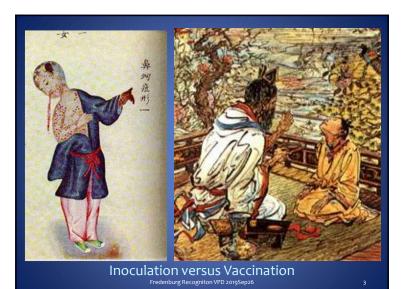
Staying on the Defense: Clinical Recognition of Vaccine Preventable Diseases

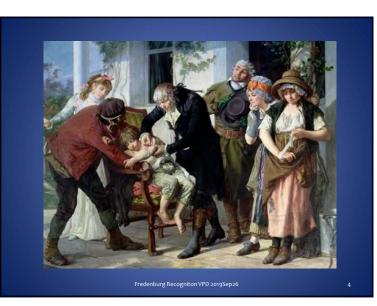
David C Fredenburg MD MPH MA FAAP NH Immunization Conference 2019Sep26



Following this session, participants will (or rather might had could) be able to:

- Recognize the major features in the presentation of the diseases for which NH children are routinely vaccinated.
- Explain the changing epidemiology of the current vaccine preventable diseases and impact of immunization or lack thereof.
- Communicate the prevalence of vaccine preventable diseases, the success of vaccinations and risks of vaccine refusal in counselling of their patients and parents.

Fredenburg Recogniton VPD 2019Sep26

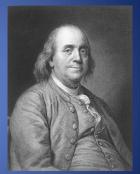




Vaccinia vs Cowpox Inocculation

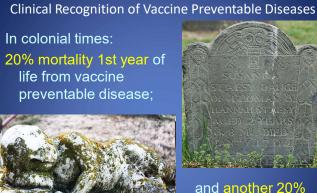
ox Progressive (necrotizing) Vaccinia Clinical Recognition of Vaccine Preventable Diseases In 1736 I lost one of my sons, a fine

boy of 4 years old, by the smallpox...I long regretted bitterly and I still regret that had not given it to him by innoculation; 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.



Benjamín Franklín

Fredenburg Recogniton VPD 2019Sep26

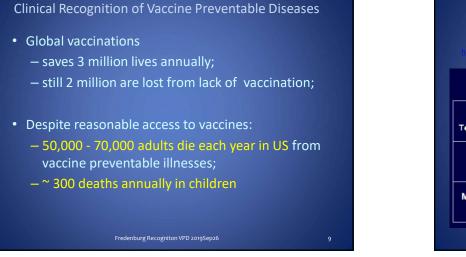


Fredenburg Recogniton VPD 2019Sep26

and another 20% mortality by 5 years of age

Where we're at...

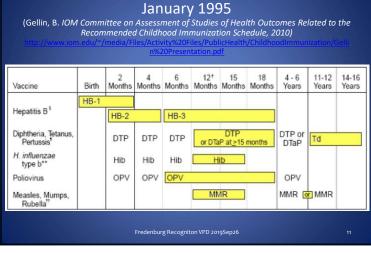
Comparison of 20th Century Annual Morbidity and Current Morbidity: Vaccine-Preventable Disease 20th Century 2011 Percent Disease Annual Morbidity Reported Cases †† Decrease 29,005 100% Smallpox 0 Diphtheria 21,053 0 100% 530,217 212 Measles > 99% Mumps 162,344 370 > 99% Pertussis 200,752 15.216 92% Polio (paralytic) 16,316 0 100% Rubella 47,745 > 99% Congenital Rubella Syndrome 152 0 100% 580 Tetanus 98% 20,000 > 99% CDC Fredenburg Recogniton VPD 2019Sep26



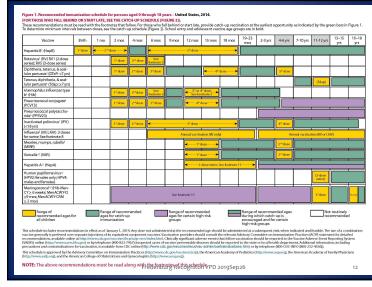
Recommended Childhood Vaccine Schedule 1982 (adapted from Gellin, B. IOM Committee on Assessment of Studies of Health Outcomes Related to the Recommended Childhood Immunization Schedule, 2010) 2 mo 4 – 6 yr 4 mo 6 mo 15 mo 18 mo 12 mo Diphtheria, DTP DTP DTP DTP DTP Tetanus, Pertussis OPV OPV OPV OPV Polio Measles, Mumps, MMR Rubella

10

9



Recommended Childhood Vaccine Schedule US,



So, now, what we're here for: Clinical Recognition of Vaccine Preventable Diseases

- Whirlwind tour of 17 vaccine prevented (one so far) & preventable diseases (16 not so much)
 - Disease incidence pre- / post- vaccine
 - Transmission / pathogenesis if uniquely curious, and not too boring
 - Clinical features specific to the disease
 - Specific complications
 - Please do not attempt to take notes
 - Fredenburg Recogniton VPD 2019Sep26

<section-header><section-header><text><text><text><text><text>

14

Smallpox Transmission

- person to person by infected aerosols and air droplets
- also possible via ventilation systems
- contaminated clothes and bedding, though the risk of infection from this source is much lower
- infectious till smallpox scabs fall off



Fredenburg Recogniton VPD 2019Sep26

Smallpox Clinical Features

- incubation period usually 12–14 days (range 7–17), healthy, not infectious
- sudden onset of influenza-like symptoms including fever, malaise, headache, back pain and, less often, abdominal pain and vomiting
- 2-3 days later, defervescence with improved symptoms, rash appears, first on the face/hands/forearms then trunk, mucous membranes with viral shedding
- centrifugal distribution of lesions, macules to papules to pustules
- 8 to 14 days, pustules scabs leaving depressed depigmented scars

Clinical Forms of Smallpox Variola Major / Minor

- variola major (30% fatal) - severe, most common form of smallpox, extensive rash, higher fever (~ 90% of cases)
- variola minor (< 1% fatal) - less common, less severe



WHO photo, October 1975 of a 3-yearold Bangladeshi girl named Rahima Buna, "the last case of smallpox on the Asian subcontinent.", as well as the last case of wild variola major in the world.

Fredenburg Recogniton VPD 2019Sep26



Fredenburg Recogniton VPD 2019Sep

18

17

	SMALLPOX	CHICKENPOX	Differentia	ting Varicall
EVER	2 to 4 days before rash	At time of rash		ting Varicell
RASH • Appearance	Pocks in same stage	Pocks in several stages		oox Rash an
• Development	Slow	Rapid	Diseas	e Course
• Distribution	More pocks on arms and legs	More pocks on body		
• On paims and soles	Usually present	Usually absent	632	6
DEATH	Usually 1 in 10 die	Very uncommon		
		P		
		P.	SMALLPOX	CHICKENPOX

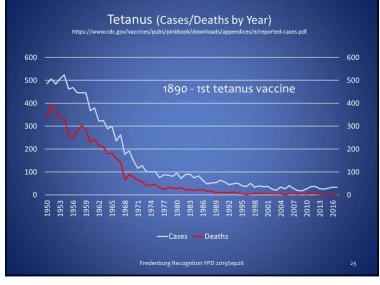
Smallpox Vaccination

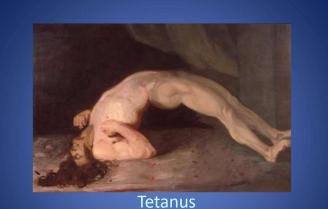
- 1960s: US: Landmark Neff/Lane Surveys (active surveillance for risk/benefit of variola vaccine)
- 1972: US: Routine Childhood vaccination stopped
- 1976: US: Routine HCW vaccinations stopped
- 1977: Global: Last naturally occurring smallpox case (Somalia)
- 1980: Global: WHO declared Smallpox eradicated
- 1982: Global: Int'l travel req lifted US: vaccine production
 halted
- 1984: US: Military program restricted to basic training settings
- 1990: US: Military recruit immunization discontinued
- 1990-pres US: Laboratorians targeted

