1th International Conference on:

THE DIAGNOSIS, MANAGEMENT AND TREATMENT OF HYPOPARATHYROIDISM

HIGHLIGHTS

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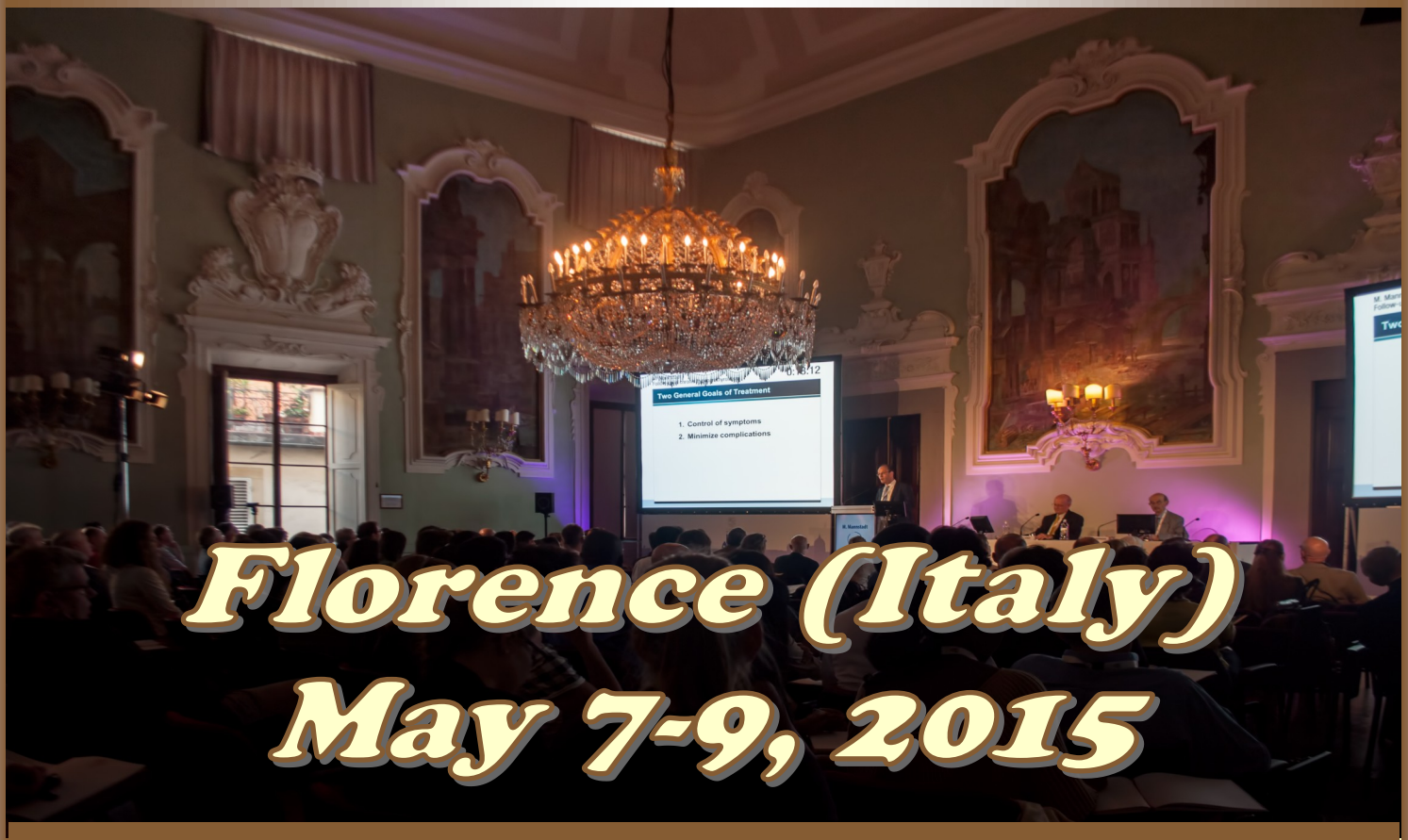


