

Viral Flu : An Update

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Objectives

1. Share latest update on viral flu

2. Flu Pandemic

3. Role of Pharmacists (Preparedness plan..)

- Govt / Community
 - Information / Prevention
 - Point of contact
 - Patient Management / referral



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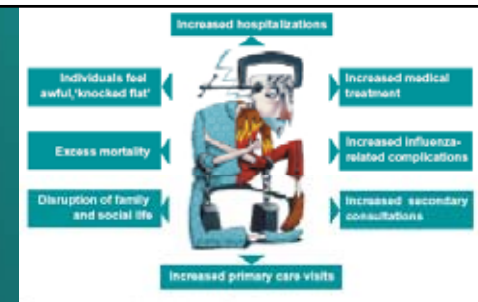
Viral Flu : Some Facts

- Every year is an influenza year
- Outbreaks last 6 – 8 weeks
- Everyone of us at risk from flu and its complications
- Flu is highly contagious and affects the whole body
- Two forms (A and B) cause disease in humans
- Symptoms are direct result of virus replication, host cell death and cytokine release



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Flu and its Impact...



- Major burden to society, individuals, businesses and healthcare systems
- Healthy people greatly affected
- Significant loss of productivity and absenteeism from work / school
- Outbreaks are associated with increased primary care visits, hospitalisations and deaths

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Epidemiology ...Everybody should be concerned

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NA/WE /Japan : 100 Mio affected / year

Children are the first to be affected



1 child in 3

Children infect adults



1 Adult in 10

Deaths



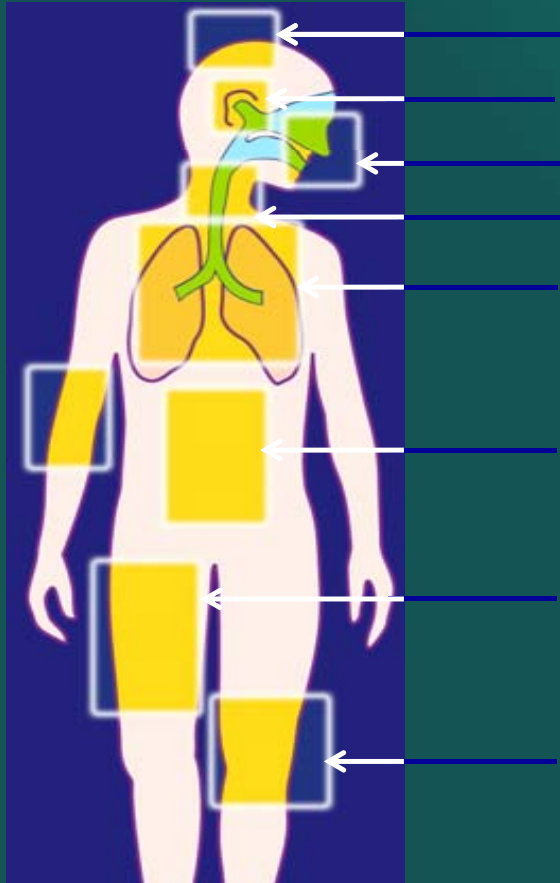
10.000 - 40.000

*En Amérique du Nord, en Europe et au Japon

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Clinical symptoms

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**Sudden onset
of symptoms
at various
sites ...**

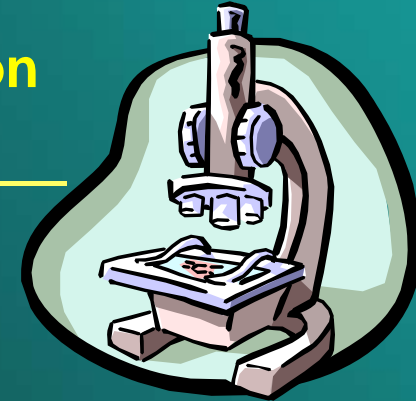
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Plan du module

Influenza v/s Common Cold

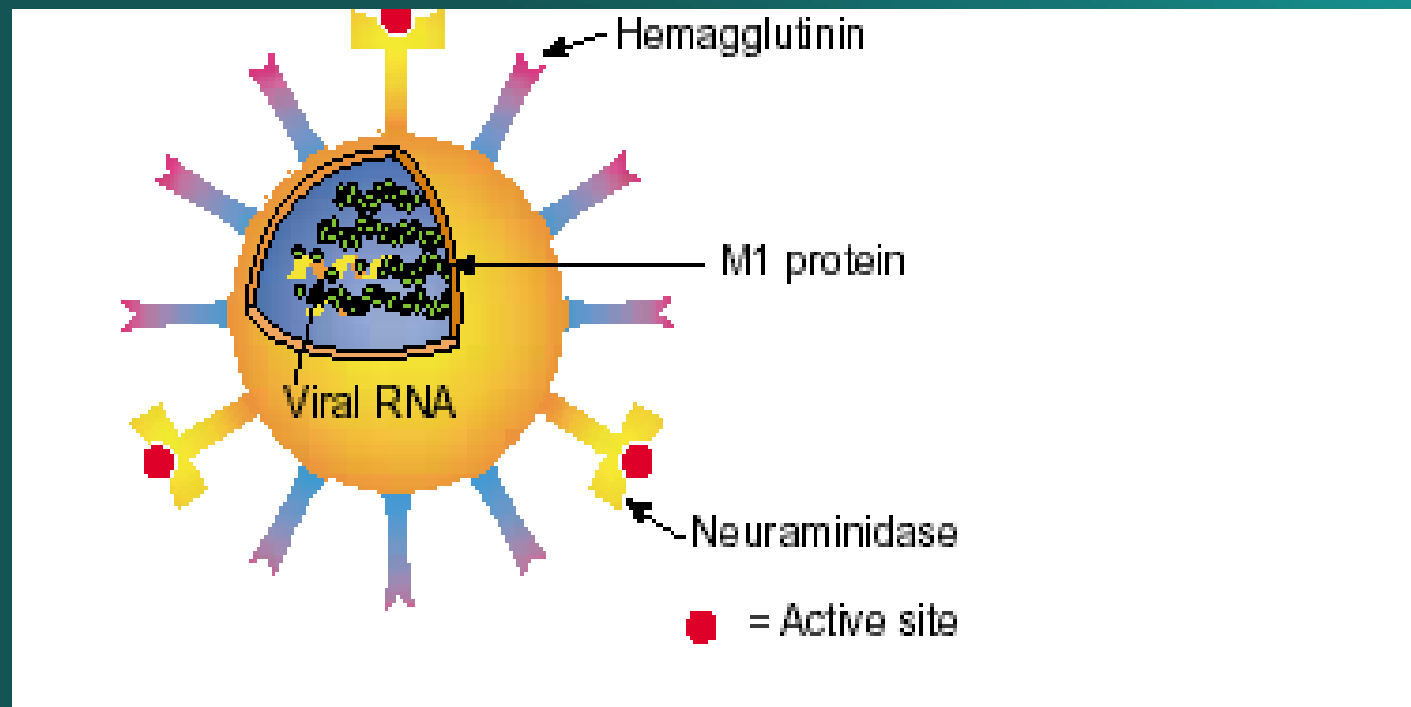
Signs & symptoms

	Influenza	Common cold
<i>Onset</i>	<i>Sudden</i>	<i>Gradual</i>
Fever/chills	Common	Rare
Cough	Usual; severe	Less common: mild-moderate
Headache	Prominent	Rare
Myalgia	Usual; often severe	Slight
Fatigue/ weakness	Can last up to 2-3 weeks	Very mild



