What Every Practitioner Should Know About the Current Vaccination Campaign

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Objectives

- At the conclusion of this presentation, the attendee will be able to
  - Identify current vaccine schedule recommendations and know where to find them
  - List current vaccine constituents
  - Describe the role of common constituents
  - Recognize the difference between historical and current vaccines and vaccination schedules

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What This Presentation IS and IS NOT

- IS
  - Report of current common vaccination recommendations
  - Static
- IS NOT
  - Replacement for individualized medical advice
  - Comprehensive of all vaccines and recommendations
  - A guide for vaccine storage and administration

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Conflict of Interest Statement

- The speakers have no conflict of interest to disclose

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Hollie Resseguie

- Kansas State University 2004, Bachelors of Music Education
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Vaccines

Taboo:

Religion, Politics

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Vocabulary

- Adjuvant—A substance, distinct from antigen, that enhances T cell activation by promoting the accumulation of antigen-presenting cells at a site of antigen exposure and by enhancing the expression of costimulators and cytokines by the antigen-presenting cells[1]
- Antibody--A type of glycoprotein molecule, also called immunoglobulin (Ig), produced by B lymphocytes, that bind antigens, often with a high degree of specificity and high affinity[1]
- Antigen--A molecule the binds to an antibody or a T cell antigen receptor (TCR). Antigens that bind to antibodies include all classes of molecules. Most TCRs bind only to peptide fragments of proteins complexed with major histocompatibility molecules; both the peptide ligand and the native protein from which it is derived are called T cell antigens [1]
- Excipient = constituent = component

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Vocabulary

- Immunity—resistance to disease, specifically infectious disease [1]
- Vaccine—A preparation of microbial antigen, often combined with adjuvants, that is administered to individuals to induce protective immunity against microbial infections. The antigen may be in the form of live but avirulent microorganisms, killed microorganisms, or purified macromolecular components of microorganisms[1]
- Vaccination vs. Immunization
  - "You can be vaccinated but if there is no immunity, you are not immunized. You can be unvaccinated, but if you have had the disease and have protection, you are immune; therefore you are immunized."[2]

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Antigen Types

- Live attenuated vaccine
- Inactivated vaccine
  - Whole cell
  - Fractional
    - Polysaccharide
    - Subunit
    - Toxoid
    - Conjugated polysaccharide

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Who Makes Vaccine Recommendations?

- Advisory Committee on Immunization Practices (ACIP)
  - United States Federal Government agency that advises Centers for Disease Control and Prevention (CDC)
- CDC ultimately makes recommendations published in Morbidity and Mortality Weekly Report (MMWR)
- CDC publishes Epidemiology and Prevention of Vaccine-Preventable Diseases "Pink Book"
  - All official vaccine information and recommendations

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CDC-Recommended Provider Behavior

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Immunization Strategies for Healthcare Practices and Providers[3]

- CDC recommendations for healthcare provider behavior regarding vaccines
- Levels of disease are "late indicators" of soundness of immunization SYSTEM
  - "Greater understanding of strategies to increase and sustain immunization levels is necessary in order to create lasting, effective immunization delivery system."
- AFIX—recommended by government and non-government vaccine programs and medical professional societies

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AFIX[3]

- Assessment of immunization coverage of public and private providers
  - CDC-developed software that electronically assesses medical records
- Feedback of diagnostic information to improve service delivery
- Incentives to motivate providers to change immunization practices or recognition of improved or high performances
- exchange of information among providers
- "Does NOT attempt to persuade clients to be vaccinated, but instead focuses on changing healthcare provider behavior"

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Federal Programs Regarding Vaccine Rates

- Vaccines for Children (VFC)—federal funding to purchase vaccines to make them available at no cost to those who meet income and eligibility requirements
  - www.cdc.gov/vaccines/programs/vfc/default.htm
- Immunization Information System (IIS)
  - Optional database to keep individual vaccine records
  - cdc.gov/vaccines/programs/iis/index.html

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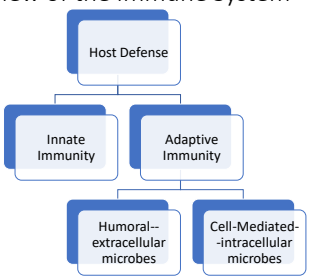
Brief Review of the Immune System



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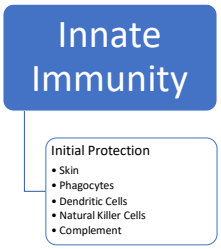
Brief Review of the Immune System



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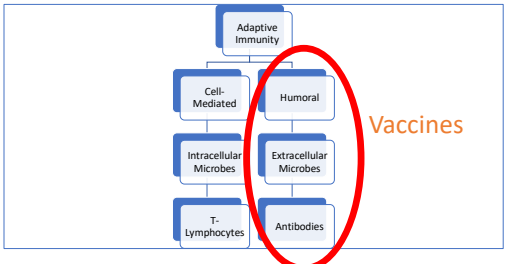
Brief Review of the Immune System



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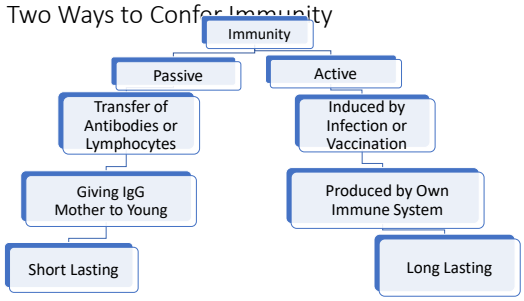
Two Ways to Confer Immunity



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Vaccines: Miracle or Scary? And Why?

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Vaccines—Miracle?

