

***Influenza***

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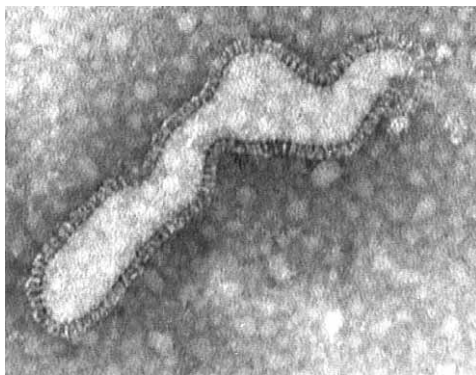
## Human Influenza

- Influenza is a highly contagious, acute respiratory disease caused by influenza viruses.
- Influenza viruses are unique among respiratory viruses. They undergo antigenic variation resulting in frequent epidemics and periodic pandemics. Annually, around 0.5-1.0 million die and 600-1200 million people become sick due to influenza epidemics worldwide, resulting in significant mortality, morbidity and economic loss.

### Clinical features

**Abrupt onset of fever with chills, running nose, sore throat, cough, headache, bodyache, weakness.**

**Bronchitis, pneumonia, ear infection are complications.**



### The virus

Irregularly shaped particles, 80-100 nm diameter; single stranded RNA virus; belongs to family *Orthomyxoviridae*.

## Types and subtypes

There are three types of influenza viruses: A, B and C.

- Type A causes frequent epidemics (due to minor antigenic variation) and periodic pandemics (due to major antigenic variation).
- Type B causes local epidemics.
- Type C causes common cold like illness.
- The virus has two surface glycoprotein antigens; haemagglutinin (H) and neuraminidase (N), which show antigenic variations.
- Influenza type A viruses have 15 H and 9 N subtypes; they occur in different combinations that infect humans, animals and birds.

## Laboratory diagnosis

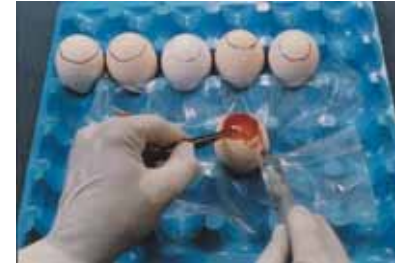
### NIV has facilities for :

- Virus isolation.
- Immunofluorescence test.
- Hemagglutination (HA) test.
- Hemagglutination Inhibition (HI) test
- ELISA - antigen detection.
- PCR.



Collection of sample

## Host systems for influenza virus isolation

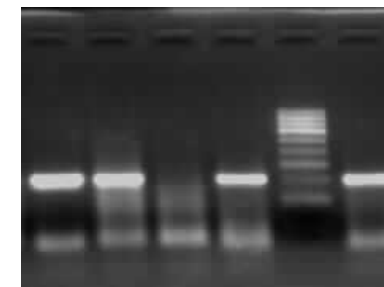


Embryonated eggs



MDCK cells

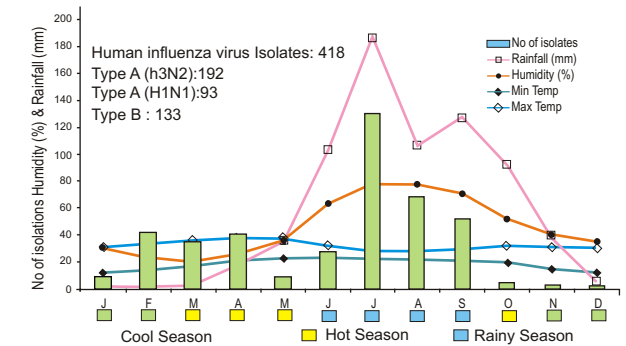
Detection of influenza A from clinical samples (throat swab) by RT-PCR



+ sample  
+ sample  
Negative control  
+ sample  
100bp ladder  
+contrl

## Epidemiology

(Surveillance in Pune, 1976-2003)



### Human influenza

- Studies on influenza were initiated at NIV in 1976 .
- NIV is recognized by the WHO as a National Influenza Center since 1980 and became part of WHO FLUNET in 2000.
- During the period of surveillance from 1976-2003, over 16,000 influenza like cases, mainly children, were investigated in Pune. These included several outbreaks.
- Out of the 16,000 respiratory specimens collected, about 9,500 (59%) were processed in chick embryos and about 7,000 (44%) in MDCK cell line for influenza virus isolation.
- A total of 418 influenza virus isolates of types A and B have been obtained comprising 43 antigenic variant strains during these outbreaks.
- These included several important global strains that caused extensive epidemics, e.g. A/USSR/90/77 (H1N1) in 1978, A/Singapore/6/86 (H1N1) in 1986, B/Yamagata/16/88

in 1990, A/Wuhan/359/95 (H3N2) in 1996, A/Sydney/05/97 (H3N2) in 1998, 99, A/New Caledonia/20/99 (H1N1) in 2000, B/Victoria/2/87 in 1989, 2002 and A/Panama/2007/99 (H3N2) in 2003.

