General characteristic of group of infections with the airborne mechanism of transmission.

INFLUENZA and ARVD

INFLUENZA and ARVD

Influenza and ARVD occupy the first place by amount of causes of diseases in the world and make annually 95 % of all infectious diseases .

Influenza affects annually 15 % of the population of a planet.

As against influenza - ARVD - (acute respiratory viral diseases) are collective name of major number respiratory disease caused more than 100 viruses.

What has allowed to unite them in one group:

All they are:

- **of a viral etiology**
- **primary injure an epithelium URT (upper respiratory tract) also are accompanied by intoxication (various expressiveness)**
- **spread from person to person by aerosol or droplet transmission**
- **meet everywhere, can cause epidemics and pandemics (influenza A)**

Among this group of diseases the main role belongs to the nfluenza.

The names of disease come:

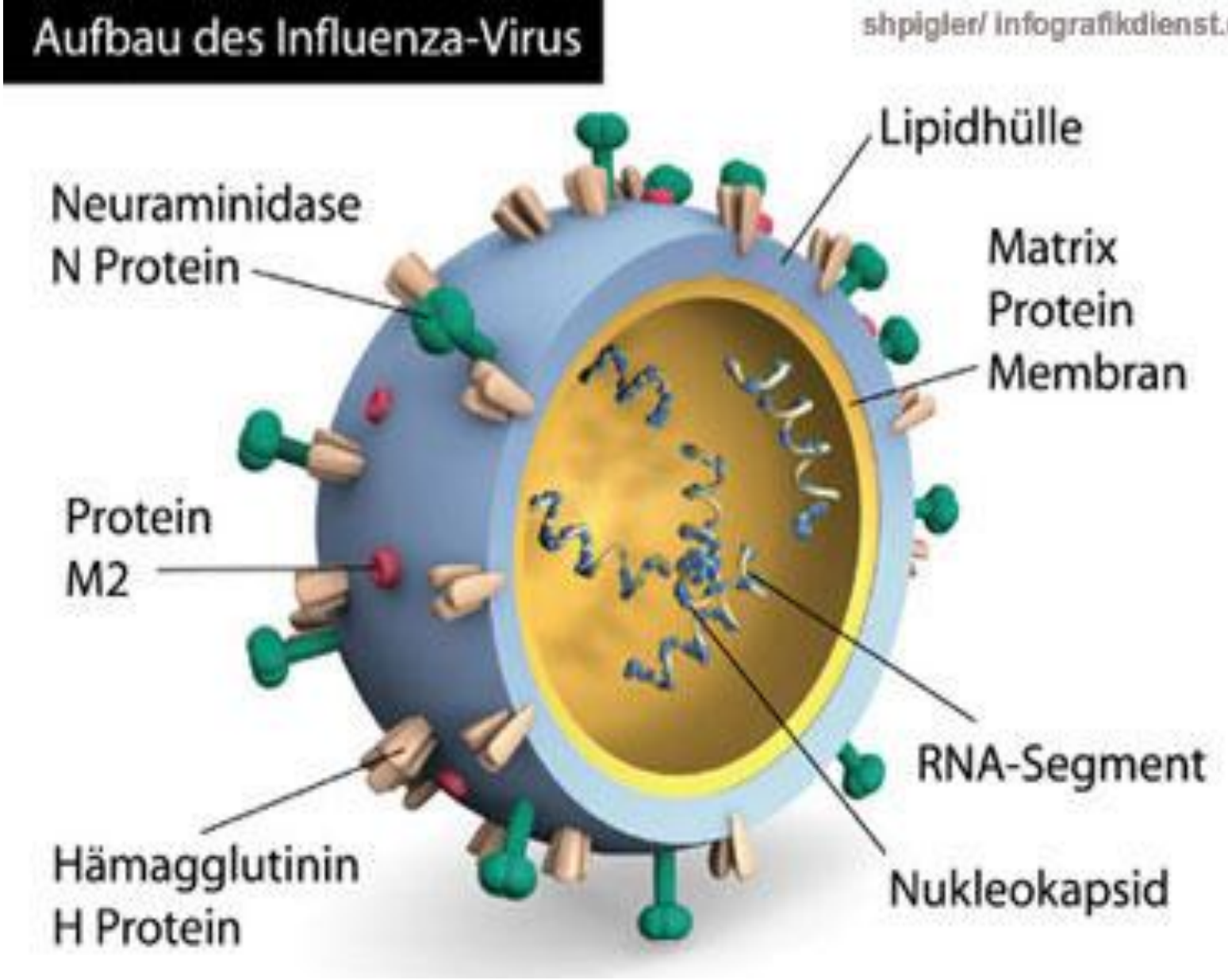
- from the French word "gripper" - to attack, to seize
- from a Latin word “influenza" - to invade, to flow into

The virus of an influenza A is allocated in 1933 year (W.Smith et all),
the virus of an influenza B - is allocated in 1940 year (T. Fransis et all)
the virus of an influenza C - is allocated in 1947 year (R.M.Taylor et all)

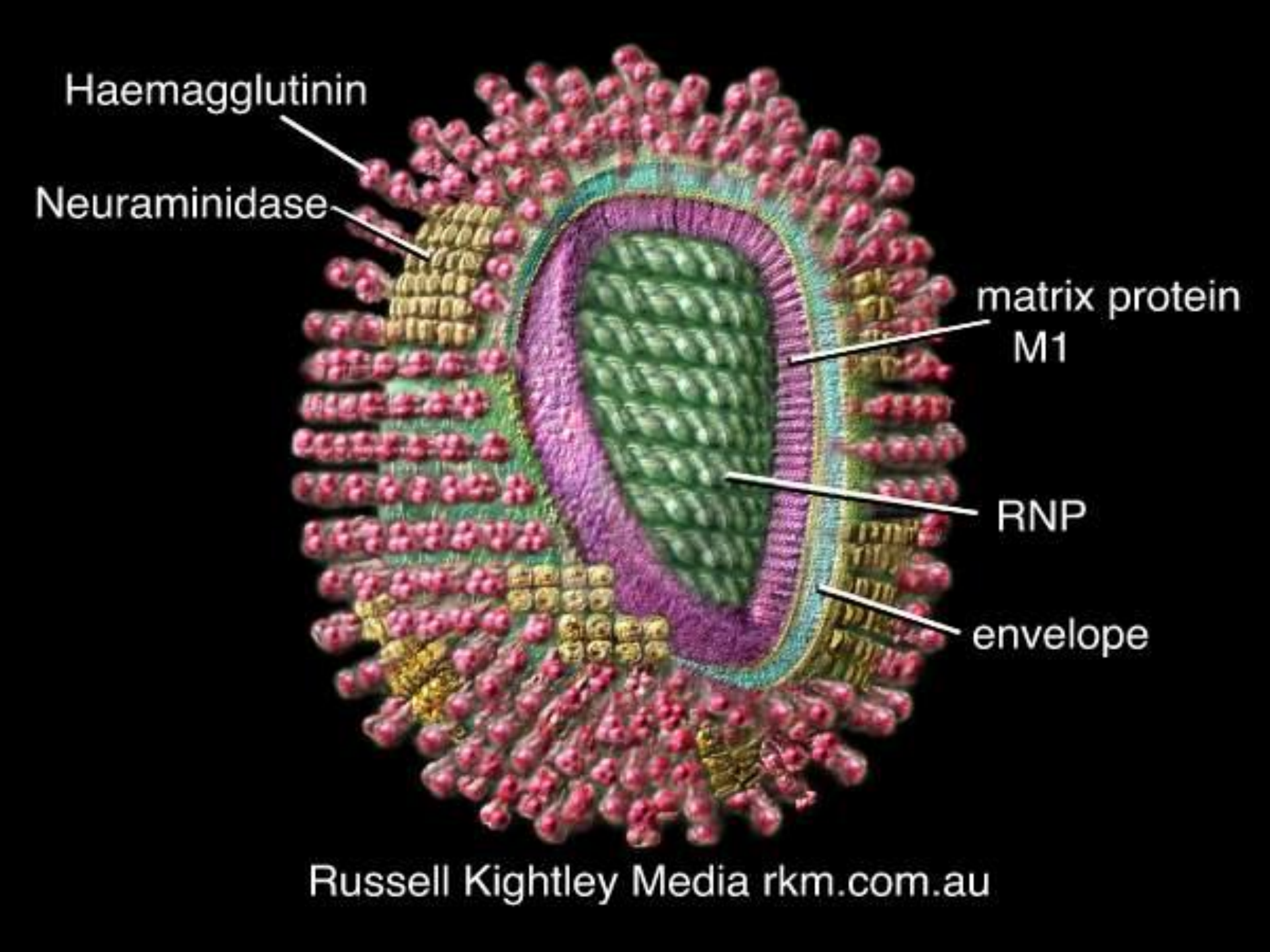
F. Orthomyxoviridae, G. Mixovirus Influenza.

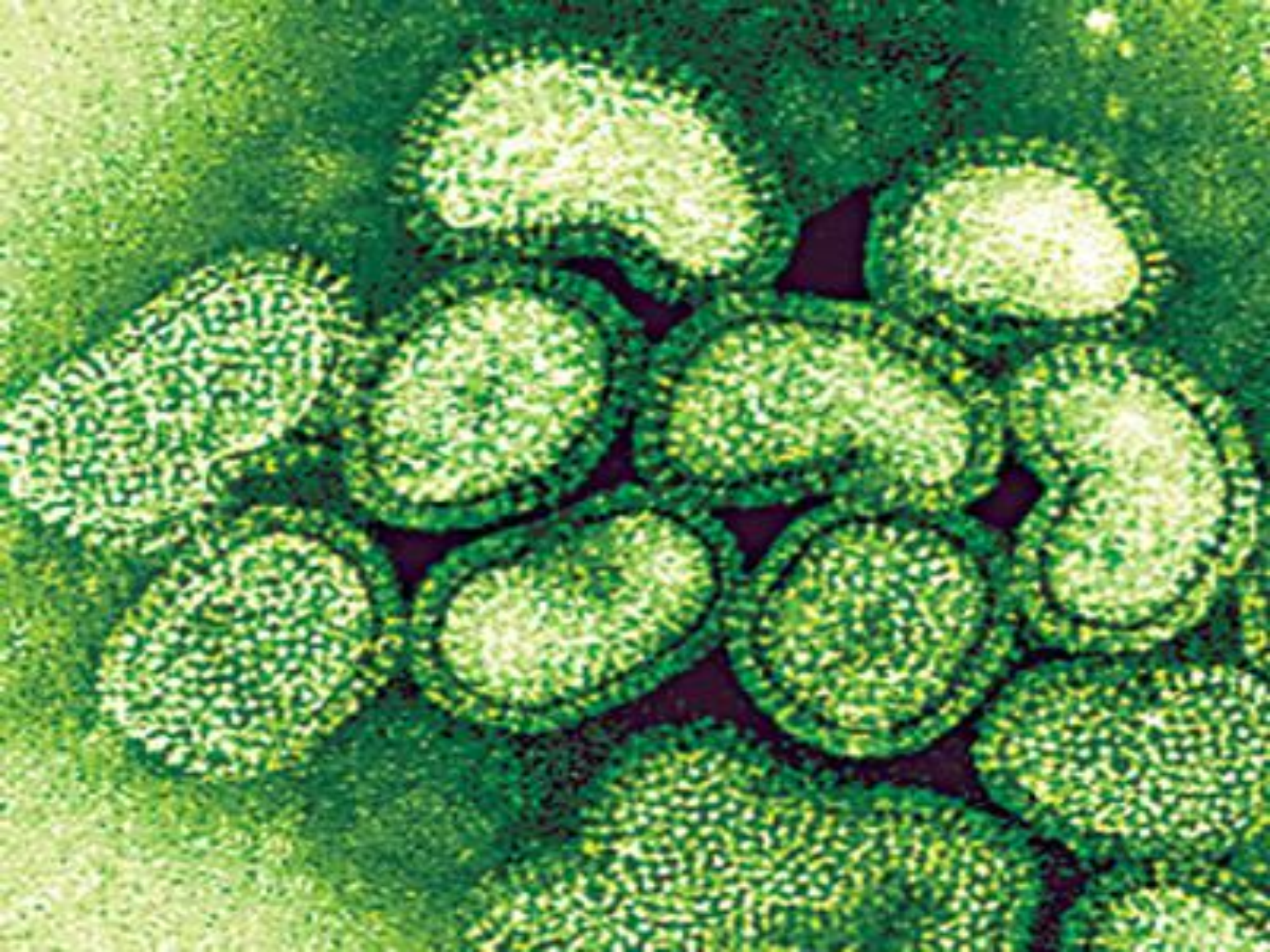
A spherical virus by a size 80 - 120 nm. The core contains one-filamentous RNA (-), divided on 8 fragments, which encodes to formation of 10 viral protein and united among themselves by common protein envelope (M1) formating a nucleocapsid.

