# Vaccine Vacuum



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### Goals

- Three things:
  - Things you will never see
  - Things you may see
  - Things you will see
- Vaccine Heroes
- Work to do

# **Timeline of Vaccines US**

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- 1945 Inactivated influenza vaccine trivalent
- 1948 Diphtheria, tetanus, and pertussis
  vaccines combined to form DTP
- 1955 Inactivated polio vaccine (shot)
- 1962 Live polio vaccine (oral)
- 1963 Measles vaccine
- 1967 Mumps vaccine
- 1969 Rubella vaccine
- 1971 MMR combination
- 1981 Hepatitis B vaccine
- 1985 Hib vaccine
- 1992 DTaP vaccine
- 1995 Varicella vaccine
- 1995 Hepatitis A vaccine

- 2000 Pneumococcal conjugate vaccine
- 2003 Intranasal influenza vaccine trivalent
- 2005 Meningococcal (ACWY) conjugate vaccine
- 2005 Tdap vaccine
- 2006 HPV vaccine for females (2 or 4 types)
- 2006 Rotavirus vaccine (RotaTeq<sup>®</sup>)
- 2006 Shingles vaccine (Zostavax<sup>®</sup> for≥ 60 yrs)
- 2008 Rotavirus vaccine (RotaRix<sup>®</sup>)
- 2009 HPV vaccine for males (4 types)
- 2013 Intranasal influenza vaccine quadrivalent
- 2014 Meningococcal B vaccine
- 2014 HPV vaccine (9 types of HPV [Gardasil<sup>®</sup> 9])
- 2017 Second shingles vaccine (Shingrix<sup>®</sup> ≥50 yrs)
- 2017 Adult hepatitis B vaccine (Heplisav-B<sup>®</sup>)

Multiple types of enhanced flu vaccines at various years.

<u>https://www.chop.edu/centers-programs/vaccine-education-center/</u> vaccine-history/vaccine-availability-timeline; https://www.historyofvaccines.org/timeline/all

#### 56 Organisms!!

#### US Impact of Vaccines in the 21<sup>st</sup> Century

Disease	Pre-vaccine Annual Morbidity	2017 Total	% Decrease
Smallpox	48,164	0	100
Diphtheria	175,885	0	100
Pertussis	200,752	18,975	90.5
Tetanus	1,314	33	97.5
Polio (paralytic)	16,316	0	100

https://wonder.cdc.gov/nndss/static/2017/annual/2017-table3.html

#### US Impact of Vaccines in the 21<sup>st</sup> Century

Disease	Pre-vaccine Annual Morbidity	2017 Total	% Decrease
Measles	503,282	120	100
Mumps	186,000	6,109	97
Rubella	47,745	7	100
Congenital rubella	823	5	99.9
Varicella	4,085,120	8,775	97.9
Haemophilus	20,000	34	99.8
influenzae b	(est.)	(est.)	

1. MMWR 1999; 48:243-8 2. MMWR 2004; 51:1-84; 3. <u>https://wonder.cdc.gov/nndss/static/2017/annual/2017-table3.html</u>;

4. https://www.cdc.gov/mumps/outbreaks.html

## Death

In 1900, 21,064 smallpox cases were reported, and 894 patients died. In 1920, 469,924 measles cases were reported, and 7575 patients died. In 1920, 147,991 diphtheria cases were reported, and 13,170 patients died. In 1922, 107,473 pertussis cases were reported, and 5099 patients died.

