# Gonorrhea Treatment Strategies: Needs & Emerging Data to Address Future Challenges

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# Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020

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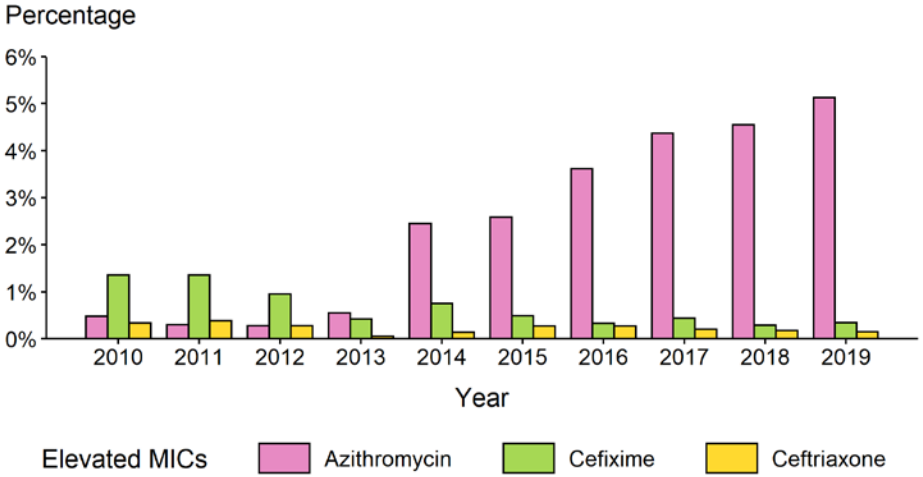
**Ceftriaxone 500 mg IM in a single dose**




**BOX. CDC recommended regimens for uncomplicated gonococcal infections, 2020**

**Regimen for uncomplicated gonococcal infections of the cervix, urethra, or rectum:**

Ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg (300 lb)

- For persons weighing ≥150 kg (300 lb), 1 g of IM ceftriaxone should be administered.
- If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.

**Alternative regimens for uncomplicated gonococcal infections of the cervix, urethra, or rectum if ceftriaxone is not available:**

Gentamicin 240 mg IM as a single dose plus azithromycin 2 g orally as a single dose OR

Cefixime 800 mg orally as a single dose. If treating with cefixime, and chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.

**Recommended regimen for uncomplicated gonococcal infections of the pharynx:**

Ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg (300 lb)

- For persons weighing ≥150 kg (300 lb), 1 g of IM ceftriaxone should be administered.
- If chlamydia coinfection is identified when pharyngeal gonorrhea testing is performed, providers should treat for chlamydia with doxycycline 100 mg orally twice a day for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.
- No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with a history of a beta-lactam allergy, a thorough assessment of the reaction is recommended.*
- For persons with an anaphylactic or other severe reaction (e.g., Stevens Johnson syndrome) to ceftriaxone, consult an infectious disease specialist for an alternative treatment recommendation.

**Abbreviation:** IM = intramuscular.

# Gaps & Challenges

- Clinical trials generally emphasize urogenital outcomes, but pharyngeal infection represents a major reservoir and AMR mechanism
- No universal option for oral therapy; parenteral therapy required
- No practical regimen for CTX alternative
- IDSA, other groups have focused on AMR; limited success
  - No new antibiotics FDA approved since 2019!
- PASTEUR act: a good first step

