

# National Interim Gonococcal Reference Laboratory

## Annual Report 2019

Compiled by:

Ms. Sinead Saab, Senior Medical Scientist, St. James's Hospital

Dr. Aoife Colgan, Surveillance Scientist, Health Protection Surveillance Centre



National Interim Gonococcal Reference Laboratory (GCRL)

Department of Clinical Microbiology,

Central Pathology Laboratory

St. James's Hospital,

James's Street,

Dublin 8

Ireland

Tel: (+353 1) 410 2917

Fax: (+353 1) 428 4351

**For advice on:**

**Patient treatment/management**

Dr. Brendan Crowley (01) 416 2968

Dr. Breida Boyle (Deputy Director) (01) 416 2917

**Laboratory aspects of Gonococcal**

Ms. Antoinette Power (Chief Medical Scientist) (01) 4162986

Ms. Sinéad Saab (Senior Medical Scientist) (01) 4162917

**Surveillance data**

Dr. Aoife Colgan (01) 876 5353

## Contents

1.	The Establishment and Funding of the Service.....	1
2.	Gonorrhoea.....	1
3.	Services Available.....	2
■	Monitoring, alert and response .....	2
■	Technical advice .....	2
■	Clinical advice.....	2
■	Collaboration and research.....	2
4.	2019 Isolates .....	3
■	Patient demographics .....	3
5.	Antimicrobial resistance .....	3
■	High-Level Azithromycin in Ireland 2019 .....	4
6.	Euro-GASP collection 2019 .....	5
7.	Continuous Education and Professional Development .....	7
8.	Publications and presentations.....	7
9.	Acknowledgements.....	7
10.	References: .....	8

## 1. The Establishment and Funding of the Service

The Interim National Gonococcal Reference Laboratory (GCRL) Service was established in April 2016 by the Health Service Executive (HSE). The laboratory is funded by a central allocation to St. James's Hospital. Funding is provided for consumable costs and staffing, which consists of a medical scientist, a senior medical scientist and a surveillance scientist. In 2019, the GCRL also received funding from the Antimicrobial Resistance and Infection Control (AMRIC) Division to develop services for the surveillance of antimicrobial resistance in Ireland. This funding is currently being used to develop Whole Genome Sequences within the laboratory.

The National Interim Gonococcal Reference Laboratory is located within the Central Pathology Laboratory Microbiology Department within St. James's Hospital and is administered within the Laboratory Medicine (LabMed) Directorate. This is the third Annual Report of the GCRL and details the output of the GCRL service in 2019.

## 2. Gonorrhoea

Gonorrhoea is a sexually transmitted infection (STI) caused by the bacterium *Neisseria gonorrhoea* (*N. gonorrhoea*); these infections primarily involve the mucosal surfaces of urethra, endocervix, rectum, pharynx and conjunctiva<sup>1</sup>.

There is a significant burden of gonococcal disease globally with higher rates in less developed countries<sup>2</sup>. Gonorrhoea has been a notifiable disease in Ireland since 1943<sup>3</sup>. Current in Ireland gonorrhoea is the second highest notifiable STI after chlamydia and provisional 2019 data from Health Protection Surveillance Centre (HPSC) indicates there were 2823 reported gonorrhoea cases, giving a provisional notification rate of 59.9 per 100,000 population in 2019 representing a 9.4% increase from 2018 rates.

For further information the website of the HSE – HPSC provides a useful guide <https://www.hpsc.ie/a-z/sexuallytransmittedinfections/gonorrhoea>

### 3. Services Available

The interim National Gonococcal Reference Laboratory provides the following services:

#### ■ Monitoring, alert and response

- Antimicrobial susceptibility testing – provision of extended antimicrobial susceptibility testing for *N. gonorrhoeae* to identify and monitor current resistance profiles in Ireland.
- In collaboration with the HPSC, determining what is representative gonococcal sentinel sampling
- Contribution to and participation in gonococcal surveillance including the European - Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) and relevant Public Health Departments
- Participation and provision of technical advice/expertise in the context of an outbreak.
- Provision of an annual report on activity and future objective to the Sexual Health and Crisis Pregnancy programme (SHCPP).

#### ■ Technical advice

- Development and dissemination of guidance on appropriate diagnostic methods, including storage and transport of isolates.
- Proactive and reactive provision of advice and information to other laboratories that carry out *N. gonorrhoeae* identification and antimicrobial susceptibility testing.
- Support and advice to other laboratories that carry out *N. gonorrhoeae* nucleic acid amplification testing (NAAT).

