MOTORE SANITÀ
Cure the Future

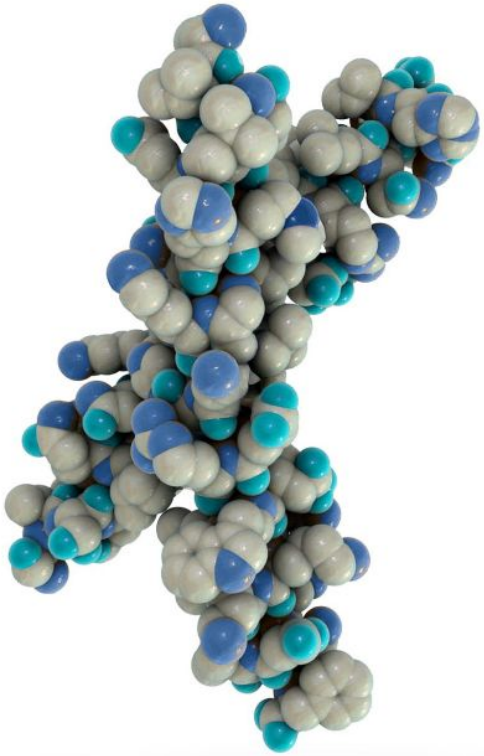
Innovazione organizzativa
nei percorsi di diagnosi,
cura, follow-up

Focus on
IPOPARATIROIDISMO

REGIONE PIEMONTE

TORINO
NH Hotel Santo Stefano
Via Porta Palatina, 19

9 GIUGNO 2025
dalle **10.00** alle **13.30**



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Ipoparatiroidismo nel contesto delle malattie rare endocrinologiche

malattie rare

Rete Interregionale per le Malattie Rare del Piemonte e della Valle d'Aosta

Cosa sono le malattie rare

Per malattia rara si intende una patologia che colpisca meno di 5 persone su 10.000 nella Comunità Europea.

L'Organizzazione Mondiale della Sanità (OMS) stima che esistano dalle 6000 alle 8000 differenti malattie rare e che circa il 10% della popolazione mondiale sia affetto da una qualche malattia rara.

La rarità di tali patologie fa si che i pazienti che ne sono affetti sperimentino maggiori problematiche rispetto ai pazienti affetti da patologie comuni sia per le **difficoltà diagnostiche** e le **carenze di informazione** anche fra gli operatori sanitari, sia per la carenza di **opzioni terapeutiche**, soprattutto farmacologiche sia per l'impatto emotivo e il **vissuto di isolamento** che affligge i pazienti e i loro familiari.

Oltre a queste caratteristiche, si tratta spesso di malattie che **minacciano la vita** o che sono **cronicamente debilitanti**.

Per affrontare questo gruppo di malattie occorre un particolare **impegno congiunto**, una **conoscenza specifica** ed una **informazione capillare**.

In Italia il Decreto Ministeriale 279 del 2001 ha cercato di fornire le prime risposte concrete ai pazienti affetti da malattia rara. In particolare:

1) ha identificato **341 malattie o gruppi di malattie** rare ritenute **meritevoli di esenzione** dai costi sanitari per le prestazioni comprese all'interno dei **Livelli Essenziali di Assistenza** (LEA). Nel 2005 e nel 2007 prima la Regione Piemonte e successivamente la Regione Valle d'Aosta hanno esteso l'esentabilità ad altre 40 patologie (**NB:** queste patologie sono esentate solo in Piemonte e in Valle d'Aosta); il DPCM del gennaio 2017, ha aggiornato i LEA e ridefnito, all'Allegato 7, il numero delle patologie esentate dalla compartecipazione al costo, che è salito a 456.

