

An Interferent No More: Measuring Thyroglobulin in the Presence of Anti-Thyroglobulin Autoantibodies

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Outline:

- Why measure thyroglobulin (Tg)?
- What measurement issues exist?
- How can we avoid these issues?
- When is MS testing for Tg most cost-effective?

Thyroglobulin (Tg): Background



drchadedwards.com

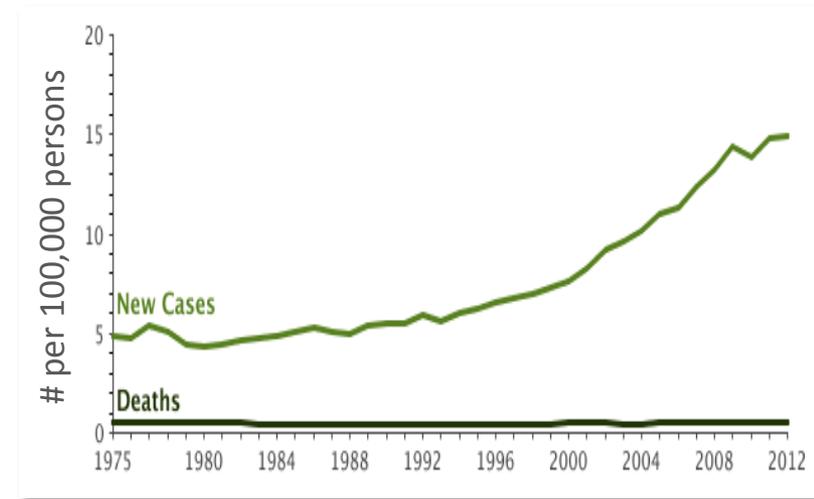


commons.wikimedia.org

- Secreted by the thyroid gland
 - Thyroid hormone precursor
 - T3 and T4
- Large protein
 - Dimer, 660 kDa
 - 19 different epitopes

Thyroglobulin (Tg): Background

- Why measure?
 - Thyroid cancer
 - Most common endocrine cancer
 - Rapidly increasing; < 55yo, F > M
 - **Treatable**
 - Full/partial thyroid resection
 - Biomarker for cancer recurrence
 - Monitor, every 6 to 12 months¹
 - Concentrations >2 ng/mL may indicate disease¹

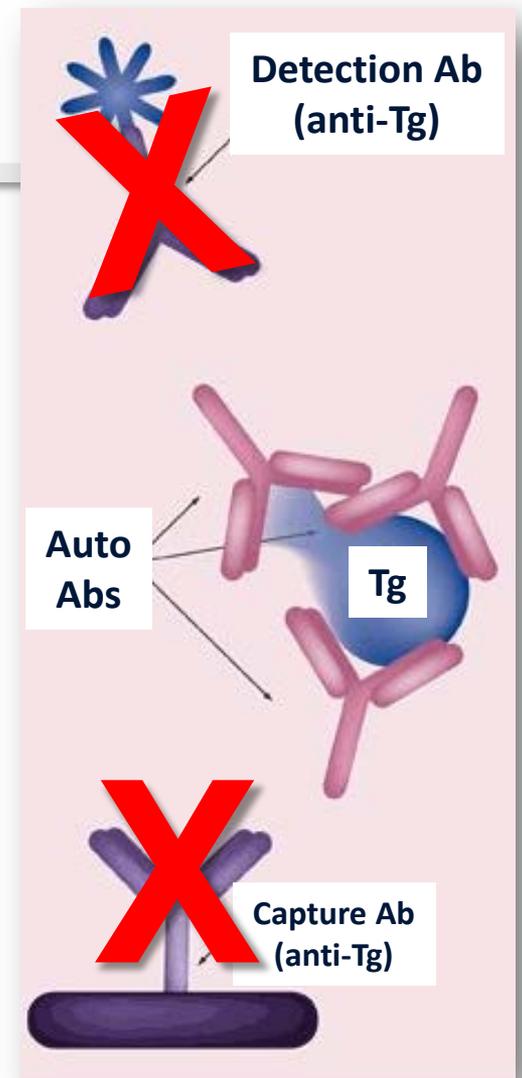


seer.cancer.gov/statfacts/html/thyro.html

¹ATA Guidelines, Thyroid (2009);19:1

Thyroglobulin (Tg): Interference

- Autoantibodies against Tg (TgAb)
 - Approximately 25% of thyroid cancer patients¹
 - 10% of general population¹
- TgAb interfere with Tg immunoassays
 - Falsely low Tg



