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Insights from the 78th Annual Meeting of the American Thyroid Association

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The 2008 American Thyroid Association meeting in New York provided a number of important contributions to clinical thyroidology. Several presentations addressed the still-open question of whether to treat patients with subclinical hypothyroidism (i.e. asymptomatic patients with elevated TSH levels but normal free thyroid hormone levels). N Rodondi *et al*. (Lausanne, Switzerland) evaluated >3,000 adults older than 65 years who were free of congestive heart failure for potential changes in cardiac function owing to subclinical hypothyroidism. Stratification was based on serum TSH values (0–4.5, 4.5–9.9 or ≥10.0 mIU/l). Over 12 years, those with TSH values ≥10.0 mIU/l (not given levothyroxine replacement) had approximately twice the incidence of congestive heart failure events than did euthyroid participants, a highly significant difference. In another study, SS Razvi *et al*. (Newcastle-on-Tyne, UK) re-evaluated the 20-year follow-up data from the Whickham (UK) community cohort for an association between subclinical hypothyroidism (TSH >6.0 mIU/l) and ischemic heart disease. Analyses showed a hazard ratio of 1.85 (95% CI 1.25–2.75) for ischemic events among patients with subclinical hypothyroidism. A further subgroup analysis showed that ischemic events and mortality were significantly increased only in women with subclinical hypothyroidism. The results of these studies argue strongly for prospective clinical trials to determine whether thyroid hormone therapy would benefit individuals with subclinical hypothyroidism.

The success of screening programs for congenital hypothyroidism—which has resulted in the early treatment of patients—has been a signal accomplishment. Patients in whom the hypothyroidism was severe or in whom early treatment was suboptimal have now reached an era when more-sophisticated neurological evaluations are possible. A study by S Sekaran and J Rovet (Toronto, ON) combined neuropsychological assessment and parental questionnaires with MRI evaluation of the size of the caudate in a group of adolescents with a history of congenital hypothyroidism and a group of controls. In 11 patients with congenital hypothyroidism due to thyroid dysgenesis, smaller caudate volumes were found than in controls, and the caudate volume was inversely correlated with the frequency of parental descriptions of attention disorders. Higher initial doses of levothyroxine and a more mature bone age at diagnosis were positively associated with larger caudate size. These results point to the need for rapid screening and early and effective levothyroxine treatment, with careful monitoring, to optimize the long-term outcomes for individuals with congenital hypothyroidism.

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A goal of many endocrinologists has been to take advantage of the ameliorative effects of thyroid hormone excess on hyperlipidemia whilst avoiding the induction of adverse effects on the heart or bone. Progress towards this goal is being made by the design of thyroid hormone analogs that are targeted to specific tissues, such as the liver. Three such agents were discussed at this meeting: 'MB07344' and 'MB07811' (Metabasis Therapeutics, San Diego, CA) by BR Ito *et al*. (La Jolla, CA); and 'KB2115' (Karo Bio, Huddinge, Sweden) by EC Ridgway and colleagues (Denver, CO). In rats, MB07811 stimulated T_3-dependent proteins in the liver, but not in the heart or pituitary. In primates and rabbits, additive improvements in lipid profiles were found when MB07811 or MB07344 was combined with a statin. Phase II human studies of KB2115 demonstrated significant decreases in LDL-cholesterol and lipoprotein(a) levels, with no effect on TSH, although a significant decrease in free T_4 and T_3 occurred. These studies provide proof-of-principle of the tissue-specific targeting of these drugs, which thereby enables adverse effects to be minimized or avoided whilst the desired therapeutic goals are achieved. Eventually, such approaches could lead to the development of tissue-specific thyroid hormone analogs for the treatment of obesity or the metabolic syndrome—an exciting prospect.

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Competing interests
The author declared no competing interests.

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doi:10.1038/ncpendmet0793