C A P E NEWS

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METABOLIC SYNDROME IN CHILDHOOD: THE DARK SIDE OF OBESITY

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India is in the midst of a rapidly escalating 'epidemic' of Type 2 Diabetes (T2DM) and Coronary Heart Disease (CHD). Indians as an ethnic group are particularly at high risk for the metabolic syndrome (insulin resistance), which is the harbinger of T2DM and CHD. It is now emerging convincingly that these disorders begin in childhood or even earlier, in fetal life (Barker hypothesis), and manifest due to interactions and accumulation of various risk factors, throughout the life course. Obesity seems to have a central role in the development of this cluster (Table 1).

In association with obesity and the metabolic syndrome, the prevalence of lipid abnormalities in children is on the rise. Because all these problems in childhood have been shown to persist into adulthood, the epidemic of increased cardiovascular (CV) risk may soon burgeon into an epidemic of premature CV disease. It is imperative that this process be forestalled by diligent prevention and control of obesity and aggressive management of co-morbidities, especially dyslipidemia, during childhood and adolescence.

Metabolic Syndrome (Syndrome X): is widely recognized as an important risk for diabetes and cardiovascular disease in adults. In children, this constellation of conditions—obesity (particularly central adiposity), hyperinsulinemia/ insulin resistance (IR), hypertension, and lipoprotein abnormalities—confers a significantly increased risk for cardiovascular disease. Obesity seems to have a central role in the development of this cluster. Autopsy studies of men 15-34 years old who died in accidents, and of 204 persons 2-39 years old, have shown that the severity and extent of asymptomatic coronary and aortic atherosclerosis were directly related to obesity, dyslipidemia, and other components of the metabolic syndrome. Other studies have confirmed the strong association of childhood obesity with the development of IR and increased CV risk.

Obesity is a global epidemic: According to WHO at least 50% adults and 20% children in UK and USA are currently overweight. Childhood obesity doubled in Australia in 10 years, and tripled in Canada in 20 years. The International Obesity Task Force has shown that childhood obesity is 'unequally distributed', prevalence ranging from >30% in the Americas to <2% in sub-Saharan Africa. Indian studies have documented this trend of escalating obesity in both adults and children, in direct correlation with better socioeconomic status and urban habitation. 50-80% of obese children become obese adults, with all complications of adult obesity made worse if obesity begins in childhood.

Obesity, IR and T2DM: Overweight and obesity increase the risk for T2DM. Formerly dubbed "maturity-onset diabetes" because it occurred most frequently in obese, middle-aged adults, T2DM is currently on the rise in younger patients, in association with obesity and the consequent IR. Obese individuals develop different degrees of IR and not all of them develop

glucose intolerance. It is recommended that overweight

TABLE 1: Metabolic syndrome

Glucose Intolerance
Central Adiposity
Small, dense LDL
Increased Triglycerides
Decreased HDL-C
Hypertension
Increased Fibrinogen & Plasminogen Activator Inhibitor 1
Uricemia

children with risk factors be tested for DM as at early as 10y (Table 2).

TABLE 2 (ADA guidelines 2005): Criteria for testing children for T2DM

Overweight (BMI > 85th percentile for age and sex, weight for height > 85th percentile, or weight >120% ideal for height) *plus any 2 of the following risk factors*:

1. Family history of T2DM in first or second degree relative.

2. Race/ ethnicity (native American, African American, Latino, Asian American, Pacific islander).

3. Signs of IR or conditions associated with IR (acanthosis nigricans, hypertension, dyslipidemia, PCOS)

Age of initiation: 10 y or at onset of puberty, if puberty occurs at younger age.

Frequency: every 2 years

Test: Fasting plasma glucose (FPG) preferred

IR and Hypertension: A number of studies have shown the association between IR and BP identified in adults, may also be found in children and adolescents. The Bogalusa Heart Study showed a positive correlation between BP and fasting insulin, even after adjustment for BMI, as early as 5 y of age. Mechanisms proposed for this association include IR leading to chronic sodium retention and altered sodium sensitivity, changes which are reversible with weight loss and exercise. Increased forearm vascular resistance seen in obese, IR-adolescents is reversed with weight loss.

