Learn from emerging virus infections（1)

Emerging viruses are zoonotic infectious viruses.

●Humans interrupted peaceful codependent relationships between viruses and natural hosts.

●Modern society invited viruses which existed in places far away from humans.

Social activities of humans keep widening.

⇒New viruses keep emerging.

Learn from emerging virus infections（2)

Marburg disease（1967）

The source of infection was an African green monkey airlifted from Uganda.
Infections with a fatality rate of 23% broke out in west Germany
（Bering Lab. in Marburg, Ehrlich Lab. in Frankfurt) and Yugoslavia (Belgrade Lab).
（note）：500 monkeys were imported to Tokyo around the same time.

The virus was separated in the University of Marburg.
(note)：by classical protection by mask, lab-coat, and gloves
now, BSL (Biosafety level) 4

Natural host is still unknown.

Learn from emerging virus infections（3)

Lassa fever（1969）

1969～1970　group infection in a Nigerian hospital. Fatality rate of 36～67%.

Natural host is mastomys（a large rodent）. No pathogeny in mastomyses; they live with the virus

The virus is a Lassa virus, belonging to the Arenaviridae family.

The virus is shed in mastomys excreta. ⇒It infects humans by aerosol.

（note）：dangers of imported diseases

1976　An American woman who returned from Sierra Leone was found to be infected with the
552 people (including 5 Japanese on the same airplane) who may have had contact with
were kept under medical supervision for 3 weeks.

1987　A Japanese engineer who returned from Sierra Leone was hospitalized in
the Institute of Medical Science at the University of Tokyo, and later found to be
infected with the Lassa virus.

Learn from emerging virus infections（3)

Ebola hemorrhagic fever（often after 1976）

Hospitals are responsible for the infection in all cases.

Causes of the spread of infection：

1. Repeated use of un-sterilized hypodermic needles
2. The customs (rituals) for cleaning and dressing the dead
3. Medical treatment without wearing a protective gown

（note）：Rapid treatment is important to minimize victims.

BSL4 level laboratory

Vaccines

bacteria：**pertussis vaccine, diphtheria toxoid、tetanus toxoid, cholera vaccine, leptospirosis vaccine, pneumococcus vaccine**

virus：**polio vaccine, influenza vaccine, Japanese encephalitis vaccine, measles vaccine, mumps vaccine, rubella vaccine, rabies vaccine yellow fever vaccine, chicken pox vaccine, hepatitis B vaccine, hepatitis A vaccine**

