Are we entering an era of untreated gonorrhoea?

Dr Ranmini Kularatne
Department of Clinical Microbiology & Infectious Diseases
University of the Witwatersrand and National Health Laboratory Service
Gonorrhoea

• “Flow of seed” (Greek)
• “The clap” – derived in 1378 from the name of a Parisian brothel (Les Clapiers)
• Caused by *Neisseria gonorrhoeae*
  – sexually transmitted
  – obligate pathogen of humans
• Complications
  – PID
  – Ectopic pregnancy
  – Epidymo-orchitis
  – Disseminated gonococcal infection
  – Infertility
• 2008 (WHO): 106 million new cases globally
  – 21% increase since 2005
Prevalence of gonococcal infection:
- **MUS** – 71% (n=217)
- **VDS** – 13.1% (n= 206)
Major public health concern

- Short incubation period
- High transmission efficiency. Co-efficient of infection:
  - female to male = 0.6; male to female = 0.7
Fivefold increase in HIV transmission\textsuperscript{1}

Asymptomatic urogenital infections in $\geq 50\%$ infected women

Rectal and pharyngeal gonorrhoea (MSM) mostly asymptomatic

Eradication from oropharynx more difficult than from urogenital sites\textsuperscript{2}
  – Differential concentration of antimicrobials
  – Selection for antimicrobial resistance

Remarkable capacity acquire genetic antimicrobial resistance determinants

\textsuperscript{1}WHO/RHR/11.14  2011
\textsuperscript{2}Curr Opin Infect Dis 2014; 27 (3): 282-283
Mechanisms of antimicrobial resistance in *Neisseria gonorrhoeae*

Plasmid or chromosome mediated

• 1. Antimicrobial destruction/ modification by enzymes
• 2. Target modification or protection leading to reduced affinity
• 3. Decreased antimicrobial influx (porin mutations)
• 4. Increased antimicrobial efflux (upregulation of efflux pumps)
Mechanisms of antimicrobial resistance in *Neisseria gonorrhoeae*

**a** Spectinomycin and macrolides
- 16S rRNA (Spectinomycin)
- 23S rRNA (Azithromycin)

**b** Fluoroquinolones
- gyrA
- parC

**c** β-lactams (including cephalosporins)
- ponA
- penA

**d** β-lactams (including cephalosporins) and others
- porB

**e** β-lactams (including cephalosporins) and others
- mtrR

**f** β-lactams
- blaTEM-1

**g** Tetracyclines
- tetM

OM IM

---

Resistance evolution in *Neisseria gonorrhoeae*

![Diagram showing the resistance evolution timeline for *Neisseria gonorrhoeae*. The timeline includes the introduction years and the resistance reporting years for various antibiotics.](image)

**Figure 1** | The history of *Neisseria gonorrhoeae* antimicrobial resistance.

---

Antimicrobial resistance and gonococcal fitness

• In *Neisseria gonorrhoeae*, antimicrobial resistance does not appear to confer a fitness cost
  – Resistance mutations persist in the absence of antimicrobial selection pressure

• Some resistance determinants (*gyrA* mutations, MtrCDE efflux pumps) may enhance biological fitness

• Fitness retained due to additional compensatory/ stabilizing/ repairing mutations

_Clin Micro Rev 2014; 27(3): 587-612_
Proportion of *N. gonorrhoeae* strains resistant to ciprofloxacin and/or other quinolones reported in countries, 2010

Source: GASP 2013
The ciprofloxacin resistant phenotype was significantly associated with HIV serostatus (p = 0.034).

Lewis et al., Sex Transm Infect 2008; 84: 352-355
MALE URETHRITIS SYNDROME (MUS)

Patient complains of urethral discharge or dysuria

Take history and examine. Milk urethra, if no visible discharge. Emphasise HIV testing.

Discharge and/or dysuria present?

YES

Treat with:
- Cefixime, oral, 400 mg single dose**
- Doxycycline, oral, 100 mg twice daily for 7 days

Ask patient to return in 7 days if symptoms persist

If symptoms persist

- Unprotected intercourse?
- Poor adherence?

YES

Repeat treatment

NO

Treat with:
- Metronidazole 2g immediately as a single dose

Ask patient to return in 7 days if symptoms persist

Improved?

NO

Treatment failure: Refer

YES

Discharge patient
**Extended-spectrum cephalosporin (ESC) resistance in Neisseria gonorrhoeae**

- ESCs: last antimicrobial class suitable for widespread single-dose single-agent treatment.
  - Cefixime is the only oral ESC that met criteria for effective treatment of pharyngeal gonorrhoea ($\geq 95\%$ cure rate).
  - SA: cefixime 400mg single-dose introduced into STI syndromic management guidelines (MUS, VDS) in 2008.

