



Il Pediatra tra Famiglia,
Protocolli e Linee Guida

11 - 18 Luglio 2008

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3) Autoimmune polyglandular syndrome

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Criteria for defining a disease as autoimmune

- Major criteria (Witebsky and Rose 1957)
- Presence of circulating autoantibodies or cellular immune-mediated events.
- Presence of lympho-plasmocytic infiltration in the target tissues.
- Induction of the disease in animals by injection of autoantigens and passive transfer of the disease by serum or lymphocytes.

- Minor criteria (Rose and Bona 1993)
- Correlation with the MHC genes.
- Response to immunosuppressive therapy.
- Association with other autoimmune diseases.

Definition

The Autoimmune polyglandular syndrome (APS) is defined as the coexistence of multiple autoimmune glandular failure or best (of multiple autoimmune diseases) in a patient.

Neufeld and Blizzard 1980

CLASSIFICATION OF APS

APS-1 (APECED)	Addison's disease, Hypoparathyroidism, Chronic candidiasis (<i>2 or 3 present</i>)
APS-2 (Schimdt's syndrome)	Addison's disease (<i>always present</i>) + Thyroid autoimmune diseases and/or Type 1 diabetes mellitus
APS-3 (Thyro-gastric syndrome)	Thyroid autoimmune diseases (<i>always present</i>) + other autoimmune diseases (<i>escluding: Addison's or hypoparatiroidism</i>)
APS-4	Two or more organ-specific autoimmune diseases not falling into APS-1, 2 or 3.

Neufeld and Blizzard 1980

Genetic Dissection of Autoimmune Polyendocrine Syndrome Type 2

Common Origin of a Spectrum of Phenotypes

ANNALISA BALLARINI AND MIN AE LEE-KIRSCH

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TABLE 1. Comparison of APS1 and APS2

	APS1	APS2
Major diseases		
Mucocutaneous candidiasis	Yes	No
Hypoparathyroidism	common	No
Autoimmune Addison's disease	~70%	~70%
Type 1 diabetes	14%	~50%
Autoimmune thyroid disease	Rare	Common
Associated features	Ectodermal dystrophy chronic atrophic gastritis/pernicious anemia, intestinal dysfunctions, hepatitis, hypogonadism, alopecia, vitiligo	Celiac disease, chronic atrophic gastritis/ pernicious anemia, hypogonadism, alopecia, vitiligo
Age at onset	Infancy	Young adulthood
Gender difference	No	Female preponderance
Genetic locus	Chromosome 21q22.3, AIRE gene	Unknown
HLA association	None	DR3, DR4

APS-1 or

APECED (Autoimmune polyendocrine-candidiasis-
Ectodermal-dystrophy)

