



New Option for Influenza Protection: An
Influenza Vaccine for Older Adults and
New Strategies in Pertussis Prevention:
Expanding Targets and Reducing
Disease



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Faculty Disclosure

Thanks to Sanofi pasteur for sponsoring this
morning's presentation

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Presentation Outline

- I. Influenza Immunization of Adults**
New challenges, new opportunities
- II. Fluzone High-Dose Vaccine**
Designed to improve the immune response
in people 65 years of age and older
- III. Fluzone Intradermal Vaccine**
A new option for influenza prevention
- IV. Adacel Vaccine**
Focusing on pertussis prevention

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Universal Influenza Immunization of Adults: New challenges, new opportunities

“A universal vaccination recommendation for all persons aged ≥6 months eliminates the need to determine whether each person has an indication for vaccination and emphasizes the importance of preventing influenza among persons of all ages.”¹

Reference: 1. Centers for Disease Control and Prevention (CDC). *MMWR*. 2010;59(RR-8):1-62.

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Influenza: An Annual Epidemic

- **5%-20%:** Percentage of the US population that becomes ill with influenza each year¹
 - 15-60 million cases
- **3000-49,000:** Range of estimated annual influenza-related deaths¹
 - Influenza and pneumonia: Eighth leading cause of death in the US (all ages)²
- **55,000-431,000:** Range of estimated annual influenza-related hospitalizations^{3,4}

References: 1. CDC. <http://www.cdc.gov/flu/about/qa/disease.htm>. Accessed May 26, 2011. 2. Xu J, et al. *Nat/ Vital Stat Rep*. 2010;58(19):1-135. 3. CDC. *MMWR*. 2010;59(RR-8):1-62. 4. Thompson WW, et al. *JAMA*. 2004;292(11):1333-1340.

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Influenza Vaccination Coverage Rates

Healthy People 2020 goals^a
90% for persons ≥65 years of age, high-risk adults 18-64 years of age, residents of long-term care, health-care personnel; 80% for all others^b

Age Group	Percent of Persons Vaccinated
≥65	69.6%
50-64	45.0%
18-49 High-risk	38.2%
18-49 Non-high-risk	28.4%
6 mo-17 yr	43.7%
Pregnant women	49%
Health-care personnel	62%

^a Rates are actual for 2009-2010 influenza season. ^b Rates are projected for 2010-2011 influenza season.

References: 1. Healthy People 2020. <http://www.healthypeople.gov/2020/topics/objectives/2020/objectiveslist.aspx?topicid=23>. Accessed May 26, 2011. 2. CDC. http://www.cdc.gov/flu/professionals/vaccination/coverage_0910estimates.htm. Accessed May 26, 2011. 3. Weinbaum C. <http://www.cdc.gov/vaccines/recs/ACIP/downloads/mfp-slides-feb11-06-3-flu-vac.pdf>. Accessed May 26, 2011.

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Influenza and Older Adults: A Disproportionate Burden of Disease

- Older adults represent:
 - ~15% of the US population¹
 - 63% of influenza-related hospitalizations²
 - >90% of influenza-related deaths³
 - 64% of the economic burden of influenza⁴
- Influenza and pneumonia: No. 7 cause of death in the US in persons ≥65 years of age⁵
- Vaccination rates for seniors have hovered in the 65%-70% range for a decade

References: 1. CDC. *MMWR*. 2003;52(6):101-106. 2. Thompson WW, et al. *JAMA*. 2004;292(11):1333-1340. 3. CDC. *MMWR*. 2010;59(RR-8):1-62. 4. Molinari NM, et al. *Vaccine*. 2007;25(27):5086-5096. 5. Xu J, et al. *Natl Vital Stat Rep*. 2010;58(19):1-135.


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Burden of Influenza in Younger Adults

- Adults 18-64 years of age:
 - Represent 31% of the total US economic burden of influenza¹
 - Accounted for ~35 million cases, 160,000 hospitalizations, and 9570 deaths in the US in the 2009 influenza A (H1N1) pandemic²
- National health officials are concerned that pandemic-like viruses will continue to circulate and that a “substantial portion” of young adults might be susceptible³
- Morbidity and mortality among younger adults occur in every influenza season³
 - Some have no previously identified risk factors for influenza
 - Some have risk factors but are unaware that they and their close contacts should be vaccinated

References: 1. Molinari NM, et al. *Vaccine*. 2007;25(27):5086-5096. 2. CDC. http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm. Accessed May 26, 2011. 3. CDC. *MMWR*. 2010;59(RR-8):1-62.