- CDC lists vaccines as great public health achievement of 20th century
- Curing an illness helps that person, preventing it helps everyone
- Herd immunity protects those unable to be vaccinated
  - Vaccine mandates scare some, vaccine choice scares some
  - "Recent outbreaks show that even vaccinated people are at risk for disease if there is not adequate vaccine coverage for a population" [3]

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Vaccines—Miracle?[3]

- Vaccine Injury Compensation Program
  - Vaccine Adverse Event Reporting System (VAERS)
  - Anyone can report
  - Available at vaers.hhs.gov or wonder.cdc.gov/vaers
  - Number of reports ~28,000/year
  - Number of vaccines given ~10 million/year[3]
- Vaccine Safety Datalink
  - 10 large managed care organizations gather data on those vaccinated at their sites allowing for planned safety studies and timely investigations
  - http://cdc.gov/vaccinationsafety.vsd

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Vaccines—Miracle?[3]

- Clinical Immunization Safety Assessment Network
  - Resource for practitioners to manage individual patients with vaccine related side effects
  - http://cdc.gov/vaccinesafety/Activities/cisa.html
  - Vaccine Analytic Unit
  - Monitors safety of vaccines given to military
  - CDC and DoD
  - Study vaccines infrequently used in general population
    - Currently studying specific vaccine potential adverse effects regarding autoimmune thyroid disease and Guillain-Barré syndrome (GBS)

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Vaccines—Miracle?[3]

- National Childhood Vaccine Injury Act and National Vaccine Injury Compensation Program
  - Diphtheria/Tetanus/Pertussis claims paid despite no scientific evidence of causation
    - Manufacturers disincentivized from making vaccines
    - Vaccine cost went up
    - Availability went down
    - Health care officials got worried
  - No fault program
    - Don't have to prove negligence
  - Compensates for certain events following a vaccine
  - Covers all childhood vaccines and those vaccines if administered to an adult and a certain list of events following them

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Vaccines—Miracle?

- Vaccine Injury Table
  - www.hrsa.gov/vaccinecompensation/vaccineinjurytable.pdf

Vaccine	Illness, disability, injury or condition covered	Time period for first symptom or manifestation of onset or of significant aggravation after vaccine administration
I. Vaccines containing tetanus toxoid (e.g., DTaP, DTP, DT, Td, or TT)	1.Anaphylaxis 2.Brachial Neuritis 3.Shoulder Injury Related to Vaccine Administration 4.Vasovagal syncope	<4 hours 2-28 days (not less than 2 days and not more than 28 days) <48 hours<1 hour
II. Vaccines containing whole cell pertussis bacteria, extracted or partial cell pertussis bacteria, or specific pertussis antigen(s) (e.g., DTP, DTaP, P, DTP- Hib)	1.Anaphylaxis 2.Encephalopathy or encephalitis 3.Shoulder Injury Related to Vaccine Administration 4.Vasovagal syncope	<4 hours<72 hours<48 hours <1 hour

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Vaccines—Miracle?

- Countermeasures Injury Compensation Program
  - Like above but for vaccines/treatments administered in preventative situations—flu pandemic, anthrax, etc
  - Includes those given to military personnel
- Vaccine Information Statements given prior to any vaccine
  - cdc.gov/vaccines/pubs/vis or immunize.org
- Confirmation bias

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Vaccines--Scary?

- Confirmation bias
- As preventable diseases have become less common, fear of vaccine as become more common
  - 28,000 reports of vaccine adverse reactions/effects each year
    - More people know someone believed to have an adverse effect than on of the preventable diseases [3]
- Giving a healthy patient a drug—higher standard of safety expected to maintain public confidence
  - Given to infants—very low tolerance for any adverse events
  - Widespread vaccine use means and adverse event could affect many people

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Vaccines--Scary?

- "Hi-jacking" immune system by bypassing cell-mediated immunity and provoking immunity
  - Linked by some to increasing autoimmunity[4]
- Distrust of the medical community
  - Changing recommendations (fat, cholesterol)
  - Vaccines and drugs withdrawn from market
- Seemingly contradictory vaccine recommendations
  - Hepatitis B, polio

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Vaccines--Scary?

- Vaccine or living conditions?
- Vaccine invented vs. in use
- Changing definition of diseases

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Vaccines--Scary?

- Vaccines for diseases that "aren't severe" or "aren't likely"
  - Chicken pox, shingles, hepatitis B
- Vaccines causing further illness
  - Varicella→shingles[5]
  - Pneumococcal strain replacement[3, 5]

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Vaccines--Scary?

- What's in it?
- "It's SO many these days"

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https://blog.supplysideliberal.com/

VACCINES PROVOKE WHICH PART OF THE IMMUNE SYSTEM?

Humoral

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Vaccine Schedule History

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Vaccine Schedule History[6]

- By mid-1980's 7 vaccines were available
  - Children received 5 shots by age 2 and not more than 1 at a single visit
- Now as many as 27 shots by age 2 and 5 per visit

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1989

- DTP
- MMR
- Polio
- Hib
- 8 vaccines in 4 shots

2019

Childhood
- DTaP
- MMR
- Polio
- Hib
- Hep B
- Varicella
- Hep A
- Pneumococcal
- Influenza
- Rotavirus

14 vaccines in 10 shots plus boosters

Adolescent
- Tdap
- HPV
- Meningococcal conjugate
- Influenza
- Meningococcal B

Adult
- Influenza
- Tdap
- Shingles
- Pneumococcal

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http://www.innomind.org

WHO PUBLISHES OFFICIAL VACCINE RECOMMENDATIONS AND INFORMATION?

