# Changes to Guidelines for Treatment of Gonorrhoea & their Role in Gonorrhoea Control

**2019 Australasian Sexual Health Conference, Perth**

**16 September 2019**

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THE UNIVERSITY OF SYDNEY

# Disclosures

- **GSK**: External Advisory Support for Gepotidacin development for treatment of gonorrhoea (current)
- **GARDP-Entasis**: External Advisory Support for Zoliflodacin development treatment of gonorrhoea (2017-2019)
- **SpeedX**: ResistancePlus™ MG assay research samples, video production

# Antibiotic Prescribing Guidelines

- Antibiotic prescribing guidelines should be used in all health care settings where antibiotics are prescribed.
- They guide prescribers on antibiotic treatment, including:
  - choosing the best antibiotic
  - correct dose
  - when and how it should be taken
  - how long it should be taken
- In some settings, there are local guidelines to guide decision making based on local or regional differences in resistance patterns
- Increasingly, clinicians must choose from numerous, sometimes differing, and occasionally contradictory, guidelines
- Adoption of guidelines of questionable validity can result in ineffective interventions, inefficient use of scarce resources and harm to patients

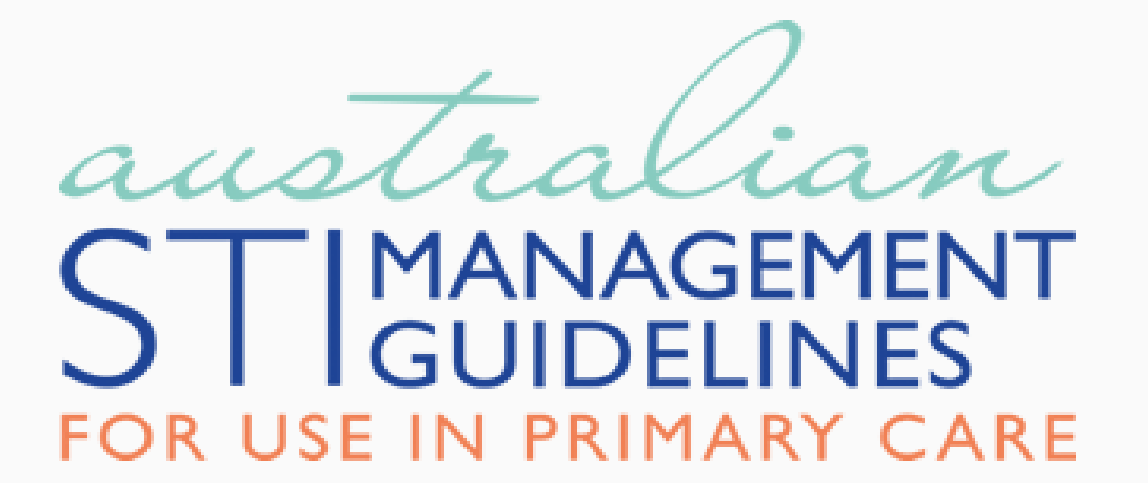
Therapeutic Guidelines

- Analgesic
- Antibiotic
- Bone and Metabolism
- Cardiovascular
- Dermatology
- Diabetes
- Gastrointestinal
- Neurology
- Oral and Dental
- Palliative Care
- Psychotropic
- Respiratory
- Rheumatology
- Sexual and Reproductive Health
- Toxicology and Wilderness
- Ulcer and Wound Management


- *eTG complete* is leading source of accurate, independent and practical treatment advice for clinical conditions.
- Includes explicit instructions for therapy, assisting practitioners in decision-making to ensure patients receive the best treatment

Antibiotic

- Approach to *Neisseria gonorrhoeae* infection




- The Australian Sexual Health Alliance (ASHA) is a committee formed under the constitution of the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM)

- Facilitates multidisciplinary collaborations to support the Australasian sexual health workforce in relation to policy, educational and resources

