The 2012 IUSTI ECCG report on the diagnosis and management of *Neisseria gonorrhoeae* infections in Europe.

Produced for and on behalf of the ECCG, Mr Ben Brooks
The European Collaborative Clinical Group (ECCG)

The ECCG was inaugurated at the 26th International Union against Sexually Transmitted Infections (IUSTI) Congress in Riga, Latvia 2011. The ECCG is a network of over 100 Sexually Transmitted Infection specialists who have come together to conduct questionnaire based research across the European Region. It is expected that this work will focus and direct guideline development.

A central core group of the ECCG has also been established who are responsible for identifying suitable survey questions that will be carried out but only after approval by the full ECCG Board. The ECCG aims to conduct a maximum of 2 projects per year which will be presented at the annual regional congresses and published as appropriate.

ECCG Members 2012

Prof. Uladzimir Adaskevich
Dr Immy Ahmed
Dr Sibel Alper
Dr Maider Arando
Prof. Karen Babayan
Dr Jeyhun Babirov
Dr Eszer Balla
Dr Josefina Belda Ibanez
Dr Vasile Benea
Dr Isabel Sanz Bereciartu
Prof. Mircea Betsiu
Prof. Gleb Bondarenko
Dr Philip Carabot
Prof. Zaza Chanturaia
Prof. Krasimir Chudomirova
Dr Marco Cusini
Dr Antonietta D’Antuono Bologna
Dr Maia Datuashvili
Dr Josefina Lopez de Munain
Dr Jorge del Romero
Dr Rocco Della Torre
Dr Sergio Delmonte Torino
Dr Aldo Di Carlo Roma
Dr Gilbert Donders
Dr Maria Dudas
Prof. Anatoly Dudun
Prof. Nicolas Dupin
Dr Ursu Elena
Dr Igen Ertam
Dr Vugar Eyvazov
Prof. Dan Forsea
Dr Sebastien Fouere
Dr Derek Freedman
Prof. Deniz Gokengin
Prof. Mikhail Gomberg
Dr Sahak Hakobyan
Dr Usha Hartgill
Prof. Ulrich Hengge
Dr Eija Hiltunen-Back
Dr Hovhannes Hovhannisyan
Dr Rashad Ismailov
Prof. Peter Itin
Dr Ilze Jakobsone
Dr Michel Janier
Prof. Mir’Riad Javadzada
Dr Jorgen Skov Jensen
Dr Anika Johnsson
Dr Marisa Junquera
Dr Antonios Kanalleas
Prof. Alexei Khrianin
Dr Andrezj Klepacki
Dr Josephhe Kobakhidze
Prof. Vladimir Kovalykh
Dr Helle Kiellberg Larsen
Dr Francois Lassau
Prof. Stefan Lautenschlager
Prof. Mikhail Lebeduk
Prof. Aleksandr Litus
Dr Aliaksandr Lukyanau
Dr Charlotta Magnusson
Prof. Farid Mahmudov
Dr Sergei Maltsev
Prof. Filomena Exposto
Dr Alberto Matteelli Brescia
Prof. Gennadiy Mavrov
Prof. Harald Moi
Prof. Electra Nikolaidou
Dr Paulina Nuutinen
Dr Elsbet Nylander
Dr Tabuica Oleg
Dr Anne Olsen
Dr Joseph Pace
Dr Oleg Pankratov
Dr Rafael Pasternack
Dr Rajul Patel
Dr Juraj Pec
Dr Airi Poder
Prof. Catalin Mihai Popescu
Dr Marko Potocnik
Dr Keith Radcliffe
Prof. Jonathan Ross
Dr Andris Rubins
Dr Silvestr Rubins
Dr Leyla Razayева
Dr Marcis Septe
Dr Jackie Sherrard
Dr Irina Shymanskaya
Dr Mihael Skerlev
Prof. Angelika Stary
Dr Irene Stefanaki
Dr Christina Stefanaki
Dr Ylva Svedberg
Dr Turid Thune
Dr Julie Timsit
Dr Timea Tisza
Dr Laurence Tootuot Trellu
Dr Tatia Tugushi
Dr Petra Tunback
Prof. Gabriela Turcu
Dr Idil Unal
Dr Andrius Vagoras
Dr Marti Vall Mayans
Dr Willem Van der Meijden
Dr Viktoria Varkonyi
Dr Tine Vestergaard
Dr Gogu Vladislav
Dr John White
Dr Karl Arne Wikstrom
Dr Janet Wilson