The CDC

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Current Vaccine Schedules and Recommendations

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Anatomy of a Vaccine Schedule

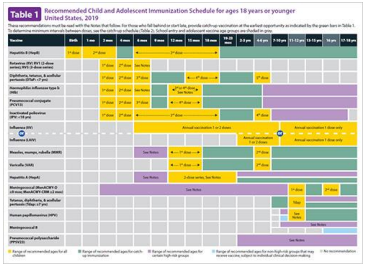

Table 1 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger
United States, 2019

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Table 2 Catch-up immunization schedule for persons aged 4 months–18 years who start late or who are more than 1 month behind, United States, 2019

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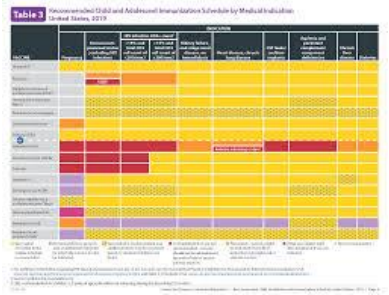

Table 3 Recommended Child and Adolescent Immunization Schedule by Medical Indication
United States, 2019

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Current Vaccine Schedule

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Diphtheria/Tetanus/Pertussis--Vaccine[3]

- *Diphtheria, tetanus, whole-cell pertussis (DTP)*
  - *No longer used in US*
- Primary vaccine pediatric: diphtheria, tetanus toxoids, acellular pertussis (DTaP)
- Primary vaccine pediatric: diphtheria, tetanus (DT)
- Booster: reduced diphtheria, tetanus (Td)
- Booster adult: reduced diphtheria, tetanus, acellular pertussis (Tdap)
- Also available combined with inactivated polio or inactivated polio and *Haemophilus influenzae* type B

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Diphtheria/Tetanus/Pertussis--Schedule[3]

- Childhood
  - DTaP
    - 5 dose series at 2,4,6, 15-18 months, 4-6 years
- Adolescent
  - Tdap
    - 1 dose at 11-18 years once full series of DTaP is completed
- Adult
  - Tdap—1 dose, then
  - Td—every 10 years
  - Pregnancy
    - 1 dose Tdap each pregnancy regardless of number of pregnancies, spacing, etc.

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Contraindications, Precautions, Adverse Events and Reactions

Contraindication (CI)	• Condition increasing likelihood of serious adverse reaction • Vaccines typically not given[3]
Precaution (Prec'n)	• Condition that might increase likelihood or severity of adverse reaction • Defer vaccine[3]
Adverse Event (AE)	• Untoward effect of vaccine or administration typically not causally related
Adverse Reaction (AR)	• Untoward effect of vaccine that are related to the vaccine

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Diphtheria/Tetanus/Pertussis--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis
Prec'n	• Moderate or severe acute illness • Neurological condition, high temp, collapse or shock-like state, persistent inconsolable crying, convulsions, GBS, Arthus reaction
AE	• Severe systemic reactions: urticaria, anaphylaxis, neurological complications, GBS
AR	• Injection site reaction, mild systemic reactions, severe systemic reactions, extensive limb swelling, hives, anaphylaxis, neurological complications

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Diphtheria/Tetanus/Pertussis--Other Notes

- "No study has assessed the safety of repeated doses of Tdap in pregnant women. CDC will monitor and assess the safety of Tdap use during pregnancy." [3]

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Diphtheria/Tetanus/Pertussis--Other Notes

- Evolution of pertussis virus
  - "Epidemiology of pertussis has changed in recent years, with an increasing burden of disease among fully-vaccinated children and adolescents, which is likely being driven by transition to acellular vaccines in the 1990's"[3]
  - Vaccine-resistant strains emerging[5, p. 87-99]
  - Greater number of whooping cough in vaccinated than unvaccinated children[5, p. 102]
  - Vaccinated individuals can still spread disease[5, p. 104]
    - Different strains
    - Declining immunity[5, p. 88]

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Diphtheria/Tetanus/Pertussis--Components[3]

- DT—aluminum phosphate, isotonic sodium chloride, formaldehyde
- DTaP (1)-aluminum phosphate, formaldehyde, glutaraldehyde, 2-phenoxyethanol
- DTaP (2)-formaldehyde, aluminum hydroxide, sodium chloride, polysorbate 80 (Tween 80)
- DTaP-IPV (1)-Formaldehyde, aluminum hydroxide, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B
- DTaP-IPV (2)-formaldehyde, aluminum phosphate, 2-phenoxyethanol, polysorbate 80, glutaraldehyde, neomycin, polymyxin B sulfate, bovine serum albumin
- DTaP-HepB-IPV-formaldehyde, aluminum hydroxide, aluminum phosphate, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B, yeast protein
- DTaP-IPV/Hib-aluminum phosphate, polysorbate 80, sucrose, formaldehyde, glutaraldehyde, bovine serum albumin, 2-phenoxyethanol, neomycin, polymyxin B sulfate

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Haemophilus Influenzae Type B--Vaccine[3]

- *Haemophilus influenzae* type B (Hib)
  - Several manufacturers
- Also available as combination
  - Diphtheria, tetanus, acellular pertussis, inactivated poliovirus, and Hib (DTaP-IPV/Hib)

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Haemophilus Influenzae Type B--Schedule[3]

- 2 or 3 dose series depending on product used
  - 2, 4, +/- 6 months
- Booster at 12-15 months

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Haemophilus Influenzae Type B--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • Age younger than 6 weeks of age
Prec'n	• Moderate or severe acute illness
AR	• Injection site reaction, systemic and serious reactions not common

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Haemophilus Influenzae Type B--Other Notes

- Vaccination against Hib has decreased cases of b strain, but increased cases caused by a strain (Hia) and non-typeable strains [5, p. 114-118]

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Haemophilus Influenzae Type--Components[3]

- DTaP-IPV/Hib-aluminum phosphate, polysorbate 80, sucrose, formaldehyde, glutaraldehyde, bovine serum albumin, 2-phenoxyethanol, neomycin, polymyxin B sulfate
- Hib (1)-sodium chloride, formaldehyde, sucrose
- Hib (2) -formaldehyde, sodium chloride, lactose
- Hib (3)-amorphous aluminum hydroxyphosphate sulfate, sodium chloride

