

Vaccine-Preventable Diseases and the Newborn Infant: The Importance of Maternal Vaccination Both Before and During Pregnancy

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Disclosures

- Potential conflicts
 - Safety Review Committee
 - Gardasil or 4-valent human papillomavirus vaccine in males (Merck)
 - Gardasil®9 or 9-valent human papillomavirus vaccine (Merck)
 - Data and Safety Monitoring Board
 - Adult and infant 15-valent pneumococcal conjugate vaccine (Merck)
- No off-label use discussion

Learning Objectives

- Upon completion, you will be able to
 - Identify all the vaccines a woman should have before she becomes pregnant
 - Describe how to catch-up a woman on her vaccines before she becomes pregnant
 - Explain what prenatal screening a woman needs with each pregnancy with respect to vaccine-preventable diseases
 - Vaccinate a pregnant woman during her pregnancy on purpose
 - Plan post-pregnancy vaccines if needed

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Pre-Pregnancy Vaccine Needs

- Average age in US of first pregnancy is 26.4 years
- Five adult, non-pregnant vaccine needs
 - Influenza, one dose annually
 - Usually Tdap once, Td every 10 years
 - 1 to 2 doses MMR depending
 - 2 doses VAR
 - HPV 2-3 doses depending

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Influenza



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Influenza as a Disease

- Very contagious: cough, sneeze, breathing
- Fever, cough, shaking chills, body aches, extreme weakness
- Several circulating strains each season
- Season begins as early as October
- Season ends as late as May
- Most outbreaks begin with school-children

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Influenza as a Menace

- Hospitalizations in the US
 - 114,018–633,001 hospitalizations a year
 - 18,476–96,667 intensive care unit admissions
 - 30%–46% of hospitalizations in those <65 yrs old
- Deaths in the US
 - 4,866–27,810 deaths per year
 - 101 children in 2016-2017
 - 15-29% of deaths occur in those <65 yrs old

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Influenza and Healthy Adults?

- Twin Cities study of healthy working adults
- RCT of influenza vaccine versus saline placebo
- Examined differences over 4 month period
- 35% fewer upper respiratory illnesses
- 52% fewer sick-leave days due to URIs
- 24% fewer visits to physicians for URIs

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Flu Vax Recommendations

- ACIP recommends
 - Everyone get the flu vaccine each year
 - 6 months and older
 - Start providing vaccine before end of October
 - Continue catch-up thru season up to exp. date
 - Honor the rare, real contraindication
 - Serious allergy to flu vaccine/its components except eggs

Td/Tdap/DTaP for Tetanus

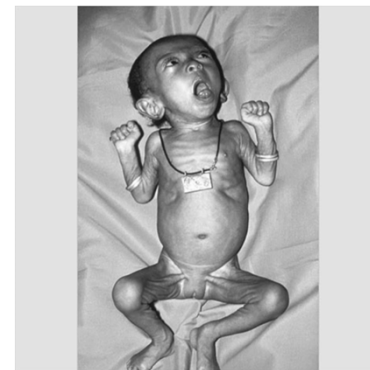
- Use of vaccine in US starting in 1930s and 1940s
- Across world 34,000 cases neonatal tetanus/year
- 96% drop from late 80s due to tetanus vaccine
- US has 40 to 50 cases a year, 13% fatal
- Missing childhood series or long lapse boosters
- Last case obstetric tetanus 2016 in Kentucky
 - Amish home birth
 - Community assistant
 - Mother hospitalized, intubated, d/c'ed after 1 month

Td/Tdap/DTaP for Diphtheria

- School age illness, cause of death
- 5-10% death rate
- Occurs worldwide, rare in US
- 1920s
 - 100,000 to 200,000 cases a year
 - 13,000 to 15,000 deaths a year
- In US now 5 cases since 2000

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Td/Tdap/DTaP for Pertussis



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Pertussis

- Cause of 100-day-cough in adolescents, adults
- Killer of babies
- Pre-vaccination in 1940s in US
 - Greater than 200,000 infantile cases a year
 - 8000 infants died each year
- Post-vaccination
 - Dramatic reduction in infant pertussis
 - More gentle acellular pertussis vaccine wanes
 - Still have significant childhood and adult disease

