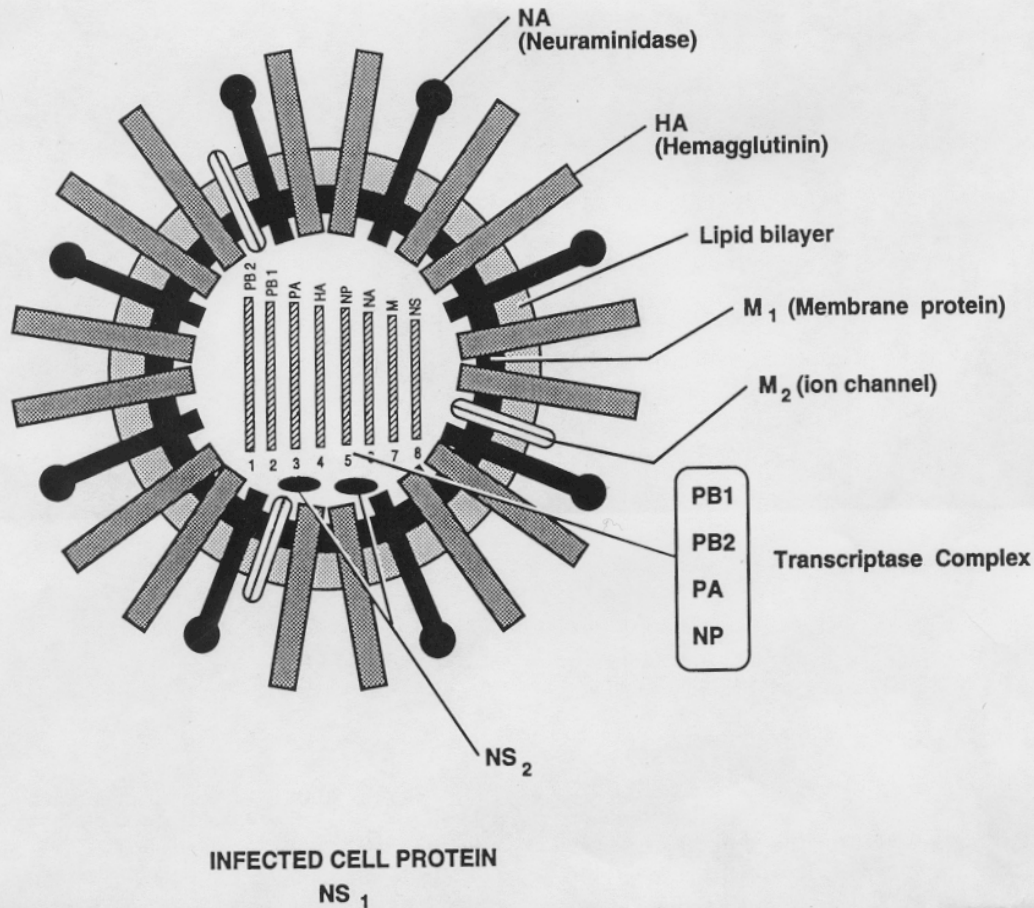


# INFLUENZA

# INFLUENZA A VIRUS

- Structure of the influenza A virus particle.



- TYPE A VIRUS HAS TWO TYPES OF SPIKES, THE HEMAGGLUTININ (H) AND THE NEURAMINIDASE (N), PROTRUDING FROM THE VIRAL ENVELOPE
- THE HEMAGGLUTININ (H) IS THE MORE IMPORTANT PROTEIN AND IS RESPONSIBLE FOR ATTACHMENT TO CELLULAR RECEPTORS. ANTI-H ANTIBODIES PROTECT AGAINST INFECTION.
- THE NEURAMINIDASE (N) IS INVOLVED IN VIRAL RELEASE FROM INFECTED CELLS AND RARELY HAS A PROTECTIVE EFFECT AGAINST INFECTION.

# INFLUENZA

- HIPPOCRATES FIRST DESCRIBED INFLUENZA IN 412 B.C.
- THE FIRST WELL-DOCUMENTED GLOBAL EPIDEMIC OCCURRED IN 1580.
- IN 1889-1890 AN H2N2 OUTBREAK OCCURRED IN RUSSIA THAT CAUSES A PANDEMIC WITH HIGH MORTALITY.
- SINCE THAT TIME THERE HAVE BEEN 30 DOCUMENTED PANDEMICS.