Smallpox Vaccination

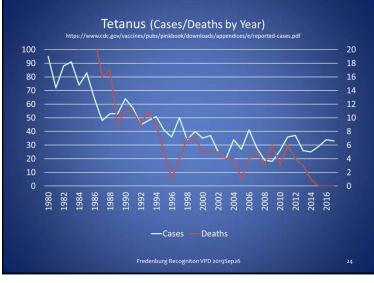
- 2001 (June) ACIP recommendations updated for laboratorians and included new guidelines for bioterrorism preparedness
- 2002 (June) ACIP updated recommendations for Smallpox Response Teams
- 2002 (Dec) Military vaccination program began: HCW, response teams and operational personnel
- 2003 (Jan) Civilian voluntary program began: smallpox response teams

21





'Lockjaw', 1st clinical descriptions from 5th century BC



Tetanus Pathogenesis

• Anaerobic conditions allow germination of spores and production of toxins



- Toxin binds in central nervous system
- Interferes with neurotransmitter release
- Leads to unopposed muscle contraction and spasm

25

Tetanus Clinical Symptoms

- Incubation period; 8 days (range, 3-21 days)
- Three clinical forms: local (uncommon), cephalic (rare), generalized (most common)
- Generalized tetanus: descending symptoms of trismus
- (lockjaw), risor sardonicus, difficulty swallowing, muscle rigidity, spasms
- Spasms continue for 3-4 weeks
- complete recovery may take months



26



•>250,000

2000-2003 • 4,712

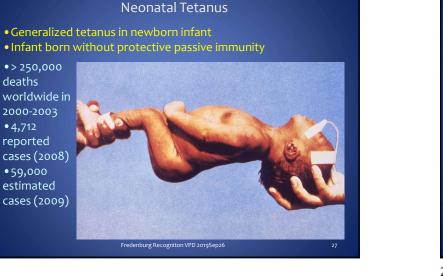
reported

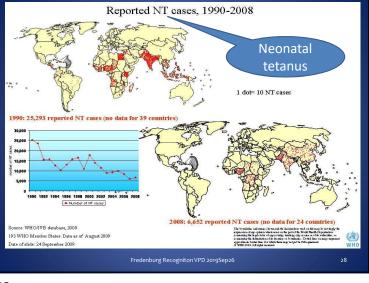
estimated

cases (2009)

cases (2008) • 59,000

deaths worldwide in







Diphtheria Epidemiology

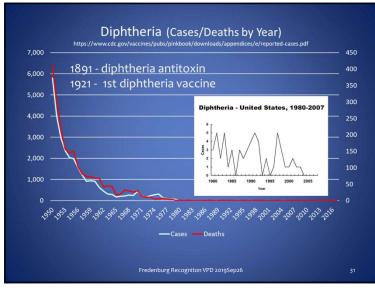
- Reservoir: Human carriers; usually asymptomatic
- Transmission: respiratory; rarely skin and fomites
- Temporal pattern: Winter and spring

30

32

• Communicability: Up to several weeks without antibiotics





Diphtheria Clinical Features • Incubation period 2-5 days (range 1-10 days) • May involve any mucous membrane or skin

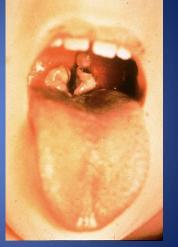




- Classified based by site of infection
 - anterior nasal
 - pharyngeal and tonsillar
 - laryngeal
 - cutaneous
 - ocular
 - genital

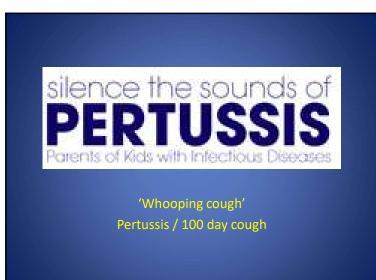
Tonsillar / Pharyngeal Diphtheria

- Insidious onset of exudative pharyngitis
- Exudate spreads within 2-3 days and may form adherent membrane
- Membrane may cause respiratory obstruction
- Fever usually not high but patient appears toxic



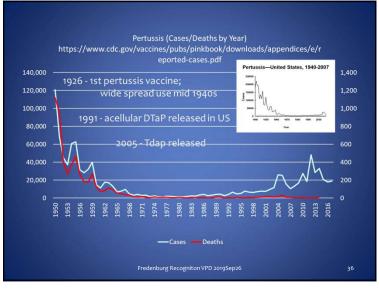
Fredenburg Recogniton VPD 2019Sep26

33



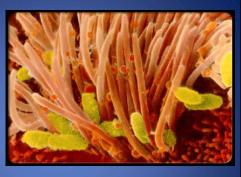
Diphtheria Complications

- Severity generally related to extent of local disease
- Most attributable to toxin (needs viral tox gene)
- Most common complications are myocarditis (60% in unvaccinated) and neuritis
- Death occurs in 5%-10% from respiratory disease
- (??) often quoted as "Guinness Book of World Records 'most resurgent disease' - with dissolution of former USSR 1990 > 150,000 cases"



Pertussis Pathogenesis

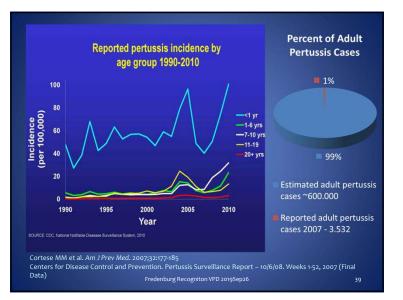
- Primarily a toxin-mediated disease
- Bacteria attach to cilia of respiratory epithelial cells



- Inflammation occurs which interferes with clearance of pulmonary secretions
- Pertussis antigens allow evasion of host defenses (lymphocytosis promoted but impaired chemotaxis)

Fredenburg Recogniton VPD 2019Sep26

37

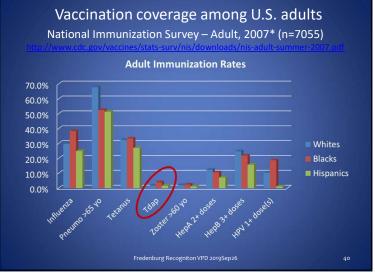


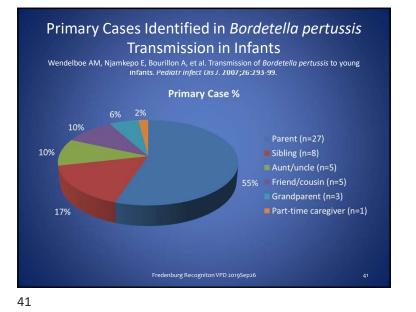
Pertussis Clinical Features

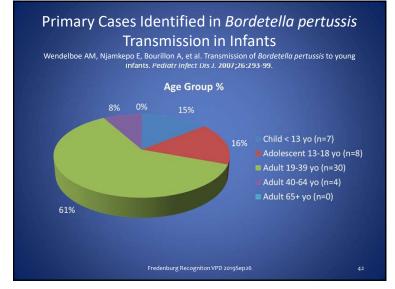
- Incubation period 5-10 days (range 4-21 days)
- Insidious onset, similar to minor upper respiratory infection with nonspecific cough
- Fever usually minimal throughout course of illness
- In adolescents and adults:
 - Disease often milder than in infants and children
 - Infection may be asymptomatic, or may present as classic pertussis
 - Persons with mild disease may transmit the infection
 - Older persons often source of infection for children