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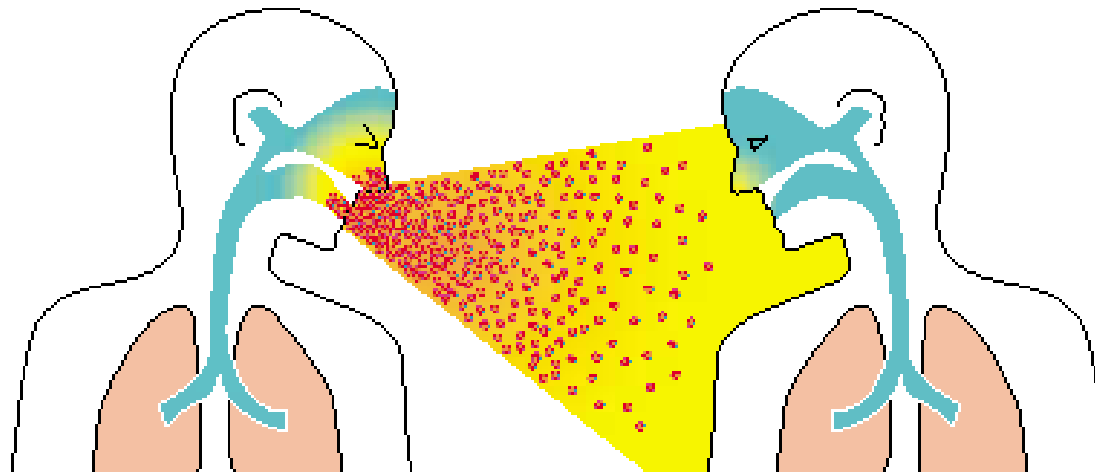
THE STRUCTURE OF THE VIRUS



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SPREAD OF THE VIRUS

Figure 1.3. Influenza is highly contagious and spread by coughing and sneezing.



Virus spread via water droplets, and small particle aerosols when coughing or sneezing

Virus enters the body through nose, mouth and eye

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The infection.....

Duration 5 – 7 days...

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Incubation : 1 – 2 days

- 1-2 days before the first symptoms appear
- 4-5 days after the first symptoms
- Most important in children
- Longer and very important in Immuno deficient pts

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Plan du module

Flu is a viral infection



To treat we need an
Antiviral !

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Antiviral drugs for treatment of influenza

- **Two classes :**
 - **Neuraminidase inhibitors**
 - Oseltamivir , Zanamivir
 - **M2 channel blockers or the Adamantanes**
 - Amantadine , Rimantidine
- **Currently (May 2009) novel influenza A(H1N1) virus samples from Mexico and USA indicate laboratory susceptibility to the neuraminidase inhibitors and resistance to the adamantanes**