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Hepatitis A--Vaccine[3]

- Hepatitis A (Hep A)
  - Several manufacturers
- Also available as combination with hepatitis A and hepatitis B

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Hepatitis A--Schedule[3]

- 2 doses at ages 1-18 years
  - 1 year and 6-12 or 6-18 months later depending on manufacturer

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Hepatitis A--CI, Precautions, AE, AR

CI	• History of severe allergic reaction/ anaphylaxis • Allergy to aluminum or 2-phenoxyethanol[3]
Prec'n	• Moderate or severe acute illness[3]
AE	• Immune thrombocytopenia purpura (ITP)[5, p. 208]
AR	• Injection site reaction • No serious adverse reactions have been reported[3]

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Hepatitis A--Components[3]

- Hep A (1)-MRC-5 cellular proteins, formalin, aluminum hydroxide, amino acid supplement, phosphate- buffered saline solution, polysorbate 20, neomycin sulfate, aminoglycoside antibiotic
- Hep A (2)-amorphous aluminum hydroxyphosphate sulfate, non-viral protein, DNA, bovine albumin, formaldehyde, neomycin, sodium borate, sodium chloride, other process chemical residuals
- Hep A/Hep B-MRC-5 human diploid cells, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein, water

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Hepatitis B--Vaccine[3]

- Hepatitis B (Hep B)
  - Several manufacturers
- Available as combination hepatitis A and hepatitis B

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Hepatitis B--Schedule [3]

- 3 doses at day 0 (birth), 1-2 months, 6-18 months
- Recommended for all under 18 years
- For unvaccinated adults only if at risk
  - Sexual exposure
  - Percutaneous or mucosal exposure to blood
  - Travel to areas with intermediate or high hepatitis B infection

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Hepatitis B--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • Hypersensitivity to yeast or other vaccine component
Prec'n	• Moderate or severe acute illness • Neurological condition, high temp, collapse or shock-like state, persistent inconsolable crying, convulsions, GBS, Arthus reaction
AE	• Alopecia (rare), GBS, chronic fatigue syndrome, neurologic disorders, rheumatoid arthritis, type 1 diabetes, autoimmune disease
AR	• Anaphylaxis

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Hepatitis B--Other Notes

- No reliable data for blood brain barrier development in neonates and infants less than 4 months of age[7a, 7b]

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Hepatitis B--Components[3]

- Hep B (1)-aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
- Hep B (2)-formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, yeast protein
- Hep B (3)-yeast protein, yeast DNA, deoxycholate, phosphorothioate linked oligodeoxynucleotide, sodium phosphate, dibasic dodecahydrate, sodium chloride, monobasic dehydrate, polysorbate 80
- Hep A/Hep B-MRC-5 human diploid cells, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein, water

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Human Papillomavirus--Vaccine[3]

- Bivalent human papillomavirus (HPV2)
- Quadrivalent human papillomavirus (HPV4)
- 9-valent human papillomavirus (9vHPV)

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Human Papillomavirus--Schedule[3]

- Female
  - HPV2, HPV4, 9vHPV 13-26 years
  - If begun at age 9-14 years: 2 dose series at 6-12 months apart
  - If begun age 15 or older: 3 dose series 0, 1-2 months, 6 months
- Male
  - HPV4 or 9vHPV 13-21 years
  - If begun at age 9-14 years: 2 dose series at 6-12 months apart
  - If begun age 15 or older: 3 dose series 0, 1-2 months, 6 months

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Human Papillomavirus--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • HPV2: allergy to latex[3]
Prec'n	• Moderate or severe acute illness • Not recommended during pregnancy[3]
AE	• Lupus, alopecia, gastroenteritis, vasculitis, GBS, thrombocytopenia[5]
AR	• Injection site reaction, fever, syncope for adolescents, nausea, dizziness, myalgia, malaise[3]

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Human Papillomavirus--Other Notes[3]

- Females: bi- or quadrivalent; males: quadrivalent only
- CAN vaccinate if already infected
- 30% of cervical cancers caused by HPV types not included in vaccines
- Most cases and deaths from cervical cancer can be prevented through routine Pap test
- High incidence of Infection, most resolve spontaneously

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Human Papillomavirus--Components[3]

- amorphous aluminum hydroxyphosphate sulfate, sodium chloride, L-histidine, polysorbate 80, sodium borate, yeast protein

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Influenza--Vaccine[3]

- Live attenuated influenza vaccine (LAIV)
  - Several manufacturers
- Inactivated influenza vaccine (IIV)
  - Trivalent or quadrivalent
  - Several manufacturers

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Influenza--Schedule[3]

- Annual vaccination for all 6 months of age and older
- 2 doses 28 days apart for 1st round for children 6 months-8 years
  - 1 dose annually thereafter
- Live vaccine (LAIV)
  - 2-49 years
  - Not recommended for pregnant women
- Inactivated vaccine (IIV)
  - All persons 6 months of age and older

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Influenza IIV--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis
Prec'n	• Moderate or severe acute illness • GBS within 6 weeks following influenza vaccine
AR	• Injection site reaction • Hypersensitivity reaction

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Influenza LIAV--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • Age younger than 2 or older than 50 • Several chronic medical conditions • Severe egg allergy • Children/adolescents on aspirin therapy • Immunosuppression • Pregnancy
Prec'n	• Moderate or severe acute illness • GBS within 6 weeks following a previous dose of influenza vaccine
AE	• Runny nose, headache, malaise
AR	• Wheezing in children 6-23 months • Cough, runny nose, nasal congestion, sore throat, chills

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Influenza--Other Notes[3]

- Inactivated vaccine approximately 60% effective in protecting people less than 65 years old, less effective in those 65 and older
  - Though not highly effective in preventing illness, is 50-60% effective in preventing hospitalization and 80% effective at preventing death from influenza[3]
- Live vaccine about 87% effective in children 60-84 months
  - Only data reported by CDC