Chronic candidiasis

Addison's disease

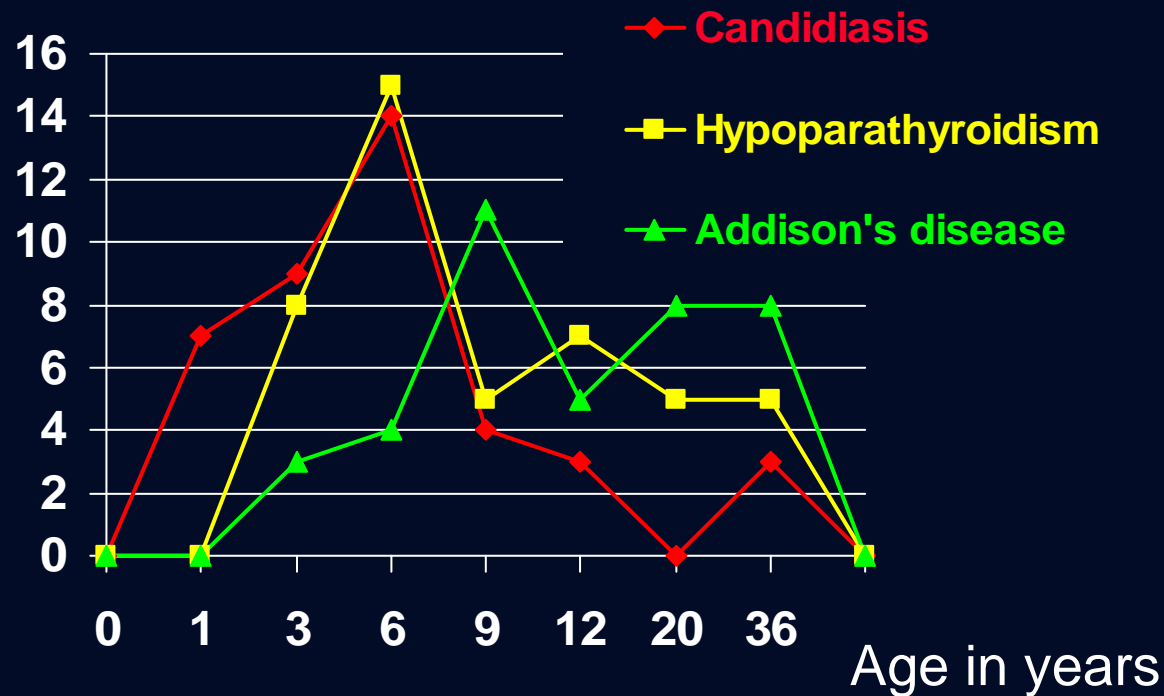
Chronic Hypoparathyroidism

PREVALENCE OF APS-1

- **110 cases / million** **Jews (Iran)**
- **60 cases / million** **Sardinia**
- **40 cases / million** **Finland**
- **12 cases / million** **Norway**
- **4-8 cases / million** **Italy**
- **1 cases / 10 millions** **Japan**

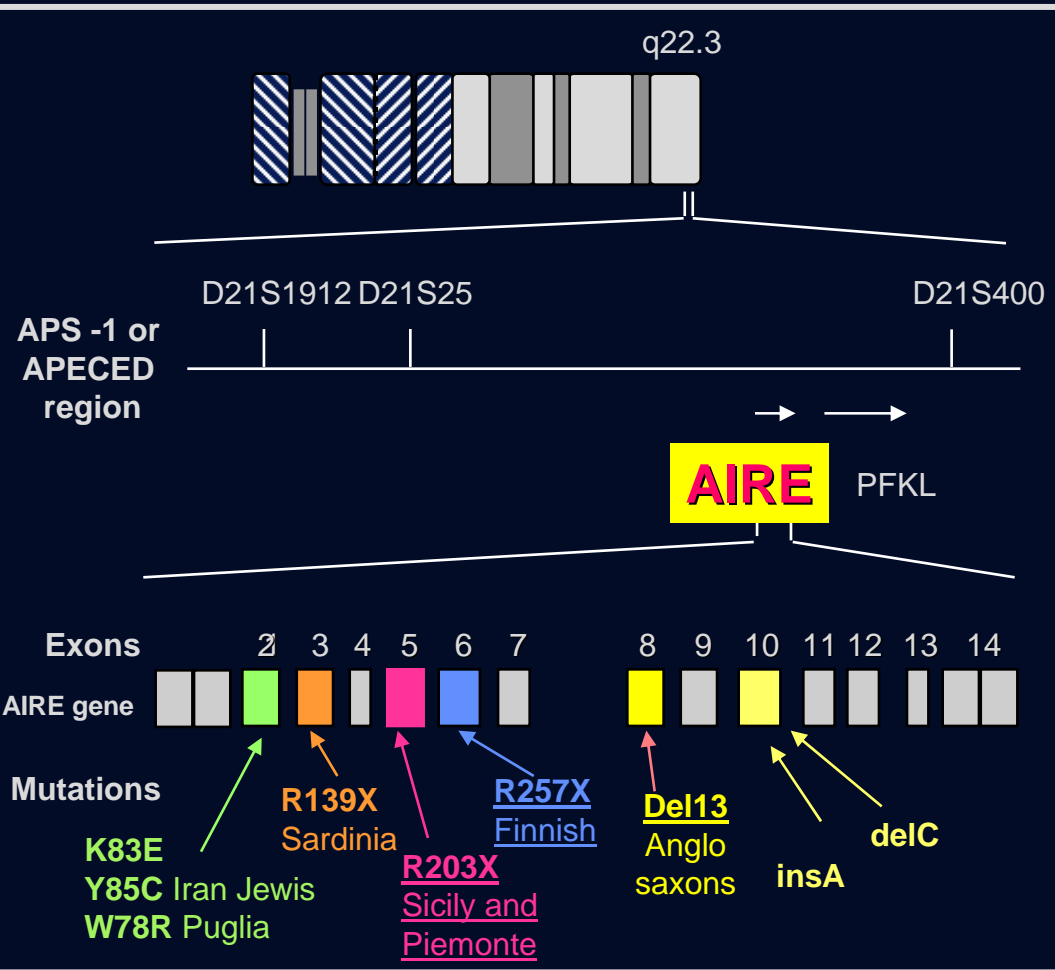
APS-1: age at onset of the three main diseases in 49 Italian patients