https://www.cdc.gov/mmwr/preview/mmwrhtml/00056803.htm

### Holy Cow! Have You Herd...?

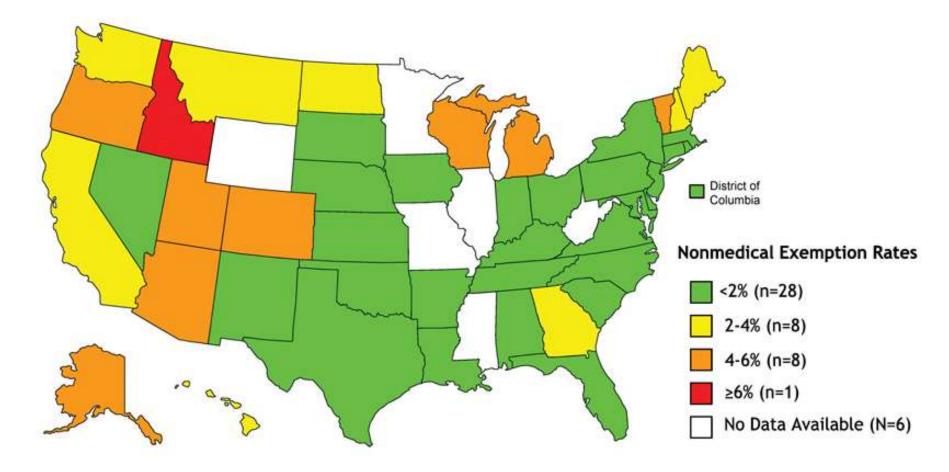
Estimated herd immunity thresholds and critical vaccination coverage using generally accepted reproductive numbers for common vaccine-preventable diseases

Vaccine-Preventable Disease	R <sub>0</sub> * <sup>59</sup> 60	Herd Immunity Threshold (%) 31	Critical Vaccination Coverage** (%) <u>31</u>
Diphtheria	4 to 5	75-80	79–84
Measles	11 to 18	91–94	96–99
Mumps	7 to 14	86–93	90 to 98
Rubella	6 to 14	83-94	87 to 99

\*\*herd immunity thresholds are adjusted to account for vaccine effectiveness.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6033611/

# Est. % Kindergarteners with Nonmedical Exemption 2015



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6033611/

# **Vaccine Victories:**

Things You Won't See (I hope!)

- Polio
- Smallpox
- Diphtheria: gray tonsillar membrane
- Tetanus: lockjaw
- Rubella: mild, arthralgia, adenopathy
- Rubella syndrome: devastating
- Meningococcal meningitis/sepsis: hearing and limb loss

I will not show you any of these with two exceptions because you won't see them! P.S. I have seen them all but one. Old...

#### **Things You Should Never See**









### **POLIO VACCINE**

CBS Television interview, on <u>See It Now</u> (12 April 1955)

Edward R. Murrow: Who owns the patent on this vaccine?

# Jonas Salk: Well, the people, I would say. There is no patent. Could you patent the sun?

Salk quotes: "The reward for work well done is the opportunity to do more." "Our greatest responsibility is to be good ancestors."

https://www.youtube.com/watch?v=erHXKP386Nk

Sabin did not patent his vaccine either! Oral vaccine stops GI transmission.

# Polio/Polio Vaccine

 Julius Younger, Byron Bennett, L. James Lewis, and secretary Lorraine Friedman were all part of Salk's team

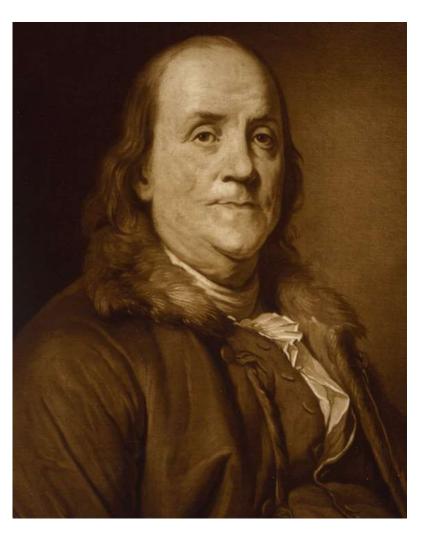


- 1.8 million children in Salk vaccine trial including his own family
- 1 in 200 infections caused paralysis
- 2019: 85 cases in Pakistan 69 and Afghanistan 16, type 1
- Type 2 last seen in 1999; WHO: eradicated from the planet!
- Type 3 last seen in 2012; to be declared eradicated next month!



