaccines and Sera RAMS

- One of the oldest Russian research institutions that has been active over 90 years.
- The Institute carries out international cooperation with a number of countries in the development of diagnostic and prophylactic preparations in accordance with international projects in the field of medical science and public health service.

## I.I. Mechnikov Research Institute for Vaccines and Sera RAMS

- Institute developed more than 20 different vaccines against viral and bacterial diseases. Among them:
- Measles, Mumps, Polio, Rabies, Influenza, Rubella
- Pertussies, Tetanus, Diphtheria

**Biological weapons are mass casualty weapons based on bacteria, viruses, rickettsiae, fungi, or toxins.**

**Biological weapons are unique in their diversity compared to nuclear, chemical, or conventional weapons.**

**10 or more of different biological agents can be used to make a biological weapon and each agent produces a markedly different disease.**

**A biological weapons attack may go undetected until victims begin to fall ill, which will complicate diagnosis, treatment, and containment efforts.**

**Once a biological attack has been detected, additional time will likely pass before the causative agent has been conclusively identified, again complicating diagnosis, treatment, and containment efforts.**

**It will be difficult to determine the size and perimeter of the contaminated areas, making it difficult to estimate the number of exposed, identify those exposed, and determine where to conduct decontamination operations if necessary.**

**The target population is not likely to be vaccinated against the threat agent.**

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**The few vaccines that exist against biological threat agents will be of very little use once an attack has taken place, since they do not reach full effectiveness until days to weeks after inoculation.**

**Treatment options are limited or nonexistent for the majority of biological threat agents.**

**The public and military health services are not well equipped in terms of personnel, equipment, or pharmaceuticals to accommodate a widespread epidemic.**

**A biological attack will incite panic and result in an influx of patients.**

# **Current Medical Defense Against Biological Weapons (3 categories)**

**Early pre-exposure prophylaxis: protective means administered long before a biological attack; this includes vaccines and means for passive immunization.**

**Urgent pre- and post-exposure prophylaxis: preemptive use of protective means before an imminent attack or administered after an attack has taken place, but before the patient develops symptoms.**

**Treatment: etiologic, pathogenic, and symptomatic therapy administered after the patient has developed symptoms.**

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**Vaccines are currently the primary means of preexposure prophylaxis.**

**However, the utility of vaccines is limited by:**

- 1. Time to reach effectiveness: a vaccine takes weeks to months to reach full effectiveness.**
  - 2. Specificity: because it works by prompting the body to produce specific antibodies; currently available vaccines protect only against one specific disease.**
  - 3. Lack of availability: for most biological weapons threat agents, no vaccine has been developed.**
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## **Vaccines can serve as effective pre-exposure prophylaxis only when:**

**The target population is well defined and can be identified well in advance of an attack.**

**The biological threat agents in the enemy's biological weapons arsenal are known.**

**Vaccines for those agents have already been developed.**

**The biological agents used are not genetically altered strains capable of circumventing a vaccine.**

# Immunological methods of Fighting Epidemics

Method	Known pathogen	Unknown pathogen
Vaccination	Yes	No
Immunotherapy	Yes	By the end of the epidemic
Activation of innate immunity	Under discussion	Under development

*Innate immunity and acquired immunity are interrelated elements of the integral immune system in 2% of metazoan organisms, including humans*

## Cellular and Soluble Components of the immune system

Type of immune system	Cellular components	Soluble components
<b>Innate immunity</b>	<b>Macrophages, Monocytes</b> <b>Neutrophils, Dendritic cells</b> <b>Basophils, Eosinophils</b> <b>NK cells, LAK cells</b> <b>Epithelial cells</b>	<b>Cytokines, Chemokines</b> <b>Complement proteins</b> <b>Acute phase proteins</b> <b>Defensins, Cathelicidins</b> <b>Histatins</b>
<b>Adaptive immunity</b>	<b>T-lymphocytes</b> <b>B-lymphocytes</b>	<b>Specific immunoglobulins</b>
<b>Overlapping (Innate-Adaptive) Immunity</b>	<b>Macrophages,</b> <b>Dendritic cells,</b> <b>NK cells</b>	<b>Cytokines</b> <b>Chemokines</b>

