### <u>THE VACCINE CRISIS</u> PREPARE FOR BACK TO THE FUTURE

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### PHYSICIAN Well Being SYMPOSIUM

#### SATURDAY OCTOBER 19

ATLANTIS COUNTRY CLUB 190 Atlantis Blvd, Atlantis, FL 33462 A 2019 Medscape survey finds physician burnout rate at 44% with 15<sup>th</sup> percent saying they experienced depression. PBCMS is committed to addressing the impact of burnout on physicians.

Join us and participate in sessions on what physicians, hospitals, medical schools and health care providers can do to combat burnout and promote well being.

#### TIME: 8:00 AM - 3:00 PM

#### \$35/Members • \$50 Non Members www.pbcms.org or call 561.433.3940

#### AGENDA

U.S. Department of Veterans Affairs

8:00 am	Registration & Continental Breaktast	
8:15 am	Welcome & Opening Remarks	Shawn Baca, MD, Chair, Physician Wellness Committee
8:30 am	Prevention & Treatment of Physician Burnout	Rebekah Bernard, MD
9:15 am	Promoting Physician Wellness through Health System Change	Kevin Taylor, MD AMA Steps Forward
10:00 am	Break	
10:15 am	PANEL – Creating an Organizational Foundation for Physician Wellness	James Goldenberg, MD - Moderator
11:00 am	PANEL - Medical Student & Resident Well Being - Creating a Positive Future for the Next Generation	Michelle Lizotte-Waniewski, PhD - Moderator
11:45 am	Physicians Heal Thyself – Building Resiliency	Bruce Saltz, MD
12:30 am	Lunch	
1:00 pm	Prevention of Medical Errors	The Doctors Company Robin L. Wessels, MBA, BSN, RN, CPHRM
3.00 nm	Adjourn	

CME/CEU provided by West Palm Beach VA Medical Center

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# PREVENTION OF INFECTIOUS DISEASES

The World was Changed by.... SANITATION & IMMUNIZATION

# Determining Development (what makes a country <u>3<sup>rd</sup> world ?</u>)

- To determine a country's development, these statistics are usually considered by the United Nations
- 1. GDP (Gross Domestic Product)
- 2. Life Expectancy
- 3. Literacy Rate
- 4. Education
- 5. Healthcare System

# Life Expectancy

Is the average age a person usually lives.
 (Infant mortality rate plays a great role)



# Healthcare System

# The <u>Prevention</u>, treatment, and management of illnesses





### **Growth in More, Less Developed Countries**

#### Billions



Source: United Nations, World Population Prospects: The 2004 Revision (medium scenario), 2005.

© 2006 Population Reference Bureau

# The global air network





# Immune System

functional system
 rather than organ
 system
 Hematopoetic
 Vasculature
 Lymphatic



# Innate vs. Adaptive Immune System – Introduction

- Innate: structural defenses; responds to <u>nonspecific</u> foreign substances
  - □ First line: external surface epithelium & membranes
  - Second line: inflammatory processes antimicrobial proteins, phagocytes, etc.





# Innate vs. Adaptive Immune System – Introduction

Adaptive: responds to <u>specific</u> foreign substances



Innate & adaptive mechanisms work together

## Adaptive Defenses: Characteristics

- Specificity: directed at specific targets
- Systemic: not restricted to initial site of infection / invasion
- Memory: after initial exposure & activation, a more rapid & more vigorous response is made to subsequent exposures to pathogens

   (secondary response)



Figure 21.11



### Vaccination is an attempt to generate immunological memory without disease pathology

- Memory is induced through immune recognition of vaccine antigens.
- Immune memory allows an accelerated humoral and cellular responses if the vaccine antigen is re-encountered.
- Immune recognition leads to:
  - Neutralization of the infectious agent before it can enter cells
  - · Destruction of infected cells before they multiply
  - Suppression of the spread of the infectious agent to other cells

### Brief History of Immunization

- Chinese noticed children who recovered from smallpox did not contract the disease again
- They infected children with material from a smallpox scab to induce immunity

### - This process known as variolation

 Variolation spread to England and America but was stopped because of risk of death

### Brief History of Immunization

- 1796 Edward Jenner discovered process of vaccination
- 1879 Louis Pasteur developed a vaccine against *Pasteurella multocida*
- Antibody transfer developed when it was discovered vaccines protected through the action of antibodies

Concerns about the safety of vaccines appeared early and often



Figure 1 | The Cow-Pock. The Cow-Pock or the Wonderful Effects of the New Inoculation! by James Gilray was published in England in 1802 by the Anti-Vaccine Society. The etching, which shows Edward Jenner among patients in the Small Pox and Inoculation Hospital at St Pancras (London), suggests the transformation into cows of individuals vaccinated by Jenner. Reproduced with permission from The Wellcome Library, London.



# WHAT TYPES OF VACCINES ARE THERE ?

Immunisation Department, Centre for Infections





#### attenuated strains which replicate in host

attenuation means the virus or bacterium has been weakened to reduce virulence so it cannot cause disease in healthy people

#### act like natural infection

live vaccines are the closest to actual infection and therefore elicit good, strong, long-lasting immune responses

### Live vaccines



#### **Advantages**

- •Single dose often sufficient to induce long-lasting immunity
- •Strong immune response evoked
- •Local and systemic immunity produced

#### **Disadvantages**

- •Potential to revert to virulence
- •Contraindicated in immunosuppressed patients
- Interference by viruses or vaccines and passive antibody
- Poor stability
- Potential for contamination

### **Inactivated vaccines**



#### Either:

#### suspensions of whole intact killed organisms

e.g. whole cell pertussis, influenza, rabies, HepA

#### Or:

#### acellular and sub-unit vaccines

contain one or a few components of organism important in protection

e.g. acellular pertussis vaccine contains between 2-5 components of the whole cell pertussis bacteria

e.g. diphtheria toxoid

e.g. Hib polysaccharide

### **Inactivated vaccines**



#### **Advantages**

•Stable

- Constituents clearly defined
- •Unable to cause the infection

#### **Disadvantages**

Need several doses
Local reactions common
Adjuvant needed
keeps vaccine at injection site
activates antigen presenting cells
Shorter lasting immunity

### **Currently Used Viral Vaccines**

Table 36-2.	Current	viral	vaccines	(2000).
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Usage	Vaccine	Live Virus, Killed Virus, or Subunit of Virus		
Common	Measles Mumps Rubella Varicella (chickenpox) Rotavirus Polio	Live Live Live Live Live Both <sup>1</sup>		
	Influenza Hepatitis A Hepatitis B Rabies	Killed Killed Subunit <sup>2</sup> Killed		
Special situations	Yellow fever <sup>3</sup> Japanese encephalitis <sup>3</sup> Adenovirus <sup>4</sup> Smallpox <sup>4</sup>	Live Killed Live Live		

<sup>1</sup>Both live and killed vaccines are used in the United States.

<sup>2</sup>Recombinant vaccine contains HBV surface antigen only.

<sup>3</sup>Used when traveling in endemic areas.

<sup>4</sup>Used for military personnel.

# Advantages/disadvantages of live and killed vaccines

Characteristic	Live Vaccine	Killed Vaccine
Duration of immunity	Longer	Shorter
Effectiveness of protection	Greater	Lower
Immunoglobulins produced	IgA <sup>1</sup> and IgG	lgG
Cell-mediated immunity produced	Yes	Weakly or none
Interruption of transmission of virulent virus	More effective	Less effective
Reversion to virulence	Possible	No
Stability at room temperature	Low	High
Excretion of vaccine virus and trans- mission to nonimmune contacts	Possible	No

Table 36-1. Characteristics of live and killed viral vaccines.

<sup>1</sup> If the vaccine is given by the natural route.

### Conjugation



•Some bacteria (e.g. Haemophilus influenzae type b, Neisseria meningitidis, Streptococcus pneumoniae) have an outer coating of sugar molecules (called polysaccharides)

•Polysaccharide coatings make it difficult for a baby or young child's immature immune system to see and respond to the bacterium inside

•Polysaccharide vaccines are poorly immunogenic in children under 2 years old and do not stimulate long term immunological memory

•Conjugate vaccines have enabled us to effectively protect children against Hib, Men C and pneumococcal diseases

### Conjugation





Carrier protein

Polysaccharide linked to carrier protein

Conjugation is the process of attaching (linking) the polysaccharide antigen to a protein carrier (e.g. diphtheria or tetanus) that the infant's immune system already recognises in order to provoke an immune response

### Advantages of Successful Conjugate Vaccines

Property	Polysaccharide	Conjugate
B-cell-dependent immune response	Yes	Yes
T-cell–dependent immune response	No	Yes
Immune memory	No	Yes
Lack of hyporesponsiveness	No	Yes
Booster effect	No	Yes
Long-term protection	No	Yes
Reduction of carriage	No	Yes
Herd protection	No	Yes

Adapted from Granoff DM, et al. In: Vaccines. 2004: 959.

