SLO Public Health Laboratory Bulletin

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Detection of Mycobacterium tuberculosis

M. tuberculosis remains a formidable infectious disease adversary, causing over a billion cases of infection worldwide and millions of deaths. In the US, the partnership of the public health and the medical communities has resulted in a decrease in the number of tuberculosis (TB) cases after a resurgence of disease in the 1980s. But that resurgence, due largely to loss of funding support for public health TB control programs, saw the appearance of multi-drug resistant TB (MDR-TB) in large numbers. More recently, extremely drug-resistant TB (XDR-TB) has been recognized as an enormous problem in Africa and Asia. Modern travel and immigration means these problems will arrive here in due time. Fortunately laboratory methods for the rapid detection of TB have also advanced. An array of laboratory tests have made their way into the medical defense system, and for the service of local medical and public health authorities by the San Luis Obispo County Public Health Laboratory.

- **M. tuberculosis amplification test.** This molecular amplification test can be performed in a day on almost any specimen and provide an accurate indication of the presence of MTB. The method, called Transcription Mediated Amplification, is very sensitive (90-95%) for acid-fast smear-positive specimens, 80-90% sensitive in smear-negative specimens. False positive results are extremely rare. This test has the greatest value in the rapid assessment of symptomatic patients.
- **Quantiferon (In tube Gold) test.** This test detects the production of gamma interferon by T cells in response to genetically-engineered specific MTB antigens. This test is 80-85% sensitive and is especially useful to evaluate patients with a history of vaccination with BCG vaccine, and/or a positive PPD skin test. Quantiferon has special value in the setting of Latent TB infection or LTBI.
- **Mycobacterial culture and Identification:** This gold standard is still the method of choice for diagnosis of the symptomatic patient and is coupled with the traditional acid-fast smear. Although only 60-70% sensitive, the acid-fast smear can be performed in about three hours (actually two tests: both a fluorochrome exam and a kinyoun stain may be examined microscopically). Combined liquid and solid medium cultures are incubated with daily examination for six weeks.
- **Hybridization Probes:** Molecular probes for MTB, M.avium-intracellulare (MAC) complex, M kasasii, and M gordonae can be performed on culture isolates and smear-positive liquid culture medium bottles. Unlike amplification methods, hybridization probes require culture growth to be performed, but produce a result in as little as 2 hours.
- **Rapid Drug Susceptibility testing (performed by the State Laboratory):** Isolates of MTB can be referred to the Microbial Diseases Laboratory for advanced molecular beacon testing for some of the most common mutations conferring resistance to Isoniazid and Rifampin. This test can also be performed in a day and can be pivotal in therapy choice for a newly recognized TB case.

What else does a public health laboratory do besides flu testing?

The SLO PHL has validated a PCR assay for poxvirus detection. This assay can be used in any situation that warrants a public health investigation of a rash illness. In recent years, this assay has been used by Laboratory Response Network laboratories to detect Monkeypox virus and rash illness in military recruits and their contacts due to vaccinia virus. In 2003, Monkeypox virus was introduced into the US by import and sale of Gambian giant rats, an exotic species now banned for importation as well as all African rodents. The virus was transmitted to prairie dogs and subsequently to pet owners.

The LRN poxvirus assay will give a positive signal for any pox virus. This includes the recently reformulated vaccinia virus vaccine strain ACAM 2000, the smallpox virus (Variola, as well as monkeypox virus, cowpox virus, the poxvirus agent of molluscum contagiosum and others.

When the orthopoxvirus PCR assay is performed, it will be coupled with a Varicella (Chickenpox) Zoster virus PCR assay (VZV PCR), allowing specific detection of the most common cause of pox virus rash illness in the US.