- Japan: in the 1990s a variety of oral ESCs with suboptimal efficacy and dosing regimens used in monotherapy
  - cephalosporin MIC creep & ultimate treatment failure with cefixime

*JAC 2010; 65: 2141-2148*
Extended-spectrum cephalosporin (ESC) resistance in *Neisseria gonorrhoeae*

- The primary resistance determinant is a specific alteration in *penA* gene that encodes PBP2
  - Transformation due to acquisition & incorporation of *penA* gene sequences from commensal *Neisseria* species in oropharynx
    - *(N. perflava, N. sicca, N. cinerea, N. flavescens)*

**Mosaic penA gene** → **mosaic PBP2**

### Criteria for decreased susceptibility to cephalosporins

<table>
<thead>
<tr>
<th>Drug</th>
<th>MICs (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefixime</td>
<td>≥0.25</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≥0.125</td>
</tr>
</tbody>
</table>

*WHO 2012*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PPNG</td>
<td>1.1%</td>
<td>0.7%</td>
<td>0.5%</td>
</tr>
<tr>
<td>TRNG (MIC ≥ 16mg/l)</td>
<td>2.2%</td>
<td>0.7%</td>
<td>0.5%</td>
</tr>
<tr>
<td>CMRNG Pen (MIC ≥ 2mg/l)</td>
<td>2.2%</td>
<td>59.3%</td>
<td>73.3%</td>
</tr>
<tr>
<td>CMRNG Tet (MIC ≥ 2mg/l)</td>
<td>11.0%</td>
<td>53.7%</td>
<td>68.8%</td>
</tr>
<tr>
<td>QRNG Levofloxacin (MIC ≥ 1mg/l)</td>
<td>27.5%</td>
<td>53.3%</td>
<td>78.3%</td>
</tr>
<tr>
<td>Cefixime decreased susceptibility (MIC ≥ 0.5mg/l)</td>
<td>0%</td>
<td>26.0%</td>
<td>30.3%</td>
</tr>
<tr>
<td>Ceftriaxone decreased susceptibility (MIC ≥ 0.5mg/l)</td>
<td>0%</td>
<td>0%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Spectinomycin resistance (MIC ≥ 128mg/l)</td>
<td>0%</td>
<td>0.7%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Emergence of Clinically Confirmed Cefixime Treatment Failures in Europe

**Rapid Communications**

**Two cases of verified clinical failures using internationally recommended first-line cefixime for gonorrhoea treatment, Norway, 2010**

M Unemo (magnus.unemo@orebro.Important), D Golparian, G Syversen, D F Vestrheim, H Moi

1. Swedish Reference Laboratory for Pathogenic Neisseria, Department of Laboratory Medicine, Microbiology, Örebro University Hospital, Örebro, Sweden
2. Department of Microbiology, Oslo University Hospital, Ullevål, Oslo, Norway
3. Olaafaklinikken, Oslo University Hospital, Oslo, Norway
4. Division of Infectious Disease Control, Norwegian Institute of Public Health, Oslo, Norway
5. Faculty of Medicine, University of Oslo, Oslo, Norway

Citation style for this article:


Article published on 25 November 2010

**Rapid Communications**

**Gonorrhoea treatment failures to cefixime and azithromycin in England, 2010**

C A Ison (catherine.ison@hpa.org.uk), J Hussey, K N Sankar, J Evans, S Alexander

1. Sexually Transmitted Bacteria Reference Laboratory, Health Protection Agency, London, United Kingdom
2. Carlton Street Clinic, Blyth, Northumberland, United Kingdom
3. New Croft Centre, Newcastle upon Tyne, United Kingdom
4. Health Protection Agency North East, Newcastle General Hospital, Newcastle upon Tyne, United Kingdom

Citation style for this article:


Article published on 7 April 2011
Emergence of Cefixime Resistant Gonococci and Cefixime Treatment Failure in South Africa

Lewis et al. JAC 2013; 1-4

- Phadebact serogroup WII/WIII
- NG-MAST ST 4822 *(porB 1903; *tbpB* 29)*
- MLST ST 1901
- Mosaic XXXIV (same as F89, MSM-linked)
- A-deletion in *mtrR* promoter
- *penB* mutations: G101K, A102N
- *ponA* mutation: L421P