### **Combination Vaccines**



•Many vaccines are combined to make it easier to give several vaccines at one time

•Combination vaccines reduce both number of clinic visits and number of injections needed

•Before combination vaccines are licensed, studies are carried out to ensure that:

- the immune response to any of the combined antigens is just as good as the response to the individual vaccines

- the rates of adverse reactions are the same as they would be if the vaccines were administered separately

### **RECOMBINANT VACCINES – DNA and ANTIGENS**



PEPTIDE VACCINES MADE OF PROTEIN ANTIGENS that have been PRODUCED In a HETEROLOGOUS EXPRESSION SYSTEM (E.G., BACTERIA OR YEAST)

The VACCINEE PRODUCES ANTIBODIES to the protein antigen providing Protection against the Pathogen

#### **DOWNSIDE of RECOMBINANT VACCINES**

- Time consuming and Expensive (\$\$\$\$) development
- Requires more skills (\$\$\$)
- More regulation to accept DNA products

### ADVISORY COMMITTEE on IMMUNIZATION PRACTICES ACIP



# ACIP (Advisory Committee on Immunization Practices)

- 15 voting members (appointed by DHH Secretary)
  - > 8 ex officio reps; 30 non-voting liaisons
  - ACIP recs become official CDC policy-signed by the CDC director, accepted by HHS Secretary, published in MMWR
- October 2010, evidence-based process GRADE
  - (Grading of Recommendations, Assessment, Development and Evaluation)
- ACIP recs:
  - Category A recommendation
    - For all persons in an age or risk factor based group
  - Category B recommendation
    - For individual clinical decision making

#### Table 1 Recommended Adult Immunization Schedule by Age Group United States, 2019

Vaccine	19–21 years	22–26 years	27–49 ye	ears	50-64 years	≥65 years		
Influenza inactivated (IIV) or Influenza recombinant (RIV)	1 dose annually							
Influenza live attenuated (LAIV)	1 dose annually							
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap, then Td booster every 10 yrs							
Measles, mumps, rubella (MMR)		1 or 2 doses depe	ending on indicat	tion (if born	in 1957 or later)			
Varicella (VAR)	2 doses (	if born in 1980 or later)						
Zoster recombinant (RZV) (preferred)					2 dc	oses		
Zoster live (ZVL)					1 d	ose		
Human papillomavirus (HPV) Female	2 or 3 doses depending on	age at initial vaccination						
Human papillomavirus (HPV) Male	2 or 3 doses depending on	age at initial vaccination						
Pneumococcal conjugate (PCV13)					1 d	ose		
Pneumococcal polysaccharide (PPSV23)	1 or 2 doses depending on indication 1 dose							
Hepatitis A (HepA)	2 or 3 doses depending on vaccine							
Hepatitis B (HepB)	2 or 3 doses depending on vaccine							
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains							
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication							
<i>Haemophilus influenzae</i> type b (Hib)	1 or 3 doses depending on indication							
	Becommended vaccination fr	ar adults who most ago requirement	at Decomm	and ad vaccing	tion for adults with an No	and the second states		

lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication No recommendation

### Table 2 Recommended Adult Immunization Schedule by Medical Condition and Other Indications United States, 2019 United States, 2019

Vaccine	Pregnancy	Immuno- compromised	HIV info CD4 c	ection ount	Asplenia, complement	End-stage renal	Heart or lung disease,	Chronic liver	Diabetes	Health care	Men who have
		(excluding HIV infection)	<200	≥ <b>200</b>	deficiencies	disease, on hemodialysis	alcoholism <sup>1</sup>	disease		personnel <sup>2</sup>	sex with men
IIV or RIV					1 dose annually						
LAIV		CONTRAII	NDICATE	D			PRECA	UTION		1 dose	annually
Tdap or Td	1 dose Tdap each pregnancy				1 dose Tdap, then Td booster every 10 yrs						
MMR	CONT	RAINDICATED			1 or 2 doses depending on indication						
VAR	CONTRAINDICATED				2 doses						
RZV (preferred)	DELAY							2 doses at a	age ≥50 yrs		
ZVL	CONT	RAINDICATED			1 dose at age ≥60 yrs						
HPV Female	DELAY	3 doses through age 26 yrs   2 or 3 doses through age 26 yrs									
HPV Male		3 doses through age 26 yrs				2 or 3 doses through age 21 yrs				2 or 3 doses through age 26 yrs	
PCV13		1 dose									
PPSV23							1, 2, or 3	doses dependin <sub>ễ</sub>	g on age and ind	lication	
НерА							2 0	r 3 doses depen	ding on vaccine		
НерВ							2 0	r 3 doses depen	ding on vaccine		
MenACWY		1 or 2 d	loses dep	pending	on indication, t	then booster eve	ery 5 yrs if risk r	emains			
MenB	PRECAUTION		2	or 3 dos	ses depending o	on vaccine and i	ndication				
Hib		3 doses HSCT <sup>3</sup> recipients only			1 d	ose					
Recommend who meet a documentat evidence of	mmended vaccination for adults meet age requirement, lack mentation of vaccination, or lack ence of past infection metation ence of past infection metation										
### Frequencies of some *scientifically proven* serious

#### reactions to vaccines

Vaccine	Reaction	Frequency
All	Anaphylaxis	1: 50,000-1,000,000
OPV	Paralytic polio	1:750,000 (first doses)
Measles	Thrombocytopenic purpura	1:22,300
Rotavirus (RotaSchild)	Intussusception	1:11,000
Mumps (Urabe Am 9)	Meningoencephalitis	1:10,000

#### THE CURRENT <u>'CLIMATE'</u> WE LIVE and WORK IN

PUBLIC'S PERSPRECTIVE

MEDICAL PROFESSIONAL'S RESPONSIBILITY



### MMR VACCINE and 'AUTISM'

#### The beginning of the autism scare

#### Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

> We have identified a chronic enterocolitis in children that may be related to neuropsychiatric dysfunction. In most cases, onset of symptoms was after measles, mumps, and rubella immunisation. Further investigations are needed to examine this syndrome and its possible relation to this vaccine.

#### NEWS

#### Downloaded from bmj.com on 16 March 2009

#### Wakefield tells GMC he was motivated by concern for children

#### Owen Dyer LONDON

The doctor at the centre of a major public health scare over vaccinations gave evidence this week before a General Medical Council panel, where he and two colleagues stand accused of research misconduct.

Andrew Wakefield, whose research paper and comments in 1998 linking the combined measles, mumps, and rubella (MMR) vaccine to autism led to a sharp fall in uptake of the vaccine, told the hearing that he was motivated by concern for autistic children.

He read out a letter that he had sent in 1997 to John Walker-Smith, now also accused of misconduct by the GMC, in which he wrote: "If these diseases are found to be linked to the MMR vaccine, these children are the few unfortunate who have been sacrificed to protect the majority."

In that letter he defended his involvement with solicitors acting on behalf of parents seeking compensation from vaccine manufacturers. Six years after the publication of a study linking measles virus to irritable bowel syndrome and autism (*Lancet* 1998;351:637-41), it emerged that 10 of 12 patients involved in the research had legal



Andrew Wakefield received more than £400 000 from the Legal Services Commission

aid backing to sue vaccine manufacturers and that the Legal Services Commission had funded his research (BMI2004:329:1293).

Dr Wakefield also received .£435643 (€550000; \$860000) from the commission in fees to investigate and write reports on the safety of the MMR vaccine—fees that were not disclosed in the *Lanest* paper. When the payments became known in 2004 the *Lanest* repudiated the paper, and its editor, Richard Horton, said that the journal was compromised by a "fatal conflict of interest."

Dr Wakefield denied that his research was

motivated by legal or financial reasons. \*The reason these parents were talking to me was nothing to do with the litigation, and litigation was not my primary concern."

He told the hearing that when he was approached by lawyers representing the families of autistic children he had consulted the BMA to ask what the "going rate" was. "They indicated that the fee was  $\pounds 150$  to  $\pounds 200$  an hour," he said. "I opted for the former of the two figures."