2) ha identificato le caratteristiche necessarie per la realizzazione della **Rete nazionale per la prevenzione, la sorveglianza, la diagnosi e la terapia delle malattie rare**. La Regione Piemonte e la Regione Valle d'Aosta hanno successivamente recepito il Decret e, a partite dal 2008 una **Rete interregionale per le Malattie Rare**

3) ha istituito un **registro nazionale** pazienti affetti da malattia rara con sede presso l'Istituto Superiore di Sar

RETE

Rete assistenziale e di ricerca

Rete assistenziale

Percorsi e raccomandazioni

Integrazione tra le Reti Europee di Riferimento (ERN)e la Rete per le Malattie Rare del Piemonte e Valle d'Aosta

Attività formative e di Ricerca

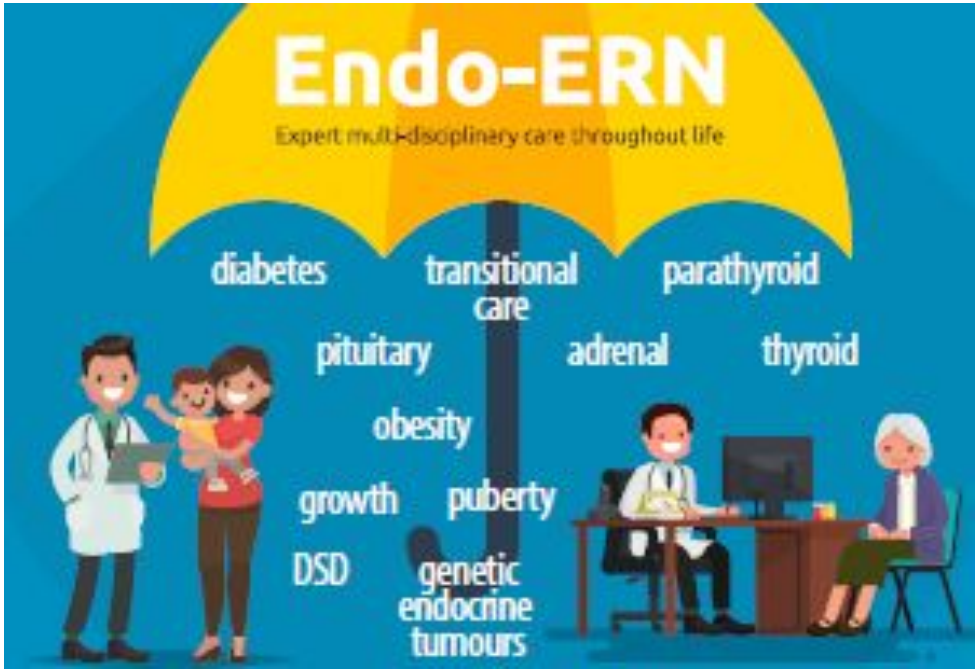
Pubblicazioni

European Reference Network on Rare Endocrine Conditions

European Reference Network

ESPE European Society for Paediatric Endocrinology

European Society of Endocrinology



Diseases/Conditions Covered by the Network

1: Adrenal: hyperadrenalism, hypoadrenalism/ adrenal cortical cancer.

2: Calcium and phosphate homeostasis: hypoparathyroidism, and other disorders further to be determined associated with calcium and phosphate homeostasis.

3: Glucose & insulin homeostasis: genetic diabetes (Sweet consortium); Syndromic obesity (Prader Willi network); Lipodystrophy

4: Growth: congenital growth disorders, acquired growth disorders, other disorders further to be determined

5: Pituitary: pituitary adenoma; aggressive pituitary tumors; hypothalamic-suprasellar tumors; congenital hypopituitarism, acquired hypopituitarism; hypophysitis,

6: Sex development and maturation: Chromosomal DSD, XX-DSD, XY-DSD (DSDnet); hypogonadotropic hypogonadism / Kallmann syndrome (GnRHnet); gender dysphoria

7: Thyroid: congenital hypothyroidism, TH signaling defects, central hypothyroidism IGSF1, thyroid cancer

8: Genetic endocrine tumour syndromes: multiple endocrine neoplasia type 1, -2. -3 and -4, SDH- and VHL mutations, Carney Complex, McCune-Albright syndrome, to be further completed

Ipoparatiroidismo: cause genetiche

Table 3 Genetic causes of hypoparathyroidism – key clinical findings and lab tests.