IR and Dyslipidemia: IR has been hypothesized to play a major role in the similar lipoprotein abnormalities seen in obese normoglycemic persons, non-obese persons with impaired glucose tolerance, and obese/ non-obese persons with T2DM. Lipoprotein abnormalities have also been reported in obese adults with the "atherogenic" profile of elevated triglycerides and LDL-c, and low HDL-c. Similar associations between obesity, IR and abnormal lipoproteins have been documented in the pediatric population. In a study comparing 82 normoglycemic, obese adolescents with 40 lean adolescents, an atherogenic profile was found in the obese adolescents. The lipoprotein abnormalities correlated with the degree of IR, which explained a significant portion of the variance in the levels of triglycerides, LDL-c and HDL-c. Investigators from the Bogalusa Heart Study reported that in comparison with their lean counterparts, overweight school children were 12.6 times more likely to have hyperinsulinemia, and 2.4-7.1 times more likely to have elevated total cholesterol, LDL-c, and triglyceride levels.

Several mechanisms fort this have been described. Hyperinsulinemia is known to enhance hepatic synthesis of VLDL, and thus may directly contribute to increased plasma triglyceride and LDL-c levels. Resistance to the action of insulin on lipoprotein lipase in peripheral tissues also may contribute to elevated triglyceride and LDL-c. IR may be responsible for the reduced levels of HDL-c observed in T2DM, despite enhanced HDL-c synthesis, because of an increased rate of apolipoprotein A1/ HDL-c degradation.

In Summary: Metabolic syndrome in childhood confers a significantly increased risk for CV disease in

TABLE 3: Recommendations for Drug Therapy of High-Risk Hyperlipidemia in Children and Adolescents

Original recommendations of the NCEP Expert Panel (1992)

1. Consider drug therapy in children ≥10 y of age (usually wait until menarche for females) and after a 6-12 mo trial of fat- and cholesterol-restricted dietary management.

2. Consider drug therapy if

LDL level remains ≥ 4.90 mmol/L (190 mg/dL) or

LDL remains > 4.10 mmol/L (160 mg/dL) and

there is a positive family history of premature CV disease

≥ 2 other risk factors are present in the child or adolescent after vigorous attempts to control these risk factors.

3. Referral to specialized lipid center may be deemed appropriate.

4. Treatment goal

Minimal, LDL < 3.35 mmol/L (130 mg/dL)

Ideal, LDL < 2.85 mmol/L (110 mg/dL)

Current modifications: Suggested AHA 2007

1. In addition to family history, overweight and obesity should trigger screening with a fasting lipid profile.

2. Overweight/ obese children with lipid abnormalities should be screened for other aspects of the metabolic syndrome (i.e., IR & T2DM, hypertension, or central adiposity).

3. For children meeting criteria for starting lipid-lowering drug therapy, a statin is recommended as first-line treatment.

4. For children with high-risk lipid abnormalities, presence of additional risk factors or high-risk conditions may also lower the recommended cutoff point LDL-c

5. Ongoing research of drug therapy of high-risk lipid abnormalities in children needed, particularly with regard to long-term efficacy and safety, and impact on the atherosclerotic disease process

adulthood. Obesity is central to the development of insulin resistance. Most obese children become obese adults, with worse prognosis for all the complications if the obesity begins in childhood**.** Aggressive weight control and lifestyle modification in children and adolescents is gaining paramount importance as obesity becomes a global epidemic.

Obesity evaluation should encompass evaluation for underlying metabolic syndrome. Obese children with two or more risk factors should have BP monitoring; undergo testing for T2DM from age 10y by FPG, repeated every 2 years if normal; and fasting lipid profile. With diet and lifestyle modifications, aggressive pharmacotherapy for DM, hypertension, and dyslipidemia should be instituted in obese children and adolescents. Statins may be started at age 10y (or after menarche in girls) as the first line of treatment in those with dyslipidemia. Urgent attention to prevention and treatment of the components of metabolic syndrome is required in obese children if the looming epidemic of rampant premature CV disease is to be aborted.

