

Targeted Laboratory Screening for Sexually Transmitted and Bloodborne Infections in Wisconsin

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ABSTRACT

Public health laboratories play an important role in screening programs for asymptomatic diseases of public health importance in high-risk and underserved populations. The implementation of targeted screening strategies for communicable diseases requires thorough planning and evaluation. The Wisconsin State Laboratory of Hygiene (WSLH) systematically selects and evaluates laboratory tests used in communicable disease control programs coordinated by the Wisconsin Division of Public Health. To do this, the epidemiologic features of the disease in potential target populations are carefully assessed, with the choice of laboratory tests based on performance as well as practical and cost considerations. Laboratory testing at WSLH plays a crucial role in screening programs for sexually transmitted and bloodborne infections. Hallmarks of these programs are cross-sector collaboration, empirical selection of laboratory testing methods, and the use of epidemiologic data to develop and evaluate targeted screening strategies.

INTRODUCTION

Public health laboratories play an important role in assuring the delivery of the essential services of public health, including monitoring health status, diagnosing and investigating health problems in the community, linking people to needed health services, assuring pro-

vision of health care when otherwise unavailable, and conducting research and evaluations of those services.¹ One critical activity of public health laboratories is the implementation of screening programs for asymptomatic diseases of public health importance in high-risk and underserved populations.

Successful application of screening programs requires systematic planning and evaluation. The Wisconsin State Laboratory of Hygiene (WSLH) has developed an expository model for the selection, use, and evaluation of laboratory testing methods for public health purposes.² The desire to achieve optimal performance characteristics of the available laboratory tests must be balanced against practical cost considerations, and the epidemiologic features of the disease in potential target populations must be carefully assessed. This model has been recognized as a useful approach to assure the cost-effectiveness of laboratory testing strategies employed for both personal health and public health purposes.³

These principles can be illustrated through consideration of the evolution of screening programs for sexually transmitted and bloodborne infections in Wisconsin, for which laboratory testing at WSLH plays a crucial role. Important features of these programs are cross-sector and interagency collaboration, systematic evaluation and selection of laboratory testing methods, and use of epidemiologic data to guide the development and evaluation of targeted screening in specific populations.

During the past two decades, numerous studies have been conducted in Wisconsin to evaluate, compare, and improve laboratory assays to screen for sexually transmitted and bloodborne infections such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). These investigations of laboratory testing methods have been integrated with epidemiologic studies to assess the distribution and de-

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terminants of infection in various populations, and to evaluate the costs and benefits of selective screening within those populations. This work has been performed by the Wisconsin Division of Public Health (WDPH) and the WSLH in collaboration with many other partners, including the Centers for Disease Control and Prevention (CDC), the Wisconsin Department of Corrections, the University of Wisconsin-Madison, local public health departments, family planning agencies, and private health organizations.

Specifically, studies have been conducted to evaluate and compare assay methods, multi-test panels, and testing algorithms. Research has also been conducted to improve existing assay performance, and to assure the quality of specimen collection, handling, and transport. Epidemiological investigations have evaluated the use of these assays in specific populations, while assessing prevalence and risk factors and developing cost-effective selective screening criteria. Target populations have included clients of sexually transmitted disease (STD) clinics, family planning clinics, community health clinics, adolescent health clinics, correctional institutions, and managed care organizations. Application of the findings from these studies has resulted in continual improvement of programs to identify, prevent, and control sexually transmitted and bloodborne infections.

SCREENING FOR SEXUALLY TRANSMITTED INFECTIONS IN WISCONSIN

The WSLH developed a panel of screening tests in 1982 to assist clinicians with the evaluation of patients at high risk for sexually transmitted infections (STIs) and to collect epidemiologic data for public health purposes. In addition to the traditional tests for gonorrhea and syphilis, this "STD Panel" included tests that were not readily available in the private sector (e.g., culture for *Chlamydia trachomatis*), tests for agents whose possible role as sexually transmitted pathogens were being investigated (e.g., cultures for *Ureaplasma urealyticum* and *Mycoplasma hominis*), and serologic tests for assessing a patient's prior exposure to agents (e.g., chlamydia microimmunofluorescence assay and herpes simplex virus enzyme immunoassay). Although culture for *Chlamydia trachomatis* had been available at WSLH since 1978, it wasn't until the inclusion of this test on the STD panel in 1982 that the demand for testing and recognition of its importance by both clinicians and public health practitioners increased.

