

# STIs - Revisited



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Division of AIDs TB and STI

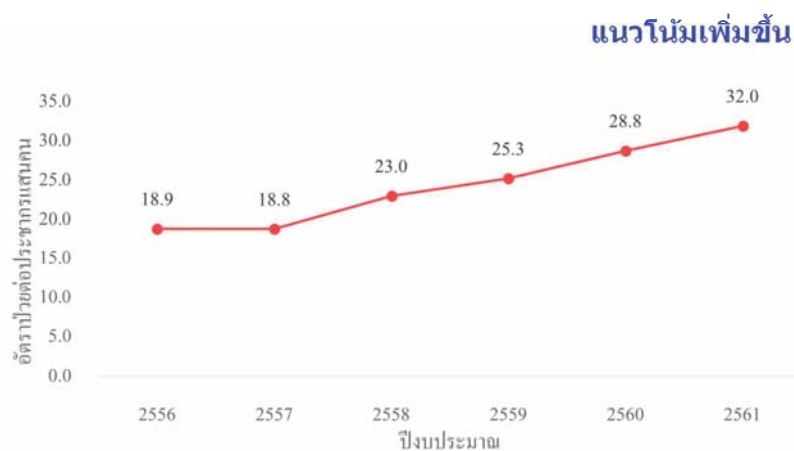
Department of Disease Control

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29/09/62

## อัตราป่วยโรคติดต่อทางเพศสัมพันธ์ 5 โรคหลัก ประเทศไทย ปีงบประมาณ 2556 -2561

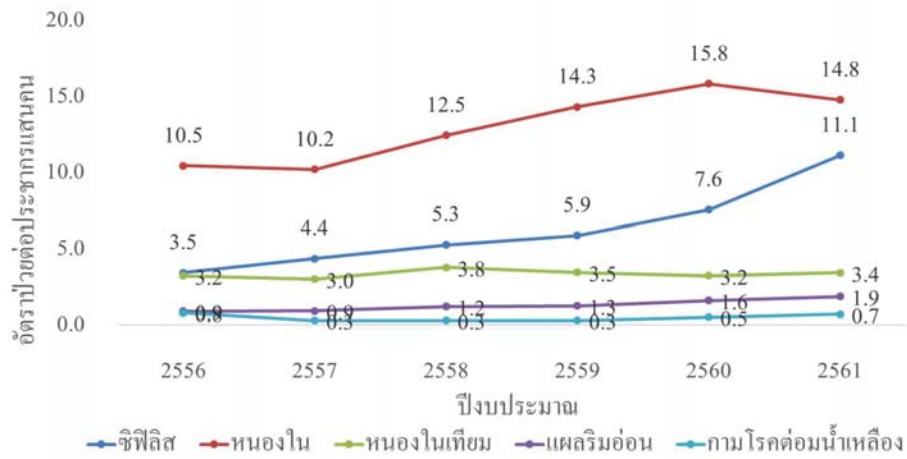


ที่มา: วิเคราะห์จากข้อมูล 506 สำนักระบาดวิทยา ปรับปรุงข้อมูล ณ วันที่ 15 กุมภาพันธ์ 2562

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### อัตราป่วยโรคติดต่อทางเพศสัมพันธ์ ประเทศไทย ปีงบประมาณ 2557 -2561 จำแนกรายโรค



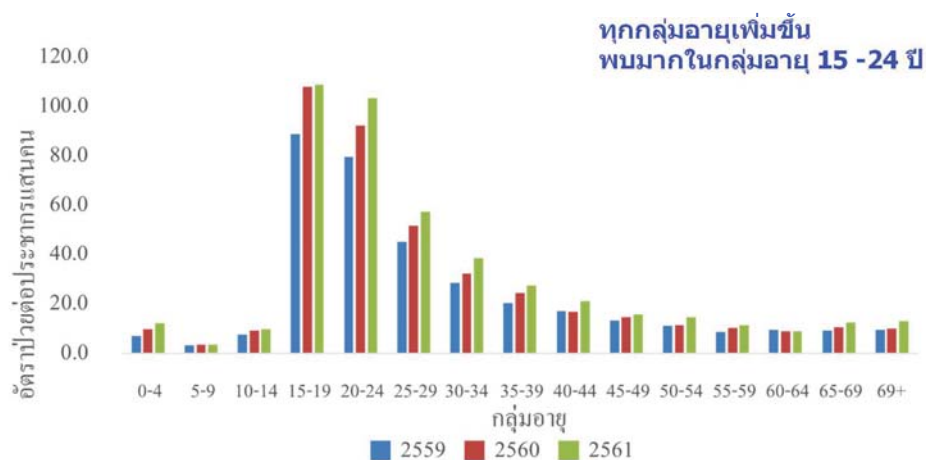
ที่มา: วิเคราะห์จากข้อมูล 506 สำนักระบาดวิทยา ปรับปรุงข้อมูล ณ วันที่ 15 กุมภาพันธ์ 2562