N° of
Patients



GENETIC OF APS-1 In Italy

CHROMOSOME 21



Italian Patients		AIRE Mutations
		Allele1 / Allele2
1.FMT	VI	R257X / R257X
2.FL	VI	R257X / R257X
3.AE	PD	R257X / R257X
4.TP	PD	del13 / del13
5.CA	brothers	R257X / R257X
6.CG	VI	R257X / R257X
7.CG	sisters	del13 / R257X
8.CE	VI	del13 / R257X
9.DGF	VE	1032delGT / del13
10.SM	RO	R139X / R139X
11.HK	BZ	del13 / del13
12.XY	BZ	R257X / R257X
13.NA	Le	W78R / W78R
14.DNM	brothers	W78R / Q358X
15.DNG	Le	W78R / Q358X
16.CV	brothers	R203X / R257X
17.CD	Me	R203X / R257X
18.GF	To	R203X / R203X

K. Nagamine, *Nat. Genet.* 17: 393;1997

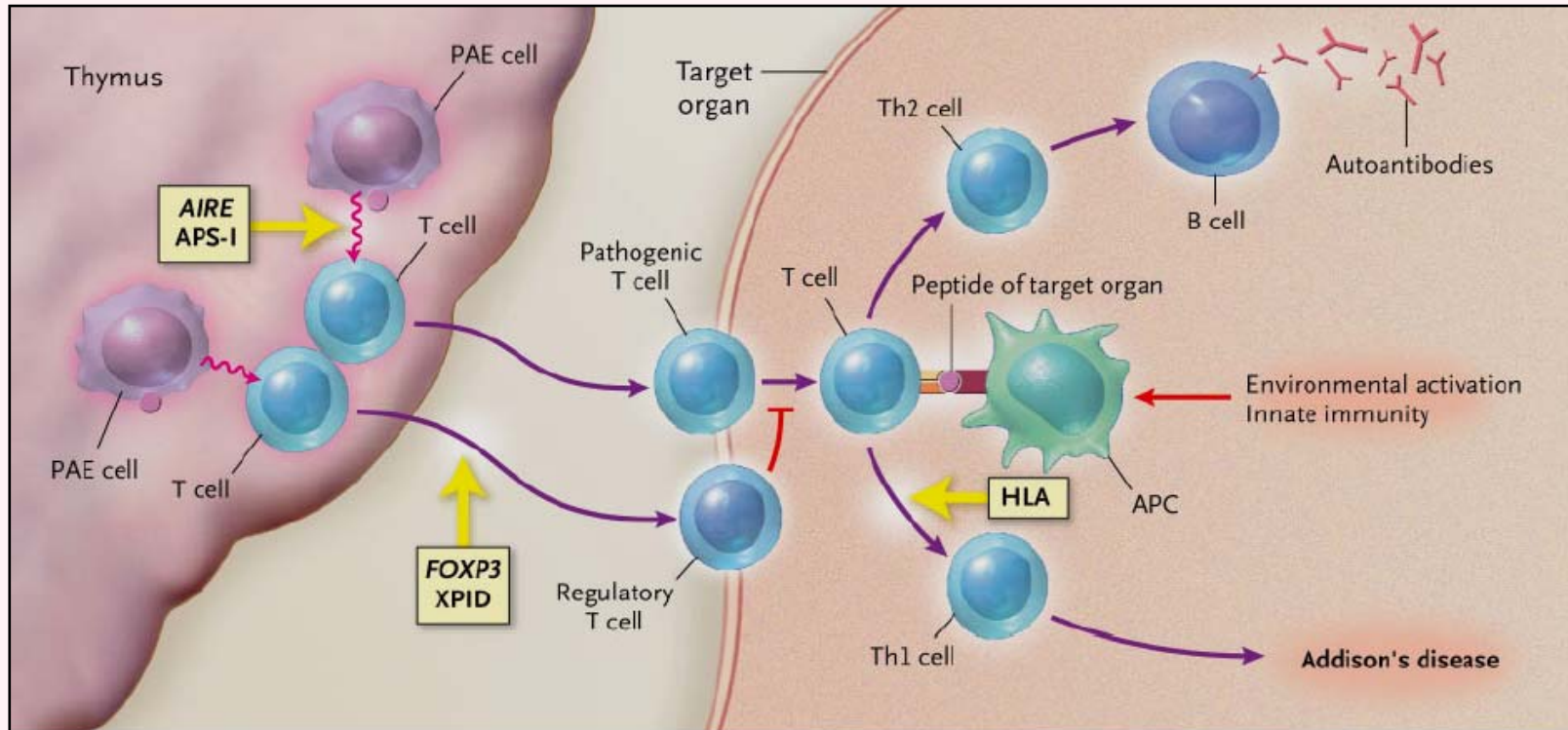
P. Peterson, *Immunol.Today* 19: 384;1998

Betterle, *Endocrine Reviews* 23: 327; 2002

Autoimmune Polyendocrine Syndromes

George S. Eisenbarth, M.D., Ph.D., and Peter A. Gottlieb, M.D.

N Engl J Med 2004;350:2068-79.



