STATE-OF-THE-ART DIAGNOSTICS FOR CHLAMYDIA & GONORRHOEA

Epidemiology & Burden

- 131 million Chlamydial infections and 78 million Gonorrhoea occur each year, making both the most prevalent bacterial sexually transmitted infections (STIs).
- In high-income countries, chlamydia is most common in young heterosexual adults (<25 years of age). Chlamydia is also common in MSM attending sexual health clinics, in whom chlamydia positivity ranges from 2% to 5% for urethral infection and 6% to 9% for rectal infection.
- *N. gonorrhoeae* burden is high in the low & middle-income countries and it has developed antimicrobial resistance to the current & recommended treatment.
- *C. trachomatis* & *N. gonorrhoeae* infections can lead to pelvic inflammatory disease, ectopic pregnancy, infertility, penile oedema, and epididymitis.

Diagnostic Methods

Table 1: . Performance and operational characteristics of diagnostic tests for chlamydia and gonorrhea (Herring, A., et al. Nature Reviews Microbiology.2006)

			Complexity‡			
Test	**Sensitivity§**	**Specificity§**	**Expertise**	**Equipment**	**Time**	**Relative cost‡**
Bacterial culture	60–70%‖	99–100%	+++	+++	48 hours	++
Microscopy (NG only)	Men: 84–95% Women: 50%	≥95%	++	+	1 hour	+
NAHT	85–90%	95–99%	+++	+++	4 hours	+++
NAAT	90–95%¶	98–100%	++++	++++	4 hours (longer to confirm)	++++
Antigen detection						
EIA	50–70%	95–99%	++	++	4 hours	++
RDT	ND	ND	+	None	30 minutes	ND

EIA, enzyme immunosorbent assay; NAAT, nucleic acid amplification test; NAHT, nucleic acid hybridization test; ND, not determined; NG, *Neisseria gonorrhoeae*; RDT, rapid diagnostic test. *Values taken from REFS 8,9,18–22,26,28–30; ‡ + denotes minimal requirements for training, equipment and cost; ++++ denotes requirement for highly trained personnel, sophisticated equipment/laboratory facilities and high cost; §Test performance compared to a combined reference standard of bacterial culture or two NAATs; ‖Bacterial culture for NG is close to 100% sensitive under optimal conditions; ¶Sensitivity is lower for urine specimens[22].

Table 2: Common diagnostic methods for *N. gonorrhoea* (WHO 2013)**

	Microscopy[a]	Culture	NAAT
Specimen types			
Endocervical swab	Yes[a]	Yes	Yes
Vaginal swab	No	Yes[b]	Yes (some assays)
Urine			
Female	No	No	Yes[c]
Male	No	No	Yes
Urethral swab	Yes[a]	Yes	Yes
Rectal swab	No	Yes	No[d]
Oropharyngeal swab	No	Yes	No[d]
Conjunctival swab	Yes	Yes	No[d]
Performance			
Sensitivity[e]	Low–high[a]	Moderate–high	Very high
Specificity[e]	Moderate–high[a]	Very high	Moderate–very high
Other considerations			
Cost	Low	Moderate	High–very high
Instrumentation	Microscope	Routine microbiology	Large footprint
Throughput/automation	Moderate/no	Moderate/no	High/possible
Technical complexity	Low	Moderate	High
Level of laboratory infrastructure	Peripheral	Peripheral–intermediate	Intermediate–central
Multiple pathogens from one sample	No	No	*C. trachomatis*, *T. vaginalis*, and HPV on some platforms

Table 3: Evaluated diagnostic methods for *C. trachomitis* (WHO 2013)**

	NAAT	Culture	DFA	POC
Specimen types				
Endocervical swab	Yes	Yes	Yes	Yes
Liquid cytology medium	Yes (some tests)	No	No	No
Vaginal swabs				
Self-obtained	Yes (some tests)	No	No	Yes (some tests)
Clinician-collected	Yes (some tests)	No	No	Yes (some tests)
Urine				
Female	Yes	No	No	No
Male	Yes	No	No	No
Male urethral swab	Yes	Yes	Yes	Yes
Rectal swab	No[a]	Yes[b]	Yes[b]	No
Oropharyngeal swab	No[a]	Yes[b]	Yes[b]	No
Conjunctival swab	No[a]	Yes	Yes	No
Performance				
Sensitivity[c]	Very high	Moderate–high	Low–moderate	Low–moderate
Specificity	Very high	Very high	Moderate	Very high
Other considerations				
Cost	Very high	Moderate	Low	Low
Transportation and storage	Ambient up to 60 days (check package insert)	4°C for 24 h –70°C after 24 h	Ambient	NA
Instrumentation	Large footprint	Routine microbiology/ virology	Fluorescent microscope	Small–none
Throughput/ automation	High/yes	Low/no	Low/no	Low/no
Technical complexity	High	High	Moderate (microscopy skills)	Low
Level of laboratory infrastructure	Reference	Reference	Central	Site
Multiple pathogens from one sample	*N. gonorrhoeae*, *Trichomonas vaginalis* and HPV on some platforms	No	No	No

