

Gonorrhea

Rossaphorn Kittiyaowamarn M.D.
Bangrak STIs Center
Bureau of AIDs TB and STIs
Department of Disease Control

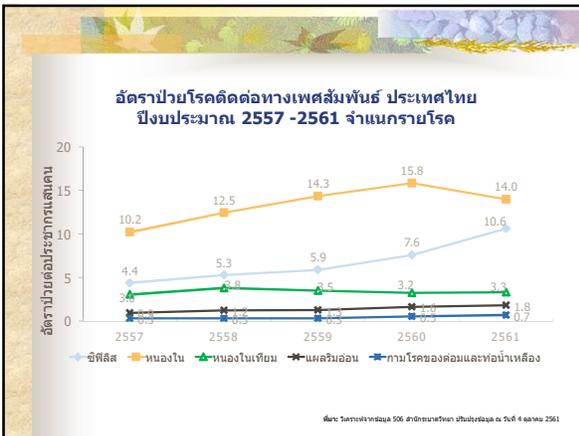
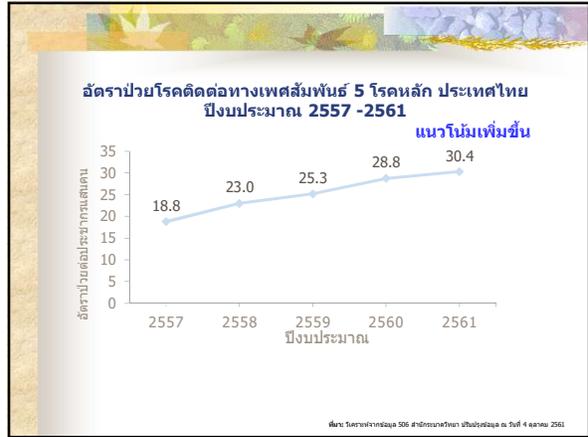
อังกฤษกังวล พบซูเปอร์หนองในดื้อยาหลังชายหนุ่มกลับจากเอเชีย

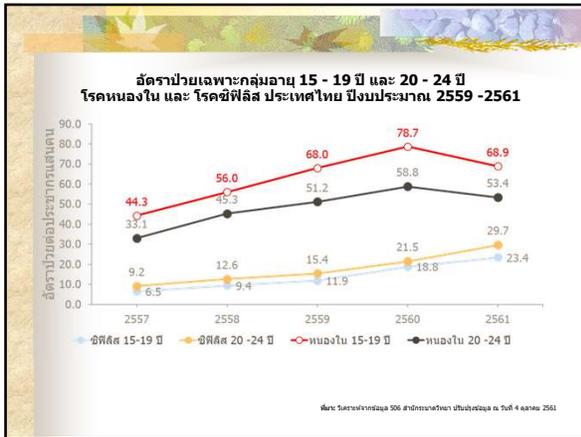
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ปมหนองใน พม.แยกพ่อลูก

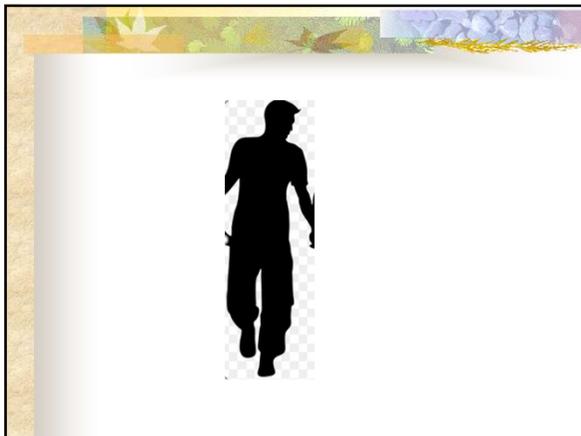




สัดส่วนของผู้ป่วยโรคติดต่อทางเพศสัมพันธ์ 5 โรคหลัก ปีงบประมาณ 2561 จำแนกตามอาชีพและกลุ่มอายุ