Dr Wakefield also disputed allegations that while at the Royal Free Hospital, London, he conducted invasive tests, including colonoscopies and lumbar punctures, not approved by the hospital's research ethics committee. Those tests were conducted for clinical, not research, purposes, he argued, and were beyond the remit of ethics approval.

Professor Walker-Smith, who is also facing the GMC panel accused of serious professional misconduct, decided which investigations were appropriate on the basis of clinical need, said Dr Wakefield.

A third consultant at Royal Free Hospital, Simon Murch, is also accused of participating in unapproved and unnecessary invasive procedures as part of the research. Professor Murch wrote to the *Lanat* in 2003 repudiating Dr Wakefield's claims about MMR vaccine, calling him "completely wrong." His testimony continues.

See EDITORIAL p729

#### Cessation of vaccination can increase disease incidence

#### **Reduced MMR Equals More Measles**

Reduced uptake of the MMR vaccine, fueled no doubt by anti-vaccine propaganda, has resulted in a recent <u>significant</u> <u>increase in Measles in the UK</u> as shown by the graph on the right. And despite what the anti-vaccine twits will tell you, Measles can be a very serious disease. According to the <u>CDC</u>:



As many as one out of 20 children with measles gets pneumonia, and about one child in every 1,000 who get measles will develop encephalitis. (This is an inflammation of the brain that can lead to convulsions, and can leave your child deaf or mentally retarded.) For every 1,000 children who get measles, one or two will die from it.

#### Early report

#### Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

#### Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3-10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rub vaccination in eight of the 12 children, with meas infection in one child, and otitis media in a All 1 children had intestinal abnormalities rangi from lymphoid nodular hyperplasia to noid u ration. Histology showed patchy chronic inflan tion in 11 children and reactive ilea perplasia in mpho seven, but no granulomas, Bel vioural diso s included autism (nine), disintegrative sy. sis (one), a ossible postviral or vaccinal encephalitis o). There were no focal neurological ab malities and and EEG tests were normal. Abno al laboratory results , are significantly raised urinary thylmal acid compared with age-03), low haemoglobin in four matched control (D= ar children. children. m IgA in

Internation e identical associated gastrointestinal discussion in a group of previously anaroma, d, which was generally associated in time, to possible environmental triggers.

Lancet 1995, 2**51:** 637–41 See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCs, A Anthony MB, J Linnell PhD, A P Dhillon MRCPath, S E Davies MRCPath) and the University Departments of Paediatric Gastroenterology (S H Murch MB, D M Casson MRCP, M Malik MRCP,

M A Thomson FRCP, J A Walker-Smith FRCP.), Child and Adolescent Psychiatry (M Berelowitz FRCPsych), Neurology (P Harvey FRCP), and Radiology (A Valentine FRCR), Royal Free Hospital and School of Medicine, London NW3 2QG, UK

Correspondence to: Dr A J Wakefield

#### Introduction

We saw several children who, after a pe of apparent normality, lost acquired skills, include nication. a COD They all had gastrointestinal mptoms, luding abdominal pain, diarrhoea, and some ating and, i cases, food intolerance. We d clinical f lings, cribe and gastrointestinal feature of these ch en.

#### Patients and methels

red to 12 children, cons department of a hi y of a pervasive paediatric gastre rology ed skills and intestinal developmental der with loss 100 amh in, bloating and food symptoms abdominal intolerance), were inv gated. All children were admitted to the ward f week, accomp ed by their parents.

#### hical investigations

took historic including details of immunisations and consure to infect us diseases, and assessed the children. In 11 cash the historic was obtained by the senior clinician (JW-S). Neuro, in bland psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.<sup>1</sup> Developmental locing included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

#### Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched previously.<sup>2</sup> Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid zones from cases to the state of the state of the state of the state of the state previously.<sup>2</sup> Chromatograms were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomyseal antibodies and boys were screened for fragile-X if this had not been done

#### THIMERSOL and NEURODEVELOPMENTAL DISORDERS

- Thimersol mercury-containing preservative
- Mercury bacteria convert to Methylmercury; enters food chain;
- neurotoxin effects
- Infants receive mercury from vaccines > EPA safety guidelines
- Thimersol contains Ethylmercury; much less accumulation
- Now NO Childhood Vaccine has Thimersol
- **META-ANALYSIS** of several epidemiologic studies

### **NO LINK TO AUTISM**

#### VACCINES and GUILLAIN-BARRE SYNDROME

- 1976 USA Swine Influenza Vaccine
- GBS risk 1 per 100,000 recipients
- 1981 2014 meta-analysis any influenza vaccine had 1 or 2 additional cases of GBS per 1 million vaccinees
- INFLUENZA infection is a STRONGER risk factor for GBS

### FLU VACCINATION 'DECREASES' RISK of GBS

### VACCINES and AUTOIMMUNITY

- Autoimmunity immune response directed against
   self-antigens
- Mechanisms present at birth prevent development of such responses
- Hepatits B Vaccine and Multiple Sclerosis –found NOT to bring on or exacerbate MS

### **ALUMINUM** in VACCINES

- Aluminum adjuvant to boost immune response
- e.g., Hepatitis A and B, Diphtheria-Tetanus, Hib, Pneumococcal
- Not in live viral vaccines, e.g., MMR, Varicella, Rotavirus, etc.
- Vaccinated children DO NOT demonstrate Aluminum levels in Toxic range
- Studies in Children found NO Correlation between infant blood or hair aluminum concentrations, vaccine history, and overall developmental status
- NO association with concerns for Macrophagic Myofasciitis

### TOO MANY VACCINES TOO SOON

**Childhood Schedule – 10 Vaccines against 14 Diseases** 

First few years of life – 26 Vaccine injections, as many as 5 at one time

**? Overwhelm the Immune System** 

**NO** – Proven that infants have the theoretical capacity to respond to at least 10,000 vaccines at ONE time

DO NOT cause long-lasting, gross alterations of immune system and NO increased risks of adverse health outcomes then or at a later time in life

# Hypothetical, **unproven**, associations between vaccines and health conditions with country of origin or originator (Andre F, Vaccine 2003)

Health condition	Vaccine incriminated	Origin
Neurological damage	DTPw	Scotland
Unexplained death	DTPw	Japan
Chronic fatigue syndrome	Hepatitis B	Canada
Sudden infant death	DTPw	France
Multiple sclerosis	Hepatitis B	France
Crohn's disease	MMR	UK
Autism	MMR	UK
Diabetes mellitus	Hib	US
AIDS	OPV	Hooper (reporter)
Mental retardation	Thiomersal	US
Autism		
Arthritis	Lyme	US
vCJD	Bovine serum	UK
Immune overload	Combinations	US

# SO DO THESE 'SHOTS' REALLY MAKE A DIFFERENCE ANYWAY ?

6

# Burden of Selected Vaccine-Preventable Diseases (VPDs)

VPD	Burden
Influenza	200,000 excess hospitalizations annually (>40% in the elderly) ~24,000 excess deaths annually (~90% elderly)
Invasive Pneumococcal Disease (IPD)	<ul> <li>~50,000 cases of bacteremia each year</li> <li>Higher rates in elderly and persons with comorbidities</li> <li>Case fatality rates ~20% (up to 60% in the elderly)</li> </ul>
Hepatitis B	<ul> <li>78,000 new infections annually (highest in young adults)</li> <li>1 million with chronic hepatitis B virus infections</li> <li>Complications include cirrhosis and hepatocellular carcinoma (80% of cases)</li> </ul>
Human Papillomavirus (HPV)	6.2 million new infections each year 2 HPV strains cause 70% of cervical cancer
Pertussis	10,454 cases reported in 2007 (3152 in adults) Most severe in infants *Source often older child or adult
Shingles	500,000 to 1 million cases annually; lifetime risk ~32% Shingles and postherpetic neuralgia increase with age

# Impact of Vaccines During the 20th Century and Into the 21st Century

Disease	Reported Cases (Year)	Reported Cases (2009)	% Decrease in Reported Cases
Diphtheria	5796 (1950)	0	100%
Tetanus	486 (1950)	18	96%
Pertussis	120,718 (1950)	16,858	86%
Measles	319,124 (1950)	71	≥99%
Mumps	152,209 (1968)	1991	99%
Rubella	46,975 (1966)	3	99%
Hepatitis A*	32,859 (1966)	1987	94%
Hepatitis B*	26,611 (1985)	3405	87%

\*Underreporting estimated at a factor of 4.3 for hepatitis A and 2.8 for hepatitis B thus actual number of cases likely substantially higher than reported numbers of cases.

CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases: The Pink Book; 2011.

Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm. Accessed June 15, 2011

Figure 17.1 Effect of immunization-overview



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### The "Vaccination Paradox" and public health

- As the pool of vaccinated individuals increases so does *herd immunity* (population protection due to a reduction in the reservoir of disease susceptible hosts) reducing disease even among the unvaccinated.
- As disease declines because of the efficiency of vaccination, the incidence of deleterious side effects becomes higher and the necessity for vaccination is questioned.

# Vaccination Rates Are Low

Vaccine	Vaccination Rate
Influenza Age 19-49, high risk Age 50-64, total Age ≥65 Healthcare workers (19-64 years old)	33.4% 40.1% 65.6% 52.9%
Pneumococcal Ages 19-64, high risk Age ≥65	17.5% 60.6%
Tetanus/pertussis since 2005 (19-64 years old)	50.8%
Shingles (60 years old and older)	10.0%
Hepatitis B (high risk, 19-49 years old)	41.8%
HPV vaccine (women, 19-26 years old)	17.1%

# Baseline Vaccination Rates vs Healthy People 2020 Goals: Gaps Persist

Vaccine and Target Group	Baseline Rate (Year)	Healthy People 2020 Goal
Influenza vaccine		
Noninstitutionalized adults 18 to 64 years old	25% (2008)	80%
Noninstitutionalized high-risk adults 18 to 64 years old	39% (2008)	90%
Noninstitutionalized adults 65 years old and older	67% (2008)	90%
Institutionalized adults 18 years old and older	62% (2006)	90%
Healthcare personnel	45% (2008)	90%
Pregnant women	28% (2008)	80%
Pneumococcal vaccine		
Adults 65 years old and older	60% (2008)	90%
High-risk adults under 65 years old	17% (2008)	60%
Institutionalized adults	66% (2006)	90%
Zoster vaccine		
Adults 60 years old and older	7% (2008)	30%
Hepatitis B vaccine		
Healthcare personnel	64% (2008)	90%

# Consumer Misconceptions About Vaccines

Category and Response	% of Respondents in Agreement
Vaccines and VPDs	
Had vaccines as a child—don't need them again	40%
Vaccines not necessary for adults	18%
Not concerned about catching VPDs	34%
Not concerned about spreading illness to others	32%
VPDs are not serious or life threatening	25%
Vaccine safety/efficacy	
Have heard vaccines are not safe	35%
Vaccines don't work	14%
A vaccine made them sick	25%

### Who Most Influences Adults' Decisions to Get Immunized?

	Ages 18-26	Age 65 and Older	All Adults
Personal physician	47%	82%	69%
Family member	33%	6%	19%
Celebrity physician, public figure, other	11%	4%	7%
None of the above	7%	6%	4%
No answer	2%	1%	1%

NFID. 2009 National Adult Immunization Consumer Survey: Fact Sheet. Available at: http://www.adultvaccination.com/doc/Survey\_Fact\_Sheet.pdf. Accessed June 15, 2011. AMA. American Medical News. Physicians asked to persuade adults to get immunized. Available at: http://www.ama-assn.org/amednews/2009/08/03/prsc0803.htm. Accessed June 13, 2011.

# Inclination to Get Vaccinated Is Higher if Physician Recommends

Physician Recommendation?	Impact on Vaccination
Yes	87% are very or somewhat likely to get vaccinated
Νο	55% would not get vaccine unless recommended by doctor



# **Influenza: Antigenic Drift and Shift**



# Past Antigenic Shifts: Pandemics in the 20th Century

Global

Deaths

- 1918 H1N1 Spanish Flu >50 million
- 1957 H2N2 Asian Flu 1-2 million
- 1968 H3N2 Hong Kong Flu 700,000



#### MOST FATAL EVENT **IN HUMAN HISTORY**

# WORLDWIDE FATALITIES: 50-100 MILLION

US FATALITIES: 675,000



# U.S. LIFE EXPECTANCY AT BIRTH

### WHAT KILLED INFLUENZA VICTIMS?





U. S. Army training camp and other military outbreaks were deadly but well studied medically/epidemiologically



6,000,000 DEATHS FROM INFLUENZA	INFLUENZA DAATH RATE IN ONTARIO
This is Estimate For World For Past 12 Weeks:	pincations as great as in the linited States centers. Toronacie dath rate is given as 327 per 100,000. Singston was the hardest his in Ormario, the rate being 644 per 100,000. Winnipeg suffered the most of any Canadian city, according to the figures now available. The death rate in that city was 744 per 100,000.
RECALLS BLACK DEATH 'Flu'' Five Times Deadlier Than World War.	The further of all it being 2.551 in the death rate of all it being 2.551 in the death rate of all it being 2.551 in the further, which cover an approxi- mate period of six weeks, are Duaths from Influence and Death Rate Complications, Rate Chiles, Chilaffy Fr 100,000 Fneumonia, Papulation.
LONDON, Dec. 19Canadian Press, via Reuter's.)-The Times' medical cor- respondent says that it memus reason- able to believe that about 6,000,000 per- sone perished from influenza pneumoria during the past 15 weeks. It has been estimated that the war caused the	le Sauk Ste. Marie 41 1- Ottawn 510 1- Ottawn 510 1- Port Arthur 510 1- Port Arthur 510 104 105 105 105 105 105 105 105 105
death of 20,000,000 persons in four and a half years. Thus, the correspondent points out, influenza has proved itself five times deadlier than war, pecause, in the same	Ay Hoston United States Figures Pirtsburg 12,647 Philadelphis 12,647 Washington 1,1644 Solution 1,1644





# SCHOOL CLASS, 1918





EXTENSIVE PUBLIC HEALTH EXPERIENCE WITH TB CONTROL HEAVILY INFLUENCED INFLUENZA PREVENTION EFFORTS IN THE U. S.

### Influenza: An Annual Epidemic

 5%-20%: Percentage of the US population that becomes ill with influenza each year<sup>1</sup>

15-60 million cases

- 3000-49,000: Range of estimated annual influenzarelated deaths<sup>1</sup>
  - Influenza and pneumonia: Eighth leading cause of death in the US (all ages)<sup>2</sup>
- 55,000-431,000: Range of estimated annual influenza-related hospitalizations<sup>3,4</sup>

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

Effectiveness of influenza vaccines in younger and older adults



Adapted from Monto AS, et al.<sup>1</sup>

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

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

# Number of Persons ≥65 Years of Age in the US, 1900-2030 (numbers in millions)



#### Influenza Immunization Rates:<sup>a</sup> Well Below *Healthy People 2010* Goals<sup>1,2</sup>



<sup>a</sup> All rates are for 2007-2008 influenza season, except 6-23 months of age and health-care personnel (2006-2007).

**References: 1.** CDC. *MMWR*. 2009;58(RR-8):1-52. **2.** Poland GA, et al. *Am J Med.* 2008;121(suppl 2):S3-S10.

#### **Staff Influenza Vaccination**



%Vaccinated %Declined %Neither

# FLU: Everyone 6 months & older needs flu vaccine every year



Even healthy people can get the flu, and it can be serious. Everyone 6 months and older should get a flu vaccine. This means you. This season, protect yourself-and those around you-by getting a flu vaccine.

http://www.flu.gov • 1-800-CDC-INFO

Get the facts. Get vaccinated.