# Innate immunity

- ✓ Quick (within minutes) recognition of pathogen
- ✓ Recognizes  
*Pathogen associated molecular patterns*
- ✓ *Patterns recognition receptors*
- ✓ located on cell surfaces.  
Their diversity allows to recognize any harmful factors (*pathogens, allergens, heat shock proteins*)

# Innate Immunity

## Concept of Emergency Protection against Pathogens

Stimulation of immunocompetent cells maturation using immunomodulators of bacterial origin.

Activation of innate immunity effector mechanisms (24 hours).

Formation of protective immunity against a concrete pathogen.

# PAMP Recognition Consequences

DC

- *maturation*
- *activation of phagocytosis*
- *APF enhancement*
- *secretion of chemokines and cytokines*

*transmission of recognition signal to lymphocytes*

*formation of acquired immunity as per types Th1 or Th2*

# THERAPEUTIC BACTERIAL VACCINE VP-4

Antigen composition:

*Klebsiella pneumoniae*

*g* -

*Proteus vulgaris*

*Escherichia coli*

*Staphylococcus aureus*

*g* +

PAMP

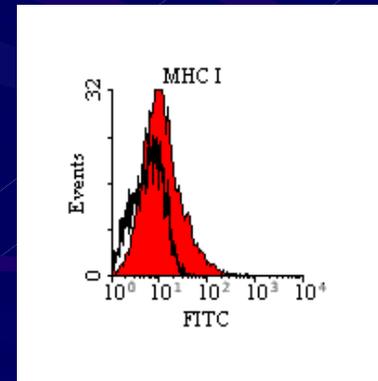
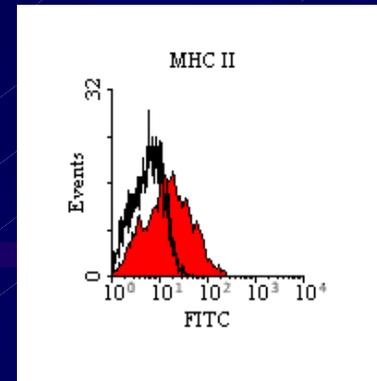
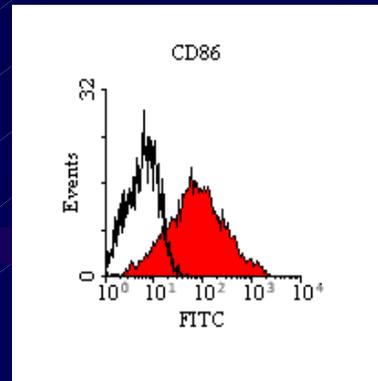
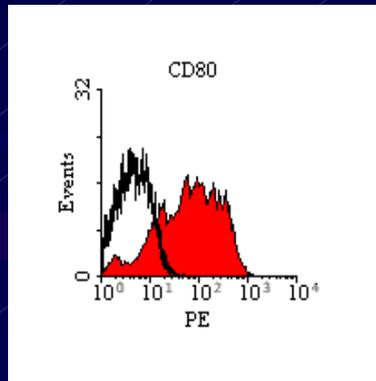
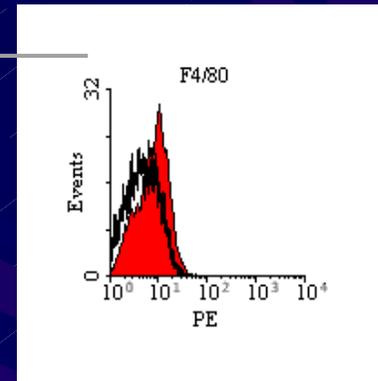
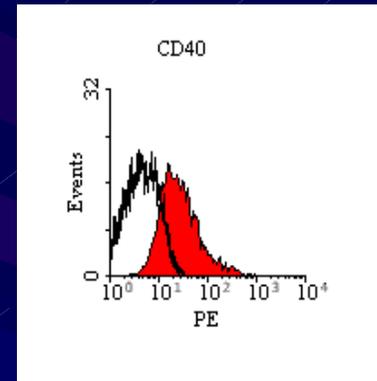
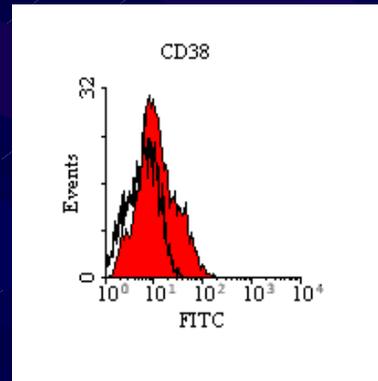
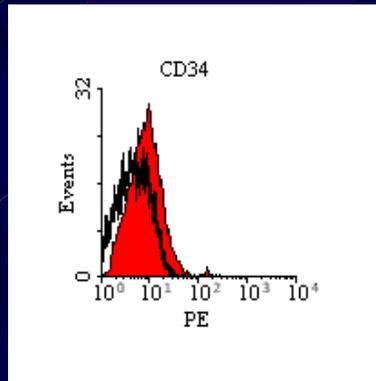