Neuraminadase inhibitors

Relenza®

(*zanamivir*); GSK,

Powder for inhalation



- Local Action
- Treatment only

Tamiflu®

(*oseltamivir*) ; Roche

Oral caps/ susp

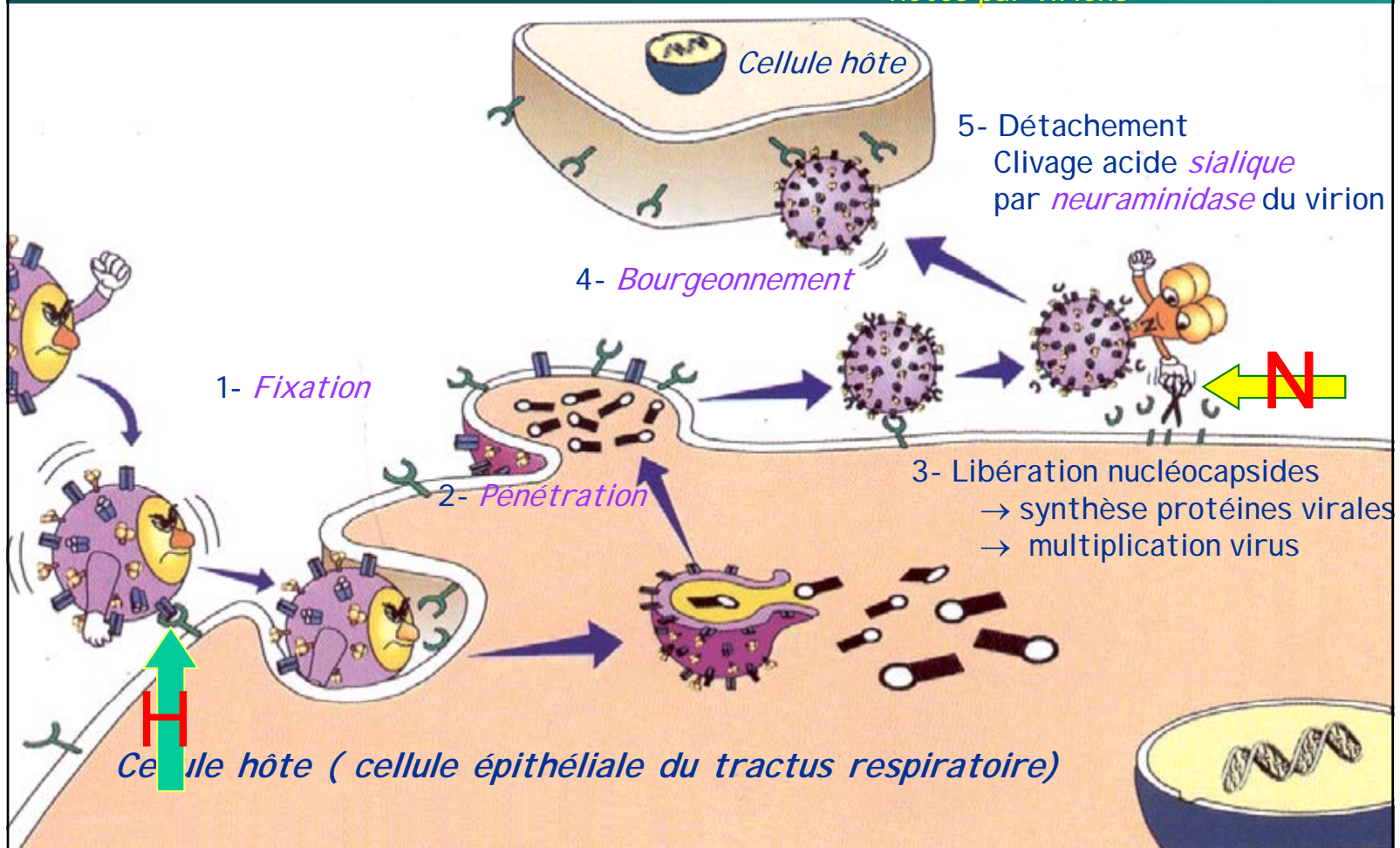


- Systemic action
- Treatment and Propylaxis

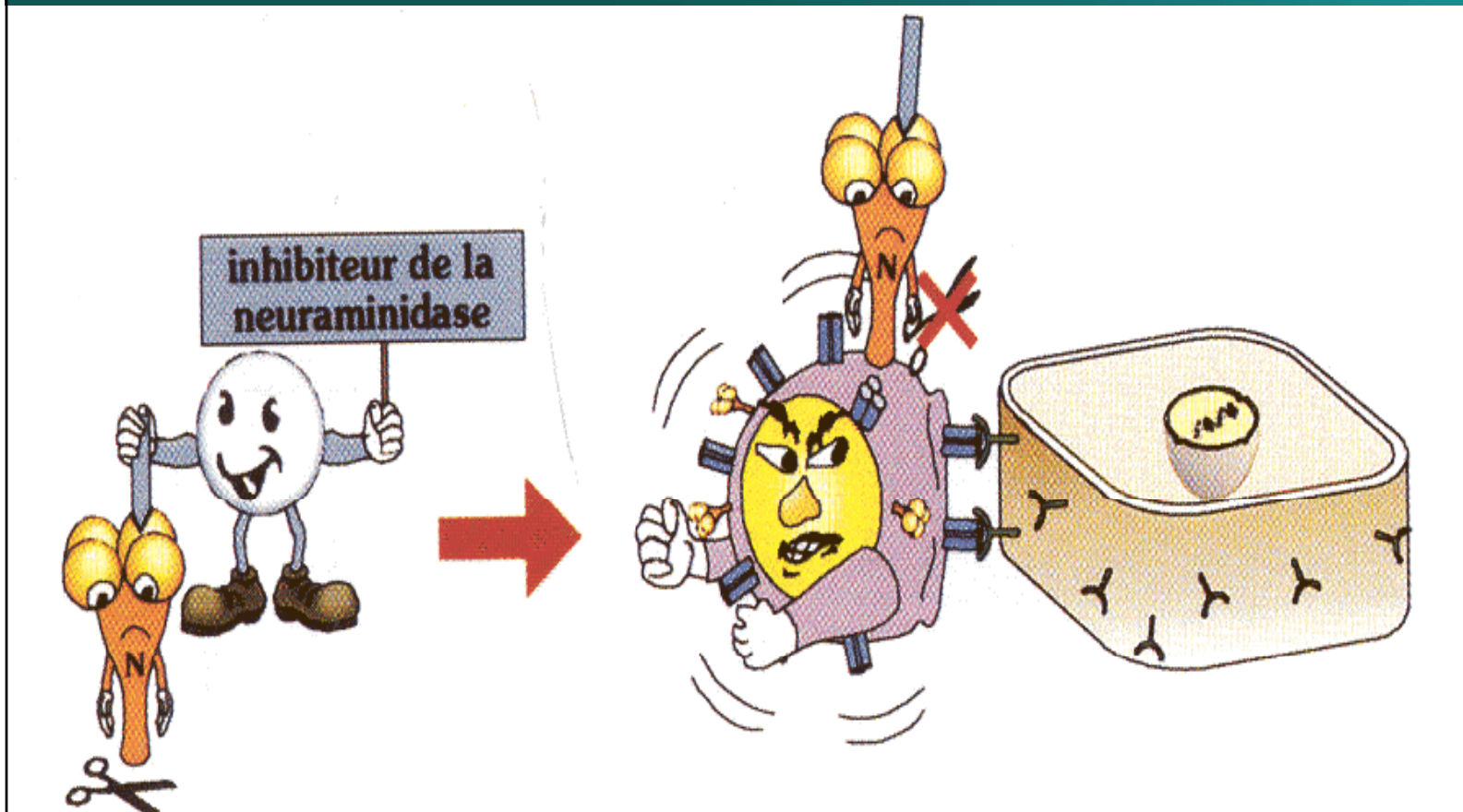
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Viral Replication

6- Fixation : infections d'autres cellules hôtes par virions

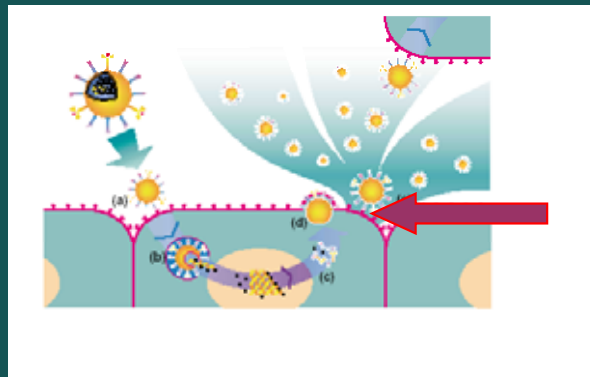


Mode of Action : Neuraminidase inhibition...



Oseltamivir (Tamiflu®) Neuraminidase inhibitor

- Effective at low concentrations
- Stops release and spread of virus from infected cells
- Specific to neuraminidases of Flu A and B
- Viral resistance is unlikely because the active site is so highly conserved and vital to influenza virus viability
- No interference with immune response of the body

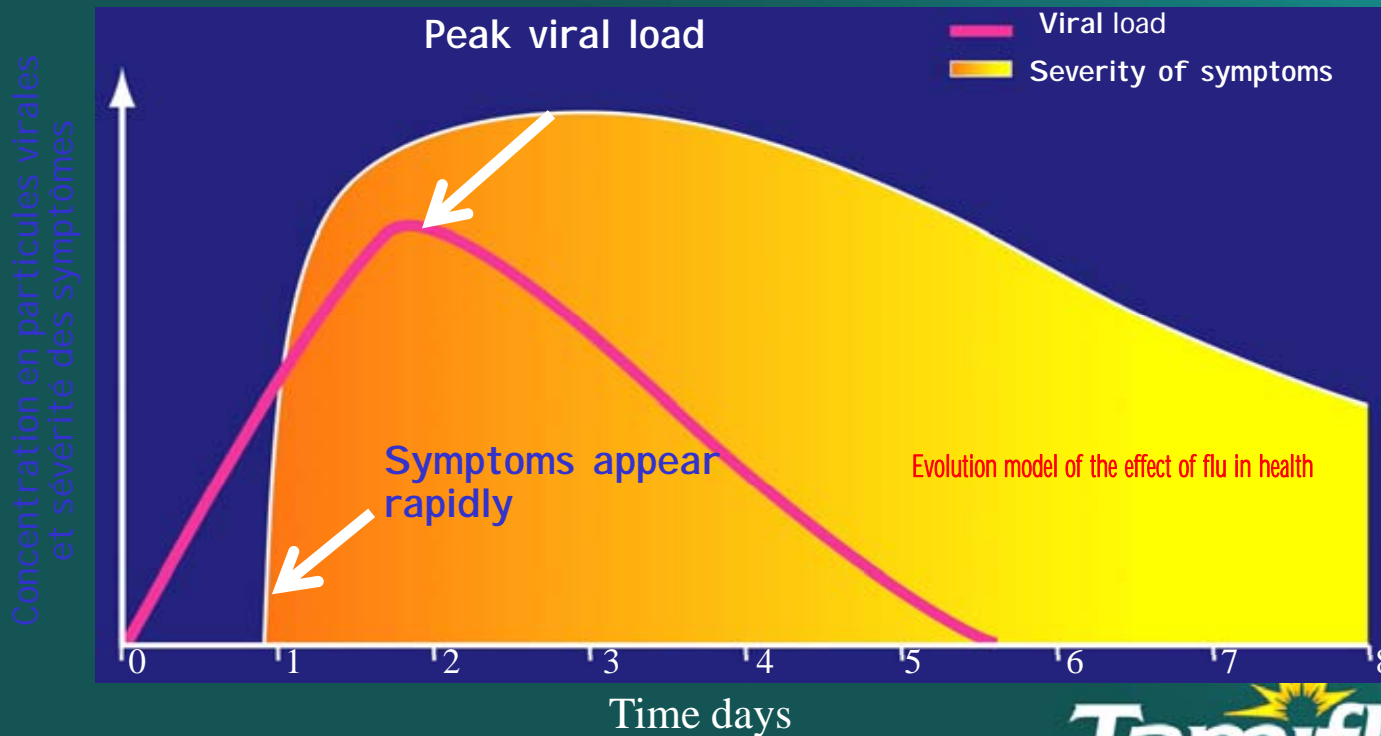


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The effects of viral replication.....