- In Pune, which has a tropical monsoon climate, influenza outbreaks predominantly occur during rainy season.
- A representative number of isolates from each outbreak were also sent to the WHO Collaborating Centre on Influenza Reference and Research, Atlanta, GA, USA, for further characterization.
- Association of influenza H3N2 strain (confirmed by RT-PCR and virus isolation) was shown in pediatric cases with encephalitis and respiratory infection in Murshidabad, West Bengal 2003.
- Serological surveys were conducted in 1981-82 and 1999 in Pune to determine the prevalence of antibodies to the pandemic and epidemic strains of influenza.
- The results indicated broadening of antibody response to a greater number of strains with advancing age. Higher prevalence of antibodies to pandemic strains and low to moderate prevalence of antibodies to epidemic strains was noticed.
- The study also demonstrated absence of antibodies to the pandemic strain H2N2 in persons < 25 years of age. The potential of its reintroduction cannot be ruled out, as H2 variants are

circulating in wild birds and immunity in human population is decreasing.

### Animal and bird influenza

- NIV has conducted serological and virological investigations in birds and animals from Pune and other parts of India.
- A duck influenza virus, having the antigenic character of H4N2, was isolated from a domestic duck from Tirunelveli town, Tamil Nadu, in 1978.
- Serological investigations have been conducted on sera from pigs, birds, horses, dogs, goats and bats.
- Pig sera (1351) collected from different states of India including Andaman and Nicobar Islands between 1968 and 1988 demonstrated presence of antibodies to human H3N2 strains (10% to 52%) and to human influenza H1N1 strain (5%). However, all the sera were negative to swine influenza H1N1 strain.
- Serological survey of equines (306) from a farm in Pune between 1987 and 1989 showed the prevalence of antibodies to equine influenza strains; H7N7 (9%) and H3N8 (6%). Study on dog sera (270) showed the prevalence of antibodies to human H3N2 strain (23%) and on bat sera (120) to human H1N1 strain (13%).
- Bird (504) and goat (320) sera tested negative for human influenza strains.

### Avian influenza

Affects domestic chickens and turkeys causing heavy mortality.



All the known 15 HA subtypes of influenza circulate among wild birds. Wild ducks do not get sick. They are the natural hosts. H5 and H7 subtypes can mutate to highly pathogenic strains after short period of circulation in poultry.

Several countries in SE Asia reported devastating avian influenza H5N1 outbreaks in poultry during 2003-04. There was no report of H5N1 outbreak in poultry from India. Some human cases with high mortality due to H5N1 have been reported from Thailand and Vietnam. However, human-to-human spread was not established.

#### Subtypes of influenza type A and host specificity

H1 to H15 - Avian species. Outbreaks reported in birds have been due to H5 and H7 subtypes.

H1, H2 and H3 - humans  
H1 and H3 - swine  
H3 and H7 - horses

The reasons / limitations for these species-specific subtypes are unknown.

### Influenza virus isolates from NIV, Pune 1976-2003 and designated by WHO as

Type A (H3N2) strains	Type A (H1N1) strains	Type B strains
A/Victoria/3/75	A/USSR/90/77	B/Hong Kong/5/72
A/Texas/1/77	A/Brazil/11/78	B/Singapore/222/79
A/Taiwan/1/79	A/India/6263/80	B/USSR/100/83
A/Bangkok/2/79	A/England/333/80	B/Hong Kong/8/83
A/Oregon/4/80	A/New Caledonia/4/83	B/Kanagawa/2/84
A/Arizona/2/80	A/Singapore/6/86	B/Texas/1/84
A/Shanghai/31/80	A/S.Carolina/6/88	B/Ann Arbor/1/86
A/Philippines/2/82	A/Czechoslovakia/2/89	B/Victoria/2/87
A/Taiwan/16/83	A/New Caledonia/20/99	B/USSR/2/87
A/Mississippi/1/85		B/Yamagata/16/88
A/Sichuan/2/87		B/Hong Kong/22/89
A/Sichuan/68/89		B/Panama/45/90
A/Beijing/353/89		B/Harbin/07/94
A/Shanghai/86/90		B/Sichuan/379/99
A/Johannesburg/33/94		B/Shizuoka/15/2001
A/Wuhan/359/95		B/Beijing/243/97
A/Sydney/05/97		
A/Panama/2007/99		

### Vaccine

Inactivated influenza vaccine, consisting of the current strains of influenza type A; H3N2 and H1N1 and type B for parenteral use in humans, is commercially available. The vaccine requires regular upgradation because of antigenic variation.

### Antiviral drugs

Amantadine hydrochloride, Rimantadine, Zanamivir and Oseltamivir are some drugs in use.