# CAPE NEWS

**Newsletter of the Indian Society for Pediatric & Adolescent Endocrinology (ISPAE)**

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## Rickets and Vitamin D: a snapshot of history


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*"If you would understand anything, observe its beginning and its development." – Aristotle*

Rickets and vitamin D are inseparable today. To visualize an era when medical science was not aware about the existence of vitamin D is difficult. The process of discovery of vitamin D, apart from winning a Nobel Prize, has many firsts to its credit, including the use of rats as experimental animals, and the establishment of the first organization for managing patents for scientific discoveries. The attempt here is to look back through the times and pay tribute to the people who made this world a little less deformed.

*Contd on page 4*

## SECRETARY'S MESSAGE

On behalf of the Executive Council of ISPAE it is my pleasure and privilege to present a report of ISPAE for the period January – March 2011. The newly elected Executive wishes to thank all members… *Contd on page 2.*

### ISPAE WEBSITE

**Have you seen our website? www.ispae.org.in.** Check it out for meetings, guidelines and other learning material, contacts in different cities…

**ISPAE 2011:** Calicut: 25-27 Nov, 2011.
**ISPAE-PET 2011 (Pediatric Endocrine Training program):** Calicut 22-25 Nov 2011. Organizing Secretary: Vijayakumar M. email: drmvijaycalicut@gmail.com

**PEDICON 2012:** 49th Annual IAP Conference: Gurgaon: 19-22 Jan 2012. Org. Secy: Dr Mahaveer P Jain,; info@pedicon2012.com; pedicon2012@gmail.com.

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## SECRETARY'S MESSAGE *Contd from page 1.*

…for their continued support. We in the Council would like to take the Society ahead with academic, scientific and patient related activities conducted under its banner. Our main focus is to encourage all members of the Society to contribute to the growth of both pediatric endocrinology and ISPAE.

The ISPAE **annual GBM** was held in Jaipur in January: minutes circulated to all of you earlier, have also been included in this issue of Capenews.

The **first EC meeting** passed a few important resolutions which I would like to share with you.

The Executive was unanimous in deciding that members should be encouraged to organize **local CME programs** under the ISPAE banner, and has streamlined and simplified the process of organizing such events. Members must write/ email in advance to the ISPAE Secretary and obtain permission of the EC. At least one member of the current EC should be a member of the Organizing Committee. The Organizing Secretary should give a brief report of the event to the ISPAE Secretary within a month of the event so that it can be included in the Society calendar of activities as well as published in Cape News and Society website.

The EC decided to invite applications for the posts of **Editor of Capenews and Web-master** for the ISPAE website, along with 3 committee members for each. As we all know, both Capenews and the website have been in extremely capable and responsible hands till date. However we also know that there are equally talented and enthusiastic members in our Society who would not only be willing to take these forward, but also rejuvenate them with fresh ideas. **You would all have received my mail regarding applications for these posts. Please note the last date for applying was 15th April: please do apply *immediately* (within a week of this dispatch) if you are interested.**

The EC also decided to invite expression of interest for the **next biennial meeting of ISPAE** scheduled for **2013**. A mail outlining the requirements for organizing the same has already been sent to all of you. We hope those of you who are interested, will apply soon.

A Special GBM held at Kanpur on 27 Feb 2011 ratified the decision taken at the Special GBM held on 9 Dec 2010 in Vellore that seed money for the Biennial ISPAE Conference may be borrowed from Society funds for organizing the conference and returned to the main corpus within a month of the conference. 25% of the profits from this meeting will be returned to the corpus along with return of the seed money. Minutes of the Special GBM, along with other decisions taken in that meeting, have also been circulated earlier to all of you. These changes now stand incorporated in the **Rules & Regulations of the Society**.

This quarter has also seen organization of two much appreciated pediatric endocrinology CME programs under the ISPAE banner. "Pedendocon" was organized by **Dr Anurag Bajpai at Kanpur on 27 February 2011**, and "Pediatric Endocrinology Conclave" was organized on **6 March 2011 at Thiruvananthapuram by Dr I Riaz**. Both meetings were well attended and educative for the delegates. The EC congratulates the organizers of both these meetings.

Much progress has been made for the forthcoming **Biennial Conference** at **Calicut**, being ably organized by Dr M Vijayakumar. Preparations for the **Pediatric Endocrine Training Program, PET 2011**, are also on the way. Information flyers have been mailed to all major Indian teaching Institutions and to members of ISPAE, Endocrine Society of India, and GDBP Chapter of IAP. The initial response is encouraging. The international faculty for ISPAE 2011 and PET 2011 has been finalized, and we are in the process of designing the programs based on the inputs received from the participants and faculty of PET 2009, experience from similar training programs held in other parts of the world, and ISPAE 2009. We look forward to an intensive curriculum in PET 2011, as well as meeting old friends and making new ones while learning and sharing during the main meeting.

**27 new members** have joined ISPAE, taking our total strength to 249. I **sincerely welcome** all of you! You would be able to check your membership number on the ISPAE website, which should help us all to stay in contact with one another.

We plan to **stay in constant e-touch with all members**. Therefore if your **email id changes**, please let us know. If you have not heard from us for a few weeks, suspect all is not well, and write to Preeti or me to find out why emails are not reaching you. We look forward to an active participation by all members of ISPAE in furthering the interest of pediatric endocrinology in India and will await your suggestions.

