New Insights

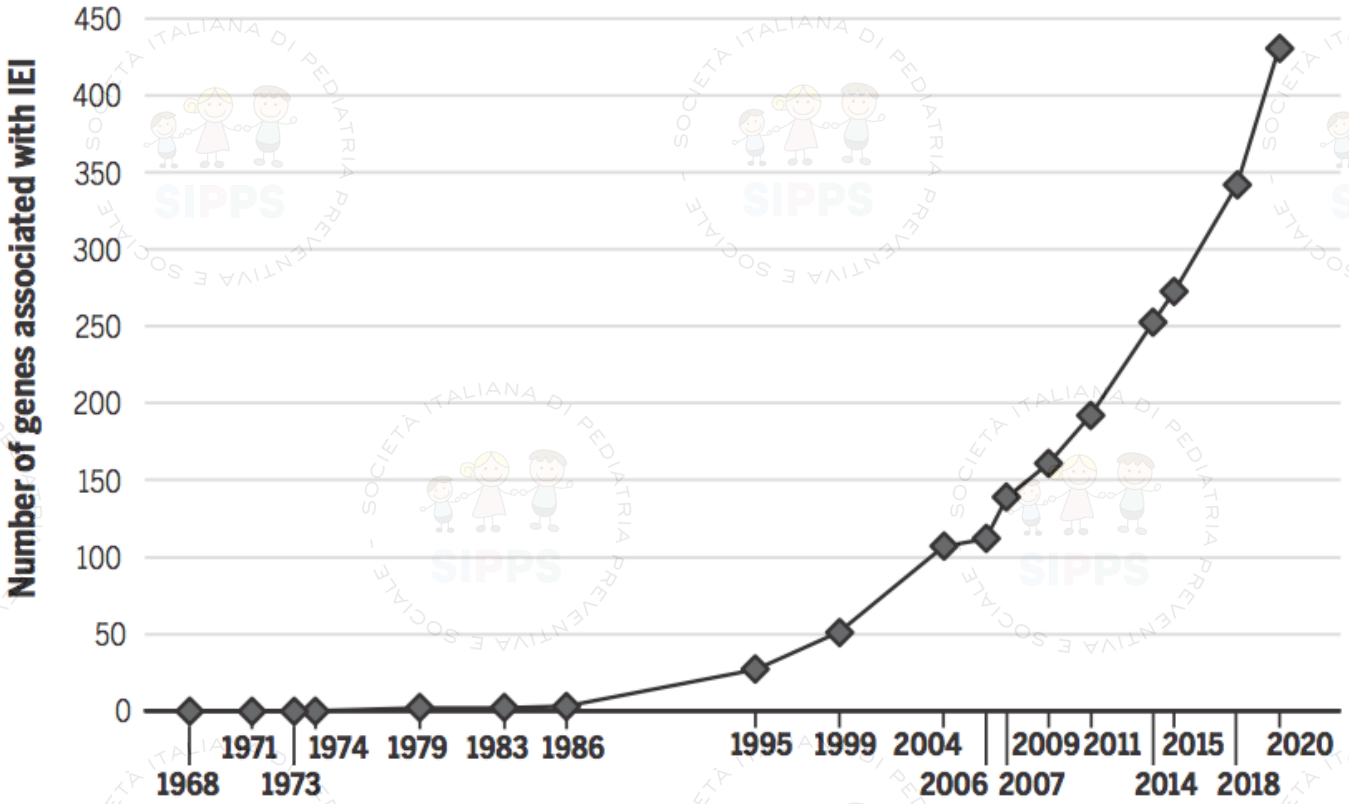
Il Difetto di IgA: perché tenere alta l'attenzione