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APPES NEWS

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The 5th biannual scientific meeting of the Asia Pacific Pediatric Endocrine Society will be held in Seoul, South Korea from Oct 29 to Nov 1 2008. The organizing committee has set up a website: www.appes2008.seoul.org

The APPES goal to provide high quality international teaching to trainees in the field is exemplified with 2 meetings for our fellows in 2007. This year 8 APPES fellows have received invitations to attend the Australasian Pediatric Endocrine Group's (APEG) Fellows Meeting in October in Broome, Western Australia. Dr Vimal M V Nambiar from Mumbai will represent India.

For this year's APPES Fellows' Meeting to be held in Taiwan in Dec 2007, dates and venues will be announced shortly on the APPES website, www.appes.org. There are 3 positions available for candidates from India. Interested candidates, preferably those in training, may get in touch with me at the email id psnmenon@hotmail.com.Don't forget - as a member of APPES, you have access to the **Hormone Research Journal** on-line. To utilize this service, log onto the members area of the APPES website.

FORTHCOMING MEETINGS

1. BSPED 2007: 35th Annual Meeting: 11-13 Sep 2007, Cambridge, UK. Details: www.bsped.org.uk/professional/meetings/index.htm

2. ISPAD 2007: 33rd Annual Meeting of the International Society for Pediatric & Adolescent Diabetes: 26-29 Sep 2007, Berlin, Germany. Contact: Olga Kordonouri, Hannover, Germany. Kordonouri@hka.de, www.ispad2007.com

3. APEG 2007: Annual Scientific Meeting: 15-18 Oct 2007, Broome, Western Australia. Email: apegasm@willorganise.com.au www.willorganise.com.au/apeg07

4. DTS 2007: 7th Annual Meeting of the Diabetes Technology Society: 25-27 Oct 2007, San Francisco, USA. Contact: Pasha Tsarinsky: tsarinsky@diabetestechnology.org. Deadline to submit abstract: 29 June, 2007. Submit online to: http://www.diabetestechnology.org/call.html

5. JSPE 2007: 41st Annual Meeting: 7-9 Nov 2007, Yokohama, Japan. Contact: Susumu Yokoya, Dept of Pediatrics, Toranomon Hospital, 2-2-2 Toranomon, Minato-ku, Tokyo 105-8470, Japan. Tel: +81-3-3588-1111, Fax: +81-3-3582-7068 Email: yokoya@toranomon.gr.jp

6. MBD: International Symposium on Metabolic Bone Disorders: 29 Nov, Tirupati, AP. Contact: Dr Harinarayanan.

7. ESICON 2007: 37th Annual Meeting of the Endocrine Society of India: 30 Nov-2 Dec 2007, Tirupati, AP. Contact: Dr CV Harinarayanan, Dept of Endocrinology, SVIMS, Tirupati 517507, AP. 0877- 2287777 ext 2315, 2314, 2312. Fax 0877- 2286803. email: esicon@rediffmail.com

8. PEDICON 2008: 45th National Conference of the IAP: 17-20 Jan 2008, Bhuvaneshwar. Contact: Dr Gadadhar Sarangi, Baidyanath Memorial Hospital, Kanan Vihar Phase I, Chandrasekharpur, Bhubaneswar 751031, Orissa. Tel: 0674 2741740, 09338415073, Fax 0674 2744231. email: iap@pedicon2008.org, www.pedicon2008.org

9. ATTD 2008: 1st International Conference on Advanced Technologies & Treatments for Diabetes: 27 Feb-1 Mar 2008, Prague, Czech Republic. Contact: Kenes International 17, Rue Du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland. Tel: +41 22 908 0488; Fax: +41 22 732 2850; attd@kenes.com; www.kenes.com/attd. Submit abstract (deadline 25 Nov 2007) online at: www.kenes.com/attd/call.asp.