http://polioeradication.org/news/





"In 1736 I lost one of my sons, a fine boy of 4 years old, by the smallpox...I long regretted bitterly and I still regret that I had not given it to him by inoculation; this I mention for the sake of parents, who omit that operation on the supposition that they should never forgive themselves if a child died under it; my example showing that the regret may be the same either way, and that therefore the safer should be chosen." -Benjamin Franklin, 1791

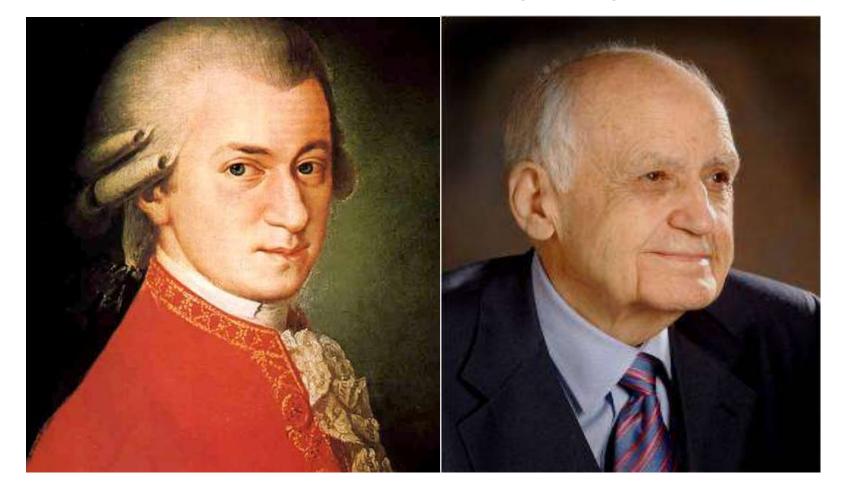






- Anthropological evidence of smallpox from 13,000 yrs ago
- Estimated 500 million deaths through time
- US 1721 Boston smallpox epidemic
- Cowpox and the milk maid: vaccinia vs variola
- Edward Jenner 1796 and Thomas Jefferson 1806
  - "You have erased from the calendar of human afflictions one of its greatest."
- 1906 purity of vaccines; eventual FDA establishment
- Last case smallpox 1977; WHO 1980 "eradicated"
- Smallpox vaccine still available; no longer used routinely
- BUT gene modification poses new threats

### Who are these people?



Wolfgang Mozart: Composer of 41 symphonies Maurice R. Hilleman: Inventor of 40 vaccines, 8 of which are on the routine schedules Including: Measles, Mumps, Rubella, Chickenpox, Hepatitis A, Hepatitis B,

Hib, and Meningitis

# Things You May See

- Measles: how many people died from measles in 2017 in the world? 110,000 mostly children
- Mumps
- Chickenpox
- Hepatitis A or B
- Pneumococcus
- Cholera







Hemophilus influenzae b





## Raold Dahl

- Olivia, my eldest daughter, caught measles when she was seven years old. I was sitting on her bed showing her how to fashion little animals... when it came to her turn...she couldn't do anything. "Are you feeling all right?" I asked her. "I feel all sleepy, " she said. In an hour, she was unconscious. In twelve hours she was dead.
- It really is **almost a crime** to allow your child **to go unimmunised**. ...it is never too late. All school-children who have not yet had a measles immunisation should beg their parents to arrange for them to have one as soon as possible.