With warm regards
Anju Seth

### Minutes of Annual General Body Meeting held on 23 January 2011 at Jaipur during PEDICON 2011

*Preeti Dabadghao, Joint Secretary*

The meeting was chaired by Dr Archana Arya, Secretary-Treasurer. The following members were present: Drs. Archana Arya, Sangeeta Yadav, Shaila Bhattacharya,

Subrato Dey, Anurag Bajpai, Sudha Rao and Preeti Dabadghao. The following agenda were discussed:

**Agenda 1. Confirmation of minutes of the last annual GBM held in January 2010 during PEDICON 2010 at Hyderabad.**
Unanimously passed.
**Agenda 2. Presentation of accounts**
This was deferred to the next meeting.
**Agenda 3. Introduction of the new executive council.**
The new executive council was introduced to the General body.
**Agenda 4. Welcoming of new members**
The General body welcomed the new executive council members.
**Agenda 5. Presentation of brief report of ISPAE 2011, ISPAE-PET 2011 to be held in Calicut.**
The names of foreign faculty who have agreed were informed. Second brochure is ready and has been circulated. It was informed that the deadline for early early bird registration is 31st January 2011. The general body was informed that some members are not receiving the information about ISPAE and PET. This will be communicated to the organizers.
**Agenda 6. Update on obesity and diabetes guidelines**
The manual on Diabetes guidelines is nearing completion. Write ups have to be collated and edited for obesity guidelines and a period of 3 months was requested by the guidelines writing committee.
**Agenda 7. Progress of the IAP Pediatric Endocrinology book.**
The editors have to correct the text and inform the authors of any required correction. IAP has given the deadline of 31st March 2011 and the work has to be completed by the deadline.
**Agenda 8. Discussion of other activities for 2011-2012, including popularizing website/ growth charts/ orchidometers.**
It was unanimously agreed that it should be done.
**Agenda 9. Scientific content of symposium in PEDICON 2012**.
Suggestions included management of inpatient endocrine diseases, neonatal endocrine emergencies like hypoglycemia and hypocalcemia and other endocrine emergencies.
**Agenda 10. Setting up of new formal pediatric endocrine courses in the country.**
The need for this was felt by all and it was suggested that the members should try hard to have formal courses.
**Agenda 11. Maintenance of 80G status to hold activities under the banner to maintain the status.**
Dr V Bhatia was unanimously congratulated for getting the status.
**Agenda 12. Any other items by permission of chair**

1. Website and CAPENEWS: There was a suggestion of involving few other members for this activity.

2. PET organization: It was suggested to have new people involved who could then takeover for the next time and to continue this process.

## ISPAE 2011, PET 2011: PROGRESS REPORT

*M Vijayakumar, Organizing Secy, drmvijaycalicut@gmail.com*

**The main meeting (**25-27 November 2011): will be held at Vasco Da Gama auditorium at Hotel Taj Gateway, situated in the heart of Calicut. The scientific committee is in the process of finalizing the academic program which will be attractive and interesting, catering to the needs of the delegates. ESPE (European Society for Pediatric Endocrinology) is sponsoring four faculty members, and APPES (Asia Pacific Pediatric Endocrine Society) one faculty member. Thus the eminent international speakers who have confirmed their participation are: Dr Jean-Claude Carel (France), Dr Franco Chiarelli (Italy), Dr Olaf Hiort (Germany), Dr Ze'ev Hochberg (Israel), Dr Reiko Horikawa (Japan), Dr Scott Rivkees (USA), and Dr Margaret Zacharin (Australia).

So far 99 delegates have registered. The early bird rate closes on 31 May, 2011. So do hurry and send in your registration! Form and all details are the website, *www.ispae.org.in*

**ISPAE-PET 2011 (**22-25 November 2011): The venue will be **Hill View Valley Nature Resort, Puduppady,** 50 km from Calicut city. The resort has small cottages for accommodation for faculty and fellows, a good auditorium to hold main sessions, and additional facilities to hold group sessions. The faculty consists of Dr Carel, Dr Hiort, Dr Horikawa, Dr Rivkees, and Dr Zacharin, and 7-9 Indian

faculty.

The format for application and all details are available at the website *www.ispae.org.in* **Please note that the last date for applications is 30th April 2011.** Dr Anju Seth, convener of the program, can be contacted at *ispae.pet@gmail.com*

Major pharmaceutical companies supporting the meetings include Novo Nordisk, LG Life Sciences, Pfizer, Eli-Lilly, Hologic, Ranbaxy, and Merck-Serono.

## NEW MEMBERS: A VERY WARM WELCOME!!

1. **Dr DEEPAK AGARWAL, Gwalior**
2. **Dr LATIKA BHALLA, Delhi**
3. **Dr REGI CHANDRAN, Thiruvananthapuram**
4. **Dr RAMESH GOMEZ, Thiruvananthapuram**
5. **Dr ASHWANI GULERIA, Una**
6. **Dr ANJANA HULSE, Bangalore**
7. **Dr LALITHA KAILAS, Thiruvananthapuram**
8. **Dr SANJIV KAKKAR, Lucknow**
9. **Dr DEEPAK KHANDELWAL, Delhi**
10. **Dr K KISHORE, Hyderabad**
11. **Dr BINDU KULSRESHTHA, Delhi**
12. **Dr SHOBA KUMAR, Thiruvananthapuram**
13. **Dr ANJALI MAINI, Lucknow/ Qatar**
14. **Dr VINOD KUMAR MAURYA, Varanasi**
15. **Dr VIKAS MEHROTRA, Aligarh**
16. **Dr MEENA KUMARI MOHAN, Coimbatore**
17. **Dr GIRISH M PARMAR, Mumbai**
18. **Dr ANUJ RASTOGI, Meerut**
19. **Dr UMA KAIMAL SAIKIA, Guwahati**
20. **Dr NUPUR SARKAR, Bhopal**
21. **Dr DIPTI SARMA, Guwahati**
22. **Dr BM SHASHI, Mysore**
23. **Dr RISHI SHUKLA, Kanpur**
24. **Dr RAJINDER SIHAG, Sirsa**
25. **Dr REKHA SINGH, Guwahati**
26. **Dr RUPA DALMIA SINGH, Kanpur**
27. **Dr USHMA SINGH, Delhi**

**Members with only rediffmail email ids**: please note. These sometimes bounce when emails are sent from gmail accounts. If you have an alternative id, please let me know. Thank you! Ed.