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Designed to improve the immune response in people 65 years of age and older

“Of all infectious diseases, influenza is foremost in its association with an age-related increase in serious consequences leading to hospitalization, debilitating complications, and death.”¹

Reference: 1. McElhaney JE, Dutz JP. *J Infect Dis*. 2008;198(5):632-634.

See Slides with Important Safety Information.

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Factors That Limit the Success of Vaccines in Older Adults

- Age-related decline in humoral and cellular immunity increases susceptibility to infection¹
- Older adults have decreased immunologic response to vaccines (immunosenescence)^{1,2}
- Decreased antibody responses to vaccination may leave them more vulnerable to influenza infection and severe complications¹⁻³

References: 1. Zheng B, et al. *J Immunol*. 2007;179(9):6153-6159. 2. Doria G, et al. *Mech Ageing Dev*. 1997;96(1-3):1-13. 3. Siegrist CA. *Vaccine Immunology*. In: Plotkin SA, et al, eds. *Vaccines*. Fifth edition. Philadelphia, PA: Saunders Elsevier; 2008:17-36.

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Post-vaccination GMT,^a Fluzone Vaccine,^b Younger vs Older Adults¹

Strain	Age Group	GMT
A (H1N1)	18-64 Years of Age	121
	≥65 Years of Age	38
B	18-64 Years of Age	78
	≥65 Years of Age	50
A (H3N2)	18-64 Years of Age	485
	≥65 Years of Age	258

^a GMT = Geometric Mean Titers. ^b Fluzone (Influenza Virus Vaccine).
Reference : 1. Sanofi Pasteur Inc. Data on file (Annual study GRC41), November 2009. MKT20203.

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Effectiveness of Influenza Vaccines Against Influenza-like Illness, by Age^{1,2}

Effectiveness of influenza vaccines in younger and older adults

Season	≥65 years of age (%)	15-64 years of age (%)
1998-99	~38	~65
1999-2000	~42	~75
2000-01	~32	~75
2001-02	~48	~78
2002-03	~28	~68
2003-04	~52	~68
2004-05	~40	~65

Adapted from Monto AS, et al.¹

During the 7 influenza seasons shown, the range of vaccine effectiveness was 26%-52% in persons ≥65 years of age and 62%-76% in those 15-64 years of age

References: 1. Monto AS, et al. *Vaccine*. 2009;27(37):5043-5053. 2. Legrand J, et al. *Vaccine*. 2006;24(44-46):6605-6611.

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Fluzone High-Dose Vaccine: Phase III Trial^{1,2}

- Multicenter, randomized, double-blind, controlled trial
- Purpose: To compare immunogenicity and safety of Fluzone High-Dose vaccine (60mcg HA per strain) with Fluzone vaccine (15mcg HA per strain)
- Participants: Medically stable persons ≥65 years of age living in the community
- 3876 subjects were randomized to receive vaccine in a 2:1 ratio (Fluzone High-Dose vaccine: Fluzone vaccine)
 - Blood samples were drawn before and 28 days after vaccination and antibody titers were measured using an HAI assay

References: 1. Fluzone vaccine [Prescribing Information]. Swifwater, PA: Sanofi Pasteur Inc.; 2011.
2. Falsey A, et al. J Infect Dis. 2009;200(2):172-180.