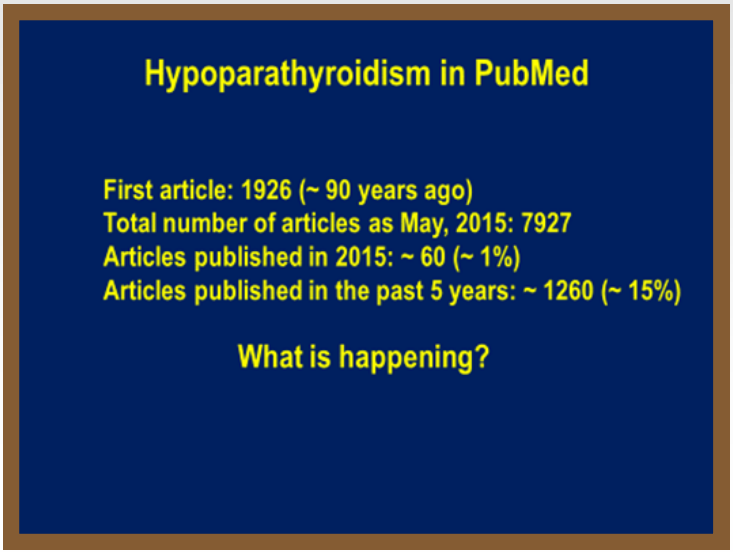
Florence (Italy)
May 7-9, 2015

HIGHLIGHTS

Maria Luisa Brandi
Florence, I

What is happening?

Prof. Maria Luisa Brandi of Florence opened the proceedings, stressing the importance of this meeting: the first international conference bringing together the world's foremost researchers to discuss diagnosis, management and treatment of hypoparathyroidism. The work of the conference was enlivened by panel meetings on the major themes discussed at the plenary session, which aimed at producing joint documents, true points of reference for new shared guidelines for hypoparathyroidism management. The event accompanies the scientific community's renewed interest in a condition that has been "forgotten" for too many years. What is happening?



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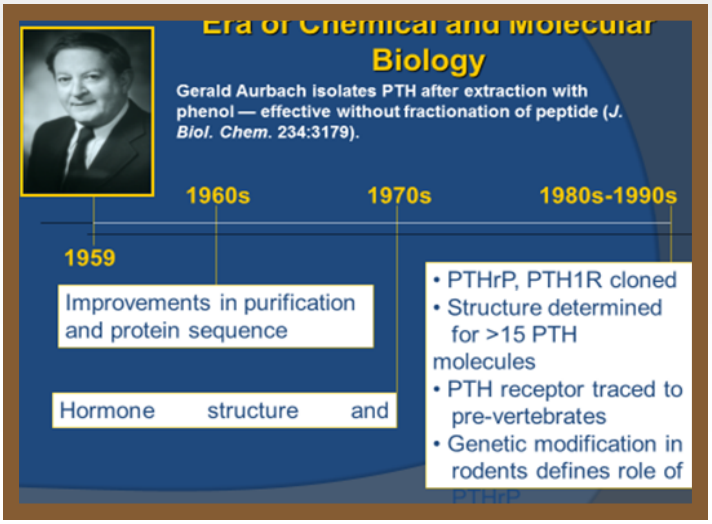
To listen to the speech by Prof. Brandi opening the Conference proceedings, go to www.fondazione-menarini.it/... Register at the site to access the multimedia material.