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

CS233062-A

# Flu Prevention: Lots of Choices Which flu vaccine to give?



Morbidity and Mortality Weekly Report

August 23, 2019

Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2019–20 Influenza Season



#### Morbidity and Mortality Weekly Report

#### Weekly / Vol. 64 / No. 30

August 7, 2015



#### **INFLUENZA VACCINE MENU**

#### TABLE 1. Influenza vaccines — United States, 2019–20 influenza season\*

Trade name (Manufacturer)	Presentation	Age Indication	HA (IIVs and RIV4) or virus count (LAIV4) for each vaccine virus (per dose)	Route	Mercury (from thimerosal) (µg/0.5mL)
IIV4—Standard Dose—Egg based <sup>†</sup>					
Afluria Quadrivalent (Segirus)	0.25-mL PFS§	6 through 35 mos	7.5 μg/0.25 mL <sup>§</sup>	IM¶	_
	0.5-mL PFS <sup>§</sup>	≥3 yrs	$15 \mu g/0.5 m L^{\$}$		_
	5.0-mL MDV <sup>§</sup>	≥6 mos (needle/syringe) 18 through 64 yrs (jet injector)			24.5
Fluarix Quadrivalent (GlaxoSmithKline)	0.5-mL PFS	≥6 mos	15 μg/0.5 mL	IM¶	_
FluLaval Quadrivalent (GlaxoSmithKline)	0.5-mL PFS	≥6 mos	15 μg/0.5 mL	IM¶	_
	5.0-mL MDV	≥6 mos			<25
Fluzone Quadrivalent (Sanofi Pasteur)	0.25-mL PFS**	6 through 35 mos	7.5 μg/0.25 mL**	IM¶	—
	0.5-mL PFS**	≥6 mos	15 μg/0.5 mL**		_
	0.5-mL SDV**	≥6 mos			_
	5.0-mL MDV**	≥6 mos			25
IIV4—Standard Dose—Cell culture based (	ccIIV4)				
Flucelvax Quadrivalent (Segirus)	0.5-mL PFS	≥4 yrs	15 μg/0.5 mL	IM	_
	5.0-mL MDV	≥4 yrs			25
IIV3—High Dose—Egg based <sup>†</sup> (HD-IIV3)					
Fluzone High-Dose (Sanofi Pasteur)	0.5-mL PFS	≥65 yrs	60 μg/0.5 mL	IM¶	_
IIV3—Standard Dose—Egg based <sup>†</sup> with M	F59 adjuvant (allV3)				
Fluad (Seqirus)	0.5-mL PFS	≥65 yrs	15 μg/0.5 mL	IM¶	_
RIV4—Recombinant HA					
Flublok Quadrivalent (Sanofi Pasteur)	0.5-mL PFS	≥18 yrs	45 μg/0.5 mL	IM¶	_
LAIV4—Egg based <sup>†</sup>					
FluMist Quadrivalent (AstraZeneca)	0.2-mL prefilled single-use intranasal sprayer	2 through 49 yrs	10 <sup>6.5–7.5</sup> fluorescent focus units/0.2 mL	NAS	_





# UPDATE ON PNEUMOCOCCAL VACCINES





CSF showing meningitis caused by S. *pneumoniae* 

Photo Credit: Content Providers(s): CDC/Dr. M.S. Mitchell - This media comes from the <u>Centers for Disease Control and Prevention's Public</u> <u>Health Image Library</u> (PHIL), with identification number <u>**#1003**</u>



### Pneumococcal Pneumonia

- Estimated 175,000 hospitalizations in U.S.
- Up to 36% of adult-community acquired pneumonia and 50% of hospital acquired pneumonia
- Common complication (bacterial) of influenza and measles
- Case fatality rate 5-7%, much higher in elderly



Pneumonia of the right middle lobe

#### Pneumococcal Bacteremia

- More than 50,000 cases per year in the United States
- Rates higher among elderly and very young infants
- Case-fatality rate ~20%; up to 60% among the elderly



Septi Chek Blood Culture Bottles

### Pneumococcal Meningitis

- Estimated 3,000–6,000 cases per year in the United States
- Case-fatality rate ~30%, up to 80% in the elderly
- Neurologic sequelae common among survivors
- Increased risk in persons with cochlear implant



Photo courtesy of CDC

 Two Pneumococcal Vaccines: FDA Approved for Adults
Pneumococcal Polysaccharide vaccine (PSV 23- Pneumovax 23 by Merck)
Licensed for routine use in adults 50 & older and age 2–49 with certain risk factors

- Pneumococcal Conjugate vaccine (PCV 13-Prevnar by Pfizer)
  - FDA approved for use in adults age 50 and older in December 2011



**NOTE:** Prevnar 13 is NOT FDA approved for age 18 to 49!

Invasive Pneumococcal Disease: Risk is increased in immunocompromised adults MMWR Oct 12, 2012, 816-819.

\*\*Risk in immunocompromised -20 x than for those without high risk conditions\*\*

> June 2012: ACIP recommended routine PCV 13 conjugate for *immunocompromised adults*:

(off label use - not FDA approved for adults < 50)

This recommendation applies to

Immunocompromised , asplenic

• "High risk" immunocompetent (CSF leaks / cochlear implants)

\*\*Risk of invasive disease in older adults is 10 times higher than in younger adults \*\*

## CAPiTA

Community Acquired Pneumonia Immunization Trial in Adults

Randomized controlled trial of PCV 13
85,000 seniors: PCV 13 or placebo

> PCV 13 was effective!

 75% effective in preventing vaccine type invasive pneumococcal disease (IPD)

 45% effective in preventing vaccine type non bacteremic pneumonia (NBP)

### *Emergency* ACIP Meeting on August 13, 2014

> Purpose: vote on routine use for PCV 13 for all seniors

> VOTE: 13 to 2- in favor of **Routine** 

 V 13 vaccination for all age 65 /+ (in addition to PPSV 23)
> Based on strong quality evidence

#### Pneumococcal Vaccination: "Ground" RULES

PCV13 & PPSV23 should not be given at same visit.

> If need both, best to give PCV 13 first.

Only <u>single</u> dose PCV13 is recommended for adults.

> Only one PPSV 23 dose at / after age 65

## Age 65 Years or Older

• If PCV13 was given before age 65 years, no additional PCV13 is needed.



# Age 19-64 Years with Underlying Conditions







All about **Pertussis** (Whooping Cough)





#### Pertussis—United States, 1980-2010





**DEPARTMENT OF HEALTH AND HUMAN SERVICES** 

96

Tdap: A Family Affair (tetanus/diphtheria/pertussis)

- Pertussis = whooping cough
- Last 10 years surge in pertussis related deaths in infants
- Cocoon in a circle of familial protection
- Household members are to blame for up to 83% of transmission

Past: moms; now: siblings



# February 2012 ACIP Tdap for Adults: Universal Recs

- > Adults age 65 + had higher rates of hospitalization than those age 19-64
- Expand Tdap booster to ALL adults age 65 and older –not just those with close contact with infants

> Universal Tdap booster for ALL adults!

#### <u>Tdap and PREGNANCY</u>

#### AT *EACH* PREGNANCY : 3<sup>RD</sup> TRIMESTER ANTIBODIES PEAK AT 10 MONTHS DECAY AFTER 1 YEAR

#### **MATERNAL AB'S PASSED TO BABY**

PROTECTION FIRST FEW MONTHS OF LIFE (OFF LABEL RECOMMENDATION)





#### Guide to Tetanus Prophylaxis with TIG in Routine Wound Management

	Clean, minor wound		All other wounds*	
History of adsorbed tetanus toxoid-containing vaccines (doses)	DTaP, Tdap or Td <sup>†</sup>	TIG‡	DTaP, Tdap or Td <sup>†</sup>	TIG‡
Unknown or <3	Yes	No	Yes	Yes
≥3	No <sup>§</sup>	No	No¶	No

VACCINATE IF LAST DOSE <u>> 5 YEAR PRIOR (Tdap if > 7 yrs and none prior)</u> TETANUS RARELY OCCURS IN PERSONS DOCUMENTED PRIMARY SERIES

‡ People with HIV infection or severe immunodeficiency who have contaminated wounds (including minor wounds) should also receive

• Do not use antibiotics for prophylaxis against tetanus. Medical experts do not recommend antibiotic prophylaxis against tetanus. However, clinicians should observe wounds for signs of infection and promptly treated if they detect signs of infection.