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The viral load reaches a peak in a very short time after infection

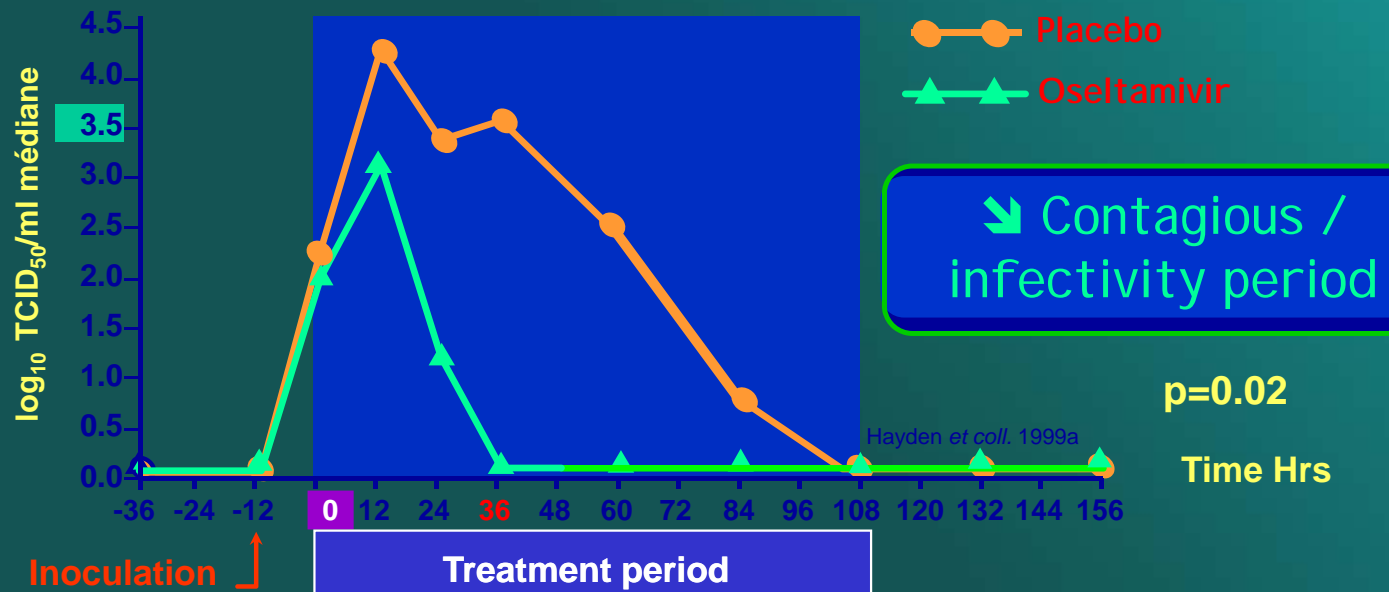


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Plan du module

Clinical studies : Viral load.....

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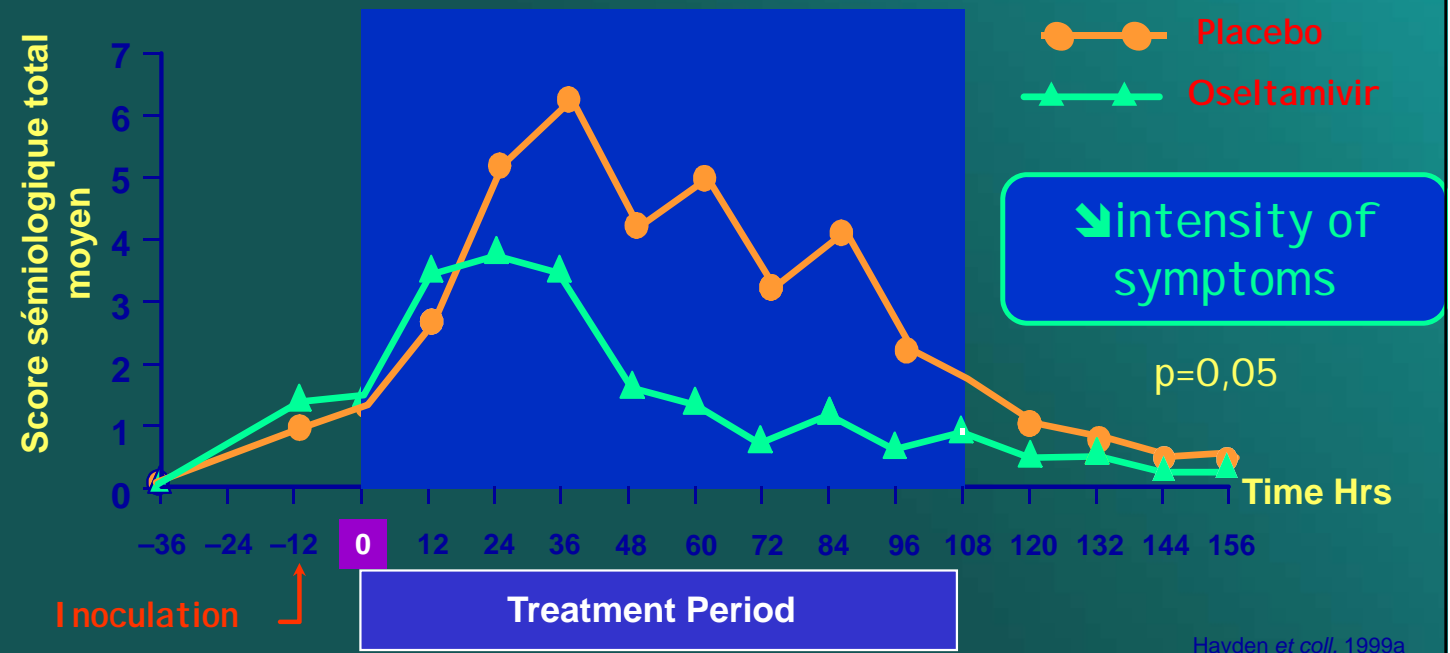


Tamiflu® reduces viral load within 24 hrs
Viral load undetectable within 1 ½ day



Clinical Studies- Symptoms...

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Hayden et coll. 1999a

Tamiflu® reduces the symptoms intensity and duration



Tamiflu® - Early treatment ...

Earliest is Best..

Treatment initiation after first symptoms



Etude IMPACT : Réduction de la durée de la maladie comparée à un début de traitement à 48 h

Latest within 48 Hrs...