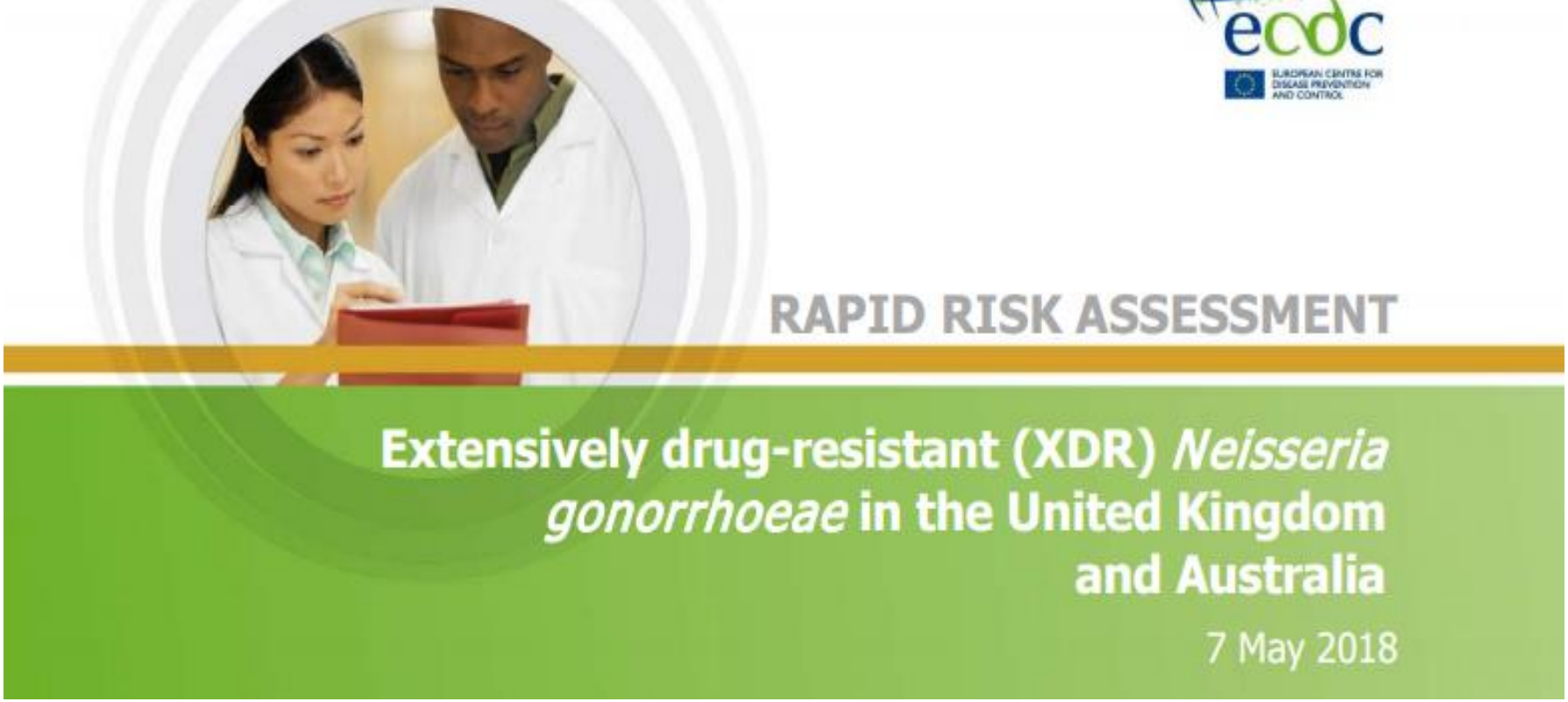
- An accepted clinical resource of the Royal Australian College of General Practitioners

# Communicable Diseases Network Australia (CDNA)

- Established in 1989 as the Communicable Diseases Control Network
- Joint initiative of NHMRC & Australian Health Ministers' Advisory Council
- Objectives:
  - To develop and co-ordinate national surveillance programs for communicable diseases
  - To develop policy, strategy and advice on the prevention and control of communicable diseases
  - To support and strengthen training and capacity building in the communicable disease field
  - To coordinate the investigation and control of multi-jurisdictional outbreaks of communicable disease
  - To engage and work with a range of national and international partners to prevent and control communicable diseases