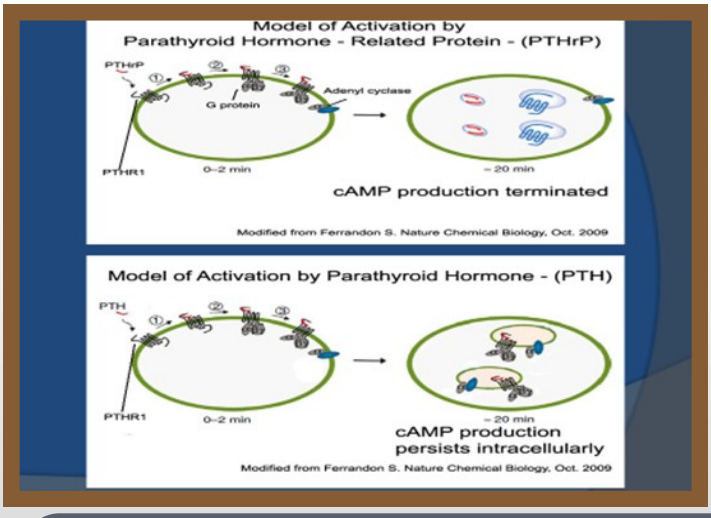
HIGHLIGHTS

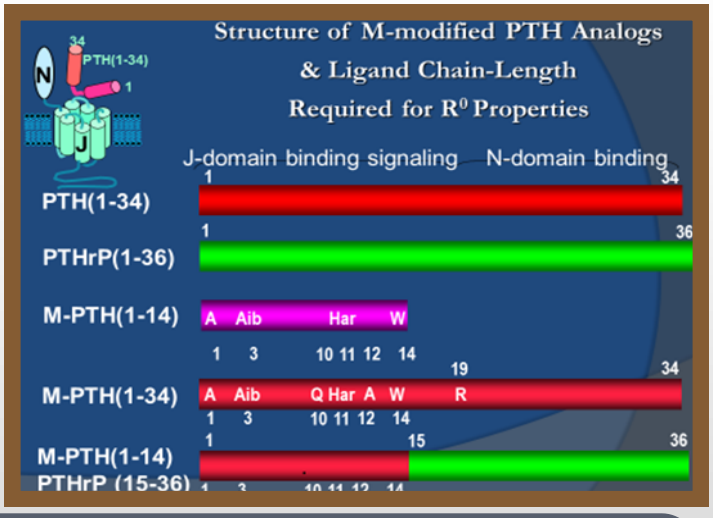
John T. Potts Jr.
Boston - USA

The history of the parathyroid glands, from 1880 to the present

A 135-year-old controversy is at the root of the progress that has been achieved above all in recent decades. Thus Prof. Potts of Boston introduced his address to the plenary session, which reviewed the history of the parathyroid glands. Since the times of their discoverer Dr. Ivar Sandström, long periods of almost total disinterest in the subject have alternated with bursts of concerted study activity that have produced significant advances in terms of understanding the physiological and clinical roles of these glands. Then came in-depth study of the ligand-receptor binding mechanisms that opened the way to discovery of new drugs, parathyroid hormone analogs. The real advances were made in the 1990s, with cloning of two parathyroid hormone ligands: PTHrP and PTH1R. Studies conducted over the last 15 years have furthered our knowledge of the cellular and molecular mechanisms of the two molecular forms of the hormone, which bind to the same receptor and determine different biological effects. This phenomenon is also known as the "Parathyroid Hormone Paradox."







How is it possible that two similar molecules bind to the same receptor and determine such profoundly different biological effects? - What are the principal parathyroid hormone analogs currently under study? - What are their effects on hypoparathyroid states?

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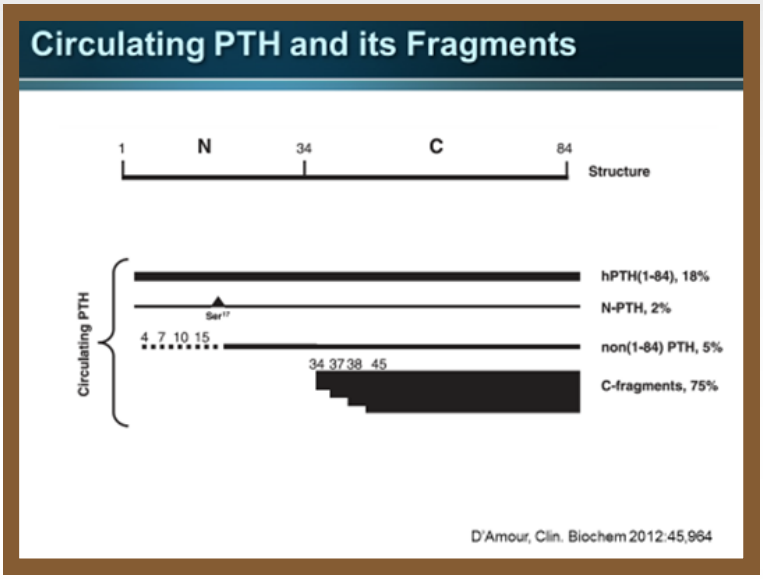
To find answers to these and other interesting queries and for more in-depth information, go to www.fondazione-menarini.it/... Register at the site to access the multimedia material.

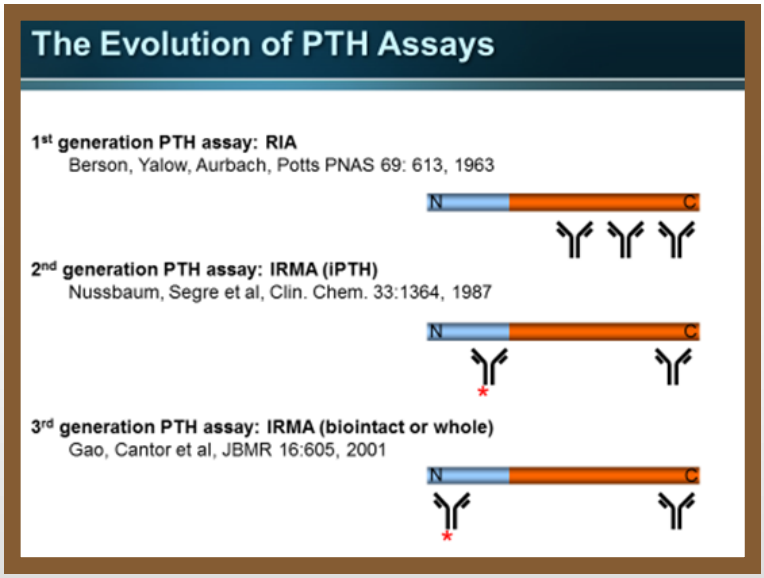
HIGHLIGHTS

Michael Mannstadt
Boston - USA

Is diagnosis of hypoparathyroidism always a linear process?