The presence of the AIRE mutated proteins may inhibit the apoptosis of autoreactive T lymphocytes at the thymic level, and these cells can migrate at the peripheral level where they can initiate an autoimmune aggression in a very young age.

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Suggestion for an autoantibody screening in children with one autoimmune disease in order to detect potential or subclinical APS

Chronic
Candidiasis
or
Hypopara
thyroidism

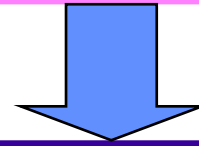
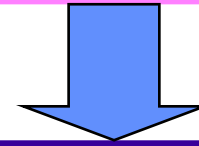
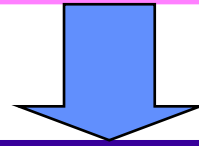
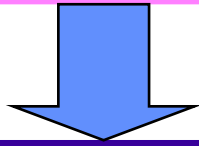
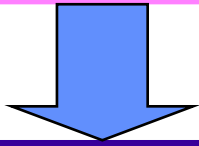
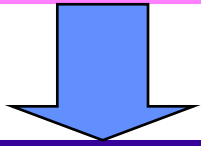
Addison's
disease

Thyroid
autoimmune
disease

Type 1
Diabetes

Celiac
Disease

Others
(Vitiligo,
Alopecia,
JRA)



ACA/21-OHAb
StCA

Thyroid Ab
PCA
Tranlutaminase
Ab
ICA/GADAb

PCA
Tranlutaminase Ab
ICA/GAD
ACA/21-OHAb

Thyroid Ab
PCA
Tranlutaminase Ab
ACA/21-OHAb

Thyroid Ab
ICA/GADAb
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