Laboratory issues in STD diagnosis and their application to disease control in an Australian context

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This issue of Microbiology Australia features a selection of articles on novel and pragmatic contributions from Australian clinical laboratories to the diagnosis, management and control of sexually transmitted diseases (STDs).

Some time ago the World Health Organisation (WHO) estimated that a total of 330 million new cases of ‘treatable’ STDs (syphilis, gonorrhoea, chlamydial infection and trichomoniasis) are acquired globally each year and these numbers may well have increased. These and other STDs are important not only for the number of infections they cause, but also for their associated morbidity and sequelae, which have profound effects, both immediate and long-term. One important and direct association with STDs is the amplification of the rate of acquisition of HIV that occurs in the presence of an STD. This arises with both ulcerative and non-ulcerative STDs and the earlier epidemiological studies that pointed to this association have now been underpinned by a better understanding of the biological processes involved. There are thus compelling reasons for seeking better control of STDs, and this was recognised by the WHO at its meeting of the World Health Assembly in 2006 when a resolution was passed calling for member states to devote more resources to this increasing problem.

Australia has a manifest need to take note of this WHO resolution regarding STD control. Rates of STDs are generally increasing in Australia, although disease incidence and prevalence of STDs is notoriously difficult to estimate with any reliability. Paradoxically, improvements in data collection, notification systems and enhanced diagnostics make it difficult to obtain valid trend data, as these improvements are rolled out progressively but variably in different jurisdictions over extended periods. Although many important and treatable STDs such as trichomoniasis are not reportable, the most current indicative data on infection rates for selected STDs were for 2005. Of these notifiable STDs, rates aggregated nationally were for Chlamydia trachomatis infections 217/100,000 population, for gonorrhoea 41.5/100,000 and for syphilis less than 10/100,000. In 2005 the per capita rate of diagnosis of hepatitis C was 63.4/100,000 and for newly acquired hepatitis B 1.2 /100,000. Age specific rates and geographic differences are substantive and vary greatly by specific STD.

With regard to STDs, in urban populations Australia experiences not only those problems common to all industrialised countries, but also a combination of other circumstances that require innovative and thoughtful approaches to their containment throughout the country. Some illustrative examples, further expanded on in the article by Lum, include the problems of disease in Indigenous populations in remote areas. Although numerically the numbers of STDs are not high in ‘outback’ Australia, the rates per head of population are 50 to 100 times those for equivalent diseases in urban settings, so that a different scale is required to compare data from the Northern Territory with those of the rest of Australia. A description of these problems and laboratory contributions to their resolution are a recurring theme in the papers presented in this edition. In urban areas too, there are important issues – some global, others local. There has been a continuing increase in the incidence and prevalence of ‘classical’ STDs, like syphilis and gonorrhoea, amongst urban populations of homosexually active men (HAM) in recent years. Also of note is the need for attention to the increasing rates of Chlamydia trachomatis infection in Australia in order to prevent the downstream sequelae attributable to these diseases.

Neisseria gonorrhoeae - a Gram stain showing Gram negative intracellular diplococci.

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Control of STDs is a complex issue. A classic formula, \( R_0 = \beta c D \), was described to provide a conceptually simple yet statistically valid means of describing how various factors can interact to affect disease rates and how different interventions may impact on them. Broadly, the disease rate \( (R_0) \) of a sexually transmitted infection is governed by the interplay between three elements – the transmissibility of the organism \( (\beta) \), the rate of effective partner exchange \( (c) \) and the duration of infectiousness \( (D) \). Put another way, \( R_0 \) depends on how well the pathogen transmits, how often it gets the chance to do so and how long this opportunity persists. When \( R_0 \) is <1, the disease is regarded as being in decline, when at or about 1 it is in a steady state, but when >1 it is essentially out of control. Each of \( \beta \), \( c \) and \( D \) has multiple inputs. For example, transmissibility of a pathogen \( (\beta) \) has factors intrinsic to the organism (such as its ability to survive, adhere, attach, invade mucosal surfaces and evade local and systemic host defences), the host (susceptibility, local and systemic innate and acquired immunity) and extrinsic considerations (condom usage, availability of diagnostic and treatment facilities, for example). Introduction of preventative measures such as condom usage on a scale sufficient to affect \( R_0 \) is not a simple process, requiring behavioural change, acceptance, availability and resources. That is, each component of \( \beta c D \) expands to involve multiple factors, and each of these must be simultaneously addressed and in place for STD control, and indeed any infectious disease control.