Cures

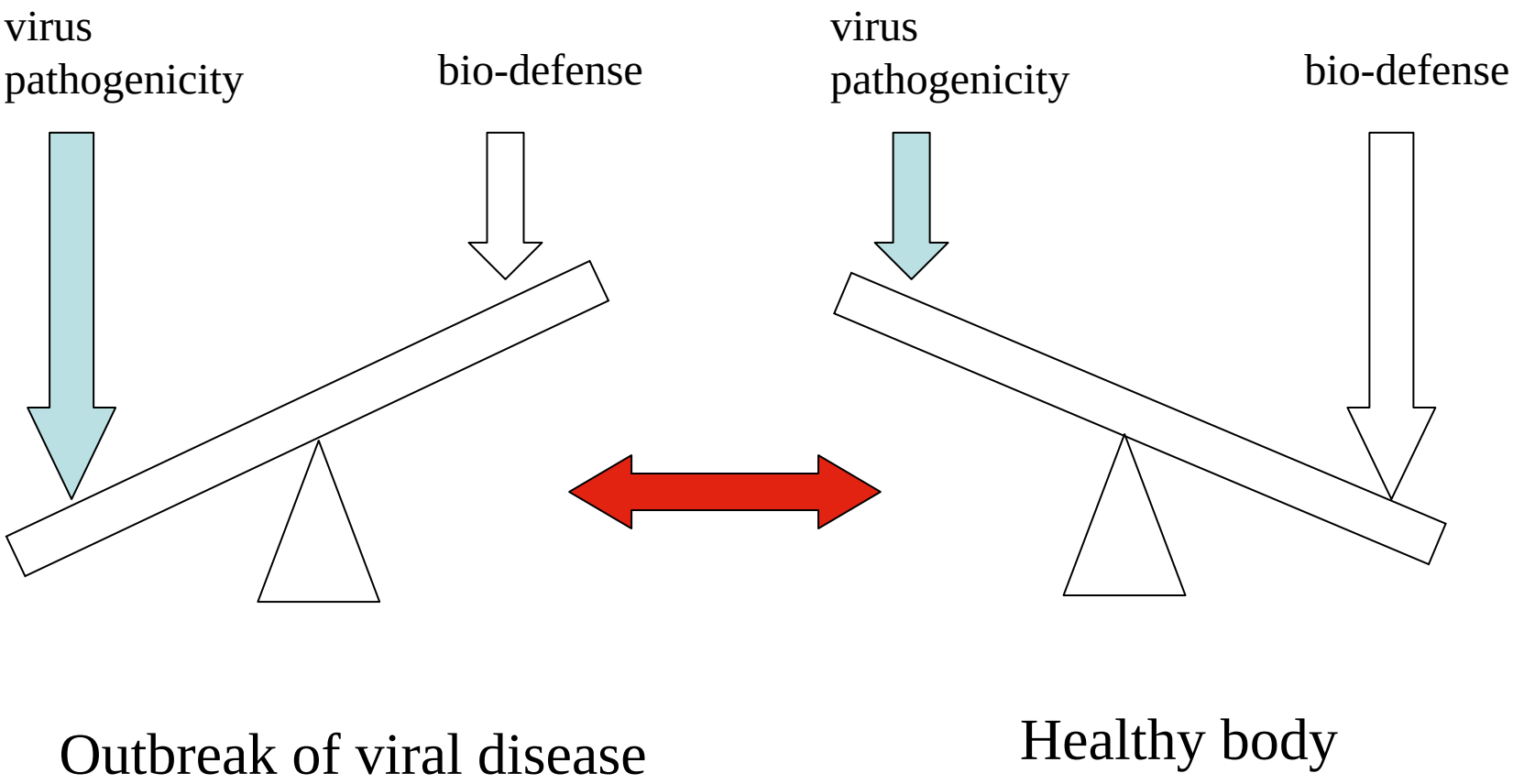
bacteria： **many kinds of antibiotics**

virus： **acyclovir, amantadine, zanamivir, r**ibavirin

Vaccines

Gives specific immunity against pathogenic microbes

Virus pathogenicity and bio-defense



Vaccines

- Raw vaccine
- Inactivated vaccine
- Component vaccine

Preventive vaccines

- Everybody
- Risk group
- Curative vaccines（drugs）

Good vaccines

- Peroral administration
- Effective in a single dose
- Multivalent vaccine

Pursuits

- Effectiveness
- Safety
- Developmental research