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### อัตราป่วยเฉพาะกลุ่มอายุโรคติดต่อทางเพศสัมพันธ์ 5 โรคหลัก ประเทศไทย ปีงบประมาณ 2559 -2561



ที่มา: วิเคราะห์จากข้อมูล 506 สำนักระบาดวิทยา ปรับปรุงข้อมูล ณ วันที่ 15 กุมภาพันธ์ 2562

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# Gonorrhea

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Health care on  **NBCNEWS.com**

# Untreatable gonorrhea spreading worldwide

HOME ON AIR LISTEN PLAYLIST VIPS PHOTOS EVENTS EXTRAS

## New 'Superbug' Strain of Gonorrhea Resists Antibiotics

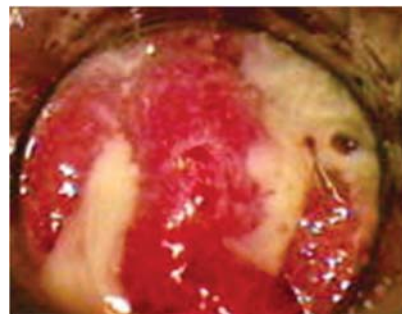
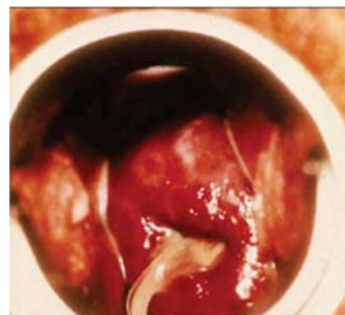
By: Amory Gritta | July 12, 2011

## Untreatable Gonorrhea a Global Threat

Sex Bug Becoming Resistant to Last Known Treatment, WHO Warns

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Characteristics of verified gonorrhoea treatment failures with ceftriaxone (250–1000 mg × 1) and causing gonococcal strain

| Country, year                  | Ceftriaxone Therapy       | Ceftriaxone MIC (mg/L)           | $fT_{>MIC}$ hours <sup>a</sup> | MLST/NG-MAST                                   | Site of failure | Final successful treatment   |
|--------------------------------|---------------------------|----------------------------------|--------------------------------|--|-----------------|--|
| Australia (n = 2), 2007 [31]   | 250 mg × 1                | 0.016–0.03 (Agar dilution)       | 41.4–50.3                      | ND/ST5, ST2740                                 |                 | Ceftriaxone 500 mg × 1/ Ceftriaxone 1 g × 1                          |
| Japan (n = 1), 2009 [30]       | 1 g × 1                   | 4.0 <sup>b</sup> (Etest, XDR)    | 0                              | ST7363/ST4220                                  |                 | None <sup>c</sup>  |
| Sweden (n = 1), 2010 [34]      | 250 mg × 1 and 500 mg × 1 | 0.125–0.25 <sup>b</sup> (Etest)  | 15.6–32.8                      | ST1901/ST2958                                  |                 | Ceftriaxone 1 g × 1  |
| Australia (n = 1), 2010 [32]   | 500 mg × 1                | 0.03–0.06 (Agar dilution)        | 41.3–49.9                      | ND ST1407, ST4950 (genogroup 1407)             |                 | Azithromycin 2 g × 1   |
| Slovenia (n = 1), 2011 [36]    | 250 mg × 1                | 0.125 <sup>b</sup> (Etest)       | 24.3                           | ST1901/ST1407 (genogroup 1407)                 |                 | Ceftriaxone 250 mg × 1 plus azithromycin 1 g × 1                     |
| Australia (n = 2), 2011 [33]   | 500 mg × 1                | 0.03–0.06 (Agar dilution)        | 41.3–49.9                      | ST1901/ST225, new variant of ST225             |                 | Ceftriaxone 1 g × 1 plus azithromycin 2 g × 1 or Ceftriaxone 1 g × 1 |
| Sweden (n = 3), 2013–2014 [35] | 500 mg × 1                | 0.064–0.125 <sup>b</sup> (Etest) | 32.8–41.3                      | ST1901/ST3149, ST3149, ST4706 (genogroup 1407) |                 | Ceftriaxone 1 g × 1  |