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Influenza--Other Notes

- Studies point to problems with yearly flu vaccine
  - Natural infection with influenza A provides protection against more lethal influenza A viruses of other unrelated subtypes[5, p.65]
  - Meta analysis of epidemiologic studies as well as studies of active duty military following H1N1 pandemic showed that recipients of the 2008-2009 influenza trivalent vaccine significantly increased the risk of requiring medical attention for H1N1 pandemic virus[5, p. 66]
  - Adults vaccinated 2 years in a row were as likely to get the flu as those not vaccinated either year[5, p. 69]
  - Vaccination 2 years in a row was a risk factor for getting the flu[5, p. 69]

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Influenza--Components[3]

- Influenza (1) Trivalent & Quadrivalent--sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, potassium chloride, calcium chloride, sodium taurodeoxycholate, ovalbumin, sucrose, neomycin sulfate, polymyxin B, beta-propiolactone, thimerosal (multi- dose vials)
- Influenza (2)--squalene, polysorbate 80, sorbitan trioleate, sodium citrate dehydrate, citric acid monohydrate, neomycin, kanamycin, barium, hydrocortisone, egg proteins, cetyltrimethylammonium bromide (CTAB), formaldehyde
- Influenza (3) Quadrivalent--octoxynol-10 (TRITON X-100), α-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), hydrocortisone, gentamicin sulfate, ovalbumin, formaldehyde, sodium deoxycholate, sodium phosphate-buffered isotonic sodium chloride
- Influenza (4) Quadrivalent--sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, polysorbate 20 (Tween 20), baculovirus and Spodoptera frugiperda cell proteins, baculovirus and cellular DNA, Triton X-100

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Influenza--Components[3]

- Influenza (5) Quadrivalent--Madin Darby Canine Kidney (MDCK) cell protein, phosphate buffered saline, protein other than HA, MDCK cell DNA, polysorbate 80, cetyltrimethlyammonium bromide, and β- propiolactone, Thimerosal (multi-dose vials)
- Influenza (6) Quadrivalent--ovalbumin, formaldehyde, sodium deoxycholate, α-tocopheryl hydrogen succinate, polysorbate 80, thimerosal (multi-dose vials), phosphate-buffered saline solution
- Influenza (7) Quadrivalent--formaldehyde, egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate- buffered isotonic sodium chloride solution, thimerosal (multi-dose vials)
- Influenza (8) High Dose--egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde
- Influenza (9) Quadrivalent--monosodium glutamate, hydrolyzed porcine gelatin, arginine, sucrose, dibasic potassium phosphate, monobasic potassium phosphate, ovalbumin, gentamicin sulfate, ethylenediaminetetraacetic acid (EDTA)

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Measles/Mumps/Rubella--Vaccine[3]

- *Inactivated measles withdrawn in 1967*
- *Live attenuated measles withdrawn in 1975*
- *Further attenuated measles strain introduced in 1965 no longer used in US*
- Measles, mumps, rubella (MMR)
- Also available as measles, mumps, rubella with varicella (MMRV)

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Measles/Mumps/Rubella--Schedule[3]

- 2 dose at 1st birthday (12-47 months) and 2nd dose at 4-6 years

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Measles/Mumps/Rubella--CI, Precautions, AE, AR

CI	• History of severe allergic reaction/ anaphylaxis including neomycin • Pregnancy (avoid for 4 weeks following) • Immunosuppression • Age >13 years[3]
Prec'n	• Moderate or severe acute illness • Receipt of blood products, history of thrombocytopenia, personal or family history of seizures (MMRV)[3]
AE	• Arthralgia (adult women), allergic reaction (rash, pruritus, purpura),[3] thrombocytopenia[5, p. 263-274]
AR	• Fever, febrile seizure, rash, orchitis, CNS dysfunction (deafness), aseptic meningitis, encephalitis[3]

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Measles/Mumps/Rubella--Other Notes[3]

- Sterility, diabetes, deafness following the mumps—MYTH
  - "Sterility from mumps orchitis, even bilateral orchitis occurred infrequently…oophoritis rates were 1% or lower…There is no relationship to impaired fertility"
  - Aseptic meningitis resolves without sequelae in 3-10 days
  - "Incidence of mumps encephalitis is reported to range from 1 in 6,000 mumps cases (0.02%) to 1 in 300 mumps cases (0.3%)"
  - "Pancreatitis is infrequent…hyperglycemia is transient and reversible"
  - "Permanent unilateral deafness caused by mumps occurred in 1 of 20,000 infected persons; bilateral, severe hearing loss was very rare"

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Measles/Mumps/Rubella--Other Notes[3]

- Does mumps vaccine confer immunity?
  - 2009 mumps outbreak
    - 90% had received 1 dose of MMR and 76% had received 2 doses
  - 2009-2010 mumps outbreak in Guam
    - Schools with most mumps cases had 99.3-100% coverage with 2 doses of MMR
  - 2 dose mumps vaccine is 66%-95% effective

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Measles/Mumps/Rubella--Components[3]

- MMR—vitamins, amino acids, fetal bovine serum, sucrose, glutamate, recombinant human albumin, neomycin, sorbitol, hydrolyzed gelatin, sodium phosphate, sodium chloride
- MMRV (Frozen: Recombinant Albumin)—MRC-5 cells including DNA and protein, sucrose, hydrolyzed gelatin, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, recombinant human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride; potassium phosphate dibasic, neomycin, bovine calf serum
- MMRV (Frozen: Human Serum Albumin)—MRC-5 cells including DNA and protein, sucrose, hydrolyzed gelatin, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride; potassium phosphate dibasic, neomycin, bovine calf serum
- MMRV (Refrigerator Stable)—MRC-5 cells including DNA and protein, sucrose, hydrolyzed gelatin, urea, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate, recombinant human albumin, sodium bicarbonate, potassium phosphate, potassium chloride, neomycin, bovine serum albumin