Pilot studies conducted in 1984 in Wisconsin family planning, STD, and university health clinics deter-

mined that the prevalence of chlamydia infection ranged from 6.5% to 19.3%.⁴ The preliminary results from these studies led to legislation in May 1984 that added *C. trachomatis* infection, as well as pelvic inflammatory disease and nongonococcal cervicitis and urethritis, to the list of STIs officially reportable to the Wisconsin Division of Health (now the Division of Public Health). Facilitated by the availability of non-culture laboratory methods, studies to assess the prevalence of *C. trachomatis* infection and to determine risk factors for infection were conducted in both rural⁵ and urban⁶ settings in 1985-1986. The introduction of an inexpensive and high-throughput laboratory enzyme immunoassay (EIA) test for *Chlamydia trachomatis* at WSLH in 1986 led to a dramatic increase in the number of tests performed by WSLH of women attending Wisconsin family planning clinics. The volume increased from 3000 tests by culture and direct fluorescent antibody (DFA) assay in 1985 to over 25,000 per year by EIA in 1987, a volume that has remained relatively constant ever since.

Analyses of demographic, clinical, and behavioral risk factors associated with *C. trachomatis* infection led to the development of selective screening criteria for use by all family planning clinics in the state. In 1990, a follow-up study to evaluate the impact of the chlamydia control program and to determine possible revisions to the selective screening criteria revealed a significant decrease in the prevalence of *C. trachomatis* infection, which was attributed to the control program efforts.⁷ Further assessment of outcomes using case reports, laboratory test records, and hospital discharge data demonstrated that following the implementation of the chlamydia prevention program in 1985, statewide declines were observed in prevalence, incidence, and complications of infection.⁸

Research on improving the EIA testing strategy resulted in implementation of supplemental testing of borderline negative specimens (thereby increasing net sensitivity), first by DFA assay in 1994, and then by nucleic acid amplification tests (NAAT) in 1996. Following comprehensive cost-effectiveness analyses, EIA testing was replaced by the more costly but much more sensitive NAAT methods. NAAT was implemented in 1997 for testing of urine specimens from high-risk males attending STD clinics, and in 2000 for testing cervical swabs or urine specimens from women attending family planning clinics or STD clinics. Over time, the chlamydia NAAT methods evaluated and employed by WSLH have included polymerase chain reaction, ligase chain reaction, and now strand displace-

Table 1. Current Selective Screening Criteria for Chlamydia and Gonorrhea in Wisconsin Family Planning Clinics