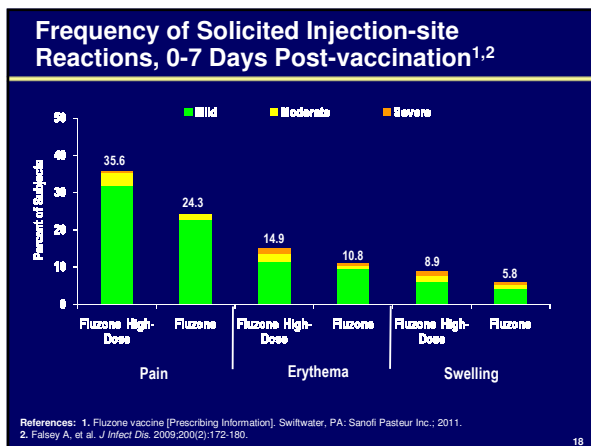
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Phase III Trial: Safety Data Collection

- Participants were observed for 30 minutes in the clinic after vaccination^{1,2}
- Participants recorded solicited injection-site and systemic symptoms on a diary card each day for 7 days following vaccination^{1,2}
- During a scheduled clinic visit 28 days after vaccination, the diary cards and unsolicited adverse events (AE) were reviewed by the study staff²
- 6 months after vaccination, participants were contacted by telephone to document any serious adverse events (SAE) and health-care provider contacts²

References: 1. Fluzone vaccine [Prescribing Information]. Swifwater, PA: Sanofi Pasteur Inc.; 2011.
2. Falsey A, et al. J Infect Dis. 2009;200(2):172-180.

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**Questions about
Fluzone High- Dose?**

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**Fluzone[®]
intradermal
INFLUENZA VIRUS VACCINE**

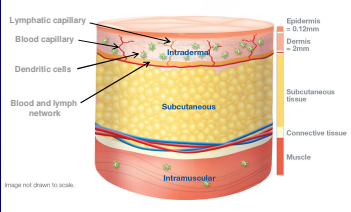
A new option for influenza prevention



See Slides with Important Safety Information.

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**Intradermal Injection:
Works by Utilizing the Skin**



- Body's first line of defense in recognizing and eliminating invading organisms¹⁻³
- Extensive blood vasculature and lymphatic network
- Rich in immune cells, including dermal dendritic cells¹⁻⁵

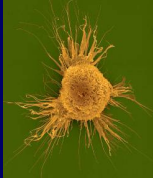
References with citations to historical developments: 1. Weniger BG, Papania MJ. Alternative vaccine delivery methods. In: Plotkin SA, et al, eds. Vaccines. Fifth Edition. Philadelphia, PA: Saunders Elsevier, 2008:1357-1392. 2. Lambert PH, Laurent PE. Vaccine. 2008;25(9):3197-3205. 3. Nicolas JF, Guy B. Exp Rev Vaccines. 2008;7(8):1201-1214. 4. Clark RA, et al. J Immunol. 2006;176(7):4431-4439. 5. Nestle FO, Nickloff BJ. J Clin Invest. 2007;117(9):2382-2385.

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The Key Role of Dermal Dendritic Cells

- Dendritic cells have distinct functional characteristics¹⁻⁴
 - Detect pathogens, capture antigens
 - Control the magnitude and quality of immune response^{3,4}
 - Possess unique ability to stimulate naïve T cells and activate B cells
 - Helps generate both cellular and humoral immune responses to viral infection
 - Contribute to the development of immune memory and long-lasting B cell response¹⁻⁴
 - Rapidly recruited into tissue after immunization^{3,4}



© Dennis Kuznetsov/Microscopy Inc./PhotoLibrary

References with citations to historical developments: 1. Weniger BG, Papania MJ. Alternative vaccine delivery methods. In: Plotkin SA, et al, eds. *Vaccines*. Fifth Edition. Philadelphia, PA: Saunders Elsevier, 2008:1357-1392. 2. Lambert PH, Laurent PE. *Vaccine*. 2008;26(26):3197-3208. 3. Stammen RM, Pope M. *J Clin Invest*. 2002;109(12):1519-1526. 4. Nicolas JF, Guy B. *Exp Rev Vaccines*. 2008;7(8):1201-1214.

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Why Intradermal Delivery?

