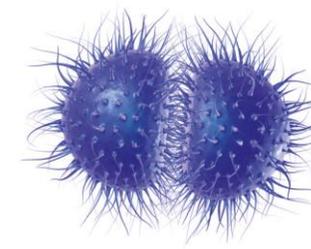




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**GONOCOCCAL
VACCINE PROJECT**

Case for Gonococcal Prevention

Cal MacLennan

Gonococcal Vaccine Project, Jenner Institute, University of Oxford

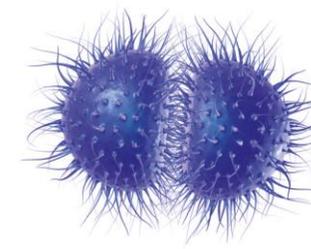
Meningitis Research Foundation Conference

2 November 2021



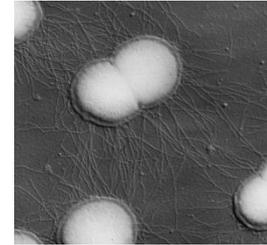
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Gonorrhoea

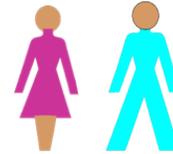


GONOCOCCAL VACCINE PROJECT

- Sexual transmitted infection
- Caused by: *Neisseria gonorrhoeae*, gonococcus, GC:
Gram Negative diplococci
Obligate human pathogen



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

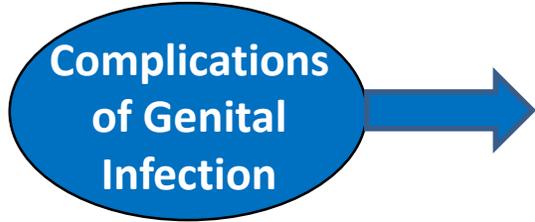


Disseminated Gonococcal Infection (DGI):
arthritis-dermatitis syndrome
endocarditis, meningitis

Urethritis
Proctitis
Pharyngeal infections
Conjunctivitis



Epididymitis (male infertility)
Abscess of Cowper's/Tyson's glands
Seminal vesiculitis
Prostatitis



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

Common coinfections with other sexually transmitted pathogens

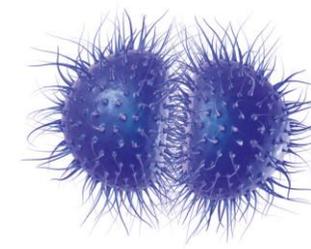
Increase risk to contract and transmit HIV

Many infections asymptomatic: 50-80 % Female
~40 % male



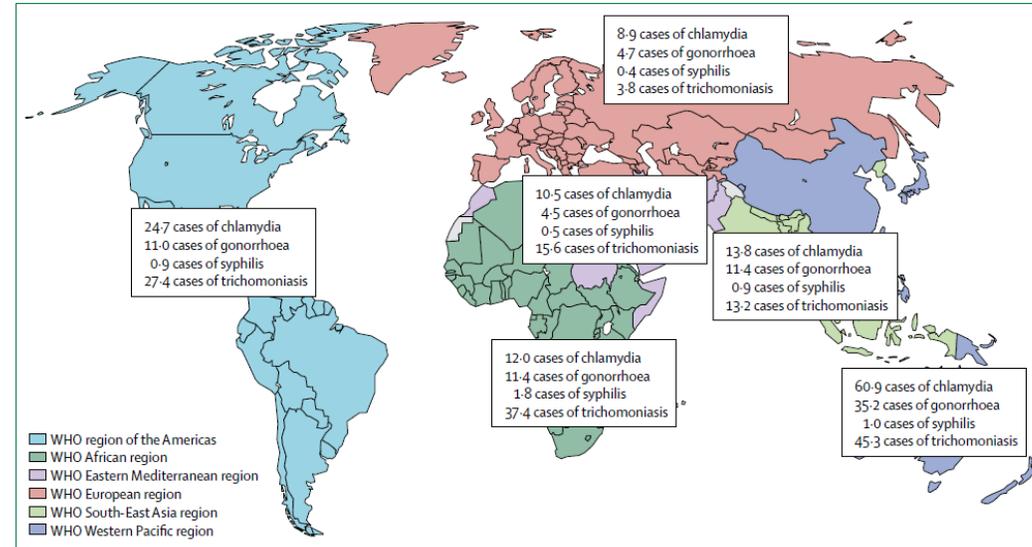
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Gonorrhoea