## APPES COUNCIL MEETING

*Vijayalakshmi Bhatia*

A teleconference of the executive council of APPES (Asia Pacific Pediatric Endocrine Society) was conducted on 29 March 2011, in which both ISPAE representatives V Bhatia and Nalini Shah were present. Matters discussed included the APPES 2011 Fellows School (9-12 November) and CME Meeting (12-13 November) being held in Hanoi. Vijayalakshmi Bhatia informed of ISPAE activities: main meeting in 25-27 November; Fellows Meeting on 22-25 November, to which ESPE (European Society for Pediatric Endocrinology) is sending 4 speakers, while APPES will be represented by Reiko Horikawa. In addition, Margaret Zacharin and Scott Rivkees are being funded by the meeting budget. The Biennial APPES Scientific Meeting 2012 is to be held in Bali, the Convenor being Aman Pulungan. Its Scientific Program Committee consists of Paul Hofman, Reiko Horikawa, Vijayalakshmi Bhatia, Xiaoping Luo, Bambang Tjadjara and Pik To Cheung. The ISPAD (International Society for Pediatric and Adolescent Endocrinology) Science School 2013, to be held in Sydney, Australia, is being convened by Maria Craig. Lyndell Wills, the manager of the APPES secretariat, informed that the APPES website will soon have a new look and useful features.

## *Rickets and Vitamin D...*

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### Rickets: A New Disease?

Conditions with bony deformities have been described in ancient medical writings. Roman physicians described bony deformities in children as early as the 1st and 2nd century AD, ascribing it to lack of nurture and hygiene by Roman mothers (1). The word 'rickets' first came in print in 1634, in the Annual Bill Of Mortality for the city of London. The condition accounted for 14 of the 10900 deaths that year, soaring to 441 by 1659 (2). The origin of the word 'rickets' is an etymological puzzle: was it from 'rachitis' (a Greek word meaning 'spinal disease'); 'riquet' (a French word meaning hunch-backed); or 'rucken' (a German word meaning 'back or spine'). An interesting but inaccurate theory is that the word is derived from the name of a Dr Ricketts in Newbury who had acquired a reputation for treating the disease (3).

In 1645, Daniel Whistler, a 26 year old English medical student published the earliest description of rickets, "Inaugural medical disputation on the disease of English children which is popularly termed the rickets"(1), as his thesis submitted for the degree of doctor of medicine in Leiden. The originality of his thesis has been in doubt and it has been postulated that he probably had access to the records of Francis Glisson, a Cambridge physician. In 1950, Glisson published a treatise on rickets titled "De Rachitide", the longest and the most detailed description of those times (4). This Latin book, translated into English the following year, remains a classic even today. Glisson thought it was a new disease barely in existence for 20 years before he wrote about it. He recognized that it was neither congenital nor

inherited and was not contagious. He thought it was due to "cold distemper, that is moist and consisting of penury or paucity of and stupefaction of spirits." His suggested treatments included cautery, incisions, blistering, and ligature of soft wool around the limb to retard the return of blood. Venesections, especially from a ear lobe, was a popular treatment modality (4). Use of rook's (crow's) liver, frog's liver, exposure of abdomen to sunlight were also mentioned as potential remedies during those times. For correction of bony deformities, Glisson proposed splinting and artificial suspension of the affected infant to make him taller!(5) Other descriptions of rickets were published by Boote and Mayow.

This explosive appearance of rickets in London in the early 17th century, at the start of the industrial era, was likely due to vitamin D deficiency from reduced UV exposure, resulting from air pollution due to coal burning, and reduced sun exposure (2). A contributory factor may have been the increasing cultural practice of wet nursing adopted by the rich, sometimes with multiple children being nursed by a single wet nurse, leading to improper feeding and calcium deficiency (6). Because of its predominance in England it came to be known as the 'English Disease'.

**Delineating etiology: Ode to Cod Liver Oil**

The late 19th and early 20th century witnessed a phenomenal expansion in the knowledge of rickets: understanding of the histopathology, advances in biochemical and radiologic testing, and clarification of the anti-rachitic features of cod-liver oil and ultraviolet light. Alfred Hess referred to this era as "the second great chapter" and the "renaissance" in the history of rickets (7). Cod liver oil played a major role in this. It had been in use for centuries as a part of folklore for its general medicinal and strengthening properties (8), and as a cure for numerous diseases including rheumatism, tuberculosis, skin diseases, measles, and puerperal fever. There is a mention of treatment of rickets with cod liver oil in the early 1800s in the German medical literature. In 1889, Bland-Sutton observed florid rickets among lion cubs on an exclusive diet of boneless lean meat at the London Zoo, with full recovery with the addition of cod-liver oil and crushed bones to their diet. He hypothesized rickets was caused by deficiency of dietary fat (1). In 1920s Edward Mellanby prevented rickets in puppies by giving them cod liver oil. Foods rich in a fat-soluble vitamin, the intake of which was able to prevent rickets, and known as fat soluble A during those times, had been recently identified (8). Mellanby postulated, "It therefore seems probable that the cause of rickets is a diminished intake of an anti-rachitic factor which is either fat-soluble A, or has a somewhat similar distribution to fat-soluble A."

In 1922 McCollum et al, at Johns Hopkins University, performed a series of experiments on rats. McCollum was one of the first researchers who visualised rats as potential experimental animals. Rachitic rats (induced by rachitogenic diets) treated with cod liver oil were healed. After cod liver oil was heated to destroy vitamin A (vitamin A is prone to denaturation by oxidation unlike vitamin D), it had no anti-xerophthalmic property but still had the anti-rachitic effect, suggesting the presence of an antirachitic factor separate from fat-soluble A. Thus vitamin D ('D' as it was the fourth vitamin) was discovered (9).