# Extensively Drug Resistant Gonorrhoea, 2018

## (dual ceftriaxone + high-level azithromycin resistance)




https://ecdc.europa.eu/sites/portal/files/documents/RRA-Gonorrhoea%2C%20Antimicrobial%20resistance-United%20Kingdom%2C%20Aust

# CDNA Working Group to Advise on Management of XDR Gonorrhoea

- ***Working Group members:*** Christopher Bourne, Marcus Chen, Monica Lahra, David Lewis, Lewis Marshall, David Paterson, Tim Read, David Speers
- ***Secretariat:*** Catherine Francis, Christine Selvey

**Aim**: To produce guidance for consideration by the eTG and ASHA guideline committees regarding treatment of XDR gonorrhoea

First-line treatment of gonorrhoea was also reviewed

# Gonorrhoea Treatment in Australia

- Ceftriaxone remains the cornerstone of therapy
- Azithromycin added (2014) to theoretically reduce the rate of emergence/transmission of ceftriaxone-resistant *N. gonorrhoeae*
- *In vitro* synergy between ceftriaxone and azithromycin always assumed – some limited clinical evidence that such synergy exists
    - reduced repeat positive oro-pharyngeal *N. gonorrhoeae* tests when azithromycin and ceftriaxone were co-administered (7.0%) vs. ceftriaxone alone (9.1%)
- Substantial decline in the number of *N. gonorrhoeae* strains with elevated MIC values to ceftriaxone during dual therapy era BUT achieved at cost of increasing azithromycin

# Treatment of Gonococcal Infection

## Australian STI Management Guidelines (ASHA), Dec 2018

| Principal Treatment Options | | |
|---|---|---|
| **Situation** | **Recommended** | **Alternative** |
| Uncomplicated genital & ano-rectal infection | Ceftriaxone 500mg IMI, stat in 2mL 1% lignocaine<br>PLUS<br>Azithromycin 1g PO, stat | Alternative treatments are not recommended because of high levels of resistance, EXCEPT for some remote Australian locations and severe allergic reactions.<br>Seek local specialist advice. |
| Uncomplicated pharyngeal infection | Ceftriaxone 500mg IMI, stat in 2mL 1% lignocaine<br>PLUS<br>Azithromycin 2g PO, stat | Alternative treatments are not recommended because of high levels of resistance, EXCEPT for some remote Australian locations and severe allergic reactions. |
| Adult gonococcal conjunctivitis | Ceftriaxone 500mg IMI, stat in 2mL 1% lignocaine<br>PLUS<br>Azithromycin 1g PO, stat | Alternative treatments are not recommended because of high levels of resistance, EXCEPT for some remote Australian locations and severe allergic reactions. |

# Special Treatment Situations

## Australian STI Management Guidelines (ASHA), Dec 2018

| Situation | Recommended |
|---|---|
| Rectal coinfection | For rectal coinfection with chlamydia, treatment should be given for gonorrhoea AND chlamydia i.e.:<br>Ceftriaxone 500mg IMI, stat in 2mL 1% lignocaine<br><br>PLUS<br><br>Doxycycline 100mg PO, BD 7 days if asymptomatic, but 21 days if symptomatic (see ano-rectal syndromes) |
| Pregnant women | Same as principal treatment option. |
| Allergy to principal treatment choice | Seek specialist advice. |
| Regional/remote | Amoxycillin 3g PO, stat<br>PLUS<br>Probenecid 1g PO, stat<br>PLUS<br>Azithromycin 1g PO, stat (when chlamydia not excluded).<br><br>If the infection is likely to have been acquired beyond local or other remote locations, use principal treatment option. |


http://www.sti.guidelines.org.au/sexually-transmissible-infections/gonorrhoea#management