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Patient A (mg/L, agar dilution)</th>
<th>Patient B (mg/L, agar dilution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefixime</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0.128</td>
<td>0.064</td>
</tr>
<tr>
<td>Penicillin</td>
<td>4 (β-lactamase –ve)</td>
<td>4 (β-lactamase –ve)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&gt; 16</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>Spectinomycin</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>
Emergence of Cefixime Resistant Gonococci and Cefixime Treatment Failure in South Africa

Lewis et al. JAC 2013; 1-4

3rd case from Cape Town and 4th case from East London with identical NG MAST genotype

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Patient A (mg/L, agar dilution)</th>
<th>Patient B (mg/L, agar dilution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefixime</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0.128</td>
<td>0.064</td>
</tr>
<tr>
<td>Penicillin</td>
<td>4 (β-lactamase –ve)</td>
<td>4 (β-lactamase –ve)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>4</td>
<td>32</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&gt; 16</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Spectinomycin</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

- Phadebact serogroup WII/WIII
- NG-MAST ST 4822 (porB 1903; tbpB 29)
- MLST ST 1901
- Mosaic XXXIV (same as F89, MSM-linked)
- A-deletion in mtrR promoter
- penB mutations: G101K, A102N
- ponA mutation: L421P
The World’s First Confirmed Gonococcal Isolate Resistant to Ceftriaxone (XDR)

- Gonococcal strain isolated from the pharynx of a female sex worker in Kyoto, Japan (H041) in 2009

- Confirmed as *N. gonorrhoeae* by 7 tests

- MIC to ceftriaxone 2-4 µg/ml and to cefixime 8 µg/ml

- Resistant to most beta-lactams including piperacillin/tazobactam, fluoroquinolones, macrolides, tetracycline, co-trimoxazole, chloramphenicol and nitrofurantoin

- Susceptible to spectinomycin, rifampicin and imipenem

*Antimicrob Agents Chemother 2011; 55 (7): 3538-3545*
Emergence of Clinically Confirmed Ceftriaxone Treatment Failures in Europe (F89 XDR) NG-MAST ST1407; MLST ST1901

High-Level Cefixime- and Ceftriaxone-Resistant Neisseria gonorrhoeae in France: Novel penA Mosaic Allele in a Successful International Clone Causes Treatment Failure

Magnus Unemo, Daniel Golparian, Robert Nicholas, Makoto Ohnishi, Anne Gallay, and Patrice Sednaoui

WHO Collaborating Centre for Gonorrhoea and Other STIs, Department of Laboratory Medicine, Microbiology, Orebro University Hospital, Orebro, Sweden; Department of Pharmacology, University of North Carolina, Chapel Hill, North Carolina, USA; National Institute of Infectious Diseases, Tokyo, Japan; Institut de Veille Sanitaire, Saint-Maurice, France; and Institut Alfred Fournier, Centre National de Référence des Gonocoques, Paris, France

Molecular characterization of two high-level ceftriaxone-resistant Neisseria gonorrhoeae isolates detected in Catalonia, Spain

Jordi Cámara, Judit Serra, Josefina Ayats, Teresa Bastida, Dolors Carnicer-Pont, Antonia Andreu, and Carmen Ardanuy

1Microbiology Department, Hospital Universitari de Bellvitge-Universitat de Barcelona-IDIBELL, L’Hospitalet de Llobregat, Barcelona, Spain; 2Microbiology Department, Hospital Universitari Vall d’Hebron, Barcelona, Spain; 3Microbiology Department, ‘Esperit Sant’ Regional Hospital, Santa Coloma de Gramenet, Spain; 4Centre d’Estudis Epidemiologics sobre les Infeccions de Transmissió Sexual i Sida de Catalunya (CEEISCAT), Institut Català d’Oncologia, Badalona, Barcelona, Spain
Countries with documented elevated minimum inhibitory concentrations to cefixime and/or ceftriaxone, 2010

Legend
- Elevated Minimum Inhibitory Concentrations (MIC*)
- No elevated MIC
- No data
- Treatment failure report

*Defined as cefixime MIC > 0.25 μg/L or ceftriaxone MIC > 0.125 μg/L

Source: GASP 2013
**Multi-Drug and Extensively-Drug Resistant Neisseria gonorrhoeae (MDR-NG and XDR-NG)**

<table>
<thead>
<tr>
<th>MDR-NG: resistant to $\geq 1$ class I antibiotic PLUS resistant to $\geq 2$ class II antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>XDR-NG: resistant to $\geq 2$ class I antibiotics PLUS resistant to $\geq 3$ class II antibiotics</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class I antibiotics</th>
<th>Class II antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>(currently recommended for use)</td>
<td>(used less frequently or proposed for more extensive use)</td>
</tr>
<tr>
<td>Injectable extended spectrum cephalosporins</td>
<td>Penicillins</td>
</tr>
<tr>
<td>Oral extended spectrum cephalosporins</td>
<td>Fluoroquinolones</td>
</tr>
<tr>
<td>Spectinomycin</td>
<td>Azithromycin</td>
</tr>
<tr>
<td></td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td></td>
<td>Carbapenems</td>
</tr>
</tbody>
</table>

*Expert Rev Anti Infect Ther 2009; 7: 822-834*
1. National change in recommended first line therapy for gonorrhoea from oral cefixime to injectable ceftriaxone.