ECCG Core Group 2012

Mr Ben Brooks
Prof. Mikhail Gomberg
Prof. Cathy Ison
Dr Marita van de Laar
Prof. Harald Moi
Dr Rajul Patel
Dr Airi Poder
Dr Keith Radcliffe
Prof. Jonathan Ross
Dr John White
Introduction

Gonorrhoea infection rates across Europe have generally remained relatively stable and near historic lows especially when discounting the wide scale adoption of nucleic acid amplification testing (NAAT) protocols that have generated increased detection. Resistance testing of clinical isolates is currently being carefully monitored through a number of laboratory initiatives. Such work has shown that the number of options for treating gonorrhoea infection is becoming limited and clinicians can no longer rely upon an oral regimen to achieve cure. The minimum inhibitory concentrations (MICs) for 3rd generation cephalosporins are rising and the recent reports of four patients failing ceftriaxone therapy in Europe including one genital infection exhibiting resistance to high dose ceftriaxone may soon mark the end of empirical single drug outpatient therapy. The ECCG felt that an urgent review of the clinical management of gonorrhoea is necessary to determine whether clinicians have adapted their prescribing practice in light of the changing resistance data.

The ECCG 2012 project looks at the clinical management of gonorrhoea, its clinical diagnosis and first line treatment choices for confirmed or suspected infections. The project determines whether clinicians provide single dose therapies, the range and doses of antibiotics used and whether tests to confirm resistance profiles and cure are arranged routinely. This builds on recently reported laboratory based studies.

Method

The survey was developed by members of the ECCG core group. In developing the survey account was taken of the recent published review of laboratory facilities across Europe for the detection of Neisseria gonorrhoeae. The core group was interested in looking at the clinical management of gonococcal infections and the extent to which laboratory services supported care. The survey was developed to look at the following areas:

1. Access to nucleic acid testing.
2. Access to culture facilities.
3. Access to culture resistance profiling.
4. Choice of sites and multiple testing using different modalities in heterosexual and homosexual patients.
5. Choice of antibiotics for definite and suspected gonococcal infection.
6. Use of combination antibiotic regimens in the management of gonococcal infection.
7. Role of co-administered chlamydial therapy.
10. Partner notification strategies and guideline choice.

Data was also collected on the type and nature of the respondents practice. The full ECCG survey is available at https://www.isurvey.soton.ac.uk/5488. A web based questionnaire administered through the University of Southampton was used to collect information regarding the diagnosis and management of gonorrhoea from 108 ECCG members across 36 European countries (2-6 clinicians from each country). The survey was translated and available in Russian. A total of 3 reminders were sent, responses could be identified to country but not to the clinician. This report represents a preliminary analysis of data collected between June and August 2012 from 74 respondents representing 82% of ECCG countries.
Results

ECCG Regions

The population coverage from the participating 28 ECCG countries totals 664 million representing 87% of the European population. Respondents were principally in urban (74%) and government (64%) practice and worked in large clinics as defined by a population coverage >250,000 (79%). Additionally 96% were clinicians with 84% involved directly in patient care in some capacity. Other roles included public health, laboratory sciences and research.

**N.B.** All participants who identified themselves as either not managing gonorrhoea or as non-clinicians were excluded from the analysis of the clinical parts of the survey.

Access to Laboratory Facilities

Only 1 clinician reported that they did not have access to laboratory facilities to confirm gonococcal infections. The ECCG had 3 responses from this clinician’s country with the remaining reporting the availability of confirmatory testing. Interestingly this clinician was only using high dose Ceftriaxone (500mg) for the management of actual and suspected gonorrhoea in homosexual patients. Some heterosexual patients may have therefore been at risk of under treatment in this centre.

Access to Microscopy
Of 65 participants 92% had access to microscopy for the immediate diagnosis of gonorrhoea. The 8% who don’t have access to microscopy represents 4 countries, 3 of which responded with mixed availability and only 1 reported no microscopy facilities.

**Access to Culture Facilities**

Of 65 participants 94% had access to gonorrhoea culture facilities. The 6% who don’t have culture facilities represents 4 countries, 3 of which responded with mixed availability of culture and only 1 reported no culture facilities.