Prof. Mannstandt of Boston spoke on the subject of diagnosis of hypoparathyroidism using specific diagnostic kits for determining levels of parathyroid hormone in the blood. The difficulties encountered by diagnosis are due to the presence, in the blood, of inactive fragments of PTH that assay out together with functionally active parathyroid hormone. In other words, the concentration of circulating PTH is not always indicative of the real active fraction of the hormone. Which organs are the major secreters of circulating PTH fragments? Since 1963, three diagnostic tests for assaying circulating PTH levels have been produced; in order of time, they are based on the RIA technique, on synthesis of an immuno-PTH (iPTH), and on synthesis of a "whole" or "biointact" immuno-PTH.





How reliable are these tests? - - - What do they really measure? - - - What is the role of the third-generation iPTHs and what are the major differences with respect to the second generation?

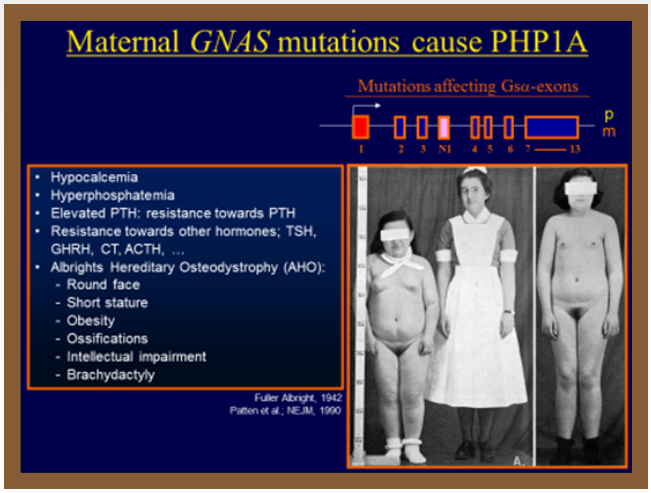
To find answers to these and other interesting queries and for more in-depth information, go to www.fondazione-menarini.it/... Register at the site to access the multimedia material.

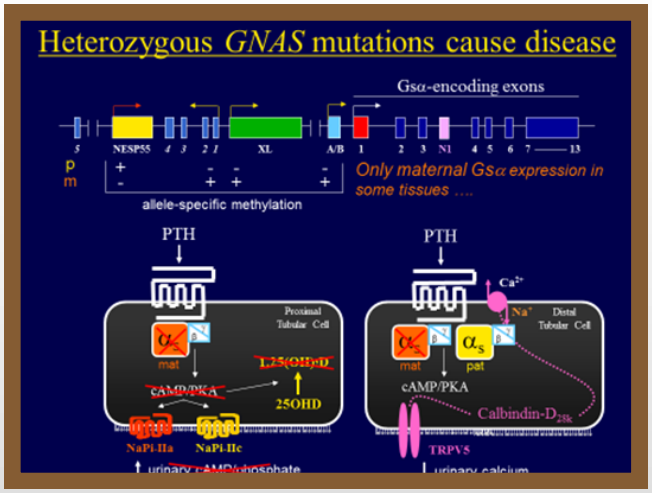
HIGHLIGHTS

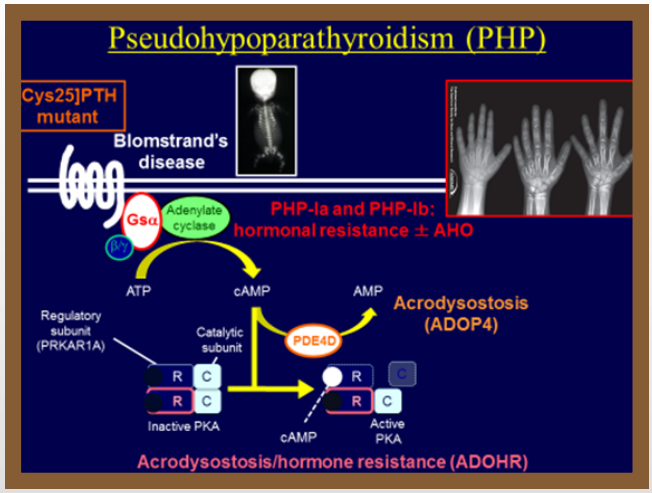
Harald W. Juppner
Boston - USA

Pseudohypoparathyroidism: a single syndrome with different, genetically-determined phenotypical manifestations