2. Dual antimicrobial therapy to treat gonorrhoea

---

**Table 1.** Various dosing regimens of ceftriaxone for *Neisseria gonorrhoeae* throughout the world

<table>
<thead>
<tr>
<th>Country</th>
<th>Ceftriaxone dose</th>
<th>Combination therapy recommended?</th>
<th>Recommended second agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>250 mg IM</td>
<td>Yes</td>
<td>Azithromycin (preferred) or doxycycline</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>500 mg IM</td>
<td>Yes</td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Europe</td>
<td>500 mg IM</td>
<td>Yes</td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Japan</td>
<td>1g IV</td>
<td>No</td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Canada</td>
<td>250 mg IM or 800 mg cefixime PO(^a)</td>
<td>Yes</td>
<td>Azithromycin</td>
</tr>
</tbody>
</table>

*Curr Opin Infect Dis 2014; 27 (1): 62-67*

*Curr Opin Infect Dis 2014; 27 (3): 282-287*
WHO: discontinue routine use of antimicrobial when resistance > 5%

Patient complains of urethral discharge or dysuria

Take history, including sexual orientation and examine. If no visible discharge; ask patient to milk urethra. Emphasise HIV testing and partner(s) tracing.

» Discharge

Y

Treatment
- Ceftriaxone, IM, 250 mg single dose
- Azithromycin, oral, 1 g as a single dose

If sexual partner has VDS, add:
- Metronidazole, oral, 2 g as a single dose

Urethral discharge persists after 7 days.

Suspected cefixime treatment failure:
- Ceftriaxone, IM, 1 g single dose
- Azithromycin, oral, 2 g as a single dose
- Metronidazole, oral, 2 g as a single dose, if not already given

Refer all ceftriaxone treatment failures within 7 days for gentamicin IM, 240 mg as a single dose

Emphasise partner's tracing
Box 1
Case definition – *Neisseria gonorrhoeae* cephalosporin treatment failure

A person who has received appropriate treatment for gonococcal infection with one of the recommended cephalosporin regimens (for example, ceftriaxone or cefixime)

AND

One of the following positive tests for *N. gonorrhoeae*:

- the presence of intracellular Gram-negative coccci on microscopy taken at least 72 h after completion of treatment; or
- isolation of *N. gonorrhoeae* by culture taken at least 72 h after completion of treatment; or
- a positive nucleic acid amplification test (NAAT) taken 2–3 weeks after completion of treatment.

AND

No history of sexual contact reported during the post-treatment follow-up period.
WHO: Global action plan to control spread and impact of AMR NG (2012)

1. Improving early detection of infection
   - Effective prevention diagnosis and control of gonorrhoea

2. Appropriate and effective treatment for patients and sexual partners
   - Awareness on correct use of antibiotics among HCW, esp in key populations e.g. MSM, CSW

3. Systematic monitoring, early detection and follow-up of treatment failures
   - Standard case definition for treatment failure

4. Effective drug regulations and prescription policies
   - Prevent unrestricted access, inappropriate selection
WHO: Global action plan to control spread and impact of AMR NG (2012)

• 5. Laboratory capacity strengthening
  – Awareness among clinicians regarding resistant NG
  – Strengthen HCW skills in specimen collection
  – Train laboratory personnel

• 6. Strengthen antimicrobial resistance surveillance in high burden countries
  – Standardized protocols for testing, external quality assurance programs
  – Regional networks of laboratories that perform quality-assured NG culture/ antimicrobial susceptibility.