**LPS**  
peptidoglycanes  
lipoproteins  
lipid A

peptidoglycanes  
TA

After introduction of VP-4 DC maturation takes place and they acquire the following phenotype:

CD34<sup>-</sup>, CD38<sup>+</sup>, CD40<sup>+</sup>, CD80<sup>+</sup>, CD86<sup>+</sup>, MHC I<sup>+</sup>,  
MHC II<sup>+</sup>, F4/80<sup>-</sup>

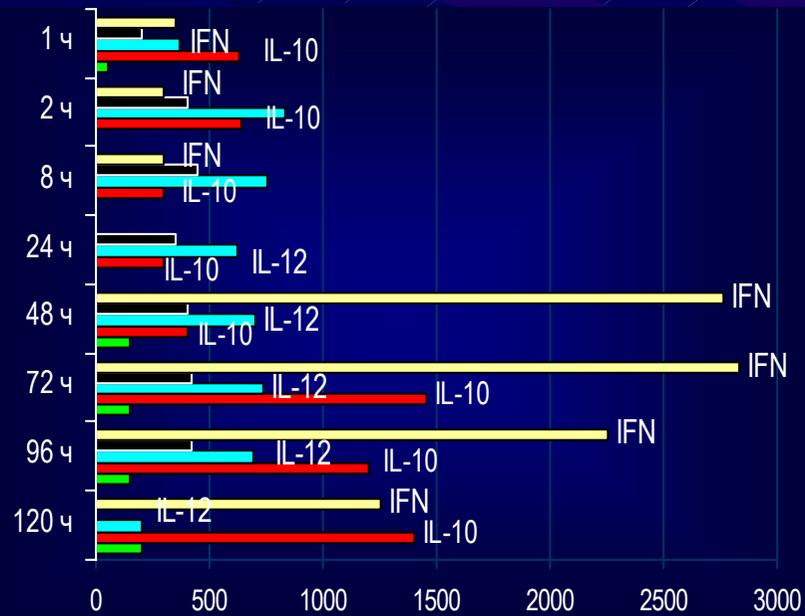


# VP-4 extends the life span of infected mice

VP-4  
(vaccinated)