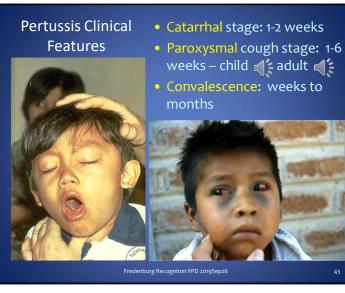
in edenburg Recogn

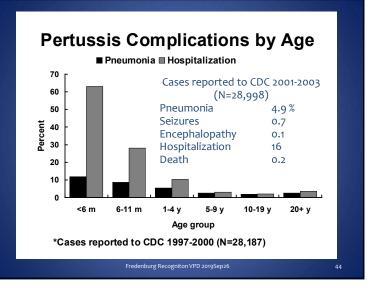
38

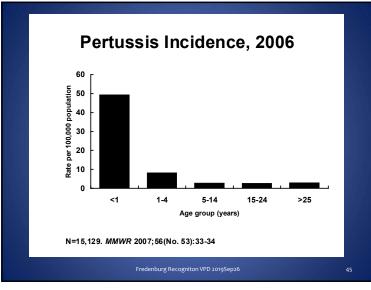


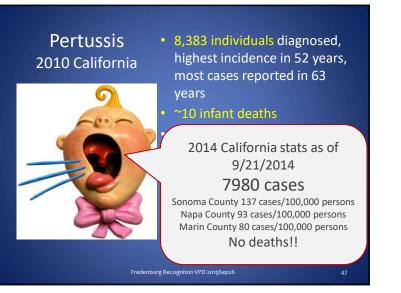


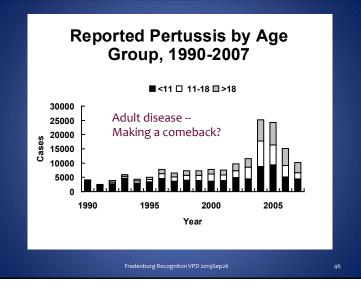












Upsurges of B. pertussis Cases

Cases of pertussis in previously vaccinated older children and adults are generally attributed to waning immunity without considering potential differences in Bordetella pertussis strains. As pointed out in 2009 by Dr Frits Mooi "There are now many studies which show that outbreaks of pertussis are often associated with changes in the B. pertussis population. Most recently, we have shown that more virulent (P3) strains have appeared which we believe to be (partly) responsible for the outbreak in the Netherlands. The P3 strains have emerged worldwide. Any discussion on the causes of sudden upsurges in infectious diseases should include changes in the pathogen population. This is even true for pertussis".

Transmission of B pertussis in Healthcare		
Index Case	Secondary Cases	
Unknown	122 cases (64 cases in healthcare personnel)	
Healthcare worker	11 newborns	
ED physician (hospital A)	5 cases among staff and visitors	
Respiratory therapist (hospital B)	3 cases among nurses	
Infant	17 symptomatic cases in healthcare workers	
Infant (source believed to be hospital worker or visitor)	3 infants diagnosed with pertussis	
?? Inpatient 80s (no work-up), husband wandering halls with chronic cough ??	??????	
	Index Case Unknown Healthcare worker ED physician (hospital A) Respiratory therapist (hospital B) Infant Infant Infant (source believed to be hospital worker or visitor) ?? Inpatient 80s (no work-up), husband	

¹ Leekha S, et al. Infect Control Hosp Epidemiol. 2009;30:467-473. ² CDC. MMWR. 2008;57(22)600-603. ³ Bagget HC, et al. Infect Control Hosp Epidemiol. 2007;28:537-543. ⁴ CDC. MMWR. 2005; 54:67-71. ³ Calugar A, et al. Clin Infect Dis. 2006;42:981-988. ⁶ Vranken P, et al. Am J Infect Control. 2006;34:550-554. (Adapted from Wright WL, ARNP. Immunization Update: What's New for 2012. Presentation 2012 NH Immunization Conference)

Fredenburg Recogniton VPD 2019Sep26

??????

49

?? Medical assistant 30s (no work-up),

outpatient dermatology office

49

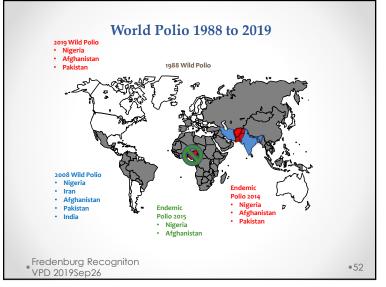
Nashua, NH 2011

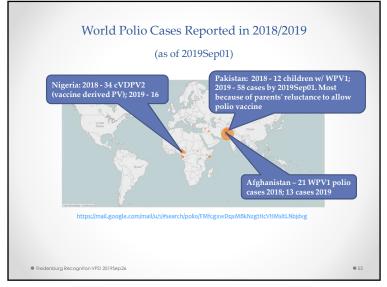


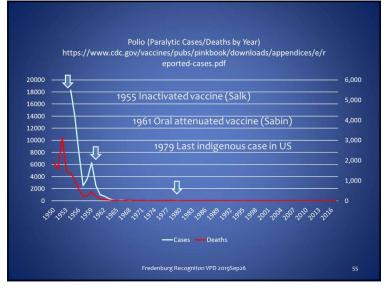
Pertussis – Please... Pertussis vaccine has incomplete efficacy at any age Clinical presentation is modified by vaccination (lack of whoop, lymphocytosis) and age Adults are routinely under-diagnosed (as in asking - when was the last time you saw pertussis?) NH DHHS-DPHS (HAN 01.26.09) Clinical case definition - your best guesses please! "Acute cough illness lasting at least two weeks with either paroxysms of coughing, inspiratory whoop, or post-tussive vomiting without other apparent cause" Nah, it's just bronchitis - maybe a different antibiotic!?

urg Recogniton VPD 2019Sep26

50

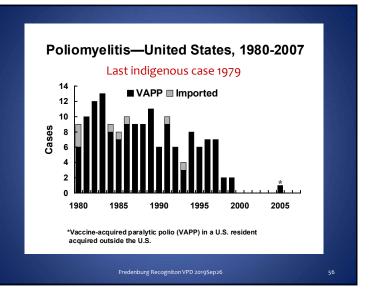






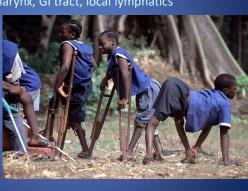




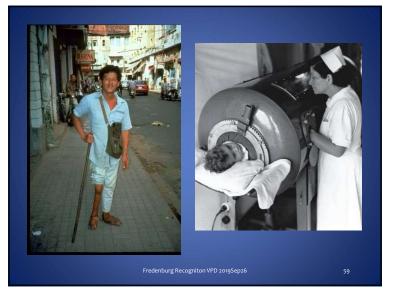


Polio Pathogenesis

- Entry into mouth
- Replication in pharynx, GI tract, local lymphatics
- Hematologic spread to lymphatics and central nervous system
- Viral spread along nerve fibers
- Destruction of motor neurons



57



Outcomes of Poliomyelitis Infections

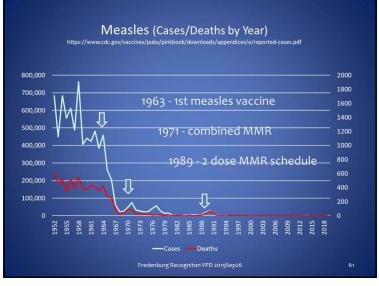
Clinical Outcome	Proportion of
	cases
Asymptomatic	90–95%
Minor illness	4-8%
Non-paralytic aseptic meningitis	1–2%
Paralytic poliomyelitis	0.1–0.5%
Spinal polio (79% of paralytic ca Bulbospinal (respiratory) polio Bulbar (brain stem) polio (2%)	
Fredenburg Recogniton VPD 2019Sep26	58

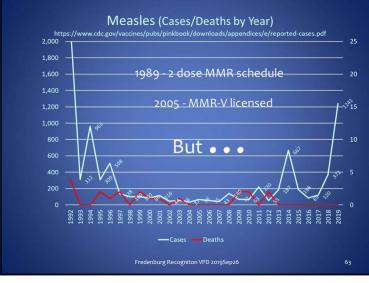
58

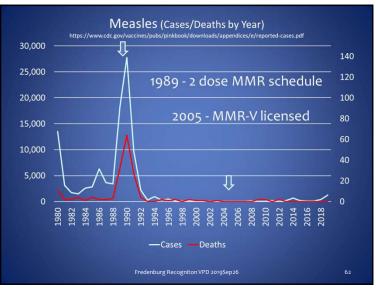


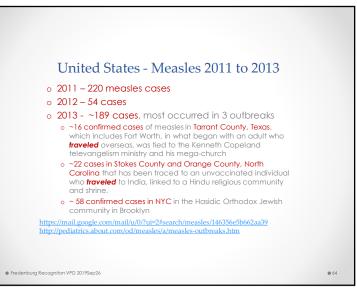
Rubeola & Morbilli Too •1st disease: measles, hard/red measles •2nd disease: scarlet fever •3rd disease: rubella (German measles) •4th disease: Duke's disease (staph scalded skin or rubella/strep variant or coxsackie) - defunct •5th disease: erythema infectiosum