<sup>a</sup>Simulation of time of free ceftriaxone above MIC ( $fT_{>MIC}$ ) based on mean pharmacokinetic parameter values. Data from Chisholm et al. [52]

<sup>b</sup>Genetic cephalosporin resistance determinants (*penA*, *mtrR*, *penB*) elucidated [3, 5–8]

<sup>c</sup>The infection was considered to have resolved spontaneously within 3 months

MIC minimum inhibitory concentration, MLST multilocus sequence typing, NG-MAST *Neisseria gonorrhoeae* multi-antigen sequence typing, ND not determined, ST sequence type, XDR extensively drug-resistant [9]

[BMC Infect Dis.](#) 2015; 15: 364.

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Table 1. Failure of Dual Antimicrobial Therapy in a Patient with Gonorrhea.\*

| Day, Symptoms, and Test Results  | Ceftriaxone<br>MIC (mg/liter) <sup>†</sup> | Azithromycin | Multilocus<br>Sequence<br>Type | Multiantigen<br>Sequence<br>Type | PBP2   | <i>mtrR</i> <sup>‡</sup> | <i>penB</i> <sup>§</sup> | 23S rRNA <sup>¶</sup> | Treatment   |
|--|--|--------------|--------------------------------|----------------------------------|--------|--------------------------|--------------------------|-----------------------|---|
| Day 1, urethral discharge and dysuria<br>Positive: <i>N. gonorrhoeae</i> culture (urethra) and <i>N. gonorrhoeae</i> PCR (urine and pharynx) | NA   | NA           | NA                             | NA                               | NA     | NA                       | NA                       | NA                    | One dose of ceftriaxone 500 mg intramuscularly plus azithromycin 1 g orally |
| Negative: <i>Chlamydia trachomatis</i> PCR (urine and pharynx)   | NA   | NA           | NA                             | NA                               | NA     | NA                       | NA                       | NA                    |   |
| Day 15, no symptoms<br>Positive: <i>N. gonorrhoeae</i> PCR (pharynx)   | NA   | NA           | ST1901                         | ST12133                          | PBP2 X | Adenine deletion         | KD                       | WT                    | None  |
| Negative: <i>N. gonorrhoeae</i> PCR (urine)  | NA   | NA           | NA                             | NA                               | NA     | NA                       | NA                       | NA                    |   |
| Day 79, no symptoms<br>Positive: <i>N. gonorrhoeae</i> PCR (pharynx)   | NA   | NA           | ST1901                         | ST12133                          | PBP2 X | Adenine deletion         | KD                       | WT                    | None  |
| Negative: <i>N. gonorrhoeae</i> PCR (urine)  | NA   | NA           | NA                             | NA                               | NA     | NA                       | NA                       | NA                    |   |
| Day 98, no symptoms<br>Positive: <i>N. gonorrhoeae</i> culture (pharynx) and <i>N. gonorrhoeae</i> PCR (pharynx)                             | 0.25, resistant                            | 1, resistant | ST1901                         | ST12133                          | PBP2 X | Adenine deletion         | KD                       | WT                    | One dose ceftriaxone 1 g intramuscularly plus azithromycin 2 g orally       |
| Negative: <i>N. gonorrhoeae</i> PCR (urine)  | NA   | NA           | NA                             | NA                               | NA     | NA                       | NA                       | NA                    |   |
| Day 112, no symptoms<br>Negative: <i>N. gonorrhoeae</i> PCR (pharynx)  | NA   | NA           | NA                             | NA                               | NA     | NA                       | NA                       | NA                    | None  |

[N Engl J Med.](#) 2016 Jun 23;374(25):2504-6

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## First verified dual treatment failure (Dec 2014)