Covered bilayer by the lipid envelope, on a surface which 2 main antigenes (H and N) of a virus are detected:

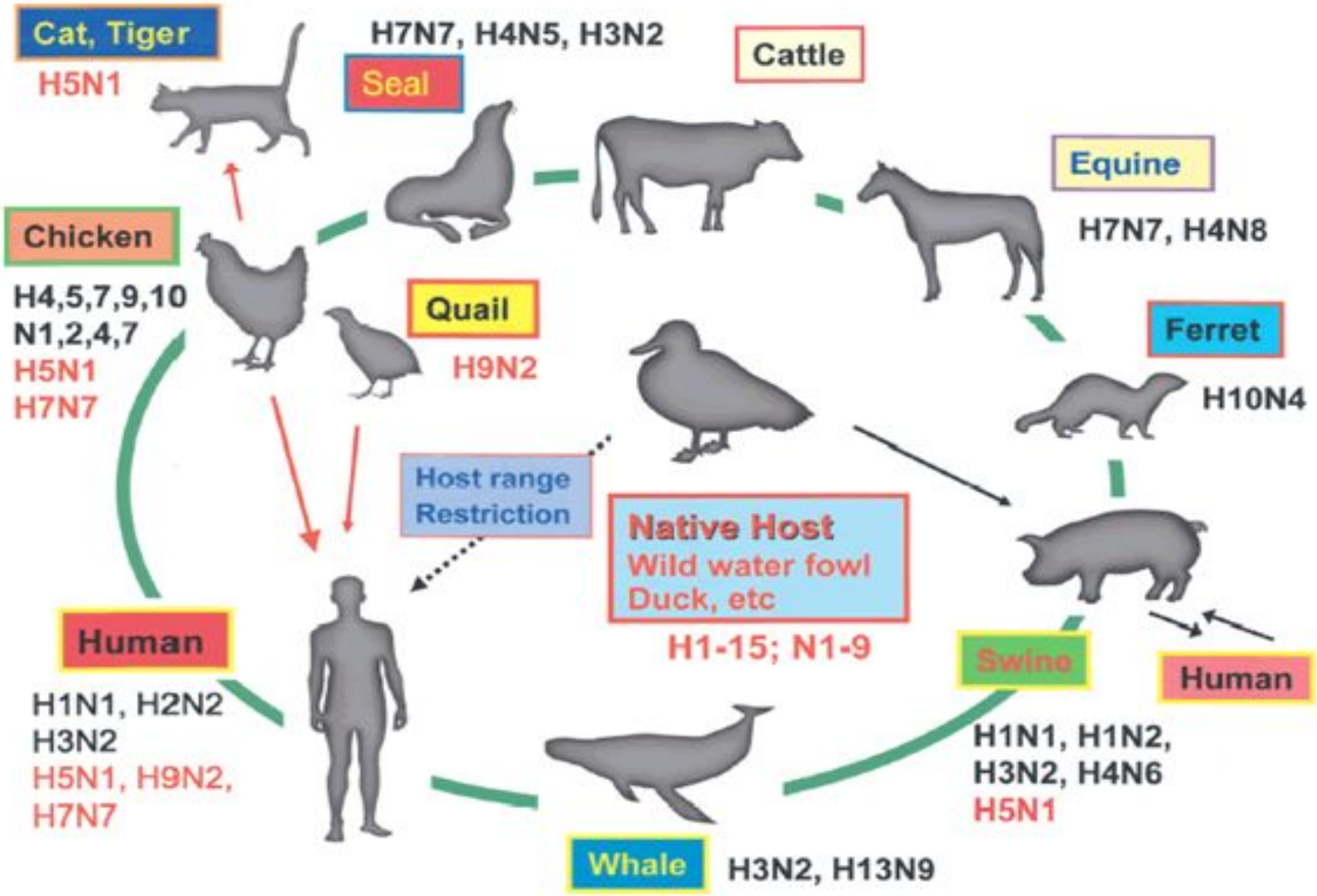


- **Virus influenza HAS - internal proteins (M 1, NP, P1, P2, P3) and external (H, N,) and extracellular proteins (NS1, NS2) RNA (-) – divided on 8 fragments. Size of the virus 100 – 120 nm**


Haemagglutinin
Neuraminidase
matrix protein
M1
RNP
envelope
Russell Kightley Media rkm.com.au



Important antigenes of influenza A (H+N) and their circulation in nature



Hemagglutinin (H) - 15 types (H1, H2, H3 - for the man) provides affixion of a virus to a cell!!!

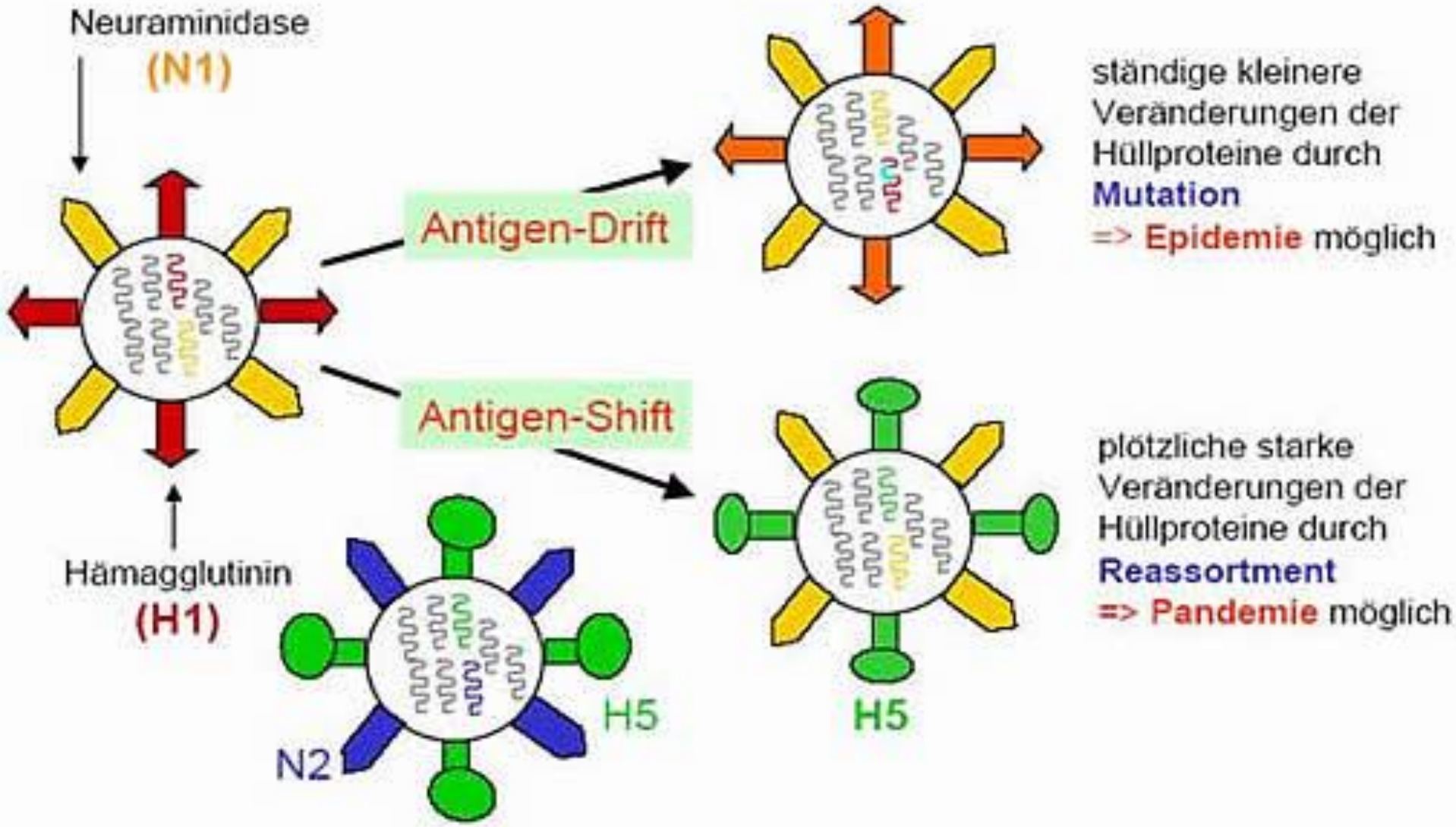
Neuraminidase (N) - 9 types (N1, N2 - for the man) provides infiltration of a virus into a host cells and facilitates going out of the viruses-descendants from the host cells, preventing their aggregation!!

The nucleoprotein (s-antigenes) has to constant structure also determines the type of a virus (A, B, C)

Hemagglutinin and neuraminidase (V - antigenes) permanently chageable also determine appearance of the different strains one virus (influenza A and B)

The virus of an influenza A permanently varies causing epidemics everyone 2 - 4 YEARS - (There is drift),

Influenza - ein variables Ziel für das Immunsystem



but everyone 10-30 years there is a complete replacement of antigenes (There is shift) - that promotes by appearance of pandemics!!

The virus B varies slowly (epidemic through 4 - 7 years)

but shift is not observed also pandemics do not arise!!

The virus of an influenza C does not change antigenes, contains only 7 fragments RNA (instead of 8) and one surface antigene (instead of 2) - supporting only sporadic case rate!!

The replication of a virus occurs in cytoplasma of an ciliated epithelium, but the synthesis RNA occurs only in a core to using RNA-transcripts of the host cells.

Unstable in the external environment, are perished:

- at 20 dg. C - through 4 - 9 hours,
- at 60 dg. C - 3-5 minutes

at boiling, effect of alcohol, bichloride of mercury, forma - linum, disinfectants - is instantly.

At fast freezing to (-) 70 dg. C - is survived by years!!!