Centers for Disease Control and Prevention

# **History of Zoster**

- Zoster: Greek for girdle
- Shingles: Latin (cingere) girdle
  Partial encircling of the trunk with rash



# First Cell Culture of Varicella-Zoster Virus (March 19, 1949)



Thomas Weller in Varicella-Zoster Virus, Cambridge Press 2000

# Zoster is Due to Reactivation of Varicella from the Nervous System



Adapted from Kimberlin and Whitley NEJM 2007
# Map of Dermatomes



Ophthalmic, thoracic, & cervical dermatomes most often affected by zoster

# Epidemiology of Zoster

- Annual rate is 3-4 cases per 1000 persons per year
- About 1 million cases in the US each year
- Rates appear to be increasing
- 30% of persons will develop zoster in their lifetime, 5% may get a second case

# **Risk Factors for Zoster**

- Age- the major risk factor for healthy persons (long duration since exposure to virus)
- Immune compromise- T cell immunity: transplant recipients, leukemia, lymphoma; HIV increases the risk up to 50 fold
- Age and immune compromise- reduced VZV-specific T cell immunity

# Cell-Mediated Immunity Declines with Age



From Plotkin et al Vaccines 2008; Data from Burke et al Arch Intern Med 1982

# Neurologic Complications of Zoster

- <u>Bell's palsy</u>: unilateral facial paralysis (reactivation in the VII cranial nerve)
- <u>Ramsay-Hunt syndrome</u>: pain and vesicles in the ear, numbness of the anterior tongue, and facial palsy (reactivation in the geniculate ganglion of the VII cranial nerve)
- Hearing impairment
- Motor neuropathy, transverse myelitis, meningitis, Guillain-Barre
- Stroke or TIAs (vasculitis of cranial arteries) during zoster, or months later



Taguchi J Infect 2011



Gilden et al NEJM 2002

# **Ocular Complications of Zoster**

 Eye disease involving any part of the eye (due to reactivation in the ophthalmic branch of the trigeminal ganglia):



 15% of zoster cases involve the eye Shaikh et al AFP 2002

- Can result in keratitis, uveitis, retinitis, glaucoma
- If eye involved, important to have ophthalmology consultation to determine if ocular therapy is needed



Photo/MN Oxman, University of California, San Diego

# Key Herpes Zoster Symptom Pain

# **Postherpetic Neuralgia**

- Pain persisting for at least one month (definitions vary) after the rash has resolved is termed postherpetic neuralgia (PHN)
- Pain may persists for months to years
- Neuron cell body and axon degeneration with scarring of ganglia
- More common in persons >50 years old
- Allodynia (sensation of pain after nonpainful stimuli)
- Paresthesias (burning, tingling)
- Dysesthesias (impaired sensation)
- Severe neuropathic pain

## **Risk Factors for Postherpetic Neuralgia**

- Age:
- -Risk of pain >30 days increases 15-fold for zoster patients >50 yo
- -PHN occurs in 25-50% of persons >50 yo
- -PHN rare in patients <40 yo
- Immune compromise is not a risk factor for PHN

# Frequency of Zoster and Zoster-Associated Pain



Kost and Straus, NEJM 2000

## Rates of Zoster and Postherpetic Neuralgia by Age in the US



\*Per 1,000 person-years. <sup>†</sup>Defined as <u>></u>30 days of pain.

Harpaz et al MMWR 2009

50% of persons reaching 85 yo will have zoster

## **Live Attenuated Virus Vaccine**



#### **ORIGINAL ARTICLE**

Volume 352:2271-2284 <u>June 2, 2005</u> Number 22

#### A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults

M.N. Oxman, M.D., M.J. Levin, M.D., G.R. Johnson, M.S., K.E. Schmader, M.D., S.E. Straus, M.D., L.D. Gelb, M.D., R.D. Arbeit, M.D., M.S. Simberkoff, M.D., A.A. Gershon, M.D., L.E. Davis, M.D., A. Weinberg, M.D., K.D. Boardman, R.Ph., H.M. Williams, R.N., M.S.N., J. Hongyuan Zhang, Ph.D., P.N. Peduzzi, Ph.D., C.E. Beisel, Ph.D., V.A. Morrison, M.D., J.C. Guatelli, M.D., P.A. Brooks, M.D., C.A. Kauffman, M.D., C.T. Pachucki, M.D., K.M. Neuzil, M.D., M.P.H., R.F. Betts, M.D., P.F. Wright, M.D., M.R. Griffin, M.D., M.P.H., P. Brunell, M.D., N.E. Soto, M.D., A.R. Marques, M.D., S.K. Keay, M.D., Ph.D., R.P. Goodman, M.D., D.J. Cotton, M.D., M.P.H., J.W. Gnann, Jr., M.D., J. Loutit, M.D., M. Holodniy, M.D., W.A. Keitel, M.D., G.E. Crawford, M.D., S.-S. Yeh, M.D., Ph.D., Z. Lobo, M.D., J.F. Toney, M.D., R.N. Greenberg, M.D., P.M. Keller, Ph.D., R. Harbecke, Ph.D., A.R. Hayward, M.D., Ph.D., M.R. Irwin, M.D., T.C. Kyriakides, Ph.D., C.Y. Chan, M.D., I.S.F. Chan, Ph.D., W.W.B. Wang, Ph.D., P.W. Annunziato, M.D., J.L. Silber, M.D., for the Shingles Prevention Study Group

# DSTAVAX

tourse like Meril

GURCUTAWERS

# ZOSTAVAX<sup>®</sup> Zoster Vaccine Live

# ZOSTAVA)

Construction of

-Desire Swall

ZOSTAV

SHINGRIX – "THE NEW SHINGLES VACCINE" > FACTS AND RECOMMENDATIONS

Not a LIVE vaccine (recombinant)
Given after age 50
SUPERIOR protection and LASTS >90
2 Doses (IM) separated by 2-6 months
Increased soreness at injection site
Cost \$280 for 2 doses (old one \$223)

# **COMMON SHINGRIX** QUESTIONS SHOULD | STILL GET SHINGRIX ? 44<mark>|</mark>=" >- I once had shingles – YES >- I had the other vaccine - YES >- I have this condition - YES

>- I live with someone sick –YES

>- I take this medication - YES

# **NEISSERIA MENINGITIDIS**



## A Peak of Meningococcal Disease Incidence Occurs in 15- to 19-Year-Olds\*



\*Average annual incidence rate by age in Maryland, 1992–1999 1. Harrison LH, et al. *JAMA*. 2001;286:694.

# Gangrene Caused by *N meningitidis* Infection



Courtesy of R Rudoy, MD, Honolulu, Hawaii, USA

# Ecchymoses



Courtesy of R Rudoy, MD, Honolulu, Hawaii, USA

## Severe Late-Stage Meningococcal Infection in a 15-Year-Old Boy



Reprinted with permission from Schoeller T, Schmutzhard E. N Engl J Med. 2001;34:1372.

#### MENINGOCOCCAL MENINGITIS



## **MENINGOCOCCAL VACCINATION – ADULTS 2019**

**MenACWY** – MENACTRA® or MENVEO® (Conjugated Vaccine)

2-Dose Series, >8-weeks apart, REVACCINATE q-5 years

Special Situations – Anatomic or Functional Asplenia HIV, Complement Deficiency, Eculizumab use

**1-Dose**, (revaccinate if q-5 years if risk remains)

**TRAVEL** to Countries with **HYPERENDEMIC** or **EPIDEMIC** disease

FIRST year COLLEGE STUDENTS living in RESIDENTIAL HOUSING (NOT previously vaccinated)

**MILITARY RECRUITS** 







# The Meningococcal Meningitis Belt



Table 9-04. International mass gathering events, 2019–2022				
EVENT TYPE	EVENT NAME	LOCATION	UPCOMING DATES	PROJECTED ATTENDANCE
Religious events	Kumbh Mela	Multiple locations in India: Allahbad, Haridwar, Madhya Pradesh, Maharashtra	2019 in Allahbad 2022 in Haridwar	40 million
	Arba'een Pilgrimage	Karbala, Iraq	October 2019	22 million
	Grand Magal of Touba	Touba, Senegal	October 2019	3 million
	Најј	Mecca, Saudi Arabia	August 10, 2019 July 30, 2020	2.5 million
	Iztapalapa Passion Play	Mexico City, Mexico	Good Friday (annually)	2 million
	Urs of Fariduddin Ganjshakar	Pakpattan, Pakistan	September 2019	500,000
Sporting events	2020 Summer Olympics	Tokyo, Japan	July 24–August 9, 2020	7.5 million
	FIFA World Cup	Qatar	November 21– December 18, 2022	3 million
	2022 Winter Olympics	Beijing, China	February 4–20, 2022	1 million
Art and music festivals	Edinburgh Festival Fringe	Edinburgh, Scotland	August 2–26, 2019	2.5 million
	Street Parade	Zurich, Switzerland	2nd Saturday in August	1 million

# <u>Men B Vaccines</u>

FDA approved in 2014

- MenB-FHbp: brand name Trumenba (Pfizer)
   Three-dose series (1, 2, 6 months)
- MenB-4C brand name Bexsero (Novartis)
   Two-dose series (0, 1 months)
- > Both are FDA approved only for those age 10-25.