- Day 1 : Urethral discharge and dysuria (Rx)
  - Positive *N. gonorrhoeae* culture (urethra)
  - Positive *N. gonorrhoeae* PCR (urine and pharynx)
- Day 15 : No symptom
  - Positive *N. gonorrhoeae* PCR (pharynx)
  - Negative *N. gonorrhoeae* PCR (urine)
- Day 79 : No symptom
  - Positive *N. gonorrhoeae* PCR (pharynx)
  - Negative *N. gonorrhoeae* PCR (urine)
- Day 98 : No symptom (Rx Ceftriaxone 1 g and Azithromycin 2 g)
  - Positive *N. gonorrhoeae* culture and PCR (pharynx)
  - Negative *N. gonorrhoeae* PCR (urine)

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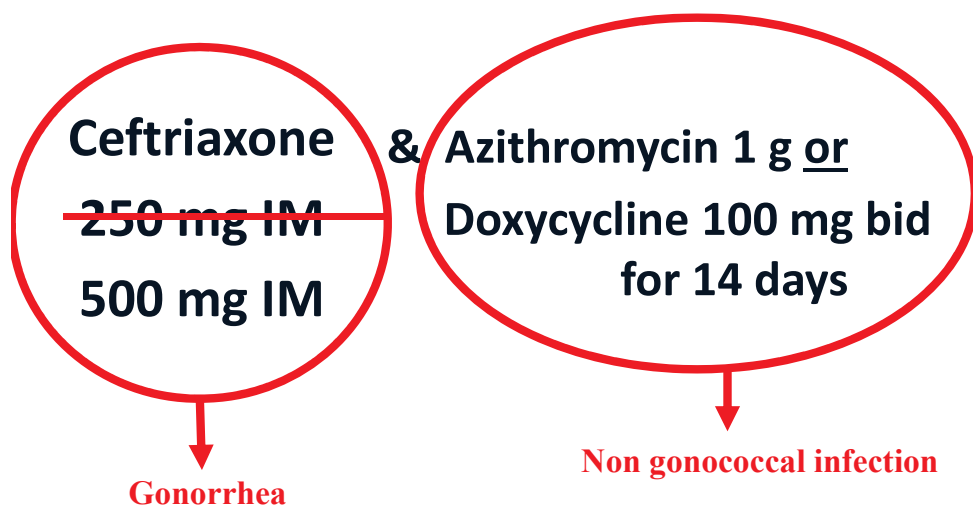
## First reported ceftriaxone-resistant, highlevel azithromycin resistant *N. gonorrhoeae* (Feb 2018)

- Day 1 : Urethral discharge and dysuria
  - (Rx Ceftriaxone 1 g and Doxycycline 7 days)
  - Positive *N. gonorrhoeae* culture and AST (urethra)
  - Positive *N. gonorrhoeae* PCR (urine)
- Day 13 : No symptom
  - Negative *N. gonorrhoeae* PCR (urine)
  - Positive *N. gonorrhoeae* culture (pharynx)
- Day 20 : No symptom
  - (Rx Ertapenam IV for 3 days)
- Day 41 : No symptom
  - Negative *N. gonorrhoeae* culture and PCR (urine and pharynx)

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## Uncomplicated urogenital, anorectal and pharyngeal gonorrhea



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## Uncomplicated urogenital, anorectal and pharyngeal gonorrhea

### Second Line Drug

- Cefixime 400 mg plus Azithromycin 1 g
- Spectinomycin (not suitable for pharyngeal gonorrhea)

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## Allergic to Ceftriaxone

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

CDC STD Treatment Guidelines 2015

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## The New Medication - Zoliflodacin

- Zoliflodacin is a new antibiotic that inhibits DNA biosynthesis.
- Zoliflodacin (also known as AZD<sub>0914</sub> or ETX<sub>0914</sub>) is an investigational spiropyrimidinetrione antimicrobial agent.
- Inhibit microbial biosynthesis by arresting the cleaved covalent gyrase complex and the formation of fused circular DNA required for biosynthesis

n engl j med 379;19

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# The New Medication - Zoliflodacin

