

BUREAU OF EPIDEMIOLOGY

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INFLUENZA VACCINES, 1983-1984

The following article first appeared in the Centers for Disease Control (CDC) publication, Morbidity and Mortality Weekly Report, Vol. 32/No. 26, July 8, 1983.

#### Introduction

Influenza virus infections occur every year in the United States but vary greatly in incidence and geographic distribution. Infections may be asymptomatic, or they may produce a spectrum of manifestations ranging from mild upper-respiratory infection to pneumonia and death. Influenza virus types A and B are responsible for only a small proportion of all respiratory disease, but they are unique in their ability to cause periodic widespread outbreaks of febrile respiratory illness among adults and children.

Influenza epidemics are frequently associated with deaths in excess of the number normally expected. More than 200,000 excess deaths are estimated to have occurred in association with influenza epidemics in the United States during 1968-1982. Excess deaths in this period were attributable mainly to influenza A viruses, although influenza B epidemics were occasionally associated with excess deaths, as in 1979-1980. Epidemics of influenza B, and to a lesser extent, influenza A infection have been associated with an increased incidence of Reye syndrome among children and adolescents in the United States.

Efforts to reduce the impact of influenza in the United States have been aimed at protecting persons at greatest risk of serious illness or death. Observations during influenza epidemics indicate that most influenza-related deaths occurred among two groups of persons: the chronically ill and the elderly. Annual vaccination is. therefore, recommended for these medically high-risk persons.

Influenza A viruses are classified into subtypes on the basis of two antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1,H2,H3) and two subtypes of neuraminidase (N1, N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens, especially hemagglutinin, reduces the likelihood of infection and the severity of disease if a person does become infected. However, there may be sufficient antigenic variation (antigenic drift) within the same subtype over time, so that infection or vaccination with one strain may not induce immunity to distantly related strains of the same subtype. Although influenza B viruses have shown much more antigenic stability than influenza A viruses, antigenic variation does occur. As a consequence, the antigenic characteristics of current strains provide the basis for selecting virus strains to be included in the vaccine.

During the 1982-1983 winter, influenza activity occurred at moderate levels in the United States. The number of virus isolates reported to CDC was more than double that of the 1981-1982 winter when influenza activity was generally low. Excess mortality was slightly elevated throughout the epidemic period, starting in January 1983. The viruses implicated as the major cause of nationwide epidemic activity were influenza A(H3N2) strains, and in particular, these H3N2 viruses were shown to cause nearly all outbreaks in nursing home or hospital settings for which laboratory diagnosis was obtained. Influenza A(H1N1) viruses, isolated in about half the states, were not proven responsible for outbreaks in the aged or infirm but occasionally were isolated from school outbreaks, sometimes concurrently with influenza A(H3N2)

Texas Department of Health - NON-CIRCULATING

Texas Preventable Disease News, week no. 36

strains. Influenza B viruses were isolated infrequently early in the season, although their prevalence increased toward the end of the season, including outbreaks in several schools and nursing homes in April and May.

Almost 80% of influenza virus isolates reported in the United States were type A(H3N2) strains, mostly similar to A/Bangkok/79(H3N2), a strain included in the vaccine for the last 3 years. However, variants that are poorly inhibited by animal sera to A/Bangkok/1/79 (reference strain A/Philippines/2/82) have accounted for an increasing proportion of H3N2 strains recovered in Asia since mid-1982 and have also been identified during the 1982-1983 winter in Europe and North America. These considerations and animal studies showing that A/Philippines/2/82 induces antibodies that react broadly with the Bangkok strain, as well as with other recent variants, suggest that the A/Philippines/2/82 strain should replace the A/Bangkok/79(H3N2) component in the vaccine. Antigenic analysis of influenza A(H1N1) viruses isolated in recent months confirms their close resemblance to A/England/333/80 strains that have circulated during the past 2 years. Measurement of antibody responses of persons receiving vaccines containing A/Brazil/11/78 antigen, however, continues to indicate that these vaccines should protect against A/England/333/80-like strains. Antigenic analysis of infuenza B viruses isolated during the past year shows that these strains remain similar to B/Singapore/222/79, a strain included in the vaccine for the past 3 years.

