In Focus
New CDC Guidelines Intensify “Race” for QuantiFERON Gold

The US Centers for Disease Control and Prevention (CDC) today released updated guidelines for TB testing, which will have a major impact on the screening for TB infection in special populations.

Imagine homeless Shelter A in Big City, USA—the ‘front line’ of American life. Thirteen residents of this 600+-bed refuge are diagnosed with isoniazid (INH)-resistant active TB over several months, and quick identification of those residents with TB infection is paramount to limit future exposure to others. Immediately a contact investigation begins. Three days of questionnaires, blood sampling, medical exams and histories, chest X-rays, and treatment prescription later, some startling results emerge. Six additional active TB cases are identified, requiring admission to the local hospital. The known TB infection rate is 41% at the conclusion of the investigation.

The catch is that Shelter A, its contact investigation, and the statistics are real and not imagined. Last year Shelter A, located in Fulton County, Georgia, was the epicentre of a large contact investigation and subsequent analysis that was run by a team from the CDC (Powell et al. Shelter-based on-site active case-finding during a tuberculosis outbreak among homeless persons—Fulton County, Georgia 2009 [Abstract only]. IUATLD, Mar 2010).

One of the largest ever (n = 311) to use QuantiFERON® (QFT®) in a US-born population, this contact investigation followed the CDC’s own contact investigation guidelines, which allow for the use of QFT in place of the tuberculin skin test (TST) during contact investigations. The major outcome of such a large and dangerous outbreak was that containment was successful using the active case-finding method (vs traditional name-based methods); QFT was fundamental to the success of this method. Of the 286 participants, including residents and staff, tested with a valid QFT, 117 (41%) were QFT-positive.
The high rates of TB in this setting should reinforce the continued relevance and importance of TB diagnosis and treatment today.

As stated in the abstract and presentation, the benefits of using QFT for this contact investigation were:

- Testing for other infections with a single venous puncture were achievable
- Only one clinical encounter for asymptomatic participants with negative results
- Results are not visible to other shelter residents (i.e., potentially less stigma associated with a positive QFT result as compared with a highly-visible TST-positive result).

Historically, homeless populations suspected of latent TB infection are very difficult to medically manage due to compliance issues (i.e., non-returns for TST reading; incomplete preventive therapy), but at Shelter A changing from TST to QFT, at least anecdotally, contributed to a significant improvement in treatment compliance. Barb Kragor, the Cellestis representative who assisted with the investigation, spoke with long-term Shelter A resident John (not his real name) about his experiences with TB. Despite knowing how deadly TB is (his mother died of TB) and despite regularly testing TST-positive for TB, John has continually refused treatment because he feels that “everyone has a positive TST.” In other words, John doesn’t believe TST results. During the recent contact investigation, John was tested for latent TB infection using QFT. Upon learning of his QFT-positive status, John said, “now that I know [TB] is in my blood, I will take the treatment.”

Distrust of the TST is not completely without cause. At the time of the contact investigation, Sam (not his real name), an HIV-positive one-time Shelter A resident, was undergoing INH treatment for latent TB infection that was diagnosed with TST. When Sam’s liver function began to deteriorate two months into treatment, the physician re-tested with QFT and discontinued INH upon receiving a QFT-negative result. Sam was spared further debilitating hepatotoxicity.

More success stories like the Fulton County experience are likely to occur thanks to the capabilities enabled by the newly updated CDC guidelines. The improvement in health and well-being of the people of Shelter A will potentially be replicated in many more communities in the US and world-wide now that new CDC guidelines have been released.

Quantitative results: How to interpret QFT?

The CDC Guidelines 2010 Update recommends that “both the standard qualitative test interpretation and the quantitative assay measurements should be reported, together with the criteria for test interpretation...to permit more refined assessment of results and promote understanding of the tests.”

So, the CDC now recommends the reporting of not only the qualitative result (positive, negative, or indeterminate), but also the quantitative reading of the IGRA.

While the FDA-approved Package Insert states that “The magnitude of the measured IFN-γ level cannot be correlated to stage or degree of infection, level of immune responsiveness, or likelihood for progression to active disease,” the updated CDC guidelines highlight the considerations of many QFT users regarding the quantification of IFN-γ levels. Cellestis proactively supports these guidelines and recommends the use of its free, validated QFT Analysis Software, which provides customers with both qualitative and quantitative results.

To help you document this response in your files, a guidance letter from Cellestis regarding quantitative results can be downloaded for Europe/Middle East/Africa, USA, International customers.

Other helpful documents...

For more information on how QFT can help you meet the new CDC guidelines, please go to www.tackletb.com

Also, you can now take the CDC guidelines with you wherever you go with the new CDC Guidelines Pocket Guide. To receive your copy, please email info@cellestis.com
In “Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection, United States,” published in today’s Morbidity and Mortality Weekly Report, the CDC recommends:

- IGRA testing may be used in place of (and not in addition to) TST in all situations in which CDC recommends TST as an aid to diagnosing *M. tuberculosis* infection.
- IGRA testing is the preferred method for testing:
  - Persons from groups that have historically poor TST return rate
  - Persons who have received BCG (as a vaccine or for cancer therapy)
- IGRA testing may be used in place of TST for:
  - Contact tracing
  - Serial and periodic TB screening (ie. surveillance programs for healthcare workers)
- Due to insufficient evidence at the time of writing the guidelines, the CDC guidelines continue to recommend the TST in children aged less than 5 years. However, they suggest that a strategy involving TST with subsequent IGRA can be used to increase diagnostic sensitivity. Other recommendations on IGRA testing in children are available from the American Academy of Pediatrics’ IGRA guidelines. For details, please see below.
- Both qualitative and quantitative assay measurements should be reported. Please see page 2 for a summary of quantitative results interpretation for QFT.