- Phase 2 trial was evaluated for the treatment of uncomplicated gonorrhea

n engl j med 379;19

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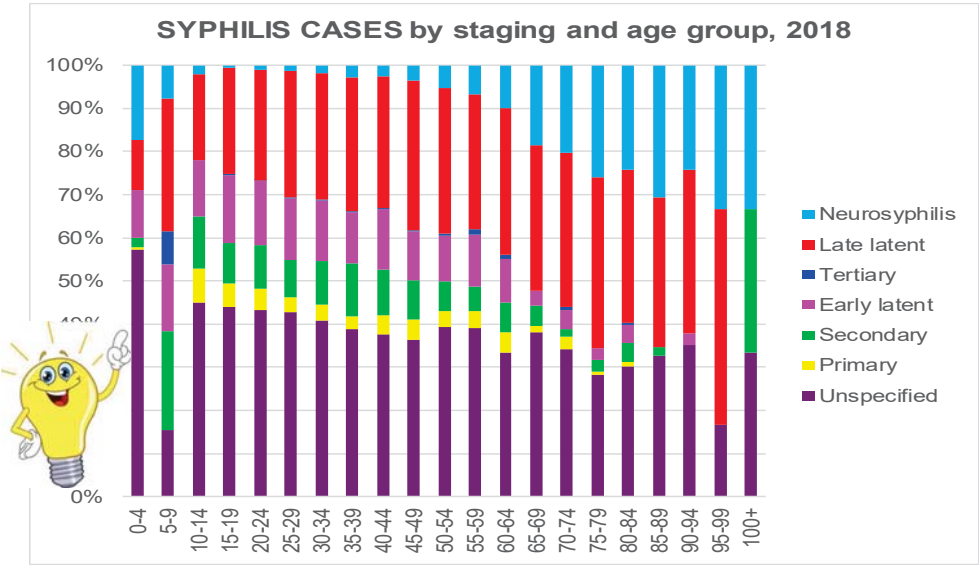
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| Table 2. Microbiologic Cure Rates at Test-of-Cure Visit — Micro-ITT and Per-Protocol Populations. |                      |       |                    |
|---|----------------------|-------|--------------------|
| Population, Site, and Treatment   | Confirmed Infections | Cures | Microbiologic Cure |
|   | number               |       | % (95% CI)         |
| <b>Micro-ITT</b>  |                      |       |                    |
| Urethra or cervix   |                      |       |                    |
| Zoliflodacin, 2 g   | 57                   | 55    | 96 (88–100)        |
| Zoliflodacin, 3 g   | 56                   | 54    | 96 (88–100)        |
| Ceftriaxone, 500 mg   | 28                   | 28    | 100 (88–100)       |
| Rectum  |                      |       |                    |
| Zoliflodacin, 2 g   | 5                    | 5     | 100 (48–100)       |
| Zoliflodacin, 3 g   | 7                    | 7     | 100 (59–100)       |
| Ceftriaxone 500 mg  | 3                    | 3     | 100 (29–100)       |
| Pharynx   |                      |       |                    |
| Zoliflodacin, 2 g   | 8                    | 4     | 50 (16–84)         |
| Zoliflodacin, 3 g   | 11                   | 9     | 82 (48–98)         |
| Ceftriaxone, 500 mg   | 4                    | 4     | 100 (40–100)       |
| <b>Per protocol</b>   |                      |       |                    |
| Urethra or cervix   |                      |       |                    |
| Zoliflodacin, 2 g   | 49                   | 48    | 98 (89–100)        |
| Zoliflodacin, 3 g   | 47                   | 47    | 100 (92–100)       |
| Ceftriaxone, 500 mg   | 21                   | 21    | 100 (84–100)       |
| Rectum  |                      |       |                    |
| Zoliflodacin, 2 g   | 4                    | 4     | 100 (40–100)       |
| Zoliflodacin, 3 g   | 6                    | 6     | 100 (54–100)       |
| Ceftriaxone, 500 mg   | 3                    | 3     | 100 (29–100)       |
| Pharynx   |                      |       |                    |
| Zoliflodacin, 2 g   | 6                    | 4     | 67 (22–96)         |
| Zoliflodacin, 3 g   | 9                    | 7     | 78 (40–97)         |
| Ceftriaxone, 500 mg   | 4                    | 4     | 100 (40–100)       |

n engl j med 379;19

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## Stage of Syphilis Infection

- Primary syphilis
- Secondary syphilis
- Latent syphilis
  - Early latent syphilis
  - Late latent syphilis
- Tertiary syphilis

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## Diagnostic tests

- Demonstration of spirochetes
- Serology
  - Non-treponemal test (NTT) : VDRL, RPR
  - Treponemal test: TPHA, TPPA, FTA-ABS, CIA, EIA

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## Screening test(s) for syphilis?