# INFLUENZA

- INFLUENZA PANDEMICS ALMOST ALWAYS BEGIN IN GUANGDONG PROVINCE (FORMALLY CANTON) CHINA.
- THERE THEY HAVE VIRUS-INFECTED WATERFOWL, SWINE, AND HUMANS ALL LIVING TOGETHER IN CLOSE PROXIMITY.
- THE ORIGINAL INFLUENZA WAS (H1N1). IT CAUSED A PANDEMIC IN 1918-1919.

# 1918 PANDEMIC

- THE INFLUENZA PANDEMIC OF 1918 WAS EXCEPTIONAL IN BOTH BREATH AND DEPTH.
- THE FIRST WAVE OF THE EPIDEMIC OCCURRED IN THE SPRING AND SUMMER OF 1918. IT WAS HIGHLY CONTAGIOUS BUT CAUSED FEW DEATHS.
- IT WAS UNUSUAL IN THAT IT DIDN'T SEEM TO BEGIN IN CHINA, BUT IN THE UNITED STATES

- IT APPEAR TO HAVE BEGUN IN HASKELL COUNTY, KANSAS, WHICH LIES WEST OF DODGE CITY IN WESTERN KANSAS.
- FARMERS THERE LIVED IN CLOSE PROXIMITY TO HOGS AND FOWL, WITH CATTLE, PIGS AND POULTRY EVERYWHERE AND THERE WAS INFLUENZA.
- YOUNG MEN DRAFTED INTO THE ARMY FROM HASKELL COUNTY CARRIED INFLUENZA 300 MILES EAST TO CAMP FUNSTON IN THE VAST FORT RILEY MILITARY RESERVATION.

- THE SECOND VERY VIRULENT WAVE BEGAN IN AUGUST 1918 AND FROM AUGUST TO NOVEMBER SWEEPED THE GLOBE. THROUGH JUNE 1919 IT IS ESTIMATED TO HAVE KILLED 40 TO 100 MILLION PEOPLE WORLDWIDE AND 650,000 PEOPLE – INCLUDING 43,000 SERVICEMEN, IN THE UNITED STATES.
- MOST DEATHS OCCURRED AMONG YOUNG ADULTS (15-TO 34-YEAR-OLDS).
- IT WAS CALLED THE “SPANISH FLU” BECAUSE IT WAS FIRST REPORTED IN SPANISH NEWSPAPERS.



- IT INFECTED APPROXIMATELY ONE-THIRD OF THE AMERICAN POPULATION AND LOWERED THE AVERAGE LIFE SPAN BY 10 YEARS.
- EVIDENCE SUGGESTS THAT THE 1918 INFLUENZA WAS A TYPE A (H1N1) CLOSELY RELATED TO SWINE FLU.

- IN 1957, THERE WAS A MAJOR SHIFT TO (H2N2) THAT RESULTED IN AN “ASIAN FLU” PANDEMIC.
- IN 1968, THERE WAS ANOTHER MAJOR SHIFT TO (H3N2) THAT RESULTED IN A “HONG KONG FLU” PANDEMIC.
- IN 1977, THE (H1N1) SUBTYPE REAPPEARED AS “RUSSIAN FLU”.
- SINCE 1977 BOTH THE H1N1 AND THE H3N2 SUBTYPES CO-CIRCULATE.
- ALL OF THESE MAJOR SHIFTS REQUIRED AN EXCHANGE OF GENES BETWEEN HUMANS AND OTHER ANIMALS.

# INFLUENZA VIRUSES

- THREE TYPES OF INFLUENZA ARE KNOWN – A, B, AND C. MAN IS THE ONLY KNOWN HOST FOR B AND C. TYPE A IS FOUND IN A WIDE RANGE OF SPECIES – SWINE, HORSES, SEALS, WATERFOWL AND HUMANS.
- INFLUENZA A VIRUS CAUSES EPIDEMICS TO OCCUR EVERY 2-4 YEARS, AND PANDEMICS TO OCCUR MUCH LESS FREQUENTLY.

