WHAT'S NEW WITH VACCINATIONS IN 2016?

MenB and a Few Other Changes

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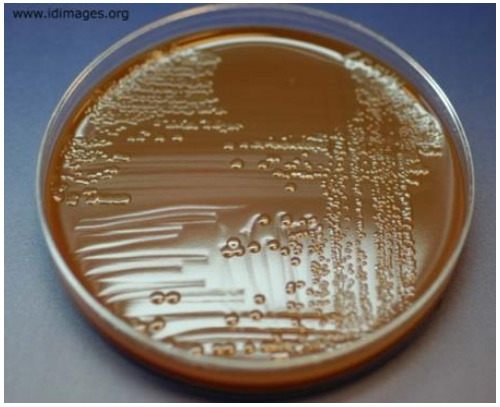
Disclosure

- No conflict of interest
- Will discuss an off-label ACIP recommendation for meningococcal serogroup B vaccines

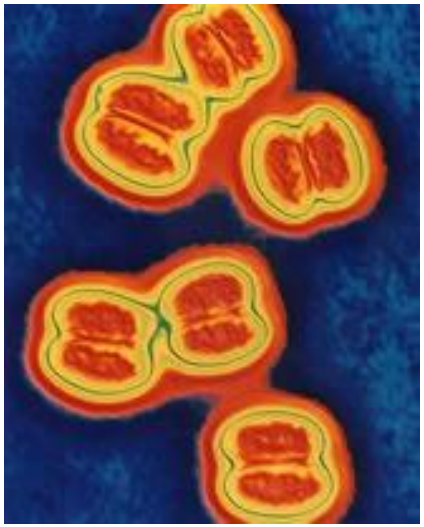


Objectives

- Review *Neisseria meningitidis disease,* risk factors and epidemiology
- Discuss vaccines used to prevent *N meningitidis,* particularly for serogroup B
- Discuss meningococcal vaccine recommendations
- Highlight other recent changes to immunizations

Invasive meningococcal disease

- Caused by *Neisseria meningitidis*
  - Gram negative diplococci
  - Polysaccharide capsule has protective features against human immune response
  - At least13 serogroups, most invasive disease caused by serogroups A, B, C, Y, W-135
- Humans are only reservoir
  - 5-15% adults have nasopharyngeal carriage
- Droplet transmission



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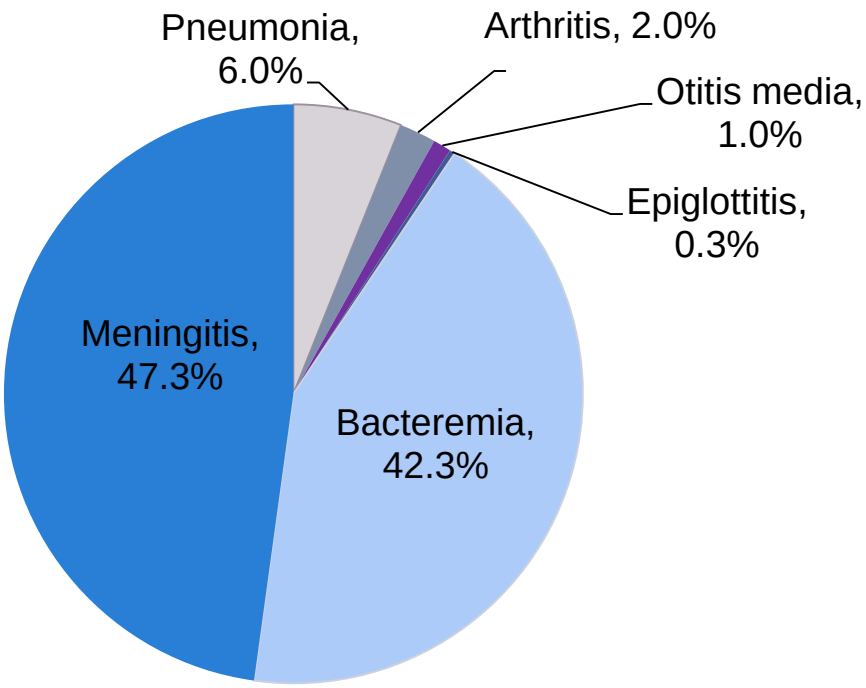
Clinical Manifestations

- Meningitis (~50%)
- Bacteremia (~45%)
  - Case fatality rate: 10% (higher with bacteremia)
  - Disease sequelae: 20%



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Risk Factors for Invasive Meningococcal Disease