# INFLUENZA VACCINES FOR 1983-1984

The specific antigens and their potency in the 1983-84 vaccine will be: 15  $\mu$ g each of hemagglutinin of A/Brazil/78(H1N1), A/Philippines/82(H3N2), and B/Singapore/79 viruses per 0.5-ml dose.

Adults and children older than 12 years will require only one dose. Children 12 years of age and younger are less likely than older children or adults to have been previously infected with strains related to each of the vaccine components. Therefore, because of their potentially lower level of immunologic priming, children in the 12-and-under age group should receive two doses of vaccine. However, children who have already had at least one of the influenza vaccines recommended for use from 1978 to 1983 will require only one dose of the 1983-1984 vaccine. The 1983-1984 vaccines will be available as whole-virion (whole-virus) and sub-virion (split-virus) preparations. Past data indicate that split-virus vaccines have been associated with somewhat fewer side effects among children than whole-virus vaccines. Thus, only split-virus vaccines are recommended for those 12 years and under.

## VACCINE USAGE

# General Recommendations

Annual vaccination is strongly recommended:

- 1. For all older persons, particularly those over 65 years, because the risk of death during influenza outbreaks generally increases with age.
- 2. For all persons (children and adults) who are at increased risk of adverse consequences from infections of the lower respiratory tract because of a pre-existing medical condition.

Conditions predisposing to such increased risk include:

- a) Acquired or congenital heart disease with actual or potential alterations in circulatory dynamics (e.g., mitral stenosis, congestive heart failure, or pulmonary-vascular overload).
- b) Any chronic disorder or condition that compromises pulmonary function (e.g., chronic obstructive pulmonary disease, bronchiectasis, heavy smoking, tuberculosis, severe asthma, cystic fibrosis, neuromuscular and orthopedic disorders with impaired ventilation, broncho-pulmonary dysplasia following the neonatal respiratory distress syndrome).
- c) Chronic renal disease with azotemia or nephrotic syndrome.

- d) Diabetes mellitus or other metabolic diseases.
- e) Severe chronic anemia, such as sickle cell disease.
- f) Conditions that compromise the immune mechanism, including certain malignancies and immunosuppressive therapy.

In balancing the benefits, risks, and costs for the community, some localities have elected to vaccinate persons who provide essential community services and medical-care personnel who also are at increased risk of exposure. Vaccination of medical-care personnel may also reduce spread of influenza to patients in hospitals and other settings. While consideration should be given to providing vaccine for such groups, vaccination of persons specified to be at high risk should take precedence.

Table 1 summarizes vaccine and dosage recommendations by age group for 1983-1984.

### Use in Pregnancy

Physicians should evaluate a pregnant woman's need for influenza vaccination on the same basis used for other persons; i.e., vaccination should be advised for a pregnant woman who has any underlying high-risk condition. Only in the pandemics of 1918-1919 and 1957-1958 was there persuasive evidence that influenza infection increased maternal mortality.

There is no evidence to suggest that influenza vaccine carries any maternal or fetal risk, and, because it is inactivated, the vaccine does not share any of the theoretical risks of live-virus-vaccine infection of the fetus. Nonetheless, when vaccine is to be given in pregnancy, waiting until the second or third trimester is a reasonable precaution to minimize any concern over teratogenicity.

#### Side Effects and Adverse Reactions

Vaccines used in recent years have generally been associated with only a few reactions; less than one third of vaccinees have been reported to have local redness and induration for 1 or 2 days at the site of injection.