Pathogens whose vaccines are difficult to develop

- Multiple antigenicity
- Changing antigenicity
- Reinfection and out breaks

New vaccines

- DNA vaccines
- Immunostimulating vaccines
- Mucosa vaccines

	polio virus	HIV
molecular mechanism of infection and pathogeny	unknown	unknown
vaccine	exists	difficult
clinical condition	acute	chronic

Pathogenicity (pathogen tropism)

- Proliferation
- Transmission in body
- Clinical conditions

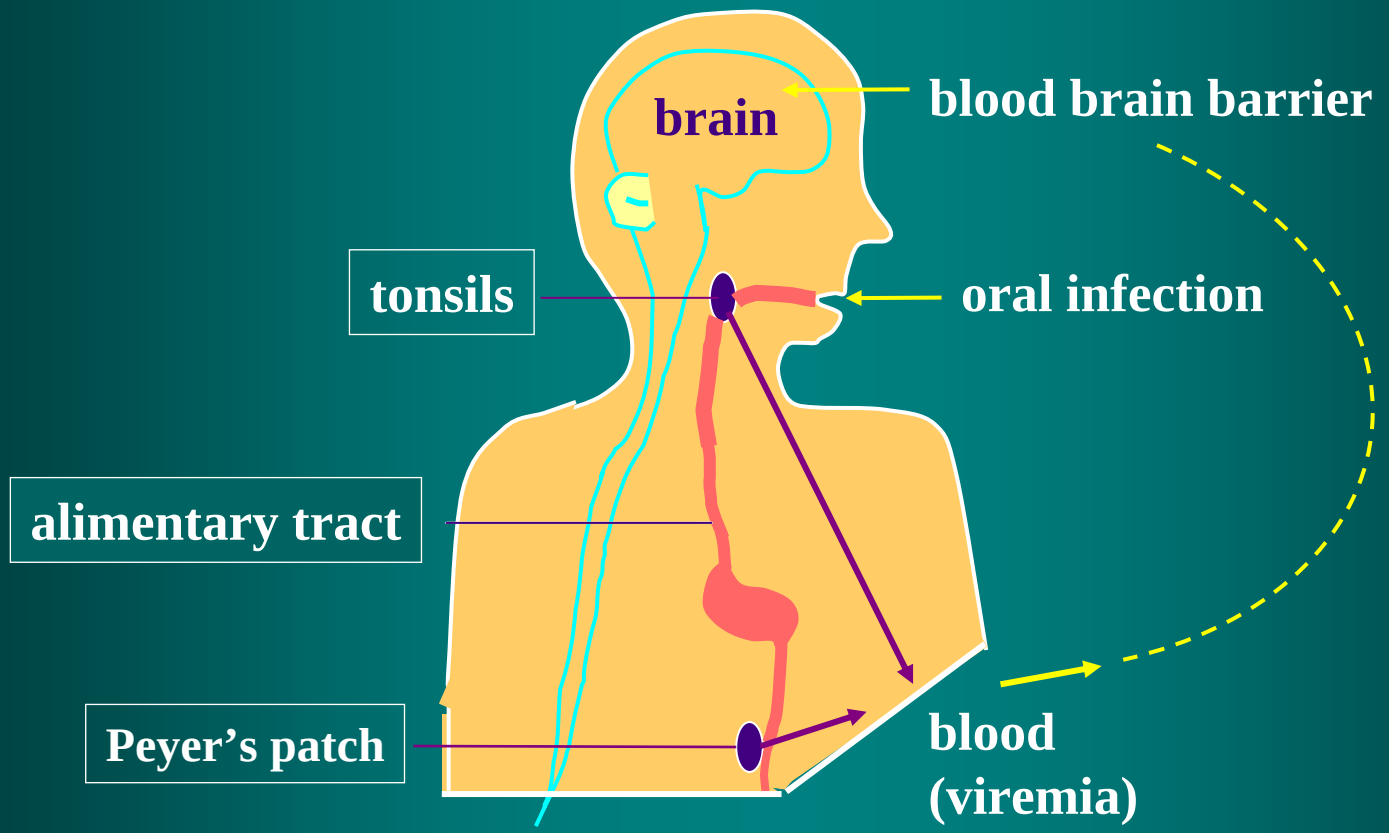
Research on infection process breeds strategies to control infections