 6th disease: roseola infantum or exanthem subitum



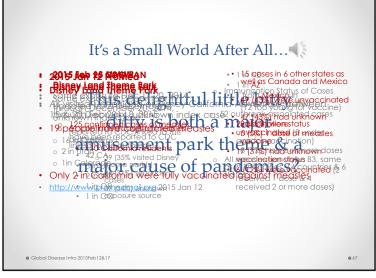


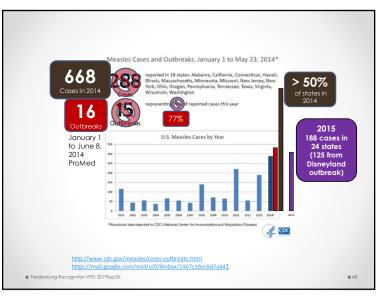


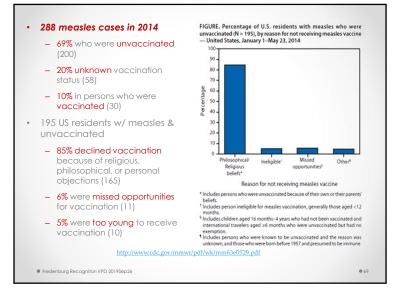




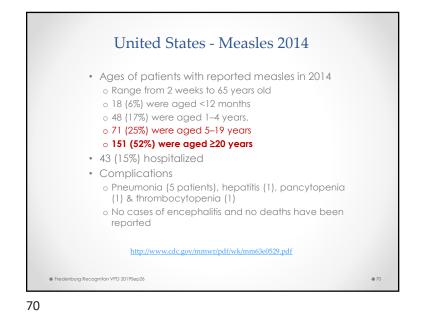


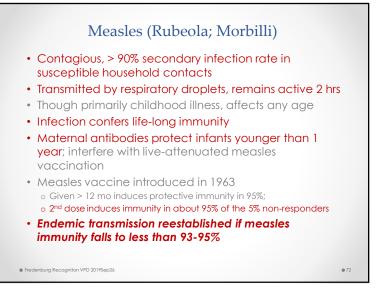


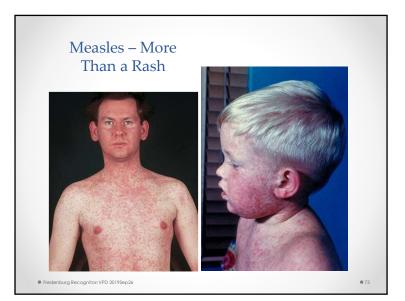














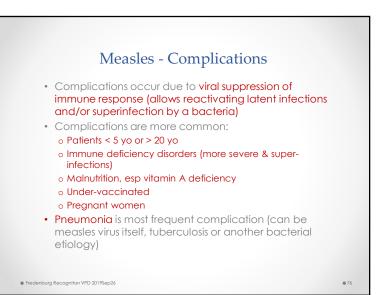
- Incubation period 10-12 days (range 7-14 days)
- Communicable 1-2 days before symptoms; until 4 days after rash onset (immunocompromised can be contagious for duration of the illness)
- 1st sign usually a step-wise fever (repeated viremias) often >104° F [40° C] lasting 4-7 days
- Prodromal phase malaise, fever, anorexia
- Classic triad (the '3-Cs'):
- Conjunctivitis
- Cough (may be the final symptom to appear)
 Coryza
- Also possible photophobia, periorbital edema, and myalgias

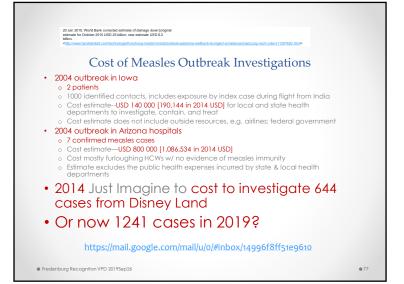
Fredenburg Recogniton VPD 2019Sep26



•75









'Epidemic parotitis' described by Hippocrates in 5th century BC

MMR and Autism

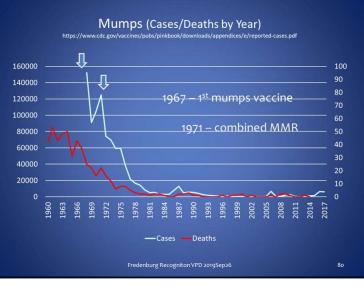
- 1998 Lancet publishes article by Andrew Wakefield linking MMR with regressive autism and bowel disease, "new syndrome"
- January 2011 BMJ published 3 articles/editorials charging Wakefield's study not just bad science but "an elaborate fraud"

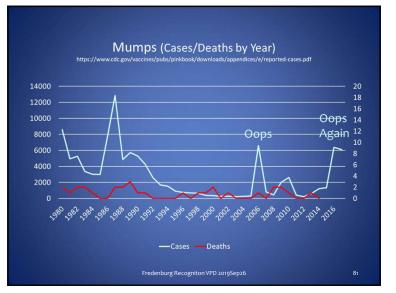


- None of the 12 patients in the study were "free of misreporting or alteration"
- 2003 to 2004 vaccination rate of 80% has now recovered slightly in the United Kingdom
- measles epidemic was also declared in England and Wales in 2008

Deborah Brauser. Autism and MMR Vaccine Study an 'Elaborate Fraud,' Charges BMJ.

Fredenburg Recogniton VPD 2019Sep26





Mumps 2006 Factors Contributing to Outbreak

- College campus environment
- Lack of a 2-dose MMR college entry requirement or lack of enforcement of a requirement
- Delayed recognition and diagnosis of mumps
- Mumps vaccine failure
- Vaccine might be less effective in preventing asymptomatic infection or atypical mumps than in preventing parotitis
- Waning immunity



Vaccine waning and mumps re-emergence in the United States.

Lewnard JA and Grad YH. Sci Transl Med. 2018 Mar 21; 10(433): eaao5945. doi: 10.1126/scitranslmed.aao5945

- Loss of immunity
 - Now estimated that vaccine-derived immune protection against mumps wanes on average 27 years (95% confidence interval: 16 to 51)
 - Peak of recurrence in adolescents and adults
- Emergency of heterologous virus genotypes changing vaccine effectiveness appears unlikely
 - Re-emergence more likely to occur in younger children
- Mumps vaccine booster at 18 yo or throughout adulthood possible solution to waning immunity

Mumps Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes



- Viremia 12-25 days after
 exposure with spread to tissues
 - Multiple tissues infected during viremia

Fredenburg Recogniton VPD 2019Sep26

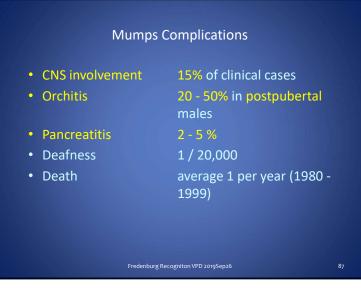
Mumps Clinical Features

- Incubation period 14-18 days
- Nonspecific prodrome of myalgia, malaise, headache, low-grade fever
- Parotitis in 30%-40%
- Up to 20% of infections asymptomatic





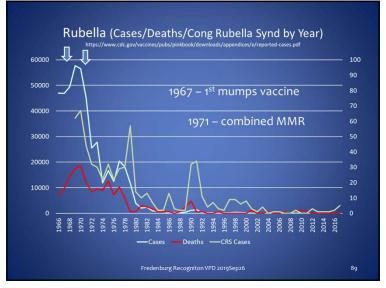
redenburg Recogniton VPD 2019Sej

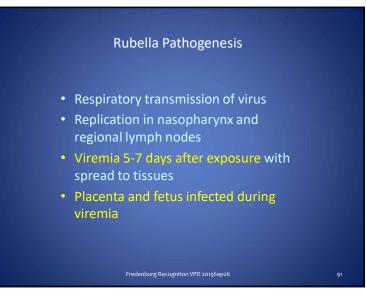


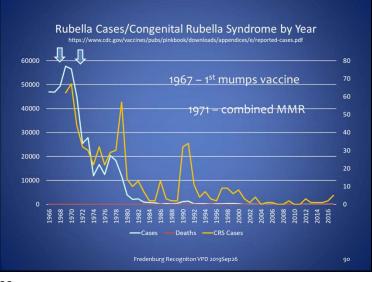


Rubella

Latin 'little red', or 3rd disease (initially thought a possible variant of measles or scarlet fever), then 1814 'German measles'







<section-header><section-header><list-item><list-item><list-item><list-item><list-item>