Prof. Juppner of Boston presented recent data on this important theme. Pseudohypoparathyroid states are associated with serious pathological manifestations such as Albright's Hereditary Osteodystrophy, multiple hormone resistance, mental retardation, hypocalcemia, and hyperphosphatemia. Behind these clinical pictures are specific mutations of the GNAS gene, which is fundamental for cell-level regulation of various hormones, including PTH. These mutations can be genetically transmitted via the paternal or maternal line, even in conditions of heterozygosity. Mutations transmitted through the paternal line generally manifest with less serious pathological pictures than do mutations transmitted through the maternal line. The principal forms of pseudohypoparathyroidism are PHP1A and PHP1B. The clinical pictures are mainly coincident, although with certain significant differences linked above all to the presence or lack of PTH resistance, a factor which has a significant effect on the phenotypic manifestation of the condition in terms of varying degrees of severity, from Albright's syndrome in its classic pathological presentation to forms of pseudohypoparathyroidism with no somatic manifestations.







What are the biohumoral parameters specific for diagnosis of pseudohypoparathyroidism? - - - What are the principal genetic mutations? - - - What are the genetic differences that determine the different forms of pseudohypoparathyroidism?

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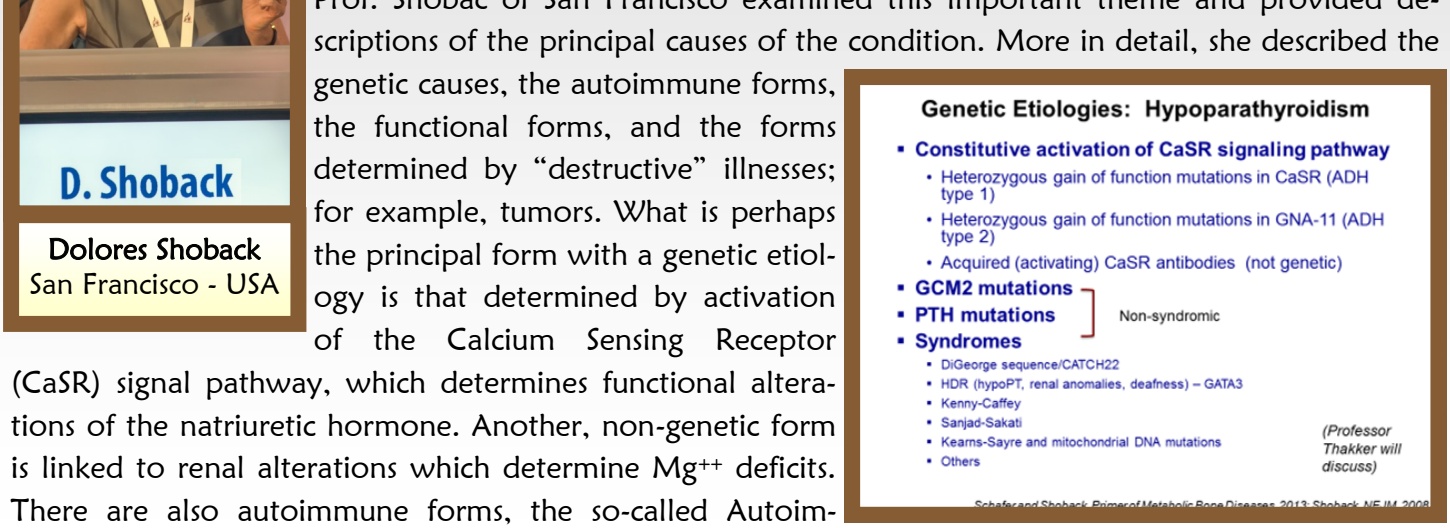
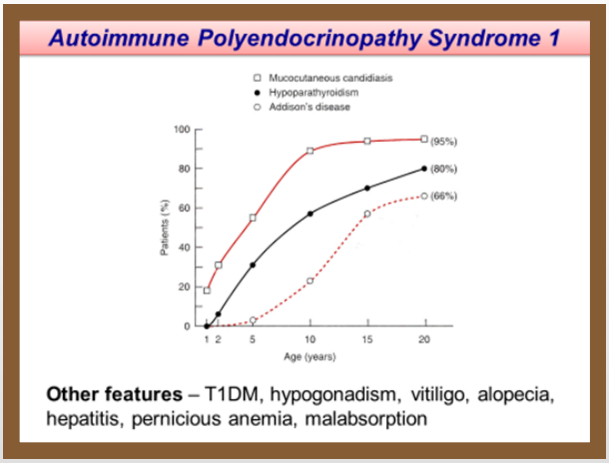
HIGHLIGHTS