# Meningococcal B Facts

- Men B causes half of all cases of meningococcal disease in those age 17-22
- Each year, about 55-65 young people age 16-24 get sick with Men B
- Strikes quickly, unforgiving, often deadly.
- Men B NOT limited to college campuses
  - About 30-60% of cases occur in young people NOT in college

# Men B vaccination (June 12, 2015 MMWR)

ACIP expanded age indication to anyone age 10 & <u>older</u> at increased risk of Men B disease: *Category A recommendation* 

- > Patients with complement deficiencies
- Patients with anatomic or functional asplenia
- Microbiologists at risk through work exposure
- > Those exposed during outbreaks. (Expanded age indication is off-label use)

**NEW ACIP Recommendation for Men B** Vaccination (June 24, 2015) Category B recommendation  $\succ$  "May" be administered to age 16-23 Preferred vaccination age range: 16-18 Either vaccine product may be used The same product should be used for all doses in the series. No Men B boosters (after initial series) recommended at this time



## **GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION**



52



# Widespread person-to-person outbreaks of hepatitis A across the United States

Since the outbreaks were first identified in 2016, 30 states have publicly reported the following as of September 6, 2019

- Cases: 25,484
- Hospitalizations: 15,330 (60%)
- Deaths: 254
- The following groups are at highest risk for acquiring HAV infection or developing serious complications from HAV infection in these outbreaks and should be offered the hepatitis A vaccine in order to prevent or control an outbreak:
  - People who use drugs (injection or non-injection)
  - People experiencing unstable housing or homelessness
  - Men who have sex with men (MSM)
  - People who are currently or were recently incarcerated
  - People with chronic liver disease, including cirrhosis, hepatitis B, or hepatitis C

### State-Reported Hepatitis A Outbreak Cases as of September 6, 2019



## January 1, 2018 – October 5, 2019



The number of reported hepatitis A cases more than doubled from 2016 to 2017 and nearly doubled again in 2018 after remaining relatively stable in previous years. Case counts in 2019 have already surpassed those in 2018.





<u>COUNTIES</u> BROWARD – 18 BREVARD – 116 DUVAL - 20MIAMI-DADE - 31 HILLSBOROUGH – 148 LAKE - 135 LEE - 78MANATEE - 124MARTIN - 40PASCO - 66PALM BEACH - 66




### Hepatitis A Surveillance

September 2019

98% never vaccinated







#### Hepatitis A Surveillance January 1, 2018-August 10, 2019

From January 1, 2018 through August 10, 2019, 2,740 hepatitis A cases were reported.

The number of reported hepatitis A cases more than doubled from 2016 to 2017 and nearly doubled again in 2018 after remaining relatively stable in previous years. Case counts in 2019 have already surpassed those in 2018. Counties that reported a hepatitis A case in week 32 (8/4/19-8/10/19) are **outlined in black**. Since January 1, 2018, 98% of cases have likely been acquired locally in Florida.





There were 68 hepatitis A cases reported in week 32 (8/4/19–8/10/19). Weekly case counts have steadily increased overall since week 1, 2018.



#### **Hepatitis A Outbreak**

### What Clinicians Can Do

Half of states across the country have reported outbreaks of hepatitis A. Since first identified in 2016, more than 22,000 cases with over 50% hospitalizations and at least 200 deaths have been reported.

One dose of single-antigen hepatitis A vaccine has been shown to control outbreaks of hepatitis A – and provides up to 95% seroprotection in healthy adults.

#### **Assess and Vaccinate:**

- People who use drugs (injection or non-injection)
- People experiencing unstable housing or homelessness
- People who are currently or were recently incarcerated
- Men who have sex with men
- People with chronic liver disease (cirrhosis, hepatitis B, or hepatitis C)



www.cdc.gov/hepatitis/HepAOutbreak August 2019







#### Table 4-02. Vaccines to prevent hepatitis A

VACCINE	TRADE NAME (MANUFA CTURER)	AGE (Y)	DOSE	ROUTE	SCHEDUL E	BOOSTER
Hepatitis A vaccine, inactivated	Havrix (GlaxoSmit hKline)	1–18 ≥19	0.5 mL (720 ELU) 1.0 mL (1,440 ELU)	IM IM	0, 6–12 mo 0, 6–12 mo	None
Hepatitis A vaccine, inactivated	Vaqta (Merck & Co., Inc.)	1-18	0.5 mL (25 U)	IM	0, 6–18 mo	None
		≥19	1.0 mL (50 U)	IM	0, 6–18 mo	None
Combined hepatitis A and B vaccine	Twinrix (GlaxoSmit hKline	≥18 (primary)	1.0 mL (720 ELU HAV + 20 µg HBsAg)	IM	0, 1, 6 mo	None
		≥18 (accelerated )	same as above	IM	0, 7, 21–30 d	12 mo



### Prevalence of hepatitis B virus infection



# Hepatitis B In the World

- 2 billion people have been infected (1 out of 3 people).
- 400 million people are chronically infected.
- 10-30 million will become infected each year.
- An estimated 1 million people die each year from hepatitis B and its complications.
- Approximately 2 people die each minute from hepatitis B.

# Hepatitis B In the United States

- 12 million Americans have been infected (1 out of 20 people).
- More than one million people are chronically infected .
- Up to 100,000 new people will become infected each year.
- 5,000 people will die each year from hepatitis B and its complications.
- Approximately 1 health care worker dies each day from hepatitis B.

### ACTUAL and ESTIMATED <u>ACUTE</u> HEPATITS B UNITED STATES 2010-2017



How common is chronic HBV infection in the United States? In 2016, the number of people living with HBV infection was 862,000 (3).



#### Table 4-04. Vaccines to prevent hepatitis B

VACCINE	TRADE NAME (MANUFACT URER)	AGE (Y)	DOSE	ROUTE	SCHEDULE	BOOSTER
Hepatitis B vaccine, recombinant with novel adjuvant (1018)	Heplisav-B (Dynavax Technologies)	>18	0.5 mL(20 μg HBsAg and 3000 μg of 1018)	ІМ	0, 1 mo	None
Hepatitis B vaccine, recombinant <sup>1</sup>	Engerix-B (GlaxoSmithKli ne)	o−19 (primary) 0−10 (accelerated) 11−19 (accelerated) ≥20 (primary) ≥20 (accelerated)	0.5 mL (10 μg HBsAg) 0.5 mL (10 μg HBsAg) 1.0 mL (20 μg HBsAg) 1.0 mL (20 μg HBsAg) 1.0 mL (20 μg HBsAg)	IM IM IM IM	0, 1, 6 mo 0, 1, 2 mo 0, 1, 2 mo 0, 1, 6 mo 0, 1, 2 mo	None 12 mo 12 mo None 12 mo
Hepatitis B vaccine, recombinant <sup>1</sup>	Recombivax HB (Merck & Co., Inc.)	0−19 (primary) 11−15 (adolescent accelerated) ≥20 (primary)	0.5 mL (5 µg HBsAg) 1.0 mL (10 µg HBsAg) 1.0 mL (10 µg HBsAg)	IM IM IM	0, 1, 6 mo 0, 4–6 mo 0, 1, 6 mo	None None None
Combined	Twinrix	≥18 (primary)		IM	0, 1, 6 mo	None

# Post-Vaccination Serologic Testing

- Not routinely recommended following vaccination of infants, children, adolescents, or most adults
- Recommended for:
  - -Infants born to HBsAg+ women
  - -Hemodialysis patients
  - -Immunodeficient persons
  - -Sex partners of persons with chronic HBV infection
  - -Certain healthcare personnel









# Human Papillomavirus (HPV)

### What is **HPV**?

- The most common sexually transmitted infection (STI) in the U.S.
- Transmitted person to person by close contact
- Most people infected with HPV are asymptomatic or may not develop symptoms until years after infection (This Makes the virus easier to spread)

### **HPV Prevalence & Incidence**

- Most sexually-active females and males will be infected with at least one type of HPV at some point in their lives
  - Estimated 79 million Americans currently infected
  - 14 million new infections/year in the U.S.
  - HPV infection is most common in people in their teens and early 20s



# Female Genital Warts





### Genital Warts in a Male



*Source*: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

*Source*: Cincinnati STD/HIV Prevention Training Center

# **Perianal Warts**



Source: Cincinnati STD/HIV Prevention Training Center

# HPV Warts on the Thigh



Source: Cincinnati STD/HIV Prevention Training Center

### **HPV-Related Health Problems**

- 40 different types
- Most go away on their own and do not cause health problems
- Cases that do not go away can cause serious health problems such as genital warts or cancer:
  - \* Cervical \* Oropharyngeal \* Anal
  - \* Vulvar \* Vaginal \* Penile



# HUMAN PAPILLOMAVIRUS CAN CAUSE SEVERAL TYPES OF CANCER



#### cancer.gov/hpv

### Cancer Types, Other Than Cervical Cancer, Attributable to HPV



**Cancer Type** 



**González Intxaurraga MA et al.** *Acta Dermatovenerol.* 2002;11:1–8. (From Merck)

#### Every year in the United States 27,000 people are diagnosed with a cancer caused by HPV

That's 1 case every 20 minutes





### **HPV-Associated** Cervical Cancer Rates by State, 2006-2010



(2012)

#### HPV-Associated <u>Oropharyngeal</u> Cancer Rates by State, 2006-2010





# Human Papillomavirus (HPV) PREVENTION





### THE GARDASIL VACCINE CONTROVERSY

#### Gardasil Vaccine Linked to:



Infertility
POTS (heart disease)
HPV related cancers
Auto Immune Disease
DEATH

in solution and in solution (1981)



#### Human Papillomavirus in 2019: An Update on Vaccines and Dosing Recommendations

 Gardasil 9 targets HPV types 6, 11, 16 and 18 along with 31, 33, 45, 52, 58—these cause 90% of cervical cancer cases and most cases of genital warts<sup>5</sup>—making it the most effective vaccine available; Gardasil 9 is the only HPV vaccine currently available in the United States.