# Rationale for 2g Azithromycin to Treat Oro-Pharyngeal Gonococcal Infection

- Dual antibiotic therapy is recommended to create a pharmacological barrier to the development of further antimicrobial resistance
- Cure rates are higher with the 2g dose vs. 1g dose
- Dose is important when strain's MIC is near clinical breakpoint
- Rise in low-level azithromycin resistance in Australia
- Reports of treatment failure in oro-pharyngeal infections associated with *N. gonorrhoeae* isolates with ceftriaxone MICs in the susceptible range
- Lower efficacy of most alternative agents at the oropharyngeal site (no data for ertapenem)

# Practice Points

- For patients treated for confirmed/presumptive ano-genital gonorrhoea prior to a positive oro-pharyngeal *N. gonorrhoeae* test do NOT require an additional 2g azithromycin dose

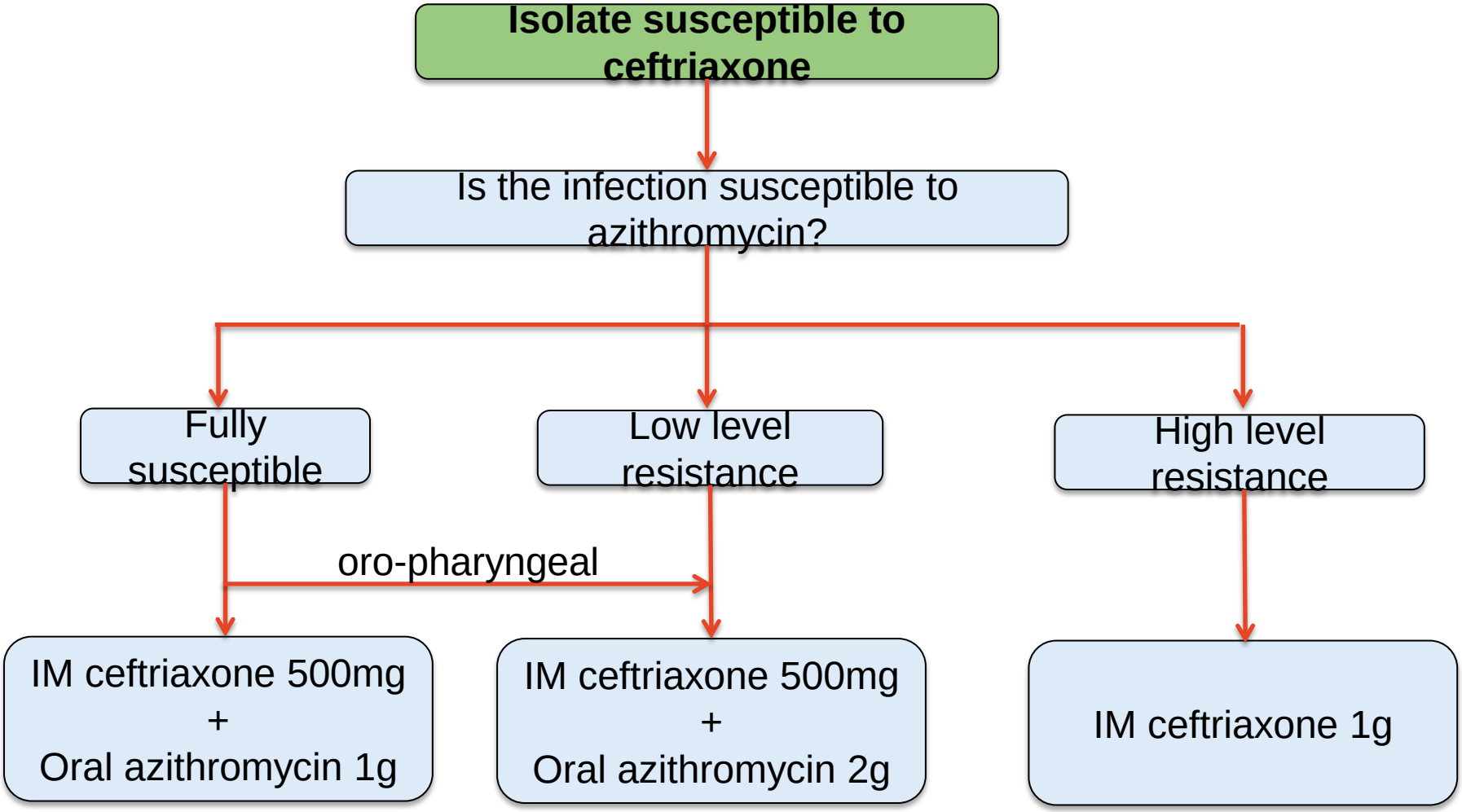
- 2g azithromycin may increase gastrointestinal side effects such as nausea, vomiting and diarrhoea
  - advise patients to eat prior to taking azithromycin
  - provide an anti-emetic for those patients perceived to be at risk of vomiting