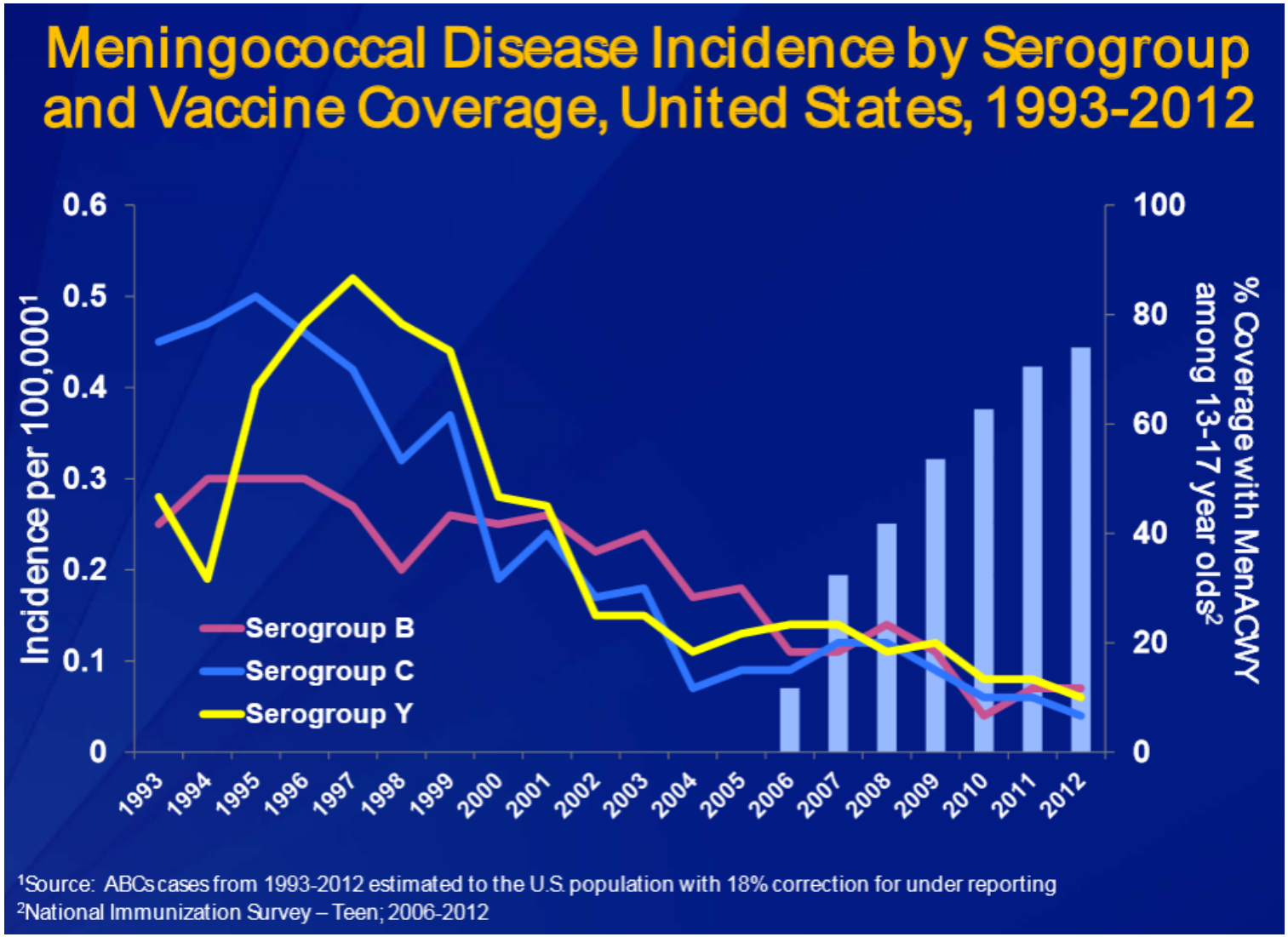
- Host factors
  - Terminal complement pathway deficiency
  - Asplenia
  - Genetic risk factors
  - HIV infection - emerging
- Exposure factors
  - Household exposure
  - Concurrent upper respiratory tract infection
  - Demographic and socioeconomic factors and crowding
  - Active and passive smoking
  - Laboratory work with N. meningitidis
  - Travel to endemic or hyperendemic areas

Prevention: Meningococcal vaccination

- Pre-2005: Quadrivalent (A, C, Y, W-135) polysaccharide meningococcal vaccines
  - 2000: Permissive recommendation for college students, particularly freshmen living in campus housing
- 2005: Quadrivalent (A, C, Y, W-135) conjugate meningococcal vaccines licensed
  - 2005: Routine adolescent recommendation:
    - One dose at 11-12 years of age
- 2010: Added booster dose at age 16 years
  - Duration of immunity shorter than anticipated
  - Certain at-risk persons recommended to receive 2-dose series

Prevention: Meningococcal vaccination

- 2011 and 2013:
  - Expanded age licensures for both MenACWY vaccines
    - Menactra to age 9 months as a 2-dose primary series
    - Menveo to age 2 months as a 3-dose primary series
  - Combination Hib-menCY (MenHibrix) vaccine licensed
    - 3-dose primary series, Hib component counts toward Hib vaccination
  - Vaccination of at-risk infants