Infection with  
*S.typhimurium*  
50 LD<sub>50</sub>



Lethality, %

VP-4

Control

24 h - 0

16,7

48 h - 0

33,3

72 h - 0

83,3

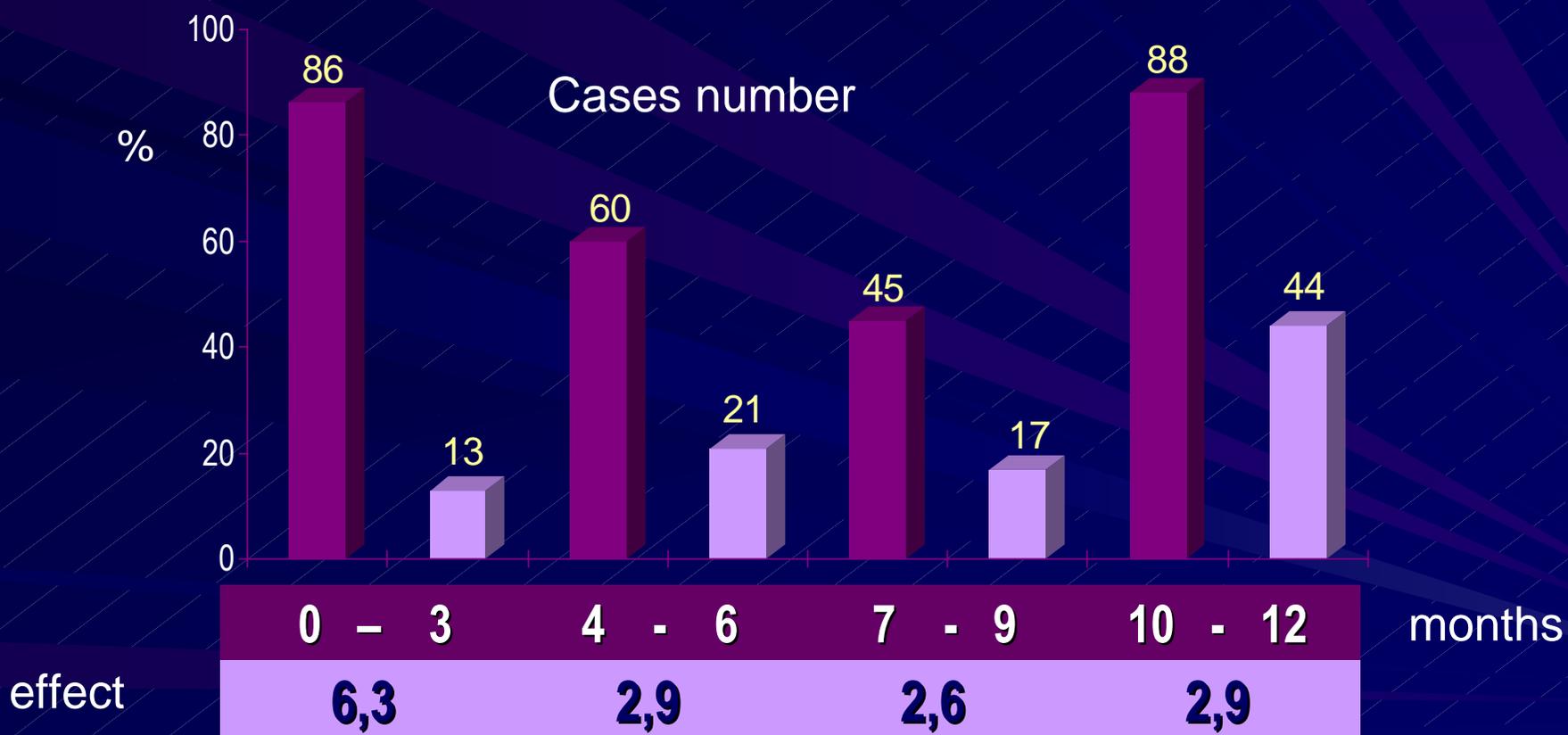
96 h - 0

83,3

120 h - 60

100

# Dynamics of ARD of children with bronchial asthma during one year after VP4 vaccination



In the Institute is developed the vaccine elicits the rapid and non-specific immunological resistance against bacterial and viral infection. The vaccine consists of the antigens of opportunistic pathogens

# International Advisory Group (IAG) on Biosecurity and Biosafety

## Main Objectives

1. To strengthen global biosafety
2. To implementation provisions of international treaties on the prohibition of biological weapons and ensure global biological safety
3. To increase awareness of the importance of biosafety and biosecurity within the scientific community, government, industry (public private cooperation) and society more broadly.