http://roalddahl.com/roald-dahl/timeline/1960s/november-1962

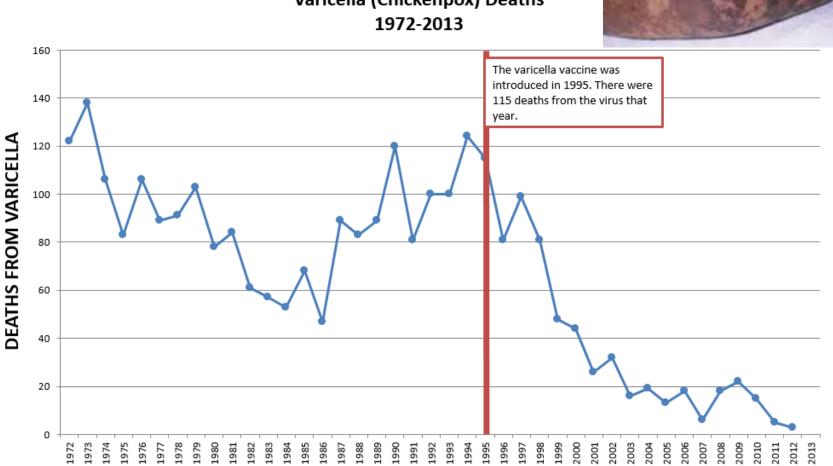
• 1,250 cases in US 2019

https://www.cdc.gov/mmwr/volumes/68/wr/mm6840e2.htm?s\_ cid=mm6840e2\_e&deliveryName=USCDC\_921-DM10756

### Varicella

https://www.cdc.gov/vaccines/pubs/pinkbook/varicella.html

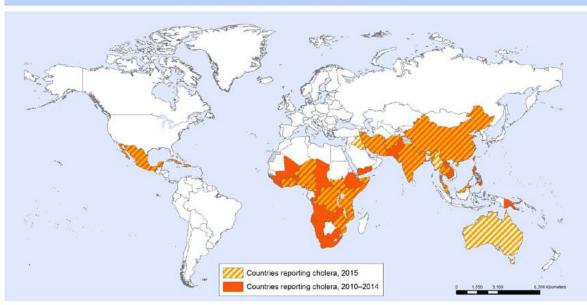




Varicella (Chickenpox) Deaths

## Cholera

#### Countries reporting cholera, 2010-2015





The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, diy or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization Map Production: Information Evidence and Research (IER) World Health Organization

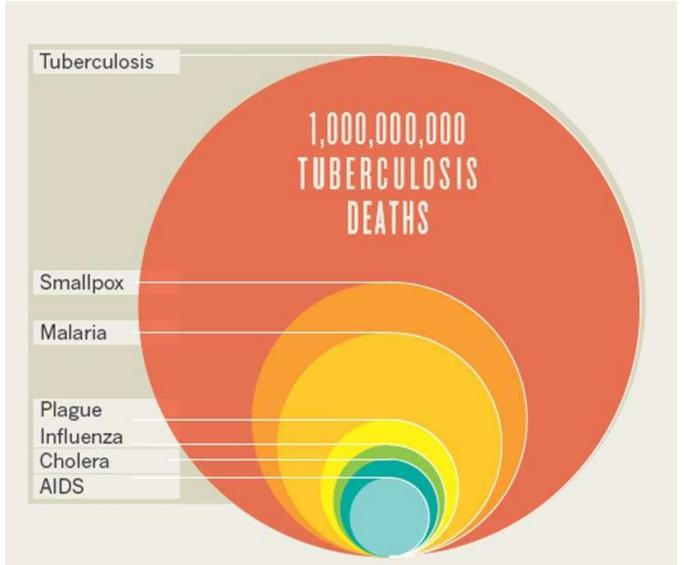
World Health Organization



# QUIZ: What is the greatest infectious disease killer of all time?

- A) plague
- B) malaria
- C) influenza
- D) tuberculosis
- E) smallpox
- F) cholera
- G) HIV
- H) measles

### **Tuberculosis**



http://theconversation.com/four-of-the-most-lethal-infectious-diseases-of-our-timeand-how-were-overcoming-them-78101