Conventional vaccines : prevent infection/outbreak by neutralizing antibodies

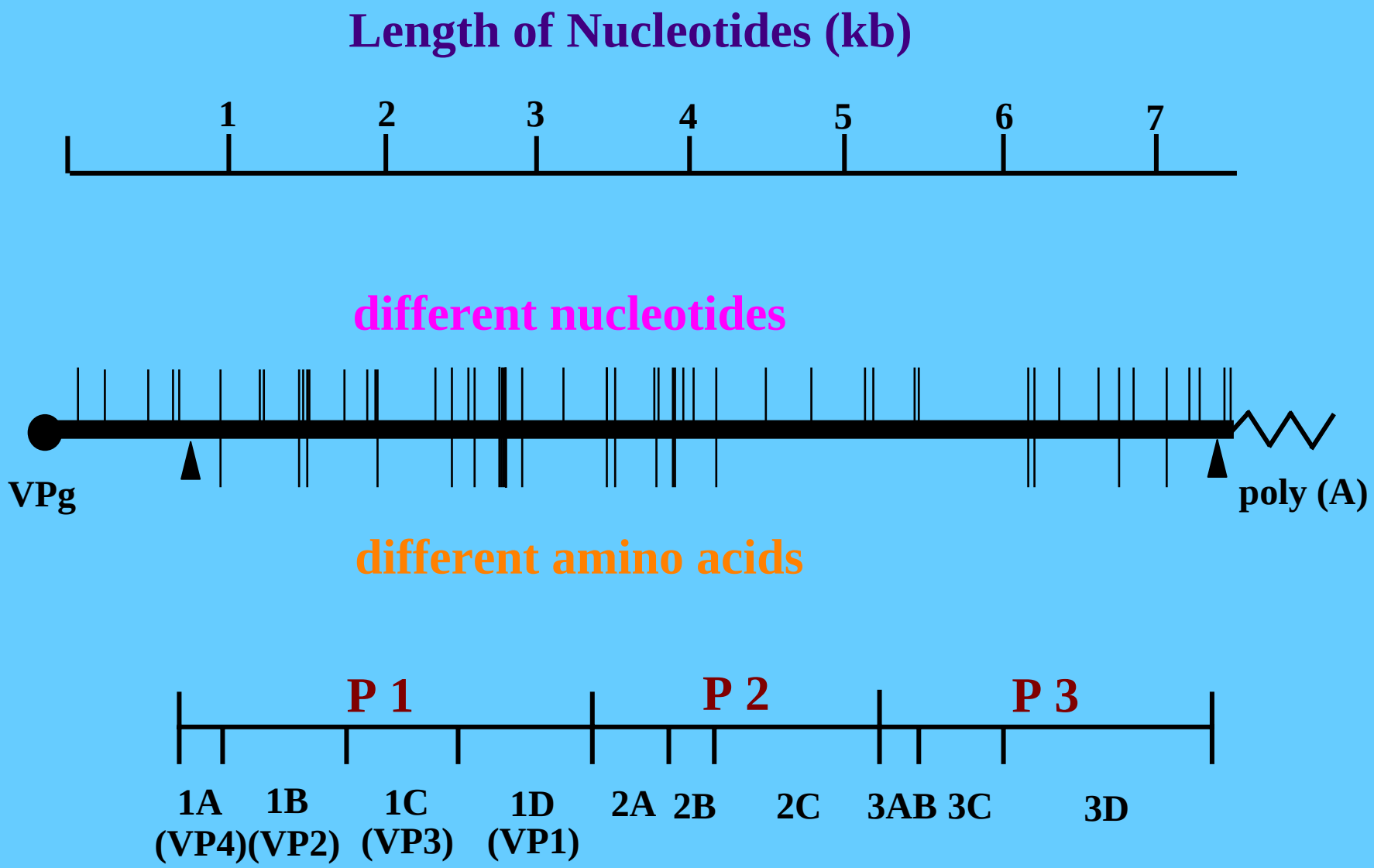
Preventing infection : discover the molecular mechanism of infection process in the first target cell

