

AACE, ATA, TES  
Pharmacovigilance Surveys  
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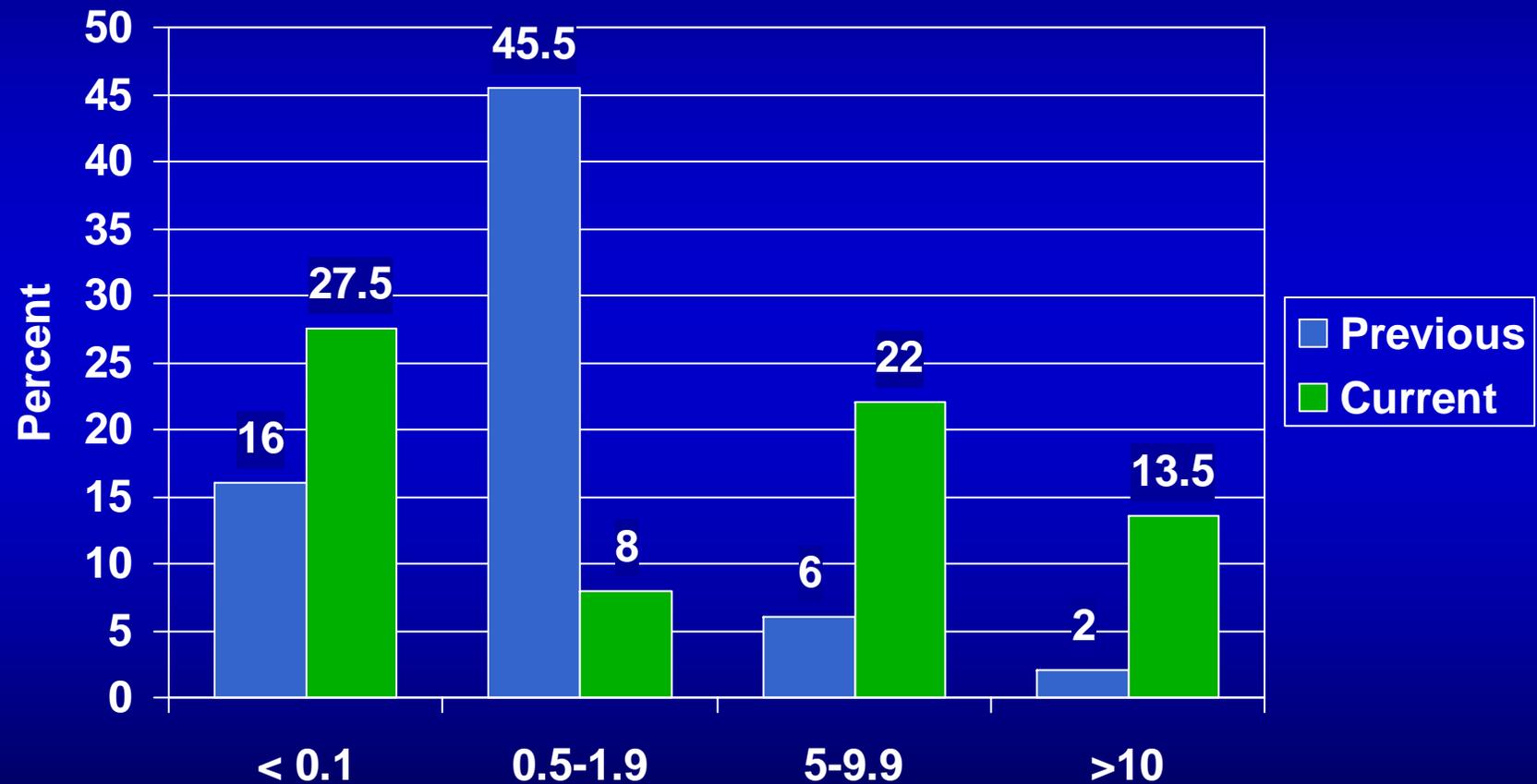
# Pharmacovigilance: Survey 1&2