- INFLUENZA B VIRUS CAUSES EPIDEMICS RARELY. INFLUENZA C DOESN'T PLAY MUCH OF A ROLE IN EPIDEMICS
- IN TYPE A VIRUSES THERE ARE 15 VARIANTS OF HEMAGGLUTININ (H) AND 9 VARIANTS OF NEURAMINIDASE (N)

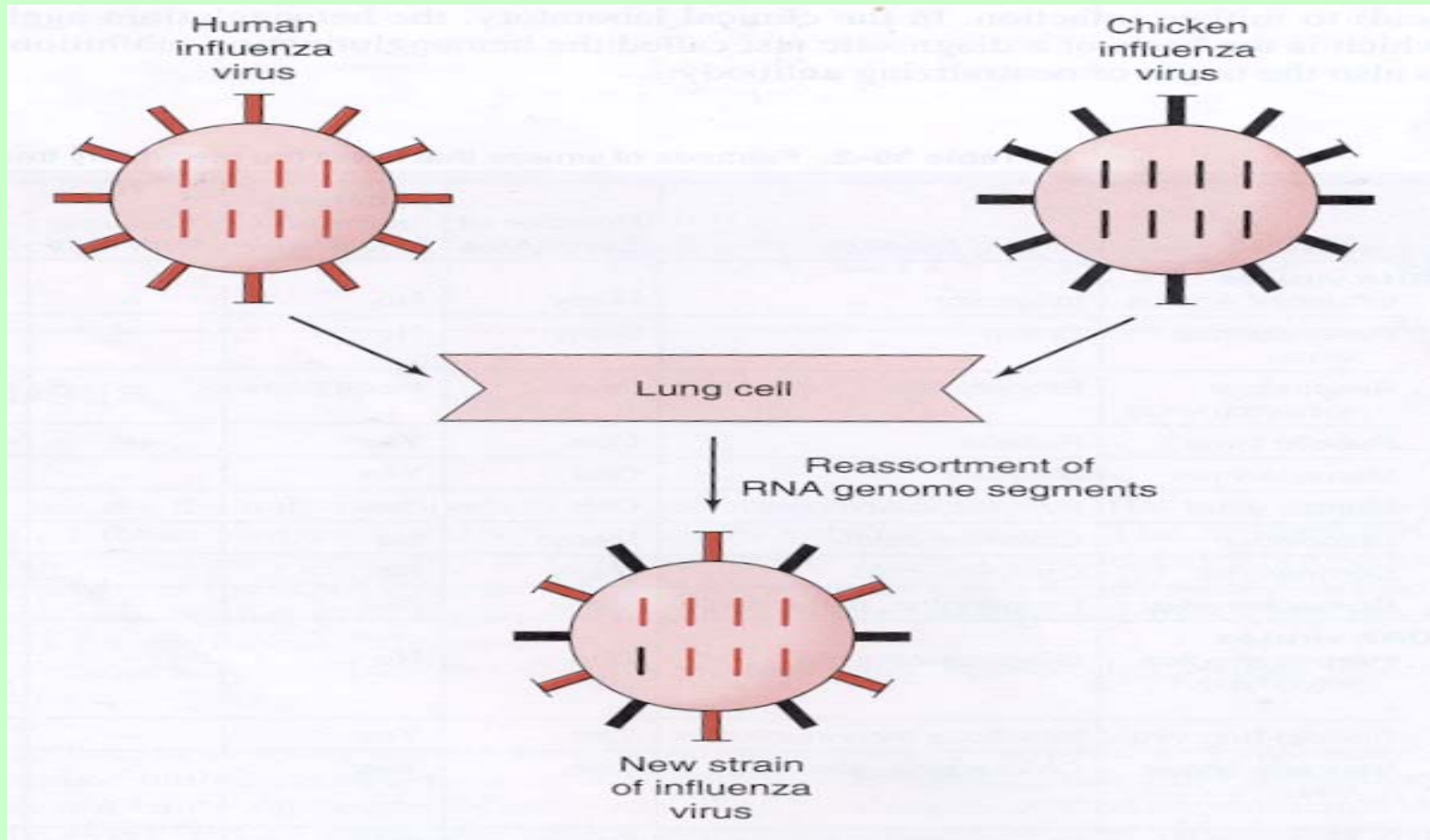
# TYPE A HEMAGGLUTININ SUBTYPES

LOCATION	H 1	H 2	H 3	H 4	H 5	H 6	H 7	H 8	H 9	H 10	H 11	H 12	H 13	H 14	H 15
BIRDS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PIGS	+		+	+	+				+						
HUMANS	+	+	+		+		+		+						

