

# Rapid diagnostics – warts and all: a final preview of the BSMT conference

This year's British Society for Microbial Technology Annual Microbiology Conference will be held on 2 May at the UKHSA, Colindale, North London.

Here, BSMT Chair Dr Mark Wilks continues his preview of the meeting focusing on antimicrobial resistance, the UK government's ambitious programme to control it, and how likely it is to succeed.

'Contained and controlled: the UK's 20-year vision for antimicrobial resistance' is the admirably optimistic title of the government policy paper on solving the problem of antimicrobial resistance (AMR) by the year 2040. The action plan covers action across human and

veterinary medicine, food production, agriculture and research, and focuses on three key ways of tackling AMR: i) reducing need for, and unintentional exposure to, antimicrobials; ii) optimising use of antimicrobials; and iii) investing in innovation, supply and access.

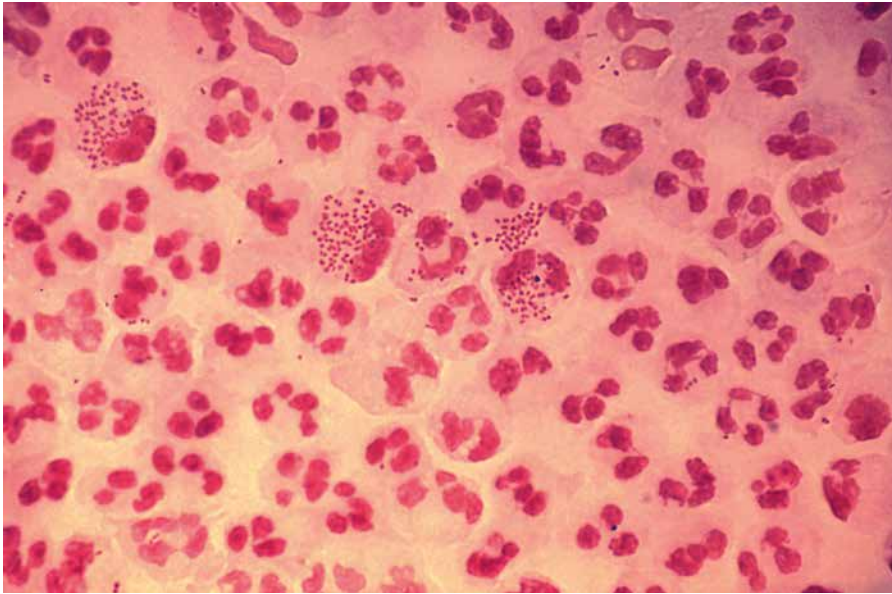
A laudable ambition and it's hard to argue against these three key ways, but how are things going so far? The UK's current five-year National Action Plan (NAP) on tackling AMR, which runs from 2019 to 2024, is coming to an end and as the next five-year NAP is currently being launched, progress made thus far towards the UK's commitments on AMR is being analysed. It should be pointed out that COVID-19 has had a derailing effect on this programme as in every other aspect of healthcare; indeed, several of our speakers have been seconded to work on different aspects of the COVID-19 outbreak from their normal areas of work.

It's worth looking at the outcomes of a meeting held in November 2022 of UK experts from across the human and animal sectors to discuss their thoughts on progress to date, as well as any recommendations and key considerations they thought should be taken forward.<sup>1</sup> Overall, it was agreed that there was a major disparity between the increasing ambitions of the NAP, and the reducing financial support for achieving said ambitions. We will look at how this plays out in the area of STIs later in this article. The gap between evidence generation and implementing recommendations into real-world settings also presents a key challenge to overcome if the NAP's commitments are to be achieved.

A lack of communication and funding appeared to underpin many of the barriers that prevent the successful delivery of current NAP commitments and were therefore highlighted as key areas of concern for policymakers to consider when looking to tackle AMR. The consensus of the meeting was that the focus should be on successfully implementing and delivering the current NAP commitments rather than identifying future ambitions.



The UK Health Security Agency, Colindale, North London: this year's venue for the the 39th Annual Microbiology Conference of the British Society for Microbial Technology.



An acute case of gonococcal urethritis (Gram staining).