อายุปี	รับจ้าง/กรรมกร	ภาครัฐ	ไม่ทราบอาชีพ/ไม่ชัด	เกษตร	อื่น ๆ	งานบ้าน	ทหาร/ตำรวจ	ค้าขาย	ข้าราชการ	อาชีพพิเศษ	นักศึกษา	ประมง	บุคลากรสาธารณสุข	ครู
0-4	0.0	0.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5-9	0.0	0.4	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
10-14	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
15-19	3.3	12.9	4.5	0.4	0.5	0.5	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
20-24	8.9	6.1	3.8	0.7	1.1	0.7	1.6	0.3	0.1	0.1	0.1	0.1	0.1	0.0
25-29	7.2	1.0	1.9	0.7	0.6	0.4	0.3	0.2	0.2	0.2	0.1	0.0	0.0	0.0
30-34	5.4	0.2	1.3	0.6	0.5	0.1	0.1	0.2	0.2	0.1	0.0	0.0	0.0	0.0
35-39	3.8	0.1	1.1	0.7	0.4	0.2	0.1	0.2	0.2	0.1	0.0	0.1	0.0	0.0
40-44	3.0	0.0	0.8	0.7	0.2	0.1	0.1	0.2	0.1	0.0	0.0	0.0	0.0	0.0
45-49	2.0	0.0	0.6	0.7	0.2	0.1	0.0	0.2	0.1	0.0	0.0	0.0	0.0	0.0
50-54	1.5	0.0	0.4	0.8	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0
55-59	0.8	0.0	0.3	0.6	0.1	0.1	0.1	0.1	0.2	0.0	0.0	0.0	0.0	0.0
60-64	0.3	0.0	0.3	0.5	0.1	0.1	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0
>65	0.5	0.2	0.9	1.3	0.2	0.7	0.0	0.1	0.2	0.0	0.1	0.0	0.0	0.0

ที่มา: วัณโรคฯ จากข้อมูล 506 สำนักวิชาแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ ปีที่ 4 ตุลาคม 2561



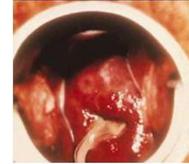
Gonococcal Urethritis

- 95% of cases have urethral discharge, dysuria



Gonococcal Cervicitis

- 85% - asymptomatic



Gonococcal Pharyngitis

- Relatively common
- >90% - asymptomatic
- Reservoir for infection



Gonococcal Proctitis

- <10% - symptomatic
- Pruritus ani, constipation, mucopurulent anal discharge
- Normal physical examination, or there may be visible pus with erythematous mucosa

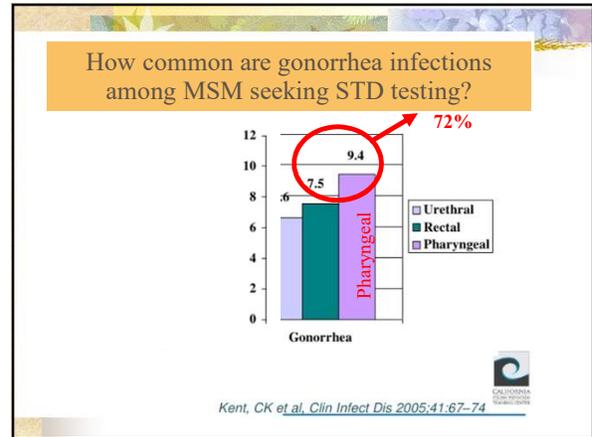
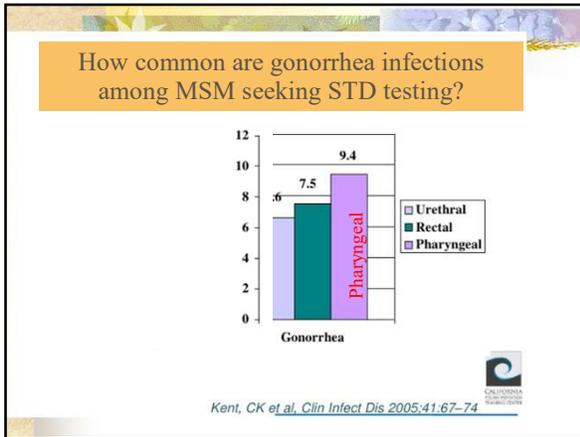


Postgrad Med J. 2006 Nov; 82(973): 733-736.