Preventing outbreak : discover the molecular mechanism of whole process from infection to outbreak

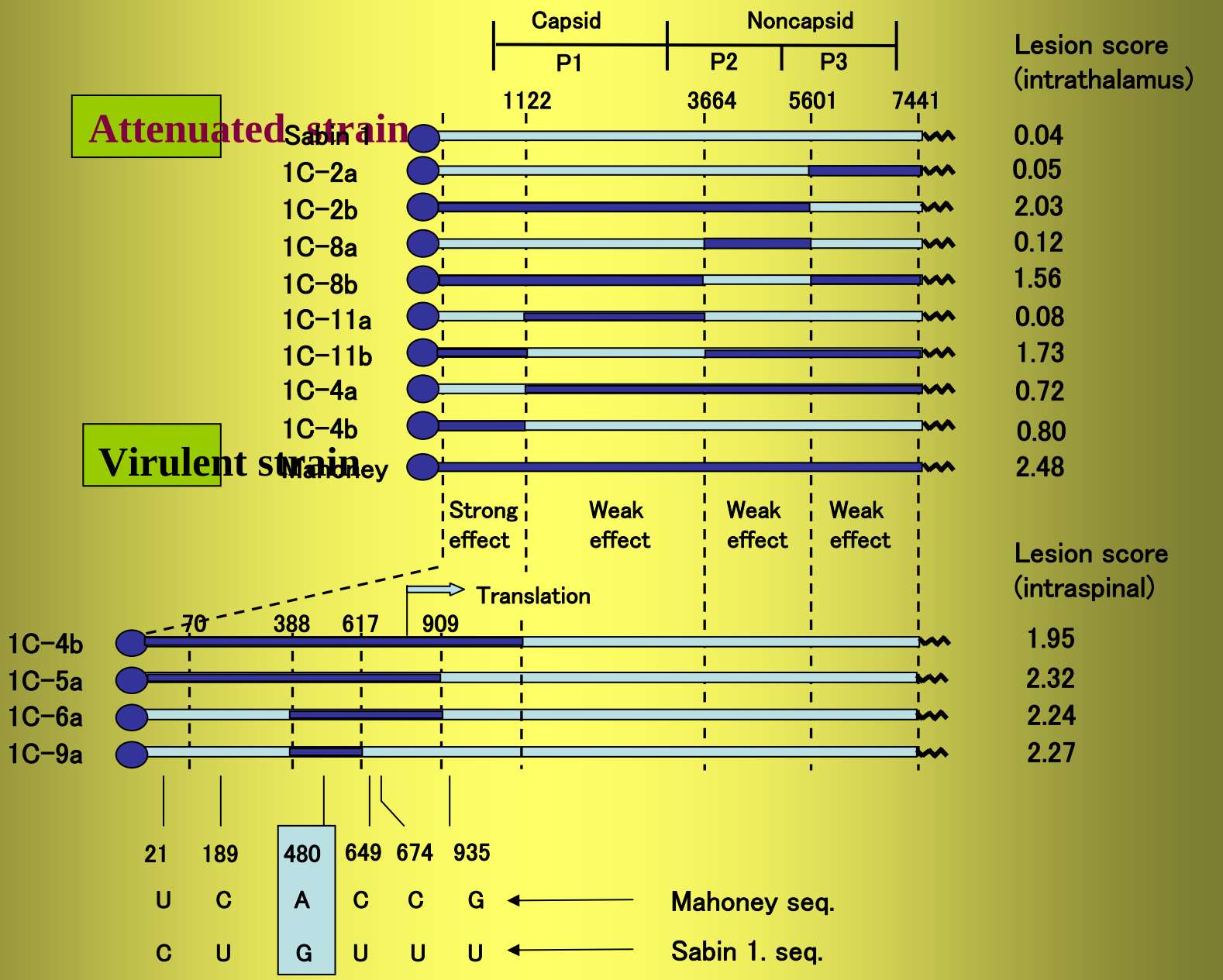
Dissemination of Polio Virus in Humans



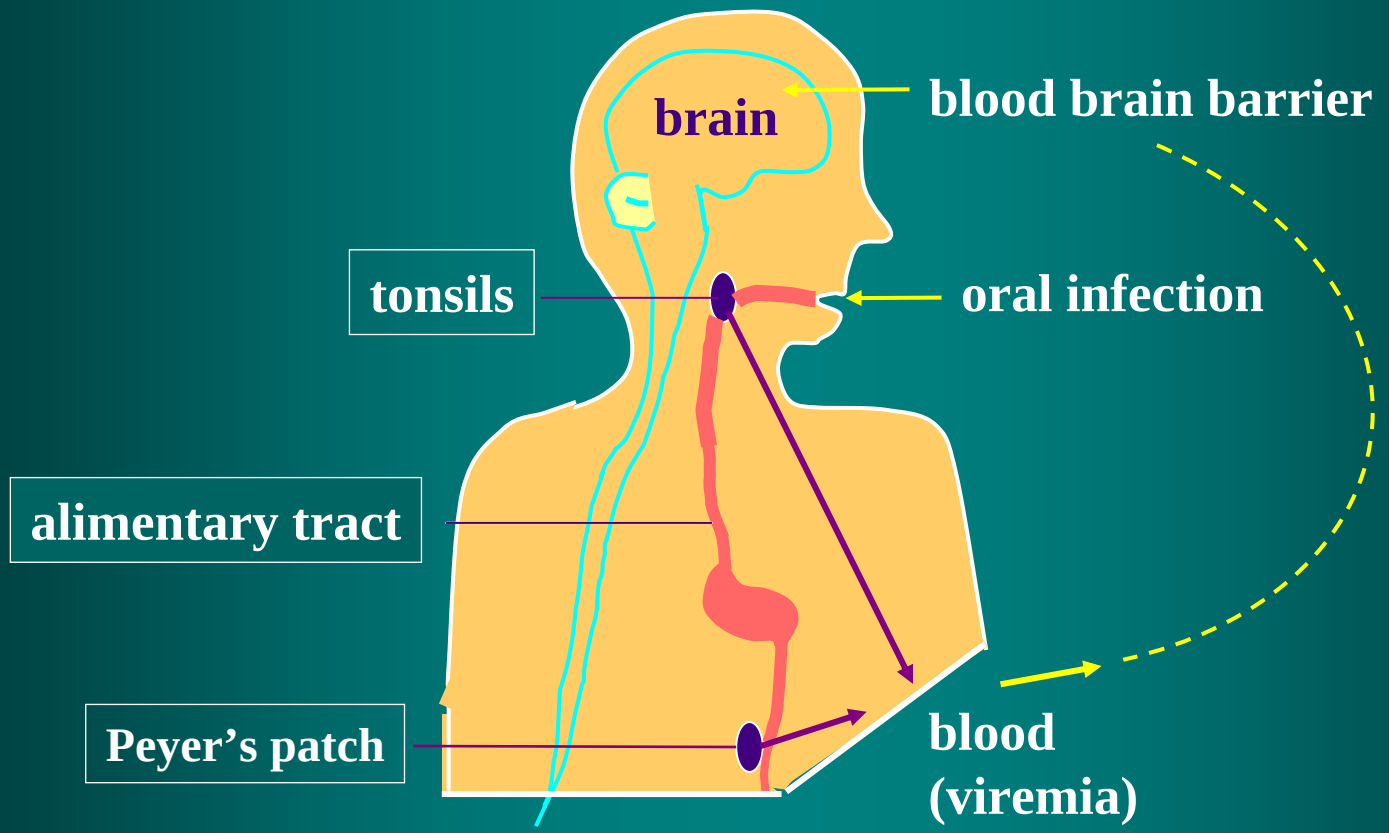
	alimentary tract	viremia	CNS
Virulent strain	○	○	○
Attenuated strain	○	×	×


Length of Nucleotides (kb)
1
2
3
4
5
6
7
different nucleotides
VPg
poly (A)
different amino acids
P 1
P 2
P 3
1A
(VP4)
1B
(VP2)
1C
(VP3)
1D
(VP1)
2A
2B
2C
3AB
3C
3D