## **Tuberculosis Vaccine?**

- 1/3 of world's pop. has TB!!
- BCG (bacille Calmette-Guerin) good for infants + children; not so good for adults



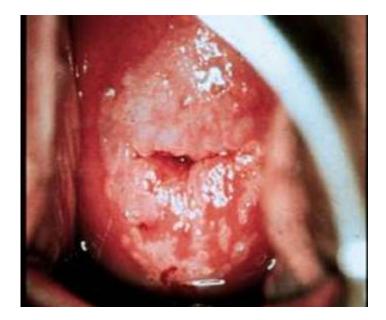
- GSK's Investigational Vaccine Candidate: M72/AS01E shows promise for prevention of TB disease in a Phase 2b trial conducted in Kenya, South Africa and Zambia; VE =54%
- TB drug resistance strains; HIV

# Things You Will See

- HPV: no more Pap smears?
- Pertussis
- Shingles
- Rotavirus
- Influenza



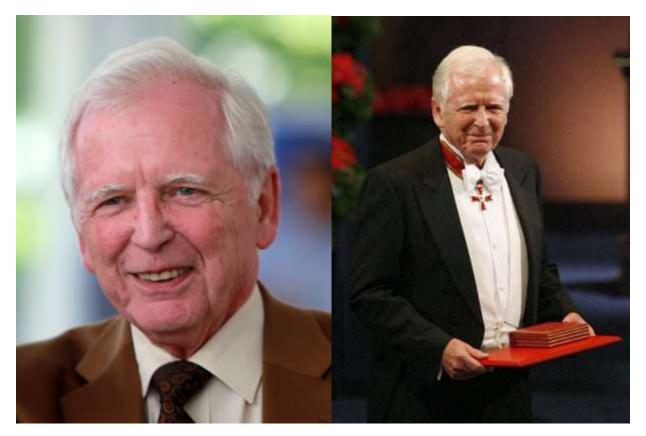






### QUIZ

#### Who is this person?



Harald zur Hausen

How many years did it take to develop his HPV vaccine? 21 years for HPV4

# Finding HPV

- Age 21 to 29: Every 3 yrs with cytology (Pap testing).
- Age 30 to 65: Every 5 yrs with HPV test alone (primary HPV testing), OR every 3 yrs with cytology alone, OR every 5 yrs with HPV co-test (Pap + HPV test). U.S. Preventive Services Task Force prefers primary HPV testing OR Pap testing alone.
- Younger Than Age 21: Screening is not recommended for women <21 yrs of age. (Too many self-resolving HPV infections!)
- Older Than Age 65/no screening: if adequate prior screening adequate (3 consecutive negative cytology results within 10 yrs or 2 consecutive negative HPV results within 5 yrs, with most recent test occurring within 5 yrs) and not at high risk for cervical cancer.
- No Cervix: No Screening; if cervix removed for benign reason.

"...the era of classic PAP smear is indeed coming to an end..."