#### ■ Clinical advice

- A point of contact for clinical queries from clinicians and other clinical microbiologists.
- Proactive dissemination of information to clinicians and other clinical microbiologists in relation to gonococcal diagnostics

#### ■ Collaboration and research

- International research collaboration
- Supporting clinical and laboratory based research, at both MSc and PhD level

## 4. 2019 Isolates

In 2019 the GCRL tested a total of eight hundred and seventy six *N. gonorrhoea* isolates. These isolates were recovered from patients attending community medical practitioners, GUIDE clinics, Gay Men's Health Service and hospitals throughout the Republic of Ireland.

### ■ Patient demographics

Of the isolates received 876 isolates received, 6.8% (60/876) were female, 92.9% (814/876) were male and the remaining of 0.2 % (2/876) isolates the sex was not stated. Among female isolates the predominant site from which isolates were recovered was cervical at 66.7% (40/60) other sites included vaginal, rectal, pharyngeal and blood. The age range among females was 17-65 years old (median age = 29 years). Rectal was the predominant site of recovery from male representing 41.8 % (340/814) while the remaining sites included urethral, pharyngeal, penile, and synovial fluid. The age range among males isolates was 16-64 years old (median age = 29 years).

## 5. Antimicrobial resistance

*Neisseria gonorrhoea* has rapidly acquired resistance to all antimicrobial drugs used as front-line monotherapy to treat gonorrhoea infection, including the extended spectrum cephalosporin class of antimicrobials which is typically considered to be the last remaining treatment option<sup>4</sup>. Traditional clinical guidelines recommended the use of a dual therapy regimen comprising the cephalosporin, ceftriaxone and the macrolide, azithromycin in the treatment of gonorrhoea infections<sup>1</sup>. This dual therapy was comprised in 2018 when the first global report of a high level azithromycin resistant *N. gonorrhoea* which is also resistant to ceftriaxone was imported to the UK<sup>5</sup>. As a result of this and a case of ceftriaxone resistant in Ireland in 2018<sup>6</sup>, the current recommended therapy in the treatment of uncomplicated *N. gonorrhoea* infections is Ceftriaxone 1g IM single dose<sup>7</sup>.

Isolates received in the GCRL were tested against varying antimicrobial panel which include six antimicrobials (azithromycin, ceftriaxone, cefixime, ciprofloxacin, tetracycline and spectinomycin) using Gradient minimum inhibitory concentration (MIC) strips from Biomérieux and Iiofilchem®. Interpretations were based upon the European Committee on

Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints- bacteria table V9.0<sup>8</sup>.  $\beta$ -lactamase testing was performed using the Hodge plate and confirmed when positive by Nitrocefin™ discs (mast group).

In 2019, 99.9% (875/876) of isolates tested susceptible to the third generation cephalosporin's cefixime and ceftriaxone. All isolates (100% 876/876) tested against ceftriaxone displayed susceptible MICs according to EUCAST 2019 breakpoints, these MICs ranged from <0.002- 0.064  $\mu$ g/ml. Cefixime MICs ranged from <0.016-0.25  $\mu$ g/ml, where by one isolate displayed reduced susceptibility to cefixime with an MIC of 0.25  $\mu$ g/ml.

Resistance to ciprofloxacin and tetracycline varied among 2019 isolates. In 2019 of the isolates that were tested against ciprofloxacin, resistance was seen in 44.8% (193/431) of isolates where MICs were > 0.064 $\mu$ g/ml. Similar to ciprofloxacin the MICs to tetracycline varied among the 2019 isolates. Of the hundred and twenty six isolates against tetracycline 6.8% (12/176) displayed a resistant phenotype with MICs ranging from 2.0 - 16.0  $\mu$ g/ml.

Of the isolates tested in 2019, 44.4% (363/876) were tested against spectinomycin all isolates display a susceptible phenotype with MICs  $\leq$ 64.0  $\mu$ g/ml.

### ■ High-Level Azithromycin in Ireland 2019

There have been 25 cases of high level azithromycin resistant gonorrhoea (HL-AziR; azithromycin minimum inhibitory concentration  $\geq$ 256  $\mu$ g/ml) reported in Ireland since 2011 to 2018<sup>9</sup>. Seven further cases of HL-AziR gonorrhoea were reported in Ireland in 2019. The cases were reported from HSE-East, HSE-Midland, HSE-West, and high level azithromycin resistance was confirmed for all 7 cases, as well as extended antimicrobial susceptibility testing, in the Interim Gonococcal Reference Laboratory.