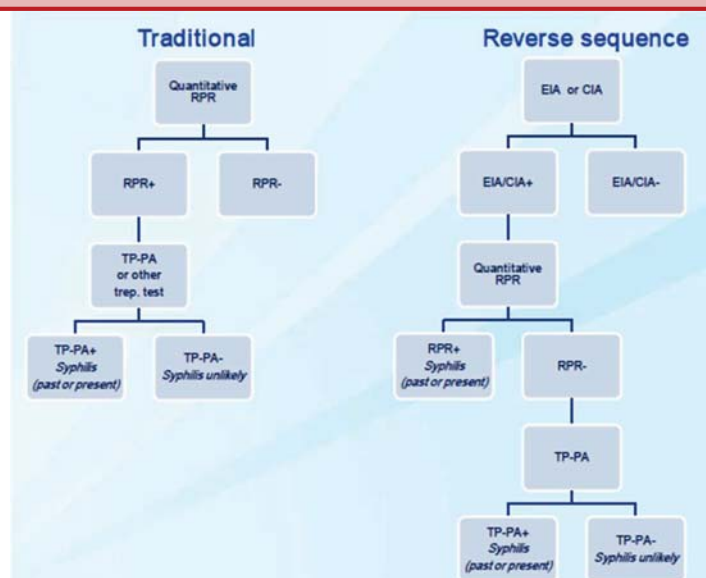
- A. RPR or VDRL
- B. TPHA or TPPA
- C. FTA-ABS
- D. RPR and TPHA

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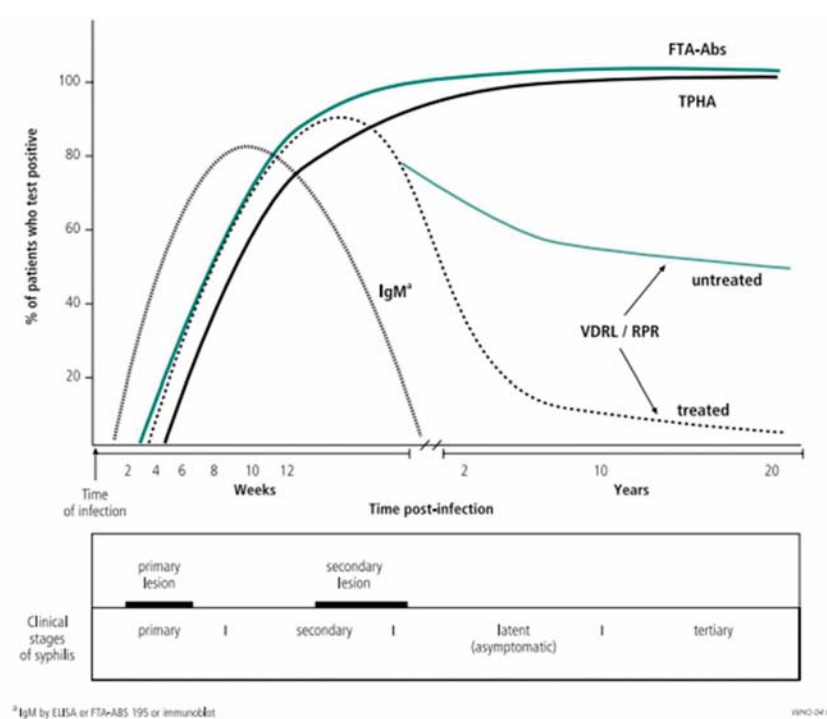
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## Syphilis Serologic Screening Algorithms