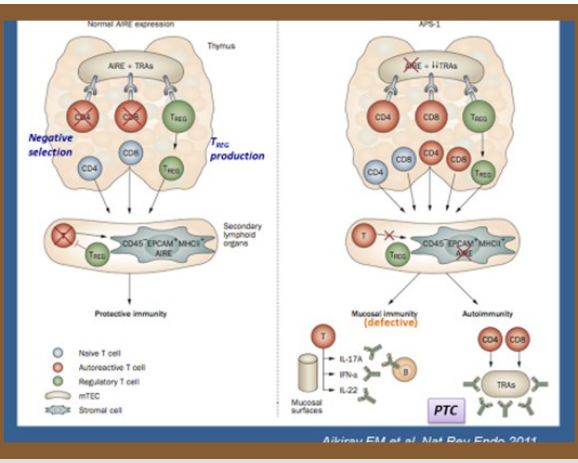
Dolores Shoback
San Francisco - USA

Hypoparathyroidism: a condition with many possible causes

Prof. Shobac of San Francisco examined this important theme and provided descriptions of the principal causes of the condition. More in detail, she described the genetic causes, the autoimmune forms, the functional forms, and the forms determined by "destructive" illnesses; for example, tumors. What is perhaps the principal form with a genetic etiology is that determined by activation of the Calcium Sensing Receptor (CaSR) signal pathway, which determines functional alterations of the natriuretic hormone. Another, non-genetic form is linked to renal alterations which determine Mg^{++} deficits. There are also autoimmune forms, the so-called Autoimmune Polyendocrine Syndrome or APS1, characterized by the simultaneous presence of hypoparathyroidism, Addison's Disease, and mucocutaneous candidiasis, the principal defect of which is characterized by mutations in the AIRE system, the gene-level autoimmune regulator of endocrine functions. The pathogenesis of this form is undoubtedly complex. There are also forms of a hypoparathyroidism defined as "destructive"; for instance, in the case of various forms of cancer. One of the main forms is secondary to the presence of β-thalassemia, in which case, however, control of the disorder via transfusions significantly reduces the risk of hypoparathyroidism.







How advanced are studies concerning the function of the AIRE system? - - - Which autoantibodies are involved? - - - What pathological forms are instead linked to disorders of renal regulation of magnesium absorption?

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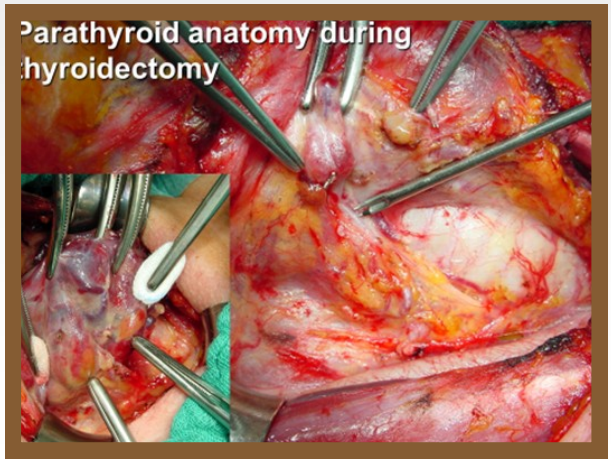
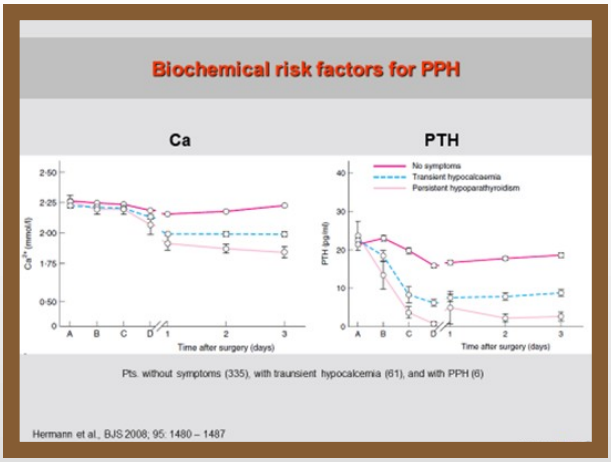
HIGHLIGHTS

Henning Dralle
Halle/Saale, D

Permanent postoperative hypoparathyroidism

Prof. Dralle of the University of Halle explored the theme of permanent hypoparathyroidism pursuant to thyroidectomy. This adverse effect of this surgical procedures is linked to the anatomy of the parathyroid glands. They are small glands embedded within or behind the thyroid; hence, the operating space between the thyroid tissue and the parathyroid glands is very limited. Another problem, typical of surgery on very young patients, is the difficulty of identifying the parathyroid glands amidst the thyroid gland tissue. Nor should we forget that at least 20% of the parathyroid gland tissue is located ectopically; for example, in the thymus or behind the esophagus; this factor certainly does not aid surgeons to preserve parathyroid tissue while operating. It is very important to check calcium and PTH levels on the first post-operative day; below-normal values for either parameter constitute a significant risk factor for hypoparathyroidism, independently of the absence/presence of symptoms. The surgeon's experience, the type of operation, and the method used during the operation to safeguard the parathyroid glands are all factors which can significantly influence the risk of permanent postoperative hypoparathyroidism.