**Resistance Profiling of Culture Isolates**

Of the 94% of clinicians with access to gonorrhoea culture facilities, 15% do not have access to resistance profiling on routine gonococcal cultured isolates.
Gonococcal Screening in Low Risk Heterosexuals

Despite having access to laboratory confirmation facilities 17% of clinicians restrict gonococcal screening in low risk populations.

Sites of testing in asymptomatic men who have sex with men (MSM)

Over 1/3 of clinicians do not perform 3 site testing in MSM. Both the pharynx and rectum are important sites of potentially difficult to treat gonococcal infection yet testing of these sites is far from universal. Most guidelines advise 3 separate specimens to be analysed independently. 18% of clinicians chose not to perform any testing in this scenario. There was no correlation with the absence of 3 site testing and whether clinicians work in the private sector.

Access to NAAT

Key:
- No access to NAAT
- Mixed access to NAAT
- ECCG member participants
- ECCG non-members/non-participants
NAAT has the potential to increase the detection of gonorrhoea. 15% of the European population have no access to NAAT and an additional 15% have limited access to NAAT.

**Type of NAAT**

<table>
<thead>
<tr>
<th>Company/Method</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siemens (Transcription Mediated Amplification)</td>
<td>21%</td>
</tr>
<tr>
<td>Abbott (Real-Time Polymerase Chain Reaction)</td>
<td>21%</td>
</tr>
<tr>
<td>Gen-Probe (Transcription Mediated Amplification System)</td>
<td>20%</td>
</tr>
<tr>
<td>Becton Dickinson (Strand Displacement)</td>
<td>18%</td>
</tr>
<tr>
<td>Roche (Polymerase Chain Reaction)</td>
<td>10%</td>
</tr>
<tr>
<td>In-house Assay</td>
<td>8%</td>
</tr>
<tr>
<td>Other</td>
<td>2%</td>
</tr>
</tbody>
</table>

In house testing was reported by clinicians in 6 countries (all clinicians in Russia and Hungary reported use of in house testing).

**Pharyngeal and Rectal site screening of asymptomatic heterosexual men and women**

<table>
<thead>
<tr>
<th>Heterosexual</th>
<th>Neither</th>
<th>Pharynx &amp; Rectum</th>
<th>Rectum</th>
<th>Pharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>91.0%</td>
<td>3.0%</td>
<td>1.5%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Men</td>
<td>95.5%</td>
<td>3.0%</td>
<td>0.0%</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

For this scenario there appears to be an element of over testing where rectal and pharyngeal swabs are taken 4.5-9.0% of the time. There was no correlation with over testing and private practice.

**First line antibiotic treatment for definite gonococcal infection**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone 500mg</td>
<td>70%</td>
</tr>
<tr>
<td>Ceftriaxone 250mg</td>
<td>60%</td>
</tr>
<tr>
<td>Ceftriaxone 1g</td>
<td>50%</td>
</tr>
<tr>
<td>Cefixime</td>
<td>40%</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>30%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>20%</td>
</tr>
<tr>
<td>Spectinomycin</td>
<td>10%</td>
</tr>
<tr>
<td>Azithromycin 1g</td>
<td>0%</td>
</tr>
<tr>
<td>Azithromycin 2g</td>
<td>0%</td>
</tr>
<tr>
<td>Doxycyclin</td>
<td>0%</td>
</tr>
<tr>
<td>No Chlamydia Cover</td>
<td>0%</td>
</tr>
</tbody>
</table>
The majority of clinicians use high dose Ceftriaxone at a dose of 500mg. Most clinicians add Azithromycin 1g (52%) although some have not adopted this strategy. Six clinicians chose to use Azithromycin at a higher dose of 2g. A range of potentially suboptimal therapies are used and many of these are given as single antibiotics. One area of particular concern is the use of Cefixime either with or without a second antibiotic. Resistance to Cefixime is now widely described and oral therapy with this agent is not recommended by a number of authorities. The presence of such prescribing may be a matter of some urgent concern.

We specifically collected data on additional therapies that would be given for possible co-existing chlamydial infection. 62% of clinicians would add Azithromycin or Doxycyclin as either part of or in addition to their regimen for the treatment of gonorrhoea. 38% of clinicians would not give any therapy which would cover a chlamydial infection in patients with gonorrhoea.