Disorder	Clinical or laboratory features prompting consideration of specific genetic or other types of testing	Molecular defect	Genetic and other testing to establish diagnosis
Autosomal dominant hypoparathyroidism (ADH) type 1 and 2	Typically asymptomatic or mild hypocalcemia with or without hypercalciuria (ADH types 1 and 2)	Gain of function mutation in CASR (type 1) or G alpha 11 (type 2)	CASR or GNA11 sequencing
ADH type 1 with Bartter's syndrome type 5	Hypocalcemia, hypomagnesemia, hypokalemia, alkalosis, hypercalciuria, and salt and water depletion may be seen depending on the severity	CASR	CASR sequencing
Isolated hypoparathyroidism	Presentation dominated by biochemical and clinical features of hypoparathyroidism		PTH, GCM2, sequencing depending on presentation
Autosomal recessive		PTH or GCM2	
Autosomal dominant		PTH or GCM2	
X-linked recessive		SOX3 locus (in males)	
Hypoparathyroidism of autoimmune etiology			
Autoimmune mediated			
Autoimmune polyendocrine syndrome type 1 (APS1)	Other autoimmune diseases and features such as mucocutaneous candidiasis, adrenal insufficiency and hypogonadism	Usually due to homozygous mutations in AIRE	AIRE sequencing Presence of 21-hydroxylase antibodies supports diagnosis of autoimmune adrenal insufficiency Testing for other hormonal insufficiency states (e.g., adrenal and gonadal insufficiency)
Isolated	May show only hypoparathyroidism	AIRE mutations or of unknown etiology	AIRE sequencing

APS tipo I

	PAS type I	
Prevalence	Very rare	
Incidence	<1:100 000/year	
M/F ratio	3:4	
Onset	Childhood	
Inheritance	Monogenic (*AIRE* gene)	
Autoimmune endocrine diseases	Hypoparathyroidism (80–85%)	(before the age of 10 years
	Addison's disease (60–70%)	(before the age of 15 years
	Type 1 diabetes (<20%)	
	Hypogonadism (12%)	
	Thyroid disease (10%)	
Concomitant disease	Mucocutaneous candidiasis (70–80%)	(before the age of 5 years)
Non-endocrine diseases	Immune gastritis, pernicious anemia, celiac disease, immune hepatitis, vitiligo, alopecia areata, Sjögren's syndrome, systemic lupus erythematodus, rheumatoid arthritis, myasthenia gravis	

Also known as **APECED** (candidiasis and ectodermal dystrophy), is a juvenile monogenetic syndrome with an autosomal recessive transmission.

The highest prevalence has been found in populations with a high degree of kindred ship or descendants of small founder populations such as Iranian Jews (1:600 to 1:9000) and Finns (1:25,000).