EPIDEMIOLOGY

Source - the sick man 24 hours prior to illness and all acute period

Mode of transmission – airborne (aerosol or droplet)

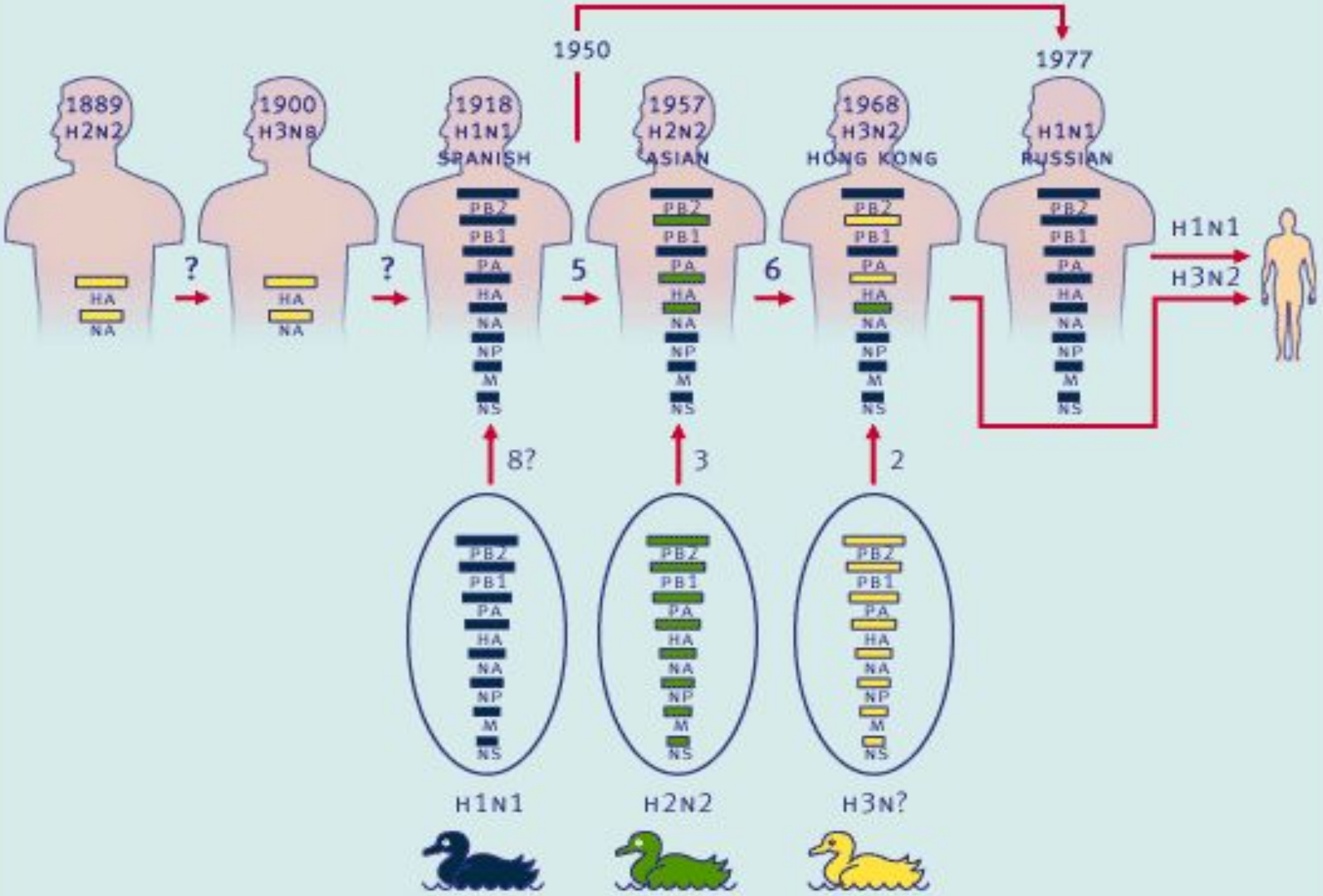
Epidemics of an influenza A - are recured everyone 2- 3 years, duration their 1 – 1.5 months with affect up to 20- 50 % of the population

The pandemics - are recured everyone 10 - 40 years

Epidemics of an influenza B - are recured through 3 - 4 years by duration their 2.5 - 3 months with affect 25 % of the population.

At an influenza C - an only sporadic case rate

Origin of human pandemic influenza A viruses



Каждые 11- 42 года (в среднем , каждые 33 года)

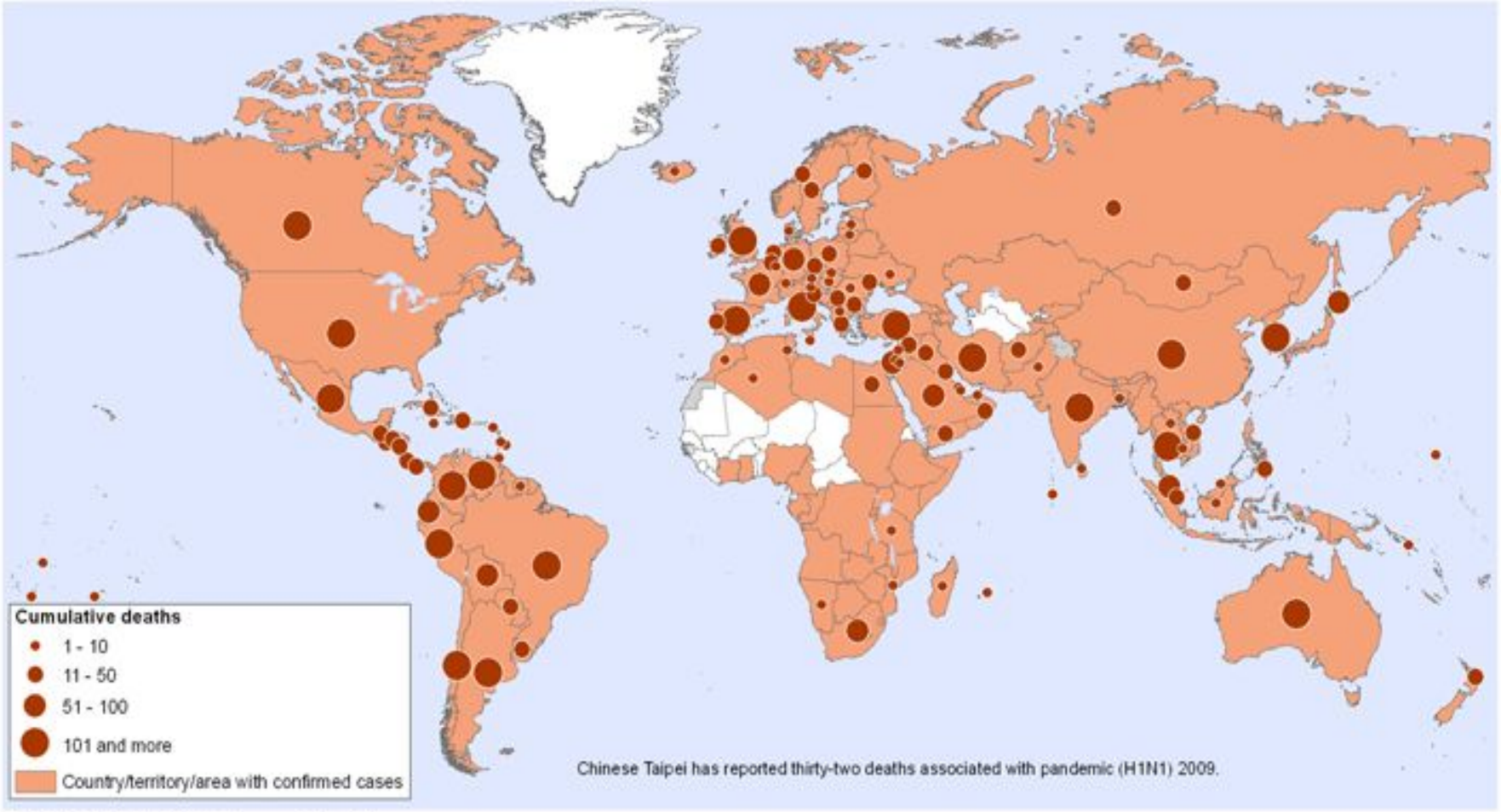
- 1889 H2N2
– 1900 H3N8
– 1918 H1N1
– 1957 H2N2
– 1968 H3N2
– 1977 H1N1 - (чаще заболевали молодые, которые были рождены после 1957 года)
- 2009 H1N1

World Health Organization

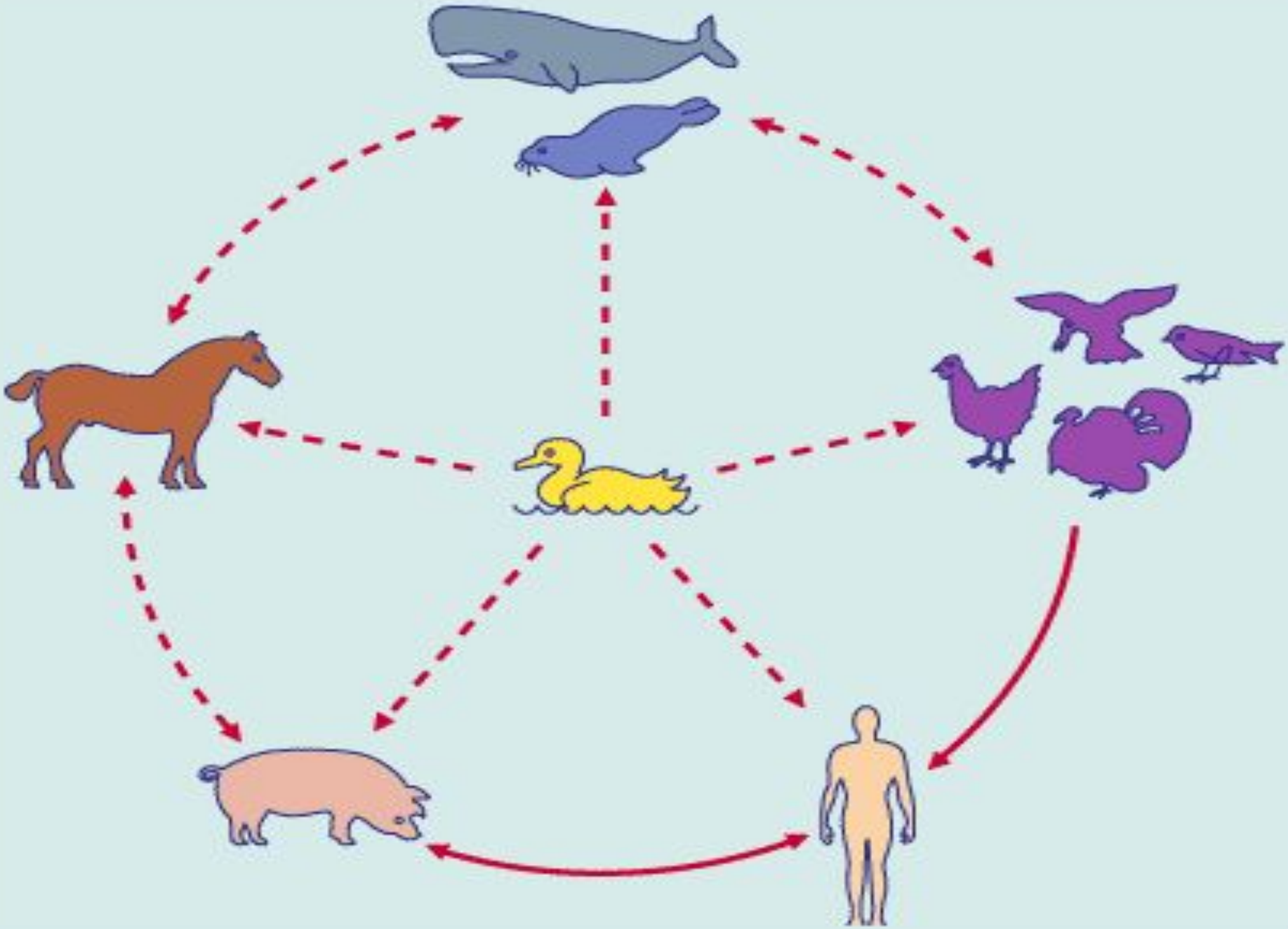
Timeline (22 July 2009 onwards)
Pandemic (H1N1) 2009 laboratory confirmed cases
And number of deaths as reported to WHO