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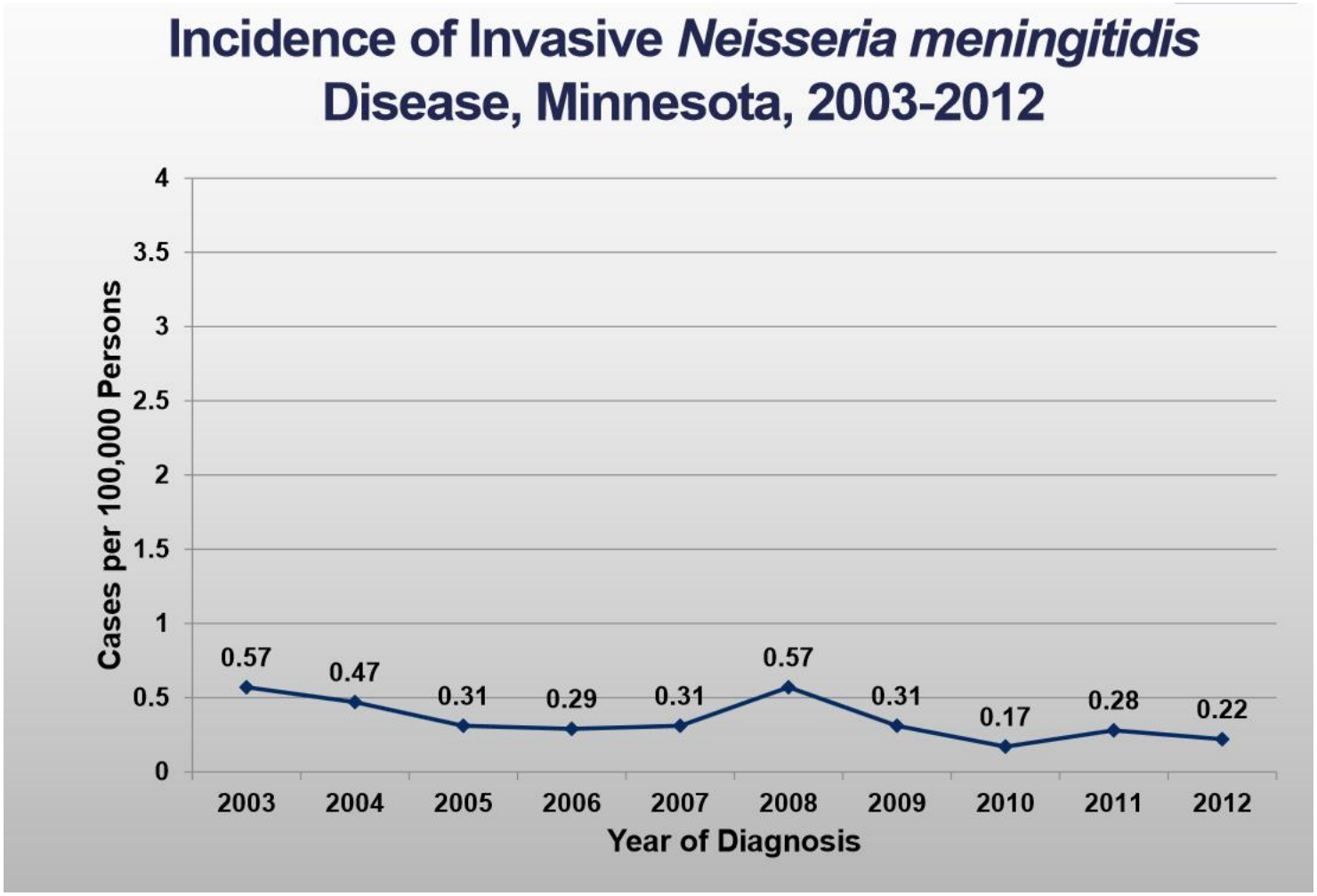
http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2014-06/Meningococcal-02-Meyer.pdf



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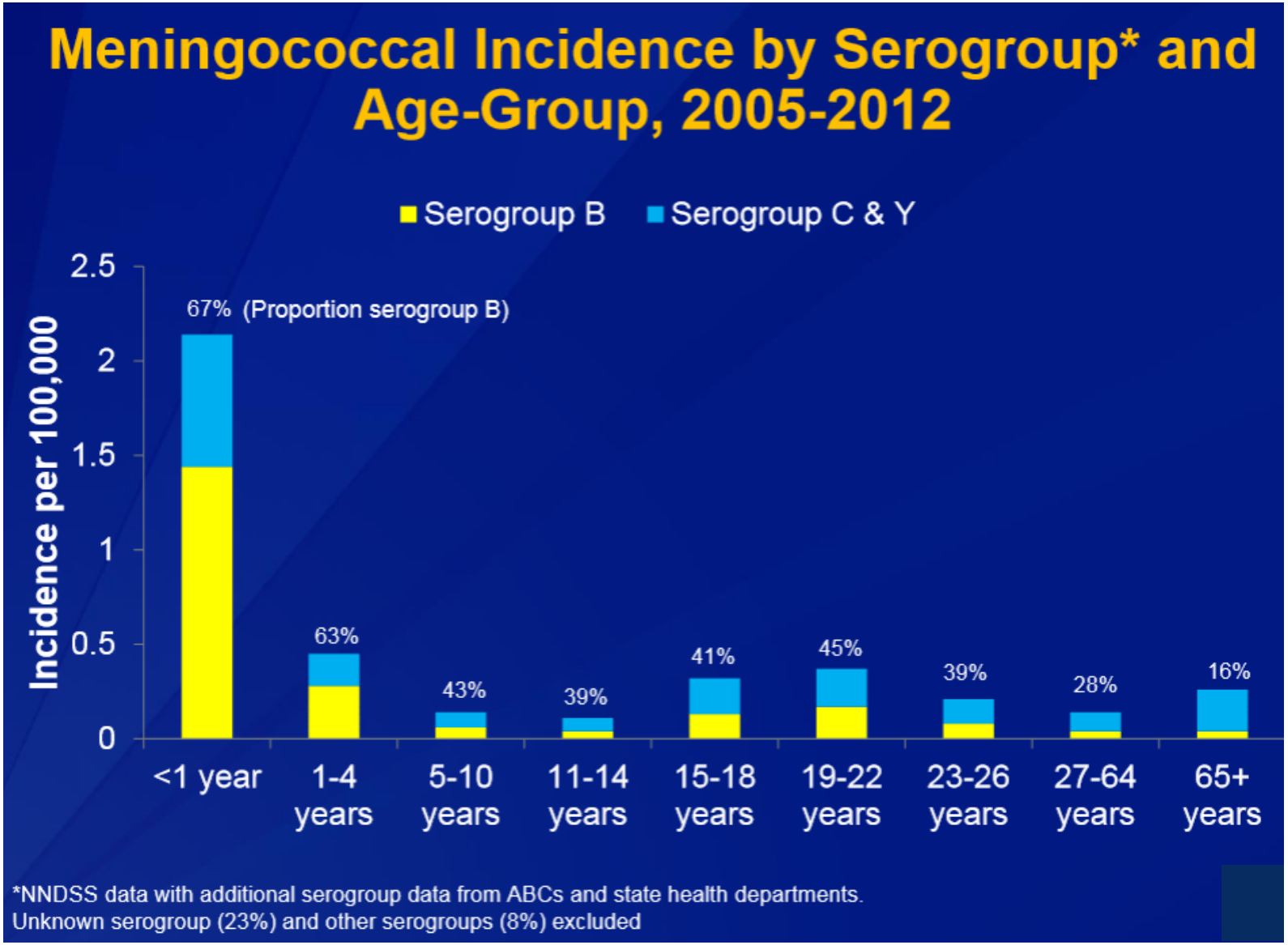
Source: MDH, Active Bacterial Core Surveillance (ABCS), 2015