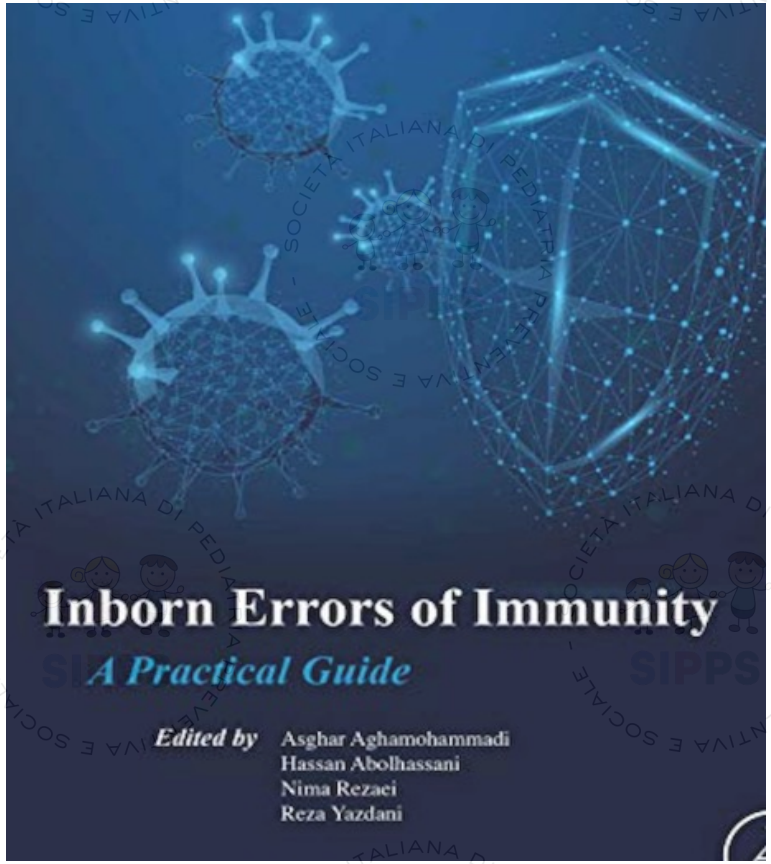
Dr. Lucia Leonardi

IMMUNODEFICIENCES

Human inborn errors of immunity: An expanding universe

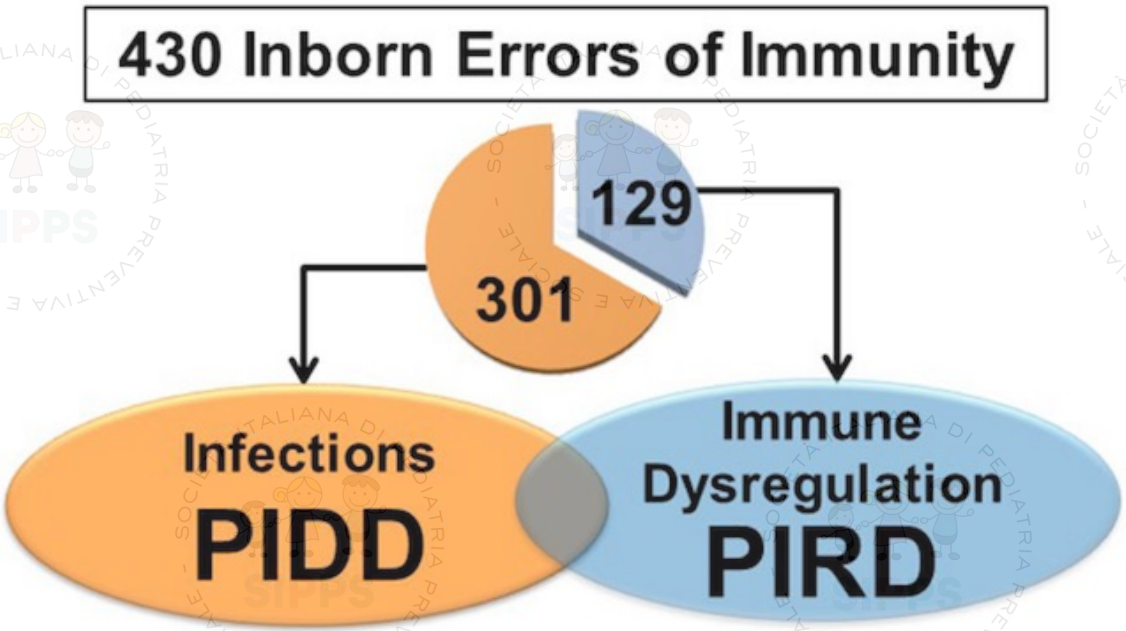
Luigi D. Notarangelo[1*†], Rosa Bacchetta[2*], Jean Laurent Casanova[3,4,5,6,7*], Helen C. Su[1*]