4.To provide information to to interested ministries, agencies and organizations on new international treaties, regulations, events, actions and initiatives related to biosafety and biosecurity

5.To assist Russian biotechnological, pharmaceutical and microbiological organizations (upon receipt of relative requests) in the implementation of new projects, programmes and other activities in the area of biosafety and biosecurity.

6.To review, assess, and offer the expertise of national and international programs in biosecurity and biosafety according to national and international standards in this area and to the current national legislation

7.To provide recommendations (including projects and programmes) for use by federal agencies, special national and international organizations (upon receipt of relative requests) to enhance national and international systems of biosafety and biosecurity.

## Russian Experts

Mikhail Paltsev, Rector, Moscow Medical Academy, Co-Chairman

Alexander Ginzburg, Director, N.F. Gamaleya Institute of Epidemiology & Microbiology

Yulia Ananyina, Deputy Director, N.F. Gamaleya Institute of Epidemiology & Microbiology

Vitaly Zverev, I.I. Mechnikov Institute of Vaccines and Sera

Ivan Dyatlov, SRC of Applied Microbiology & Biotechnology

Vladimir Kutyrev, Director of SRAI Microbe

Mikhail Kiselev, Deputy Head of Federal medico-biological agency,

Sergey Netesov, Deputy Director of SRC VB Vector

Oleg Kiselev, Director, Institute of Influenza

Dimitry Lvov, Director of Ivanovsky Institute of Virology

Petr Deryabin, Deputy director Institute of Ivanovsky Institute of Virology  
and Head of state collection of viruses

Yuri Remnev, Deputy Director NP TEMPO, Subgroup Leader on  
Education/Training

Eugene Tkachenko, Deputy Director, Institute of polio and viral  
encephalitis

Nikolay Fedorov, Blood Center

Beniamin Cherkassky Head of Department Central Research  
Institute of Epidemiology

Valentin Evstigneev, Deputy Director of BioPreparat company

Valery Loktev, Head of Department of Molecular Virology, SRC  
VB Vector,

Vasily Kholodenko, Deputy Director of Education Center, SRC of  
Applied Microbiology & Biotechnology,

Diana Pobedimskaya, Scientific Programs Coordinator, TEMPO  
(Secretary of the group)

## International Experts

Terence Taylor, Co-Chairman, ICLS

Jennifer Runyon, ICLS (1) also alternate to Terence Taylor

Heather Sheeley, UK Health Protection Agency

Rainer Wessel, CEO GANYMED Pharmaceuticals , Germany

Ali Mohammadi, World Health Organization

Martin Sanders, Centers for Disease Control. USA

Erling Myhre, University Hospital Lund, Sweden

Barry Holmes, National Type Culture Collection, UK Health Protection Agency

Maureen Ellis, Foreign Affairs Canada

Ingegerd Kallings, Swedish Institute for Infectious Disease Control

Georg Pauli, Robert Koch Institute

Takeshi Kurata, Toyama Institute of Health, Japan

David Franz, Midwest Research Institute, USA

Robert Halley, MidWest Research Institute and President of American Biosafety Association, USA

Andrew Powell, Asia Biobusiness, Singapore

Stefan Wagener, Public Health Agency, Canada

Jonathan Richmond, Jonathan Richmond and Associates, past President of the American Biosafety Association and formerly Director of the Office of Health and Safety at the Centers for Disease Control, USA

Roger Hewson, Group Leader Virus Research, Porton Down UK

Tim Brooks, Head of Novel & Dangerous Pathogens, Centre for Emergency Preparedness and Response Porton Down UK Health Protection Agency

Alexander Bartsev, Biotechnology Division, Organisation for Economic Cooperation and Development

Thank you for  
attention