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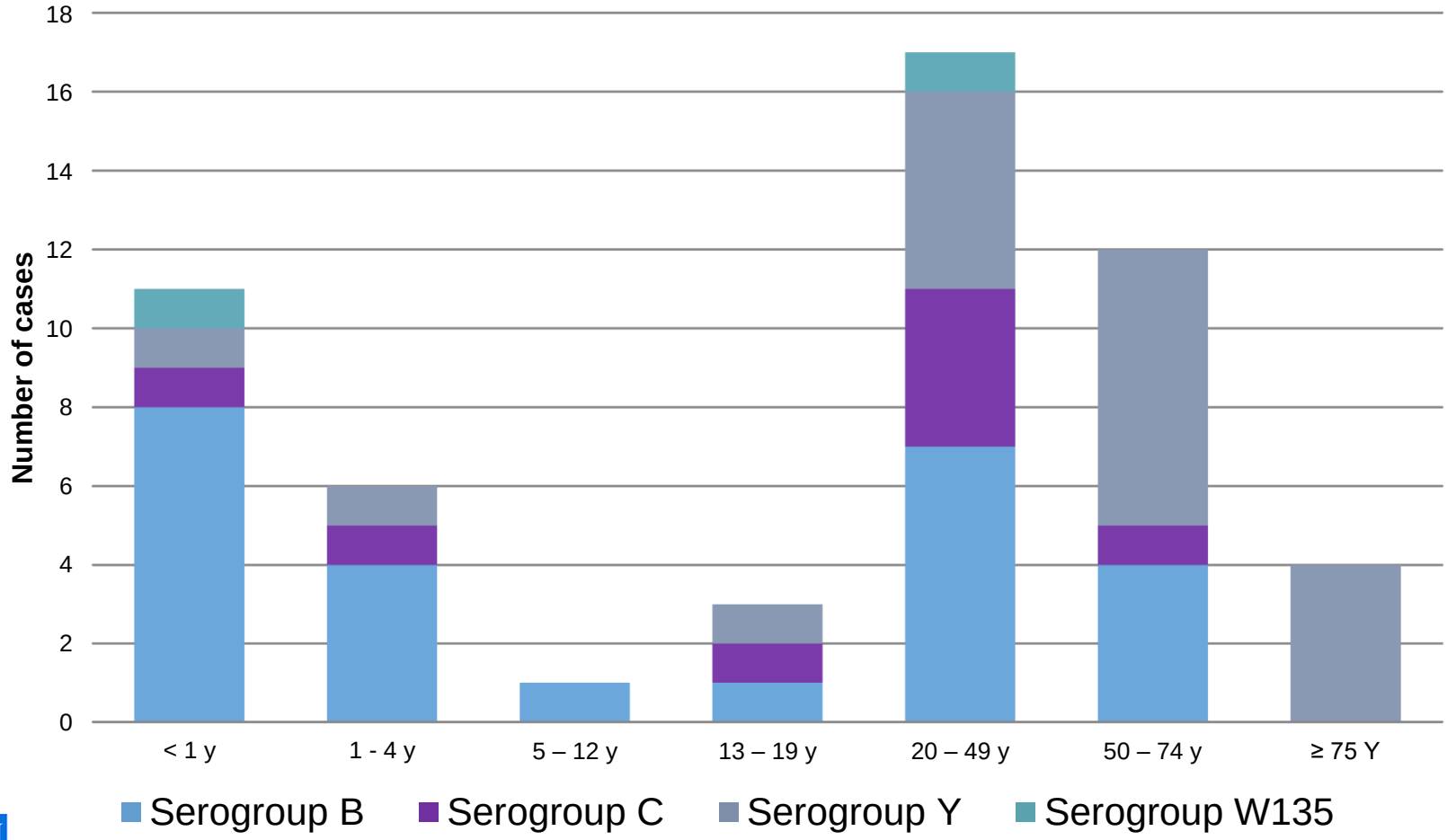
http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2014-10/mening-02-MacNeil.pdf

Cases of Invasive *N. Meningitidis* by Age-group and Serogroup, 2010-2014, Minnesota



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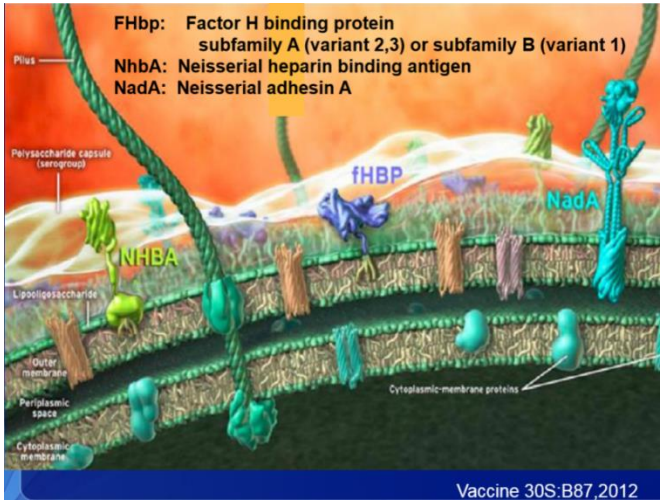
Serogroup B Meningococcal Disease Among Adolescents and Young Adults