**Sunshine and radiation**

As early as 1822, Sniadecki, a Polish physician, had observed that rickets was more prevalent among infants residing in the polluted, sunless inner-city areas of Warsaw than in rural areas, and postulated that it was caused by the lack of exposure to sunlight. In 1890, Palm advocated the systemic use of sunbaths to prevent and cure this disease. In 1919, Kurt Huldschinsky cured rickets in infants by exposing them to light rays from a mercury vapour lamp for variable time durations. He concluded that UV ray exposure was an 'infallible remedy' against rickets in children. In 1921, Hess et al also reported marked improvement in seven rachitic children exposed to sunshine (10). The fact that both sunlight exposure and ingestion of cod-liver oil could cure or prevent rickets was perplexing.

Steenbock et al realized that rachitic rats were cured when irradiated rats were introduced into their cages. This growth was attributed to consumption of 'activated' feces of the irradiated rats, irradiated dust straw or irradiated left-over food by the diseased ones. With this cue, Steenbock and Black irradiated food (with mercury vapor lamps) and realized that this promoted growth and calcium assimilation in the rats. Simultaneously similar observations were being made by Hess & Weinstock, and also Hume & Smith (11). That 'irradiation of food conferred on it antirachitic properties', was a phenomenal breakthrough, put graphically as 'The sun has been trapped' (12)! Irradiation of common food products like milk and cereal proved low cost health measures and led to the near 'eradication' of nutritional rickets. Steenbock realized the need to patent his discovery to prevent misuse by the commercial industry. Patenting of scientific discoveries and the establishment of an independent organization to handle patents was a novel concept then, and the Wisconsin Alumni Research Foundation (WARF) was formed. Interestingly, Quaker Oats Company was the first to be given the license in 1927 to irradiate food, and fortified breakfast cereals became commercially available (12).

The question still remained- how was irradiation able to confer antirachitic properties? Huldschinsky demonstrated that irradiation of one arm could cure rickets in the other, suggesting that something produced in the skin had to enter the systemic circulation to impart the cure. Hess et al isolated sitosterol (phytosterol) from cottonseed oil which was activated by ultraviolet light. The irradiated plant ergosterol was named as vitamin D2 or calciferol. 'Vitamin D fortified milk' was introduced in 1934 where milk was initially fortified with ergosterol and irradiated for antirachitic activity (13).

It was well known that ergosterol is not present in animals. So, what was the animal equivalent of ergosterol? Cholesterol had been isolated from rat brain and was seen to be activated to produce antirachitic properties. Hess et al hypothesized: "it would seem quite possible that the cholesterol in the skin is normally activated by UV-irradiation and rendered anti-rachitic—that the solar rays and artificial radiations can bring about this conversion. This point of view regards the superficial skin as an organ, which reacts to particular light waves, rather than as a mere protective covering" (1). In 1926, Helibron et al suspected some 'impurity' in the cholesterol which was getting 'activated'. In 1937, Windaus and Bock isolated and identified that 'impurity' as 7-dehydrocholesterol from hog skin. 7-dehydrocholesterol was also shown to be present in human skin and in food from animal sources and was convertible to an antirachitic substance by irradiation. The irradiated product was named vitamin D3, or cholecalciferol (11). The Nobel Prize for chemistry for 1928 was awarded to Adolf Windaus "for his studies on the constitution of the sterols and their connection with vitamins".

Since then intensive research on vitamin D continues. In the 1970s it was realised that vitamin D is a (pro)hormone and not a vitamin! A variety of tissues and cells not responsible for regulating calcium and phosphorus metabolism (pancreas, stomach, gonads, brain, breast, mononuclear cells, skin..) were found to have specific receptors for l,25(OH)2D. Vitamin D deficiency has been associated with a variety of disorders other than rickets, like type 1 diabetes mellitus, multiple sclerosis, rheumatoid arthritis, colon cancer, prostate cancer, Crohn's disease etc. (13). Research needs to continue to answer a lot of unanswered questions.

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## Excerpts from the ADA 2011 Clinical Practice Guidelines on "Diagnosis and Classification of Diabetes Mellitus" and "Standards of Medical Care in Diabetes Mellitus."

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### Classification

I. **Type 1 diabetes** (β-cell destruction, leading to absolute insulin deficiency)
A. Immune mediated
B. Idiopathic

II. **Type 2 diabetes** (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance).

III. **Other specific types**
A. Genetic defects of β-cell function.
B. Genetic defects in insulin action.
C. Diseases of exocrine pancreas.
D. Endocrinopathies
E. Drug or Chemical induced.
F. Infections
G. Uncommon forms of immune mediated diabetes
H. Other genetic syndromes sometimes associated with diabetes.

IV. Gestational diabetes mellitus.

### Criteria for the diagnosis of diabetes

A1C ≥ 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

OR

FPG ≥ 126 mg/dl. Fasting is defined as no caloric intake for at least 8 h.

OR

2-h plasma glucose ≥ 200 mg/dl during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl.

In the absence of marked hyperglycemia with decompensation, these criteria should be confirmed by repeat testing on a different day.

### Categories of increased risk for Diabetes

FPG 100-125 mg/dl [IFG]
2-h PG in the 75-g OGTT 140-199 mg/dl [IGT]
A1C 5.7–6.4%. [***Comment: The variable reliability of A1C reports must be kept in mind while using this last criterion.***]

### Therapy

Recommended therapy for type 1 diabetes (T1DM) consists of the following components: 1) use of multiple dose insulin injections (three to four injections per day of basal and prandial insulin) or CSII therapy; 2) matching of prandial insulin to carbohydrate intake, premeal blood glucose, and anticipated activity; and 3) for many patients (especially if hypoglycemia is a problem), use of insulin analogs.