- THE VIRUS FOUND IN WILD BIRDS DOESN'T REPLICATE WELL IN HUMANS. THEREFORE, IT MUST GO FIRST TO AN INTERMEDIATE HOST – SUCH AS A HORSE, SEAL, OR SWINE THAT DRINKS WATER CONTAMINATED WITH WILD BIRD FECES.
- THE INTERMEDIATE HOSTS MAY SICKEN AND DIE BUT, THE SWINE IS ABLE TO LIVE A LONG TIME WITH THE VIRUS AND SERVES AS A “MIXING VESSEL”.
- THE BIRD IS USUALLY UNAFFECTED BY THE VIRUS.

- ANTIGENIC **SHIFT** OCCURS AS A RESULT OF REASSORTMENT OF CHROMOSOMES IN THE VIRUS.
- ANTIGENIC **DRIFT** IS CAUSED BY MUTATIONS IN (H) AND (N) GENES. THAT'S WHY WE NEED A NEW VACCINE EVERY YEAR.

# INFLUENZA



- Antigenic shift (caused by reassortment in influenza A virus).



- IN HONG KONG IN 1997, A VERY VIRULENT AVIAN STRAIN (H5 N1) INFECTED PEOPLE DIRECTLY WITHOUT ANY ANIMAL INTERMEDIARY. IT WAS NOT TRANSMITTED FROM PERSON TO PERSON.
- 18 PEOPLE BECAME INFECTED AND 6 PEOPLE DIED.
- OVER 1 MILLION CHICKENS WERE KILLED TO PREVENT THE SPREAD OF THE VIRUS.
- IN 2004 THE SAME STRAIN CAUSED DEATHS IN VIETNAM.
- OFFICALLY, THERE HAVE BEEN 39 BIRD TO HUMAN INFECTIONS WITH 28 FATALITIES.
- IN 2003, 83 POULTRY WORKERS IN THE NETHERLANDS CONTRACTED AVIAN STRAIN H7 N7.

# H1N2

- DURING THE WINTER OF 2001-2002 A NEW H1N2 VIRUS APPEARED IN THE UK.
- IT GETS THE H1 FROM THE PREVAILING H1N1 VIRUS AND ALL OF THE OTHER GENES FROM THE PREVAILING H3N2 STRAIN.

# INFLUENZA VIRUS



- Glycoprotein spikes containing hemagglutinin or neuraminidase activity are visible on the surface of the colorized virions.

