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MORE THAN SKIN DEEP—BLOOD ASSAY FOR TUBERCULOSIS ARRIVES IN OREGON

QUANTIFERON-TB GOLD (QFT-G), a new blood assay for the diagnosis of TB, is available in Oregon. We dedicate this epistle to discussion of the principles, diagnostic utility, guidelines for use, and details of local availability of the new test.

HOW DOES IT WORK?

QFT-G is one of a new category of blood tests for diagnosing *Mycobacterium tuberculosis* infection called interferon gamma release assays.¹ It detects interferon-gamma (IFN- γ) produced by T-lymphocytes from TB-sensitized persons. Whole blood incubates overnight with synthetic antigens, which are specific to TB. Consequently, QFT-G helps distinguish infection with *M. tuberculosis* from false positive skin tests resulting from BCG vaccination or exposure to environmental mycobacteria.

WHAT IS QFT-G USED FOR?

QFT-G is likely to be useful for diagnosing latent TB infection (LTBI) in BCG-vaccinated people and others from low-prevalence areas like Oregon where false positive skin tests can result from non-tuberculous mycobacteria exposure. The Centers for Disease Control and Prevention (CDC) advises that "QFT-G can be used in all circumstances in which the skin test is used." These include contact investigations, evaluation of recent immigrants, and screening of health-care workers. Occasionally, QFT-G might be useful in helping to rule in active TB in patients with confusing

presentations. However, neither the skin test nor QFT-G should ever be the sole diagnostic test in a patient with suspected active TB. Either test can be falsely negative in $\geq 30\%$ of active disease cases.

HOW ACCURATE IS QFT-G?

Unfortunately, no gold standard exists for diagnosis of LTBI. However, QFT-G sensitivity has been estimated to be 76%—approximately equivalent to the skin test—by studies in which people with confirmed active TB were used as surrogates for LTBI. Specificity is estimated to be 97% and importantly does not appear to be lower in patients with prior BCG vaccination. In contrast, skin testing is comparably specific in BCG-unvaccinated people but only about 56% specific in BCG-vaccinated people. This means that we can expect similar numbers of people with true LTBI to be diagnosed with either the skin test or QFT-G, but many fewer false positives with QFT-G.²

QFT-G IN CHILDREN AND THE IMMUNOCOMPROMISED

In children not enough is known about the relative sensitivity and specificity of QFT-G and the skin test, and caution is required in interpretation. Only a few small studies have been con-

ducted including few infants, and sensitivity estimates vary widely. So, as noted, QFT-G may occasionally be useful in ruling in TB disease in children, but less useful for ruling it out.

In people with immune compromising conditions including but not limited to HIV infection, Diabetes Mellitus, and renal failure, caution should also be exercised.

COMPARATIVE QUALITIES OF QFT-G AND TST

As the table shows, QFT-G promises better overall diagnostic accuracy owing to equal sensitivity and better specificity for LTBI in adults. However, each test offers some comparative advantages that make it the better choice in some circumstances. Skin tests are not likely to disappear until alternatives are further refined.

RECOMMENDED CIRCUMSTANCES FOR QFT-G USE

With the proviso that accuracy is poorly understood in children, we concur with CDC's recent endorsement of QFT-G in all circumstances where TST is used. Though CDC presently recommends QFT-G as a replacement, rather than a supplement for TST, we also envision occasional use of QFT-G as an adjunctive or confirmatory test when for example, a

Tuberculin Skin Test and QuantiFERON-Gold Comparison*

	Tuberculin Skin Test	IFN- γ Release Assay
Cross-reactivity with BCG	Yes	No
Cross-reactivity with non-TB mycobacteria	Yes	Rarely
Estimated sensitivity: TB in immunocompetent adults	75 – 90%	75 – 90%
Specificity: TB in immunocompetent adults	70 – 95%	90 – 100%
Distinguish between TB infection and TB disease	No	No
Material costs	Low (<\$10)	High (\geq \$40)
Results available	48-72 hours	24 hours
Finicky specimen handling requirements	No	Yes

*Adapted from Starke³.



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positive skin test arises in a BCG recipient who is otherwise thought to have low likelihood of LTBI. Clinicians should avoid ordering QFT-G as an adjunct if a negative test (discordant with positive skin test) will not alter the LTBI treatment decision. While no position is taken by CDC on use of QFT-G as adjunct to skin test, it is consistent with current recommendations in the United Kingdom.⁴ Ultimately, LTBI treatment decisions will need to be guided by long-term studies identifying risk of progression to active disease among patients with varying combinations of skin test and QFT-G results.

We offer the following recommendations and considerations for use of QFT-G in Oregon. It may be used:

- Instead of skin test for investigation of adult contacts to confirmed cases of active TB. Avoid sole reliance on QFT-G in children aged ≤ 5 years and others at risk of rapid progression.
- Instead of, or as an adjunct to, skin test for LTBI screening in persons with definitive history of BCG or those who have immigrated from countries where BCG is commonly given and have no clinical evidence of active TB disease.
- Instead of, or as an adjunct to,

skin test for LTBI screening in adults who are members of otherwise low-risk populations (e.g., U.S.-born persons and others who have immigrated to the U.S. > 5 years ago or more recently from low TB prevalence countries; absence of immunosuppressive conditions such as HIV infection, renal failure, diabetes mellitus or alcoholism; homelessness or incarceration; known exposure to someone with active TB), and no clinical evidence of current TB disease.

- In persons who need rapid (within 24 hours) diagnosis in order to guide appropriate public health interventions.
- In high-risk patients (e.g. homelessness, immune suppression or deficiency, recent immigrant) who the treating clinician believes are unlikely to return for the TST reading.
- For health care worker screening.

WHERE CAN YOU GET QFT-G DONE IN OREGON?

The Oregon State Public Health Laboratory (OSPHL) offers QFT-G free to local health department clients and at \$40 per test for all others. Specimens for QFT-G are accepted Monday – Thursday before 2PM, but not on Friday – Sunday. The sample must consist of ≥ 6 ml of venous blood collected in a lithium heparin tube (green top) not more than 12 hours before the test is to be run in the labora-

tory and held at room temperature, *not refrigerated or frozen*. The sample must be delivered to OSPHL at 1717 SW 10th Ave, Portland. Specimen collection and transport is the responsibility of the requesting provider; no venipuncture or courier services are offered by OSPHL. Further information is available by calling 503/229-5882 and asking to speak with the General Microbiology Section.

Providence Portland Medical Center laboratory in Portland also offers QFT-G testing for a fee. Specimens must be collected in the morning and received in the main laboratory by noon Monday – Friday. A whole blood sample drawn in a lithium heparin glass tube is required. Minimum volume is 5mL. Further information is available at 503/215-6660.

REFERENCES

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