強毒株と弱毒株の組換え体ウイルスのゲノム構造

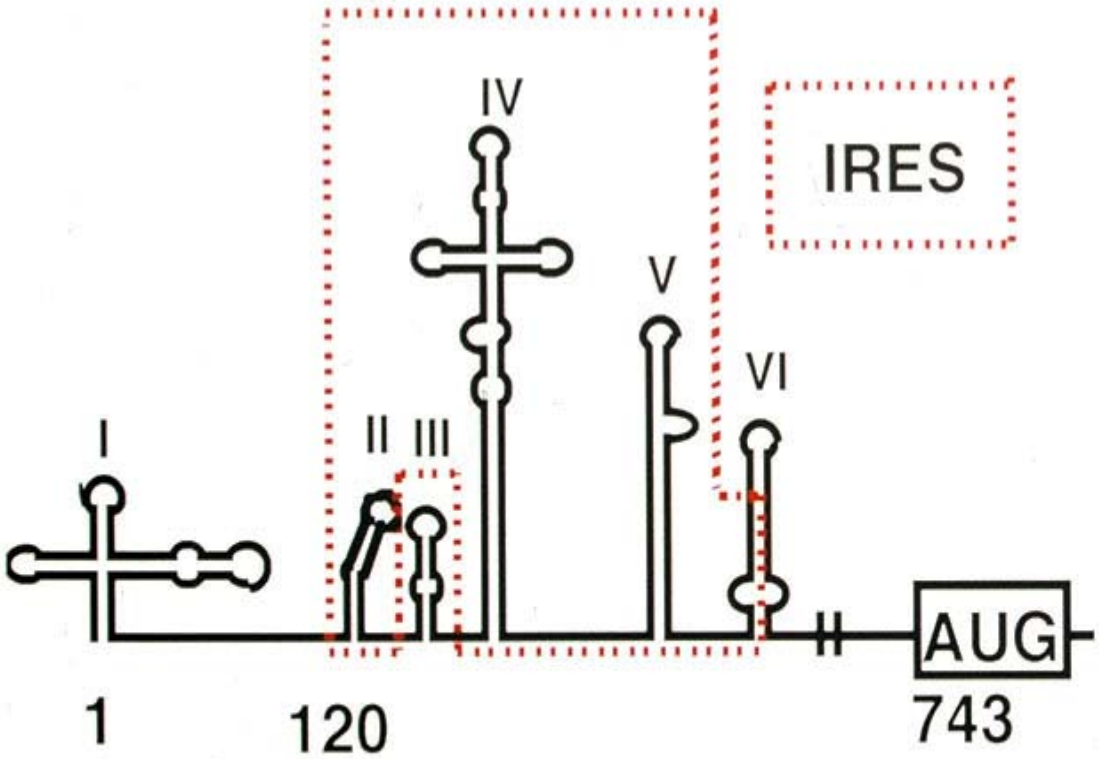


Dissemination of Polio Virus in Humans



	alimentary tract	viremia	CNS
Virulent strain	○	○	○
Attenuated strain	○	×	×

Poliovirus IRES and Host Factors



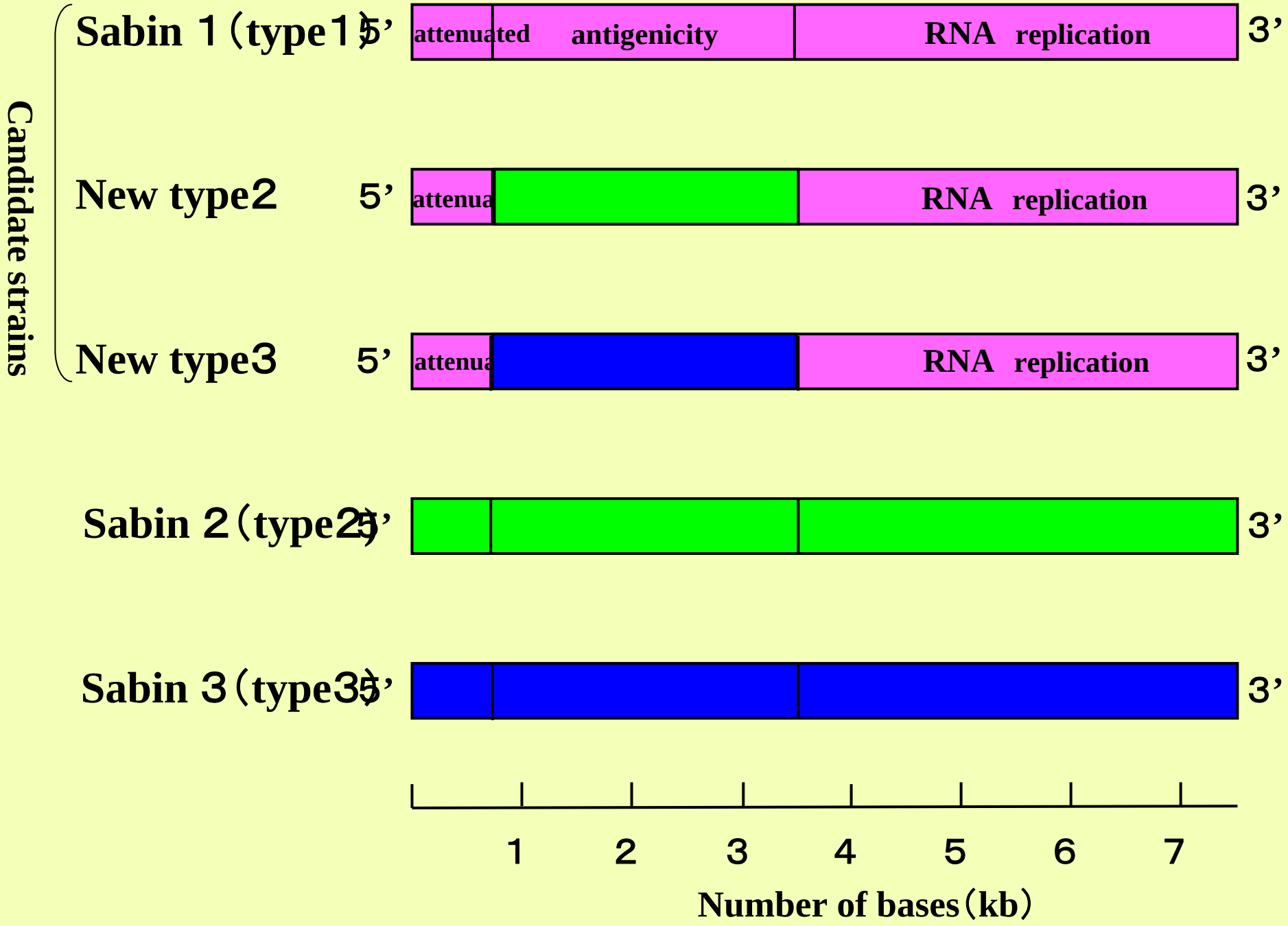
Cellular factors for IRES

La protein (SLVI)
PCBP-1,2 (SLI, IV)
PTB (SLV)