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Current Pertussis Epidemiology

- Numbers driven by
 - Recognition of pertussis in adolescents and adults
 - No whoop
 - Persistent cough
 - Ability to test with PCR
 - Acellular pertussis
 - Overcomes resistance to reactivity with whole cell
 - Delivers less immunogenic protection with more waning

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Current Situation with Pertussis

- Most recent peak 2010 27,000 cases in US
- Large proportions
 - 7 to 10 years of age thought result of acellular form
 - 13 to 14 years of age
- Tdap introduced 2005 routine 11-12 years old
- Field testing shows waning 1-2 years post dosing

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Current Pre-Pregnancy Recs

- Routine
 - DTaP 2, 4, 6, 12-15 mo, and 4-6 years of age
 - Tdap 11-12 years old
 - Td every 10 years after
- Catch-up
 - If non-pregnant adult with no or unclear history
 - Tdap now
 - Td in 4 weeks
 - Td in 6-12 months

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Measles



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Measles

- A highly contagious viral illness
- Spread by droplets through the air
- Fever, cough, coryza, conjunctivitis, and rash
- Complications occur 30% of the time
 - Diarrhea (8%)
 - Ear infections (7%)
 - Pneumonia (6%)
 - Acute encephalitis (1/1000)
 - Death (2-3/1000)
- Pre vaccine: ½ million cases, 1000 deaths a year

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Measles During Pregnancy

- Premature labor
- Miscarriage
- Low-birth weight

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The 2017 Measles Outbreak in Minnesota

- On April 10, 2017, first case reported
 - Hospitalized child aged 25 months old
 - Evaluated for fever, rash, onset 2 days before
 - No hx of measles-mumps-rubella (MMR) vaccine
 - No travel history or known exposure to measles
- By end of May, 2017
 - 79 total cases in 4 counties
 - 74 in children (ages 0-17 years), 5 in adults
 - Median age 23 months
 - **31%** were hospitalized

Measles Vaccination Status Among 79 Cases

- 71 confirmed to be **unvaccinated**
- 3 had 1 dose of measles-mumps-rubella or MMR vaccine
- 3 had 2 doses of MMR
- 2 are unknown/pending

Race/Ethnicity among the Measles Cases

- 64 **Somali Minnesotans**
- 11 White/Non-Hispanic
- 3 White/Hispanic
- 1 Black/Non-Hispanic

Measles in US Linked to International Travel

- From 1997 to 2016, 56 cases in MN
- Of these 50 linked to international travel
- Still prevalent in Europe, Asia, and Africa
- For 2017 **source** not yet identified

Measles and Somali Minnesotans

- 2011 outbreak among Somali Minnesotans
 - 21 cases of which 8 were Somali
 - Index case 30-month-old who visited Kenya
- Before 2008, MMR coverage **90%**
- Decline then with concerns over autism
- In 2011 rate had fallen from 90% to **54%**
- Belief autism higher in Somali Minnesotans
- Belief that MMR caused this increase
- **Wakefield** met with community repeatedly

Mumps

- Pre-vaccine 200,000 reported cases a year
- Complications awful but deaths rare, 10 a year
- Continued outbreaks still with ~1000 cases a yr
 - College campuses
 - Pro hockey teams
- Occurrences
 - Complications still occur
 - Complications include those who had **2 MMRs**

Complications

- In 301 cases of mumps at U of Iowa
 - 20 (**7%**) had complications
 - 15 (5%) orchitis
 - 3 (1%) transient hearing loss
 - 2 mastitis
 - 1 meningitis
 - All 20 had documentation 2 doses **MMR**

The Mumps Vaccine of MMR

- Unlike the measles vaccine of MMR
 - **Less** immunogenic
 - Median effectiveness
 - For 1 dose 78%
 - For 2 doses 88%
 - Measurable **waning**

Management of Outbreaks

- Role for 3rd MMR in targeted populations
 - 2 dose coverage >90%
 - Intense exposure
 - Sustained transmission >2 weeks
 - High attack rates >5 cases per 1000
- Some evidence 3d dose is immunogenic
- In outbreaks
 - Rates declined after third dose intervention
 - Statistically significant only in one outbreak
 - Rates drop even when 3rd dose **not** used