| Bacteria (WHO category) | WHO (2017) | Indian* (2021) | CDC (2019) | CDC (2013) | ESKAPE (2008-9) |
|---|---|---|---|---|---|
| *Acinetobacter baumannii*, carbapenem-R | Critical | Critical | Urgent (carbapenem-R) | Serious (MDR) | Yes |
| *Pseudomonas aeruginosa*, carbapenem-R | Critical | Critical | Serious (MDR) | Serious (MDR) | Yes |
| *Enterobacteriaceae*, carbapenem-R, 3rd-gen ceph-R (ESBL+) | Critical | Critical | Urgent (carbapenem-R)<br>Serious (ESBL+) | Urgent (carbapenem-R)<br>Serious (ESBL+) | Yes |
| *Enterococcus faecium*, vancomycin-R | High | High | Serious (VRE) | Serious (VRE) | Yes |
| *Staphylococcus aureus*, methicillin-R, vancomycin-I/R | High | High | Serious (MRSA) | Serious (MRSA)<br>Concerning (VRSA) | Yes |
| *Helicobacter pylori*, clarithromycin-R | High | | | | |
| *Campylobacter* spp., fluoroquinolone-R | High | | Serious (drug-R) | Serious (drug-R) | |
| *Salmonellae* spp., fluoroquinolone-R | High | High (drug-R) | Serious (drug-R, Typhi & non-typhoidal) | Serious (drug-R) | |
| *Neisseria gonorrhoeae*, 3rd-gen ceph-R, fluoroquinolone-R | High | | Urgent (drug-R) | Urgent (drug-R) | |
| *Neisseria meningitidis*, 3rd-gen ceph-R, fluoroquinolone-R | | Medium | | | |
| *Streptococcus pneumoniae*, penicillin-NS | Medium | Medium | Serious (drug-R) | Serious (drug-R) | |
| *Haemophilus influenzae*, ampicillin-R | Medium | Medium | | | |
| *Shigella* spp., fluoroquinolone-R | Medium | Medium | Serious (drug-R) | Serious | |
| Staphylococcus, coagulase-neg, Van/Lzd-R | | Medium | | | |
| *Clostridium difficile* | | | Urgent | Urgent | |
| *Candida* spp. fluconazole-R | | | Urgent (C. auris)<br>Serious (Drug-resistant) | Serious (Flu-R) | |
| *M. tuberculosis* | | | Serious (drug-R) | Serious (drug-R) | |
| Group A *Streptococcus* | | | Concerning (erythro-R) | Concerning (erythro-R) | |
| Group B *Streptococcus* | | | Concerning (clinda-R) | Concerning (clinda-R) | |
| *Aspergillus fumigatus* | | | Watch (azole-R) | | |
| *Mycoplasma genitalium* | | | Watch (drug-R) | | |
| *Bordetella pertussis* | | | Watch (drug-R) | | |

***Note that the Indian PPL sometimes differs slightly from WHO in terms of precise patterns of qualifying R.**

# What's new?
# Pew Development Pipeline December 2020

- 43 New antibiotics in development
  - > 95% small companies; > 70% pre-revenue
  - 15 phase 1 - Not a good sign!
  - 13 phase 2
  - 13 phase 3
    - 60% likely to make it to FDA approval
- 19 + potential to treat G- ESKAPE pathogens
  - 15/19 + potential activity against carbapenem-R organisms
- 10 + potential to treat *N. gonorrhoeae* or *C. difficile*
- 1 in 4 = novel drug class or mechanism of action
- Initial indications: cUTI, cIAI, ABSSSI

**Focus on systemically available antibiotics in phase 2 or beyond**

https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2014/antibiotics-currently-in-clinical-development

# PASTEUR Act

***Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act***

- **Goals:**
  - **Support the development of new antibiotics and promote appropriate use of existing ones**
  - **Limit increase and spread of resistant infections**
    - **Good stewardship**

# PASTEUR Act

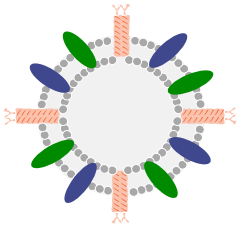
- Subscription program to provide federal payments for critically needed new antibiotics
- Payments delinked from sales —provides predictable return on investment that aligns with appropriate use goals
- Establishes a new HHS committee to determine details of subscription contracts (including preferred characteristics of drugs that should receive subscription payments); input from advisory group of non-government experts
- Payments made after drug's approval over a period of up to 10 years
- Establishes new HHS grant program to support hospital implementation of antibiotic stewardship programs and hospital reporting of antibiotic use/resistance data to CDC National Healthcare Safety Network

# PASTEUR Act

- **Bipartisan leadership:**
  - **Senators Bennet (D-CO) and Young (R-IN)**
  - **Reps. Doyle (D-PA) and Ferguson (R-GA)**
- **Supported by 40+ organizations, including: IDSA, AdvaMedDx, ASM, BIO Cystic Fibrosis Foundation, Research!America, Society of Critical Care Medicine, Society of Hospital Medicine, Society of ID pharmacists, The Joint Commission, multiple academic centers**
- **Reflects consensus recommendations from multiple expert bodies and reports: PACCARB, UK AMR Review, Duke Margolis Center for Health Policy, PCAST, DRIVE-AB**