Chlamydia (CT)	Gonorrhea (GC)
<p>Females</p> <p>Sex Partner Risk: <i>All within past 90 days</i></p> <p>Patient had more than one partner</p> <p>Patient had a partner who had more than one partner</p> <p>Patient had a new partner</p> <p>Contact</p> <p>Patient had a partner with symptoms or diagnosis of CT, GC, NGU, epididymitis, or other STD within past 90 days</p> <p>Symptomatic</p> <p>Current diagnosis of (or evaluation for) gonorrhea</p> <p>Current diagnosis of or symptoms of PID</p> <p>Cervicitis - mucopurulent discharge or friable cervix</p> <p>Cervical erythema greater than 50%</p> <p>Purulent vaginal discharge</p> <p>History of STD (<i>note: NOT "Test of Cure"</i>)</p> <p>Confirmed or self-reported CT infection in past 5 years</p> <p>Other</p> <p>Protocol testing: Prior to an IUD insertion</p> <p>Pregnancy - prenatal visit</p> <p>Special Age Criteria *</p> <p>Patients not meeting above criteria, but under a specified age may be tested in selected clinics.</p>	<p>Level 1** Females and Males</p> <p>Contact</p> <p>Patient had a partner with symptoms or diagnosis of Chlamydia, GC, NGU, epididymitis, syphilis or PID within past 90 days (confirmed or self-reported)</p> <p>Symptomatic</p> <p>Cervicitis-mucopurulent discharge (MPC) or friable cervix</p> <p>Current diagnosis of NGU or PID</p> <p>Penile discharge</p> <p>Current Positive Chlamydia</p> <p>Current positive test for Chlamydia on this specimen</p> <p>History of STD (<i>note: NOT "Test of Cure"</i>)</p> <p>Diagnosed with GC, Chlamydia, or PID within the past year</p> <p>Level 2** Females and Males (limited)</p> <p>Contact</p> <p>Patient had partner with GC (confirmed or self-reported)</p> <p>Symptomatic</p> <p>Patient has discharge suggestive of GC infection</p> <p>Current Positive Chlamydia</p> <p>Current positive test for Chlamydia on this specimen.</p>
<p>Males</p> <p>Contact</p> <p>Patient had a partner with symptoms or diagnosis of Chlamydia, GC, NGU, syphilis or PID within past 90 days (confirmed or self-reported)</p> <p>Symptomatic</p> <p>Males presenting with symptoms suggestive of CT infection</p> <p>Positive LET</p> <p>Males who are not contacts and present with no symptoms, but with a urine dipstick Leukocyte Esterase Test (LET) result of trace or higher.</p>	
<p>* Special Age Criteria: different age cutoffs apply at selected clinics.</p> <p>** Level 1 clinics are located in high-morbidity areas for GC. Level 2 clinics are in areas where GC is uncommonly seen.</p>	

ment amplification that allows for simultaneous detection of *C. trachomatis* and *N. gonorrhoeae* from the same specimen, either swab or urine.

Subsequent epidemiologic studies, enhanced by using NAAT technology, were conducted in 1996-1997 and again in 2000 to identify further changes in the prevalence of infection and to re-evaluate and revise the *C. trachomatis* selective screening criteria for women attending family planning clinics. The 2000 study also provided data for the development of empirical screening criteria for *N. gonorrhoeae* infection. Based on these new criteria (Table 1), selective screening of

74.8% of women for *C. trachomatis* and 43.9% for *N. gonorrhoeae* would detect 91.2% and 89.2% of these infections respectively.

SCREENING FOR BLOODBORNE INFECTIONS IN WISCONSIN

The WSLH introduced a screening panel for the evaluation of patients at risk for HIV infection prior to both the identification of HIV as the causative agent of AIDS in 1983-1984 and the development of laboratory tests for HIV antibody in 1985. This battery of tests was used to establish baseline and prognostic markers

and included antibody assays to detect prior infection with Hepatitis A and B viruses, herpes simplex virus, cytomegalovirus, Epstein-Barr virus, toxoplasma, syphilis, and *C. trachomatis*, as well as immunochemical and immunologic markers, such as beta-2 microglobulin, C-reactive protein, immunoglobulins, and complement markers. From the results of this screening panel, even in the absence of an agent-specific laboratory test, the clinician was able to determine a patient's index of risk for AIDS or the so-called "AIDS-related complex" syndrome.

The first enzyme-linked immunosorbent assay (ELISA) test for antibody to HIV became available in March 1985 and was immediately introduced at WSLH. In June 1985, the Wisconsin Division of Health established a network of counseling and testing sites comprised of existing local non-profit public health clinics, state-associated non-profit medical clinics, and community health clinics. This strategy allowed individuals at high-risk to be evaluated for HIV infection anonymously in an alternative setting to blood and plasma collection facilities, with testing performed at no charge by WSLH. During the first 18 months of operation, these sites collectively tested an average of 170 clients per month; by early 1987, this number had increased to 500 clients tested per month.