¹JCEM 1998;83:1121-7

Thyroglobulin (Tg): Interference

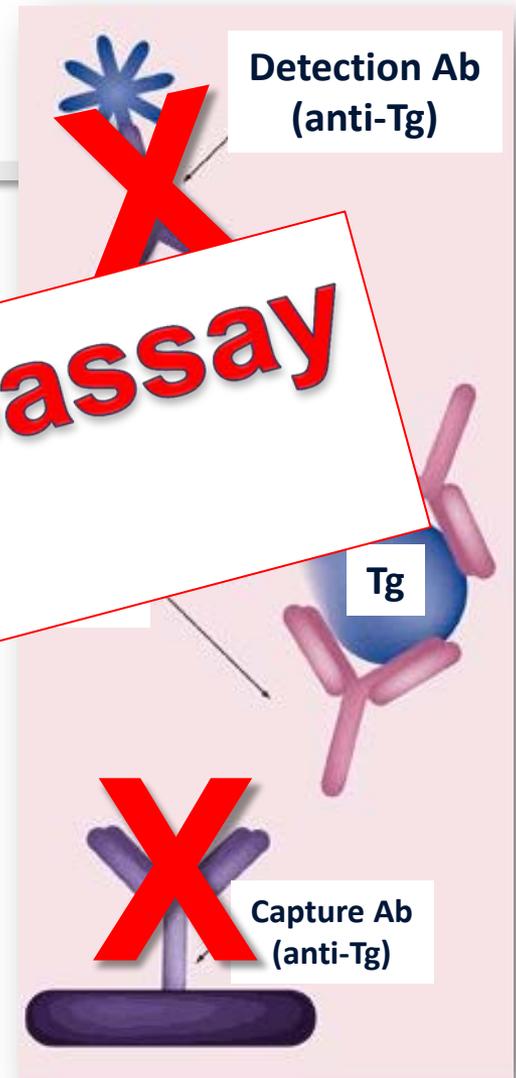
- Autoantibodies against Tg (TgAb)