10. ISPAD 2008: 34th Annual Meeting: 12-16 Aug 2008, Durban, South Africa. Contact: Kuben Pillay, West Ville Hospital Westville, 7 Spine Road, Suite 561, IDurban 3600 4013, South Africa. Tel: +27 31 2655377, Fax: +27 31 2655378, email: kubenpillay@worldonline.co.za, www.ispad2008.com

11. ESPE 2008: 47th ESPE Meeting: 20-23 Sep 2008, Istanbul, Turkey. Contact: Atilla Buyukgebiz, Prof Dokuz Eylul Faculty of Medicine, Dept of Paediatric Endocrinolgy & Adolescence, Inciralti, IZMIR, TR-35340, Turkey. Tel: +90 232 278 8411 / 4644540, Fax: +90 232 278 8411/ 4649240, E-mail: atilla.buyukgebiz@gmail.com www.congrex.com/espe2008/

12. JSPE 2008: 42nd Annual Meeting: 2-4 Oct 2008, Yonago, Tottori, Japan. Contact: Susumu Kanzaki, E-mail: smkanzak at grape.med.tottori-u.ac.jp

13. APPES 2008: 5th Biennial Meeting of the Asia Pacific Pedistric Endocrine Society: 29 Oct- 1 Nov 2008, Seoul, Korea. Email: apegasm@willorganise.com.au.

14. ICE 2008: 13th International Congress of Endocrinology: 8-12 Nov 2008, Rio de Janeiro, Brazil. www.ice2008rio.com/

15. ESPE/LWPES: 8th Joint Meeting: 9-12 Sep 2009: New York, USA. www.lwpes-espe2009.org

16. ISPAD 2009: 35th Meeting: 16-18 Sep 2009, Ljubljana, Slovenia. Tadej Battelino, tadej.battelino@mf.uni-lj.si

17. ISPAD 2010: 36th Meeting: 5-11 Sep 2010, Buenos Aires, Argentina. Olgar Ramos, ramoso@interlink.com.ar.

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INTERNATIONAL UPDATE IN PEDIATRIC ENDOCRINOLOGY

Current Trends in Diagnosis and Management

Under the joint auspices of
Indian Academy of Pediatrics - Pediatric & Adolescent Endocrinology Chapter
Asia Pacific Pediatric Endocrine Society (APPES)
Supported by
European Society of Pediatric Endocrinology (ESPE)

14-17 February, 2008
Venue: RD Choksi Auditorium, Tata Memorial Hospital, Parel, Mumbai 400012, INDIA

CHAIRPERSON: **Meena P Desai** • meena_desai@vsnl.net
SECRETARY GENERAL: **Nalini S Shah** • secretariatpedendo@gmail.com / nalinishah@gmail.com
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SCIENTIFIC HIGHLIGHTS

• Molecular basis of pediatric endocrine disorders: Clinical lessons from genetic mutations (GH deficiency, puberty, thyroid disorders, disorders of sexual differentiation, persistent hyperinsulinemic hypoglycemia of infancy)
• Endocrine Disorders in Pregnancy: Impact on fetus and newborn: Optimal care for successful outcome
• Growth, endocrine and metabolic consequences of IUGR
• Decision making in Neonatal Endocrinology
• Pharmacogenomics of Growth Hormone treatment
• Management issues: Problems in Therapy and Monitoring
• Diabetes type 1 & 2 (Pathogenesis and preventive strategies, current trends in optimal management, molecular basis of micro- and macroangiopathies)
• Neonatal Diabetes
• Spectrum of thyroid disorders in childhood
• Evaluation and treatment of pediatric osteoporosis and rickets
• Endocrine neoplasia
• **MINI POSTER SESSION**

INTERNATIONAL FACULTY:

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Chris Cowell, Australia
Annette Gruters, Germany
Khalid Hussain, UK
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Category	**Before 30 Sep 07**	**Upto 31 Dec 07**	**Onsite**
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APPES Member	125 US$	150 US$	175 US$
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Grand Rounds with case discussion, Thu 14 Feb 2008
Registration is free but Compulsory
Restricted to 100 delegates registered for full update ☐ Attending ☐ Not-Attending

One day registration available for practicing pediatricians for Sun 17 Feb 2008

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