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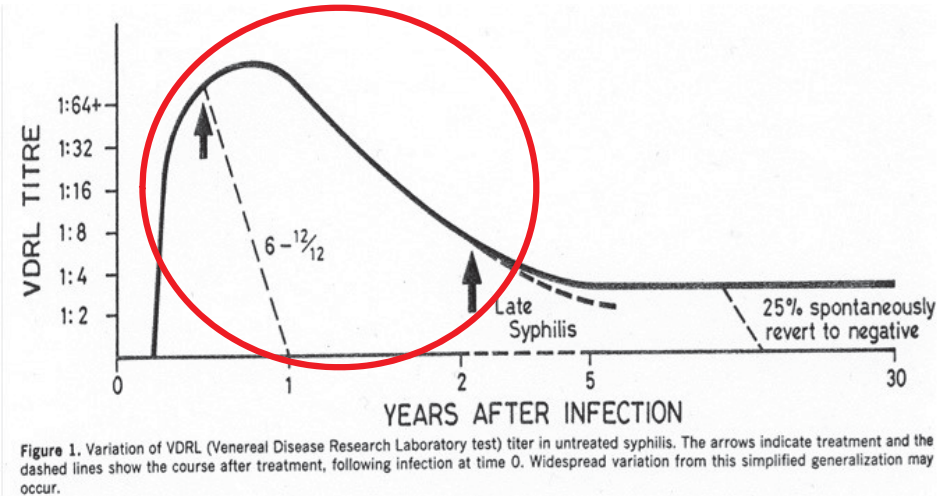
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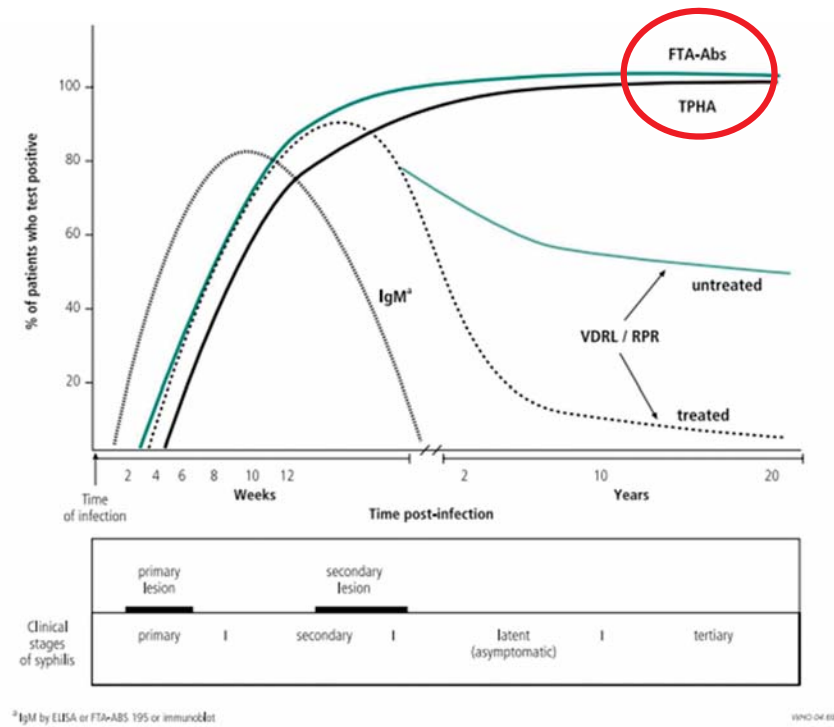
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# Nontreponemal antibodies (VDRL/RPR)



