In 2006, a new variant of *Chlamydia trachomatis* (nvCT) was discovered in Sweden [1]. Due to a deletion in the target sequence for PCR amplification, nvCT has escaped detection by the nucleic acid amplification tests Abbott m2000 (Abbott Laboratories) and Cobas AmpliCtor/TaqMan48 (Roche Diagnostics) which together were used for 65% of all chlamydia tests in Sweden. The third test commonly used in Sweden, ProbeTec ET (Becton Dickinson [BD]), does detect the new variant because it uses a different DNA target sequence in the cryptic plasmid.

The nvCT is spread all over Sweden and in early 2007, it accounted for between 20% and 65% of all chlamydia cases in Swedish counties where Abbott/Roche test systems were used [2]. In the four counties that used the BD system, the proportion of nvCT was only between 7% and 20% in the same time period. Ongoing studies are now following the spread of the nvCT in several counties.

The areas most heavily affected by the spread of nvCT were in almost the same situation as at the time before chlamydia was recognised as a pathogen. In many sexual networks cases have therefore escaped diagnosis, treatment and mandatory contact tracing. Moreover, figures from 2007 confirm that – irrespective of the emergence of nvCT – the number of reported chlamydia cases has reached an all time high in Sweden (see Figure) [3,4].

Although the new variant is widely spread in Sweden, surprisingly few cases have been detected in other countries [2,5], and many of the detected cases had epidemiological links to Sweden.

When it was realised that nvCT was prevalent in Sweden, all affected laboratories had to change from Abbott/Roche methods to adequate test systems that detect nvCT. For a temporary period, alternative test systems have been used (Artus C trachomatis Plus PCR, Qiagen; LightMix 480HT, TIB Molbiol) or BD ProbeTec has replaced the previous system. Most of the 14 affected laboratories had changed their test system by February 2007, and three months later all laboratories in Sweden had reliable diagnostic test systems in place.

Now Abbott has replaced their old assay for the m2000 platform with a new version (Abbott RealTime CT assay) that has two target regions in the cryptic plasmid of *C. trachomatis*. This modification has drastically decreased the risk for detection failure due to a mutation, and maintains a high sensitivity based on the copy number of 5-10 copies of the plasmid per cell. Roche has also developed a new assay version (CT Test, v2.0) for their COBAS TaqMan system. This assay also relies on a dual target, with one target on the cryptic plasmid and the other in the chromosomal *ompA* gene. Thus it has a slightly lower sensitivity for detection of nvCT strains that are lacking the plasmid target sequence, but the chromosomal target will enable detection of strains with any kind of mutation on the plasmid. Both tests are now CE-labeled. Quality assurance by independent reference laboratories would be useful, but resources are lacking in most countries.

The emergence of nvCT has taught us several things: First, the diagnostic tests must be designed carefully. The targets should not only be conserved genetic elements but also essential for the organism. Although not an issue for commonly used *C. trachomatis* assays, specificity is a problem for detection of other bacterial pathogens [6-8]. Another point to consider is the importance of using several test systems on a national level. If a single test system dominates a market too much, it will be more difficult to notice the appearance of a mutant, and the lack of alternative detection systems will make laboratory diagnostics even more vulnerable. The thrilling story of nvCT has also highlighted the importance of epidemiological surveillance in the discovery of unexpected biological changes that have impact both on diagnostics and public health.
References


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