***[Comment: In a resource limited setting, the treatment plan needs to be individualized based on the patient's age, socioeconomic status, understanding of the disease, frequency of self home blood glucose (SMBG) and ease of access to the diabetes care team].***

## Plasma BG and A1c goals for T1DM by age group

| | Plasma blood glucose goal range (mg/dl) | | |
|---|---|---|---|
| | Before meals | Bedtime/overnight | A1C (%) |
| Toddlers and preschoolers (0–6 years) | 100–180 | 110–200 | <8.5 |
| School age (6–12 years) | 90–180 | 100–180 | <8 |
| Adolescents and young adults (13–19 years) | 90–130 | 90–150 | <7.5 |

## Screening and management of chronic complications in children & adolescents with T1DM

i. **Nephropathy**

Annual screening for microalbuminuria, with a random spot urine sample for albumin-to-creatinine (ACR) ratio, should be considered once the child is 10 years of age and has had diabetes for 5 years. Confirmed, persistently elevated ACR on two additional urine specimens from different days should be treated with an ACE inhibitor, titrated to normalization of albumin excretion if possible.

ii. **Hypertension**

Treatment of high-normal BP (systolic or diastolic BP consistently > 90$^{th}$ percentile for age, sex, and height) should include dietary intervention and exercise aimed at weight control and increased physical activity, if appropriate. If target BP is not reached with 3–6 months of lifestyle intervention, pharmacologic treatment should be considered.

Pharmacologic treatment of hypertension (systolic or diastolic BP consistently > 95$^{th}$ percentile for age, sex, and height or consistently > 130/80 mmHg, if 95% exceeds that value) should be initiated as soon as the diagnosis is confirmed. ACE inhibitors should be considered for initial treatment, following appropriate reproductive counseling due to its potential teratogenic effects. The goal of treatment is a BP consistently < 130/80 or below the 90th percentile for age, sex, and height, whichever is lower.

iii. **Dyslipidemia**

If there is a family history of hypercholesterolemia (total cholesterol ≥240 mg/dl) or a cardiovascular event before age 55 years, or if family history is unknown, then a fasting lipid profile should be performed on children ≥ 2 years of age soon after diagnosis (after glucose control has been established). If family history is not of concern, then the first lipid screening should be considered at puberty (≥10 years). For both age-groups, if lipids are abnormal, annual monitoring is recommended. If LDL cholesterol values are within the accepted risk levels (<100 mg/dl [2.6 mmol/l]), a lipid profile should be repeated every 5y.

Initial therapy should consist of optimization of glucose control and medical nutrition therapy (MNT) using a Step 2 AHA diet aimed at a decrease in the amount of saturated fat in the diet. After age 10y, the addition of a statin in patients who, after MNT and lifestyle changes, have LDL cholesterol ≥160 mg/dl (4.1 mmol/l), or LDL cholesterol ≥130 mg/dl (3.4 mmol/l) and one or more CVD risk factors, is reasonable. The goal of therapy is an LDL cholesterol value <100 mg/dl.

iv. **Retinopathy**

The first ophthalmologic examination should be obtained once the child is 10 years of age and has had diabetes for 3–5 years. After the initial examination, annual routine follow-up is generally recommended. Although retinopathy most commonly occurs after the onset of puberty and after 5–10 years of diabetes duration, it has been reported in prepubertal children and with diabetes duration of only 1–2 years.

v. **Celiac disease**

Children with T1DM should be screened for celiac disease by measuring tissue transglutaminase or anti-endomysial antibodies, with documentation of normal total serum IgA levels, soon after diagnosis of diabetes. Testing should be repeated in children with growth failure, failure to gain weight, weight loss, diarrhea, flatulence, abdominal pain, or signs of malabsorption, or frequent unexplained hypoglycemia or deterioration in glycemic control.

***[Comment: Due to the lack of uniform availability and affordability of antibody testing and the marked heterogeneity in the incidence of celiac disease; antibody testing must be used judiciously as per the pediatrician's discretion].***

vi. **Hypothyroidism**

Children with T1DM should be screened for thyroid peroxidase and thyroglobulin antibodies at diagnosis. TSH concentrations should be measured after metabolic control has been established. If normal, they should be re-checked every 1–2y, or if the patient

develops symptoms of thyroid dysfunction, thyromegaly, or abnormal growth rate. Subclinical hypothyroidism may be associated with increased risk of symptomatic hypoglycemia and reduced linear growth. Hyperthyroidism alters glucose metabolism, resulting in deterioration of metabolic control.

### The Importance of Lifetime Exposure to LDL cholesterol in Primary Prevention of Ischemic Heart Disease Events

*Chittaranjan Andrade*

** Benn M, Nordestgaard BG, Grande P, Schnohr P, Tybjaerg-Hansen A. PCSK9 R46L, low-density lipoprotein cholesterol levels, and risk of ischemic heart disease: 3 independent studies and meta-analyses. J Am Coll Cardiol 2010; 55: 2833-2842.

Benn et al (2010) examined the effect of the R46L polymorphism of the PCSK9 gene on LDLc, IHD events, and mortality in the prospective Copenhagen City Heart Study (CCHS; n=10,032). They validated the results in the cross-sectional Copenhagen General Population Study (CGPS; n=26,013) and in the case-control Copenhagen Ischemic Heart Disease Study (CIHDS; n=9,654). Finally, they performed meta-analyses of data from present and previous studies (n=66,698). This study is of considerable public health importance, but curiously, has received little attention in the scientific media. The 46L allele of the PCSK9 gene (carried by 2.6% of the CCHS and CGPS study populations) is associated with a 11-16% reduction in LDLc in subjects aged 20-80+ years in the general population. The approximately 30% lower risk of IHD events in 46L carriers is far larger than is predicted by the observed reduction in LDLc alone. A likely explanation is that lifetime exposure to LDLc is a better predictor of IHD risk than LDLc levels measured cross-sectionally in midlife or later. After all, cholesterol deposit in arteries has been detected even before the age of 20 years. Lowering LDLc should therefore be a lifelong goal, starting from teenage years, itself.