Systemic reactions have been of three types:

- 1. Fever, malaise, myalgia, and other systemic symptoms of toxicity, although infrequent, most often affect children and others who have had no experience with the influenza virus antigens contained in the vaccine. These reactions, which begin 6-12 hours after vaccination and persist 1-2 days, are usually attributed to the influenza antigens (even though the virus is inactivated) and constitute most of the side effects of influenza vaccination.
- 2. Immediate, presumably allergic, responses such as flare and wheal or various respiratory expressions of hypersensitivity occur extremely rarely after influenza vaccination. They probably result from sensitivity to some vaccine component—most likely residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, on rare occasions they can induce hypersensitivity reactions. Individuals with anaphylactic hypersensitivity to eggs should not be given influenza vaccine. This would include persons who, on eating eggs, develop swelling of the lips or tongue or experience acute respiratory distress or collapse.
- 3. In 1976, a temporal association (i.e., within 10 weeks of vaccination) was noted between administration of A/New Jersey/76 (swine) influenza vaccine and Guillain-Barre syndrome (GBS). Vaccinated adults had an excess frequency of GBS at the rate of approximately 10 cases/million persons vaccinated. This incidence of GBS was five to six times higher than the comparable average reported incidence for unvaccinated persons. An active surveillance system for GBS was initiated in 1978 and was maintained for 3 years. No significant excess risk of GBS was found for recipients of influenza vaccine during the influenza seasons 1978-1979 through 1980-1981. Available evidence indicates that any

risk of GBS from influenza vaccine appears to be far lower than the risks associated with influenza among persons for whom the vaccine is indicated.

#### OTHER MEASURES

Annual vaccination continues to be the most important way to prevent influenza and should be routine for all persons at high risk of serious and/or fatal disease. Measures intended to reduce the likelihood of exposure in community outbreaks, such as limiting the number of gatherings of large groups, may delay spread but are not uniformly effective.

Amantadine hydrochloride, an antiviral drug, can help prevent influenza A for certain persons and circumscribed groups. It is not a substitute for vaccine and is not generally applicable to public health practice, but it may be useful for persons who have not been vaccinated and need protection during outbreaks.

Amantadine protects only against influenza A, not influenza B, infection and must be taken each day for the duration of the epidemic (6-8 weeks, generally) or until active immunity can be expected to develop after vaccination (about 10-14 days). Precautions must be taken for patients with certain chronic conditions, and there are sometimes mild but occasionally troublesome side effects—especially among older patients. Amantadine is a prescription drug and must be ordered and monitored by a physician. Dosage, precautions, and other information on use are specified in the drug's labeling.

# PDN Editorial Note:

The Immunization Division, Texas Department of Health (TDH will neither purchase influenza vaccines nor conduct influenza immunization programs during the 1983-1984 season. These vaccines may be purchased from the manufacturer footnoted in Table 1. The TDH Tuberculosis Control Program will continue to provide influenza vaccine for tuberculosis patients only.

	Table 1	1:	Influenza	vaccine*	dosage,	by	age		United	States,	1983 <b>–</b> 1984
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Age group	Product	Dosage	Number o doses			
6-35 months	Split virus only	0.25ml †	2 §			
3-12 years	Split virus only	0.5ml	2 §			
over 12 years	Whole or split virus	0.5ml	1			

\*Contains 15  $\mu$ g each of A/Brazil/78(H1N1), A/Philippines/82(H3N2), and B/Singapore/79 hemagglutinin antigens in each 0.5 ml. Manufacturers include Connaught Laboratories, Inc. ("FLUZONE": whole and split), Parke-Davis ("FLUOGEN": split), and Wyeth Laboratories ("Influenza Virus Vaccine, Trivalent": split).

†Based on limited data. Since the likelihood of febrile convulsions is greater for this age group, special care should be taken in weighing relative risks and benefits. Four weeks or more between doses; both doses recommended for maximum protection. Twever, if the individual received at least one dose of any influenza vaccine recommended from 1978-79 to 1982-83, one dose is sufficient.