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Meningococcal--Vaccine[3]

- Meningococcal polysaccharide vaccine (MPSV4)
  - Quadrivalent (A, C, W, Y)
- Meningococcal conjugate vaccine
  - Quadrivalent (A, C, W, Y)
  - MenACWY-D
  - MenACWY-CRM
- Meningococcal B
- Also available as combination with *Haemophilus influenzae* type B (Hib-MenCY-TT)
  - Bivalent (C, Y)

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Meningococcal--Schedule[3]

- Meningococcal conjugate vaccine (MenACWY-D or MenACWY-CMR)
  - Age 11-12 years 1 dose
    - booster at 16 years
  - 1 dose only if over 16 years old
  - See Pink Book for special childhood populations
- No official recommendation for meningococcal B currently

83

Meningococcal Conjugate--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis including diphtheria toxoid
Prec'n	• Moderate or severe acute illness • GBS—removed by ACIP, remains in package insert
AE	• Fever, headache, dizziness, syncope • 6.6% coded serious, 0.3-0.4% deaths reported • Injection site redness
AR	• Injection site reaction

84

Meningococcal--Components

- Meningococcal (MenACWY 1)—sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde, diphtheria toxoid
- Meningococcal (MenACWY 2)—formaldehyde, CRM197 protein
- Meningococcal (MenB 1)—aluminum hydroxide, sodium chloride, histidine, sucrose, kanamycin
- Meningococcal (MenB 2)—polysorbate 80, aluminum phosphate, histidine buffered saline[3]
- Haemophilus b meningococcal—aluminum hydroxyphosphate sulfate, sodium chloride[8]

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Pneumococcal--Vaccine[3]

- Pneumococcal polysaccharide vaccine
  - 14-valent pneumococcal polysaccharide vaccine licensed in 1977
  - Replaced by 23-valent pneumococcal polysaccharide (PPSV23) in 1983
- Pneumococcal conjugate vaccine
  - 7-valent pneumococcal pneumococcal conjugate vaccine (PCV7) licensed in 2000
  - Replaced by 13-valent pneumococcal conjugate vaccine (PCV13) in 2010

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Pneumococcal--Schedule[3]

- Childhood
  - 13-valent pneumococcal conjugate vaccine (PCV13)
    - 3 doses at 2, 4, 6 months of age
    - Booster at 12-15 months
- Adult
  - Age 65 and older
  - 1 dose PCV13 and 1 dose 23-valent pneumococcal polysaccharide (PPSV23)
- See Pink Book for additional recommendations for special and at-risk populations

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Pneumococcal--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis
Prec'n	• Moderate or severe acute illness • Safety in pregnancy not evaluated
AR	• Injection site reaction, fever, decreased appetite, irritability

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Pneumococcal--Other Notes[3]

- NOT "the pneumonia vaccine"
  - PCV13 approximately 45% effective in preventing pneumonia in adults, no data for children
  - PPSV23 60-70% effective in preventing invasive disease and "less effective in preventing pneumococcal pneumonia"
- PCV13-covered antigens responsible for
  - 61% of cases of invasive pneumococcal disease (IPD) in children
  - 20-25% IPD in adults 65 years and older
    - 10% community-acquired pneumonia
- PPSV23 contains antigen from 23 types of pneumococcal bacteria that cause 60-76% of invasive disease

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Pneumococcal--Other Notes

- Strain replacement
  - Decreases in IPD seen after introduction of PCV7 were offset by IPD caused by serotypes not included
  - 2 years before introduction of PCV13, PCV7 strains causing less than 2% of IPD[3]
  - Strains targeted by PCV13 were reduced in healthy children 6-23 months old, but non-vaccine strains increased for all children
  - 2 years after PCV13 introduction, 94% of all pneumococcal strains in healthy children were non-vaccine targeted types [5, p. 125]

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Pneumococcal--Components[3]

- Pneumococcal (PCV13)—CRM197 carrier protein, polysorbate 80, succinate buffer, aluminum phosphate
- Pneumococcal (PPSV-23)—phenol

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Poliomyelitis--Vaccine[3]

- Oral live polio vaccine (OPV)
  - Not available in US since 2000
  - 95% of incidents of paralytic polio since 1980 caused by live oral vaccine
  - Last case reported in 2009
- Inactivated poliovirus vaccine (IPV)
  - Only polio vaccine available in US

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Poliomyelitis--Schedule[3]

- Inactivated poliovirus vaccine (IPV)
  - 3 dose at 2, 4, 6 months old
  - Booster at 4-6 years
  - Not recommended for adults due to "very low risk of exposure to wild poliovirus"

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Poliomyelitis--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis
Prec'n	• Moderate or severe acute illness
AR	• Injection site reaction • Allergic reaction

94

Poliomyelitis--Other Notes

- Adverse reactions for combination vaccines are very different than monovalent vaccine
  - Not reported in Pink Book—not available in U.S.