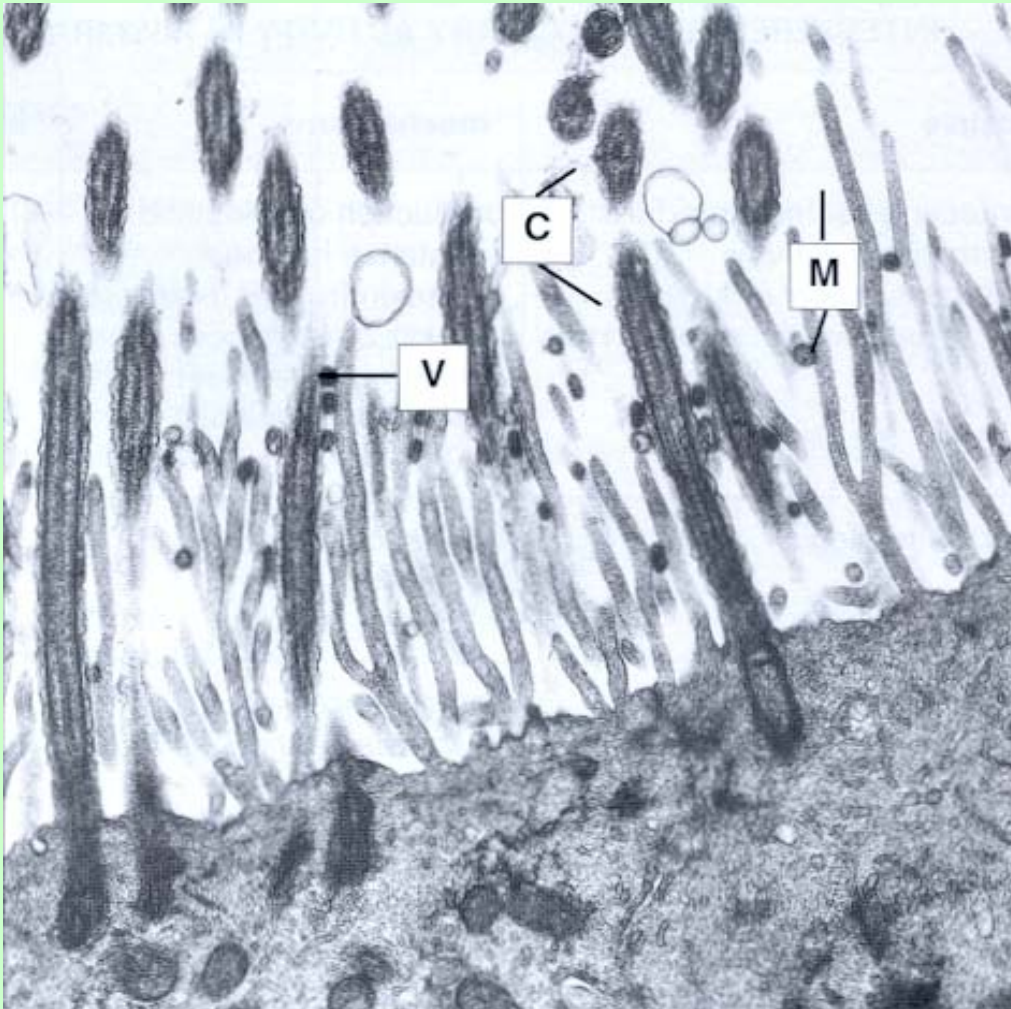
# INFLUENZA VIRUS



- Colorized transmission electron micrograph of influenza virus.