- Azithromycin is available on private prescription in Australia (about $10-15 for 2x 500mg) – no PBS restricted benefit for gonorrhoea treatment

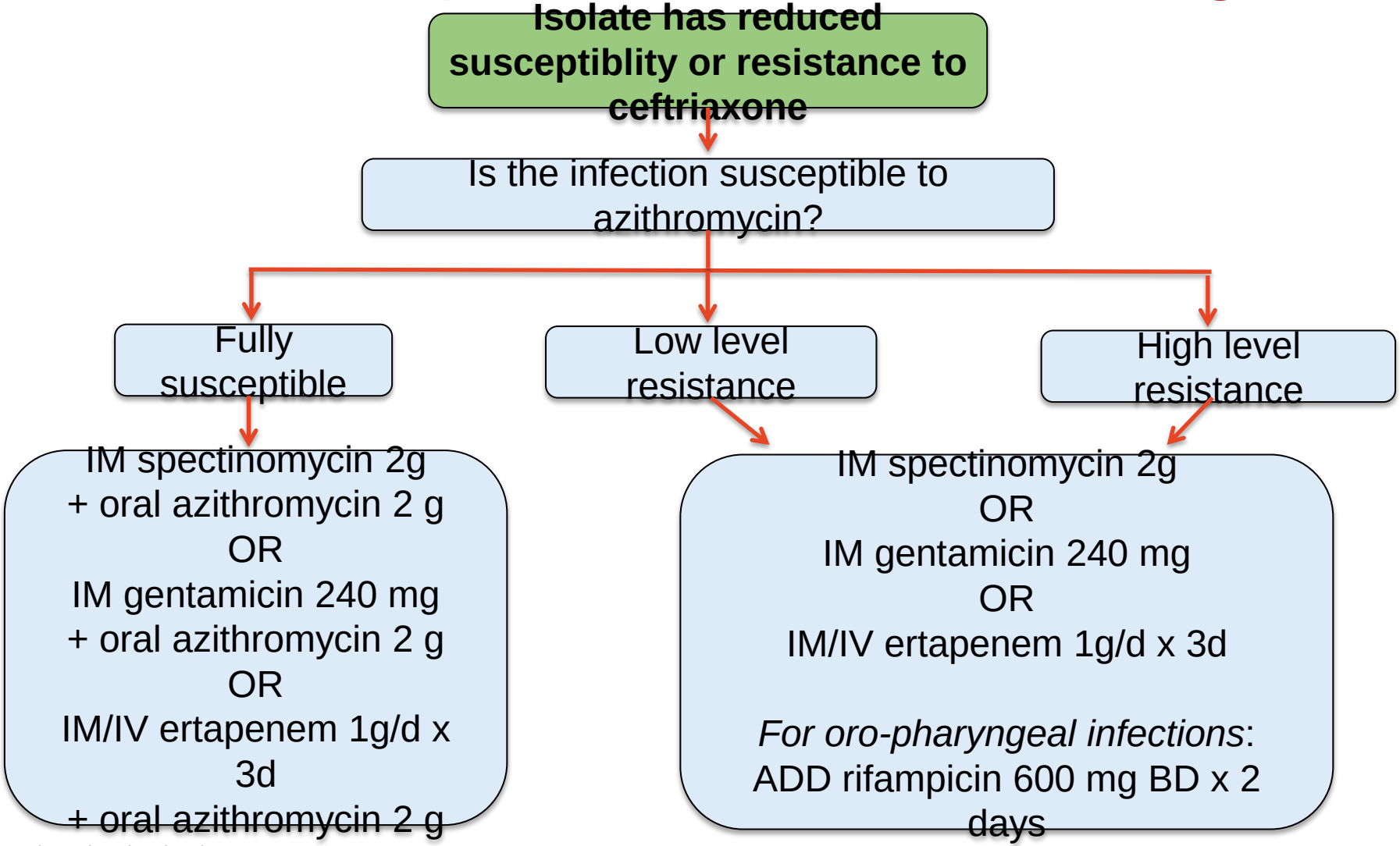
- People having difficulty accessing private treatment can be referred to public sexual health services