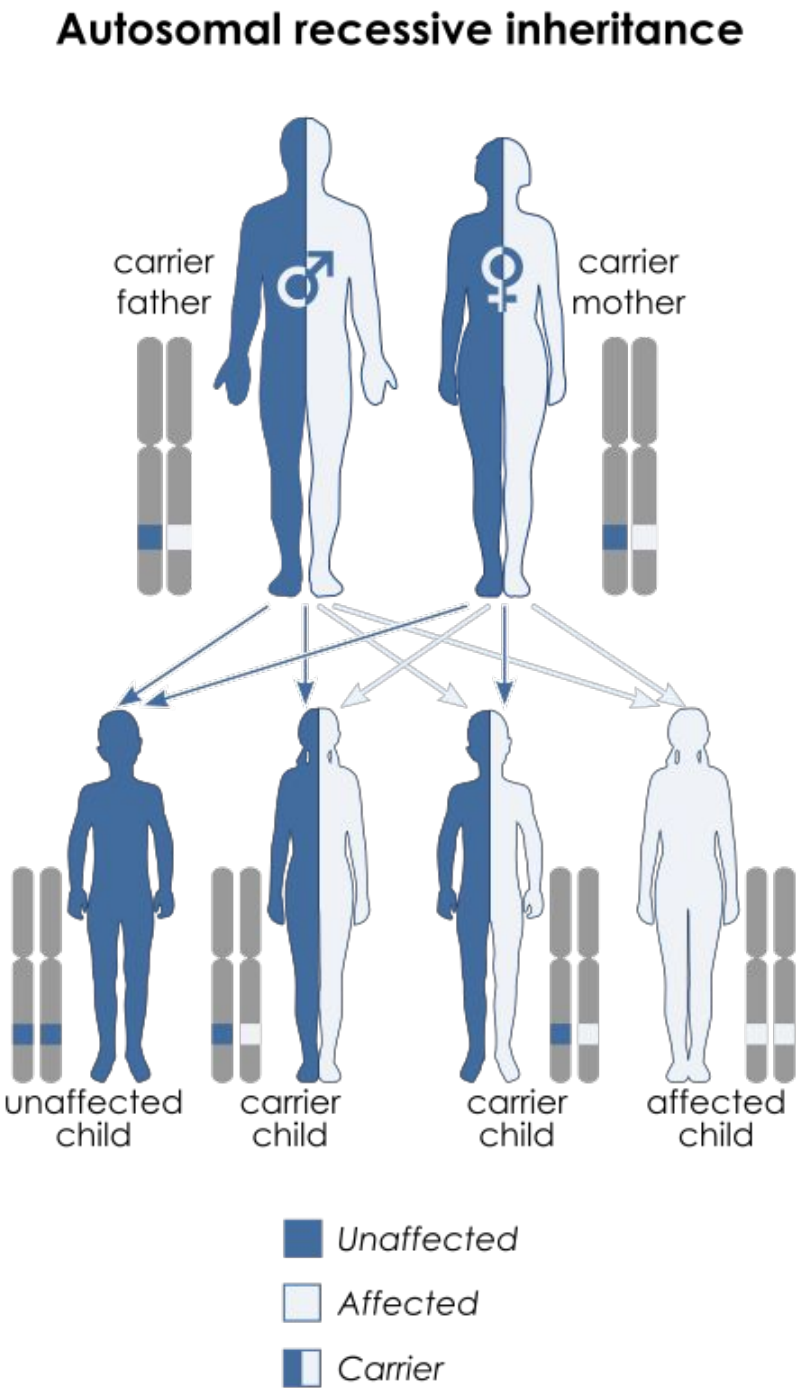
It is related to the **autoimmune regulator (AIRE) gene**, located on the long arm of chromosome 21, involving 14 exons.

Autosomal recessive inheritance.

The AIRE gene codes for the AIRE protein, a transcription factor, which interferes with immune regulation, and contributes to the negative selection of autoreactive thymocytes.

AIRE also regulates reactions against microbial agents, especially against mycosis.

AIRE deficiency contributes to an alteration in the intracellular communication between monocytes and T helper (Th) cells.



	Adult		
AP (ORPHA: 282196) Subtypes	**II (ORPHA:3143)**	**III (ORPHA:227982)**	**IV (ORPHA:227990)**
Prevalence	1:20,000		
Sex ratio (male/female)	1:3		
Onset	Adulthood		
Endocrine disorders / manifestations	AD Hypoparathyroidism AITD T1D	AITD T1D Hypogonadism	Hypogonadism Hypoparathyroidism Hypopituitarism AITD T1D
Non - endocrine disorders / manifestations	Autoimmune gastritis Celiac disease Inflammatory bowel disease Autoimmune pancreatitis Vitiligo Alopecia Urticaria Psoriasis Rheumatoid arthritis	Autoimmune gastritis Pernicious anemia Celiac disease Inflammatory bowel disease Autoimmune pancreatitis Autoimmune hepatitis Primary biliary cirrhosis Vitiligo Alopecia Urticaria Psoriasis Neurodermitis Rheumatoid arthritis Systemic lupus erythematosus Myasthenia gravis Sicca/Sjögren-syndrome	Autoimmune gastritis Pernicious anemia Celiac disease Inflammatory bowel disease Autoimmune pancreatitis Primary biliary cirrhosis Vitiligo Alopecia Urticaria Pemphigus Psoriasis Neurodermitis Myasthenia gravis Sicca/Sjögren syndrome
Inheritance	Polygenic		
HLA haplotypes / *AIRE gene*	*DRB1*04:04-DQA1*03:01-DQB1*03:02*	*DRB1*04:01-DQA1*03:01-DQB1*03:02*	*HLA-DRB1*03:01-DQA1*05:01-DQB1*02:01*
Single nucleotide polymorphisms	*PTPN22+1858 C/T (rs2476601), CTLA-4 C/T60 (rs3087243), Bsm I (rs1544410), Aps I (rs7975232), Taq I (rs731236), IL2-Ra CD25 (rs10795791), TNF-α -308 (rs1800629)*		
Auto-antigens	21-OH CaSR TSH-R TPO Tg GAD Insulin IA-2 Islet cell ZnT8	TSH-R TPO Tg GAD Insulin IA-2 Islet cell ZnT8	17-OH CaSR TSH-R TPO Tg GAD Insulin IA-2 Islet cell ZnT8

Table 3 Genetic causes of hypoparathyroidism – key clinical findings and lab tests.