The contributions that clinical laboratories can make to reduction in \( R_0 \) are most obvious in the area of improved diagnostics. In Australia, an aetiological based system of disease diagnosis and management is in place as opposed to the ‘syndromic’ approaches used where resources for diagnostic testing are not available or reliable. This aetiological approach enables focused treatment and management of the individual so that accurate and rapid diagnosis, if followed by effective treatment and management, reduces both \( \beta \) (transmissibility) and \( D \) (duration of infectiousness). Further, epidemiological analyses of diagnostic data can properly determine sorely needed data on
disease rates, thereby ensuring relevant resource allocation to enhance public health control of the most prevalent diseases.

Australia has many examples of novel solutions to diagnostic dilemmas in the area of STDs. In this edition of *Microbiology Australia* Bastian describes pioneering work on the diagnosis of donovanosis, Robertson the status of resolution of problems surrounding aspects of the serological diagnosis of syphilis, Tabrizi the experience of the Melbourne group in relation to the diagnosis of chlamydial disease and Whiley the solutions to some, but not all, issues surrounding the molecular diagnosis of gonorrhoea.

Diagnostic laboratory practice can also materially enhance therapeutic interventions for STDs. Again, these measures constitute essential components of any disease control approach through their capacity to materially affect β and D, and by this means, Ro. Significant advances have been made in our knowledge relating to vaccine based prevention of human papilloma virus associated malignancies and this topic is dealt with by Garland. Other viral STDs too are extremely important and surprisingly common and herein Smith offers insights into hepatitis virus acquisition through sexual contact. While the antimicrobial treatment of most bacterial STDs (such as syphilis or chlamydial disease) is relatively unaffected by problems of antimicrobial resistance, the choice of an appropriate antibiotic treatment for gonococcal infection is complicated by the seemingly remorseless and uninterrupted emergence and spread in Australia of *Neisseria gonorrhoeae* resistant to multiple antibiotics. The Australian response to this problem, a long running national programme of antibiotic resistance surveillance, is detailed herein by Limnios. Again these laboratory procedures if utilised and applied effectively provide material benefits to public health extending beyond those attributable to the wellbeing of the individual patient.

The articles presented here do not set out to provide an exhaustive examination of the depth and breadth of issues surrounding STD diagnostics and their applications — such an endeavour would require a very substantial publication that may well be out of date by the time it is completed given the rapid advances that are occurring in this field. For example, there is the emerging problem of diagnosis of lympho-granuloma venereum (LGV). This disease, caused by particular sub-types of *C. trachomatis*, has appeared overseas in HAM and is now also seen in these groups in Australia.

Other extensions of laboratory diagnostics in the control of STDs too have not been mentioned. For example, proper application of laboratory typing methods can help define sexual networks and allow interventions appropriate for their interruption thus contributing to a reduction in the rate of effective partner exchange. Additionally typing of STD pathogens is extremely important to determine the components required for any vaccine.

Finally, there is the continuing search for the ‘holy grail’ of STD diagnostics – cheap, sensitive, specific, non-invasive, rapid and robust tests that can be used and reliably interpreted at the point of care. Given the evidence presented in the group of papers in this issue of Microbiology Australia, on Australian applications of emerging technology to the conditions that prevail here, it is anticipated that future issues of this journal will be needed to describe advances in this important area.

**References**

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