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AIDS CASES IN TEXAS BY YEAR OF DIAGNOSIS

1980	1981	1982	<u>1983</u>
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ASEPTIC MENINGO- ! HEPATITIS: ! IMMUNIZABLE: | RICKETTSIAL: | VENEREAL: |

	ASEPTIC MENIN- GITIS	MENINGO- COCCAL INFEC	ı	A	PATIT B SERUM		I IMMU	NIZABLE: RUBELLA	RIC END TYP		- 1	V ENER	EAL:   P&S   SYPH	MISC. FLU & FLU-LIKE	TUBER-
PUBLIC HEALTH REGION	12 MID	LAND, TX		PHON	ΙΕ:			POPULA	TION	= 364	,329				
COUNTIES															
DAWSON ECTOR HOWARD REEVES WARD CASES THIS WEEK CUMULATIVE 1983	6	1	***	46	1 1 16	4 1 5 78	* * * * * * * * * *	5	***	1 1 1	***	15 15 601	86	*  *  *  5  *  1  *  *  *  *  6  *  2,322	16
OTHER COUNTIES:	NO	COMMUNIC	CABL	E DISE	ASES:	0	o	THER DISEA	SES 0	NLY: 2		NOT	REPORTIN	G: 10	
OTHER REPORTING SOURCE	E S														
ARMED FORCES V.A. HOSPITALS			*				*		*		*	21	5	*	
CASES THIS WEEK CUMULATIVE 1983	5	2	*	18	18	21	* *	1	* *		*	21 1,662	5 111	* * * 5,051	

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OTHER REPORTABLE DISEASES	REPORTED 1982	THIS WEEK 1983	C UM U 1982	LATIVE 1983
ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)		4		
AMEBIASIS	13	2	338	37 25 <i>3</i>
ANTHRAX	0	Õ	9,00	
BOTULISH	ō	ī	ő	2
BRUCELLOSIS	ũ	0	13	57
CHICKENPOX	14	23	9765	13675
CHOLERA	٥	0	0	O
DIPHTHER IA	9	a	1	0
ENCEPHALITIS, ST. LOUIS ENCEPHALITIS, WESTERN EQUINE	1	a	3	1
ENCEPHALITIS, VENEZUELAN EQUINE	0	0	1_	O
	0	0	0	0
ENCEPHALITIS, ALL OTHER	6	2	102	77
LEPROSY (HANSENS DISEASE) LEPTOSPIROSIS	0	0	22	21
MALARIA	1 0	0 0	10	0
MALARIA ACQUIRED OUTSIDE USA	G.	1	0 37	0
	<b>.</b>	1	3 (	34
MUMPS	4	4	157	157
PERTUSSIS	3	2	53	60
PLAGUE POLIOMYELITIS, PARALYTIC	0	0	1	Ō
PSITTACOSIS PARALITIC	0	0	0	0
1 3 2 1 1 1 1 0 0 3 1 3	U	2	6	5
Q FEVER	U	٥	1	0
RABIES IN MAN	Û	Ō	٥	0
RELAPSING FEVER RHEUMATIC FEVER	Ű	0	<u>1</u>	ō
RUBELLA CONGENITAL SYNDROME	. o	0 0	7	11
ROBELER CONGENTIAL STRONGIE	Ů,	U .	0	0
SALMONELLOSIS	49	31	1264	1376
SHIGELLOSIS	40	45	1428	1033
STREP THROAT & SCARLET FEVER	540	379	34683	27178
REYE SYNDROME TETANUS	C	0 0	-	13
TCTRAOS	U	IJ	5	3
TRICHINOSIS	a	a	0	1
TULAREMIA	1	<u>o</u>	5	7
TYPHOID FEVER TYPHUS, EPIDEMIC	<b>0</b> 0	3 0	19	30
YELLOW FEVER	ຍ ວ	U D	0 0	0
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RABIES IN ANIMALS