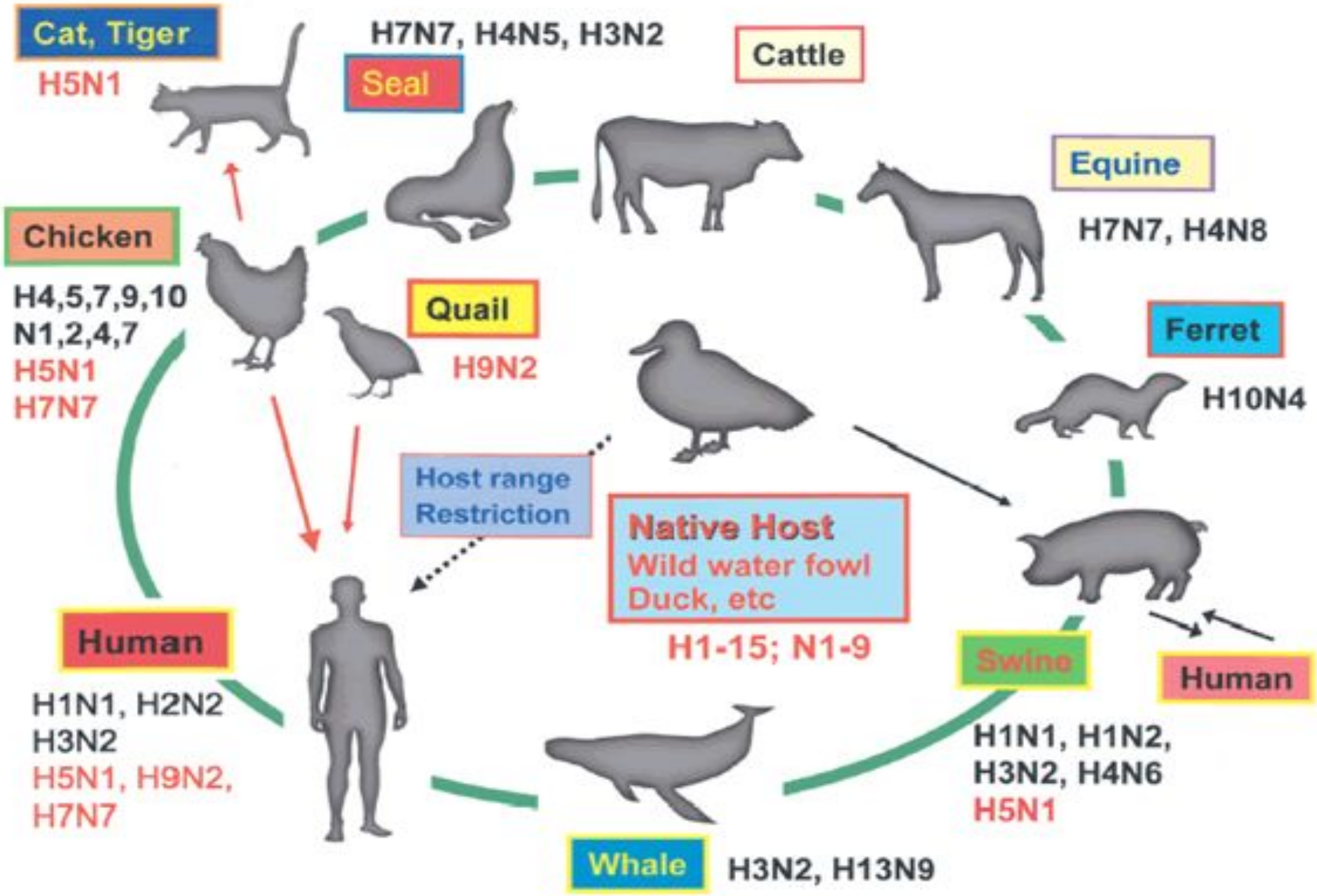
Status as of: 06 December 2009

Previous



The reservoir of influenza A viruses




Cat, Tiger
H5N1
H7N7, H4N5, H3N2
Seal
Cattle
Equine
H7N7, H4N8
Chicken
H4,5,7,9,10
N1,2,4,7
H5N1
H7N7
Quail
H9N2
Ferret
H10N4
Host range
Restriction
Native Host
Wild water fowl
Duck, etc
H1-15; N1-9
Human
H1N1, H2N2
H3N2
H5N1, H9N2,
H7N7
Swine
H1N1, H1N2,
H3N2, H4N6
H5N1
Human
Whale
H3N2, H13N9

Epidemics arise:

- autumn and winter (Northern hemisphere)
- spring and summer (Southern hemisphere)
- the year round (along equator)

The level of a case rate depends on number the population of city:

- 1 million and more - ARVD- 29,7 % of an Influenza - 11,3 %
- 500 т. - 1 million. - ARVD - 24,1 % of an Influenza - 10,3 %
- It is less 500 т. - ARVD - 22,1 % of an Influenza - 9,7 %

The village inhabitants are sick less often (less density of the population)

Duration of postinfectious immunity:

- at an influenza A-1 - 3 years
- at an influenza B - 3 - 6 years,
- at an influenza C - all children have immunity to it to 10 years of life.!!!