Isolates were recovered from both male (57.1% 4/7) and female (42.9% 3/7) with ages ranging in age from 18 – 40 years (median age 22). In all four of the male cases the site of infection was the urethral while the 3 female isolates were recovered endocervix, pharyngeal and rectal. All HL-AziR isolates were susceptible to ceftriaxone, with MICs ranging from 0.008  $\mu$ g/ml to 0.032  $\mu$ g/ml. All seven of the isolates were susceptible to cefixime, ciprofloxacin and spectinomycin no isolates produced  $\beta$ -lactamase.

## 6. Euro-GASP collection 2019

The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) is a sentinel surveillance programme, run by the European Centre for Disease Control (ECDC), established to detect emerging and increasing trends in antibiotic resistance in gonorrhoea isolates throughout the participating member states in Europe. The annual de-centralised testing model requires that sentinel laboratories perform antimicrobial susceptibility testing on a selection of isolates, enhanced surveillance is collected on the selected isolates and this information is reported to the ECDC. Linking susceptibility and epidemiological information informs disease prevention interventions. The programme ensures quality and comparability across all participating laboratories and provides training in gonococcal culturing and antimicrobial susceptibility testing. Ireland has participated in Euro-GASP since 2010, and has participated via de-centralised testing since 2013. The GCRL in St. James's Hospital is the Irish sentinel laboratory.

The collection period for Euro-GASP samples commences annually in September. Euro-GASP guidelines recommend that 100 consecutive samples should be collected but countries should aim to capture approximately 10% of the total number of national Gonorrhoea cases per year. For countries where 100 isolates is much lower than 10% of the national total of gonorrhoea cases, additional isolates should be collected to achieve a more representative sample size. Samples should be selected from groups that represent different geographical regions and patient groups to reflect the distribution of gonorrhoea cases nationally. When more than one isolate is submitted for a patient it is considered one episode of infection if the specimens were recovered  $\leq 4$  weeks apart. In these cases only one isolate should be submitted for Euro-GASP according to the following hierarchy:

**Male:** 1) pharyngeal, 2) rectal, 3) urethral, 4) other

**Female:** 1) pharyngeal, 2) cervical, 3) other anogenital (high vaginal swab, rectal, urethral), 4) other

By August 2019 the number of gonorrhoea notifications in Ireland had already exceeded 1000 so 200 consecutive gonorrhoea isolates were selected for submission to Euro-GASP for 2019. Data on 200 *N. gonorrhoea* isolates collected between August and November 2019



were reported to ECDC as part of Euro-GASP 2019; this represented 7% of total national gonorrhoea notifications in 2019.

In Ireland 92% ( $n=184$ ) of the isolates in the 2019 Euro-GASP submission were recovered from male patients while the remaining 8% ( $n=16$ ) were recovered from females. The male patients ranged in age from 16-56 years (median age=28 years) while female patients were 17-35 years (median age=28 years). The mode of transmission was available for 85% ( $n=170$ ) where known MSM 83% ( $n=141$ ), Heterosexual 16% ( $n=27$ ) and other 1% ( $n=2$ ). Where information on concurrent STI was available 51% were concurrently infected with another STI, most commonly chlamydia in over 70% of cases. The majority of isolates (88%) came from patients who attended the GUIDE or Gay Men’s Health Service STI clinics in Dublin. Table 1 shows the original clinical or laboratory source of all isolates included the 2019 Euro-GASP submission.

**Table 1.** 2019 Euro-GASP isolates

Clinic/laboratory	Number of isolates
Bon Secours Tralee	1
Gay Men’s Health Service	96
General Practitioner	3
Guide	82
MRH Portlaoise	2
Naas Hospital	1
National Maternity Hospital	1
Our Lady of Lourdes Drogheda	1
Tallaght Hospital	1
University Hosp. Limerick	12

2019 was a “snapshot year” for testing sensitivity to extended panel isolates were investigated for susceptibility against azithromycin, ceftriaxone, cefixime, ciprofloxacin, tetracycline, spectinomycin, gentamicin and for the production of  $\beta$ -lactamase. No isolates exhibited resistance cefixime, ceftriaxone and spectinomycin. Of two hundred isolates tested 3.5% 9 ( $n=7$ ) exhibited azithromycin MICs  $>1.0$  mg/L, 47% ( $n=94$ ) were resistant to ciprofloxacin and 20% ( $n=40$ ) tested positive for B-lactamase activity. There are currently no resistance breakpoints defined for gentamicin by EUCAST.