Gonococcal Conjunctivitis

- Rare in adults
- Autoinoculation





Gonorrhea Diagnostic Tests

- Gram stain
- Culture
- NAATs

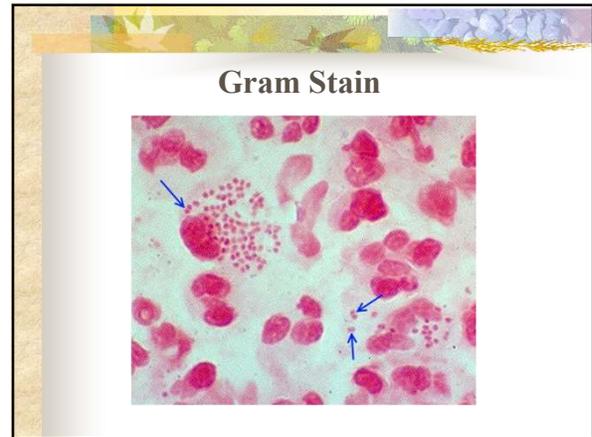


Table 35-2. Sensitivity and Specificity of Gram-Stained Smears for Detection of Genital or Anorectal Gonorrhea

Site and Clinical Setting	Sensitivity ^a	Specificity ^b
<i>Urethra</i>		
Men with symptomatic urethritis	90-95	95-100
Men with asymptomatic urethral infection	50-70	95-100
<i>Endocervix</i>		
Uncomplicated gonorrhea	50-70	95-100
Pelvic inflammatory disease	60-70	95-100
<i>Anorectum</i>		
Blind swabs	40-60	95-100 ^c
Anoscopically obtained specimens	70-80	95-100 ^c

^aSensitivity—percent of patients with positive cultures who have positive Gram-stained smears.
^bSpecificity—percent of patients with negative cultures whose Gram-stained smears also are negative.

Culture

- Sensitive to oxygen and cold temperature
- Require prompt placement in high-CO2 environment (candle jar)
- In cases of suspected sexual abuse, culture is the only test accepted for legal purpose

MMWR March 14, 2014

Specimen Collection



Specimen must be plate on warm media ASAP



Candle Jar

FDA-approved specimen

	Culture	NAAT
Endocervix	√	√
Urethra(men)	√	√
Vagina		√
Rectum	√	***
Pharynx	√	***
Conjunctiva	√	
Urine		√

MMWR March 14,2014

Treatment

Recommended Regimens for Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum (CDC)

Drug	2006	2007	2010	2015
Ciprofloxacin	500 mg PO	-	-	-
Ofloxacin	400 mg PO	-	-	-
Levofloxacin	250 mg PO	-	-	-
Ceftriaxone	125 mg PO	125 mg IM	250 mg IM	250 mg IM plusAZ
Cefixime	400 mg PO	400 mg PO	400 mg PO	-
And Doxycycline 100 mg twice a day for 7 day OR Azithromycin(AZ) 1 g orally in a single dose IF CHLAMYDIAL INFECTION IS NOT RULED OUT				-

Uncomplicated urogenital, anorectal and pharyngeal gonorrhea

Ceftriaxone & Azithromycin 1 g 250 mg IM

Dual therapy

Avoid sex for 1 week following treatment

CDC STD Treatment Guidelines 2015



Health care on NBCNEWS.com

Untreatable gonorrhea spreading worldwide

HOME ON AIR LISTEN PLAYLIST VIPS PHOTOS EVENTS EXTRA!

New 'Superbug' Strain of Gonorrhea Resists Antibiotics

By Amy Gritta | July 12, 2011

Untreatable Gonorrhea a Global Threat

Sex Bug Becoming Resistant to Last Known Treatment, WHO Warns

Gonorrhea becoming resistant to last available class of antibiotics

Published: Monday, August 20, 2012, 4:00 PM Updated: Monday, August 20, 2012, 5:21 PM

อังกฤษกังวล พบซูเปอร์หนองในดื้อยาหลังชายหนุ่มกลับจากเอเชีย

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Gonorrhoea treatment failure caused by a *Neisseria gonorrhoeae* strain with combined ceftriaxone and high-level azithromycin resistance, England, February 2018

David W Eyre¹, Nicholas D Sanderson¹, Emily Leof¹, Natasha Kapilford-Reimer¹, Kevin Chau¹, Leanne Barker¹, Markus Morgan¹, Robert Newman¹, Daniel Galparian¹, Magnus Unemo¹, Derrick W Cook^{1,2}, Tim EA Peto^{3,4}, Owenda Hughes⁵, Michelle J Cole¹, Helen Filler¹, Anne Edwards¹, Monique Andersson⁶

1. Big Data Institute, University of Oxford, Oxford, United Kingdom
2. Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom
3. Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom
4. WHO Collaborating Centre for Gonorrhoea and Other STIs, National Reference Laboratory for STIs, Örebro University Hospital, Örebro, Sweden
5. National Infection Service, Public Health England, Colindale, United Kingdom
6. National Institute for Health Research Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, University of Oxford, Oxford, United Kingdom
7. The authors contributed equally to this work

We describe a gonorrhoea case with combined high-level azithromycin resistance and ceftriaxone resistance. In February 2018, a heterosexual male was diagnosed with gonorrhoea in the United Kingdom following sexual intercourse with a locally resident female in Thailand and failed treatment with ceftriaxone 1 g and azithromycin 1 g and subsequently spectinomycin. Resistance arose from two mechanisms combining for the first time in a genetic background similar to a commonly circulating strain. Urgent action is essential to prevent further spread.