- Approximately 25% of cancer patients have TgAb

Well-known immunoassay interference

- Immunoassays

- Falsely low Tg



A New Way: Tg by LC-MS/MS

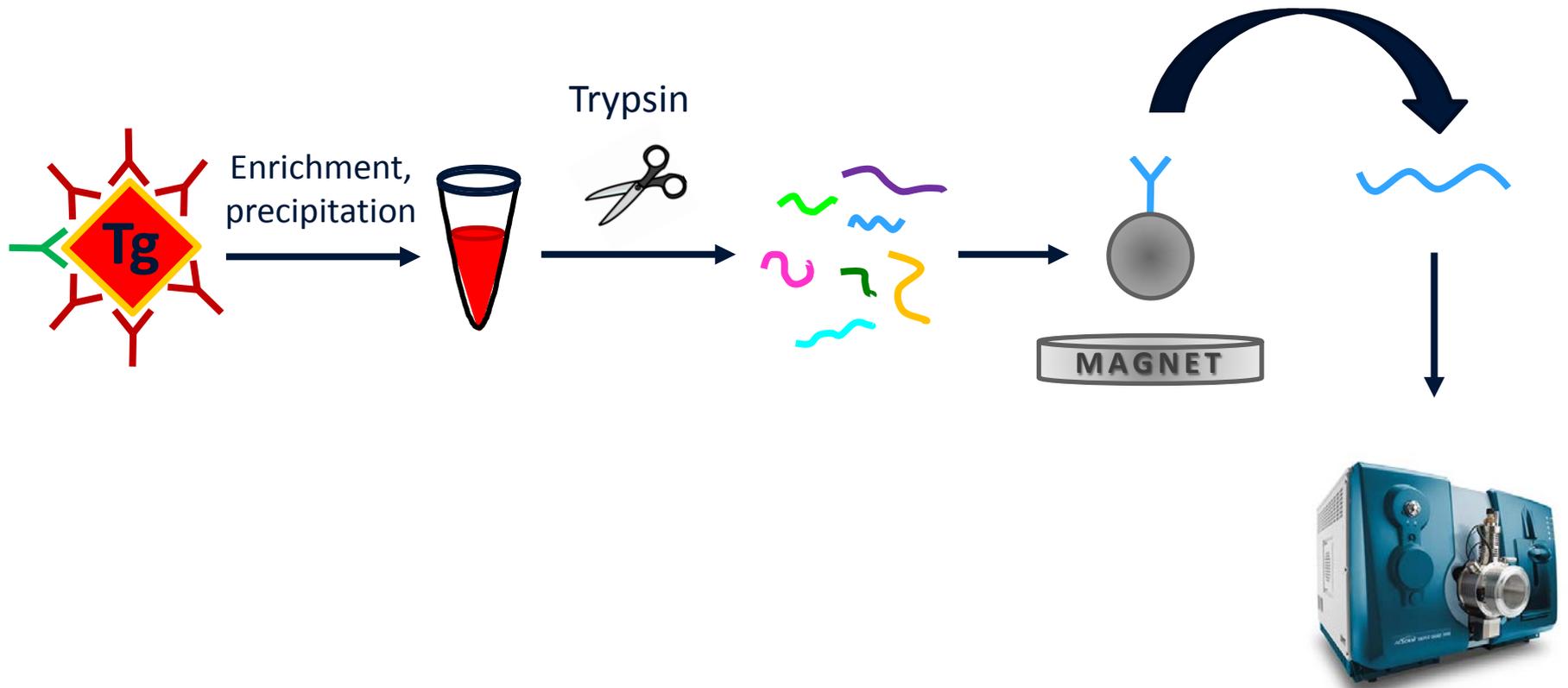
Clinical Chemistry 59:6
982–990 (2013)

Proteomics and Protein Markers

Measurement of Thyroglobulin by Liquid Chromatography–Tandem Mass Spectrometry in Serum and Plasma in the Presence of Antithyroglobulin Autoantibodies