Disorder	Clinical or laboratory features prompting consideration of specific genetic or other types of testing	Molecular defect	Genetic and other testing to establish diagnosis
Hypoparathyroidism, deafness, renal anomalies (HDR) syndrome	Sensorineural deafness, renal anatomic abnormalities and renal dysfunction, autosomal dominant inheritance	GATA3	GATA3 sequencing, hearing testing, renal imaging
DiGeorge syndrome	Cardiac defects (present in ~80% including ventriculoseptal defect, tetralogy of Fallot, interrupted aortic arch, truncus arteriosus), immunodeficiency (recurrent infections, thymic hypoplasia or aplasia, T cell lymphopenia), hypoparathyroidism, pharyngeal and laryngeal abnormalities, cleft palate, behavioral and psychiatric problems, ophthalmic anomalies, hearing loss	Variety of defects and deletions and microdeletions in chromosome 22q11.2	Fluorescence in situ hybridization (FISH) is the traditional test most commonly done Two other diagnostic approaches are used with greater frequency than FISH including PCR-based multiplex ligation-dependent probe amplification and SNP) array. In some case, TBX sequencing is done
Kenny–Caffey syndrome			
Type 1 or Sanjad–Sakati syndrome (autosomal recessive)	Short stature, growth retardation, small hands and feet, cortical thickening and medullary stenosis of the long bones, delayed fontanelle closure, abnormal eyes, dysmorphic facies, hypoparathyroidism	TBCE	TBCE sequencing
Type 2 (autosomal dominant)	Gracile bone dysplasia, short stature with cortical thickening and medullary stenosis of tubular bones, delayed closure of anterior fontanelle, eye abnormalities, and hypoparathyroidism	FAM111A	FAM111A sequencing

Table 3 Continued.

Disorder	Clinical or laboratory features prompting consideration of specific genetic or other types of testing	Molecular defect	Genetic and other testing to establish diagnosis
Hypoparathyroidism associated with mitochondrial disorders		Mutations in the mitochondrial genome	Mitochondrial DNA sequencing
Kearns Sayre syndrome	Ophthalmoplegia, retinal pigmentary and cardiac conduction abnormalities, proximal and bulbar weakness, possibly ataxia	mtDNA large-scale deletion	Specialized clinical assessments depending on the manifestations (cardiac, ophthalmologic, neurologic, endocrinologic and others)
MELAS	Encephalomyopathy, lactic acidosis, and stroke-like episodes along with external ophthalmoplegia, diabetes, hearing loss, early-onset stroke symptoms, migraine, and cognitive dysfunction	Mutations in the mitochondrial tRNA Leu gene	
MTPDS	Disordered fatty acid oxidation associated with neuropathy, retinopathy and fatty liver	Mutations in mitochondrial genome	

Evaluation and Management of Hypoparathyroidism Summary Statement and Guidelines from the Second International Workshop

Aliya A. Khan,[1] John P. Bilezikian,[2] Maria Luisa Brandi,[3] Bart L. Clarke,[4] Neil J. Gittoes,[5] Janice L. Pasieka,[6] Lars Rejnmark,[7] Dolores M. Shoback,[8] John T. Potts,[9] Gordon H. Guyatt,[10] and Michael Mannstadt[9]

J Bone Miner Res. 2022 Dec;37(12):2568-2585. doi: 10.1002/jbmr.4691. Epub 2022 Nov 14.