NGS-->Caratterizzazione molecolare di oltre 480 IEI

Primary immune regulatory disorders: a growing universe of immune dysregulation

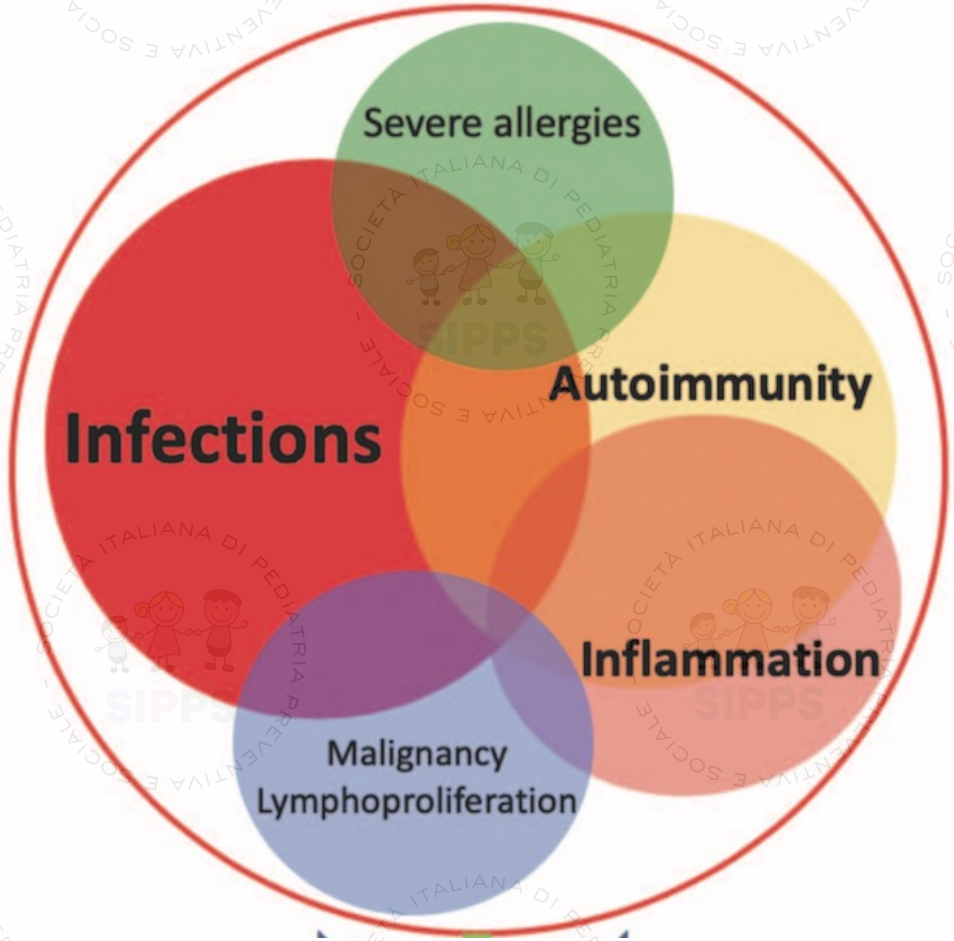


Primary Immune Deficiency Disorders (PIDD)

- Infection-dominant pathology
- Therapies focused on infection treatment or prevention
- Example: SCID

Primary Immune Regulatory Disorders (PIRD)

- Immune-mediated pathology dominant
- Therapies focused on immune modulation
- Example: IPEX