- Approximately 50 cases annually among 11-24 year olds
  - Approximately one third of cases among 18-23 year olds occur in college students
  - 29% of serogroup B cases in all 18-23 year olds occurred among college students during 1999-2012
    - From 2008-2012: ~11 cases (and ~1 death) annually

Making a Meningococcal B Vaccine: challenging

- Polysaccharide capsule vaccine target for MenACWY, but poorly immunogenic for MenB
- Next option was to find specific proteins in the capsule that would have a broad coverage as possible and stimulate an immune response
  - This took decades



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Meningococcal B Vaccines

- **MenBfHbp** (Trumenba®) – licensed October 2014 (Pfizer) AKA meningococcal B, recombinant
  - 10 – 25 years of age
  - 2-dose (0, 6 month intervals – no skimping!)
  - 3-dose series (0, 2, 6 month intervals)
- Immunogenicity: met all end-points, duration of protection unknown
- Safety:
  - Local: injection site pain
  - Systemic: malaise, headache, myalgia, chills
- Concomitant studies: HPV4 and Tdap-IPV booster –
  - Remained immunogenic and
  - No additional safety concern

- rLP2086 (recombinant lipidated protein 2086)
- fHBP subfamily A/v2,3; subfamily B/v1

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Meningococcal B Vaccines

- **MenB-4C** (Bexsero®) – licensed February 2015 (Novartis) AKA Meningococcal B, OMV
  - 10 -25 years of age
  - 2-dose series (0, 1-6 months)
  - Adjuvanted
  - Given intramuscularly
- Immunogenicity: met all end-points, immunity wanes by 5-25% at two years
- Safety:
  - Local: injection site redness and pain,
  - Systemic: malaise, myalgia and headache
- Concomitant studies were not done

- fHBP subfamily B/v1,
- NHBA,
- NadA,
- PorA1.4

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Recommendation Considerations

- Current epidemiology
- Vaccine coverage (effectiveness)
- Cost effectiveness
- Implementation
- At risk populations

CONSIDERATIONS FOR USE OF MENB VACCINES

- Rates of meningococcal disease at historic lows
- Vaccination with MenACWY at 11-12 years of age and a booster at 16 years of age
  - Increasing vaccination coverage contributing to decreasing rates in adolescents
- Serogroup B accounts for ~40% of meningococcal disease
- 50 cases annually among adolescents in recent years

Challenges to the Considerations

- Extent of strain coverage *estimated*; actual unknown
- Duration of protection unknown
- Impact on carriage unknown
- Impact of vaccine pressure on circulating strains unknown
- Different multi-dose schedules make implementation challenging
- Burden of MenB disease is low and not all cases will be prevented with vaccination

Options for Use of MenB vaccines

- Recommendation for high risk groups only
  - Medical conditions high risk for meningococcal disease
    - Persistent complement component deficiencies
    - Anatomic or functional asplenia
  - Microbiologists
  - Outbreak response
- Routine recommendation for expanded groups
  - Adolescent
  - College students

Men B Recommendation, Part 1: February 2015

- Vaccinate persons age 10 years and older at-risk for invasive serogroup B meningococcal disease
- Either vaccine may be used
- ACIP recognizes the off-label recommendation for persons over age 25 years

Who are the “At-risk?”

- Medical conditions
  - Terminal complement pathway deficiencies
  - Treatment with Eculizumab, a monoclonal antibody - used to treat atypical HUS or paroxysmal nocturnal hemoglobinuria – inhibits complement cascade
  - Anatomic or functional asplenia, including sickle cell disease
- Microbiologists
- Outbreak response - threshold defined as:
  - 2 cases in population under 5,000 persons
  - 3 cases in population of 5,000 or more persons

Men B Recommendation, Part 2: June 2015

- ACIP approved a "*B recommendation*" for meningococcal B vaccination:
  - MenB vaccine series *may be* administered to adolescents and young adults 16 through 23 years of age for short term protection against meningococcal B disease.
  - The preferred age for MenB vaccination is 16 through 18 years of age.

An ACIP *B recommendation* means that the recommendation is clinician-based rather than population-based; it will still be covered by insurance

Implementing a B Recommendation for MenB

- Timing – when giving booster dose of MenACWY
- Educate:
  - Licensed meningococcal vaccine product exists to prevent some/most serogroup B infections
  - Benefits and risks are addressed on the VIS
  - Limitations – duration of protection and inability to protect against all serogroup B infections – this is what drove lack of a strong recommendation
- Vaccinate or refer
- May be given with MenACWY
- The products are NOT interchangeable – use the same product to complete the series

Future considerations for expanded recommendations

- Concomitant vaccination
- Additional safety data
- Additional immunogenicity data to evaluate coverage and efficacy data
- Duration of protection

THE OTHER THINGS

- HPV
- Influenza
- Product updates
- More other things

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HPV Vaccines

- 9vHPV received approval for license expansion in males 15-26.
  - Merck is planning to retire 4vHPV by the end of 2016
- Discussion continues regarding 2 versus 3 dose schedule for HPV vaccines
  - WHO changed their HPV vaccination recommendation:
    - 2 doses, at least 6 months apart
    - Girls age 9-14 years
    - A 3-dose schedule is still recommended for persons 15-26 years and for immunocompromised and/or HIV-infected