Surgical risk factors for PPH

- surgeon experience
- extent of surgery/disease
- unintentional PTx
- vascularization of PG
- autotransplantation of PG
- number of in situ preserved PG

What solutions to these problems does Prof. Dralle propose?

What are the most efficacious surgical aids?

HIGHLIGHTS

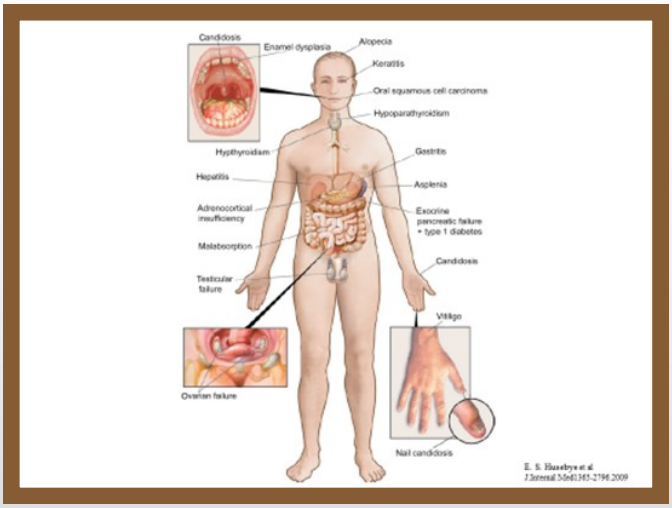
Karen K. Winer
Bethesda - USA

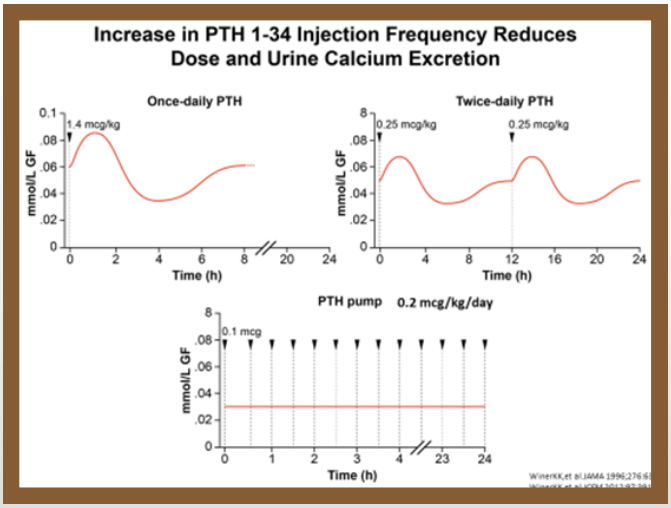
Resistant Hypoparathyroidism

Prof. Winer of Bethesda spoke on this important topic, presenting interesting data on innovative treatment options. In particular, she discussed congenital autoimmune forms of hypoparathyroidism, of which Autoimmune Polyglandular Syndrome, also called APS-1, is a representative example. Patients affected with this form exhibit the classic triad of mucocutaneous candidiasis, hypoparathyroidism, and Addison's Disease in addition to deficits affecting other vital organs which determine onset of hypothyroidism, Type 1 diabetes, and gonadal deficit. Treatment of these patients is complex, since the "treatment window" is very narrow. These patients need high doses of PTH, frequent IV administrations of calcium and high doses of calcitriol, although the complications of such treatment can include nephrocalcinosis and hypercalciuria. Maintaining the calcium balance is, obviously, a central issue in management of such patients.

Type 1 Autoimmune Polyglandular Syndrome (APS-1)
Autoimmune Polyendocrinopahy Candidiasis Ectodermal Dystrophy (APECED)

- Classic Triad: At least 2 of the following
  - Mucocutaneous Candidiasis
  - Hypoparathyroidism
  - Addison's Disease (Primary Adrenal Insufficiency)
- Autoimmune regulator gene (AIRE) mutations
  - AIRE gene modulates transcription of peripheral self-antigens in the thymus





How can we deal with and resolve these problems?

Are there efficacious, safe treatment protocols for these patients?