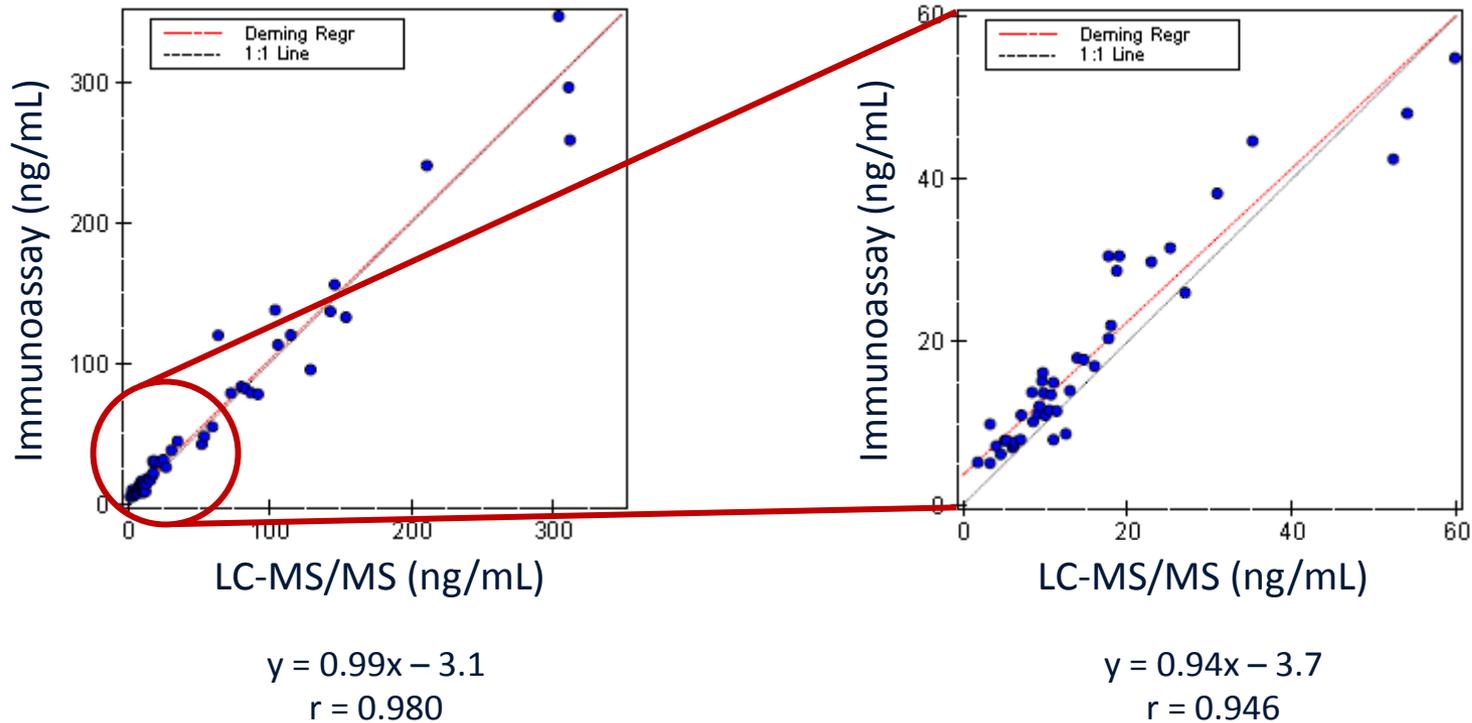
Mark M. Kushnir,^{1,2,*} Alan L. Rockwood,^{1,2} William L. Roberts,[†] Dev Abraham,³
Andrew N. Hoofnagle,⁴ and A. Wayne Meikle^{1,2,3}