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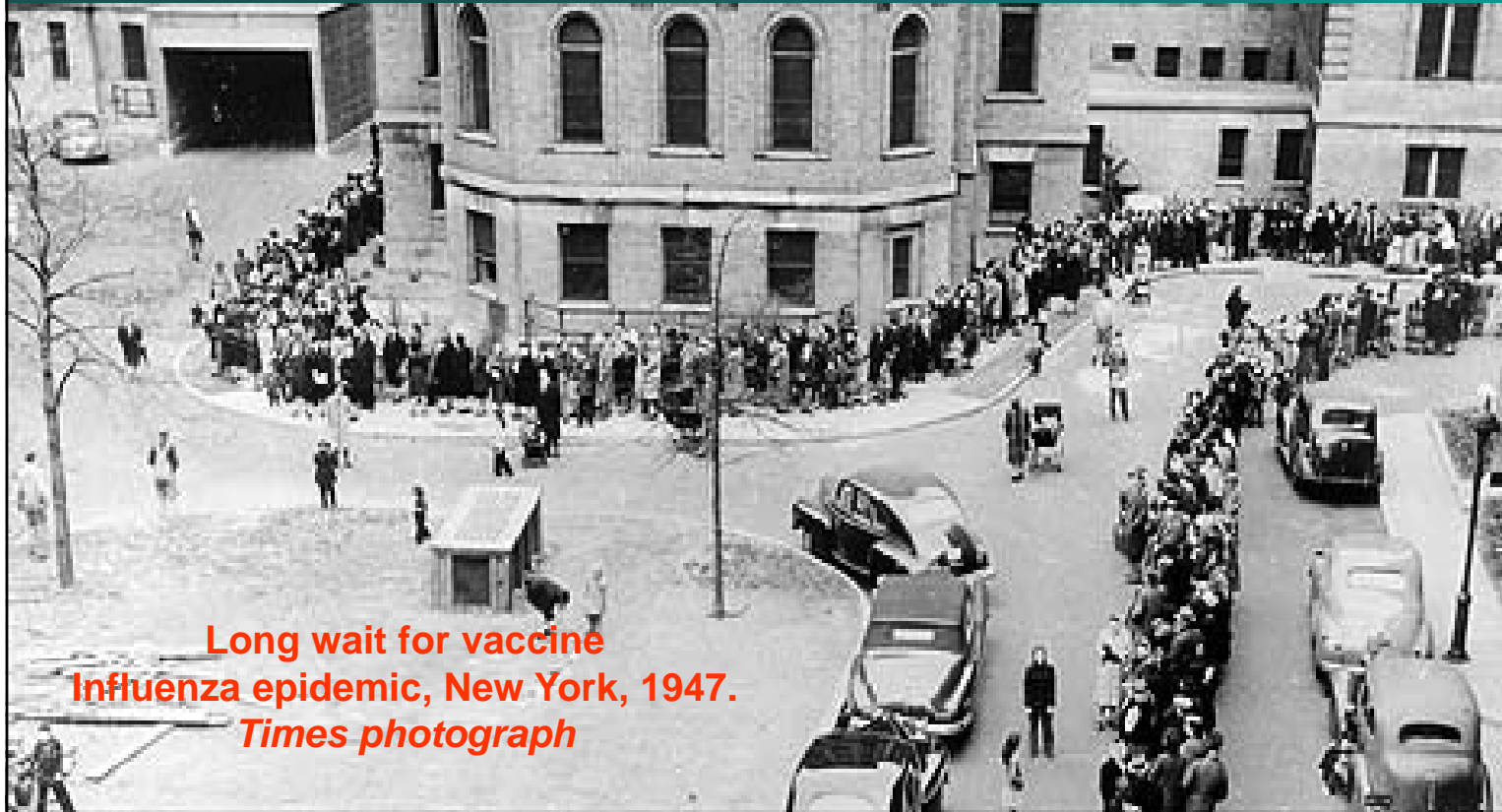
Champions League Final
Which team will be the winner tonight ?

Manchester
United
V/S
Barcelona



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Influenza Pandemic planning



Long wait for vaccine
Influenza epidemic, New York, 1947.
Times photograph

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Influenza

Seasonal influenza
“The Flu”

Human influenza virus that **mutates** slightly each year

Swine influenza
“Swine Flu”

Influenza virus in **swine population**. Limited number of human cases from exposure to infected pigs

Pandemic influenza
“A Pandemic”

Virus to which the human population has **little or no immunity**. It is transmitted human-to-human and can quickly spread globally. Pandemics can cause unusually high morbidity (illness) and mortality (death)

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The Next Influenza Pandemic ???

- Influenza pandemics occur approximately every 30 - 40 years
- Experts caution that it **is a case of when, not if**, the next pandemic will strike.



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Influenza Pandemics / Threats



- 1918-1919 : H1N1 virus Spanish Flu (50 Mio deaths)
- 1957 : H2N2 virus (4 Mio deaths)
- 1968 : H3N2 Hong Kong Flu (1 Mio deaths)
- 1997 : H5N1 Avian flu in H Kong (6 deaths)
- Jan 2004 : H5N1 Avian Flu (26 deaths)
 - 200 + deaths to date from Bird flu....
- April / May 2009 : 80+ deaths Swine flu... H1N1
- 2005- 20XX : WHO Experts - New Flu virus !!!!
Approx 10 Mio deaths predicted

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What's in a name?

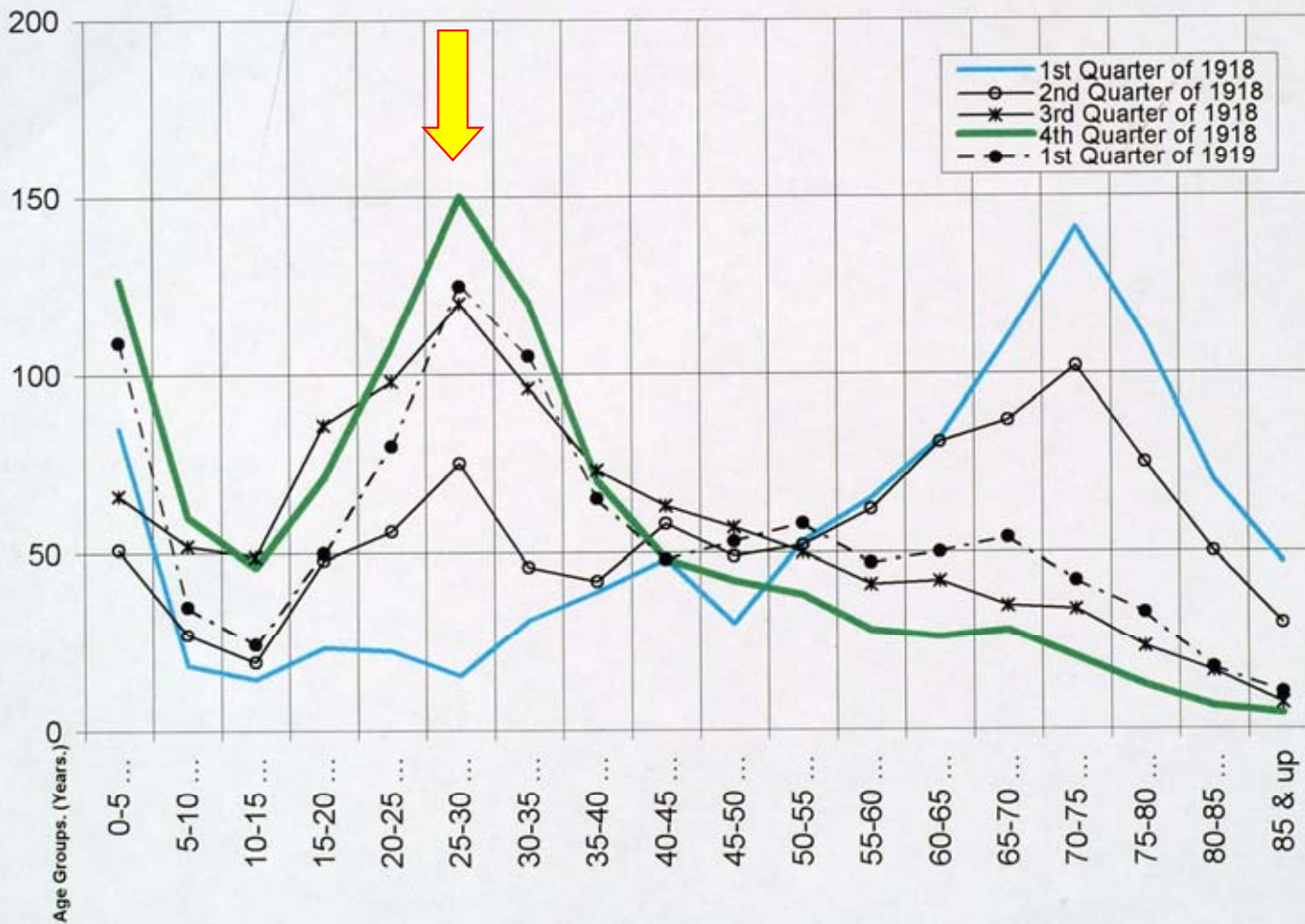
- **1918:**
 - 50 mio deaths
 - 50% of world's population infected
 - 25% clinically ill
 - Mortality significantly greater in young adults
 - Clinical manifestations were horrid
 - Population is immunologically naive
- **40 years since the last pandemic**
- **Spread of pandemic will be rapid**
- **WHO : 1/3 of the population at risk (2009)**
- **Will society cope better or worse than previously ?**
- **This time we have the weapons to attack a pandemic & a window of opportunity in which to prepare**



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Proportion
per 1,000 Deaths
at All Ages.