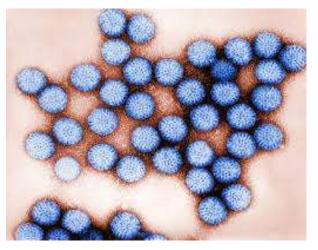
#### **Don't forget warts**



Rotavirus vaccine: 73% uptake

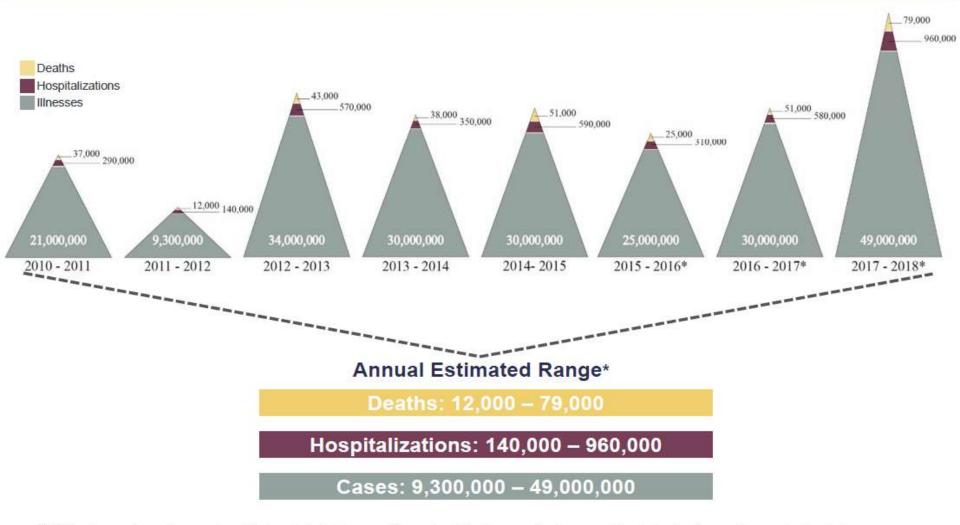


- Median annual % of stool tests + for rotavirus:
  - Prevaccine: 25.6% (range = 25.2–29.4)
  - Postvaccine: 6.1% (range = 2.6–11.1)
- Median annual peak in rotavirus positivity:
  - Prevaccine: 43.1% (range = 43.8–56.3)
  - Postvaccine: 14.0% (range = 4.8–27.3)
- Season duration:
  - Median of 26 weeks (range = 23–27)
  - Median of 9 weeks (range = 0-18).



https://www.cdc.gov/mmwr/volumes/68/wr/mm6824a2.htm

#### Estimated Influenza Burden in the United States



\* Estimates are based on mathematical models that account for under-detection, medical care seeking behavioral surveillance, deaths that occur outside of the hospital or associated with/without respiratory and circulatory causes **Reference: 1.** CDC https://www.cdc.gov/Laboratory-confirmedinfluenza-associatedhospitalizationflu/about/burden/index Accessed July 30, 2019.

#### **Despite current vaccines!!**

# Available But Not Routinely Used Vaccines

- Japanese encephalitis: routine in guess where?
- Rabies: when to use? Drives me batty...
- Adenovirus: military, type 4 and 7
- Tickborne encephalitis
- Typhoid fever: travel
- Cholera: outbreaks
- Yellow fever: travel
- Hepatitis E



## Activity: discuss with a neighbor

• What improvements in current vaccines would you like to obtain? List 2.

• Other than TBC, malaria, and HIV, what 3 diseases need a good vaccine?

# Vaccine Pipeline

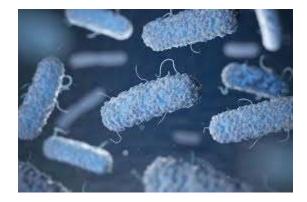
- <u>E. coli</u>\* (major sepsis; death)
- <u>Respiratory syncytial virus</u>\* (11,000 die)
- <u>Cytomegalovirus</u>
- <u>Clostridium difficile</u>\* (15,000 die)
- Lyme disease\*
- <u>Dengue fever</u>\* (current vaccine +/-)
- Ebola virus
- <u>Zika virus</u>
- <u>Malaria</u>
- <u>HIV</u>
- <u>Tuberculosis</u>
- <u>Streptococcus pneumoniae</u>\*
- <u>Streptococcus pyogenes</u>
- <u>Tuberculosis</u>
- Universal Influenza Vaccine\*

#### <u>......</u>

\* We see lots!!!