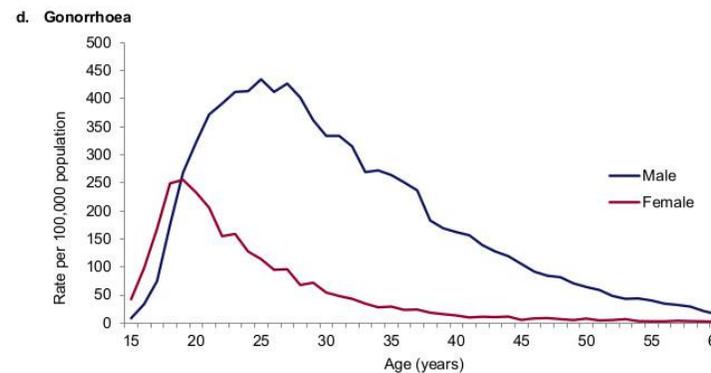
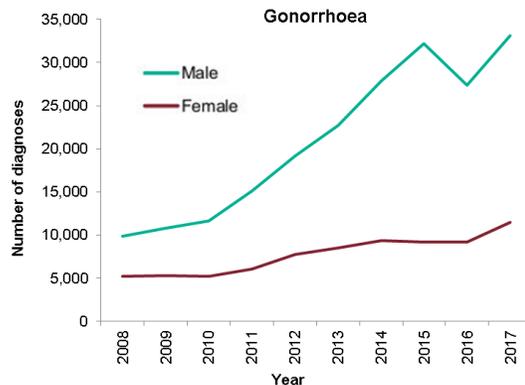
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- Second most common bacterial STI
- Global incidence of over 78 million cases per year 21 % increase incidence between 2005 and 2012 (WHO).
- Rates vary: incidence is 12.5 cases/100,000 population in Europe and ≈6,000 cases/100,000 population in parts of sub-Saharan Africa



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

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

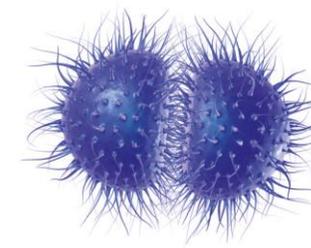


Public Health England. Health Protection Report. June 2018.



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Control of *N. gonorrhoeae*



GONOCOCCAL VACCINE PROJECT

- Antimicrobial resistance is a major problem:

Public Health England
Protecting and improving the nation's health

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

Health Protection Report Advanced Access Report
Volume 12 Number 11
29 March 2018

- First clinical use
- Last clinical use
- Development of resistance

Untreatable gonorrhoea?

Quillin SJ, Seifert. Nat Rev Microbiol. 2018

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Health

Man has 'world's worst' super-gonorrhoea

By James Gallagher
Health and science correspondent, BBC News

28 March 2018

f t Share



A man in the UK has caught the world's "worst-ever" case of super-gonorrhoea.

Gonorrhoea has the potential to become untreatable (WHO)

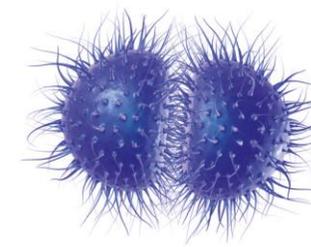
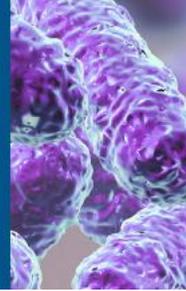
Urgent need for a vaccine



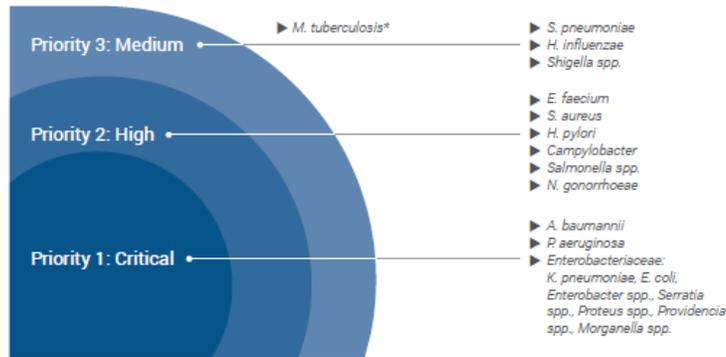
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Vaccines to tackle drug resistant infections