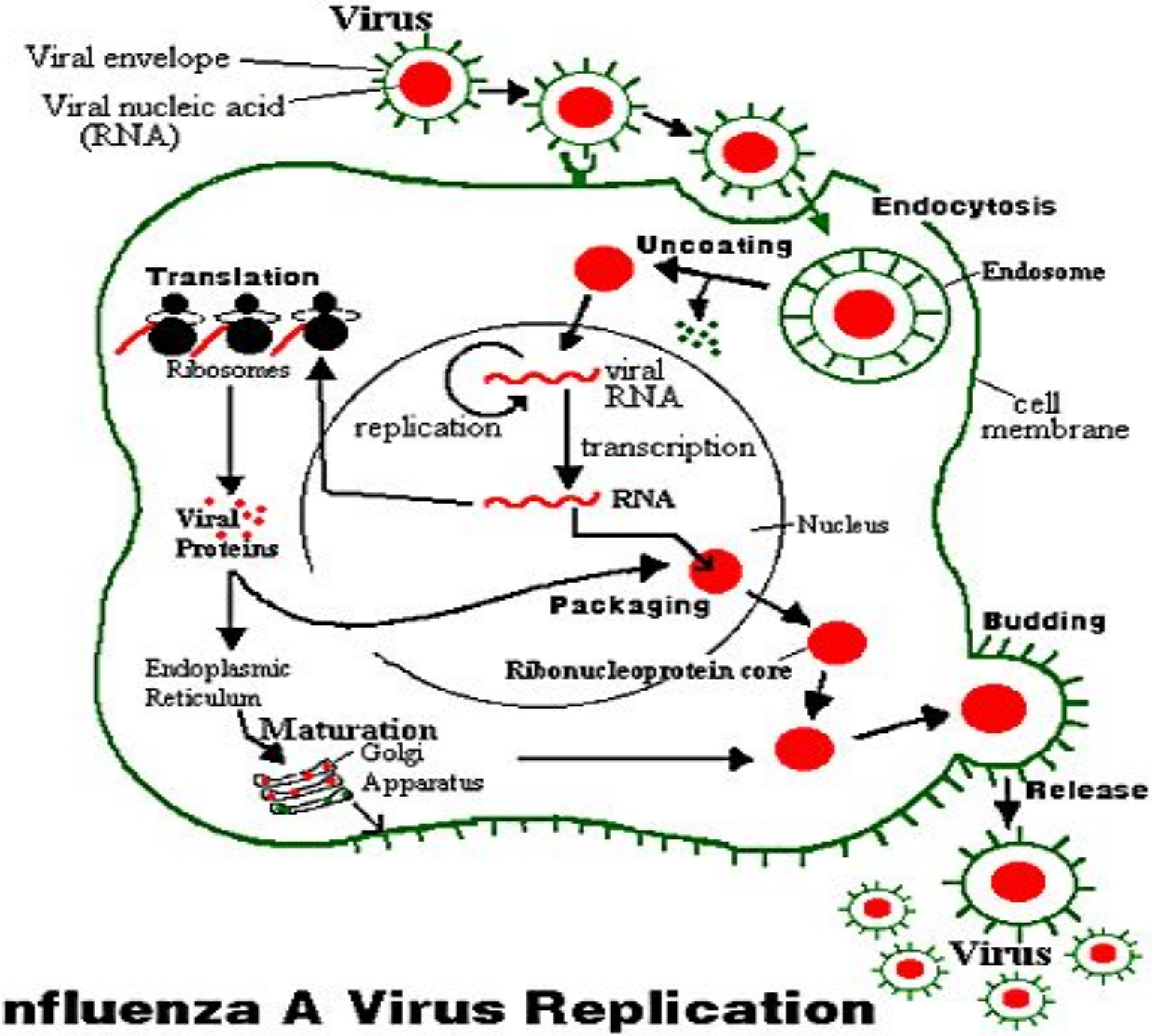
PATHOGENY

1. The virus gets on mucous with a ciliated epithelium (nose, trachea), overcoming its protection:

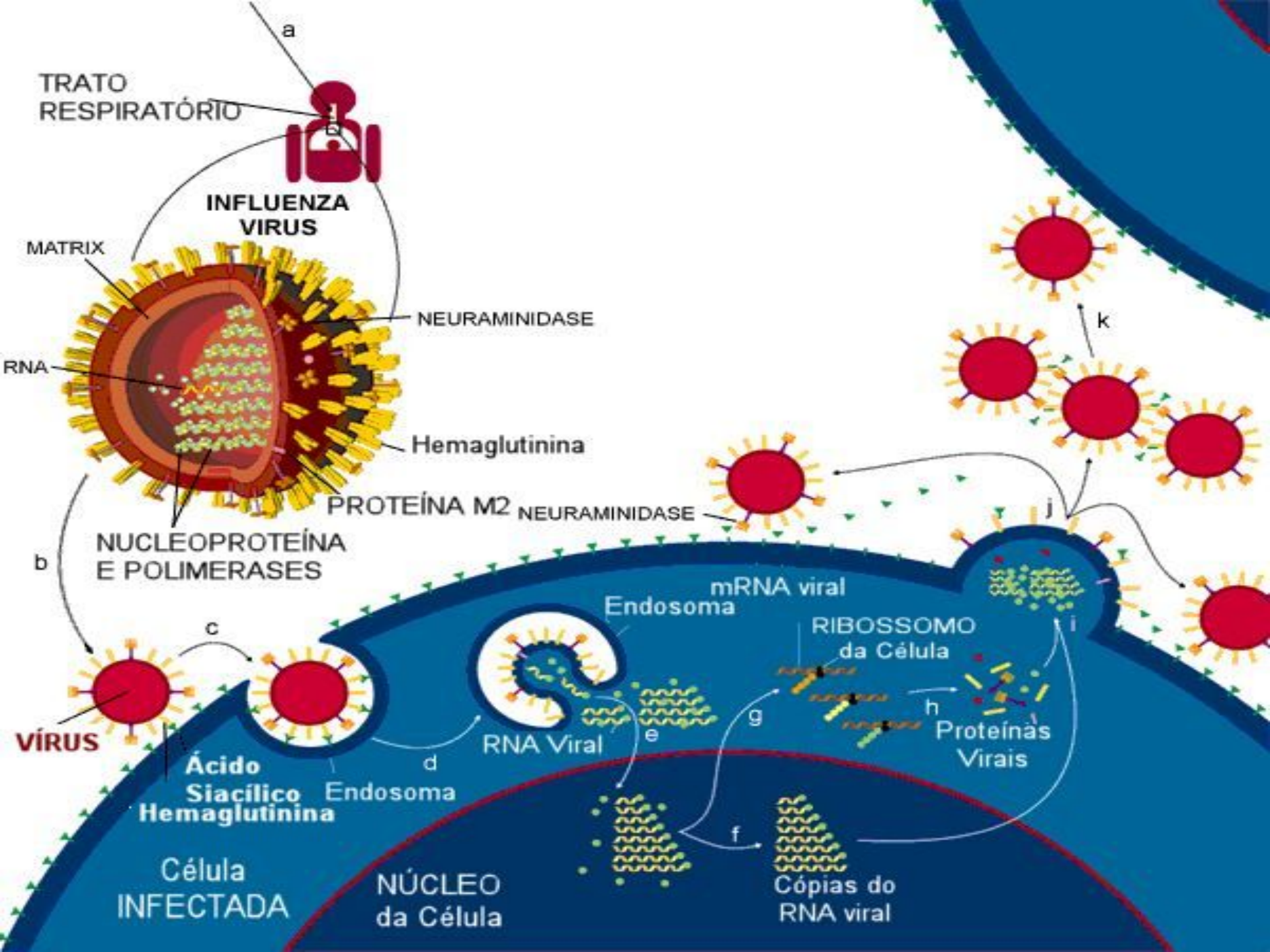
- viscous slime
- constant a motion of villies of a ciliated epithelium
- absorption by macrophages
- secretion of a mucous immunoglobulin A
- overcoming effect of interferons

2. Attachment (with helps a hemagglutinin- attach to receptors of sialic acid on epithelium URT (upper respiratory tract), with subsequent implantation in cells of an epithelium, "uncoating"of a virus, beginning of replication with creation of the viruses - descendants. One cycle of replication lasts 4-6 hours.

In 24 hours from one virus there are some hundreds millions viruses - descendants!!!!



Influenza A Virus Replication


a
TRATO RESPIRATÓRIO
INFLUENZA VIRUS
MATRIX
NEURAMINIDASE
RNA
Hemaglutinina
PROTEÍNA M2
NUCLEOPROTEÍNA E POLIMERASES
NEURAMINIDASE
b
c
d
e
f
g
h
i
j
k
mRNA viral
Endosoma
RIBOSSOMO da Célula
Proteínas Virais
VÍRUS
Ácido Siacílico
Hemaglutinina
Endosoma
RNA Viral
Célula INFECTADA
NÚCLEO da Célula
Cópias do RNA viral

3. Exit of the viruses-descendants and damage of new host cells.

Core and protein of a virus are shaped in cytoplasma with the subsequent exit through the envelope cell, transmuting a part it in own!!! Final creation of a virus occurs on surface of a cell, then a virus - descendant introduces into healthy host cell.

4. The neuraminidase at this stage plays the important role, impedeing aggregation of the viruses- descendens at them going out from a cell.

5. The left by viruses cells enter a stage degenerations, but their link with a basal membrane mucous survives 1 - 2 days.

That results to retard appearances catarrhal of a syndrome - the hypersecretion mucous only starts in 1-2 days!!!

6. Appearance of a virusemia and toxemia - from the first hours of disease.

The expressed toxicosis - distinguishes of an influenza from others ARVD!!

7. The toxicosis results to TIS, toxic edema lungs and brain cardiovascular unsufficiency, damage of adrenal glands, damage of a liver and kidneys, diarrhoea, oppression cellular of immunity and phagocytosis and always causes IMMUNODEPRESSION!!

8. Reconvalescence and creation of immunity:

- elaboration an interferon and activation Tκ
- reinforced shaped IgA mucous, and then Ig G
- the antibodies are worked out not earlier of the 7-th day

PATHOMORFOLOGY

At typical current of change it are found out only on mucous, covered by ciliated epithelium (nose, trachea) as its desquamation. The necrosis considerably exceeds sites of a visible inflammation!!! The secretion of an epithelium is reduced (dryness mucous).

Restoring mucous starts with 3-5 days of illness with derivation statifield plane epithelium, which only for 15 days is substituted on ciliated. Immunodepression and bacteria slow down this process.

At severe current - the necrosises become numerous, there is lymphatic infiltration and hemorrhagic syndrome with a damage lungs, brain, myocardium, total damage of the all capillary network!!

CLASSIFICATION of an INFLUENZA

1. For the type (A, B, C. etc.) For a type A is underlined the type Hemagglutinin (H1, H2, H3) and neuraminidase (N1 N2)

2. On gravity of current: mild, midlle-severe, severe and fulminant (hypertoxical form)
3. The atypical forms of an influenza: an influenza without a fever or without an inflammation URT (upper respiratory tract)

4. Presence of complications stipulated by a virus:
   - hemorrhagic pulmonary edema, false croup
   - edema brain, arachnoiditis, polymyeloradiculoneuritis
   - glomerulonephritis
   - myocarditis, syndrome of sudden mors
   - the syndrome Reae (is more often at H1N1)

   or stipulated by affixion bacterial agents:
   (pneumonia, sinusitises, otites, pharyngitis etc.)

Example of the diagnosis: an influenza A (H1N1), severe.
Complications: a myocarditis, purulent pansinusitis.

Incubation interval - some hours - 2 days

Major clinical syndromes of an influenza:

- syndrome of an intoxication
- catarrhal a syndrome

Acute beginning, fever up to 39 - 40 dg. C, hyperemia of the skin, injection of vessels of scleras, headache in frontal areas, myalgia, arthralgia, expressed weakness, losses of appetite, thirst, pain of an eyes, dry painful cough, tearing, photophobia,

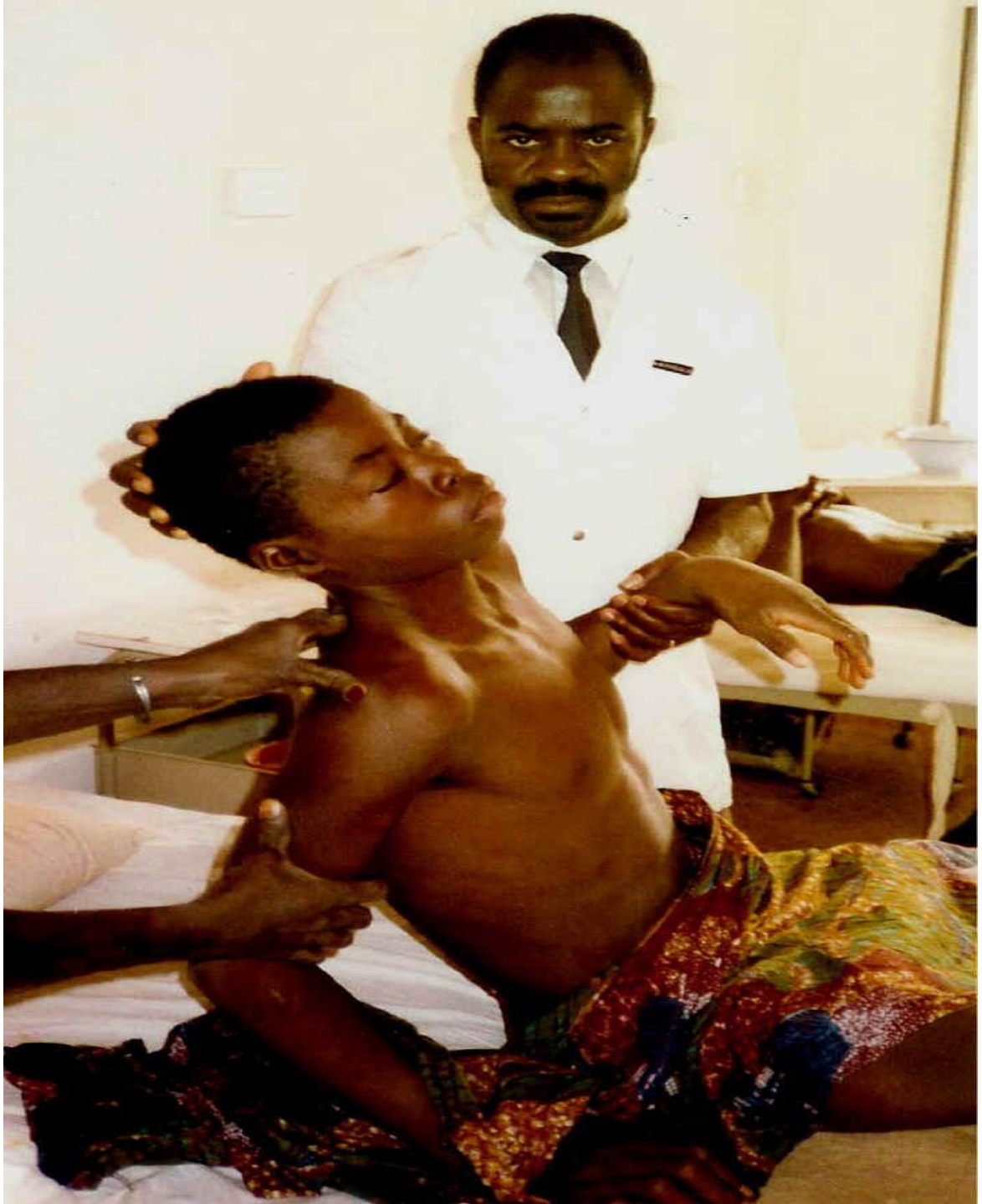
The high fever keeps 2-3 days, then it is reduced, but the cough amplifies and 4-7 days (sometimes 1 - 2 weeks) are keeped

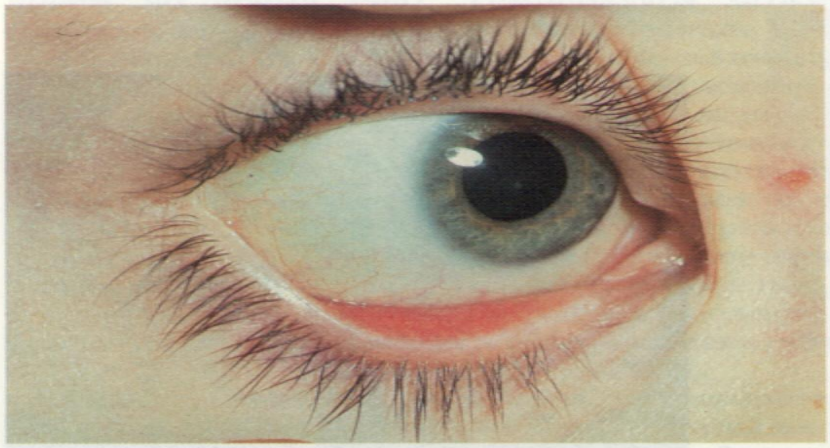
For influenza A is typically - intoxication, violation of consciousness