Rubella

- Mild fever and rash
- German measles
- 50% have no symptoms
- Often undiagnosed
- Prevacination epidemic in 1964-1965
 - 12.5 million infections
 - 20,000 babies developed congenital rubella sx

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Rubella

- A highly contagious viral illness
- Spread by droplets through the air
- Children get a rash starting on the face
- Most who get it do not get ill or only mildly ill
- Complications
 - Arthritis, usually temporary (70% adult women)
 - Encephalitis (1/6000)
 - Low platelets and hemorrhage (rare)
- Major concern is non-immune pregnant woman
 - Miscarriages
 - Serious birth defects (congenital rubella syndrome or CRS)

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Congenital Rubella Syndrome



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Congenital Rubella Syndrome

- Infections in the first trimester
 - Fetal death
 - Premature delivery
 - Serious birth defects (85%)
 - Deafness
 - Eye defects including cataracts
 - Congenital heart disease
 - Cognitive impairment
 - Autism (15% of CRS)

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Vaccine-Era CRS Epidemiology

- Routine vaccination in US led to elimination 2004
- Rubella eliminated but not eradicated
- Congenital rubella syndrome in US
 - From 2004 to 2012 6 cases
 - Five cases mothers infected while in Asia or Africa

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MMR Vaccine Recommendations

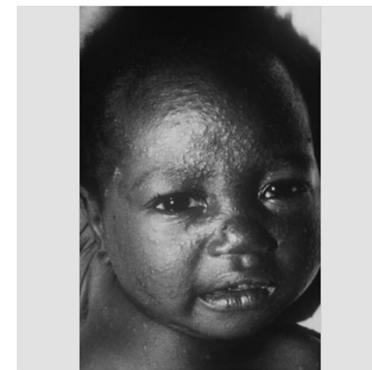
- Routine
 - 1st dose MMR at 12 to 15 months of life
 - 2nd dose MMR 4 to 6 years of life
- Catch-up
 - Two doses 28 days apart thru 18 years of life
 - Recs a little different for adults 18 years and older

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MMR Recs for Adults

- **Everyone needs measles immunity**
- Vaccines, lab serology, or birth before 1957
- Non-immune adults born 1957 or later
 - 1 dose MMR routinely
 - 2 doses 28 days apart if student, healthcare, international travel
- Contraindications
 - Severe immunodeficiency
 - Pregnancy

Varicella (Chicken Pox)



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Varicella

- Spread person-to-person through air
- Extremely contagious
- Wasn't reportable, ~ entire birth cohort
- Rash, fever, coughing, fussiness, headache, anorexia
- 5-10% had serious complications
 - Serious skin infections
 - Pneumonia
 - Brain damage
 - 100-200 deaths a year

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Congenital Varicella Syndrome

- Infections in the first 20 weeks of gestation
 - Low birth weight
 - Hypoplasia of an arm or leg
 - Skin scarring
 - Localized atrophy of muscles
 - Encephalitis
 - Cortical atrophy
 - Chorioretinitis
 - Microcephaly

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Varicella Vaccination

- Routine
 - 1st dose MMR at 12 to 15 months of life
 - 2nd dose MMR 4 to 6 years of life
- Catch-up
 - Two doses 3 months apart thru 12 years of life
 - Two doses 4 weeks apart if 13 through 18 years old

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Adult Rules for Varicella

- If no evidence of immunity
 - 2 doses 4-8 weeks apart
- Evidence of immunity?
 - 2 doses at least 4 weeks apart
 - Healthcare provider diagnosed or verified cases of
 - Varicella
 - Zoster
 - Lab evidence of immunity or disease
 - US born before 1980 (except if pregnant, healthcare)

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Contraindications to Varicella

- Live vaccine just like MMR
 - Severe immunodeficiency
 - Pregnancy

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“As Common as the Flu”

- Human papillomavirus or **HPV** infections
- Spread by direct contact
- 14 million new genital infections a year in US
- Cf. influenza causing 9 to 60 million infections
- 7 million new infections high-risk HPV type
- Most persist 1 to 2 years
- Silent, contagious, undiagnosed
- Some persist for years, progress to **cancer**

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The Cancers HPV Causes

- **30,700** new cancers a year in the US caused by HPV
 - 19,200 among women
 - 11,600 among **men**
 - 10,700 cervical
 - 11,000 **oropharynx**

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Cervical Ca Treatable?