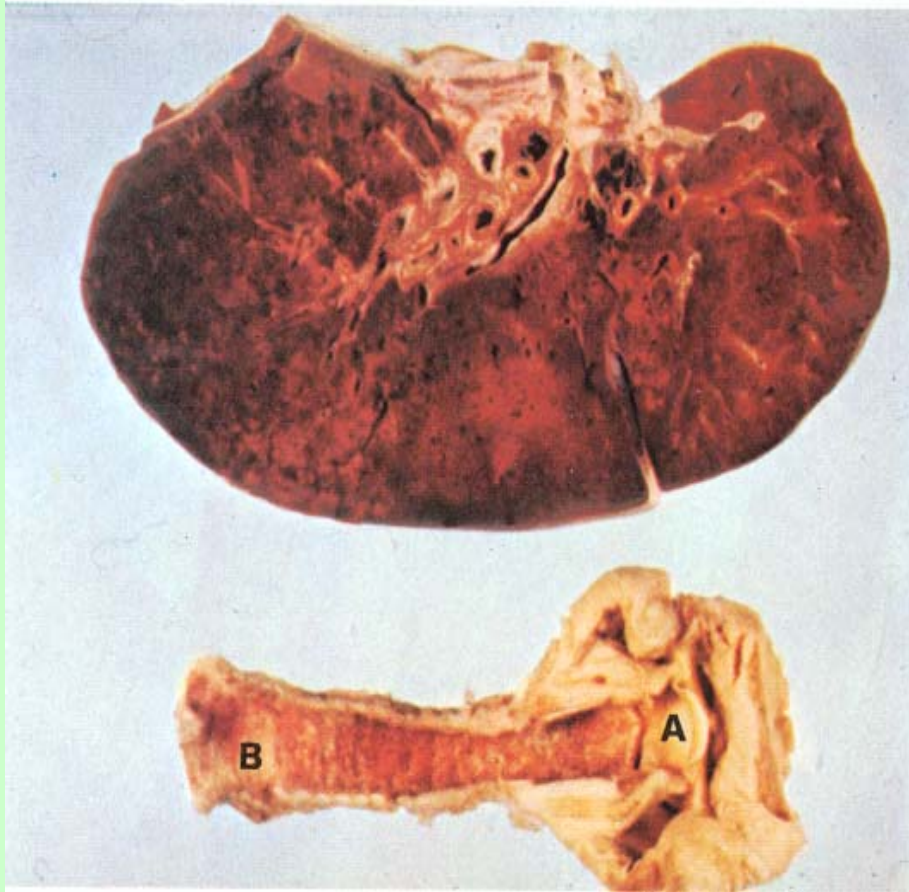


# INFLUENZA VIRUS



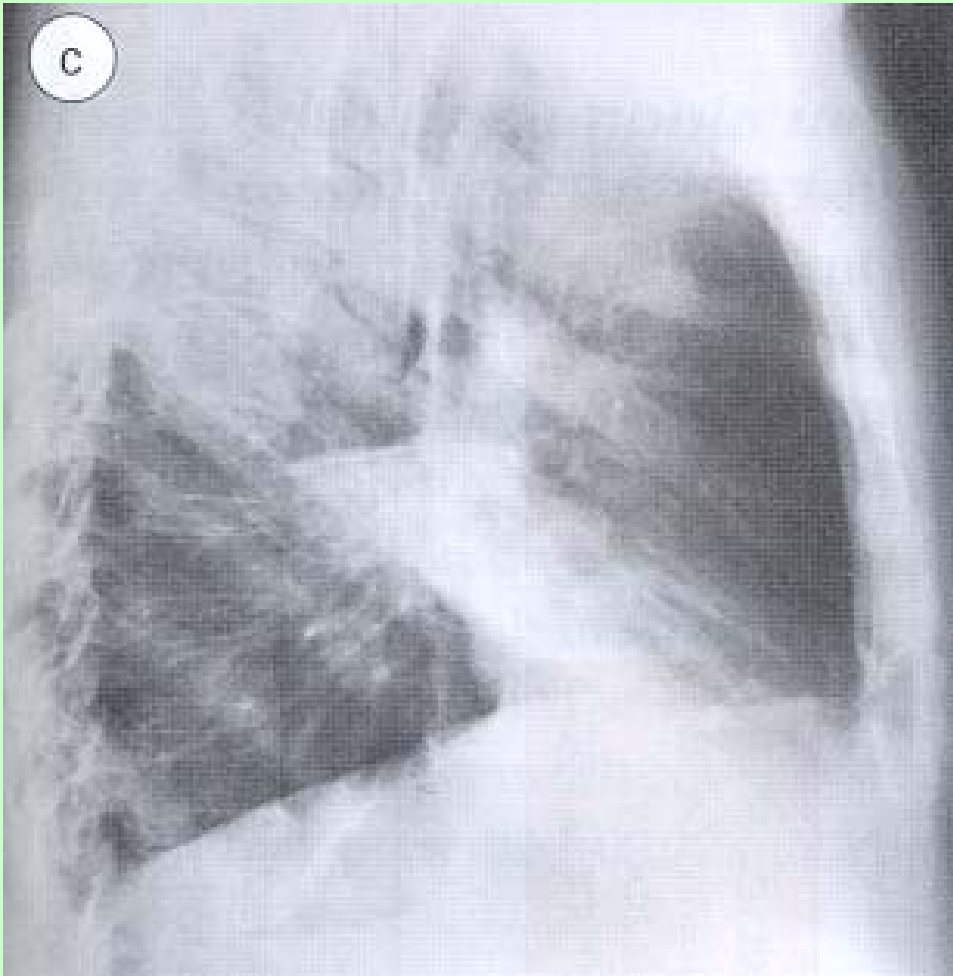
- Influenza virus particles (V) attach to cilia (C) and microvilli (M).