***** WHO Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus 2013***

Table 4: Pooled performance of the POC antigen detection and near-patient NAATs (Source: Systematic review by Kelly H, et al. Sex Transm Infect 2017 in press)

	Antigen detection point-of-care tests			Near-patient NAATs		
Specimen type	**No. of studies (No of study subjects)**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**No. of studies (No of study subjects)**	**Sensitivity % (95% CI)**	**Specificity % (95% CI)**
Cervical swab	8 (4,588)	53.1% (34.7 - 70.8)	98.9% (98.0 - 99.4)	1 (1,713)	97.4%	99.6%
Vaginal swab	10 (6,252)	36.6% (22.9 - 52.9)	96.9% (94.0 - 98.4)	1 (1,710)	98.7%	99.4%
Male urine	5 (2,568)	62.5% (43.2 - 78.5)	98.0% (95.1 - 99.0)	1 (1,386)	97.5%	99.9%
Female urine	-	-	-	1 (1,718)	97.6%	99.8%
Male rectal swab	-	-	-	1 (409)	86%	99.2%

NAAT-nucleic acid amplified test; POC-point of care, CI-confidence intervals

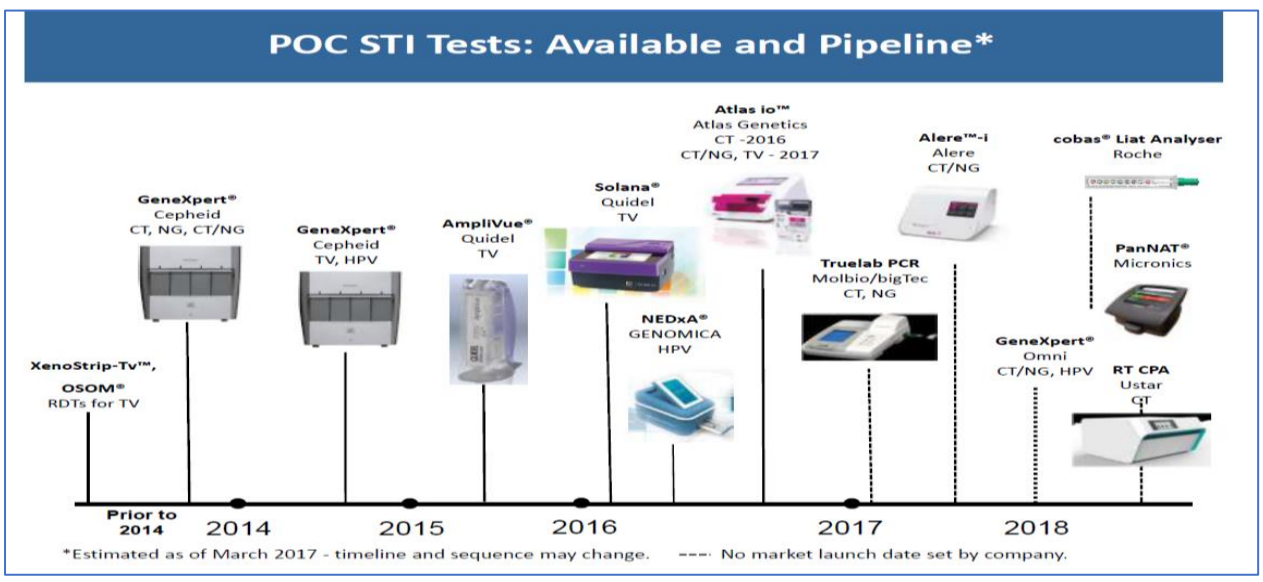

Fig 1: Point-of-care tests or near point-of-care diagnostics for N. gonorrhoea, C. trachomitis & other STIs (Source: http://www.who.int/reproductivehealth/topics/rtis/Diagnostic_Landscape_2017.pdf)

Unmet Diagnostic Needs

- Development of more affordable and sensitive point-of-care diagnostics for Chlamydia and Gonorrhoea

References:

- Herring, A., et al. (2006). Evaluation of rapid diagnostic tests: chlamydia and gonorrhoea. Nat Rev Micro.
- Kelly H, Coltart CEM,Pant Pai N et al. (2017). Systematic reviews of point-of-care tests for the diagnosis of urogenital *Chlamydia trachomatis* infections. Sex Transm Infect.
- Murtagh, M. M. (2016). The point-of-care diagnostic landscape for sexually transmitted infections (STIs).*World Health Organization, Geneva, Switzerland*. Accessed from: http://www.who.int/reproductivehealth/topics/rtis/Diagnostic_Landscape_2017.pdf
- Sexually transmitted infections (STIs). World Health Organization. 2016. Accessed from: http://www.who.int/mediacentre/factsheets/fs110/en/
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