Rubella Complications

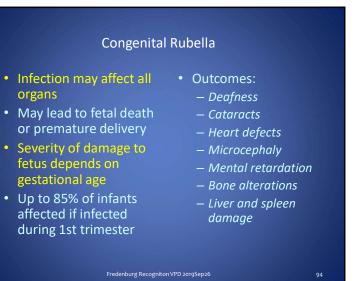
ı A	rthralgia or arthritis adult female children	up to 70% rare	
ı Tl	hrombocytopenic purpura	1 / 3000 cases	
ı Ei	ncephalitis	1 / 6000 cases	
ı N	euritis	rare	
ı O	rchitis	rare	
	Fredenburg Recogniton VPD 2019Sep26		93

Congenital Rubella Blueberry Muffin generalized hemorrhagic purpuric eruptions that on histopathology showed dermal erythropoiesis (TORCH)





Cataracts secondary to congenital rubella



94

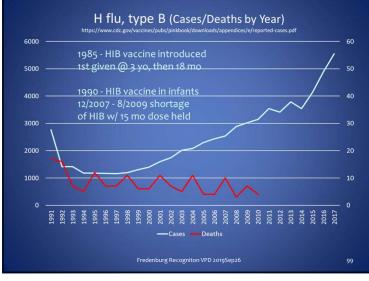
Rubella Epidemic - United States, 1964 - 1965

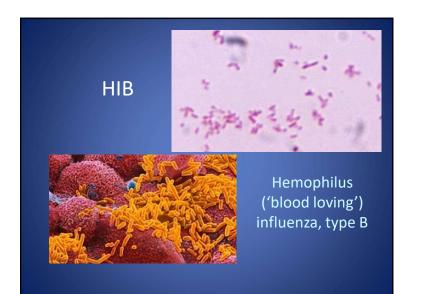
- 12.5 million rubella cases
- 2,000 encephalitis cases
- 11,250 abortions (surgical/spontaneous)
- 2,100 neonatal deaths
- 20,000 CRS cases
 - deaf 11,600
 - blind 3,580
 - mentally retarded 1,800

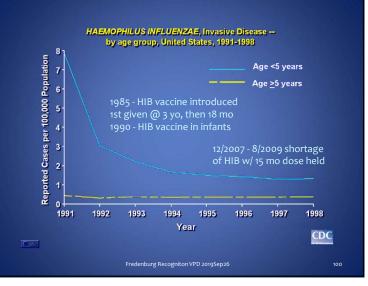
MMR/Rubella Vaccination During in Pregnancy Outcomes 1971-1989

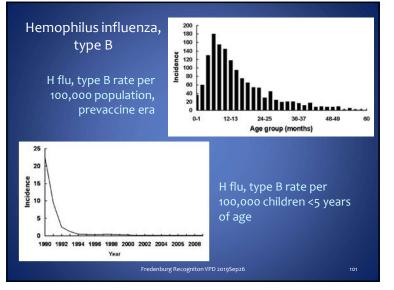
- 321 women received rubella vaccine during pregnancy or near the estimated time of conception
- 324 live births
- No observed CRS
- 95% confidence limits 0%-1.2%

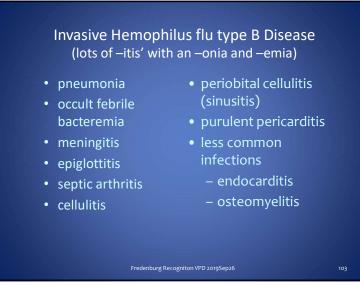
97











HIB Transmission and Risk Groups

- Transmission direct contact with respiratory droplets from nasopharyngeal carrier or case patient
- Risk Groups:
 - infants and young children
 - household contacts
 - day-care classmates
 - American Indian/Alaska Native populations

redenburg Recognition VPD 2019Sep

102

104

Epiglotitis

High fever, toxic appearance, drooling, dysphagia, muffled voice, inspiratory retractions, soft stridor



Complications of Sinusitis



Complications (due to contiguous spread)

 Orbital preseptal / orbital cellulitis

(from ethmoid) Osteomyelitis o

the frontal bone (Pott's puffy tumor) (from frontal sinus)

Occasionally cheek cellulitis (from maxillary)



Fredenburg Recogniton VP

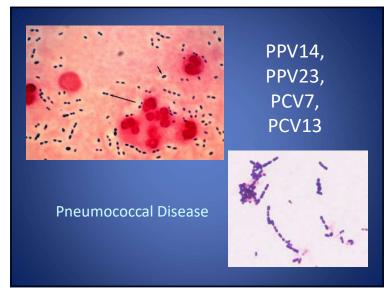
105

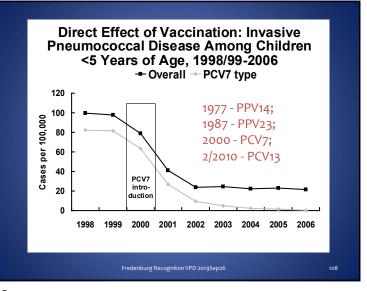
Sequelae of H flu type B Disease

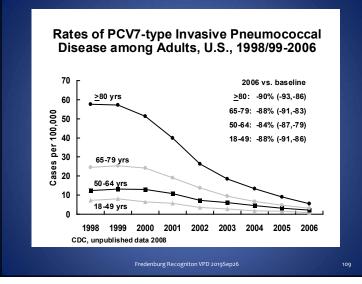
- 3%-6% of cases are fatal
- up to 20% of surviving patients have permanent hearing loss or other long-term sequela per CDC estimate

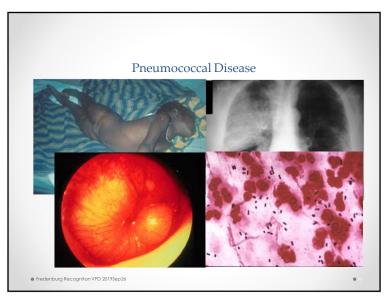
- BU1

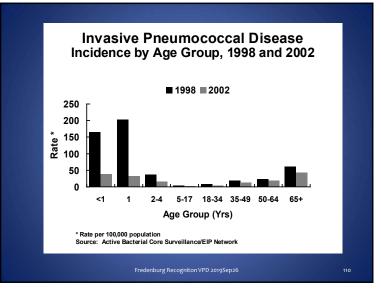
- 2009 2010 literature review 1433 children (1970 to 2010) survivors of childhood bacterial meningitis
 - 705 (49.2%) have 1 or more long-term sequelae
 - 455 (45.0%) behavioral and/or intellectual disorders
 - 68 (6.7%) hearing changes
 - 145 (14.3%) gross neurologic deficits

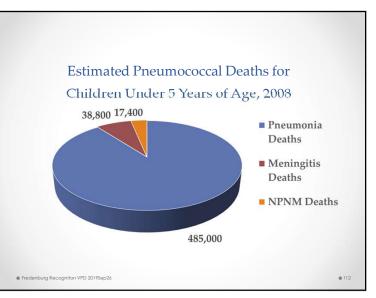




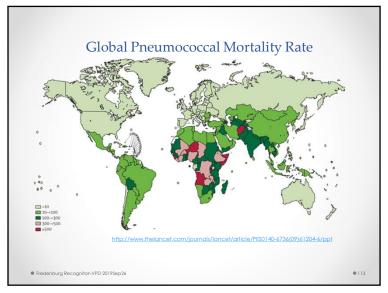




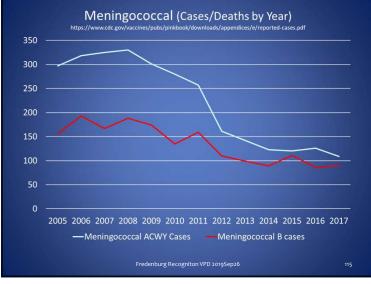




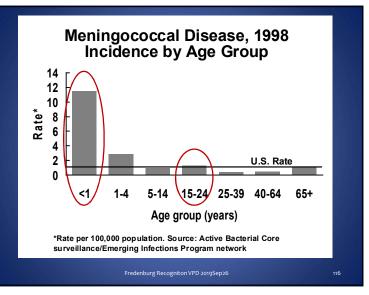












Meningococcal Disease in the United States

- Distribution of cases by serogroup varies by time and age group
- In 1996-2001:
 - 31% serogroup B
 - 42% serogroup C
 - 21% serogroup Y
 - 65% of cases among children younger than 1 year of age caused by serogroup B