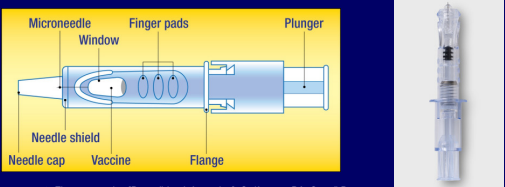
- Antigen injected through the epidermis into upper layers of the dermis^{1,2}
 - Access via the skin allows the use of a smaller needle
- Introducing vaccine antigens to a large number of antigen-presenting cells in the epidermis and dermis induces an immune response¹⁻³
- For some antigens, intradermal vaccination can be accomplished with a lower dose of antigen than the intramuscular (IM) route while inducing similar antibody responses¹⁻³
- Various clinical studies conducted since the 1930s have documented the "equivalence and occasionally improved immunogenicity"³ of intradermal influenza vaccination by needle-syringe compared to larger doses by the subcutaneous and IM routes³⁻⁹

References: 1. Lambert PH, Laurent PE. *Vaccine*. 2008;26(26):3197-3208. 2. Nicolas JF, Guy B. *Exp Rev Vaccines*. 2008;7(8):1201-1214. 3. Weniger BG, Papania MJ. Alternative vaccine delivery methods. In: Plotkin SA, et al, eds. *Vaccines*. Fifth Edition. Philadelphia, PA: Saunders Elsevier, 2008:1357-1392. 4. Francis TF, Jr, McGill TP. *J Exper Med*. 1937;69(2):251-259. 5. Bruyn HB, et al. *J Immunol*. 1949;62(1):1-11. 6. Hilleman MR, et al. *JAMA*. 1958;168(10):1134-1140. 7. Saslaw S, Carlisle HN. *Am J Med Sci*. 1964;248(Sep):273-284. 8. Brown H, et al. *J Infect Dis*. 1977;136(suppl 3):S466-S471. 9. Halperin W, et al. *Am J Public Health*. 1979;69(12):1247-1251.

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A New Microinjection Device^{1,2}

- Single-use glass syringe prefilled with 0.1mL dose
- 30-gauge, short-bevel needle permanently affixed to the end of the syringe
- Depth of insertion limited to 1.5mm from the skin's surface




References: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011. 2. Laurent PE, et al. *Vaccine*. 2007;25(52):8633-8642.

Becton Dickinson Soluvia™ Microinjection System

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Advantages of the New Becton Dickinson Microinjection System¹

1. 90% smaller needle
 - Short needle (1.5mm) reduces possibility of damage to nerves and blood vessels
 - Volume injected is 0.1mL
2. Consistent depth of injection
 - Ensures reliable delivery of an accurate dose of antigen into the dermal layer
 - No need to vary needle length or injection technique by patient age, gender, muscle mass, or body mass index




Courtesy and © Becton, Dickinson and Company.

Reference: 1. Laurent PE, et al. *Vaccine*. 2007;25(52):8833-8842.

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Advantages of the New Becton Dickinson Microinjection System¹ (cont'd)

3. Ease of administration
 - No air bubble purging of syringe is required
 - Minimal training needed
 - Affixed microneedle eliminates need to prepare injections
4. Patient acceptance
 - Needle is shorter, thinner, not readily visible
 - May enhance compliance in needle-averse individuals²
5. Needle shield feature, activated post-vaccination
 - Helps reduce risk of contamination, injury, and infection in health-care personnel
 - Also helps prevent re-use of needles



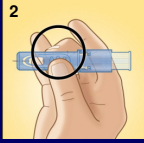
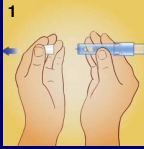
Courtesy and © Becton, Dickinson and Company.

Reference: 1. Laurent PE, et al. *Vaccine*. 2007;25(52):8833-8842. 2. Nir Y, et al. *Am J Trop Med Hyg*. 2003;68(3):341-344.

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Intradermal Injection Technique¹

1. Remove the needle cap from the microinjection system
2. Hold microinjection system between thumb and middle finger
 - Place only the thumb and middle finger on the finger pads
 - Index finger remains free
 - Do not place fingers on the windows



Reference: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011.



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Intradermal Injection Technique¹ (cont'd)

3. Insert the needle rapidly and perpendicular to the skin, in the deltoid region, in a short, quick movement

4. Inject using the index finger

- Once the needle has been inserted, maintain light pressure on the skin surface
- Do not aspirate
- Inject using the index finger to push on the plunger




Reference: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011.

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Intradermal Injection Technique¹ (cont'd)

5. Remove needle from skin and activate needle shield by pushing firmly on plunger

- Remove the needle from the skin; direct it away from you and others
- With the same hand, push very firmly with the thumb on the plunger to activate the needle shield
- You will hear a click when the shield extends to cover the needle



Reference: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011.