Influenza

- Vaccine efficacy, early season: 59%! Specifically, for AH1N1-51% and B-76%.
- New product:
  - Adjuvanted influenza vaccine, trivalent (aIIV3) - Fluad®
    - 65 years and older
    - Contains adjuvant, MF59®, a squalene based oil-in-water emulsion
    - Immune response higher compared to standard formulation
    - Higher rates of local injection site pain and tenderness

Egg allergies and Influenza Vaccine

Presentation by Dr. John Kelso, ACIP, February 2016:

- 2700 published studies involving more than 4100 allergic subjects, including known anaphylaxis to egg ingestion
  - Received influenza vaccination without serious reactions, including respiratory distress or hypotension
  - Minor reactions such as hives, mild wheezing, but seen equally among non-egg allergic controls
  - Additional information about safety of receipt of LAIV is available

Recommendations of the Joint Task Force on Practice Parameters (2012):

- All patients with egg allergy of any severity, including anaphylaxis, should receive IIV annually, using any age-approved brand of IIV in an age-appropriate dose.
- Such patients can receive the vaccine as a single dose without prior vaccine skin testing.
- Either egg-based or egg-free IIV can be used.
- Special precautions regarding medical setting are not warranted
- Language that describes egg-allergic recipients as being at increased risk compared or requiring special precautions should be removed from guidelines and product labeling.

Ann Allergy Asthma Immunol 111 (2013) 298e305

https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/Update-on-influenza-vaccination-of-egg-allergic-patients-2014.pdf

2016-17 Influenza Vaccine Recommendations

- Risk of anaphylaxis due to egg allergy small compared to risk of hospitalization and death due to influenza
- 2016-17 Flu recommendations: change in egg allergy language
  - ACIP voted to remove the egg allergy algorithm
    - Person with egg allergies should receive influenza vaccine, including LAIV
    - Persons who have previously experienced a severe anaphylactic reaction to eggs should be vaccinated by their primary care provider/clinic

Product updates

- Hib PRP-T (Hiberix) – now approved for the primary series: 2m, 4m, 6m
- 9vHPV – age expanded for males age 22 through 26 years
- 4vHPV – will be discontinued by the end of the year, no longer available through MnVFC
  - (MnVFC-related: 2vHPV no long available to order)
- Influenza
  - Fluad – New product with adjuvant
  - Coming soon? – Quadrivalent Recombinant Influenza Vaccine
- Coming soon?: Combination hexavalent vaccine:
  DTaP-IPV-Hib-HepB

More other things: Good-bye Type 2

- On April 25, 2016 the world outside the U.S. switched from a trivalent OPV (tOPV)to a **bivalent OPV (bOPV)**: types 1 and 3
- Last Type 2 wild poliovirus case was 1999
- No Type 3 wild poliovirus since 2012
- Endemic wild poliovirus cases only occurring in two countries – Pakistan and Afghanistan

Photo from http://www.polioeradication.org/

Acknowledgements

- CDC – ACIP slides and notes: www.cdc.gov/vaccines/acip
- Kathy Como-Sabetti, MPH, MDH, Epidemiologist, Emerging Infections
- Lori Triden, MDH, ABC Surveillance