95

Poliomyelitis--Components[3]

- Calf bovine serum albumin, 2-phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B, M-199 medium

96

Rotavirus--Vaccine[3]

- *1998 tetravalent rotavirus vaccine (RRV-TV)*
  - Recommended for routine immunization of U.S. infants
  - Withdrawn from the market within the year
    - Association with intussusception
- Rotavirus 5 (RV5)
- Rotavirus 1 (RV1)

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Rotavirus--Schedule[3]

- RV5
  - 3 oral doses at 2, 4, and 6 months
- RV1
  - 2 oral doses at 2 and 4 months
- Per CDC do not give to child older than 8 months
  - Per manufacturer maximum age RV5 32 weeks, RV1 24 weeks

98

Rotavirus--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • History of intussusception • Severe combined immunodeficiency • RV1: latex allergy
Prec'n	• Moderate or severe acute illness • Moderate or severe acute gastroenteritis
AE	• Intussusception still being studied
AR	• Diarrhea, vomiting, otitis media, nasopharyngitis, bronchospasm, cough, runny nose, irritability

99

Rotavirus--Components[3]

- Rotavirus (RV5)-sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, fetal bovine serum [DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.]
- Rotavirus (RV1)-Dextran, Dulbecco's Modified Eagle Medium (sodium chloride, potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids, L-glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red), sorbitol, sucrose, calcium carbonate, sterile water, xanthan [Porcine circovirus type 1 (PCV-1) is present in Rotarix. PCV-1 is not known to cause disease in humans.]

100

Varicella--Vaccine[3]

- Varicella vaccine
  - Also available as measles/mumps/rubella/varicella vaccine
- Herpes zoster vaccine

101

Varicella--Schedule[3]

- Varicella
  - 2 doses at 12-15 months then 4-6 years
  - Plus any adolescent or adult without evidence of varicella immunity
- Herpes zoster
  - Single dose at age 60 or older

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Varicella--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • Immunosuppression • Pregnancy/attempting to become pregnant
Prec'n	• Moderate or severe acute illness • Receipt of blood products • Personal or family history of seizures • Avoid use of salicylates for 6 weeks after vaccination
AR	• Injection site reaction • Varicella-like rash • Zoster caused by vaccine • MMRV: febrile seizure

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Herpes Zoster--CI, Precautions, AE, AR[3]

CI	• History of severe allergic reaction/ anaphylaxis • Immunosuppression • Pregnancy/attempting to become pregnant
Prec'n	• Moderate or severe acute illness • Receipt of recombinant human immune mediators and modulators • Current treatment with antiviral drugs active against herpesviruses
AR	• Injection site reaction

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Varicella--Other Notes

- Vaccinating against chickenpox increases risk of shingles in teenagers and adults[3, 5, p. 153-160]
- Some studies showing vaccinated children still contract chicken pox
  - Did not have milder symptoms than unvaccinated children[5, p. 161]

105

Varicella--Components[3]

- Varicella Frozen—MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, sodium phosphate monobasic, potassium phosphate monobasic, potassium chloride, EDTA, neomycin, fetal bovine serum
- Varicella Refrigerator Stable—MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed gelatin, sodium chloride, monosodium L-glutamate, urea, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, neomycin, bovine calf serum
- Zoster Frozen—MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed porcine gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride; neomycin, bovine calf serum
- Zoster Refrigerator Stable—MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed porcine gelatin, urea, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, neomycin, bovine calf serum

106

WHAT WAS THE MOST COMMON

CI?

PRECAUTION?

ADVERSE REACTION?

107

More Vaccine Schedules

- See CDC Pink Book or website for more information
  - Special populations
  - Catch up schedules
  - Vaccines for travel
  - Vaccines for military

108

Vaccine Components

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What's In It?

- CDC
  - Pink Book or website
- Package inserts
  - https://dailymed.nlm.nih.gov/dailymed/

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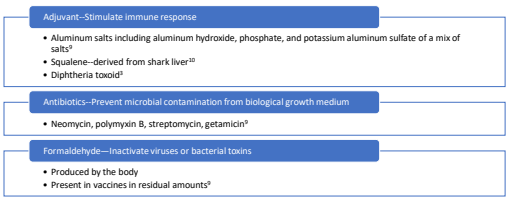
Vaccine Components—General Categories



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Vaccine Components—General Categories[9]

Stabilizers

- Sugars--sucrose, lactose
- Amino acids--glycine, monosodium glutamate, trace amounts of human and bovine serum proteins

Growth Medium--For viral antigen

- Human, monkey, dog, and bovine DNA, cell parts, serum, albumin; baker's yeast; chicken eggs
- Trace amounts still present and listed on package insert

Preservatives--Inhibit bacterial growth for multi-dose vials

- Thimerosal

112

Components Explained

- Aluminum
  - Adjuvant
  - No known biochemical reaction requires aluminum and deleterious effects have been studied[11]
  - What does the FDA say?
    - "the benefits of aluminum-containing vaccines administered during the first year of life outweigh any theoretical concerns about the potential effect of aluminum on infants. Of note, the most common source of exposure to aluminum is from eating food or drinking water"
    - Also, though, "When evaluating a vaccine for safety and efficacy, FDA considers adjuvants as a component of the vaccine; they are not licensed separately"[9]

113

Components Explained

- Aluminum cont'd
  - Injecting aluminum bypasses gastrointestinal tract
    - Changes pharmacodynamics
  - Many have continuous exposure in daily life
    - Vaccines may be small fraction
    - Antiperspirant, cookware/food storage, food sources (baking powder, food preservatives, food dye), pharmaceuticals[11]

114

Components Explained[3]

- Vaccines containing aluminum
  - All tetanus and diphtheria
  - 1 manufacturer's *Haemophilus influenzae* type B
  - Hepatitis A
  - Hepatitis B
  - 9-valent human papilloma virus
  - All meningococcal
  - Pneumococcal conjugate
  - Other less commonly used vaccines (anthrax, Japanese encephalitis)

115

Components Explained[3]

- Antibiotics
  - Inhibit growth of bacteria from biological growth medium
- Vaccines containing antibiotics
  - Neomycin
    - Most diphtheria/tetanus containing vaccines
    - Hepatitis A
    - Varicella
    - Zoster
    - Other less commonly used (rabies, yellow fever etc)

116

Components Explained[3]

- Antibiotics cont'd
  - Polymyxin
    - Most diphtheria/tetanus containing vaccines
    - Inactivated poliovirus vaccine
  - Streptomycin
    - Inactivated poliovirus vaccine
  - Gentamicin
    - 2 manufacturers' quadrivalent influenza vaccines