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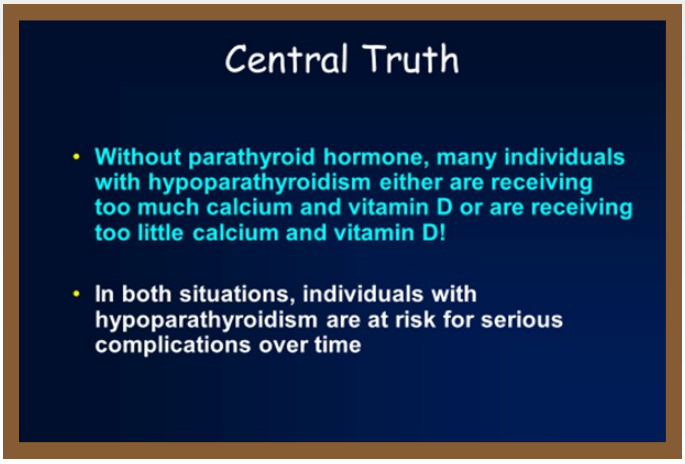
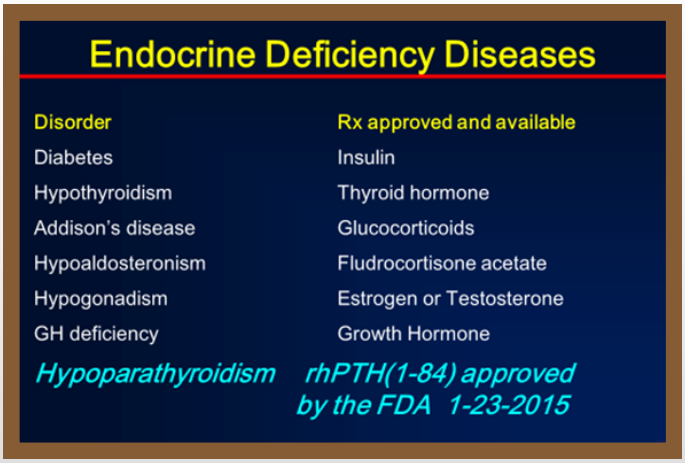
HIGHLIGHTS

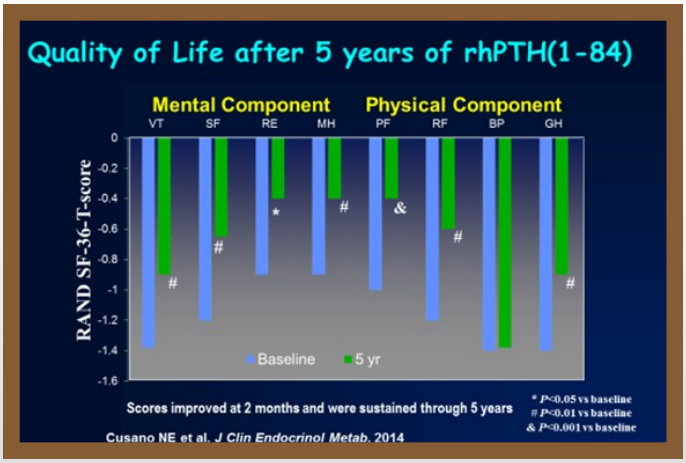
John P. Bilezikian
New York - USA

Replacement therapy with PTH peptides

Prof. Bilezikiandi of New York explained this important, innovative technique. The central problem linked to replacement therapy is adequate management of calcium and Vitamin D dosage, and this is not always an easy goal to attain. How much Vitamin D need we administer to these patient for adequate control of calcemia and what is the price they pay? How can we counteract the negative effects of this replacement therapy on bone metabolism? How can we maintain quality of life at acceptable levels? According to Prof. Bilezikian, the real problem is that patients affected with hypoparathyroidism often receive excessively high or insufficient doses of calcium and Vitamin D and, in both cases, the outcome for their health can be serious. Hypoparathyroidism is the only specific hormonal deficit disorder not currently treatable via a well-defined hormone replacement therapy. Or at least this was true until today, since in January 2015 the FDA approved marketing of a new releasing hormone denominated rhPTH (1-84) for use in treatment of patients with hypoparathyroidism.







What data have been published on this new treatment adjunct? - - - What is its effect on bone metabolism? - - - What is its effect on calcemia? - - - And on quality of life?

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HIGHLIGHTS

"We have a Plan for Patients and Doctors"

At the end of the meeting sessions, Prof. Brandi closed the Conference with these words: **"Now, we have a plan for patients and for our endocrinologist colleagues. For patients, to improve their treatment and optimize their quality of life so that it will be rarer to find people diagnosed with hypoparathyroidism. For the doctors, to help them further their knowledge of this important subject: hypoparathyroidism. This discussion we completed today must not remain within strictly scientific bounds but must be communicated to the social sphere."**

These are just a few of the subjects touched on during the Conference work. For more information, consult the Fondazione Internazionale Menarini website, where you'll find full-text versions of all the papers presented to the Conference. Go to www.fondazione-menarini.it/.... Register at the site to access the multimedia material.

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