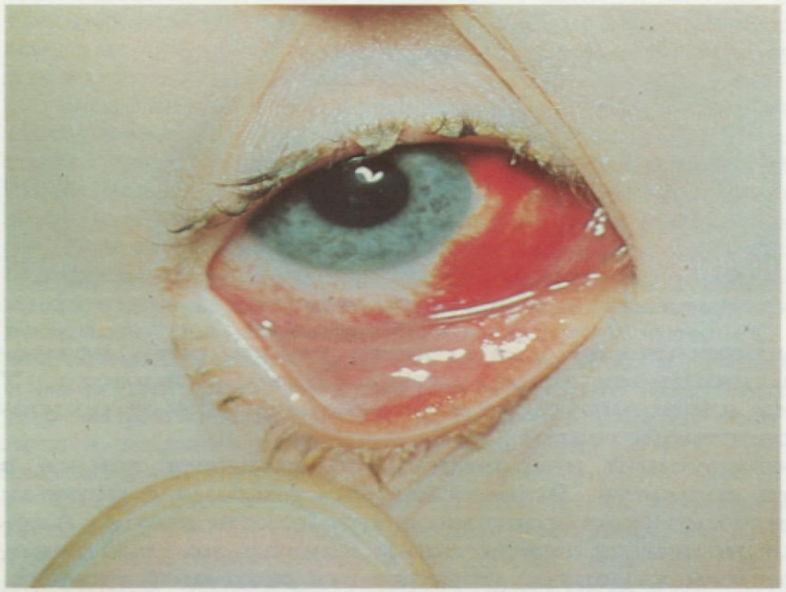
For influenza B is typically - damage of a nasopharynx and eyes

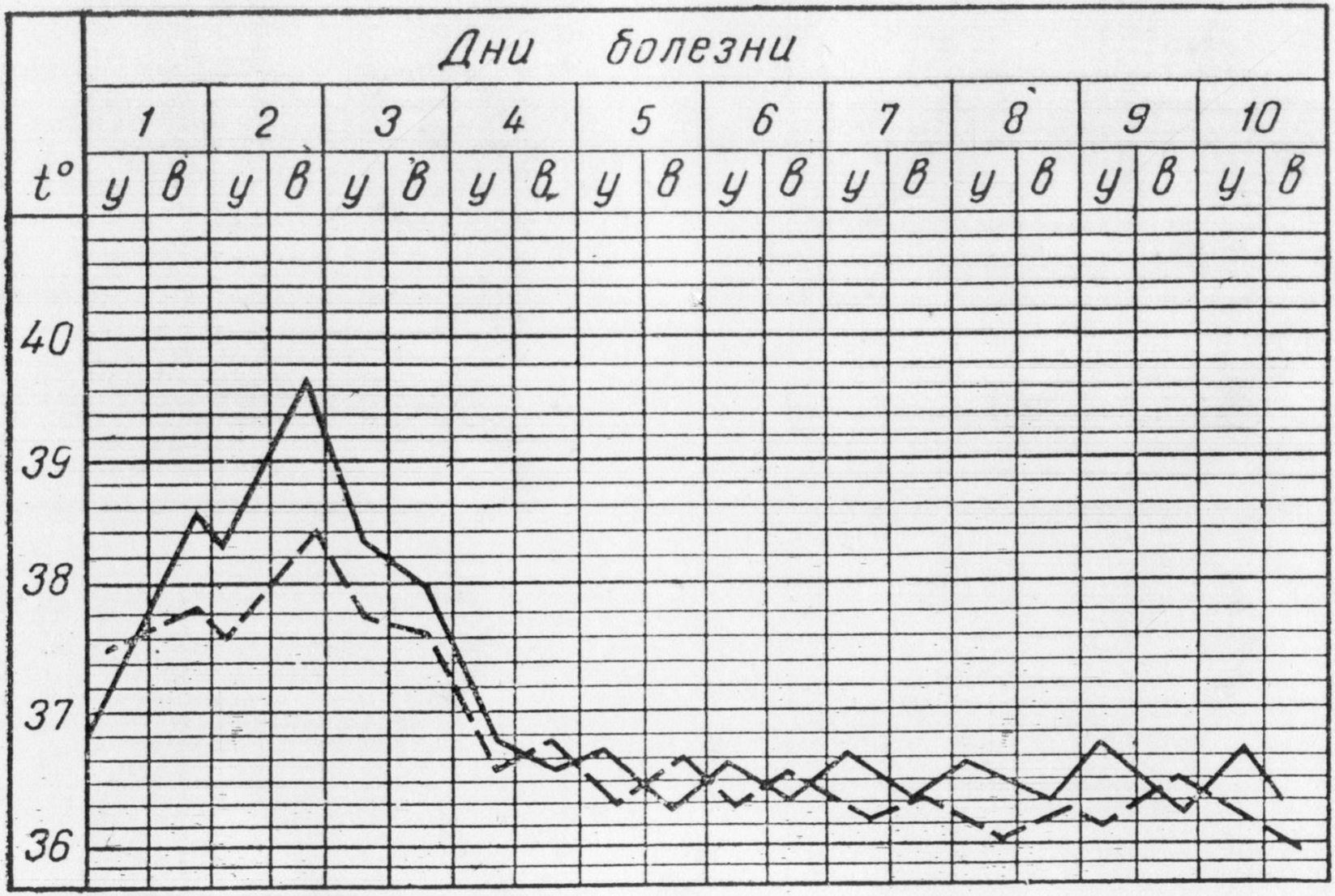
Frequency of signs at an influenza:

- chill and fever	76-100 %
- dry painful cough	51 - 75 %
- headache	51 - 75 %
- pharyngalgia	51 - 75 %
- prostration	26 - 50 %
- stuffiness of a nose	26 - 50 %
- the diarrhoea (is more often at H1N1)	26 - 50 %
- giddiness	1 - 25 %
- myalgia	1 - 25 %
- vomiting	1 - 25 %
- irritation and pain in eyes	1 - 25 %









Температурная кривая у больного неосложненным гриппом.

Usually of an influenza proceeds thus, but can proceed in the atypical form or at the inadequate immune answer and low level of interferons in a blood develop the hypertoxical forms with neurotoxic, hemorrhagic edema lungs, TIS, edema brain and without adequate treatment to result in death of the patient per the first days of illness.

DIAGNOSIS

- virologic inspection smears from a nose and stomato - pharynxes with the subsequent cultivation on culture cells or chicken embryos
- PCR - reveal of an antigene in smears with mucous, blood, CSF.
- immunological research (ELISA, RA, RPHA, RN, CFtest) on 1st and 7th - 14th days of illness - (a fourfold increase of antibody before and after an interval of 1-2 weeks -conferms diagnosis)

- IFM inspection smears - express - diagnostics!
- X-ray lungs, plating and microscopy of a sputum
- WBC - leukopenia, lymphomonocytosis
- coagulogram - at a hemorrhagic syndrome

TREATMENT of an INFLUENZA

Antiviral therapy:

Rimantadine - 300 mg the 1-st day, then 100 mg PO in q12h 3- 4 days

oseltamivir (tamiflu) - 75 mg PO in q12h - 5 days

Arbidol - 200 mg PO in q8H - 3 - 5 days

Адапromin - 150 mg PO in q24h - 3 - 5 days

Ribaverin - 200 mg PO in q6-8h - 3 - 5 days

Maintenance therapy:

- apply of an interferon in a nose, application of an antiflu-immunoglobulin for 3- 6 mls / day

- inductors of an endogenic interferon

- antibiotics (all old men, attenuated, children old 6 months and at bacterial complications)

DIF. DIAGNOSTICS

It is necessary to exclude: VHA, ornithosis, malaria, typhoids, rickettsioses. Measles (before appearance of an eruption), brucellosis, hemorrhagic fevers in initial period, pneumonia, ARVD of other aetiology etc. At hypertoxical forms: inhalational anthrax, pulmonary form of a plague

TABLE 1. Symptoms and signs of inhalational anthrax, laboratory-confirmed influenza, and influenza-like illness (ILI) from other causes

Symptom/Sign	Inhalational anthrax (n=10)	Laboratory-confirmed influenza	ILI from other causes
Elevated temperature	70%	68%–77%	40%–73%
Fever or chills	100%	83%–90%	75%–89%
Fatigue/malaise	100%	75%–94%	62%–94%
Cough (minimal or nonproductive)	90%	84%–93%	72%–80%
Shortness of breath	80%	6%	6%
Chest discomfort or pleuritic chest pain	60%	35%	23%
Headache	50%	84%–91%	74%–89%
Myalgias	50%	67%–94%	73%–94%
Sore throat	20%	64%–84%	64%–84%
Rhinorrhea	10%	79%	68%
Nausea or vomiting	80%	12%	12%
Abdominal pain	30%	22%	22%

PROPHYLAXIS (common and special)

- Common - rise of stability of an organism to catarrhal diseases (walk, vitamin therapy etc.)

- Specific - introduction of inactivated vaccines:
  - subunit (containing only H and N antigenes)- Infuvac (Holland)
  - split - Fluarix (Holland), Vaxigrip (France)

(At usage of split vaccines reduced in 2,6 times were sick by others ARVD less often!!!

Emergency prophylaxis usage of remantadinum, arbidol, adapromil in preventive doses, and intranose will be utillized by 0,25 % oxolinic and florenalic of unguents!!

Rhinoviral an INFECTION

The virus - rhinoviruses (114 serotypes)

Incubation - 2 3 days

Beginning of disease - acute

Current - acute

Main on clinical syndrome - catarrhal

Intoxication - weak, duration 1 - 2 days

Fever - subfebrile or normal

Catarrhal of the phenomenon - are expressed since the first day

Rhinitis – plentiful serous of secretion, nasal the respiration misses or laboured!!!

Cough - dry

Mucosas - weak hyperemia

Main on syndrome - RHINITIS!!

Eyes - injection of vessels of scleras, eyelids, tearing

PARAINFLUENZA (10 - 20 %)

The virus - PARAMYXOVIRIDAE - has 4 serotypes

The incubation - 2 - 7 days (is more often than 3- 4 days)

Beginning of disease - step-by-step

Current - subacute

Main on clinical syndrome - catarrhal

Intoxication - weak or moderate

Fever - 37 38 d. C can durably be kept!!!

Catarrhal of manifestation - are expressed since the first day, of a hoarse voice

Rhinitis - stuffiness of a nose

Cough – dry - "barking", is saved 12 - 21 days

State mucous - moderate hyperemia

Carrying on syndrome - laryngitis, less often false croup

Increase of lymph nodes

ADENOVIRAL INFECTION (5 - 8 % among ARVD)

The virus – (49 serotypes) maintains DNA

Incubation - 4 - 14 days

Beginning of disease - step-by-step

Current - lingering, wavy

Main on clinical syndrome - catarrhal

Intoxication - moderate,

Fever - febrile or subfebrile, duration 8-10 days

Catarrhal of manifestation - are expressed since the first day

Rhinitis - a plentiful mucoserous secretion

State a mucous - hyperemia of tonsils and back wall of a pharynx

Lungs - dry rales at a bronchitis

Carrying on syndrome - rhinopharyngoconjuctivitis, tonsilitis

Lymph nodes - there can be a polyadenitis

Liver and lien - are enlarged

Damage of an eyes - keratoconjuctivitis

The damage of internal bodies - can be an exanthema and diarrhoeia.