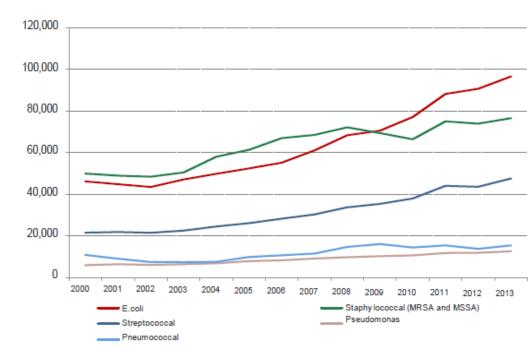
- <u>Campylobacter jejuni</u>
- <u>Chagas Disease</u>
- <u>Chikungunya</u>
- Enterovirus 71 (EV71)
- Group B Streptococcus (GBS)
- Herpes Simplex Virus\*
- <u>HIV-1</u>
- Human Hookworm Disease
- Leishmaniasis Disease
- <u>Nipah Virus</u>
- Nontyphoidal Salmonella Disease
- <u>Norovirus</u>\*
- Paratyphoid fever
- <u>Schistosomiasis Disease</u>
- <u>Shigella</u>
- <u>Staphylococcus aureus</u>\*

# Escherichia coli



- E. coli 0157:H7
- US: UTI/sepsis
  - 7 million UTIs/yr
  - 400,000 hospital
- UK, incidence of E. coli bacteremia is est. at 90/100,000 population case fatality rate of 11/100,000 population

E.coli bacteremias have overtaken MRSA/MSSA as a leading cause of hospital admission in the US



Bacteremia: hospital admissions\* by etiology US, 2000-20131

\* based on principal diagnosis

# Estimate based on currently available data in case no preventive measurements are undertaken

### **Combat Vaccine Resistance**

- Avoid vaccinator vaccine fatigue: better vaccines coming!
- Assess every patient on every office visit for vaccination needs: like a vital sign
- Office vaccine champion(s) but engage entire staff
- Use presumptive rather than participatory approach
- Use patient reminders: iPhone, email, texts, postcards
- Use standing orders
- Default appointments:

"Your next appointment for flu vaccine is ..."

 Document adult vaccines: wallet card, iPhone



### Resources

• CDC schedules

https://www.cdc.gov/vaccines/schedules/index.html

- Shots Immunizations by AAFP/STFM <u>www.aafp.org/shots</u>
- Online resources: CDC and IAC
- ACIP email

#### https://www.cdc.gov/Other/emailupdates/

 Full list from Immunization Action Coalition (IAC) at

http://www.immunize.org/resources/apps.asp http://www.immunize.org/express/

Favorites	WEB SECTIONS	PRINTABLES
1. Handouts (ed and Staff	lucational materials	) for Patients
2. Vaccine Infor	mation Statements	
3. Ask the Expe	rts	
4. IAC Express		
5. Subscribe to	IAC Express	
6. Clinic Tools		
7. Standing Ord	ers for Vaccination	
8. Screening Ch	ecklists for Vaccina	ation
9. Vaccinating A	dults: Step-By-Step	o Guide
10. ACIP Recom	mendations	
11. Package Inse	erts	
12. Technically S	peaking Columns	
13. PowerPoint S	lide Sets	
14. Photos		
15. State Laws a	nd Mandates	
16. CDC Schedu	les	
17 Unprotected	People Stories	

- 18. Contact Info for States
- 19. Shop IAC



#### 11:07 Shots Immunizations SCHEDULES CHILD/TEEN CHILD CATCH-UP ADULT COMBO VACCINES VACCINES BY PROFILE BY CONDITION INFO BY TYPE

11:07	ā.			•				
<		Adult						
Viicolites	19-21y	22-26y	27-49y	50-64y				
Flu (IEV)		3	dose annos	ev.				
Flu (LAIV)	Annua	il vaccine 1 d	ose only					
Tdap			See note					
MMB	1 or 2 di	born in 195		tion ()f				
VAR	7 doses	(if born in 1f or later)	980					
RZV (pref)				28	dai			
ZVL					1			
HPV-E	dependin	a doses to pruspe at initiation						
HPV-M	2.or.3 doses	2.01.2 dooes						
PCV13		Ses	note		l			
PPSV23	1 ar	2 doses depe	nding on int	Scation				
HenA	2 or 3 doses depending on vaccine							
HepB		2 or 3 doses depending on vaccine						
Men	T or 2 doses depending on indication, then booster years if risk remains							
MenB	2.07	i dosen depo	midling oo va	ccine and ind	ic.			
HID		1 or 3 dose	s depending	on indication	1			