# INFLUENZA



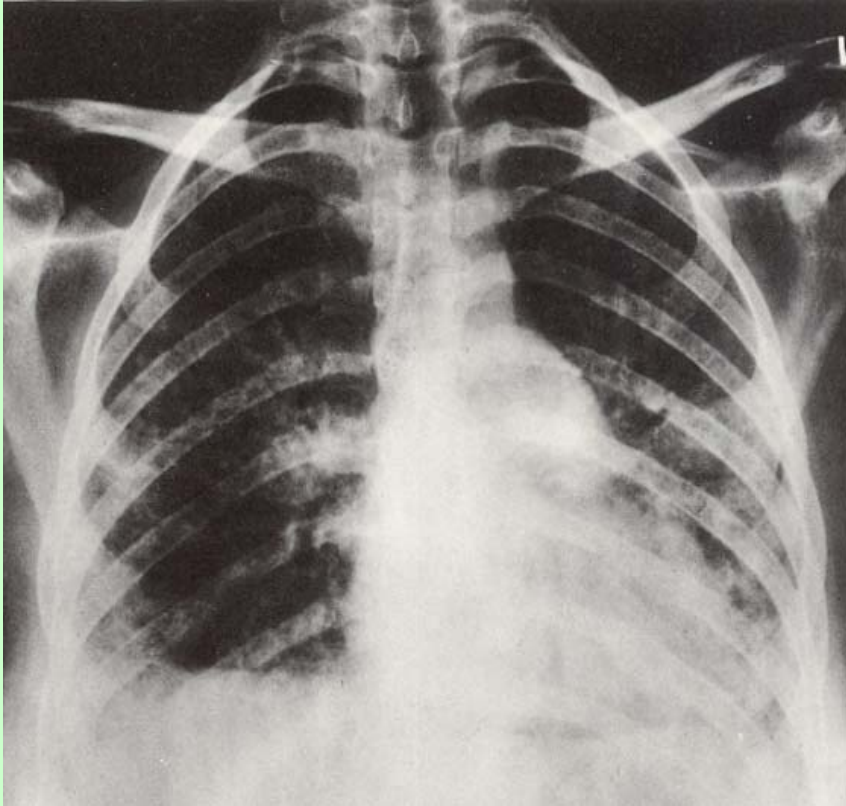
- Influenza- appearance of trachea and lungs. The trachea (B) and bronchi are congested. The lungs are brightly mottled with subpleural hemorrhages. (A=larynx).

# INFLUENZA



- Interstitial pneumonia due to influenza virus. Interstitial pneumonia involves invasion of the lung interstitium.

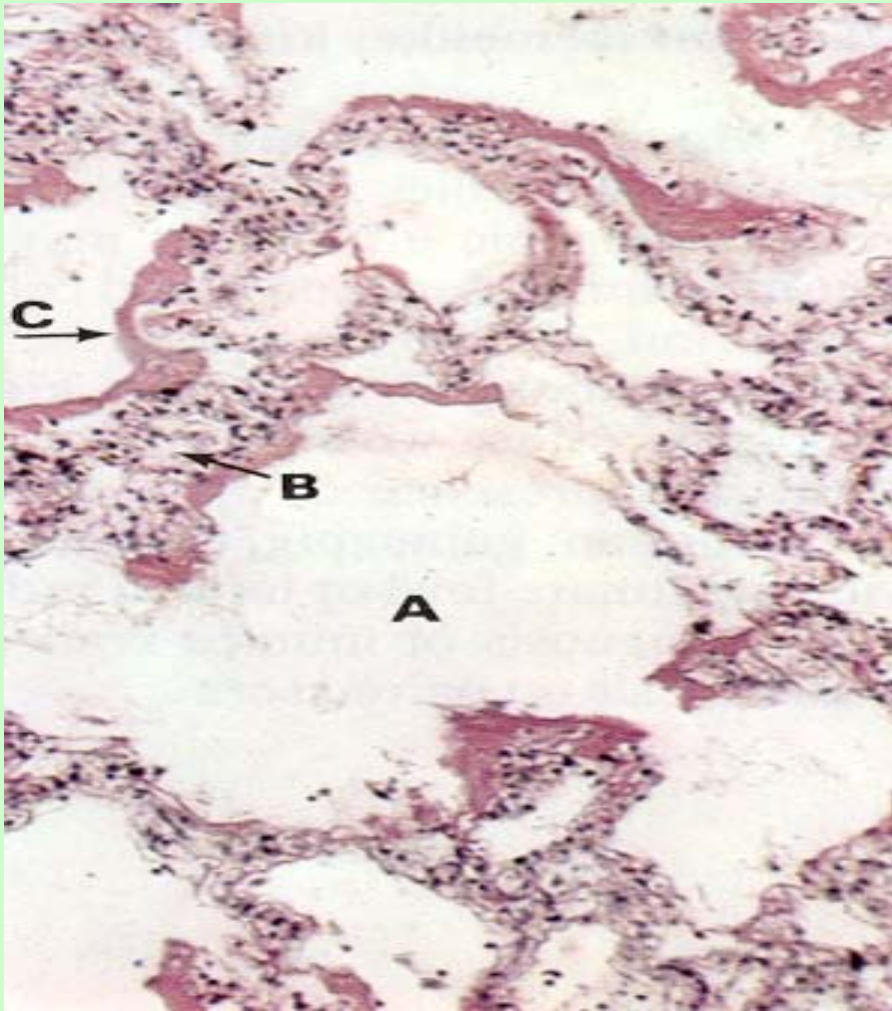
# INFLUENZA VIRUS



- Another radiological appearance of viral interstitial pneumonia shows diffuse patchy shadowing in both lung fields with sparing of the apices.