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Fluzone Intradermal Vaccine: Indication, Dosing, and Administration¹

- Fluzone Intradermal vaccine is an inactivated influenza virus vaccine indicated for active immunization of persons 18-64 years of age against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine
- Persons 18-64 years of age should receive a single annual 0.1mL intradermal dose
 - Recommended site is over the deltoid

Reference: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011.

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Important Safety Information for Fluzone Intradermal Vaccine

Indication

Fluzone Intradermal vaccine is an inactivated influenza virus vaccine indicated for active immunization of persons 18 through 64 years of age against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.

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Important Safety Information for Fluzone Intradermal Vaccine

Safety Information

The most common local and systemic adverse reactions to Fluzone Intradermal vaccine include erythema, induration, swelling, pain, and pruritus at the vaccination site; headache, myalgia, and malaise. Other adverse reactions may occur. Fluzone Intradermal vaccine should not be administered to anyone with a severe allergic reaction (eg, anaphylaxis) to any vaccine component, including egg protein, or to a previous dose of any influenza vaccine. The decision to give Fluzone Intradermal vaccine should be based on the potential benefits and risks, especially if Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine. Vaccination with Fluzone Intradermal vaccine may not protect all individuals.

Before administering Fluzone Intradermal vaccine, please see full Prescribing Information.

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Summary of Clinical Trial Findings for Fluzone Intradermal Vaccine

- Injection-site reactions were more frequent due to administration of influenza antigens into the dermal space
 - Generally mild-to-moderate in intensity and resolved in 3-7 days
- Systemic safety profile, including unsolicited AEs and SAEs, was comparable to that of IM vaccine
- Fluzone Intradermal vaccine induces a robust immune response in adults 18-64 years of age

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Fluzone Intradermal Vaccine: Practical Advantages

- Microinjection system facilitates vaccine administration
 - Shorter needle with a needle shielding system
 - Ensures consistent administration whatever the patient's physical characteristics
 - Ensures accurate and reliable delivery of antigen into the dermis
- Should be well accepted by providers and patients
 - Needle length is 90% shorter
 - Technique intuitive, easy to learn
- Fluzone Intradermal vaccine is an attractive new option in influenza prevention and should help increase immunization coverage rates among adults 18-64 years of age

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Frequency of Injection-site Reactions by Intensity, 0-7 Days Post-vaccination^{1,2}

		Fluzone High-Dose Vaccine (%)	Fluzone Vaccine (%)
Pain	Any	35.6	24.3
	Moderate	3.7	1.7
	Severe	0.3	0.2
Erythema	Any	14.9	10.8
	Moderate	1.9	0.8
	Severe	1.8	0.6
Swelling	Any	8.9	5.8
	Moderate	1.6	1.3
	Severe	1.5	0.6

Local injection-site reactions occurred more frequently in recipients of Fluzone High-Dose vaccine than in recipients of Fluzone vaccine.

References: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011. 2. Falsey A, et al. *J Infect Dis.* 2009;200(2):172-180.

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Frequency of Systemic Reactions by Intensity, 0-7 Days Post-vaccination^{1,2}

		Fluzone High-Dose Vaccine (%)	Fluzone Vaccine (%)
Myalgia	Any	21.4	18.3
	Moderate	4.2	3.2
	Severe	1.6	0.2
Headache	Any	16.8	14.4
	Moderate	3.1	2.5
	Severe	1.1	0.3
Malaise	Any	18.0	14.0
	Moderate	4.7	3.7
	Severe	1.6	0.6
Fever	Any	3.6	2.3
	Moderate	1.1	0.2
	Severe	0.0	0.1

Systemic complaints occurred more frequently in recipients of Fluzone High-Dose vaccine than in recipients of Fluzone vaccine.

References: 1. Fluzone vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2011. 2. Falsey A, et al. *J Infect Dis.* 2009;200(2):172-180.