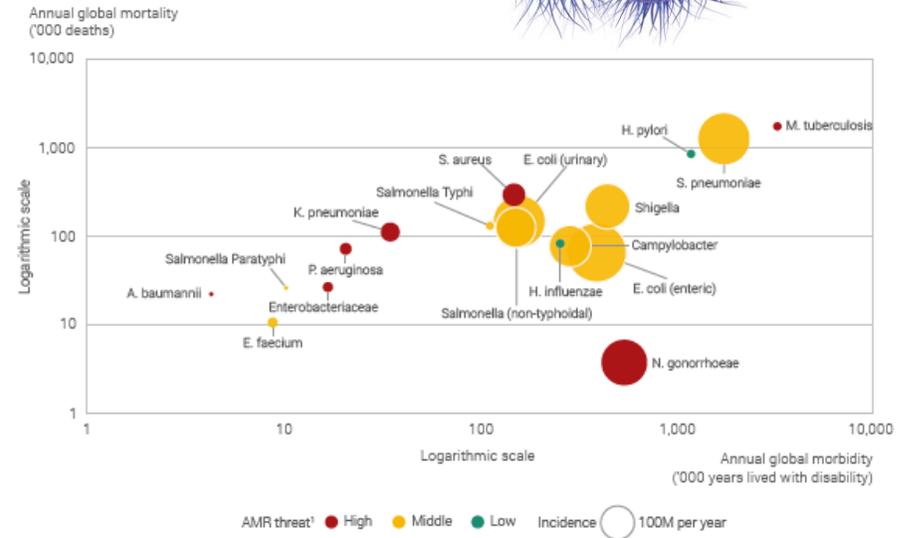
An evaluation of R&D opportunities



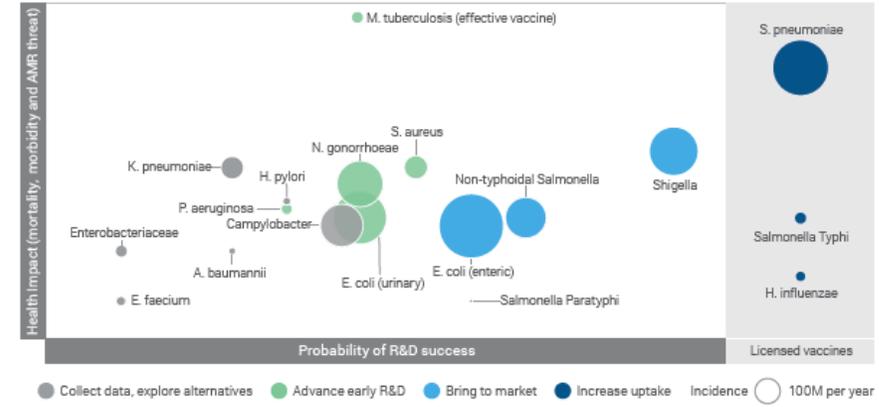
GONOCOCCAL VACCINE PROJECT



Note: WHO 2017: Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics; *M. tuberculosis was not subjected to review for inclusion in the WHO priority list. However, it was specifically acknowledged as a globally established priority for which innovative new treatments are urgently needed. We therefore included this pathogen in our analysis.



1) Colour code for AMR threat different from pathogen scorecards. Source: WHO and IHME 2016 global disease burden datasets and literature review – full source list and methodology in appendix.



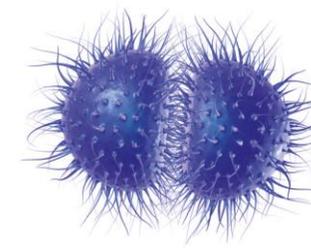
Weighting used for chart
Health Impact – Mortality (50%), Morbidity (20%), AMR (30%).
Prob. of R&D success – Pathogen biology (30%), Pre-clinical and clinical R&D (30%), Pipeline robustness (40%).

(published 5 October 2018)



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Difficulties in vaccine development



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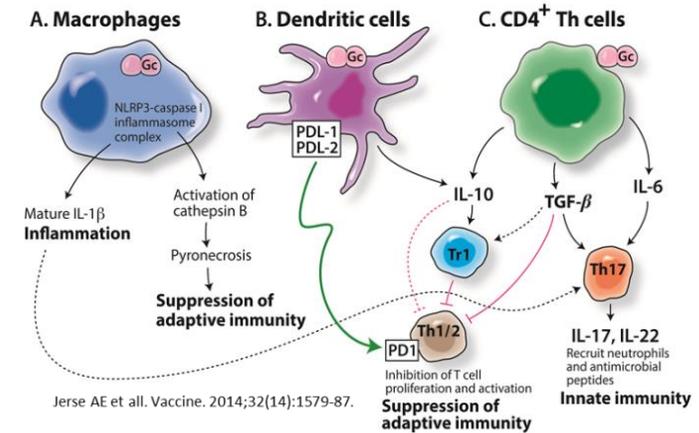
- Lack of knowledge of the immune response against GC
 - Antibody production is low and not necessarily protective
 - Able to avoid and actively suppress innate and adaptive immune response:

- 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 response might confer protection:

- **Natural infection does not induce protection → 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 *in vitro* correlate of protection : induction of mucosal IgG and IgA antibodies, and a bactericidal serum response, did not predict protection (Zhu W. Front Microbiol. 2011;2:124).
- 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





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Vaccines against *N. gonorrhoeae*



- Vaccines against gonorrhoea

1) Whole cell vaccine sterilized with thimerosal : **No efficacy**

Sex workers in Nairobi (1973) Greenberg et al, Canad. J. Publ. Health, 1974

2) Pilus vaccine : **No efficacy**

Boslego et al, Vaccine, 1991

US Army trial in Korea (1983)

3) Protein I-based vaccine (PorB) vaccine: **No efficacy**

Medical student volunteers (1986) Rice et al, In Neisseria 1994



- Vaccines against meningococcus

Effectiveness of a group B outer membrane vesicle
meningococcal vaccine against gonorrhoea in New Zealand:
a retrospective case-control study



(Lancet, 2017)

Helen Petousis-Harris, Janine Paynter, Jane Morgan, Peter Saxton, Barbara McArdle, Felicity Goodyear-Smith, Steven Black

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)