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Components Explained[3]

- Formaldehyde
  - Inactivate virus
  - Detoxify bacterial toxin
- Vaccines containing formaldehyde
  - All tetanus containing vaccines
  - 2 manufacturer's *Haemophilus influenzae* type B
  - 1 manufacturer's hepatitis B
  - Most influenza
  - Meningococcal conjugate
  - Other less commonly used (typhoid, anthrax)

118

Components Explained[3]

- Growth medium
  - Used to grow antigen-containing virus
  - Not completely removed during manufacturing
  - Listed as ingredient in package insert and on CDC
- Vaccines containing residual growth medium
  - Baker's yeast—hepatitis B
  - Chicken egg—live attenuated influenza

119

Components Explained[3]

- Growth medium cont'd
  - Madin Darby Canine Kidney (MDCK)—1 manufacturer's trivalent inactivated influenza
  - Chick embryo fibroblast—all measles and mumps containing vaccines
  - Monkey kidney tissue culture (Vero cell line)—1 manufacturer's inactivate poliovirus
  - Fetal bovine serum—rotavirus, varicella, 2 manufacturers' zoster

120

Components Explained[3]

- Growth medium cont'd
  - Calf serum albumin—inactivated poliovirus
  - Human albumin—measles, other less commonly used vaccines (small pox, rabies)

121

Components Explained

- Growth medium cont'd
  - Human diploid fibroblasts
    - MRC-5 Cell line from lung fibroblasts from fetus aborted in 1964[12, 13]
  - Vaccines containing MRC-5
    - Hepatitis A
    - All rubella containing vaccines
    - 1 manufacturer's inactivated poliovirus
    - Varicella
    - Zoster[3]

122

Components Explained

- Thimerosal
  - Ethyl mercury containing compound
    - 49.6% mercury by weight [15]
  - Preservative to inhibit bacterial growth for multi-dose vials
  - Public Health Service and American Academy of Pediatrics recommended it be discontinued in 1999
  - 2003 was last expiration date of thimerosal containing childhood vaccine[14]
  - Still used in multi-dose flu vaccines[3]

123

Components Explained

- Thimerosal Con't
  - "Compared to CDC's pre-2000 recommended vaccination schedule, the maximum lifetime exposure to thimerosal from vaccines has actually increased"[5, p. 41]

Thimerosal	Influenza	FluShield	Wyeth	0.025 mg
	Influenza	Fluzone	Aventis Pasteur	0.025 mg
	Diphtheria-tetanus	DT (pediatric)	Aventis Pasteur	0.025 mg
	Pneumococcal polysaccharide	Pneu-Immune 23	Wyeth	0.05 mg
	Meningococcal	Menomune	Aventis Pasteur	0.025 mg
	Japanese encephalitis virus	JE-Vax	Aventis Pasteur	0.007 mg

https://pediatrics.aappublications.org/content/112/6/1394.long

124

Components Explained

- Excipients common in products other than vaccines
  - Monosodium Glutamate
  - Sucrose, D-manose, D-fructose, dextrose, anhydrous lactose, lactose, hydrolyzed casein
  - sodium chloride, citric acid, sodium bicarbonate, sodium carbonate, phosphate buffered saline solution
  - Glutaraldehyde
  - amino acid supplement, asparagine, L-histadine
  - Potassium phosphate, potassium, magnesium stearate, magnesium sulfate, ascorbic acid, potassium chloride, calcium chloride
  - Microcrystalline cellulose, polysorbate 80 (Tween 80), polysorbate 20
  - Cellulose acetate phthalate
  - Alcohol, acetone, glycerin
  - Castor oil
  - FD&C Yellow #6 aluminum lake dye
  - Sodium phosphate, Monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, sodium citrate dehydrate
  - hydrocortisone
  - α-tocopheryl hydrogen succinate
  - Ethylenediaminetetraacetic acid (EDTA), phenol, benzethonium chloride
  - Sorbitan trioleate
  - Disodium phosphate dihydrate

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Components Explained

- All other excipients listed
  - Plasdone C
  - Polacrilin
  - Iron ammonium citrate
  - 2-phenoxyethanol
  - Sodium borate
  - Other process chemical residuals
  - Deoxycholate
  - Phosphorothioate linked oligodeoxynucleotide
  - Dibasic dodecahydrate
  - Monobasic dehydrate
  - Sodium taurodeoxycholate
  - Ovalbumin
  - Beta-propiolactone
  - Barium
  - Cetyltrimethylammonium bromide (CTAB)
  - Octoxynol-10 (TRITON X-100)
  - Sodium deoxycholate
  - Baculovirus and Spodoptera frugiperda cell proteins
  - Baculovirus and cellular DNA
  - Protein other than HA
  - β- propiolactone
  - CRM197 protein
  - M-199 medium
  - beta-propriolactone

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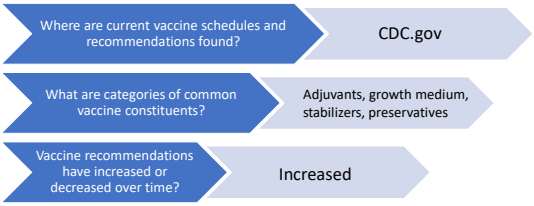
Show What You Know



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Helpful Resources for the Health Care Professional

- CDC.gov
  - Official resource of vaccine information and a wealth of information
- Epidemiology and Prevention of Vaccine-Preventable Diseases "Pink Book"
  - Official vaccine handbook found on CDC.gov
- http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm
  - Official FDA roster of vaccines approved in the US
- https://dailymed.nlm.nih.gov/dailymed/
  - Repository of package inserts

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What Every Practitioner Should Know About the Current Vaccination Campaign

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