RESPIRATORY-SYNSYTIAL INFECTION (RSI)

The virus - RS-virus (1 serotype, there are a lot of subtypes)

Incubation - 3 - 6 days

Beginning of illness - step-by-step

Current - subacute, sometimes lingering

Main on syndrome – catarrhal, respiratory unsufficiency

Intoxication – moderate or weak, 2 7 days

The fever - moderate or normal

Catarrhal of the phenomenon - are expressed and amplify

Rhinitis - stuffiness of a nose, scanty secretion

Cough - dry, attacks, morbid, 2 - 3 weeks

Mucosas - weak hyperemia

Lungs - dry and (less often) moist rales, pneumonia

Carrying on syndrome - bronchitis, bronchiolitis, bronchospasm

Liver - signs of a toxic hepatitis

SARS

Corona-virus - of new group

Incubation - 2 - 7 days (about 10 days)

Beginning of disease - acute

Current of disease - acute

Intoxication - expressed, 5 - 10 days

Fever - 38 d. C and is higher

Catarrhal of manifestation - are moderately expressed

The rhinitis - is possible in a start of illness

Cough - dry, moderately expressed

LUNGS - with 3 - 5 days of illness signs interstitial pneumonias with a generalisation!!!

Main on syndrome - bronchitis, acute respiratory distres The damage of an eye - is rare

Damage of internal bodies - frequently diarrhoea in a start the diseases

AVIAN INFLUENZA

Virus of an influenza A (H5N1, H7N7 etc.)

Beginning of disease - acute

Current of disease - acute

Main on syndrome - fever, respiratory failure

Intoxication - strong, duration 7 - 12 days

Fever - 38 d. C and is higher

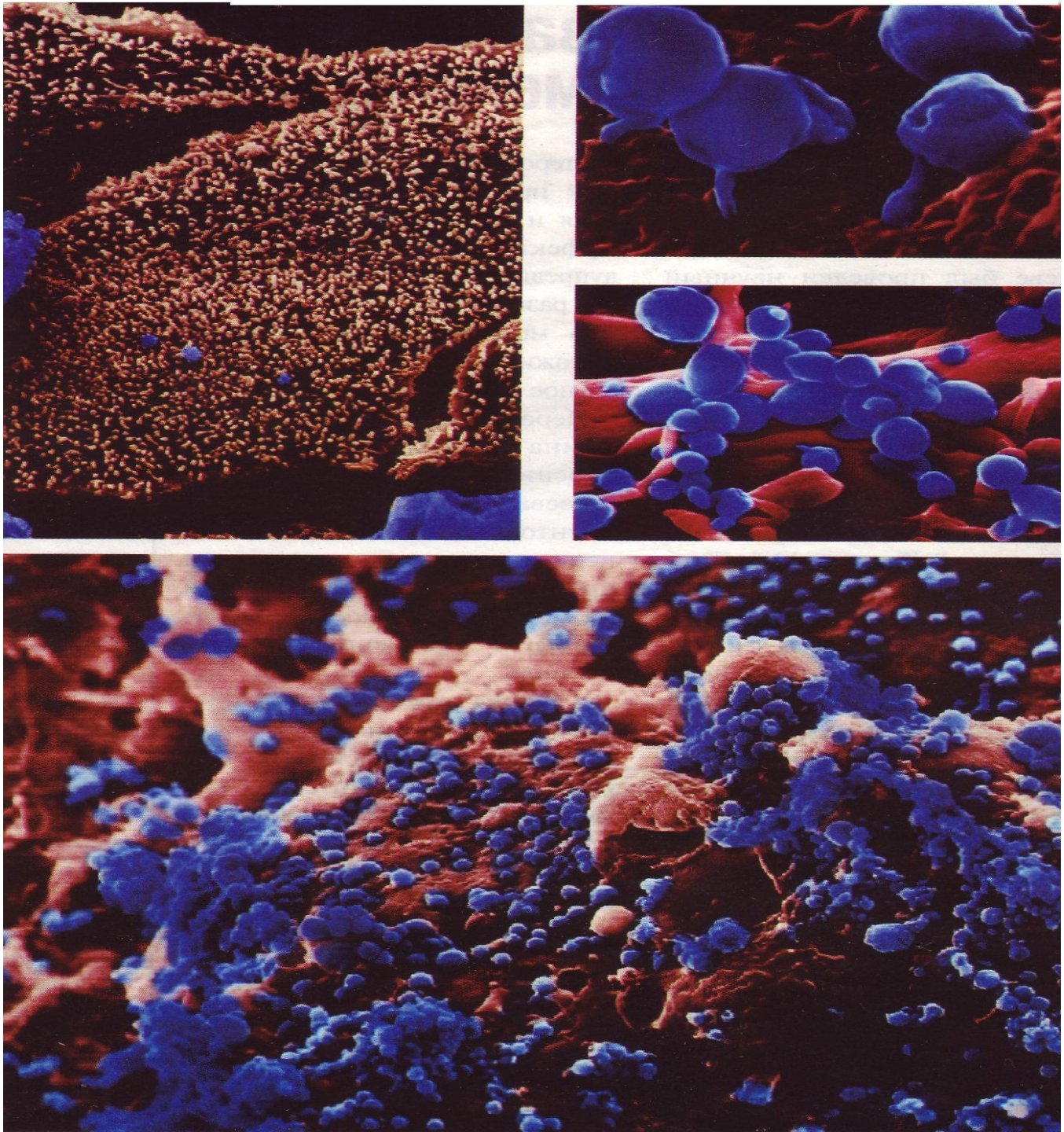
Cough - expressed

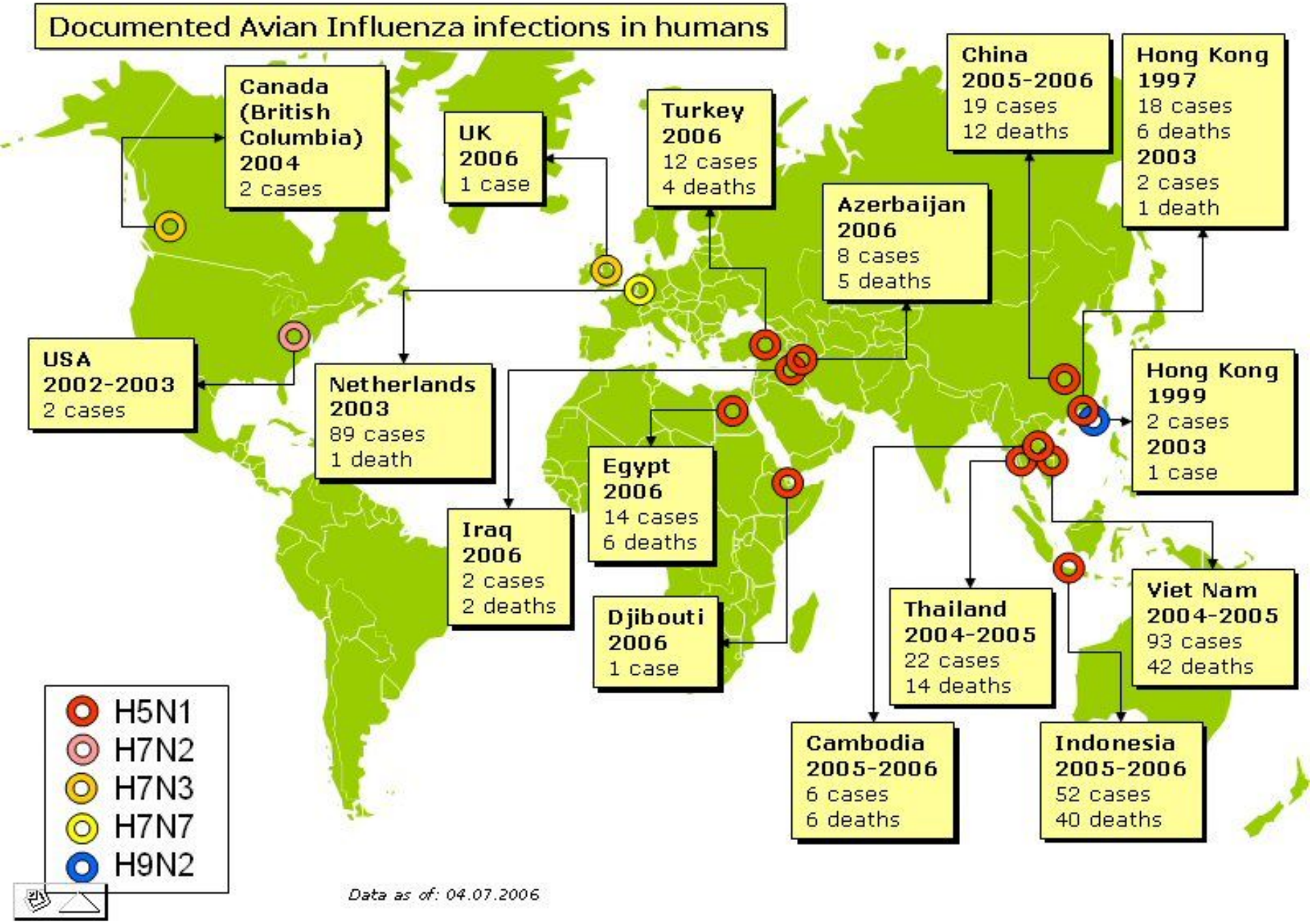
Damage lungs - since 2-3 days of illness