# INFLUENZA VIRUS



- Section of lung in influenza. The alveolar walls are thickened and infiltrated by mononuclear cells. There is a heavy deposit of hyaline on the surface. A = air sac, B= alveolar wall, and C= hyaline material.

# EXAMPLE OF FLU VACCINE PRODUCTION

- **MID-JANUARY** A GOVERNMENT LABORATORY SENDS THE FIRST VIRUS (B) TO THE PRODUCTION FACILITY WHERE THE VIRUS IS GROWN IN FERTILE CHICKEN EGGS . IT TAKES ABOUT 6 WEEKS.
- **EARLY MARCH** THE SECOND STRAIN (H1N1) IS SENT. IT TAKES ANOTHER 6 WEEKS TO GROW.

- **LATE APRIL** THE THIRD STRAIN IS SENT (H3N2). IT TAKES ANOTHER 6 WEEKS TO GROW.
- **JUNE** SAMPLES ARE SENT TO THE FDA WHICH CHECKS FOR PURITY AND CONCENTRATION.
- **JULY** WITH FDA APPROVAL, THE STRAINS ARE BLENDED INTO THE VACCINE.
- **AUGUST** SHIPPING BEGINS.
- **SEPTEMBER AND OCTOBER** PATIENTS BEGIN GETTING FLU SHOTS.

# 1993 - 1994

- A / TEXAS / 36 / 91 (H1N1)
- A / BEIJING / 32 / 92 (H3 N2)
- B / PANAMA / 45 / 90

# 1994 - 1995

- A / TEXAS / 36 / 91 (H2N1)
- A / SHANGDONG / 09 / 93 (H3N2)
- B / PANAMA / 45 / 90

# 1995 - 1996

- A / TEXAS / 36 / 91 (H1N1)
- A/ JOHANNESBURG (H3N2)
- B / HARBIN / 07 / 94

# 1996 - 1997

- A / TEXAS / 36 / 91 (H1N1)
- A / NANCHANG / 933 / 95 (H3N2)
- B / HARBIN / 07 / 94

# 1997 - 1998

- A / JOHANNESBURG / 82 / 96 (H1N1)
- A / NANCHANG / 933 / 95 (H3N2)
- B / HARBIN / 07 / 94



# 1998 - 1999

- A / BEIJING / 262 / 95 (H1N1)
- A / SYDNEY / 5 / 97 (H3N2)
- B / BEIJING / 184 / 93 - LIKE

# 1999 - 2000

- A / BEIJING / 262 / 95 (H1N1)
- A / SIDNEY / 5 / 97 (H3N2)
- B / YAMANASHI / 166 / 98

# 2000 - 2001

- A / NEW CALEDONIA / 20 / 99 (H1N1)
- A / PANAMA / 2007 / 99 (H3N2)
- B / YAMANASHI / 166 / 98

# 2001 - 2002

- A / NEW CALEDONIA / 20 / 99 (H1N1)
- A / PANAMA / 2007 / 99 (H3N2)
- B / JOHANNESBURG / 5 / 99

# 2002 - 2003

- A / NEW CALEDONIA / 20 / 99 (H1N1)
- A / MOSCOW / 10 / 99 (H3N2)
- B / HONG KONG / 330 / 01

# 2003 - 2004

- A / NEW CALEDONIA / 20 / 99 (H1N1)
- A / PANAMA / 2007 / 99 (H3N2) (25%)
- A / FUJIAN (WOULD HAVE BEEN BETTER BUT DOESN'T GROW WELL IN CHICKEN EGGS) (75%)
- B / HONG KONG / 330 / 2001 (1434 / 2002)

# 2004 - 2005

- A / NEW CALEDONIA / 20 / 99 (H1N1)
- A / FUJIAN / 411 / 2002 (H3N2) OR
- A / WYOMING / 3 / 2003 (H3N2) OR
- B / SHANGHAI / 361 / 2002 OR
- B / JILIN / 20 / 2003