It is important to highlight that the data supporting these guidelines are more than two years old and that even more compelling evidence for the use of IGRA and QFT is now available.

For people like Sam and John and physicians across the US, the CDC’s recognition of IGRA technology provides a valuable alternative to the TST and its high rate of false-positives, low compliance, and potential for unnecessary treatment. It is very likely that QFT, with its accuracy and reliability validated by the new guidelines, will play a major role in future TB testing across the US and around the world. For those people who are tested with QFT and experience the benefits over the TST, QuantiFERON will be a winner, so the challenge then will be to make QuantiFERON accessible to as many individuals as possible. The reward will be movement towards healthy, TB-free communities.

From AAP Red Book Section 3 TB.

The premier organization of pediatricians in the US, the American Academy of Pediatrics (AAP) has published its 2009 Red Book, the update of policies and best practices for children. In this issue, the AAP has included a section on immunologic-based testing for TB in children. While recognizing that the published experience with testing children with IGRA is less extensive than for adults, the AAP has commented that, “A number of studies have demonstrated that IGRA perform well in most children 4 years of age and older.”

In fact, the supporting literature is strong enough for the AAP to recommend that:

- IGRA be used in place of a TST to confirm cases of TB disease or latent TB infection and will likely yield fewer false-positive results than the TST in immune-competent children aged 5 years or older
- IGRA may be especially useful in children who are BCG-vaccinated to negate the risk of false positive TST results
- IGRA-positive results in children should be considered as having *M. tuberculosis* complex infection.

The AAP recommends using the TST in children younger than 5 years and in immunocompromised children of any age because there is not sufficient clinical evidence to support the use of IGRA in these groups. Furthermore, caution is urged regarding interpretation of a negative IGRA result on TST-positive children, as the long-term negative predictive value of IGRA is uncertain.
Latest News

Publications & Guidelines update
The Romanian National Health Insurances House (NHIH), which manages the health insurance system and incorporates governmental health policies and programs, has published the technical details for implementation of national health programs for 2010. The document states that IGRA tests and QuantiFERON TB Gold may be purchased and used for quick diagnosis of TB infection.
✧ View the new Romanian Instructions (In Romanian).

Updated Swiss SUVA guidelines published.
✧ View the new Swiss guidelines (In German).

Station airs TV special on epidemic of TB
On March 31, the German government TV Channel, ZDF, aired a 30-minute documentary entitled [The Fight Against Old Epidemics] about the resurgence of long-forgotten infectious diseases. This program focused mostly on TB and featured prominent TB experts, Dr Roland Diel and his team from the Gesundheitsamt Hamburg as well as the team of Dr Sabine Rüscher-Gerdes from the Research Centre Borstel, Germany. Although the episode was (unfortunately) only available in German language, it was evident that TB infection is still relevant today and should be on the public health radar. QFT is also featured in one small portion of the documentary.
✧ View the TB documentary (In German).
✧ See April QFT News for an in-depth review of Dr Diel and colleagues’ latest publication (Chest 2010. 137:952–68).

Novel TB Tests Compared video by Reuters Health/The Doctor’s Channel Daily Newscast
Reuters Health and The Doctor’s Channel Daily Newscast has aired a short video covering the results of the meta-analysis recently published in Chest and reviewed in the April QFT News InFocus article. The video highlights that QFT has a significantly higher specificity than its competitor and that both IGRA’s may out-perform the tuberculin skin test.
✧ View the full newscast video.
Product updates

Gnowee Support
With the number of Gnowee users skyrocketing, registration and support for the content and functionality of Gnowee are increasingly important.

If you experience any issues or have any technical requests regarding Gnowee, please email the dedicated help line at support@gnowee.net

If you have a Gnowee card, but have not yet registered, you may find the Gnowee Registration Presentation helpful.

If you don’t yet have a Gnowee USB card and would like one, please visit www.gnowee.net, email your interest to info@gnowee.net, or contact your local Cellestis representative.

Check the upcoming issues of QFT News for full listings of the new content available on Gnowee.

Event summaries


As part of the global outreach following the publication of the updated 2009 Technical Instructions for TB Screening and Treatment of immigrants applying to the US, the CDC’s Division of Global Migration and Quarantine and the International Panel Physicians Association (IPPA) held Panel Physician training in Ghana in March.

Over 30 physicians and a dozen consular officials from around the region attended the two-day event, which included lectures and interactive sessions focusing on the new Technical Instructions. TB infection and diagnosis is a major issue in Africa; Ghana has a TB prevalence estimated at 353 per 100,000 people, while its neighbors have prevalence estimates as high as 750 per 100,000 (World Health Organization, www.bcgatlas.org). The Instructions now recommend the use of IGRA in some circumstances (see related article on TB testing in immigrants in QFT News January).

To find out more about Panel Physician training session, please contact the IPPA on info@panelphysicians.org

For more specific information on TB-related events around the US, please visit http://tb-usaevents.com

Register your interest at www.igrasymposium.com
If you have any questions or comments about QFT-News, contact us at news@cellestis.com
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