A New Way: Tg by LC-MS/MS



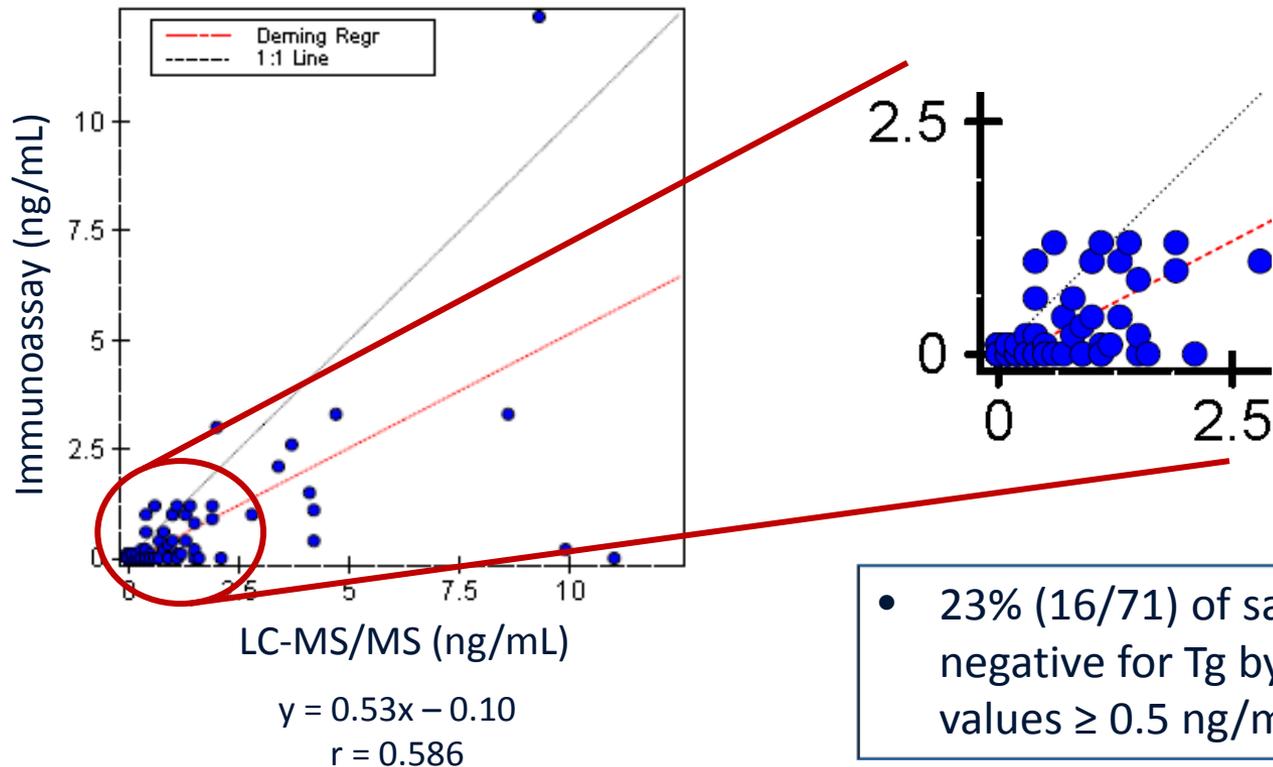
Tg by LC-MS/MS: Comparison to Immunoassay

MS vs. Immunoassay (IA): **TgAb negative** samples



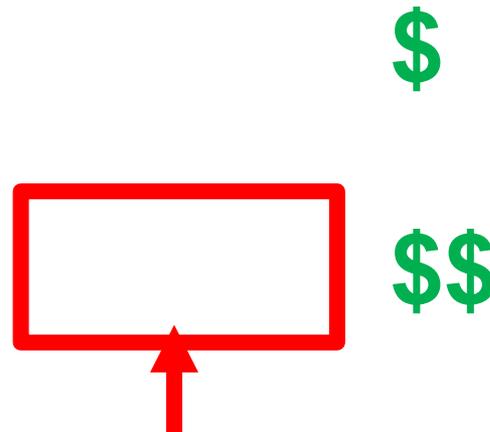
Tg by LC-MS/MS: Comparison to Immunoassay

MS vs. Immunoassay (IA): **TgAb positive** samples



Tg by LC-MS/MS: How should we use this test?

- Focus on utilization
 - LC-MS/MS preferred measurement for TgAb positive patients
 - LC-MS/MS = IA in TgAb negative patients
 - Reflex testing algorithm:



Tg by LC-MS/MS:

How should we use this test?

- Analysis of Tg testing patterns (> 100,000 orders)
 - 89% utilized reflex testing
 - 89% were TgAb negative
 - Reflex to IA vs. MS directly saved > \$3 million*
 - If ordered separately (TgAb + Tg by LC-MS/MS)
 - Reflex would save almost \$9 million*
 - 11% ordered TgAb and Tg by LC-MS/MS separately
 - 90% were TgAb negative
 - Reflex (to IA) would have saved almost \$250,000*

* Cost analysis based on average list price from 3 laboratories

Powers, Strathmann, Straseski; Poster Abstract A-068, 2015 AACC Annual Meeting

A New Way: Tg by LC-MS/MS

MS allows for accurate measurement of Tg in the presence of interfering TgAb.

Utilizing MS assays when most appropriate leads to economical use of health care resources.

Summary:

- Tg has utility in the diagnosis and monitoring of thyroid cancer recurrence.
- LC-MS/MS technology allows for the measurement of Tg in the presence of interfering autoantibodies.
- Proper test utilization in TgAb positive and TgAb negative populations can lead to substantial cost savings.

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