TABLE 1							
HPV vaccination timeline, male and female							
Age 9–14	Age 15–26	Age 21–26 (male)	Age 27–45				
2-dose HPV vaccine, 0 and 6–12 months	3-dose HPV vaccine, 0, 1–2, and 6 months	Vaccine offered, 3-dose regimen	FDA-approved, but not routinely recommended				
FDA = US Food and Drug Administration; HPV = human papillomavirus							

#### Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Adults aged >26 years. Catch-up HPV vaccination is not recommended for all adults aged >26 years. Instead, shared clinical decision-making regarding HPV vaccination is recommended for some adults aged 27 through 45 years who are not adequately vaccinated. (Box). HPV vaccines are not licensed for use in adults aged >45 years.

BOX. Considerations for shared clinical decision-making regarding human papillomavirus (HPV) vaccination of adults aged 27 through 45

Ideally, HPV vaccination should be given in early adolescence because vaccination is most effective before exposure to HPV through sexual activity. For adults aged 27 through 45 years who are not adequately\* vaccinated, clinicians can consider discussing HPV vaccination with persons who are most likely to benefit. HPV vaccination does not need to be discussed with most adults aged >26 years.

# Vaccination Trends in the U.S.





Source: Stokley et al. (2014) Note: The Healthy People 2020 Goal is for boys and girls age 13-15 years

### Vaccination Trends in the U.S. & FL





#### **HPV Vaccine Three-Dose Coverage**



#### **Among Girls in High-Income Countries**











White spots inside the mouth are common with measles (Koplik's spots)
### Spread of Measles

- The majority of people who got measles were unvaccinated.
- Measles is still common in many parts of the world.
- Travelers with measles continue to bring the disease into the U.S.
- Measles can spread when it reaches a community in the U.S. where groups of people are unvaccinated.

# Measles Outbreaks

In a given year, more measles cases can occur for any of the following reasons:

- an increase in the number of travelers who get measles abroad and bring it into the U.S., and/or
- further spread of measles in U.S. communities with pockets of unvaccinated people.

### **Global Measles Burden**

- Measles is still commonly transmitted (endemic or large outbreaks) worldwide.
- Measles remains a leading cause of vaccine-preventable infant mortality.
- Great progress has been made toward measles elimination
- From 2000-2017\*:
  - Reported measles incidence decreased 83%, from 145 to 25 cases per million persons
  - Annual estimated measles deaths decreased 80% (21.1 million deaths prevented)

#### **Number of Lives Saved by Measles Vaccine Globally**



### U.S. Measles Burden: Before 1963 Vaccine Development\*

- Each year, measles caused an estimated 3 to 4 million cases
  - Close to 500,000 cases were reported annually to CDC, resulting in:
    - 48,000 hospitalizations
    - 1,000 cases with encephalitis (brain swelling)
    - 400 to 500 deaths

### **U.S. Measles Burden: Current\***

- Measles was declared eliminated from the United States in 2000 thanks to a highly effective vaccination program and other control measures.
- However, measles remains present in many other countries and can be brought into the United States by unvaccinated travelers (Americans or foreign visitors).
  - This can result in outbreaks that are costly to control.
- Since 2000, the annual number of reported measles cases ranged from 37 people in 2004 to 667 people in 2014.
- The last measles death in the United States occurred in 2015.

# Number of Measles Cases Reported by Year

#### 2010-2019\*\*(as of October 3, 2019)



Year

### Measles Cases and Outbreaks

### Measles Cases in 2019

From January 1 to October 3, 2019, 1,250\* individual cases of measles have been confirmed in 31 states. This is an increase of seven cases from the previous week. However, only three of these cases were recently ill. The rest were identified as past cases.



#### Measles Cases Reported by Month in 2019\*

**GREATEST** NUMBER SINCE 1992; 75% LINKED TO NYC MAJORITY **UNVACCINATED** 119 HOSPITALIZED; 61 COMPLICATIONS; **PNEUMONIA** and **ENCEPHALITIS** 

# Get Vaccinated: Prevent and Stop Measles Outbreaks

When measles happens anywhere in the world...

it can travel here and spread

Since measles is still common in many countries, unvaccinated travelers will continue to bring the disease into the U.S., and it can spread to other people.

Make sure you and your family members are up-to-date on your measles-mumps-rubella (MMR) vaccine, including before traveling internationally. Ask your doctor if everyone has received all recommended doses of MMR for best protection against measles.

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#### www.cdc.gov/features/measles/



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

# Measles

- Most US measles cases result from international travel
- Measles outbreaks are going on in many countries around the world
- Travelers should be vaccinated before their trip:



- Infants 6–11 months: 1 dose of MMR (does not count toward the routine series)
- People ≥12 months with no evidence of immunity: 2 doses separated by 28 days
- People ≥12 months with documentation of 1 dose and no evidence of immunity: 1 additional dose before travel
  - A second dose was added to the routine series in 1989, so people born before then are likely to be in this category

#### MEASLES VACCINATION RATES FOR PRESCHOOLERS

Nationally, about 91 percent of 19- to 35-month-olds have been vaccinated for measles, according to data gathered from the Centers for Disease Control and Prevention. But in 17 states, fewer than 90 percent of young children have been immunized for the disease, which puts those states at a higher risk for widespread infection.



# **Rate of Nonmedical Vaccine Exemptions By State**

Percentage of kindergartners with nonmedical exemptions, 2012-13 school year



Note: Children with exemptions may still be vaccinated. Source: Centers for Disease Control



# **Dengue Vaccine**

- May 1, 2019: FDA approved **Dengvaxia** 
  - First live, attenuated dengue vaccine to protect against all 4 virus serotypes
- Indicated in children ages 9–16 who live in endemic areas and have laboratory confirmation of previous dengue infection
- In people not previously infected, Dengvaxia appears to increase the risk of severe dengue through antibody-dependent enhancement
- Use in international travelers is expected to be limited



# Viral Hemorrhagic Fevers (VHFs)

Viral group	Representative viruses
1 – Filoviruses	Ebola V and Marburg V
2- Flaviviruses (82 members)	-Yellow fever V -West Nile V - Dengue Fever V
3- Bunyaviruses	(Rift Valley fever virus (RVV), Crimean-Congo hemorrhagic fever (CCHF) virus, and <u>Hantavirus</u> pulmonary syndrome (HPS).
2- Arenavirus	Lassa Fever V New World Arena Viruses



#### Ebola Virus Outbreaks by Species and Size, Since 1976

Country	Town	Cases	Deaths	Species	Year
Dem. Rep. of Congo, Uganda	multiple	ongoing	ongoing	Zaire ebolavirus	2018-2019
Dem. Rep. of Congo	Bikoro	54	33	Zaire ebolavirus	2018
Dem. Rep. of Congo	Likati	8	4	Zaire ebolavirus	2017
Dem. Rep. of Congo	multiple, Équateur province	66	49	Zaire ebolavirus	2014
Multiple countries	multiple	28652	11325	Zaire ebolavirus	2014-2016



Incubation period: 2-21 days for Ebola (Mean 8 -10).
3-10 days for Marburg
9.6 days (mean) from symptom onset to death









# Merck's Ebola vaccine helps combat deadly outbreak in the Congo as the virus spreads

WHO data shows the Merck vaccine had a 97.5% efficacy rate for those who were immunized compared to those who were not.

"There are risks and costs to action. But they are far less than the long range risks of comfortable inaction". John F. Kennedy