- **300,000** invasive tests and treatment a year
 - Costly and anxiety-provoking
 - Long-lasting effects
 - Infertility
 - Second trimester pregnancy loss
 - Premature rupture of membranes
 - Preterm delivery

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HPV Vaccine Efficacy

- Large clinical trials
 - Per protocol cervical intraepithelial neoplasia (CIN)
 - 4vHPV
 - 2 double-blind, placebo-controlled trials
 - Types 16 and 18
 - Among HPV naïve, **97-100%** for CIN2 or more severe
 - 9vHPV
 - Single international trial with 4vHPV as control
 - Types 31, 33, 45, 52, 58
 - Among HPV naïve, **97%** for CIN2 or more severe

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Uptake of HPV Surprising Poor

- Introduced 2006 a year after Tdap and MCV4
- More **effective** than either
- Just as **safe** or **safer**
- Diseases prevented far more common
- Among 13 to 17 year olds
 - Tdap at 88.0%
 - First dose MCV4 82.2%
 - Second dose MCV4 39.1% among 16-17 yr olds
 - HPV UTD **37.5** male and **49.5%** female

Specifics of Current Recs

- Routinely recommended **11-12** years of age
- Permission to start at 9-10 years of age
- Catch-up for initiation with 1st dose
 - Through 26 years of age for females
 - Through 21 years of age for males
 - For males 22 through 26 years
 - If desiring immunity (option)
 - If at increased **risk** (recommended)

High Risk Males

- HIV
- Immune compromise
- Males who have sex with males

Pre-December 2016 Dosing

- **Three doses**
 - 0, 1-2 months, 6 months
 - Minimum intervals
 - 4 weeks between 1st and 2nd doses
 - 12 weeks between 2nd and 3rd doses
 - 24 weeks between 1st and 3rd doses

New as of December 2016

- **Two doses**
 - 0 and 6-12 months
 - Immunocompetent males and females
 - First dose <15 years of age
 - Minimum interval **5 months**
 - May start as early as 9 or 10 years of age

Why the Change?

- 2 doses 6-12 mo apart
 - Just as or more immunogenic
 - 9-14 yrs seroconvert >97.9%
 - Higher antibodies than 3 doses in 16-26 yrs
- Duration of protection
 - 10 years out from trials **no waning** w/ 3 doses
 - 2 doses expected to be the same
- Health impact, cost-effectiveness
 - More likely to complete schedule
 - 2 doses will be cost saving

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Notes on Two-Dose Rec

- Past vaccine doses count
 - E.g., 18-year-old who got a 4vHPV age 12
 - She only needs only 1 dose HPV now
 - Can finish with 9vHPV now and be done
- Some patients are **already** done!
 - 16-year-old got a 4vHPV at 11 & a 9vHPV at 15
 - He's done!
- Have to be immune competent, start <15 yr
- NB: 2v for females and 4v or 9v for all count

Also New

- **No more 2vHPV or 4vHPV in US**
 - 2vHPV Cervarix (was only licensed for females)
 - 4vHPV Gardasil
- Only HPV now available 9vHPV Gardasil 9
- Can complete any schedule of valid doses

Prenatal Screening is Key

- Screen for rubella immunity by serology
 - If non-immune, baby at risk for CRS
 - Vaccines are live viral but asap post delivery, vaccinate!
- Also screen for hepatitis B with each pregnancy...