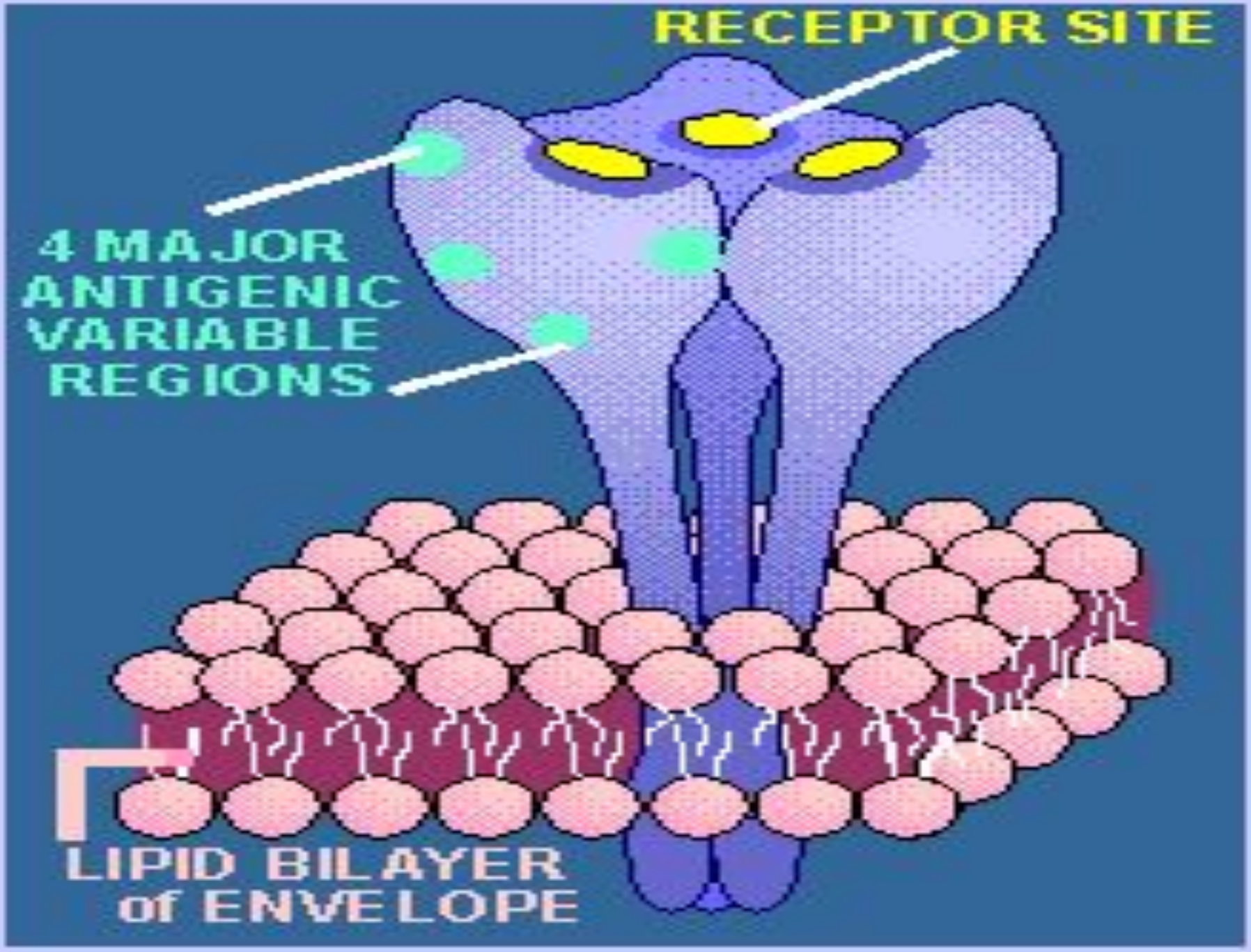
Main on clinical syndrome - lower respiratory

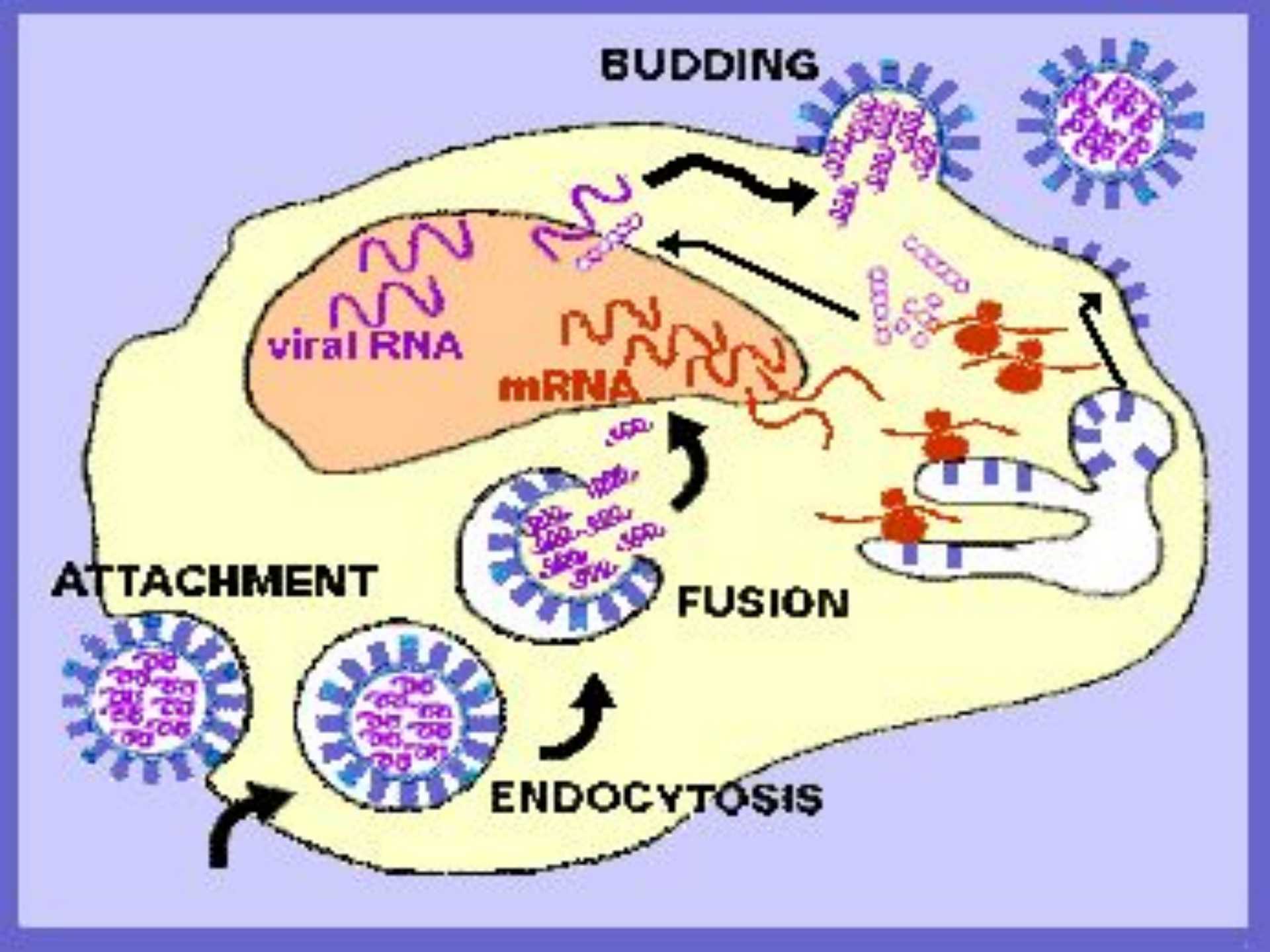
The increase of a liver and spleen - is possible

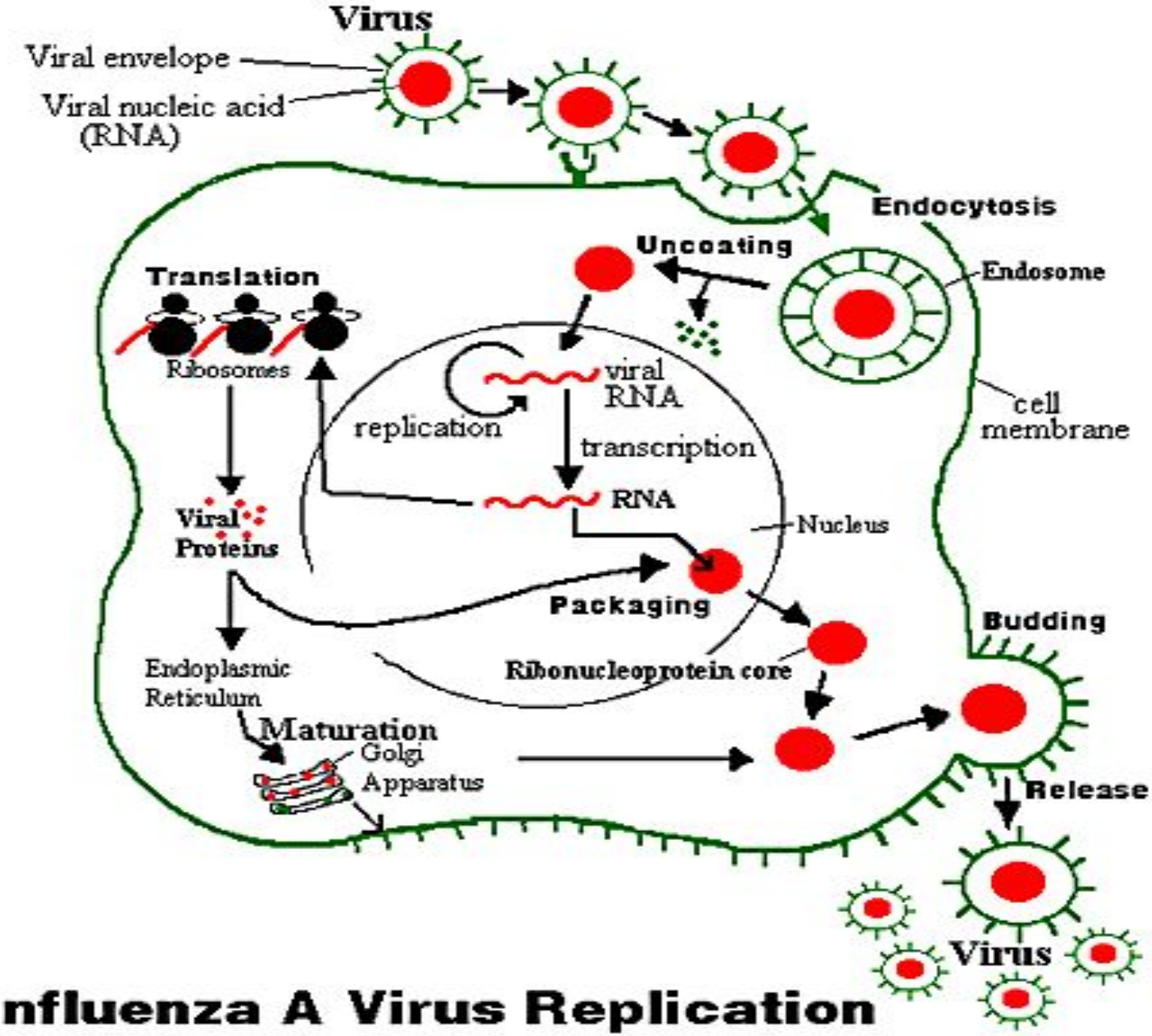
Damage of internal bodies - diarrhoea, damage liver, kidneys, leuco- lympho- thrombocytopenia




Documented Avian Influenza infections in humans
Canada (British Columbia) 2004
2 cases
UK 2006
1 case
Turkey 2006
12 cases
4 deaths
China 2005-2006
19 cases
12 deaths
Hong Kong 1997
18 cases
6 deaths
2003
2 cases
1 death
Azerbaijan 2006
8 cases
5 deaths
USA 2002-2003
2 cases
Netherlands 2003
89 cases
1 death
Hong Kong 1999
2 cases
2003
1 case
Egypt 2006
14 cases
6 deaths
Iraq 2006
2 cases
2 deaths
Djibouti 2006
1 case
Thailand 2004-2005
22 cases
14 deaths
Viet Nam 2004-2005
93 cases
42 deaths
Cambodia 2005-2006
6 cases
6 deaths
Indonesia 2005-2006
52 cases
40 deaths
H5N1
H7N2
H7N3
H7N7
H9N2
Data as of: 04.07.2006


RECEPTOR SITE
4 MAJOR ANTIGENIC VARIABLE REGIONS
LIPID BILAYER of ENVELOPE


BUDDING
viral RNA
mRNA
ATTACHMENT
FUSION
ENDOCYTOSIS



Influenza A Virus Replication