IRES: Internal Ribosome Entry Site

Genetic stability of nucleotides that influence the attenuation phenotype of the polio virus.

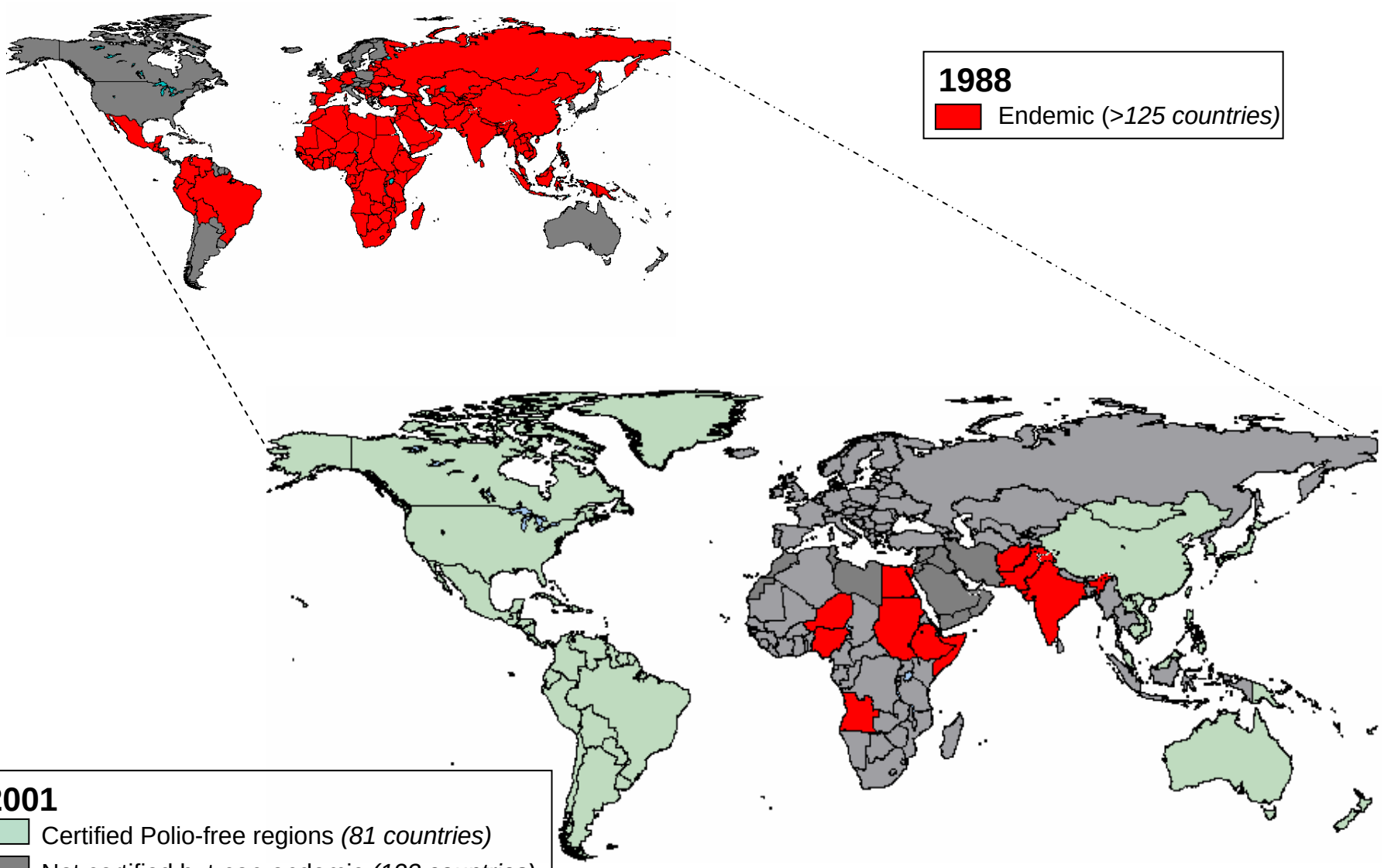
	N480(Type 1)	N481(Type 2)	N472(Type 3)
Nucleotide in Sabin strain genomes	G	A	U
Nucleotides detected in excreted viruses	G(83%) A(17%)	A(28%) G(72%)	U(0%) C(100%)