Age Distribution of Deaths of Females from Influenza in each QUARTER of 1918
and in the First QUARTER of 1919.



Pandemic vs. Seasonal influenza

Pandemic influenza

- Every 30-40 years
- Disease and death worldwide (nationwide epidemics) in a short period of 2-3 months, often returning in 2-3 waves
- No (or little) immunity
- No vaccine until months after pandemic begins

Seasonal Influenza

- Yearly
 - Causes epidemics on a smaller scale
 - Some immunity already
 - Vulnerable such as the elderly are most at risk
 - Vaccine available in some countries
- Pandemic influenza can be viewed many large nationwide epidemics occurring at the same time



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WHO Recommendations

- “Stockpiling drugs in advance is presently the only way to ensure that sufficient supplies are available at the time of a pandemic.”¹
- That countries stockpile enough Tamiflu for their population(**range is approx 25% of the population²**)

1 “Avian influenza: assessing the public threat” WHO January 2005

2 Various press articles



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“WHO checklist for influenza pandemic preparedness planning” March, 2005



Depending on the policy, consider:

1. Mechanisms for ensuring a secure supply of antiviral drugs
2. If a secure supply cannot be guaranteed, consider central or private stockpiling of antiviral drugs
3. In the latter case, a formal national policy is needed to ensure the safe purchase and use of these drugs
4. Plan how to distribute available antiviral drugs based on priority groups
5. Monitor antiviral drug use and adverse events, as well as antiviral drug resistance

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- Diagnosis can be easy -

Literature: Diagnosis of influenza 1-5

- More accurate with knowledge of a local outbreak
- Sudden onset of symptoms is characteristic
- Certain symptoms increase the predictive value

During a local influenza outbreak, patients presenting with a sudden onset Influenza Like Illness (ILI) having both cough and fever are likely to have influenza



1: Lina B, J Clin Microbiol 1996; 2: Cate TR, Am J Med 1987; 3: Snacken R, Dis Manage Health Outcomes 2000; 4: Govaert TM, Fam Pract 1998; 5: Monto AS, Arch Intern Med 2000

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Effective management of influenza in primary care

Knowledge that
influenza is
in the locality



Accurate clinical
diagnosis
of influenza



Surveillance



Effective management
Optimal effective antiviral therapy
Burden reduced, including improper
antibiotic use

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Influenza Like Illness (ILI) case definition:

1. Previously healthy patients (13-80 years)
2. <36 hrs of symptom onset



- Plus fever ($\geq 38^{\circ}\text{C}$)
- Plus one or more respiratory symptoms (cough, nasal congestion, sore throat)
- Plus one or more constitutional symptom (fatigue, headache, myalgia, chills/sweats)

This case definition achieves 70% diagnostic agreement with subsequent laboratory confirmation

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Symptoms that best predict influenza infection during an influenza outbreak

Sudden onset of ILI symptoms

Symptoms	Predictive Value*
Cough	74
Chills	71
Fever	70

* probability of laboratory-confirmed diagnosis of influenza infection (%)



Mauritius situation

- **Costs of stockpiling v/s costs of not stockpiling**
 - Socio economic impact
- **Government and Private stockpiling**
 - MOH
 - Individual / Corporate
- **Costs spread over a few years**
- **Impact on the Tourism based economy (Chikun..., SARS , Avian, swine flu drastically affected so many economies..)**
- **Proactive impact locally and internationally**
 - Competitive advantage
 - WHO compliance



WHO Update A H1N1

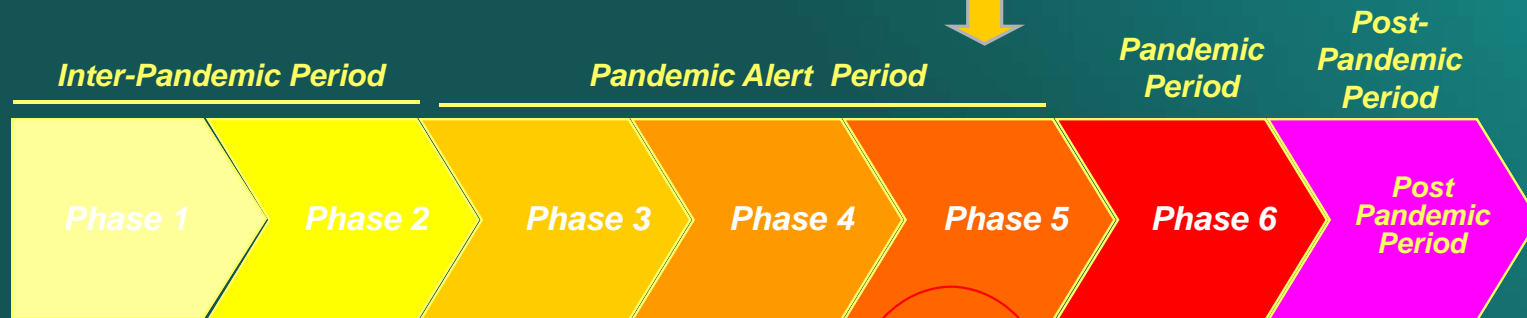
- Level 5
- 4 continents affected ?
- Could mutate further
- 46 Countries with confirmed cases
- 12,954 Cases to date
- 92 Deaths
- Africa : RSA ??
- USA has the most cases
- Mexico deaths mainly due to late access to treatment



WHO Pandemic Phases

January 2005

Current Phase of the Pandemic



- No new influenza subtypes in humans
- No new influenza subtypes in humans
- Human infections with new influenza subtype
- Small clusters of human to human transmission
- Larger clusters of human-to-human transmission
- Increased and substantial transmission in general pop.
- Return to inter-pandemic period
- Low risk of human infection from influenza present in animals
- Animal influenza subtype poses substantial risk to humans
- Rare human to human transmission of disease
- Infected areas highly localized
- Infected areas still localized
- Global pandemic risk



What should I do if I get sick?

- 1. Stay home**
- 2. Avoid contact with other people as much as possible.**
- 3. If experiencing any of the warning signs, seek medical care.**



Warning signs to look for

- **In children:**
 - Fast breathing or trouble breathing
 - Bluish skin color
 - Not drinking enough fluids
 - Not waking up or not interacting
 - Irritable, the child does not want to be held
 - Flu-like symptoms improve but then return
 - with fever and worse cough
 - Fever with a rash
- **In adults:**
 - Difficulty breathing or shortness of breath
 - Pain or pressure in the chest or abdomen
 - Sudden dizziness
 - Confusion
 - Severe or persistent vomiting



Be prepared for a pandemic

- Store a 2-week supply of water
- Store at least a 2-week supply of non-perishable food for each family member and pet
- Include medications and health supplies (both prescription and non-prescription)
- Maintain an emergency contact list
- Plan now for school closing and work stoppages



WHO treatment recommendations

Where neuraminidase inhibitors are available:

- Clinicians **should administer oseltamivir treatment (strong recommendation); zanamivir might be used as an alternative (weak recommendation).**
- Clinicians should not administer amantadine or rimantadine alone as a first-line treatment (strong recommendation).
- Clinicians might administer a combination of a neuraminidase inhibitor and an M2 inhibitor if local surveillance data show that the H1N1 virus is known or likely to be susceptible (weak recommendation), but this should only be done in the context of prospective data collection.