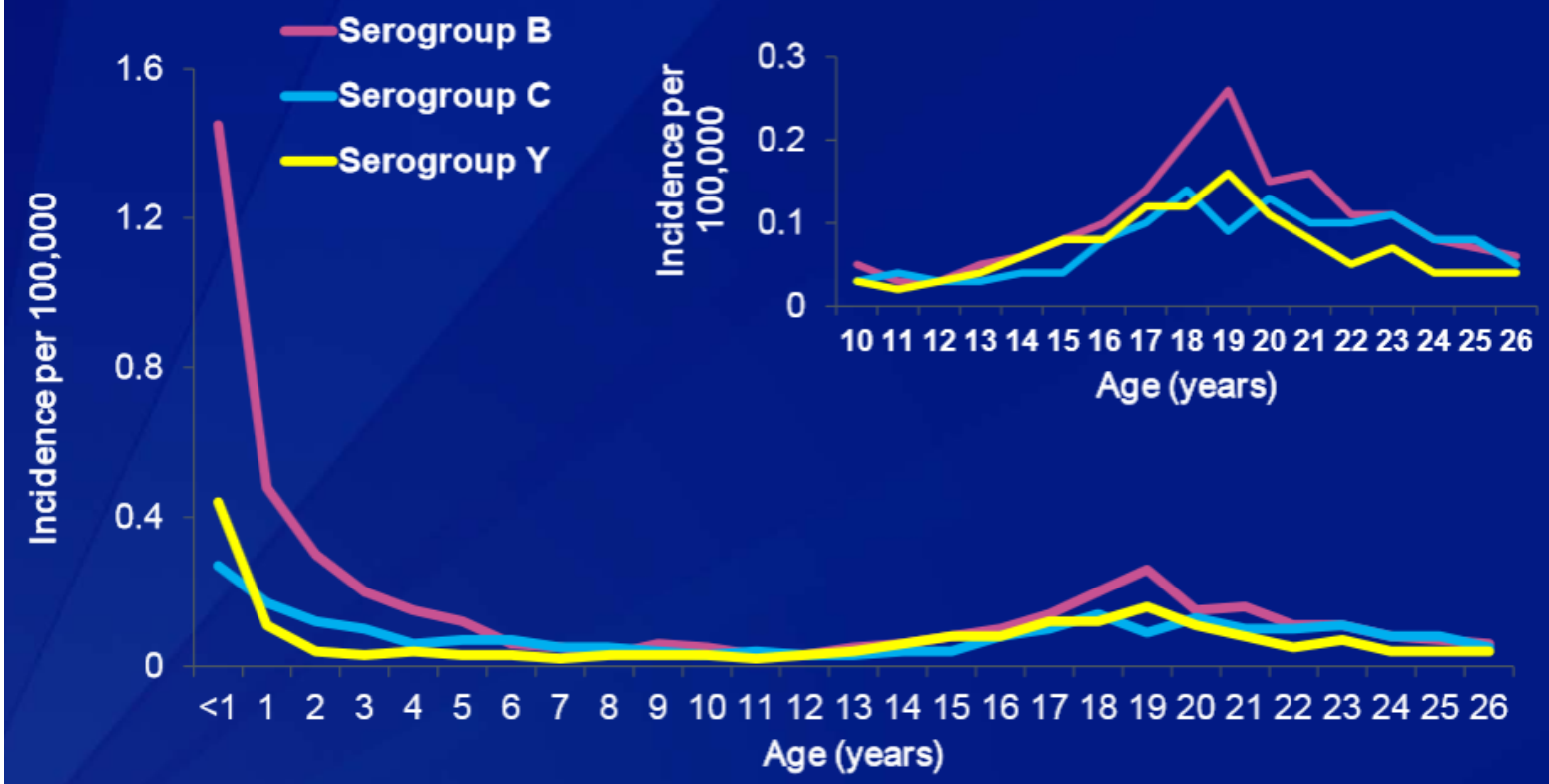
Licensed Meningococcal Vaccines

Vaccine	Components	Licensed age indication	Dose/ Route	Schedule
MenACWY-crm (Menveo®) GSK	Serogroups A, C, W-135, Y	6 weeks through 55 years	0.5 mL IM	Age-, risk-dependent
MenACWY-D (Menactra®) Sanofi Pasteur	Serogroups A, C, W-135, Y	10 through 55 years	0.5 mL IM	Age-, risk-dependent
Hib-MenCY-TT (MenHibrix®) GSK	Serogroups C and Y Hib	6 weeks through 18 months	0.5 mL	2m, 4m, 6m, 12-15m
MPSV4 (Menomune®) Sanofi Pasteur	Serogroups A, C, W-135, Y	2 years and older	0.5 mL	

Licensed Meningococcal Vaccines

Vaccine	Components	Licensed age indication	Dose/ Route	Schedule
MenB-4C MenB- OMV (Bexero®) GSK	fHbp (subfamily B) NadA PorA P1.4 NHBa	10 through 25 years	0.5 mL IM	0, 1 – 6 months
MenB-fHbp MenB-recombinant (Trumenba®) Pfizer	fHbp (subfamilies A & B)	10 through 25 years	0.5 mL IM	0, 6 months or 0, 1 – 2, 6m

Incidence of Meningococcal Disease by Age and Serogroup, United States, 2005-2012*



*Source: National Notifiable Diseases Surveillance System (NNDSS) with additional serogroup data provided by state and local health departments

http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2014-06/Meningococcal-02-Meyer.pdf

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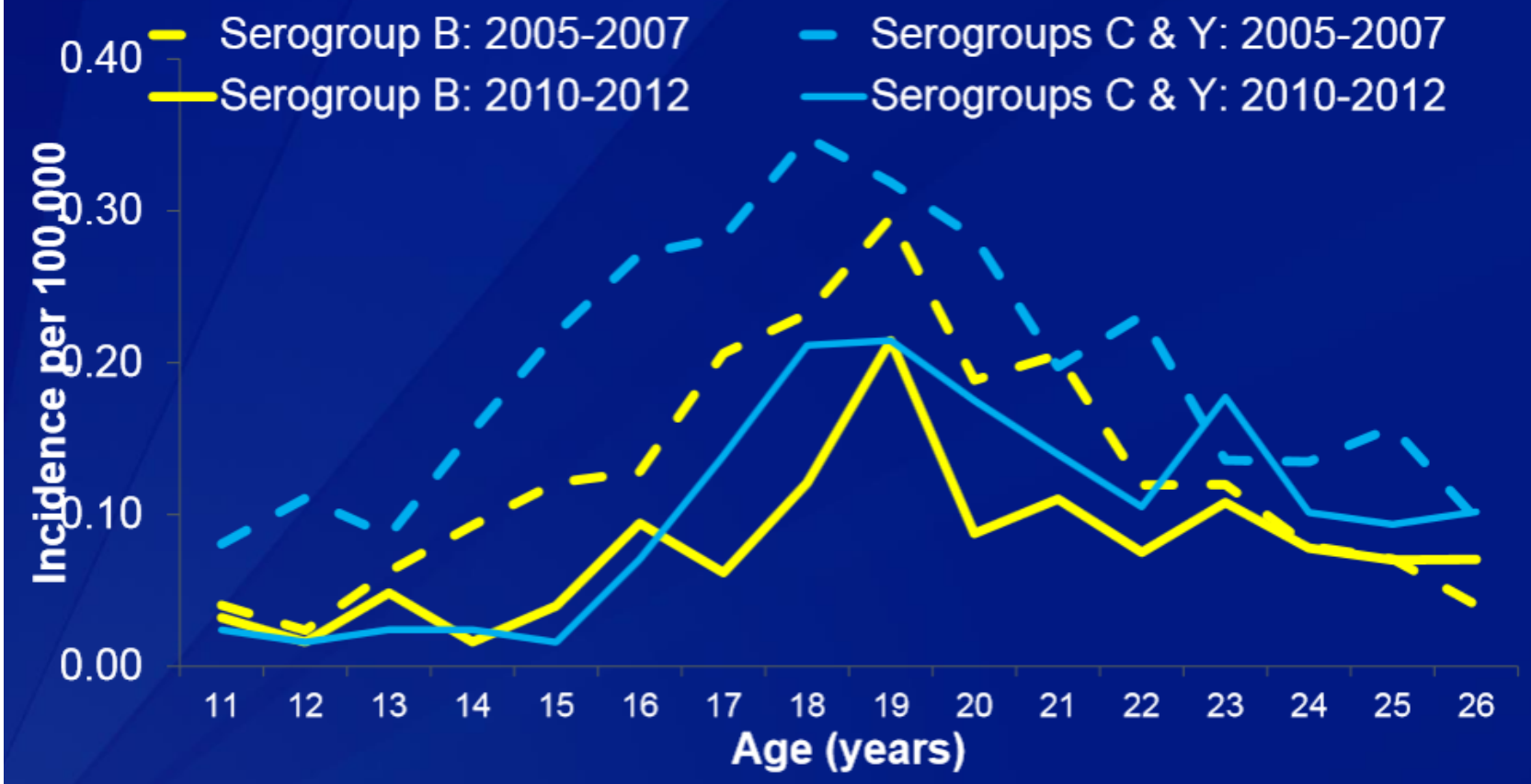
Meningococcal Incidence in Adolescents 11-26 Years of Age by Serogroup, 2005-2012