Candidate strains
Sabin 1（type1）
5’
attenuated
antigenicity
RNA replication
3’
New type2
5’
attenua
RNA replication
3’
New type3
5’
attenua
RNA replication
3’
Sabin 2（type2）
5’
3’
Sabin 3（type3）
5’
3’
1
2
3
4
5
6
7
Number of bases（kb）

1961. 6. 22

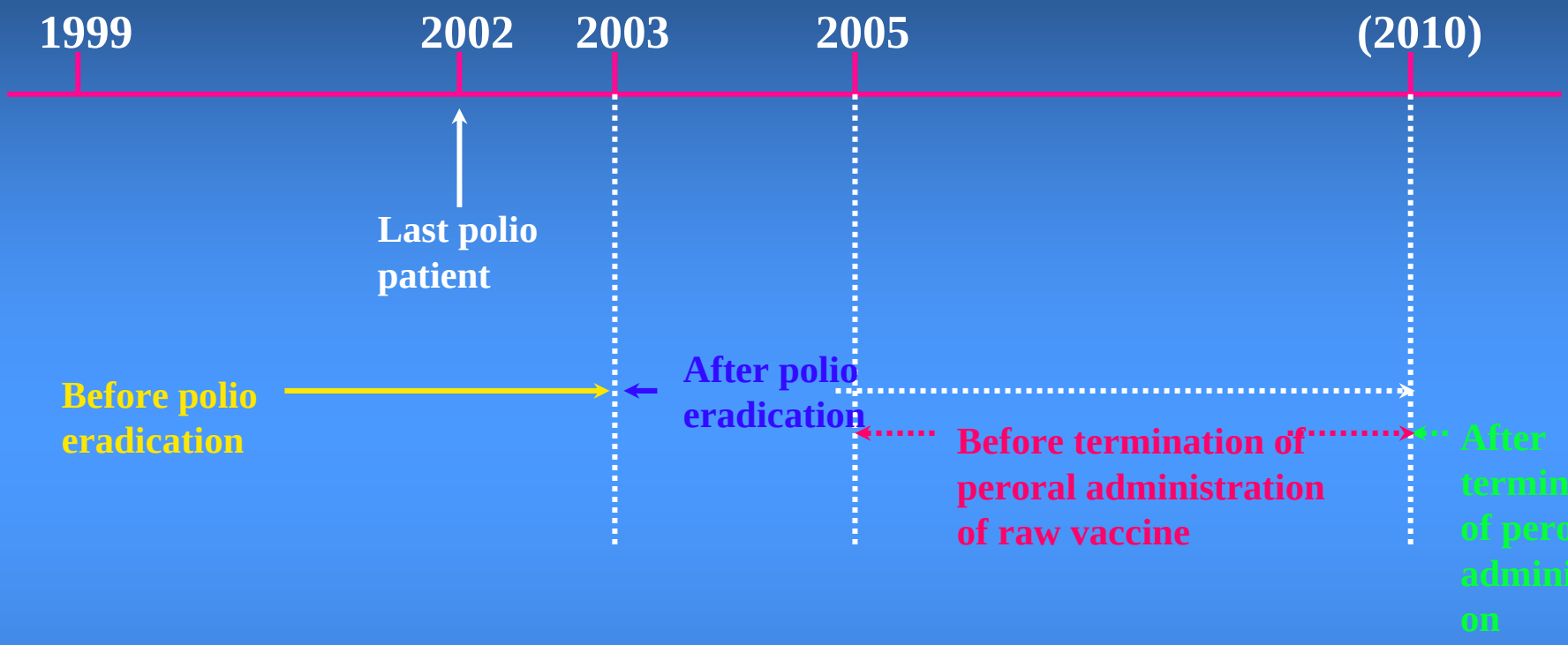
Asahi Shimbun

Polio Eradication Progress, 1988 - 2001



Source: WHO AFP surveillance database
February 2002

WHO policy for a polio eradication plan（2000）



（wild-type exists）　（wild-type eradicated）　(OPV administration sto

wild-type strain	BSL2	BSL3	BSL4
vaccine strain	BSL2	BSL2	BSL3

BSL：Bio-safety level