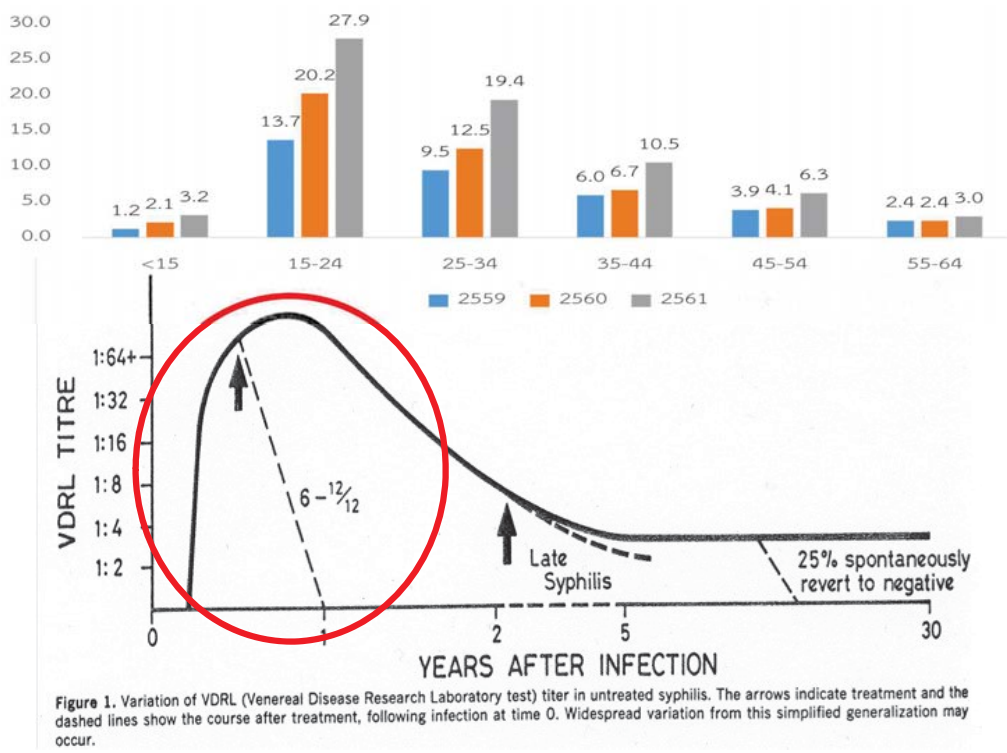
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**Table 4. Comparison of the 3 Serodiagnosis Algorithms at Different Stages of Syphilis**

| Diagnosis    | No. of Serum Samples Tested | No. (%) of Serodiagnosis Positive by: |                           |                        |
|--------------|-----------------------------|---------------------------------------|---------------------------|------------------------|
|              |                             | Traditional Testing Algorithm         | Reverse Testing Algorithm | ECDC Testing Algorithm |
| Primary      | 24                          | 18 (75.00)                            | 23 (95.83)                | 24 (100)               |
| Secondary    | 365                         | 362 (99.18)                           | 365 (100)                 | 364 (99.73)            |
| Early latent | 198                         | 155 (78.28)                           | 198 (100)                 | 195 (98.48)            |
| Late latent  | 1578                        | 1153 (73.07)                          | 1576 (99.87)              | 1569 (99.43)           |
| Tertiary     | 584                         | 396 (67.81)                           | 583 (99.83)               | 580 (99.31)            |
| Total        | 2749                        | 2084 (75.8)                           | 2745 (99.85)              | 2732 (99.38)           |

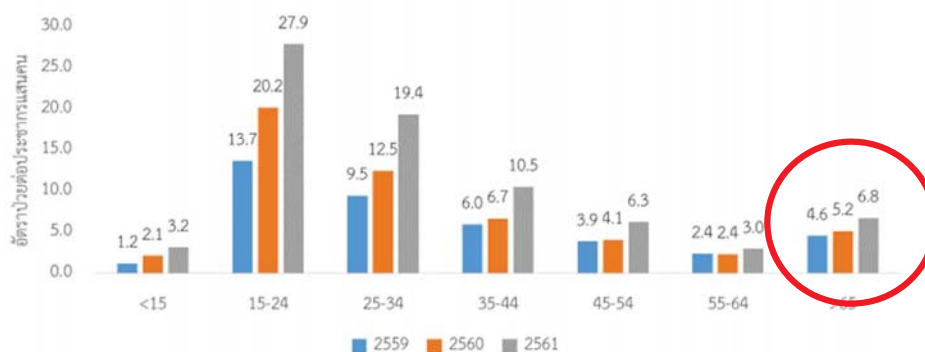
Abbreviation: ECDC, European Centre for Disease Prevention and Control.

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### อัตราป่วยเฉพาะกลุ่มอายุโรคซิฟิลิส ประเทศไทย ปีงบประมาณ 2559 -2561



ที่มา: วิเคราะห์จากข้อมูล 506 สำนักโรคติดต่อวิทยา ปรับปรุงข้อมูล ณ วันที่ 15 กุมภาพันธ์ 2562

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## Key Messages

### Gonorrhea

- The new treatment guideline for gonorrhea
- Treatment failure of gonorrhea should be aware.
- When should we start to do TOC for Thailand?



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## Key Messages

### Syphilis

- The return of congenital syphilis
- Stage of syphilis should be clearly defined.
- Screening is important.
- Traditional or Reverse algorithm
- Partner notification and treatment should be done as many cases as possible.

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