An HIV testing algorithm was developed at WSLH whereby all specimens were tested by 2 different ELISA assays, with all specimens yielding reactive or high non-reactive results repeated by ELISA and tested by a supplemental in-house Western Blot assay. This algorithm allowed for ongoing validation of the new test methods, provided enhanced specificity, and resulted in increased sensitivity for the detection of patients early in seroconversion. The WSLH actively participated with other state public health laboratories, reference, clinical and research laboratories, and blood donor centers to develop consensus recommendations for the optimal use of HIV antibody assays, including criteria for Western Blot interpretation.⁹ Over time, indirect fluorescent antibody (IFA) assays, recombinant peptide-specific procedures, HIV isolation, polymerase chain reaction methods, p24 core antigen tests, HIV-2 and HIV-1/HIV-2 combination assays, and rapid test methods, as well as assays using alternative specimen types such as dried blood spots and oral fluid have been evaluated. Several of these testing strategies have been incorporated into the WSLH repertoire as public health needs emerged.

With the availability of HIV antibody screening tests in 1985, a series of epidemiologic studies were

conducted over the next several years under the direction of the WDPH and CDC, with testing performed at WSLH, to assess the incidence and prevalence of HIV infection in several specific Wisconsin populations, including men who have sex with men (MSM),¹⁰ intravenous drug users,¹¹ prison inmates,^{12,13} childbearing women,¹⁴ and clients of STD clinics.¹⁵ The use of data from these seroprevalence studies resulted in improved services and targeted prevention interventions focused on those most likely to transmit or acquire HIV infection.

Evaluation of data from the Wisconsin HIV Counseling, Testing, and Referral (CTR) Program led to significant changes in 1999 to increase HIV case finding and prevention and to improve use of program resources.¹⁶ These changes consisted of eliminating sites that screened only low-risk individuals, intensifying efforts to focus HIV screening services on higher-risk and underserved clients, increasing outreach activities, and exploring innovative testing technologies such as oral fluid sampling and rapid point-of-care testing.

Screening programs for bloodborne pathogens other than HIV have also been implemented and evaluated in specific populations. Screening for Hepatitis B virus (HBV) infection was useful in determining susceptibility and eligibility for vaccination among MSM, immigrant refugees, and inmates of correctional institutions. HBV screening of inmates in the Wisconsin correctional system led to the implementation of a successful vaccination program starting in 1998. The Department of Corrections vaccinates susceptible inmates under the age of 18 years, or between 19 and 39 years with a sentence of less than 6 years. By the end of 2000, approximately 13,000 doses of Hepatitis B vaccine had been administered.

Two serosurveys have been conducted to assess the prevalence of hepatitis C virus (HCV) in specific populations in Wisconsin and to develop targeted screening strategies. A 1999 study of newly incarcerated inmates of the Wisconsin adult correctional system revealed that 13.5% were infected with HCV.¹⁷ An investigation of clients utilizing Wisconsin CTR clinics in 2000 who had a history of injection drug use (IDU) were nearly 18 times more likely to be positive for HCV (53%) than those with no history of IDU (3%).¹⁸ In the prison setting, selective screening of high-risk individuals was shown to be more cost-effective than universal screening. Restricting screening to those 26.8% of inmates with a history of IDU or liver disease, serologic evidence of HBV infection, or elevated alanine aminotransferase levels would have detected 90.8% of all

HCV infections. Based on the results of this study, inmates entering the Wisconsin adult correctional system are currently being selectively screened for anti-HCV according to these criteria. The HIV CTR Program study suggests that HCV counseling and testing should be offered to all clients with a history of IDU and to sexual partners of persons with a history of IDU.

SUMMARY

Our experiences with Wisconsin control programs for sexually transmitted and bloodborne infections indicate that well-planned and continually-evaluated laboratory testing strategies based on empirical data are critical components of these programs. The laboratory testing methods and testing algorithms must be selected with full cognizance of the epidemiologic features of the disease in the proposed target populations, and the costs associated with both testing and control of the disease must be thoroughly assessed. Screening programs are most efficient when focused on specific high-risk populations or individuals, and are more likely to be successful when there is coordination and collaboration among public health officials, laboratory professionals, physicians, and other clinicians. Furthermore, laboratory screening must be integrated with treatment of infected persons, counseling of patients, notification of partners or contacts, and education of clinicians.

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