Standards of care for hypoparathyroidism in adults: a Canadian and International Consensus

European Journal of Endocrinology (2019) **180**, P1–P23

Aliya A Khan[1], Christian A Koch[2], Stan Van Uum[3], Jean Patrice Baillargeon[4], Jens Bollerslev[5], Maria Luisa Brandi[6], Claudio Marcocci[7], Lars Rejnmark[8], Rene Rizzoli[9], M Zakarea Shrayyef[10], Rajesh Thakker[11], Bulent O Yildiz[12] and **Bart Clarke[13]**

Hypoparathyroidism: diagnosis, management and emerging therapies

Sarah Khan[1] & Aliya A. Khan[2]

Nature Reviews Endocrinology | Volume 21 | June 2025 | 360–374

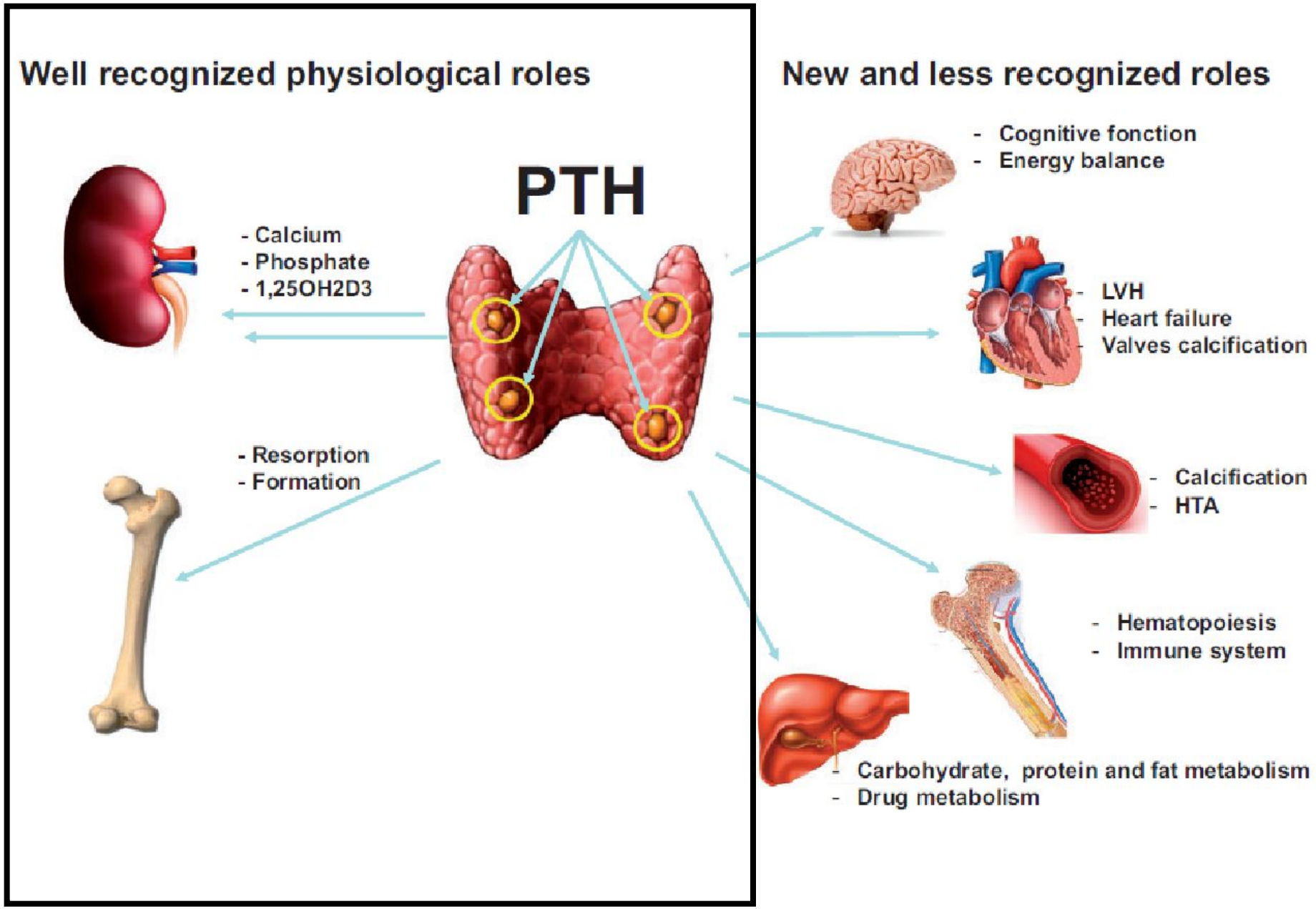
Table 4. Conventional therapy for hypoparathyroidism