• 7. Research
  – New molecular methods for detection and monitoring of resistance
  – ID alternative therapeutic strategies/ novel antimicrobials/ vaccine
WHO: Regional response plan (2012) – ESC resistance

- Local health departments should initiate epidemiological assessments to monitor spread in affected area:
  - 1. Review of clinical records to ID additional cases of treatment failure
  - 2. Epidemiological assessment to ID demographic and behavioural risk factors
  - 3. Design and implementation of clinic-based activities to enhance case detection
    - Targeted screening
    - *Test-of-cure using culture for key populations*
  - 4. Enhance laboratory capacity for culture/susceptibility testing
  - 5. Enhance local surveillance activities
  - 6. *Prioritize notification of sexual contacts*
### WHO Global Antimicrobial Surveillance network (GASP) – baseline report 2012

#### Number of countries participating in the Gonococcal Antimicrobial Surveillance Programme (GASP) network

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Regional GASP focal points</th>
<th>Number of countries participating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>Currently none</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Formerly, until February 2012, Sexually Transmitted Infections Reference Centre, National Health Laboratory Service, Johannesburg, South Africa</td>
<td></td>
</tr>
<tr>
<td>The Americas</td>
<td>Sexually Transmitted Infections Reference Centre, National Institute of Infectious Disease, Buenos Aires, Argentina</td>
<td>13 plus Canada and the USA</td>
</tr>
<tr>
<td></td>
<td>University of Saskatchewan, Saskatoon, Canada</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA</td>
<td></td>
</tr>
<tr>
<td>The Eastern Mediterranean</td>
<td>STD Laboratory, Bacterial Department, National Institute of Hygiene, Rabat, Morocco</td>
<td>1</td>
</tr>
<tr>
<td>Europe</td>
<td>Sexually Transmitted Bacteria Reference Laboratory, Health Protection Agency Centre, London, UK</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>WHO Collaborating Centre for Gonorrhoea and Other STIs, Department of Laboratory Medicine, Microbiology, Orebro University Hospital, Orebro, Sweden</td>
<td></td>
</tr>
<tr>
<td>South-East Asia</td>
<td>WHO GASP South-East Asia Regional Reference Laboratory, VMMC and Safdarjang Hospital, New Delhi, India</td>
<td>6</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>WHO Collaborating Centre for STD – South Eastern Area Laboratory Services (SEALS), The Prince of Wales Hospital, Sydney, Australia</td>
<td>15</td>
</tr>
</tbody>
</table>

**Status of the data:** **Gonococcal Antimicrobial Susceptibility Programme**

Although 62 countries participate in the GASP network, only 50 countries had available data for 2009–2010 on ceftriaxone (or cefixime), azithromycin, and quinolones (Table 3). Data on quinolones are the most widely available data (all countries reporting), whereas data on ceftriaxone (or cefixime) were available for 32 countries and on azithromycin for 29 countries.
1. Alternative single dose options
   - Spectinomycin: costly, low cure rate for pharyngeal NG, rapid emergence of resistance
   - Gentamicin: limited \textit{in vitro} data; need efficacy data for extragenital NG
   - Azithromycin: ESC non-susceptible NG show reduced susceptibility; high level resistance with monotherapy; side effects associated with 2g dose

2. Novel treatment options
   - Ertapenem: increasing MICs seen in ESC non-susceptible NG; parenteral
   - Tigecycline: active \textit{in vitro} against ESC non-susceptible strains; use in urogenital infections questionable; parenteral
   - Solithromycin: fluoroketolide undergoing phase 2 clinical trials
   - New broad-spectrum fluoroquinolones: avarofloxacin, delafloxacin

3. New targets
   - Novel inhibitors of bacterial topoisomerases/ efflux pumps
   - Therapeutic vaccine

\textit{JAC} 2014; 69: 2086-2090
Future developments (Diagnostics)

• 1. Resistance prediction by genotype association
  – NG-MAST: DNA sequencing of two variable outer membrane protein genes (porB & tbpB)
  – NG-MAST sequence types in a given geographical area possess similar resistance profiles (e.g. NG-MAST ST 1407 related to XDR strain F89)
  – Need representative number of sample isolates from a region for an unbiased assessment of resistance

• 2. Detection of specific genetic mechanisms of resistance
  – Chromosomal resistance relies on synergistic effect of multiple mutations
  – Need to define targets that are fundamental to resistance (e.g. gyrA PCR for quinolone resistance)

• Molecular surveillance
  – International database of NG penA ST associated with ESC resistance
  – Complementary to culture-based surveillance

Key Points

1. Incidence of gonorrhoea increasing worldwide

2. Antimicrobial resistance in NG increasing, XDR strains characterized by high ESC MICs

3. Use of high dose ceftriaxone as national first line therapy may slow spread of XDR NG

4. Combination treatment with azithromycin may curtail emergence of XDR NG

5. Enhanced national and regional culture-based surveillance (public & private sectors) essential, particularly in key populations
   - Political advocacy, evidence-based guidelines, funding, and investment in laboratory infrastructure & training
“Although we have not yet had the ‘knockout’ punch, the gonococcus appears to be winning on points”

Lewis, D. Sex Transm Infect 2010; 86: 415-421