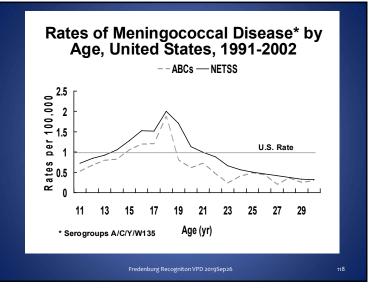
Fredenburg Recogniton VPD 2019Sep26

• Quadrivalent vaccines - only A, C, Y, W-135

117

Meningococcal Disease Among Young Adults, United States, 1998-1999

•	18-23 years old	1.4 / 100,000	
•	18-23 years old not college student	1.4 / 100,000	
•	Freshmen	1.9 / 100,000	
	Freshmen in dorm	5.1 / 100,000	
	Bruce et al, <i>JAMA</i> 2001;286;688-93		
	Fredenburg Recogniton VPD 2019Sep26		11

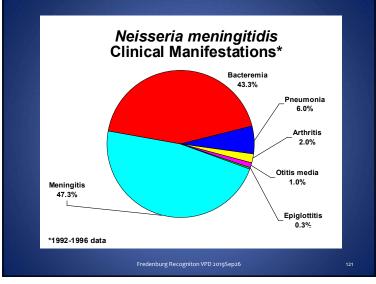


118

Meningococcal Pathogenesis & Clinical Features

- Organism colonizes nasopharynx
- In some persons organism invades bloodstream and causes infection at distant site
- Antecedent URI may be a contributing factor
- Incubation period 3-4 days (range 2-10 days)
- Abrupt onset of fever, meningeal symptoms, hypotension, and rash
- Fatality rate 9%-12%; up to 40% in meningococcemia

Fredenburg Recogniton VPD 2019Sep26

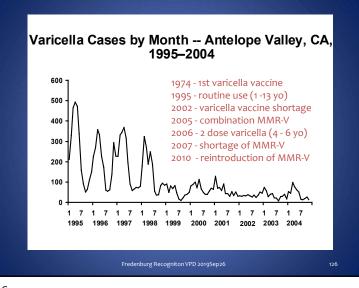


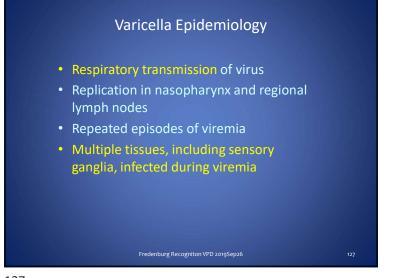
<section-header><section-header><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><table-row>

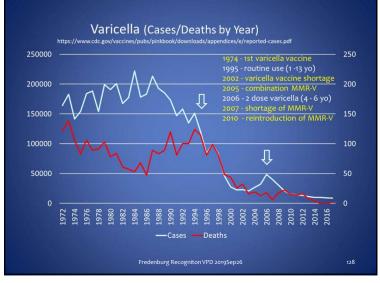














129

Varicella Clinical Features

- Incubation period 14-16 days (range 10-21 days)
- Mild prodrome for 1-2 days
- Rash generally appears first on head; then most concentrated on trunk
- Successive crops over several days with lesions present in several stages of development



Fredenburg Recogniton VPD 2019Se

130

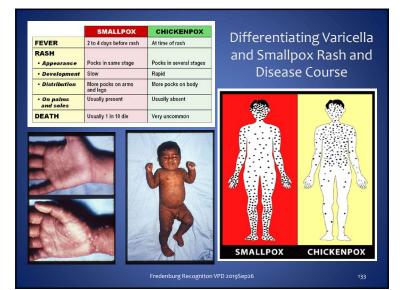
130



132

Varicella Complications

- Bacterial super-infection of skin lesions
- Pneumonia (viral or bacterial)
- Central nervous system manifestations postvaricella cerebellitis/encephalitis)
- Reye's syndrome (ASA)
- Hospitalization: 2-3 per 1,000 cases
- Death: 1 per 60,000 cases
- Postherpetic neuralgia (complication of zoster)



Varicella Vaccine Efficacy - AAP Report 2007 • 1 dose schedule, from 1997 to 2005 vaccinations increased

from 27% to 88% (1 - 4 year olds)

71% - 84% decrease in varicella cases
88% decrease in hospitalizations
92% decrease in deaths

immunized and unimmunized children)

and 1-vaccine eras

- 80 - 85 % prevention of disease of any severity

100% efficacy for prevention of severe disease
70% less hospitalizations in < 20 year olds, also 65% less hospitalizations in 20 + year olds between the pre-vaccination

• Peak age shifted from 3-6 years old to 9-11 years old (both

• 2 dose varicella vaccine (99% of children protective antibody)

Fredenburg Recogniton VPD 2019Sep26

- 98% prevention of any varicella disease (94% - 1 dose)

133

Varicella Zoster Reactivation of varicella zoster virus

- Associated with:
 - aging
 - immunosuppression
 - intrauterine exposure
 varicella at younger than
 - 18 months of age

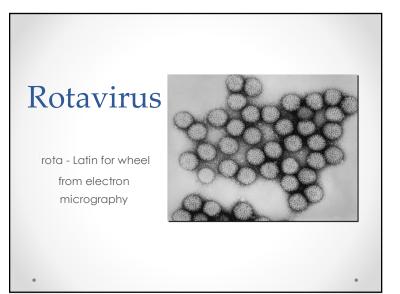




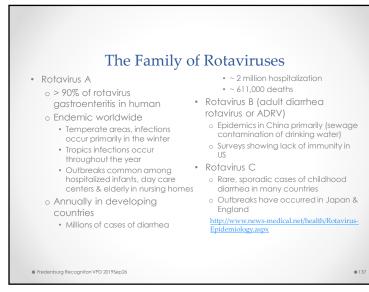
- Postherpetic neuralgia (PHN)
- Ophthalmic zoster
- Dissemination with generalized skin eruptions and involvement of the central nervous system, lungs, liver and pancreas