Medication	Dose	Comments/half-life
Calcium carbonate or calcium citrate	Ranges from 500–3000 mg three times daily preferably with meals to enhance phosphate binding effects	Calcium citrate preferred in presence of Proton Pump Inhibitor (PPI) use
Vitamin D3 (cholecalciferol)	1000 IU/day to 100,000 IU/day based on 25-hydroxy vitamin D level	4–6 hours plasma half-life
Vitamin D2 (ergocalciferol)	50,000 IU weekly to daily based on 25-hydroxyvitamin D levels	4–6 hours plasma half-life
Calcitriol	0.25–3 µg /day total dose administered in divided doses	5–8 hours plasma half-life
Alfacalcidol	0.5–6 µg/day	3–6 hours plasma half-life
Thiazide diuretics	25–100 mg/day	6–12 hours plasma half-life

4. rhPTH(1–84) replacement therapy in hypoparathyroidism – when and how to proceed?

1. inadequate control of serum calcium,
2. oral calcium or vitamin D medications required to control serum calcium or symptoms that exceed 2.5 g calcium or >1.5 µg calcitriol per day,
3. hypercalciuria, renal stones, nephrocalcinosis, stone risk or reduced creatinine clearance or eGFR (<60 mL/min),
4. hyperphosphatemia and/or calcium-phosphate product that exceeds 55 $mg^2 dL^2$ (4.4 $mmol^2 L^2$) (74).

PTH: effetti biologici



Principio attivo TERIPARATIDE

Ricerca | Reimposta | Indietro

12 risultati trovati (2 pagine) **1** | **2** succ ultim

	Descrizione Farmaco	Farmaco	Codice principio attivo	Descrizione principio attivo	Formulazione
○	TERROSA 20MCG/80MCL 1 PENN	TERROSA	H05AA02	Teriparatide	20MCG/80MCL 1 PENN
○	PATRIDE 20MCG/80MCL 1 PEN	PATRIDE	H05AA02	Teriparatide	20MCG/80MCL 1 PEN
○	SONDELBAY 20MCG/80MCL 1P 2,4	SONDELBAY	H05AA02	Teriparatide	20MCG/80MCL 1P 2,4
○	TERROSA 20/80MCG 1CART+1PEN	TERROSA	H05AA02	Teriparatide	20/80MCG 1CART+1PEN
○	OSEFFYL 20MCG/80MCL 1CAR	OSEFFYL	H05AA02	Teriparatide	20MCG/80MCL 1CAR
○	MOVYMIA 20MCG/80MCL 1CAR+1PE	MOVYMIA	H05AA02	Teriparatide	20MCG/80MCL 1CAR+1PE
○	LIVOGIVA 20MCG/80MCL SC 1PEN	LIVOGIVA	H05AA02	Teriparatide	20MCG/80MCL SC 1PEN
○	TERIPARAT TEV 20MCG/80MCL 1P	TERIPARAT TEV	H05AA02	Teriparatide	20MCG/80MCL 1P
○	TERROSA 20MCG/80MCL 1CART	TERROSA	H05AA02	Teriparatide	20MCG/80MCL 1CART
○	MOVYMIA 20MCG/80MCL 1CART	MOVYMIA	H05AA02	Teriparatide	20MCG/80MCL 1CART

12 risultati trovati (2 pagine) 1 | 2 prima prec

	Descrizione Farmaco	Farmaco	Codice principio attivo	Descrizione principio attivo	Formulazione
○	FORSTEO 20MCG/80MCL 1PENNA	FORSTEO	H05AA02	Teriparatide	20MCG/80MCL 1PENNA
○	YORVIPATH 420MCG/1,4ML 2PEN	YORVIPATH	H05AA05	Palopegteriparatide	420MCG/1,4ML 2PEN

12 risultati trovati (2 pagine) 1 | 2 prima prec