- 12,000 e-mails sent to AACE, ATA, TES
- 18,000 e-mails: frequent LT4 Rxers
- 5,000 e-mails: frequent Thyroid Extract Rxers
- 1421 (4.7%) responded
- **210** LT4 Rxers completed **AE** surveys:
- Results:
  - **96%** of patients were considered **compliant**
  - **77.5%** noted no confounding medication use

# Survey 1&2 Results

- |         | <u>Previous TSH</u> | <u>Most recent TSH</u> |
|---------|---------------------|------------------------|
| < 0.1   | 16%                 | 27.5%                  |
| 0.5-1.9 | 45.5%               | 8%                     |
| 5-10    | 6%                  | 22%                    |
| > 10    | 2%                  | 13.5%                  |

# Survey 1&2: TSH in AE patients



# Survey 1&2 Results

- LT4 dose changed between visits?
  - **NO: 75.5%**
- Was type of LT4 changed?
  - Brand to generic n=129/210 **(61%)**
  - Brand to another brand n=21/210 **(10%)**
  - Generic to generic n=8/210 **(3.8%)**
  
  - **Total changed** n=160/210 **(75%)**



# Case 1 from Survey 1

A patient from Georgia got a **recurrence** of her thyroid **cancer**, and experienced hypothyroid symptoms (dry skin, tiredness) and change in serum TSH after a switch from brand to generic had been made at the pharmacy without the knowledge of the treating Endocrinologist. The patient was considered compliant with LT4 therapy by both verbal verification and pill count/ pharmacy records and had not been started on medications that would be expected to alter absorption or metabolism of LT4. The patient was not pregnant. The TSH was noted to be between 5 to 10 mIU/ml after a change from brand to generic whereas it had been less than 0.1 when previously checked while on the brand product.

# Case 2 Survey 1

A patient from Pennsylvania with CAD was treated with LT4 for hypothyroidism and was changed from a name brand LT4 product to a generic with the subsequent development of thyrotoxicosis and symptoms. Problem abated when changed back to the name brand. The substitution occurred by a mail order Rx plan. The AE was suspected by the onset of new symptoms (hyperthyroid symptoms, palpitations, weight loss, difficulty sleeping). Compliance was verified by verbal confirmation and no absorption nor metabolism altering medications were noted. The post substitution TSH was less than 0.1 and had been 0.5 to 2 while on stable brand name therapy.

# Case 3 Survey 1

A compliant hypothyroid US Army aviator living in Kentucky was grounded from flying duties when the name brand LT4 preparation he had been treated with was switched to a generic at the pharmacy without the treating endocrinologist's knowledge. His TSH rose into the 5 to 10 mIU/ml range following the substitution while it had been stable at 0.5 to 2 mIU/ml previously. His endocrinologist (Flight Surgeon) noted that to remain on flying status hypothyroidism must be adequately treated, i.e. TSH in the normal range; the change to generic resulted in his TSH rising into hypothyroid range, grounding him from flying duties: expensive missed work!

# Case 4 Survey 1

This compliant thyroid cancer patient developed atrial fibrillation after a switch to generic LT4. Patient was followed in Minnesota to maintain suppression of TSH in order to minimize TSH stimulation of residual thyroid cancer tissue. Both symptoms (palpitations) and a change in TSH document this AE. On the generic, the TSH less than 0.1 mIU/ml whereas it was 0.1 to 0.4 on stable brand name LT4 treatment. The change to generic occurred at the pharmacy without the knowledge of the treating endocrinologist

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# Conclusions

- In 1997 FDA took action (NDA process) after receiving 58 adverse drug experience reports (ADER) on the potency of LT-4 products
- In 2006 we have received 210 AE reports
  - AEs indicate both super and subpotency
  - 75% of the AEs were associated with a change in LT4 source reported by the health care professional
  - Following these switches, 31.4% had SAE
    - Missed work, urgent ER/clinic visits, hospitalizations, other events (Cancer recurrence etc.)

# Request for Action

- AACE, ATA and TES request that the FDA CDER reconsider current methods for the determination of Thyroxine Bioequivalence.
- The societies advocate the incorporation of pharmacodynamic markers of thyroxine action such as the serum TSH into the process of thyroxine bioequivalence assessment.
- In so doing we believe that greater assurance of true interchangeability of products determined to be therapeutically equivalent can be achieved.