Fredenburg Recogniton VPD 2019Sep26

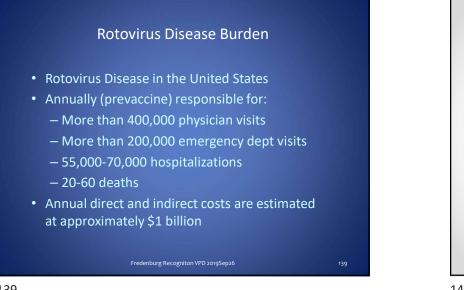
134

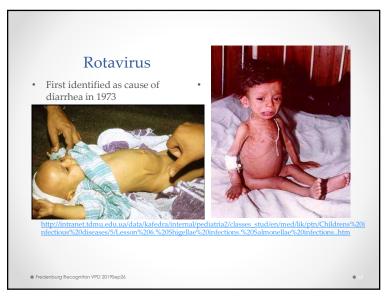


136

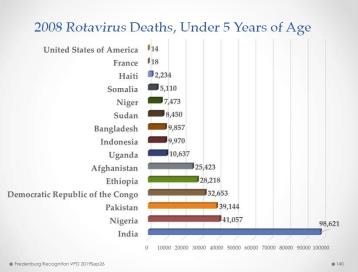




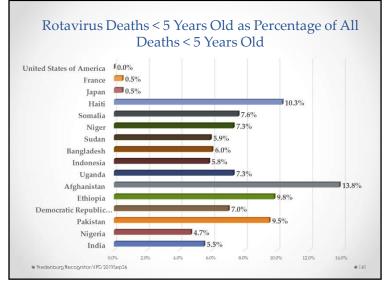


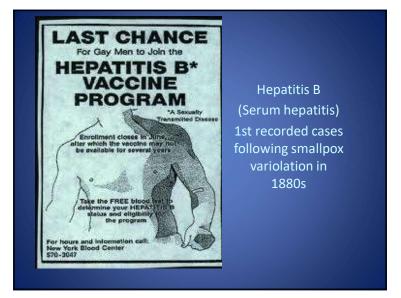


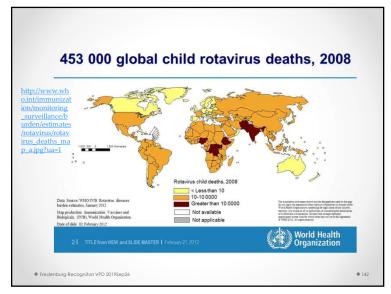


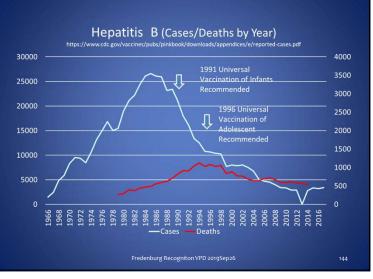


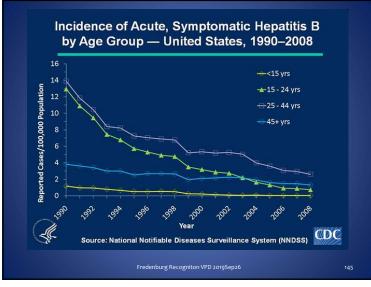












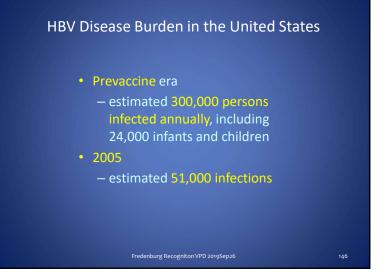
145

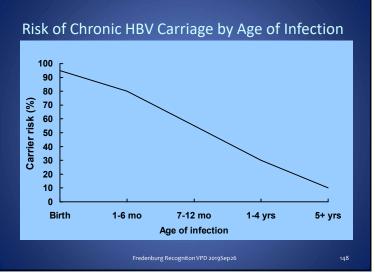
Clinical Features / Complications of Hep B

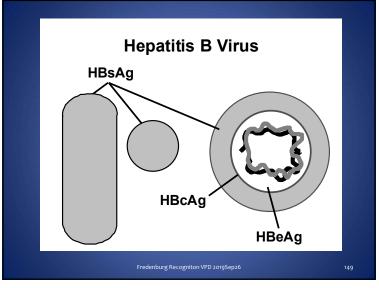
- Incubation period 60-150 days (average 90 days)
- Nonspecific prodrome of malaise, fever, headache, myalgia
- Presenting symptoms not specific for hepatitis B
- At least 50% of infections asymptomatic
- Complications

 - Hospitalization
 - Cirrhosis
 - Hepatocellular carcinoma
 - Death







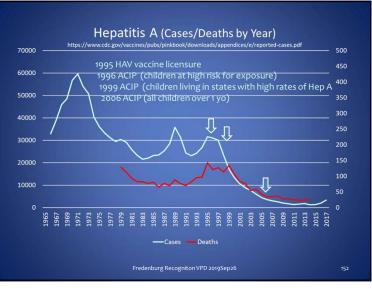


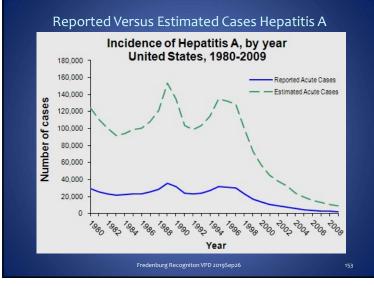
149



Hepatitis A Epidemic/infectious jaundice, 1st described by Hippocrates in 5th century BC Hepatitis B Perinatal Transmission (in absence of postexposure prophylaxis)

- If mother positive for HBsAg (surface antigen) and HBeAg (produced when virus is actively replicating)
 - 70%-90% of infants infected
 - 90% of infected infants become chronically infected
- If positive for HBsAg only
 - 5%-20% of infants infected
 - 90% of infected infants become chronically infected



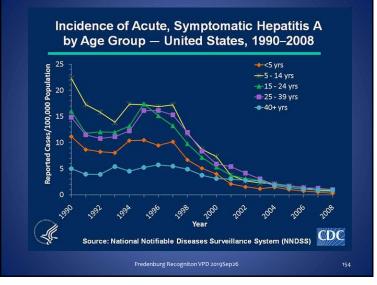


153



- Entry into mouth (fecal-oral transmission)
- Viral replication in the liver
- Virus present in blood and feces 10-12 days after infection
- Virus excretion may continue for up to 3 weeks after onset of symptoms
- Incubation period 28 days (range 15-50 days)
- Illness not specific for hepatitis A
- Likelihood of symptomatic illness directly related to age
- Children generally asymptomatic, adults symptomatic

Fredenburg Recogniton VPD 2019Sep26



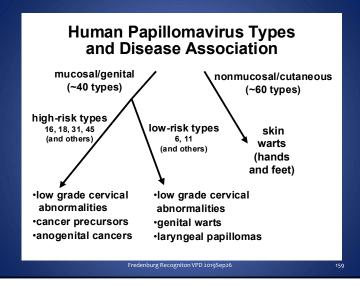


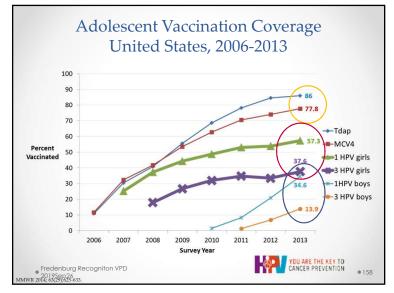
Human Papillomavirus (HPV)

- Tumors of the skin and mucous membranes
- > 100 HPV types known
- People with multiple sexual partners; who already have persistent HPV infection are at increased risk for acquiring additional HPV strains
- 2 main clinical categories:
 o Anogenital or mucosal
 - Nongenital cutaneous



Fredenburg Recogniton VPD 2019Sep26







HPV Associated Disease			
Туре	Women	Men	
16/18	70% of Cervical Cancer	70% of Anal Cancer	
	70% of Anal/genital Cancer	Transmission to women	
	Transmission to men		
6/11	90% of Genital Warts	90% of Genital Warts	
	90% of RRP lesions	90% of RRP lesions	
	Transmission to men	Transmission to women	
	Fredenburg Recogniton VPD 201	9Sep26 160	

HPV Clinical Features

- Most HPV infections are asymptomatic and result in no clinical disease
- Clinical manifestations of HPV infection include:
 - anogenital warts
 - recurrent respiratory papillomatosis (RRP)
 - cervical cancer precursors (cervical intraepithelial neoplasia)
 - cancer (cervical, anal, vaginal, vulvar, penile, and some head and neck cancer)

Fredenburg Recogniton VPD 2019Sep26

HPV Disease Burden

- Anogenital HPV is the most common sexually transmitted infection in the US
 - Estimated 20 million currently infected
 6.2 million new infections/year
- Common among adolescents and young adults





Estimated 80% of sexually active women will have been infected by age 50 Infection also common in men

Fredenburg Recogniton VPD 2019Sep26

162

Laryngeal Papillomatosis



A 48-year-old woman presents with inspiratory stridor, dyspnea, and hoarseness. On direct laryngoscopy, extensive respiratory papillomatosis were diagnosed as the cause of her symptoms.

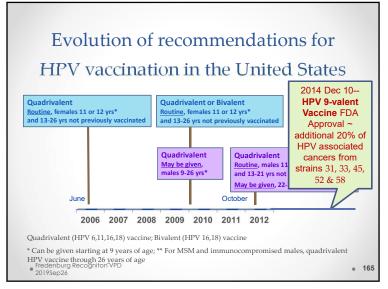
Endoscopy reveals the characteristic wart-like lesions of laryngeal papilloma. JORRP is more common and more severe than AORRP. JORRP is caused by exposure to HPV during the peripartum period.