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Hepatitis B



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Hepatitis B

- Contagious
 - Mother-to-baby in utero, blood, environmental
- Serious but stealthy
 - Can lead to serious illness, hospitalization, death
 - Can lie dormant or undetected for decades
 - Can leave person contagious for a lifetime
 - Can be transmitted sexually, blood
 - Can cause liver failure or cancer later in life
 - 15% spread non-household environmental

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Prenatal Screening for HepB

- Screen for hepatitis B chronic infection
 - If positive for Hepatitis B surface antigen (HBsAg)
 - Give HBIG to infant first 12 hours of life
 - Start Hepatitis B vaccine series in 1st 12 hours of life
 - Finish series with 2 to 3 more doses over next 6 months
 - Test for hepatitis B status if mother HBsAg positive
 - Hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs)
 - 9-12 months of life (previously 9 to 18 months of life)
 - 1-2 months after series if dosing delayed

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More on Screening for HepB

- If HBsAg unknown at birth
 - Start Hepatitis B vaccine series in 1st 12 hours of life
 - If less than 2000 grams , give HBIG in 12 hours too
 - Determine maternal HBsAg status
 - If positive and >2000 grams, give HBIG asap, 1st 7 days
- If HBsAg negative at birth
 - Start Hepatitis B vaccine series in 1st 24 hours of life
 - Finish series with 2 to 3 more doses over next 6 months

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Congenital Hepatitis B

- 90% of infants infected become chronically infected
- 25% of chronically infected die prematurely
 - Liver cancer
 - 1000-1500 persons die each year in US
 - Cirrhosis
 - 3000-4000 persons die each year in US

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More Prenatal Screening

- Screen mothers for all vaccines due
 - Use medical records, state registry (WIR, MIIC, IRIS)
 - Do NOT accept oral reports except flu vaccine
 - Access the ACIP adult schedule at <https://www.cdc.gov/vaccines/schedules/hcp/adult.html>
 - Use catch-up schedule for vaccines due that can be given in pregnancy
 - Start other vaccines upon baby's delivery

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Vaccine Needs During Pregnancy

- Five adult, non-pregnant vaccine needs
 - Influenza, one dose annually
 - Usually Tdap once, Td every 10 years
 - 1 to 2 doses MMR depending
 - 2 doses VAR
 - HPV 2-3 doses depending
- Two on-purpose during-pregnancy vaccine
 - Influenza, 1 dose annually, for the mother and baby...
 - Tdap, no matter previous history, for the baby...

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Influenza in Pregnancy

- Risk of hospitalization 4 times higher
- Risk of complications in pregnancy similar to other high-risk conditions like asthma, diabetes, etc

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Influenza in First 2 Years of Life

- Hospitalization rate $\sim \geq 65$ years old
- Complications
 - Secondary bacterial pneumonia
 - More rarely primary viral pneumonia with a high fatality rate
 - Myocarditis

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Pertussis (Whooping Cough)

- Spread through the air
- Triggers such severe coughing fits that babies cannot breath
- Half of babies with whooping cough are hospitalized
- In babies, pertussis can cause
 - Seizures
 - Brain damage
 - Apnea
 - Cardio-respiratory collapse
 - Death
- Babies need 3 doses DTaP over 6 months to get immune

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Current Tdap Recs to Protect Babies

- Vaccinate all pregnant women at 27-35 weeks
- Aim to give as close to 27 weeks as possible
- Allows for developed booster response
- Provides antibodies to protect baby for 6 months
- Takes 6 months (3 doses DTaP) to protect baby

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Timing of Vaccines To Give on Purpose in Pregnancy

- Inactivated influenza vaccine
 - IIV
 - Not live attenuated influenza vaccine (nasal spray)
 - As soon as available
 - Any trimester
- Tetanus-diphtheria-acellular pertussis
 - Tdap
 - Timed between 27 and 36 weeks
- Neither affects plans to breastfeed

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Vaccines to Catch Up in Pregnancy

- If no primary series of diphtheria-tetanus-pertussis, 3 doses with two Tds and 1 Tdap*
- If high-risk and not previously vaccinated
 - 4-valent Meningococcal conjugate
 - Hepatitis A
 - Hepatitis B
 - Some vaccines for travel
- None affect plans to breastfeed

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Vaccines to Receive ASAP After Delivery

- Measles-mumps-rubella
- Varicella
- Human papillomavirus vaccine series
- None affect plans to breastfeed

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None affect plans to breastfeed

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Summary

- Pre-pregnancy IIV, Tdap/Td, MMR, Var, and HPV
- Screen for rubella, hepatitis B, adult vaccines
- During pregnancy IIV and Tdap on purpose
- During pregnancy give any non-live vaccines due
- Post-pregnancy give any live vaccines due

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