https://ashm.blob.core.windows.net/ashmpublic/Firstline%20change%20Ng%20Rx%20rationale%202019.pdf

# Recommendations for *N. gonorrhoeae* Infection, Ceftriaxone MIC < 0.125 mg/l



# Recommendations for *N. gonorrhoeae* Infection, Ceftriaxone MIC ≥ 0.125 mg/l



# Precision Management for STIs: a New Era

*Clinical Infectious Diseases*

BRIEF REPORT

**Clinical Infectious Diseases® 2017;64(9):1268–70**

## Implementation of a Rapid Genotypic Assay to Promote Targeted Ciprofloxacin Therapy of *Neisseria gonorrhoeae* in a Large Health System

Lao-Tzu Allan-Blitz,[1] Romney M. Humphries,[2] Peera Hemarajata,[2] Ashima Bhatti,[3] Mark W. Pandori,[4] Mark J. Siedner,[5] and Jeffrey D. Klausner[6,7]

## Further evidence to support the individualised treatment of gonorrhoea with ciprofloxacin

Ella Trembizki, Rebecca Guy, Basil Donovan, John M Kaldor, Monica M Lahra and David M Whiley

Lancet Infectious Diseases, The, 2016-09-01, Volume 16, Issue 9, Pages 1005-1006, Copyright © 2016 Elsevier Ltd

"Our study confirmed that the *GyrA S91* locus is highly predictive of ciprofloxacin susceptibility"

- Not to be used in pregnancy
- Not useful in countries with high pre-existing levels of QRNG
- Expect quinolone resistance to rise
- Increased QRNG prevalence may impact on response to new DNA topoisomerase II inhibitors

## *Resistance*Plus® GC

*Resistance*Plus® GC | Specifications | Resources | Ordering

***Resistance***Plus GC* is a multiplex qPCR test for detection of *Neisseria gonorrhoeae* and sequences linked to ciprofloxacin susceptibility, validated for a range of specimen types. Dual *N. gonorrhoeae* targets improve clinical specificity. Ciprofloxacin resistance and susceptibility targets are included for additional confidence.

***Resistance***Plus GC* is powered by proprietary ***Plex***PCR® technologies demonstrating improved multiplex performance compared with other probe-based tests.


CE IVD

### Related Products

***Resistance***Plus® GC Control* kit

***Plex***PCR® Colour Compensation* kit

| PERFORMANCE OF *RESISTANCE*PLUS® GC | | |
|---|---|---|
| | GC DETECTION | *gyrA* Detection |
| Sensitivity | 96.9% | 100% |
| Specificity | 99.7% | 98.6% |

- TGA clearance - 15 February 2019
- Two *N. gonorrhoeae* targets (*opa* & *porA*)
- Ciprofloxacin resistance phenotype
- Internal control

# Conclusions

- Antimicrobial resistance is worsening - threats of hard-to-treat or untreatable *N. gonorrhoeae* in the near future
- Reducing incidence of gonorrhoea is the single most important action we must accomplish whilst we have effective drugs
- Clinical practice guidelines and regulatory oversight have a key role to play in antimicrobial stewardship and increasing the longevity of existing antimicrobial agents
- Molecular susceptibility-guided therapeutic approaches enable recycling of older antibiotics
- Regional surveillance systems are critical to inform guidelines