Case for Gonococcal Prevention

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Pelvic inflammatory disease: cervicitis, salpingitis, endometritis.
Accessory gland infection
Peri-hepatitis
Pregnancy morbidity

Disseminated Gonococcal Infection (DGI): arthritis-dermatitis syndrome, endocarditis, meningitis

Urethritis
Proctitis
Pharyngeal infections
Conjunctivitis

Infertility
Ectopic Pregnancy
Spontaneous abortion
Congenital Infection:
- Ophthalmia neonatorum: destructive corneal scarring and blindness
- Skin infections

Common coinfections with other sexually transmitted pathogens
Increase risk to contract and transmit HIV
Many infections asymptomatic:
- 50-80% Female
- ~40% Male
- Second most common bacterial STI
- Global incidence of over 78 million cases per year 21% increase incidence between 2005 and 2012 (WHO).
- Rates vary: incidence is 12.5 cases/100,000 population in Europe and ≈6,000 cases/100,000 population in parts of sub-Saharan Africa

- In the UK, there has been a year-on-year increase in cases between 2008 and 2015

Data are estimated numbers of incident cases in millions for chlamydia, gonorrhoea, syphilis, and trichomoniasis in 2012. Unemo M. The Lancet. 2017

Control of *N. gonorrhoeae*

- Antimicrobial resistance is a major problem:

  - Emergence of *N. gonorrhoeae* with high-level resistance to azithromycin and resistance to ceftriaxone acquired abroad

  - UK case of *Neisseria gonorrhoeae* with high-level resistance to azithromycin and resistance to ceftriaxone acquired abroad

  - *Gonorrhoea* has the potential to become untreatable (WHO)


  - Urgent need for a vaccine
Vaccines to tackle drug resistant infections
An evaluation of R&D opportunities

GONOCOCCAL VACCINE PROJECT

(published 5 October 2018)
Difficulties in vaccine development

- Lack of knowledge of the immune response against GC
  - Antibody production is low and not necessarily protective
  - Able to avoid and actively suppress innate and adaptive immune response:
    - Elicit a Th17 drive innate inflammatory responses and suppress Th1/Th2-mediated specific immune responses
    - Production of blocking antibodies against conserve antigens: Rmp
    - Actively expelling hydrophobic antimicrobial substances: by active efflux pump system
    - Resistance to the bactericidal activity of human serum: LOS sialylation and phase variation, PorB
  - Lack of knowledge of what immune respond might confer protection:
    - Natural infection does not induce protection \(\Rightarrow\) generation of a non-native immune response

- Variability of gonococcal antigens: phase and antigenic variation difficulty finding targets common to all strains.

- Lack of knowledge on genital tract immunology


- Lack of a robust animal model:
  - 17β-estradiol and antibiotics treated BALB/C (or C57/BL6) mice
  - Host restrictions severely limit the capacity of this model
Vaccines against *N. gonorrhoeae*

- Vaccines against gonorrhoea
  1) Whole cell vaccine sterilized with thimerosal: **No efficacy**
     Sex workers in Nairobi (1973)  
  2) Pilus vaccine: **No efficacy**
     US Army trial in Korea (1983)
     Boslego et al, Vaccine, 1991
  3) Protein I-based vaccine (PorB) vaccine: **No efficacy**
     Medical student volunteers (1986)  
     Rice et al, In Neisseria 1994

- Vaccines against meningococcus

  MeNZB: *N. meningitidis* OMVs vaccine used for meningitis outbreak - 15-30 year olds
  31% (95%CI 21-39) **estimate effectiveness** against gonorrhoea
  Replicated in the mouse model with Bexsero (parenteral administration) (IPNC 2018)