## OUR MEMBERS' PUBLICATIONS

*[Editor's note: Please send us information, and even a short summary of your recent publications.]*

** Nair PS, Sobhakumar S, Kailas L. Diagnostic re-evaluation of children with congenital hypothyroidism. Indian Pediatr. 2010 Sep; 47(9):757-60.

### Congenital hypothyroidism: Life-long treatment is not the rule

*Priyanka Gupta, gims2gui@yahoo.com*

Congenital hypothyroidism (CH) is an ideal condition for newborn screening: common condition, no early clinical features, disastrous consequences of delayed diagnosis; accurate biochemical diagnosis possible, and good outcome with early treatment (2-3 weeks of age) which is inexpensive. Contrary to popular belief, CH is not always permanent. Important transient causes are iodine deficiency, trans-placental passage of maternal TSH-binding inhibitory antibodies or anti-thyroid drugs, and neonatal exposure to iodine. Recently, a very well done Indian study (Nair PS et al: see above), showed that as many as half the cases of CH may turn out to be transient. The authors studied 36 children, age > 3 yrs, on thyroxin, with diagnosis of CH. None of them had any documented proof (by radionuclear scan or thyroid ultrasonography) of permanent CH in the neonatal period,. Thyroid function tests (TFT) and thyroid ultrasound were done in all. Those who had agenesis or hemiagenesis on thyroid ultrasound were classified as having permanent CH. In the remaining, thyroxin was stopped, and of them those who developed abnormal TFT, underwent thyroid scanning with/without perchlorate discharge test. Eighteen of 36 children studied (20 boys, 16 girls) had transient hypothyroidism, i.e. TFT remained normal for up to 6 months. The commonest cause of permanent CH (15 of 36: i.e. 41.7%) was thyroid agenesis. Thus authors found that thyroxin replacement could be successfully stopped in as many as 50% patients.

This is an important piece of clinically relevant information, because all those with transient CH would have received unnecessary life-long treatment unless re-evaluated. As more and more newborns are screened across the country, we need to become aware of how to handle the babies with abnormal results. As suggested in an accompanying editorial by Prof V Bhatia, (Bhatia V. Congenital hypothyroidism is not always permanent: Caveats to newborn thyroid screen interpretation. Indian Pediatr 2010; 47: 753-754), clinicians must adhere to joint guidelines by American Academy of Pediatrics, American Thyroid Association and Lawson Wilkins Pediatric Endocrine Society. For example, it is important to remember to confirm all abnormal results before starting therapy. Moreover, if blood sampling is done too early (before the TSH surge has subsided) TSH levels as high as 40 mIU/L may be normal, and repeat sampling at 2 weeks of age is needed for confirmation. False positives due to early screen sampling, or immaturity of the HPT axis, may have subsided by then. In this study also, retrospective analysis of TSH at the time of initial diagnosis showed mean TSH lower in the transient CH group than the permanent CH (47.0±33.1 vs. 83.0±31.6 mIU/L; P=0.002). Ideally, ultrasound and radionuclide thyroid imaging of thyroid should be used to try and make an etiological diagnosis (e.g. hemithyroid, dyshormonogenetic goitre, athyreosis and lingual thyroid) before starting replacement. At the same time, initiation of therapy should not be delayed beyond age 2 weeks, to get a normal outcome. Any baby who did not have a sound documentation of permanence, merits a trial of stop thyroxin at 3 year of age, to check thyroid status and trying to establish etiology.

** Dhanwal DK, Dennison EM, Harvey NC, Cooper C. Epidemiology of hip fracture: World wide geographic variations. Indian J Orthop; 2011:45(1):15-22.

** Dhanwal DK, Kochupillai N, Gupta N, Cooper C, Dennison EM. Hypovitaminosis D and bone mineral metabolism and bone density in hyperthyroidism. J Clin Densitom. 2010 Oct-Dec;13(4):462-6. Epub 2010 Jul 21.

** Dhanwal DK, Vyas A, Sharma A, Saxena A. Hypothalamic pituitary abnormalities in tubercular meningitis at the time of diagnosis. Pituitary. 2010 Dec;13(4):304-10.

** Gupta P, Shingla S. Symptomatic transient idiopathic hypo-magnesemia in a neonate. Singapore Med J 2011, 52: 132-33.

** Priyambada L, Bhatia V, Krishnani N, Agarwal V, Bhattacharya A, Jain S, Misra SK, Marwaha RK. Primary hypothyroidism, precocious puberty and hypothalamic obesity in Langerhans cell histiocytosis. Indian J Pediatr 2011; 78: 351-353.

## MORE ISPAE NEWS

## CALICUT MEETING

*M Vijayakumar*


A CME program in pediatric endocrinology was conducted at East Avenue Suites, Calicut, on 6 Dec, 2010. Prof. P Sreekumaran, introduced the guest speaker, Prof. PSN Menon. Dr Menon's discussion on short stature and growth hormone therapy was followed by a lively discussion.

## PEDENDOCON 2011

*Anurag Bajpai, Organizing Secretary, dr_anuragbajpai@yahoo.com*

PEDENDOCON 2011, the 1st North Central Regional Update in Pediatric Endocrinology was organized on February 27 2011 at Ragendra Swaroop Auditorium, Kanpur, under the auspices of ISPAE, UP IAP and Departments of Endocrinology and Pediatrics, Regency Hospital Limited, Kanpur. The event attended by over 200 delegates from the region, was mainly focused on practical issues. Prof. PSN Menon, President ISPAE, in his presidential address, highlighted the need for increasing awareness of pediatric endocrinology amongst pediatricians.

Key areas covered in the update included growth, diabetes, obesity, metabolic bone disease, hypocalcemia and pubertal disorders. The galaxy of speakers, including Prof. Vijayalakshmi Bhatia, Prof. Anju Seth, Dr Vaman Khadilkar and Dr Preeti Dabagdhao, provided new insights to the delegates on simple management on complex disorders.