Antimicrobial resistance in *Neisseria gonorrhoeae* is a major concern. Dual therapy with ceftriaxone and azithromycin, the last two mainstream agents to which *N. gonorrhoeae* remains largely susceptible, is widely recommended internationally [1]. We describe a case of urethral and pharyngeal infection with *N. gonorrhoeae* with combined high-level azithromycin resistance and ceftriaxone resistance. Previously no such cases have been reported.

medial history. Examination revealed a creamy white urethral discharge, with 3+ pus cells and Gram-negative intracellular diplococci seen under microscopy, leading to a diagnosis of urethral gonorrhoea infection. He was treated with a single dose of intramuscular ceftriaxone 1 g and oral doxycycline 100 mg twice daily for 7 days.

A urine nucleic acid amplification test (NAAT) was positive for *N. gonorrhoeae* and *Chlamydia trachomatis*-negative. *N. gonorrhoeae* was cultured from a urethral swab. Antimicrobial susceptibility testing was undertaken by M.I.C. Evaluator Strips (Oxoid, Basingstoke, UK), according to the manufacturer's instructions, with results confirmed using Etest (BioMérieux, Marcy l'Étoile, France) at Public Health England, Colindale, UK and the WHO Collaborating Centre for Gonorrhoea and other STIs, Sweden. European Committee on Antimicrobial Susceptibility Testing resistance breakpoints were used [2]. The minimum inhibitory concentrations (MICs) of nine antimicrobials are given in Table and demonstrate high-level resistance to azithromycin

First verified dual treatment failure

- Heterosexual male presented to a UK Sexual Health Clinic with 2 weeks urethral discharge in December 2014
- Returned from Japan 10 days previously
- Urethral and pharyngeal gonococcal infection
- Treatment : Ceftriaxone 500 mg plus Azithromycin 1g

First verified dual treatment failure

- **Aymptomatic after treatment !!!**
- Test of Cure :
 - Day 15 -Throat NG NAAT +ve, Urine NG NAAT -ve
 - Day 79 -Throat NG NAAT +ve, Urine NG NAAT -ve
 - Day 98 Throat NG **C/S** and NAAT +ve
- Treatment : Ceftriaxone 1 g and Azithromycin 2 g

First reported ceftriaxone-resistant, highlevel azithromycin resistant *N. gonorrhoeae*

- In February 2018, a heterosexual male
- 4-day history of urethral discharge and dysuria
- SI 3 days earlier with a regular female partner
- SI with female in Thailand in January 2018

- PE: A creamy white urethral discharge

- Gram stain : 3 + pus cells and Gram-negative intracellular diplococci

- Rx : A single dose of intramuscular **ceftriaxone 1 g** and oral **doxycycline 100 mg** twice daily for 7 days.

- Urine NAAT : positive
- Culture : positive for *N.gonorrhoeae*
- Antimicrobial susceptibility test

TABLE 1

Antimicrobial minimum inhibitory concentrations, *Neisseria gonorrhoeae* case imported from Thailand to England, February 2018

Antimicrobial	MIC	Interpretation*
Ceftriaxone	0.5 mg/L	Resistant
Cefixime	2 mg/L	Resistant
Azithromycin	> 256 mg/L	High-level resistant
Ciprofloxacin	> 32 mg/L	Resistant
Tetracycline	32 mg/L	Resistant
Benzylpenicillin	1 mg/L	Intermediate susceptible
Spectinomycin	8 mg/L	Susceptible
Gentamicin	2 mg/L	No resistance breakpoint available (low value)
Ertapenem	0.032 mg/L	No resistance breakpoint available (low value)

MIC: minimum inhibitory concentrations.

* European Committee on Antimicrobial Susceptibility Testing resistance breakpoints were used [2].