Where neuraminidase inhibitors are not available:

- Clinicians might administer amantadine or rimantadine as a first-line treatment if local surveillance data show that the H1N1 virus is known or likely to be susceptible to these drugs (weak recommendation).

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WHO prophylaxis recommendation

Where neuraminidase inhibitors are available:

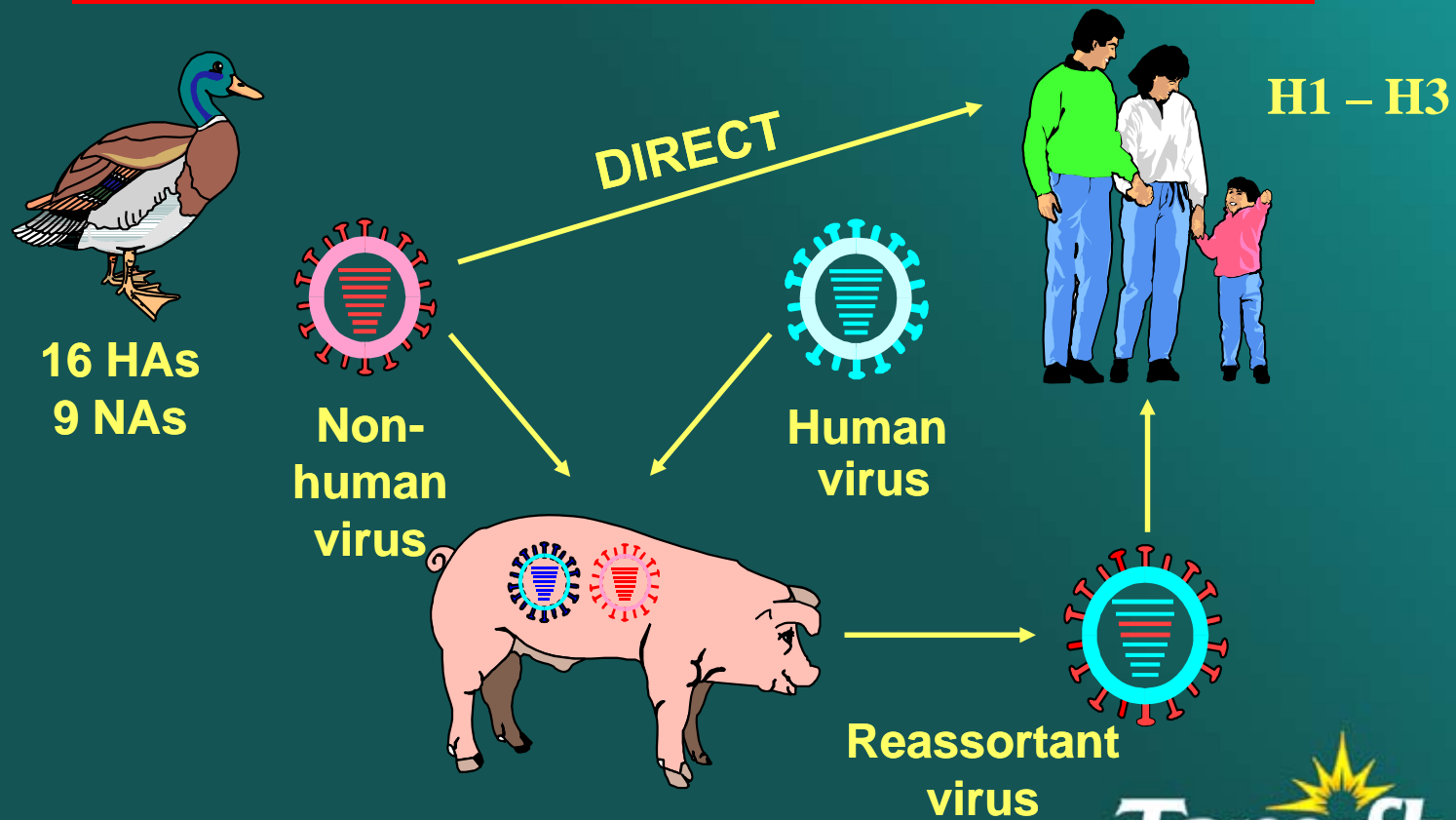
- High risk exposure groups (including pregnant women):
 - **Oseltamivir** for 7–10 days after the last exposure (strong recommendation)
 - **Zanamivir** could be used in the same way (strong recommendation) as an alternative.
- Moderate risk exposure groups (including pregnant women)
 - **Oseltamivir** might be administered for 7-10 days after the last exposure (weak recommendation).
 - **Zanamivir** might be used in the same way (weak recommendation).
- Low risk exposure groups:
 - **Oseltamivir** or **zanamivir** probably not (weak recommendation).
 - Pregnant women in the low risk group should not receive oseltamivir or zanamivir for chemoprophylaxis (strong recommendation).
 - Amantadine or rimantadine should not be administered as chemoprophylaxis (strong recommendation).

Where neuraminidase inhibitors are not available:

- No benefits of M2 inhibitors



Mutation of the flu virus



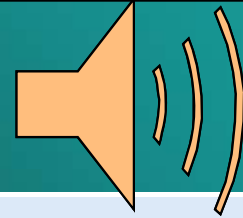
What will happen during a pandemic?

- Perhaps 2-3 waves, each lasting about 2-3 months
- Mortality impact greatest in vulnerable populations
- Heavy burden on health care facilities
- Economic and social disruption



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Information for communities during a PANDEMIC



ABOUT THE VIRUS:

- ✓ The illness and symptoms
- ✓ Mode of transmission

WHAT EVERYONE NEEDS TO DO TO PROTECT THEMSELVES:

- ✓ Cover mouth and nose for coughs and sneezes
- ✓ Keep your distance (limit time in crowded places)
- ✓ Wash hands regularly with soap & water / ash
- ✓ Ventilate households

EVERYONE NEEDS TO KNOW HOW TO:

- ✓ Protect yourself and loved ones
- ✓ Care for the sick
- ✓ Seek access to health-care (and when)
- ✓ Keep informed

What you need to tell them (1)

How do you know if you or your child has influenza?

- Symptoms can appear suddenly, beginning with headache and a feeling of illness, followed by:
 - fever ($>38^{\circ}\text{C}$)
 - dry cough
- You may also experience:
 - muscle aches and pains
 - tiredness
 - sore throat
 - chills



What you need to tell them (2)

When to seek care at health facility?

- No change in guidance for health-seeking in under 5 year olds
- Most Influenza A(H1N1) can be managed at home
- Signs of severe illness and need to go to health facility:
 - shortness of breath, difficulty breathing, weakness/unable to stand, lethargy, unconsciousness, convulsions, inability to drink fluids and dehydration, high fever.
- Risk factors for severe disease:
 - chronic illness, pregnancy, infant or young child

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What you need to tell them (3)

How do you protect yourself and your family?