*NNDSS data with additional serogroup data from ABCs and state health departments.
Unknown serogroup (23%) and other serogroups (8%) excluded

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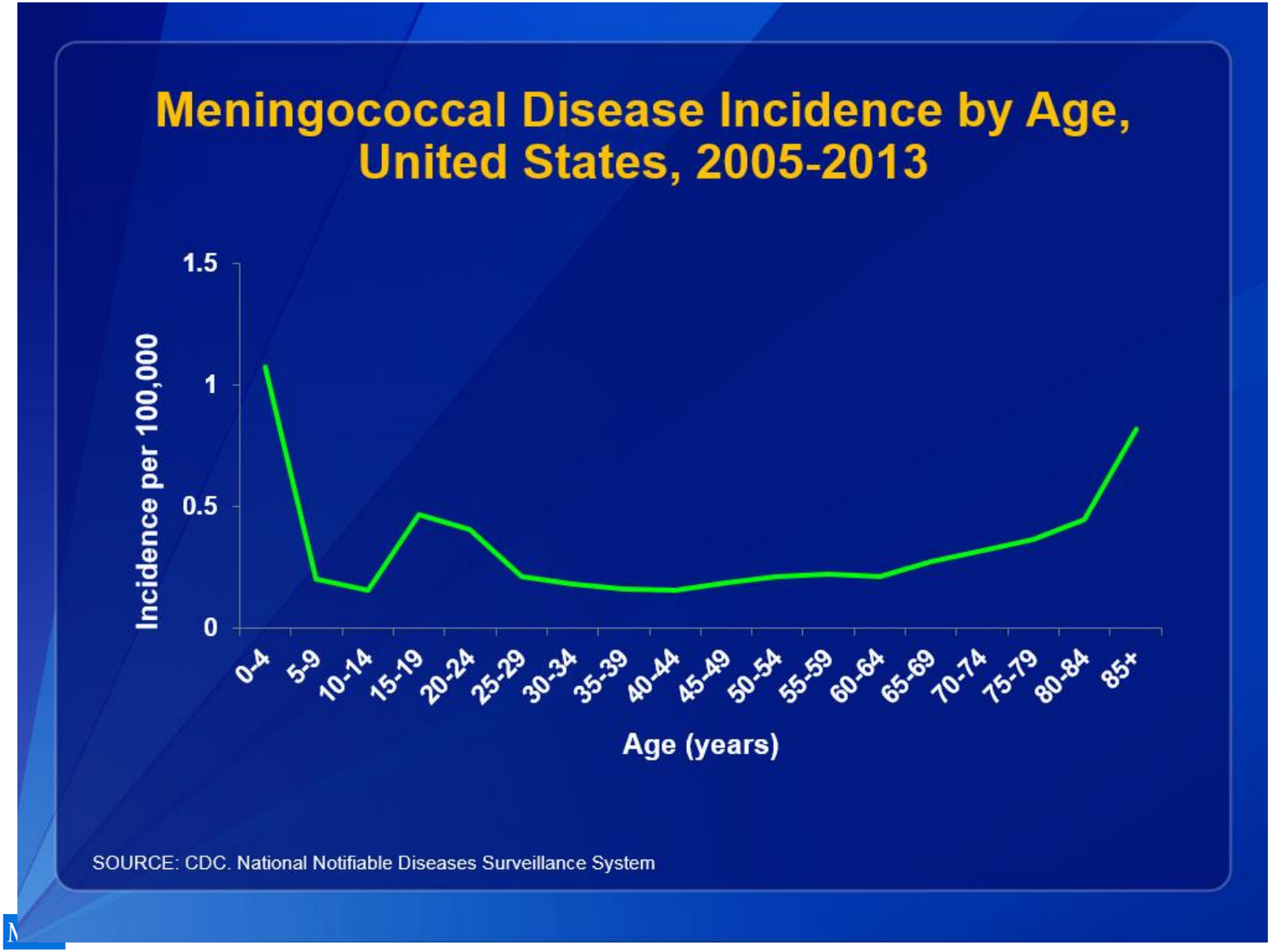

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Accessed from: http://www.cdc.gov/meningococcal/images/meningococcal-graph-lg.jpg