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**Questions about
Fluzone Intradermal?**

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Pertussis

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**Common Clinical Manifestations of
Adult and Adolescent Pertussis¹**

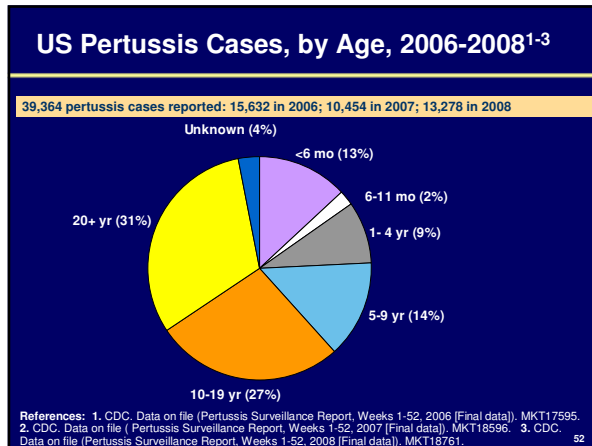
- Cough ≥ 3 weeks in 97%,
 ≥ 9 weeks in 52%
- Paroxysms ≥ 3 weeks in 73%
- Whoop in 69%
- Post-tussive emesis in 65%
- Adults missed an average of 7 days of
work; teens missed an average of 5 days of
school
- Average 14 days of disrupted sleep

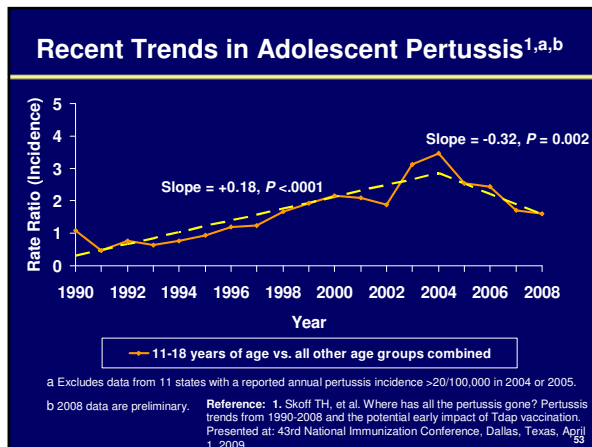


Video courtesy of the Centers for
Disease Control and Prevention
(CDC).

Reference: 1. De Serres G, et al. *J Infect Dis.* 2000;182(1):174-179.

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Explaining the Recent Decrease in Adolescent Pertussis¹

- Decline in disease incidence among adolescents (compared to other age groups) may indicate early impact of Tdap vaccination in this age group
 - However, decline began in 2004; Tdap licensed in US in 2005
- Other potential factors may be contributing to a decrease in reported cases
 - Population immunity from circulating disease (natural boosting)
 - Fluctuations in testing and reporting patterns
 - Cyclical patterns of pertussis disease

Reference: 1. Skoff TH, et al. Where has all the pertussis gone? Pertussis trends from 1990-2008 and the potential early impact of Tdap vaccination. Presented at: 43rd National Immunization Conference, Dallas, Texas, April 1, 2009.

Tdap ACIP Recommendations¹

- Adolescents (who have completed primary childhood immunization series) 11-18 years preferably at 11-12 preventative health care visit should receive a single dose Tdap.
- Adults aged 19-64 years single dose of Tdap.
- Tdap may be given at interval since the last tetanus or diphtheria toxoid containing vaccine.
- Children 7-10 years of age:
 - Single dose for those not fully vaccinated against pertussis.
 - Those never vaccinated or unknown immune status 3 doses of tetanus and diphtheria containing vaccines with the first dose Tdap.
- Adults 65 years and older:
 - Those in contact with infant less than 12 months of age, one dose Tdap.
 - Other adults aged 65 years and older, one dose Tdap.

References: 1. MMWR, January 14, 2011, Vol. 60, pages 13-15. 58

Tdap use in Pregnancy: ACIP Provisional Recommendations¹

- Vaccinate with Tdap at late second (after 20 weeks gestation) and third trimesters
- Pregnant women with unknown or incomplete immune status. Tdap 0, Td 4 weeks, 6-12 months

References: 1. accessed 8/15/2011 www.cdc.gov/vaccines/recs/provisional/default.htm 59

Websites Supporting Vaccination

Sounds of Pertussis:
<http://www.soundsofpertussis.com/#/whatispertussis>

Faces of Influenza:
<http://facesofinfluenza.org>

Voices of Meningitis:
<http://www.voicesofmeningitis.org>

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