**Treatment of asymptomatic female contacts of gonococcal infection**

![Bar chart showing the distribution of antibiotic choices for asymptomatic female contacts.]

15% of clinicians chose not to treat asymptomatic female partners of men with gonorrhoea. This is a surprising result. The choice of antibiotic and whether co-therapy is used to cover chlamydia is similar to that of the previous question. Of those who chose not to treat asymptomatic partners, 90% have access to NAAT and 80% perform 3 site testing.

**Site and type of testing in symptomatic MSM with microscopic evidence of gram negative diplococci**

![Diagram showing the distribution of testing sites and types.]

Key:
- a Pharyngeal Culture (0%)
- b Rectal Culture (0%)
- c Urethra/Urine Culture (16%)
- ab (0%)
- ac (7%)
- bc (0%)
- abc (59%)
- Neither (18%)
Nearly a half of all patients do not receive 3 site testing. Surprisingly only 1 clinician reported that they would not perform any culture or NAAT testing in this scenario yet had reported having access to such laboratory facilities. Interestingly 7% of clinicians with access to culture, resistance profiling and NAAT do not use them in this scenario where microscopic evidence of probable infection was present. There was no apparent correlation between 3 site testing and private practice.

Treatment in symptomatic MSM with probable gonorrhoea

Treatment choice in homosexual men is similar to that for heterosexuals. Interestingly some clinicians continue to use regimens which have a higher failure rate in non-genital infections. Co-therapy for possible co-existing chlamydial infection is given less consistently then for heterosexuals.
Treatment in patients with a history of mild allergy to penicillin

Current guidance states that any 3rd generation cephalosporin may be used in patients with a previous rash to penicillin. However there is a marked reduction in the number of clinicians choosing to use cephalosporins compared with previous scenarios.

Treatment in patients with a history of anaphylaxis to penicillin

Guidance advises that cephalosporins be avoided in patients with a documented history of anaphylaxis to penicillin unless patients are first desensitised. Interestingly there is a marked reduction in the choice of 3rd generation cephalosporins (Ceftriaxone, Cefixime and Cefotaxime) while there is an increase in the use of antibiotics with lower efficacy against gonococcal infections. Additionally more clinicians chose to co-administer Azithromycin.
Tests of Cure

Key:

- a Microscopy (1.5%)  
- ab (13%)  
- b Culture (10%)  
- ac (3%)  
- c NAAT (16%)  
- bc (20%)  
- abc (11%)  
- Neither (25.5%)

Surprisingly 25% of clinicians reported that they do not perform tests of cure following treatment. Additionally 1 clinician reported that they use microscopy alone to check for cure yet had already reported having access to culture and NAAT facilities.

Contact Tracing – Look Back Period

Only 1 clinician did not perform contact tracing. 3 months was the most frequent look back period chosen by clinicians. There was no correlation with the length of contact tracing and private practice.

Choice of Guidance

IUSTI guidelines are well used but most clinicians still use their own local national/regional guidelines.
**Conclusion**

There is considerable variability surrounding the clinical diagnosis and management of gonococcal infections by IUSTI experts across Europe. Some of this variation is of concern since antibiotic choices amongst many clinicians may do little to delay the development of further gonococcal resistance or may even fail to provide cure amongst patients with current infection.

**Recommendations**

Our survey found many examples of excellent and up to date care. Clinicians are often using the best available treatment strategies and providing therapy which will provide guaranteed treatment and delay the onward march of resistant infection. However, this was not universal and those involved in post graduate training, continued professional development and guidelines development should consider further developing, disseminating and justifying clinical standards around the following:

1. Guidance regarding site testing.
2. Guidance regarding antibiotic choice.
4. Guidance regarding tests of cure.
5. Guidance regarding the duration of contact tracing.
6. Clarification should also be provided as to the circumstances in which gonococcal testing can be omitted and whether epidemiological or presumptive therapy is needed if there is full access to multiple site NAAT.

**Dissemination**

This report will be distributed at the 27th IUSTI Europe Congress in Antalya, Turkey 2012 and the results presented. The report will be available on the IUSTI Europe Regional pages and selected elements will also be published in due course.

**References**


6. CDC. *Morbidity and Mortality Weekly Report* 2012;61:31. [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w)