# *N. gonorrhoeae* and *N. meningitidis* are genetically similar, with NHBA and OMV antigens present in both pathogens

**OMV**[1]



22 core proteins comprise **>90%** of OMV content

| ***Nm* OMV protein antigens** | **% ID to *Ng*** |
|---|---|
| 16 proteins | **>90%** |
| 2 proteins | **>80%** |
| 2 proteins | **<80%** |
| 2 proteins | No *Ng* homologue identified |

**NHBA**[2]

***Nm* NHBA** (present in Bexsero)

Share **67%** identity

***Ng* NHBA**

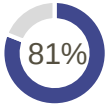
- **Surface exposed**
- Highly **conserved** in *N. gonorrhoeae* strains (>93% identity)
- Recognised by **human serum** samples from people vaccinated with Bexsero

*Ng*, *N. gonorrhoeae*; NHBA, Neisseria heparin binding antigen; *Nm*, *N. meningitidis*; OMV, outer membrane vesicle

1. Semchenko EA *et al. Clin Infect Dis* 2019;69:1101–1111; 2. Semchenko EA *et al. J Infect Dis* 2020;221:1612-1622

# In New Zealand studies, young adults vaccinated with MeNZB were less likely to have or be hospitalised with gonorrhoea

Mass MenB immunisation programme using **MeNZB** (2004–2006, 3+0 schedule)[1]




of population aged **≤20 years** received doses (~1 million individuals had 3 doses)[1]

Population included residents born 1984–1999, residing in NZ from 2004 until at least 2015[1]

Two retrospective studies investigated MeNZB effectiveness against gonorrhoea and associated hospitalisation (2004–2015/16)

Confirmed **gonorrhoea diagnoses** were assessed in a case-control study, using data from sexual health clinics[1]

1241 cases (gonorrhoea only)

12487 controls (chlamydia only)

MeNZB showed **31% effectiveness** against gonorrhea in15-30yoa (95% CI: 21–39%)

**Gonorrhoea-associated hospitalisation** was assessed in a cohort study, using hospital diagnostic coding data[2]

935,496 cohort members were included

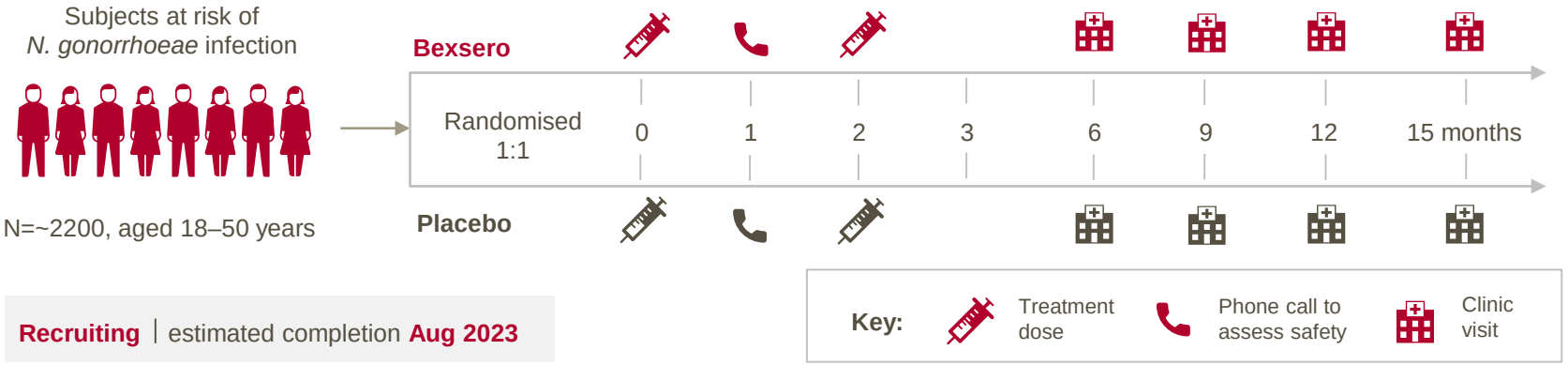
MeNZB showed **24% effectiveness** against gonorrhoea-associated hospitalization in15-30yoa (95% CI: 1–42%)