Fredenburg Recogniton VPD 2019Sep26

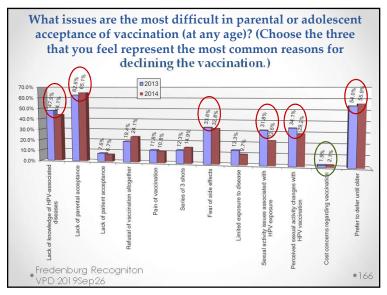
Laryngeal Papillomatosis

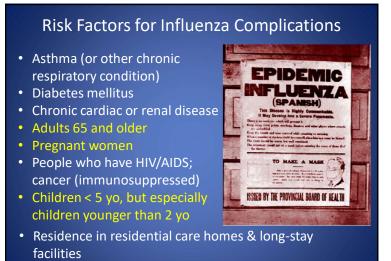
- HPV 6, 11, 16 implicated, with substantial percentage of mothers having a history of genital condylomata at delivery
- Age of onset usually 2-4 yo, but as late as juvenile onset documented, younger age worse prognosis
- Symptoms include hoarseness, voice changes, croupy cough, stridor
- Diagnosis by direct laryngoscopy
- Prevention by HPV vaccine
- Treatment by direct surgical resection (recurrences are the rule), tracheostomy occasionally required
- Spontaneous remissions do occur











Fredenburg Recogniton VPD 2019Sep26

Hospitalizations for cardiopulmonary conditions in excess of the expected:

- 104 per 10,000 children per year infants < 6 mo
- 50 per 10,000 per year infants 6-12 mo
- 19 per 10,000 per year children 1-3 yo
- 9 per 10,000 per year children 3-5 yo
- 4 per 10,000 per year 5-15 yo
- For every 100 children, ~ 6-15 outpatient visits & 3-9 courses of antibiotics were attributable to influenza
- In winter, 10-30% of the excess* number of courses of antibiotics occurred while influenza virus present

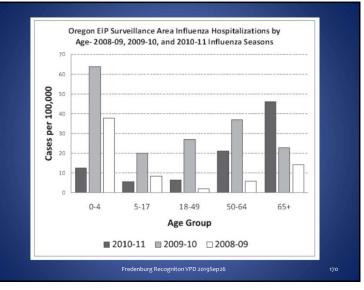
Fredenburg Recogniton VPD 2019Sep26

*above baseline

169

Impact of Childhood Influenza Vaccination on Adult Disease

- targeting school children during influenza vaccine shortages rather than directing resources at high risk adult individuals may be more effective in limiting disease in the entire population
- achieving a 20% influenza vaccination rate in children would reduce overall incidence in US by 46%, 80% vaccination rate would decrease total cases by 91%
- in another study vaccinating 20-25% of children under 19 with influenza vaccine had a protective effect on 8-18% of adults in the community over 35 years old

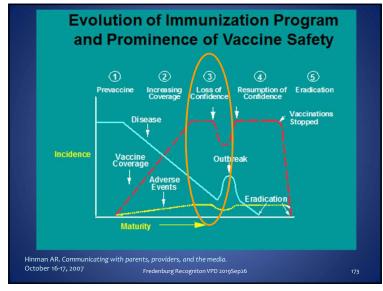


170

Why Vaccine Preventable Diseases Are Not Yet Prevented

- clinical recognition of once common vaccine preventable diseases - mumps, pertussis, measles
- modified illness due to vaccine varicella, pertussis
- vaccine shortage HIB booster, pneumococcal, flu
- inconsistent policies and funding of immunizations (e.g. Section 317 grants - discretionary funding)
- parent and clinician complacency varicella, pertussis
- Fear mongering is the disease or vaccine worse?
 So who are the better publicists?

Fredenburg Recogniton VPD 2019Sep26

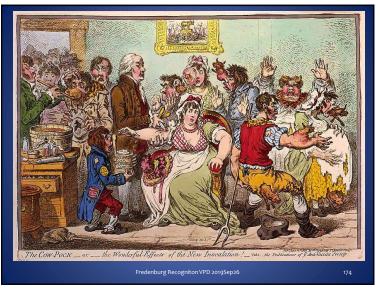


173

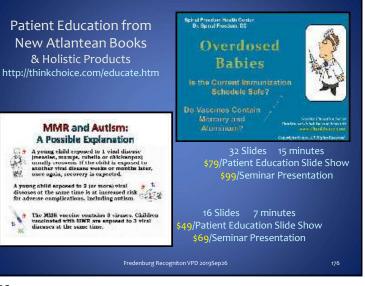
BMJ vs Andrew Wakefield*

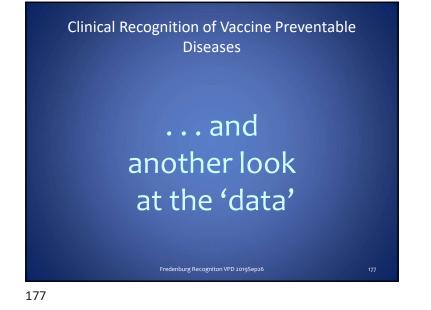
But how did a small case-control study like this set off such a panic in the first place? "I think a lot of people would like to know the answer to that," said Dr. Godlee [BMJ Editor-in-Chief Fiona Godlee, MD].

"I think Andrew Wakefield is a terrifically good publicist. He managed to convince his institution to run a press conference for this very small piece of research. The media attention for this grew, and concerns were raised with his subsequent publications."



174





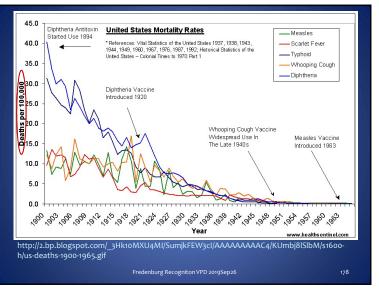
 "This [graph] shows that vaccines for measles, pertussis, and diphtheria all got introduced during the natural waning of the epidemics, making it impossible for me to conclude that the vaccine had any dramatic benefit. Child Health Safety has similar graphs referring to other vaccines."

Natural waning of epidemics, nope, not vaccines

- Don, on Blogger since May 2009
- Gender: Male
- Astrological Sign: Cancer
- Occupation: Nutritionist, Acupuncturist, Professor, Author, MA in Philosophy
- http://donmatesz.blogspot.com/2009/10/how-i-came-tovaccines.html

Fredenburg Recogniton VPD 2019Sep26

179



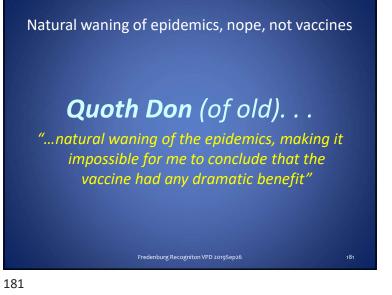
178

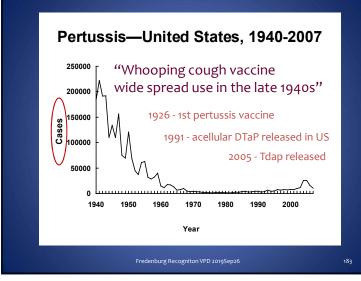
Current Evolution of Don Matesz, Author

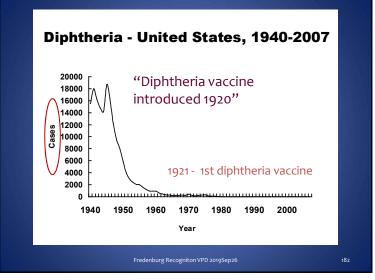


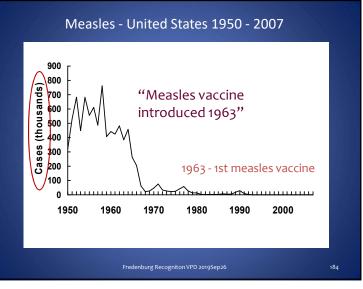
180

- Master's philosophy & Oriental medicine
- Certifications American Academy of Nutrition & International Association of Resistance Trainers
- Co-authored The Garden of Eating and was a presenter at the firstever Ancestral Health Symposium
- Author of the *Hypercarnivore Diet* (subtitle Eat Meat, Get Healthy. Plants Optional)
- Switched to a hypercarnivore diet in mid-2017 after decades of practicing and authoring books on plant-based diets to relieve his psoriasis and eczema (he's improved his skin, digestive health, and body composition dramatically)









Jenny McCarthy "I do believe sadly it's going to take some diseases coming back to realize that we need to change and develop vaccines that are safe. If the vaccine companies are not listening to us, it's their f#@&king fault that the diseases are coming back. They're making a product that's s#&t. If you give us a safe vaccine, we'll use it. It shouldn't be polio versus autism."

"Would you trust this woman to give you sound medical advice?" http://www.emagill.com/rants/eblogo77 .html



burg Recogniton VPD 2019Sep26

185