We are fortunate that Dr Alicia Demirjian from Evelina London Children's Hospital and UKHSA has agreed to speak and explain the new five-year plan to us. Dr Demirjian is a consultant in paediatric infectious diseases and immunology at Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, where she is the lead for paediatric antimicrobial stewardship, and deputy lead for infection prevention and control. In addition, she is a consultant epidemiologist in the UKHSA's Healthcare-Associated Infection & Antimicrobial Resistance division and is an expert on the new five-year plan.

In the previous article of this two-part review,<sup>2</sup> we described advances in rapid sequencing developed by Adela Alcolea-Medina, Lead, Next-Generation Sequencing, Infection Sciences, Synovis, St Thomas' Hospital, London leading to the development of a unified metagenomic method for rapid detection of bacteria, fungi and viruses in clinical samples, but it should not be forgotten that PCR as a diagnostic tool, although well-established, is also rapidly advancing.

### Multiplexing capability in diagnostics

Dr Rodriguez Manzano, Associate Professor in the Department of Infectious Disease at Imperial College London will be describing his work on infections and AMR using, among other approaches, a machine-learning method to develop high-level multiplexing in qPCR and dPCR. Dr Manzano is also a member of the National Institute for Health and Care Research (NIHR) Unit in Healthcare-Associated Infections and Antimicrobial Resistance, a partnership between Imperial College and the UKHSA,

where he contributes to shaping the UK's strategy for addressing the critical issue of AMR. The technology he and his unit have developed enables accurate multiplexing (up to 21 targets in a single well has been demonstrated). The patented approach enables the recognition of primer-characteristic molecular signatures. Hopefully this will lead to truly affordable solutions in established molecular tests, by effectively extracting the kinetic and thermodynamic information from existing real-time data.

There is a huge amount of information contained in these data which is not visible to the end user in the clinical laboratory but is normally just seen in the form of a positive or negative result. This technology should enhance diagnostic performance and has the potential to vastly increase throughput by identifying multiple nucleic acid targets in a single amplification reaction. It is compatible with a wide range of amplification chemistries (eg probe-based, intercalating dyes, and isothermal reactions), and hence can be seamlessly integrated with various laboratory workflows. Multiplexing offers a solution that reduces the requirements in physical space, time-to-result, and volume of reagents and sample.

In the microbiology laboratory, fluorescent probes are often used as markers and the number of targets is often limited by optical instrumentation and the small range of different wavelengths available for reporting. Alternative methods of detection such as post-amplification analysis may require lengthy gel-electrophoresis or expensive sequencing approaches. The technology leverages machine learning to automatically learn target-specific

information encoded in each amplification event (via real-time data), to identify the nature of nucleic acid molecules. The utility of a reliable and accurate high-level multiplexing capability in the diagnostic laboratory is clear.

### Issues in sexual health

Returning to the area of STIs mentioned above, a recent analysis by *The Guardian* of English council spending on sexual health services found national cuts of more than a third since 2013, despite a rise in consultations for STIs.<sup>3</sup> English councils spent £9.58 a head on sexual health services – including STI testing and treatment, contraception, and advice – in 2022–23, compared with £14.41 in 2013–14, after taking inflation into account.

The result of this is that people are being hospitalised for sexual health conditions that are easily treatable in local clinics. Nationally, the number of gonorrhoea and syphilis cases reached a record last year, with 146 gonorrhoea diagnoses per 100,000 people. That was up from 58 in 2013, while syphilis diagnoses increased from 6.4 to 15.4. Hospital figures show admissions for syphilis and *Chlamydia* doubled between 2013–14 and 2022–23, while gonorrhoea admissions tripled.

Advice, prevention and promotion services have seen the largest cuts to funding, with net spending down 44% since councils were made responsible for public health in 2013. Meanwhile, STI testing and treatment fell by 33% and contraception spending fell by 30%. Of course, some of this fall in funding may be as a direct result of the more widespread introduction of cheaper tests that can be performed by online requesting of a test kit without the need for clinic attendance. It remains to be seen if the ambitious targets of the UKHSA AMR plan can be realised in the face of such cuts, which are of course not confined to the field of STI testing, treatment and contact tracing.

The rise in the unnecessary hospitalisation of patients with disseminated gonococcal infection (DGI) referred to above poses its own particular problems. Diagnosis often has to rely on 16s rRNA sequencing of molecular specimens rather than culture. Here, there is no cultured isolate for phenotypic antimicrobial susceptibility testing (AST), therefore selection of an appropriate antibiotic therapy for DGI, or in other gonorrhoea infections where ceftriaxone is contraindicated, is challenging and relies on molecular methods.