Enhanced surveillance information on patients linked to each Euro-GASP isolate is collected to combine antimicrobial susceptibility patterns with epidemiological data to inform public

health policy and health promotion strategies. Data on patient country of birth, area of residence, probable country of infection, probable mode of transmission, antimicrobial treatment used to treat current incidence of infection, history of gonorrhoea infections and concurrent sexually transmitted infections is provided by clinicians and Departments of Public Health. The laboratory and epidemiological data is collated at the HPSC and will be reported to the ECDC via The European Surveillance System (TESSy).

## **7. Continuous Education and Professional Development**

The Staff of the GCRL maintains their expertise and knowledge through participation at both national and international meetings, workshops and conferences. Throughout the year all staff continued their professional development through attendance various meetings including;

- HIV club evening meetings
- SJH Journal clubs
- Focus on Infection ISCM 2019
- National Multidisciplinary Forum on Antimicrobial Resistance in *Neisseria gonorrhoeae*

GCRL staff also ensured mandatory training requirements were met in areas such as Manual Handling, Fire safety, Quality Management, GDPR training and Hand Hygiene modules.

## **8. Publications and presentations**

- Gonorrhoea antimicrobial resistance in Ireland, 2010-2017: Summary January 2019
- Antimicrobial Resistance and Infection Control Team: July 2019 Ed 8 The rise of antibiotic resistant gonorrhoea
- Epi Insight Volume 20, Issue 12 December 2019 Response to the threat of multi and extensively-drug resistant gonorrhoea: How are we doing?

## **9. Acknowledgements**

We would like to thank the Staff of the GCRL for their hard work in providing this service; The Department of Laboratory Medicine, St. James's Hospital, the Health Protection Surveillance Centre (HPSC) and users of this service for the support provided to the GCRL.

## 10. References:

<sup>1</sup> Health Protection Surveillance Centre Scientific Advisory Committee. 2017 National Guidelines for Prevention and Control of Gonorrhoea and for Minimising the Impact of Antimicrobial Resistance in *Neisseria gonorrhoeae*.

<https://www.hpsc.ie/a-z/sexuallytransmittedinfections/gonorrhoea/amrgonorrhoea/amrgonorrhoeaguidance>

<sup>2</sup> Newman L, Rowley J, Vander Hoorn S, Wijesooriya NS, Unemo M, Low N, et al. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. PLoS ONE. 2015; 10(12):e0143304. <https://doi.org/10.1371/journal.pone.0143304> PMID: 26646541.

<sup>3</sup> Government of Ireland. Infectious Diseases (amendment) Regulations 2016 SI No 276 of 2016. Ireland 2016.

<sup>4</sup> Unemo M, Shafer WM. Antimicrobial resistance in *Neisseria gonorrhoeae* in the 21st century: past, evolution, and future. Clin Microbiol Rev. 2014;27(3):587-613. doi:10.1128/CMR.00010-14

<sup>5</sup> Health Protection Report: 2018 UK case of *Neisseria gonorrhoeae* with high-level resistance to azithromycin and resistance to ceftriaxone acquired abroad Volume 12 Number 11

<sup>6</sup> Golparian D, et al. Multidrug-resistant *Neisseria gonorrhoeae* isolate, belonging to the internationally spreading Japanese FC428 clone, with ceftriaxone resistance and intermediate resistance to azithromycin, Ireland, August 2018. Euro Surveill. 2018;23(47):pii=1800617.

<https://doi.org/10.2807/15607917.ES.2018.23.47.1800617>

<sup>7</sup> Disease surveillance report of HPSC – Epi. Insight: 2019 Change in national guidance for management of infection with *Neisseria gonorrhoeae* without cephalosporin allergy. Volume 20 issue 2

<sup>8</sup> The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 9.0, 2019.

[https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST\\_files/Breakpoint\\_tables/v\\_9.0/Breakpoint\\_Tables.pdf](https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_9.0/Breakpoint_Tables.pdf)

<sup>9</sup> Health Protection Surveillance Centre 2017. High level azithromycin resistant (HL-AziR) gonorrhoea in Ireland 2011 - 2017. Health Protection Surveillance Centre 2017