students. It was observed that intervention students were less likely to experiment or initiate, receive or intention to use tobacco than their non-intervention counter parts.

Thus, for preventing onset of tobacco use such intervention programs in the early adolescent period are essential on priority basis to bring behavioral change in school students especially in Northeastern states and Bihar.

Raj Narain, L. Satyanarayana, Division of Epidemiology & Biostatistics, Institute of Cytology & Preventive Oncology (ICMR), NOIDA-201 301, India. E-mail: rajnarain2907@yahoo.co.in

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Diagnosing Adrenal Dysfunction in Thalassemic Children: A Note of Caution

The article on adrenal function in thalassemic patients by Srivatsa, et al. made interesting reading(1). However, I would like to bring to the notice of the authors, certain aspects of the study.

1. While using 1 µg ACTH stimulation tests, it is the 30 minute cortisol and not the 60 minute cortisol that forms the basis of diagnosis of adrenal insufficiency(2). Although the authors have mentioned that one patient had adrenal insufficiency by 1 µg ACTH test, the absolute values are not given in the article.

2. Standard commercial preparation of 1 µg ACTH is not available. It is usually prepared by diluting 250 µg ACTH. These are stored over time and used as and when patients are tested. However, ACTH is easily degradable and the biological activity decreases over time. The activity of the ACTH preparation has to be determined at the end of the study as described by Gandhi, et al.(3)

3. The authors have used basal cortisol <400 nmol/L (14.5 µg/dL) to define abnormal adrenal function. This is a rather high value for making a conclusive diagnosis of adrenal dysfunction despite the explanations given by the authors. A very low early morning plasma cortisol (<138 nmol/L, 5 µg/dL) is highly suggestive of adrenal insufficiency, but lacks sensitivity because most patients with adrenal insufficiency have cortisol values exceeding this value. Sensitivity is increased by raising the cut off value for a presumptive diagnosis to 275 nmoL/l (10 µg/dL), but
this considerably decreases the specificity(2). Hence using 400 nmol/L as cut off would reduce the specificity further. Furthermore, at least in the evolution of adrenal dysfunction due to primary adrenal insufficiency, stimulated cortisol values become abnormal earlier than basal cortisol values(4). Hence there is no reason to believe that it is different in secondary adrenal insufficiency, where the trophic action of ACTH is lost. In the absence of normal controls to substantiate the basal cortisol values, the authors should refrain from using the term “adrenal dysfunction” to describe patients with basal cortisol <400 nmol/L.

Hence, it is incorrect to classify a patient with “low” basal cortisol (<400 nmol/L) and normal post ACTH cortisol as having adrenal insufficiency. Obviously, such a state has no therapeutic implication. Further, it gives an impression that adrenal dysfunction is very common (9 out of 20 patients) in thalassemics who have received multiple transfusions.

Mathew John,  
Department of Endocrinology,  
Diabetes & Metabolism,  
Christian Medical College, Vellore,  
Tamil Nadu 632004, India.  
E-mail: drmathewjohn@yahoo.com

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Reply

We thank Dr. Mathew John for his interest in our article(1). His comments are very meaningful. The following paragraphs address the suggestions/comments:

Regarding the 1 µg ACTH test, only freshly prepared dilution of the standard preparation was used and it was not stored for further use. The 30 min value was used in the 1µg test to define adrenal insufficiency, in accordance with the current recommendation, though the 60 min response was also assessed. In the solitary patient, who had failed the 1µg ACTH stimulation test, the basal and 30 min cortisol levels were 230 and 300 nmol/L, respectively.

We agree with the comment that the baseline cortisol values alone cannot be used to diagnose adrenal insufficiency. It is precisely for this reason that we carefully avoided the use of the term “adrenal insufficiency” in the concluding paragraph. Instead we designated it as a subtle abnormality of adrenocortical function.

Though the baseline cortisol cut off value of 400 nmol/L may appear arbitrary but it was based on published evidence on adrenal function during stress of illness or pharmacological stress. Stewart, et al. had shown that no patient with a morning cortisol value >14 mg/dL (~400 nmol/L) failed an insulin tolerance test(2). Similarly it has been shown that