CI, confidence interval; NZ, New Zealand

1. Petousis-Harris H *et al. Lancet* 2017;390:1603-1610; 2. Paynter J *et al. Vaccines (Basel)* 2019;7:5

# A Phase II proof of concept study aims to demonstrate the efficacy of Bexsero against gonococcal infection

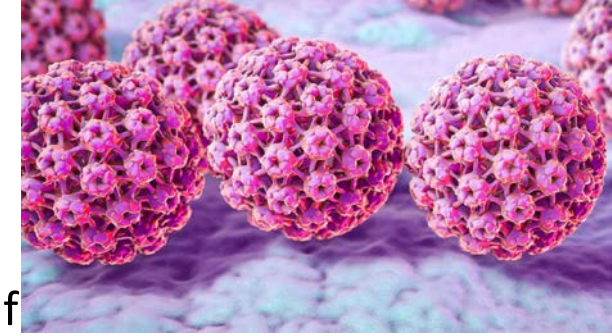
| | |
|---|---|
| **Study design** | Phase II, randomised, observer-blind, placebo-controlled trial (USA and Thailand) |
| **Primary objective** | Bexsero efficacy in preventing urogenital and/or anorectal gonococcal infection |




**Recruiting** | estimated completion **Aug 2023**

Clinical trials.gov. NCT04350138. https://clinicaltrials.gov/ct2/show/NCT04350138 (accessed February 2021)

# “STI” Immunizations



- Hepatitis A/B
- Either 9vHPV or 4vHPV vaccination through age 26 years if vaccinated previously (catch-up); shared clinical decision-making for persons 27 through 45 years
- Meningococcal vaccine in HIV+
  - MenACWY-D (Menactra) or MenACWY-CRM (Menveo)

**TABLE 1. Evidence of increased risk for meningococcal disease among HIV-infected persons compared with HIV-uninfected persons — seven study populations, 1996–2013**

| Period | Study site | Age group | No. of cases* | Increase in meningococcal disease rate among HIV-infected compared with HIV-uninfected persons | Serogroups |
|---|---|---|---|---|---|
| 1996–1999 | Australia† | All ages | 60 | 5-fold | B, C |
| 1990–2000 | London§ | All ages | 2,900 | 14-fold | B, C |
| 1988–1993 | Atlanta, Georgia¶ | 18–45 years | 132 | 24-fold | B, C, Y |
| 2003–2007 | South Africa** | All ages | 504 | 11-fold | A, B, C, W, Y |
| 2000–2008 | United States ABCs†† | 25–64 years | 491 | 13-fold | B, C, W, Y |
| 2000–2011 | New York City§§ | 15–64 years | 265 | 10-fold | C, Y |
| 2011–2013 | United Kingdom¶¶ | All ages | 2,353 | 5-fold | A, B, C, W, Y |

**Abbreviations:** ABCs = Active Bacterial Core surveillance; HIV = human immunodeficiency virus.

Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices

Emiko Petrosky, MD[1,2], Joseph A. Bocchini Jr, MD[3], Susan Hariri, PhD[2], Harrell Chesson, PhD[2], C. Robinette Curtis, MD[4], Mona Saraiya, MD[5], Elizabeth R. Unger, PhD, MD[6], Lauri E. Markowitz, MD[2] (Author affiliations at end of text)

Recommendations for Use of Meningococcal Conjugate Vaccines in HIV-Infected Persons — Advisory Committee on Immunization Practices, 2016

Jessica R. MacNeil, MPH[1]; Lorry G. Rubin, MD[2]; Monica Patton, MD[1]; Ismael R. Ortega-Sanchez, PhD[3]; Stacey W. Martin, MS[1]

Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020

# Challenges in GC Diagnosis

- Many GC infections are asymptomatic or have atypical symptoms; routine screening performance remains suboptimal, especially in HIV care settings & at sites not diagnosed by urine
  - Diagnosis often depends on presentation of clinical syndromes
- Limited availability of culture; practical barriers
- Slow uptake of point of care testing, encouraging developments in last year

binx health Receives FDA CLIA Waiver for Chlamydia and Gonorrhea Test, Expanding Critical Access to Single-Visit Diagnoses

binx

USA - English

First ever 30-minute, CLIA-waived, molecular PCR Test for CT/NG now available for OBGYN, physician offices and retail settings holding certificates of waiver

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