- **13 days** after starting ceftriaxone and doxycycline treatment

- No symptoms

- Ix : urine NAAT
Pharyngeal swab culture

- Rx : Spectinomycin 2 g

- 13 days after starting ceftriaxone and doxycycline treatment

- No symptoms

- Ix : urine NAAT - **negative for *N. gonorrhoeae***
Pharyngeal swab culture - **positive for *N. gonorrhoeae***

- Rx : Spectinomycin 2 g

- 20 days
- Dx : Treatment failure
- Rx : Ertapenam IV for 3 days

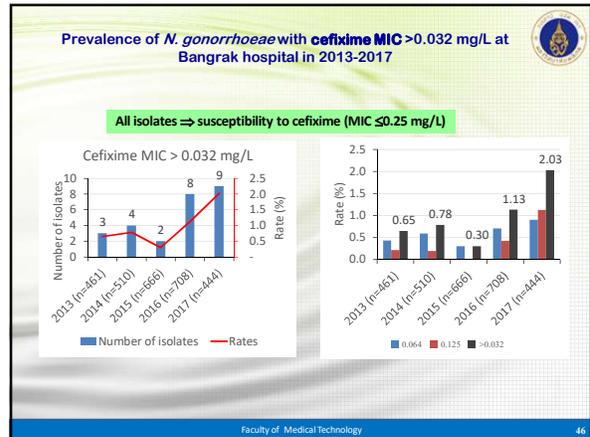
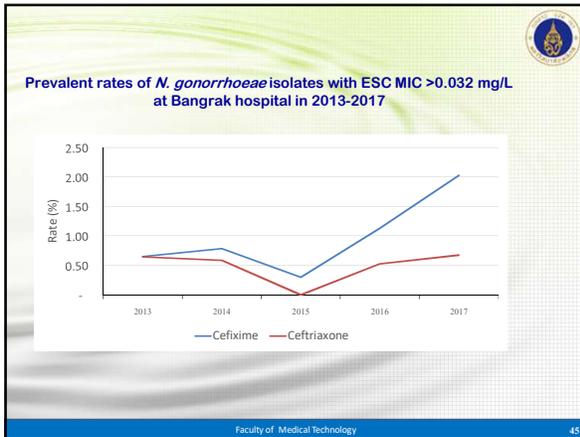
↓ 21 days

NAAT and culture of urethral and pharyngeal swabs : neagative

History of discovered and recommended antimicrobials and evolution of resistance in Neisseria gonorrhoeae, including the emergence of genetic resistance determinants, internationally.

Super Bug Status!

Magnus Unemo, and William M. Shafer Clin. Microbiol. Rev. 2014; doi:10.1128/CMR.00010-14
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Treatment

Uncomplicated urogenital, anorectal and pharyngeal gonorrhea

Ceftriaxone
~~250 mg IM~~
500 mg IM

↓

Gonorrhea

& Azithromycin 1 g or
Doxycycline 100 mg bid

↓

Non gonococcal infection

Alternative Regimens

If ceftriaxone is not available:

- **Cefixime** 400 mg orally in a single dose
PLUS
- **Azithromycin** 1 g orally in a single dose

CDC STD Treatment Guidelines 2015

Allergic to Ceftriaxone

- Gentamicin 160 mg -240 mg plus
Azithromycin 2 g
- Gemifloxacin 320 mg plus Azithromycin 2 g

CDC STD Treatment Guidelines 2015

Dual First-Line Therapy for Gonorrhea

- Ceftriaxone 500 mg + Azithromycin 1 g (UK+Australia)
- Ceftriaxone 250 mg + Azithromycin 1 g (USA+Canada)
- Ceftriaxone 500 mg + Azithromycin 2 g (Europe)
- Ceftriaxone 500 mg + Azithromycin 1.5 g (Germany)



Treatment Failure

- Symptoms do **not resolve within 3-5 days** after cephalosporins regimen treatment.
- Persons with a **positive test-of-cure** (i.e., positive culture ≥ 72 hours or positive NAAT ≥ 7 days after receiving recommended treatment)
- **Reinfection was excluded.**

CDC STD Treatment Guidelines 2015

What will we do for the case of treatment failure?

■ Report !!!!



Key Messages : *N. gonorrhoea*

- Local resistance data to determine the choice of therapy
- Use of dual therapy over single therapy
 - Ceftriaxone 250 mg or Cefixime 400 mg plus Azithromycin 1 gram
- Quinolones are no longer recommended
- Oropharyngeal infection
- Treatment Failure