## THIRUVANANTHAPURAM MEETING

*Lalitha Kailas, Organizing Chairperson;S Sobhakumar, Organising Secretary, Riaz.I , Scientific Coordinator*

A national update on Pediatric Endocrinology was held at Trivandrum on March 6th 2011, organized by Department of Pediatrics, Govt. Medical College, Trivandrum, in association with the Pediatric & Adolescent Endocrinology Chapter of IAP, and the IAP Trivandrum branch.

The program started with Prof. Vijayalakshmi Bhatia, our guest of honor, lighting the lamp. Prof. Lalitha Kailas (HOD, Dept. of Pediatrics) delivered the welcome address. Prof. KE Elizabeth introduced the conference theme. Dr PNN Pisharody (President IAP Kerala) chaired the inaugural session. Felicitations were offered by Dr PA Mohammed Kunju, President, IAP Trivandrum, and Dr Zulfikar Ahmed. Dr S Sobhakumar gave the vote of thanks.


*Dr V Bhatia lighting the lamp. Also seen: Dr PNN Pisharody, Dr Sobhakumar, Dr Kailas, Dr Elizabeth, Dr PA Mohammed Kunju and Dr Zulfikar Ahmed.*

Our eminent faculty included not only Dr Bhatia, Dr Kailas, Dr Sobhakumar, but also Dr Vaman Khadilkar, Dr Sarah Mathai, Dr Vijayakumar and Dr Veena Nair. There were sessions on growth monitoring, hypothyroidism, vitamin D deficiency, obesity, Type I diabetes, chronic steroid use in children. Interesting case scenarios were discussed.

The meeting was well attended by practicing pediatricians, faculty and students from different medical colleges in Kerala and was appreciated by all for its scientific content and its usefulness in clinical practice. On behalf of the Organizing Committee, we place on record our sincere gratitude to Dr Bhatia for her constant guidance and support from the very conception of this event for making this endeavour a grand success. We also thank the office bearers of the Chapter for their support.

## 25TH ANNUAL MEDICINE UPDATE

*Dinesh Dhanwal, Organizing Secretary, dineshdhanwal@hotmail.com*

The Endocrinology Division of Dept. of Medicine, Maulana Azad Medical College, New Delhi, organized

their 25th annual scientific feast on 3-5 March 2011, the theme being newer advances in medicine. Though the scientific program covered all the sub specialties of internal medicine, the major emphasis was on endocrine disorders, including pediatric endocrinology. The main endocrine topics covered were a symposium on growth; the key speakers were Dr Anju Virmani and Dr Rajesh Khadgawat. Other topics were insulin pump therapy, newer agents in management of diabetes, obesity: from prevention to intervention, osteoporosis, and imaging techniques including thyroid scanning. Dr SK Sarin, Chairman Medical Council of India, delivered the keynote address on hepatic dialysis. The scientific proceedings, containing write up on various topics, was also published. 200 delegates and 60 faculty members participated in this successful meeting.

## CHARITY ACTIVITIES

ISPAE is mandated to conduct some charity activities through its members, apart from educational activities. It has been supporting our member, Dr Sahul Bharti, in his selfless work in Himachal Pradesh. Glimpses of his work by provided by Dr Margaret Zacharin in her article in an earlier issue. Subsidized insulin and glucose test strips have also been provided to poor children with diabetes using donations raised for ISPAE by Dr Bhatia's and Dr Virmani's patients.

We welcome other members to similarly let us know of their charitable activities, and if possible route them thru ISPAE. As you know, donations to ISPAE are exempt from income tax under section 80 G; this could be an added incentive to your donors.

## FORTHCOMING MEETINGS

1. Update on Pediatric Endocrinology: Dept of Endocrinology, Osmania General Hospital and Osmania Medical College, Hyderabad: 24 April 2011. Details below. Contact: Sri Nagesh, 09885646917 or 7842901608, email: vsrinagesh@gmail.com; pedendoupdate2011@gmail.com.
2. ENDO 2011: Annual Meeting of the Endocrine Society (USA): Boston, Mass, USA. 4-7 June, 2011.
Email: societyservices@endo-society.org
3. EASD 2011: 47th Annual meeting: Lisbon, Portugal: 12-16 September, 2011.
4. ESPE 2011: 50th ESPE Meeting: Glasgow, Scotland: 25-28 Sep, 2011. Theme: 'Evidence-based Pediatric Endocrinology – its strengths and limitations'. http://www.eurospe.org/meetings/; www.eurospe.org
5. ISPAD 2011: 37th Annual Meeting: Miami, USA: 19-22 October 2011. Contact Dr Alan Delamater, ADelamater@med.miami.edu
6. RSSDI 2011: 39th Annual Conference of RSSDI: 4-6 November 2011, Mumbai. www.rssdi2011.org
7. PET 2011: Pediatric Endocrine Training Program: Calicut, Kerala: 22-25 November 2011. Contact: M Vijayakumar, drmvijaycalicut@gmail.com
8. ISPAE 2011: 2nd Biennial Meeting: Calicut, Kerala: 25-27 Nov 2011. Contact: M Vijayakumar, drmvijaycalicut@gmail.com
9. ESICON 2011: Annual Meeting of the Endocrine Society of India: Pune: 1-3 Dec 2011. Contact Col Narendra Kotwal, narendrakotwal@gmail.com or esicon2011@gmail.com. Website: esicon2011.com.
10. World Diabetes Congress: 4-8 December 2011, Dubai, UAE. Email: YouthLeadersDubai2011@idf.org
11. PEDICON 2012: 49th Annual Meeting of IAP: Gurgaon: 19-22 January 2012. Contact Mahaveer P Jain, info@pedicon2012.com; pedicon2012@gmail.com.
12. LWPES 2012: Annual Meeting of the Lawson Wilkes Pediatric Endocrine Society (USA): Boston, Mass. 28 April-1 May, 2012.
13. ENDO 2012: Annual Meeting of the Endocrine Society: Houston, Texas, USA. 23-26 June, 2012. Email: societyservices@endo-society.org
14. ESPE 2012: 51st ESPE Meeting: Leipzig, Germany: 20-23 September, 2012. Email: espe@eurospe.org
15. APPES: 7TH Biennial Scientific Meeting: Bali, Indonesia: email: appes@willorganise.com.au
16. LWPES 2013: Annual Meeting of the Lawson Wilkes Pediatric Endocrine Society (USA): Washington DC. 4-7 May, 2013.
17. ENDO 2013: Annual Meeting of the Endocrine Society: San Francisco, USA. 15-18 June, 2013. Email: societyservices@endo-society.org
18. ESPE-LWPES: 9th Joint ESPE/ LWPES Meeting: Rome, Italy: 19-22 September, 2013. Email: espe@eurospe.org
19. LWPES 2014: Annual Meeting of the LWPES: Vancouver, Canada. 3-6 May, 2014.
20. ENDO 2014: Annual Meeting of the Endocrine Society: Chicago, USA. 21-24 June, 2014. Email: societyservices@endo-society.org
21. ESPE: 53rd ESPE Meeting: Dublin, Ireland: 18-21 September, 2014. Email: espe@eurospe.org
22. LWPES 2015: Annual Meeting of the LWPES: San Diego, CA. 25-28 April, 2015.
23. ENDO 2015: Annual Meeting of the Endocrine Society: San Diego, CA. 20-23 June, 2015. Email: societyservices@endo-society.org
24. ESPE: 54th ESPE Meeting: Barcelona, Spain: 9-12 September, 2015. Email: espe@eurospe.org

