

## Central adrenal insufficiency is common in children with Prader–Willi syndrome

Prader–Willi syndrome (PWS) is a genetic disorder characterized by hypotonia, short stature, hyperphagia, obesity, hypogonadism, and delayed psychomotor development. The annual death rate in patients with PWS is ~3% and many of these deaths are sudden and unexplained. Patients with PWS have hypothalamic dysregulation and de Lind van Wijngaarden *et al.* hypothesized that affected patients suffer from central adrenal insufficiency (CAI) during stressful conditions such as infections, which increases their risk of sudden death.

Metyrapone blocks cortisol synthesis and causes a sudden increase in demand for adrenocorticotrophic hormone (ACTH) production, which mimics stress. The researchers performed a single-dose metyrapone test in 25 children with PWS who did not have any intercurrent illnesses at the time of the study. All patients (mean age 9.7 years) received metyrapone at 2330h and fasting blood samples were taken for the analysis of ACTH, 11-deoxycortisol, cortisol and glucose at 0730h the following day. In 16 of the 25 children, diurnal salivary cortisol profiles were also assessed.

The test results showed that 15 (60%) patients had an insufficient ACTH response and were, therefore, considered as having CAI during stressful conditions. Cortisol suppression did not differ between children with CAI and those without. All the children had normal diurnal rhythms of cortisol secretion.

The authors suggest that, unless CAI has been ruled out by a metyrapone test, hydrocortisone treatment should be considered in patients with PWS during stressful conditions.

**Original article** de Lind van Wijngaarden RF *et al.* (2008) High prevalence of central adrenal insufficiency in patients with Prader–Willi syndrome. *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-2294]

## MicroRNA profiling might improve the diagnostic accuracy of thyroid FNA

MicroRNAs act as negative regulators of protein-coding genes (including oncogenes and tumor suppressors); their dysregulation can lead to carcinogenesis. Nikiforova and colleagues have

now shown that different histological subtypes of thyroid cancer (even those of the same cellular origin) are associated with distinct microRNA expression profiles, and also that variation in these profiles correlates with the presence of known oncogenic mutations—including *BRAF* mutations that predict treatment failure and recurrence.

The researchers determined the microRNA expression profiles in 62 thyroid fine needle aspiration (FNA) samples and in 60 thyroidectomy samples (18 classical papillary carcinomas, 5 follicular-variant papillary carcinomas; 9 conventional or oncocytic follicular carcinomas; 8 conventional or oncocytic follicular adenomas; 4 anaplastic carcinomas; 4 poorly differentiated carcinomas; 2 medullary carcinomas; 5 normal thyroid specimens; 5 hyperplastic nodules). Interestingly, oncocytic tumors had a microRNA profile distinct from that of follicular tumors, which supports the rather controversial idea that they represent a distinct class of thyroid neoplasm.

Nikiforova and colleagues found that the diagnostic accuracy of preoperative FNA cytology could be markedly improved by testing for a panel of seven microRNAs (those found to be upregulated across a broad range of thyroid cancer types, and overexpressed by at least twofold in thyroid cancers compared with hyperplastic nodules). The sensitivity, specificity and overall accuracy of cancer detection were 100%, 94% and 95%, respectively, in FNA samples that evinced this degree of overexpression of one or more of these seven microRNAs.

**Original article** Nikiforova MN *et al.* (2008) MicroRNA expression profiling of thyroid tumors: biological significance and diagnostic utility. *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-2696]

## VEGF-C associated with advanced tumor stage and nodal metastases in PTC

Vascular endothelial growth factor (VEGF) promotes angiogenesis and distant metastases, whereas VEGF-C is a lymphangiogenic factor that facilitates nodal metastases. Upregulation of both growth factors can be observed in many epithelial tumors. Papillary thyroid carcinoma (PTC) frequently undergoes lymphatic spread, with a high incidence of cervical lymph-node metastases. Yu *et al.* analyzed the associations