- Cover mouth and nose (especially coughs and sneezes)
- Keep your distance / avoid time spent in crowds or large gatherings (especially if you are a young child or pregnant or have underlying chronic illness)
- Wash hands frequently with soap & water/ash
- Ventilate to allow air circulation



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What you need to tell them (4)

How to care for sick people at home:

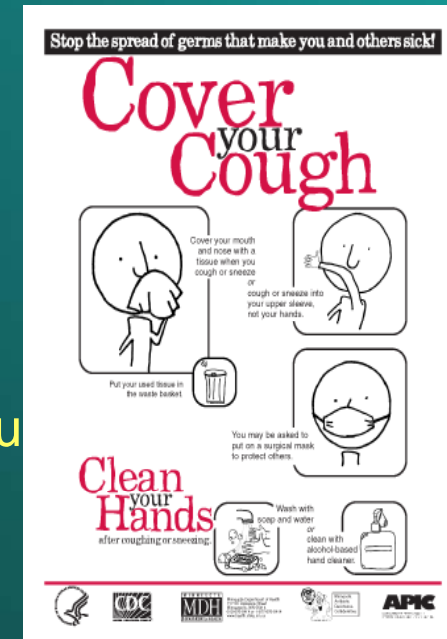
1. **Use as few caregivers as possible (ideally only 1 person)**
 - This will minimize exposure to the illness
2. **The sick person should remain in bed**
3. **The sick person should cover mouth and nose with a piece of cloth or scarf whenever in close contact with the caregiver**
4. **Keep ill people separated from the healthy as much as possible (especially from infants, young children, and pregnant women and those with chronic illnesses such as HIV, TB, heart or lung disease, diabetes)**



What can you do to protect yourself?

First and most important:

- Wash your hands.
 - Try to stay in good general health.
 - Get plenty of sleep,
 - Be physically active,
 - Manage your stress,
 - Drink plenty of fluids, and eat nutritious
- Try not to touch surfaces that may be contaminated with the flu virus.
 - Avoid close contact with people who are sick.



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What you need to tell them (5)

How to care for sick people at home:

5. Give liquids

- This will help replace the liquids lost due to fever & sweating

6. Feed normally

- Do not stop breast-feeding (sick mothers could wear mask / scarf)

7. Give medicine for fever (i.e. Paracetamol)



What you need to tell them (6)

- The ill person should avoid close contact with others for **7 days after start of illness** or for **1 day after feeling better**
- Family members should check themselves daily for fever and cough
- Family members should open windows or doors for air circulation
- Wash clothes, bed-linen and scarves of ill persons in soap and water and dry in the sun
- Dispose of used masks carefully **in a sealed bag and arrange for incineration**



How you need to tell them

- **Listen carefully** – respond sympathetically to concerns expressed and give time for people to ask questions
- **Be reassuring** – people may be frightened and confused
- **Use simple language** and avoid complicated technical terms
- **Repeat and reinforce messages** several times – people are likely to forget or misinterpret during a crisis
- **Show by example – walk your talk!** People are much more likely to value what you say if you are already doing what you advise them



Inpatient treatment includes: (1)

- Supplemental oxygen therapy (if available) by face mask
- IV or oral fluids for dehydration
- Antibiotic (oral and parenteral) treatment of secondary bacterial infections
 - Possible antibiotics include amoxicillin or cephalosporins
- Non-aspirin antipyretics for fever and pain
- Nutritional supplementation as needed



Inpatient treatment includes: (2)

- **Antiviral treatment may be indicated in some groups, if available**
 - **Prioritize**
 - pregnant women
 - patients at increased risk of severe illness (chronic medical conditions such as immunodeficiency, cardiovascular or lung disease, diabetes, etc)
 - patients with severe pneumonia or progressive disease.
 - **Resistance may develop – follow WHO recommendations as to which, if any, antivirals could be used**

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Anti-viral limitations

- **Pandemic effectiveness is anticipated but not assured**
- **For treatment to be most effective, deliver early in symptom onset**
- **Contraindications and side effects**
 - rare neuropsychiatric symptoms with oseltamavir
 - Bronchospasm with zanamavir in patients with pre-existing airways disease
- **Potential development of antiviral resistance**



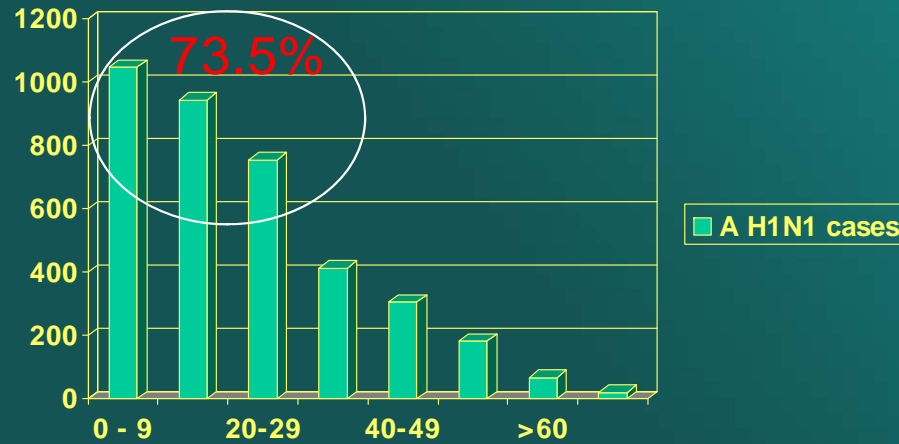
WHO Report : Human infection with new influenza A (H1N1) virus: clinical observations from Mexico and other affected countries, May 2009

Antiviral treatment. Detailed information regarding antiviral therapy in these patients is not currently available, but use of oral oseltamivir in those with serious illness or pneumonia may be beneficial. In some hospitalized patients with new influenza A (H1N1) virus infection, **delays to initiation of antiviral therapy are likely an important factor in poor outcomes.** Among 27 fatal cases in Mexico, the median time from onset of symptoms to initiation of antiviral therapy was 8 days (range, 1–26 days).¹

Age distribution (fatal cases) : 31 years (most 20 – 55 yrs)

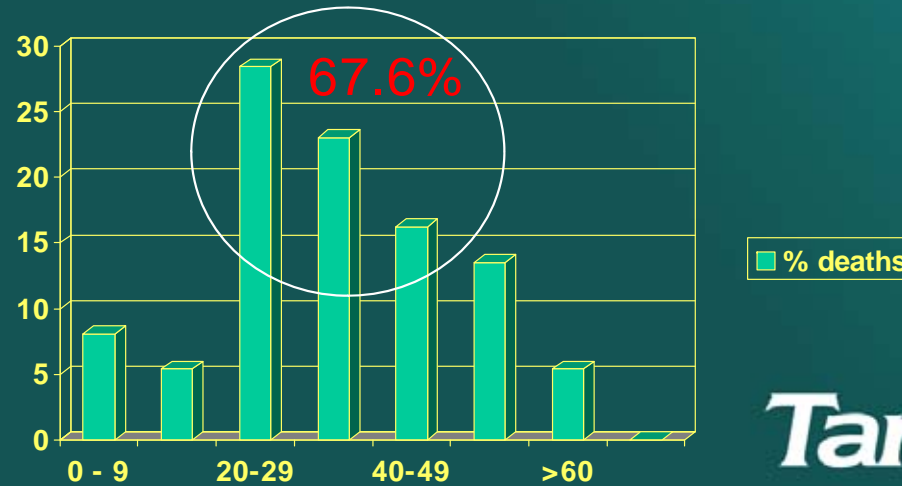


Mexico : Age distribution / mortality of confirmed cases



Cases :
3,734

Deaths : 74



Thank you