## NOTES & NEWS

*Sudha Rao, c_sudha@hotmail.com*

The **Indian Academy of Pediatrics** (IAP) has formulated an **"Essential Medicine List for Children"** in collaboration with World Health Organization. I represented our Chapter in the preparation of the list from an endocrine perspective. Each specialty list has a Core list (essential) and a Supplementary list, e.g. drugs like glucocorticoids and thyroxin are in the core list, while drugs like growth hormone, bisphosphonates, and medroxyprogesterone acetate are in the supplementary list. This novel initiative of IAP and WHO to make a national list of medicines for

children is to be an ongoing process, with lists revised every three years. We hope it will be useful to one and all.

PUBLICATIONS FROM KARGER

SERIES:

1. Yearbook of Pediatric Endocrinology 2010: Ed: Jean –Claude Carel & Ze'ev Hochberg.
2. Endocrine Development: Series Ed: P-E Mullis.
   Vol 18: Current Indications for Growth Hormone Therapy, Ed PC Hindmarsh
   Vol 17: Pediatric Neuroendocrinology: Ed: S Loche, M Cappa, L Ghizzoni, M Maghnie, MO Savage.
   Vol 16: Calcium & Bone Disorders in Children & Adolescents: Ed J Allgrove, NJ Shaw.

BOOKS:

1. Adipose Tissue Development: From Animal Models to Clinical Conditions: Ed Claire Levy-Marchal & Luc Penicaud.
2. Cytokines, Growth Mediators and Physical Activity in Children during Puberty. Ed: J Jurimae, AP Hills, T Jurimae.

## DIABETES QUIZ

*Ganesh Jewalikar, g_jewlikar@yahoo.co.in*
*(Please send answers to this email id)*

** Which of the following HLA types is highly protective of Type 1 Diabetes?

a. HLA-DQB1*0602
b. HLA-DR4
c. HLA-DQB1*0302
d. HLA-DQA1*501

** Which of the following is not a good choice of treatment of hypoglycemia?

a. Cold drinks
b. Glucose biscuits
c. Sucrose
d. Ice-cream

** Which of the following is not true in case of type 2 diabetes in children?

a. Family history of diabetes is very common
b. Hyperosmolar hyperglycemic state is an exclusive feature of type 2 diabetes
c. Ketoacidosis is not an initial presentation
d. Low birth weight is a risk factor

** A 10 kg child was admitted with diabetic ketoacidosis with 5 % dehydration. His fluid correction was planned over 48 hrs. He had received 300 ml of normal saline as boluses in outside hospital. His fluid requirement over next 48 hr will be

a. 2.5 L
b. 2.2 L
c. 2.8 L
d. 1.5 L

** One carbohydrate exchange equals how many grams of carbohydrate?

a. 10 gm
b. 15 gm
c. 20 gm
d. 25 gm

## Farewell, Dear Friend

I write these words with a heavy heart. On 13th April we received the sad news that our colleague and friend, Amita Shah, endocrinologist in Baroda, succumbed to the brain tumor which so rapidly gripped her over the last year. Amita was in the first batch of DM students at SGPGI. Intelligent, talented, conscientious, so full of life…..I can picture her neat, tiny handwriting on her detailed case sheets and the transparencies (yes, those were days of overhead projectors and transparencies), where every square centimeter was covered with tables and diagrams, to make her lucid presentations even more complete. She continued to maintain contact with the department after passing out, and we watched with admiration as she acquired a reputation as an accomplished endocrinologist. She built up a formidable endocrine practice in Baroda, but just as easily shifted to Chennai for a few years so that the family could be together while her husband Shaunak acquired advanced training and experience in cardiac surgery.

We discovered the power of the internet together; I would describe the huge changes brought about by email and internet in SGPGI, and she would describe how advanced the south of India had become in IT facilities, and how fascinating it was to "google" out information. Why do I remember this particularly? I guess because of what she once said to me when she had consulted on a particularly sick baby in the neonatal ICU: "….they trust me so much….I have to read, I can't be wrong…". Amita never stopped doing the best for her patients.

It will be difficult to come to terms with her loss. We can only pray for strength to Shaunak and her 2 lovely daughters.

Vijayalakshmi Bhatia