### Molecular approaches

Dr Michelle Cole, Interim Head of the STI Reference Laboratory, UKHSA, will be reviewing some of the molecular

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approaches to STI AMR surveillance. *Neisseria gonorrhoeae* Sequence Typing for Antimicrobial Resistance (NG-STAR) is a MLST scheme specifically developed for *N. gonorrhoeae* sequence typing and the identification of specific antimicrobial resistance determinants, thus allowing phenotypic antimicrobial susceptibility to be inferred from some alleles and sequences types (STs). The variety of NG-STAR types identified thus far should be able to show whether DGIs are caused by a single virulent clone or are related to the problem of delayed diagnosis as mentioned above, in which case we could expect to see a variety of NG-STAR types.


Dr Cole's work has also involved *Mycoplasma genitalium*, which can cause non-gonococcal urethritis in men and is associated with cervicitis and pelvic inflammatory disease in women. The sexually transmitted bacterial pathogen *M. genitalium* has proved a complex organism to work with in the laboratory setting. Owing to its extremely fastidious nature, successful growth of *M. genitalium* in the laboratory has proved elusive, particularly in the UK which has arguably lagged behind other countries in realising the importance of this organism. Antimicrobial resistance to both first- and second-line recommended therapies (macrolides and fluoroquinolones, respectively) is commonly reported. However, phenotypic susceptibility testing is not routinely performed because culture is so rare. Instead, molecular detection of known resistance determinants is used to infer susceptibility

or resistance. As with *N. gonorrhoeae*, future treatment options are extremely limited for *M. genitalium* and, if this sexually transmitted infection is to remain treatable, phenotypic susceptibility testing will have a role in evaluation of potential therapeutics. Furthermore, molecular assays are of limited use for detection of emerging resistance mechanisms, as by definition the target is unknown. As such, the ability to introduce and retain culture retention of these techniques in at least some laboratories is important.

Antimicrobial resistance in *M. genitalium* is presently a minor public health concern and not nearly as important as that of *N. gonorrhoeae* and DGI; however, surveillance remains very limited. Dr Cole has been involved in the development of a protocol for routine national surveillance of AMR in *M. genitalium* in England (MARS). The MARS protocol aims to estimate the prevalence of macrolide and fluoroquinolone resistance in *M. genitalium* infections among adults ( $\geq 18$  years) attending sentinel sexual health services (SHSs) in England, and characterise factors associated with resistance.


### A final sobering reflection

Lastly, Ivor Mitchelmore, now-retired chief biomedical scientist, Luton & Dunstable University Hospital, will describe his work in setting up a microbiology service in a low- to middle-income country from scratch. It's sobering to reflect that in spite of all the increasingly sophisticated and

expensive technology described above, the majority of the world's population does not have access to even the most basic laboratory services and the kind of work that Ivor will describe; for example, introducing a basic blood culture set-up and sensitivity testing can be transformative and achieved at a very low cost. 

### References

- 1 Neale D, Cullen L. Evaluating the National Action Plan (NAP) on antimicrobial resistance, and recommendations for the next 5-year NAP: a roundtable discussion. *Sustainable Microbiology* 2024 Jan; 1 (1): qvad001. <https://doi.org/10.1093/symbio/qvad001>.
- 2 Wilks M. Rapid diagnostics – warts and all: a microbiology conference preview. *Pathology in Practice* 2024 Feb; 25 (1): 14– 6.
- 3 The Guardian. *Hospital admissions for easily treatable STIs rise amid funding cuts in England*. 16 Feb 2024 (<https://www.theguardian.com/society/2024/feb/16/hospital-admissions-for-sexual-health-conditions-rise-amid-funding-cuts-in-england>).

As in previous years, the BSMT conference will have a full trade show supported by 12 of the most innovative companies attending to present the latest developments and newest equipment to talk to delegates about what their companies can offer laboratories. The conference provides scientists with the opportunity to discuss and debate their experiences: and a great chance to question the experts! We have restricted the number of talks to six, rather than seven, to allow more time for you to ask questions and make comments. Registration is now open, and early booking is advised as the conference last year sold out. Please check the BSMT website (<http://www.bsmt.org.uk>) to register and for any updates to the programme.  [www.bsmt.org.uk](http://www.bsmt.org.uk)

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