# Shots Immunization by AAFP/STFM

#### 11:08 11:09 **Patient Profile** Reset Hepatitis A AGE **High-Risk Indications** 13-15 yrs CONDITIONS Details on vaccination of persons with primary and secondary Add Conditions immunodeficiencies for 2018 are available at www.cdc.gov/vaccines/hcp/aciprecs/general-Diabetes recs/immunocompetence.html/www.cdc.g SPECIAL CIRCUMSTANCES OV). Add Circumstances High-risk indications include: RECOMMENDED VACCINATIONS · Persons with chronic liver disease Vaccine may be indicated if benefit outweight risk of · Persons who receive clotting-factor adverse reaction. concentrates: Pneumococcal Polysaccharide Vaccine (PPSV23) Homelessness Influenza Inactivated · Men who have sex with men · Persons who use injection and non-Live Attenuated Influenza Vaccine injection illicit drugs HPV · Persons working with nonhuman primates infected with HAV or with HAV in a research laboratory setting · Persons working in countries with a high or intermediate risk of HAV infection: all

- or intermediate risk of HAV infection: all areas except Canada, Western Europe, Scandinavia, Japan, New Zealand, and Australia. For additional information, see www.cdc.gov/travel/vaccines/(www.cdc.go y).
- Unvaccinated persons anticipating close personal contact (e.g., household contact or regular babysitting) with an international adoptee from a country of bioh or.

PATIENT NAME.

#### Screening Checklist for Contraindications to Vaccines for Adults

DATE OF BIRTH\_\_\_\_\_\_

For patients: The following questions will help us determine which vaccines you may be given today. If you answer "yes" to any question, it does not necessarily mean you should not be vaccinated. It just means additional questions must be asked. If a question is not clear, please ask your healthcare provider to explain it.

	yes	no	don't know
1. Are you sick today?			
2. Do you have allergies to medications, food, a vaccine component, or latex?			
3. Have you ever had a serious reaction after receiving a vaccination?			
4. Do you have a long-term health problem with heart, lung, kidney, or metabolic disease (e.g., diabetes), asthma, a blood disorder, no spleen, complement component deficiency, a cochlear implant, or a spinal fluid leak? Are you on long-term aspirin therapy?			
5. Do you, or does a close family member, have cancer, leukemia, HIV/AIDS, or any other immune system problem?			
6. In the past 3 months, have you taken medications that affect your immune system, such as prednisone, other steroids, or anticancer drugs; drugs for the treatment of rheumatoid arthritis, Crohn's disease, or psoriasis; or have you had radiation treatments?			
7. Have you had a seizure or a brain or other nervous system problem?			
8. During the past year, have you received a transfusion of blood or blood products, or been given immune (gamma) globulin or an antiviral drug?			
9. For women: Are you pregnant or is there a chance you could become pregnant during the next month?			
10. Have you received any vaccinations in the past 4 weeks?			
FORM COMPLETED BY	DATE		

#### Immunization Action Coalition

http://www.immunize.org/catg.d/p4065.pdf

Remember to provide your adult patients with some record of vaccination. Cell phones, wallet cards.

-	Type of Annual State	Date given monthey's	Healthcare protocommal.	Dale rest Does the	71 22	5
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Did you bring your immunization record card with you?

FORM REVIEWED BY.

yes 🗌 no 🗌

DATE

It is important for you to have a personal record of your vaccinations. If you don't have a personal record, ask your healthcare provider to give you one. Keep this record in a safe place and bring it with you every time you seek medical care. Make sure your healthcare provider records all your vaccinations on it.