Classificazione fenotipa complessa—nuovi campanelli allarme

Chan AY Torgerson RE, Curr Opin Allergy Clin Immunol. 2020

Vecchi e nuovi paradigmi nei difetti congeniti dell'immunità

1952	1996
Rare	Comuni
Infezioni multiple	Infezioni singole
Suscettibilità a + agenti infettivi	**Suscettibilità a singoli agenti infettivi**
Agenti infettivi opportunisti (es Pneumocystis)	**Agenti infettivi comuni (es herpes simplex)**
Espressione in linee emopoietiche	Espressione in tessuti non emopoietici
Malattie monogeniche	Effetto multigenico per la determinazione del fenotipo
Assenza di anticorpi verso self e non self	**Non risposta al non self, elevata risposta al self/ immunodisregolazione**

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selective IgA deficiency

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2 results

Page 1 of 1

Filters applied: Meta-Analysis, Randomized Controlled Trial, Systematic Review. Clear all

1 Cite Share

Common variants at PVT1, ATG13-AMBRA1, AHI1 and CLEC16A are associated with **selective IgA deficiency**.

Bronson PG, Chang D, Bhangale T, Seldin MF, Ortmann W, Ferreira RC, Urcelay E, Pereira LF, Marti J, Plebani A, Lougaris V, Friman V, Freiberger T, Litzman J, Thon V, Pan-Hammarström Q, Hammarström L, Graham RR, Behrens TW.

Nat Genet. 2016 Nov;48(11):1425-1429. doi: 10.1038/ng.3675. Epub 2016 Oct 10.

PMID: 27723758 Free PMC article.

Selective immunoglobulin A **deficiency** (IgAD) is the most common primary immunodeficiency in Europeans. ...These data suggest that a complex network of **genetic** effects, including genes kno to influence the biology of **IgA** production, contributes to IgA ...

2 Cite Share

Intravenous augmentation treatment and lung density in severe α1 antitrypsin **deficiency** (RAPID): a randomised, double-blind, placebo-controlled trial.

Chapman KR, Burdon JG, Piitulainen E, Sandhaus RA, Seersholm N, Stocks JM, Stoel BC, Huang L Yao Z, Edelman JM, McElvaney NG; RAPID Trial Study Group.

Lancet. 2015 Jul 25;386(9991):360-8. doi: 10.1016/S0140-6736(15)60860-1. Epub 2015 May 27.

PMID: 26026936 Clinical Trial.

METHODS: The RAPID study was a multicentre, double-blind, randomised, parallel-group, placebo controlled trial of A1PI treatment in patients with alpha1 antitrypsin **deficiency**. We recruited eligib

Europe PMC Funders Group
Author Manuscript
Nat Genet. Author manuscript; available in PMC 2017 April 10.

Published in final edited form as:
Nat Genet. 2016 November ; 48(11): 1425–1429. doi:10.1038/ng.3675.

Common variants at *PVT1*, *ATG13–AMBRA1*, *AHI1* and *CLEC16A* are associated with selective IgA deficiency

Abstract

Selective immunoglobulin A deficiency (IgAD) is the most common primary immunodeficiency in Europeans. Our GWAS meta-analysis of 1,635 IgAD patients and 4,852 controls identified four new significant ($P < 5x10^{-8}$) loci and association with a rare *IFIH1* variant (Ile923Val). Peak novel variants (*PVT1* $P = 4.3x10^{-11}$, *ATG13–AMBRA1* $P = 6.7x10^{-10}$, *AHI1* $P = 8.4x10^{-10}$ and *CLEC16A* $P = 1.4x10^{-9}$) overlapped with autoimmune markers (3/4) and correlated with 21 putative regulatory variants, including eQTLs for *AHI1* and *DEXI* and DNase hypersensitivity in *FOXP3*+ T regulatory cells. A pathway analysis of the meta-analysis results showed a striking association with the KEGG pathway for IgA production (pathway $P < 0.0001$): where 22 of 30 annotated pathway genes contained at least one variant with a *P*-value ≤0.05 in the IgAD meta-analysis. These data suggest that a complex network of genetic effects, including genes known to influence the biology of IgA production, contribute to IgAD.

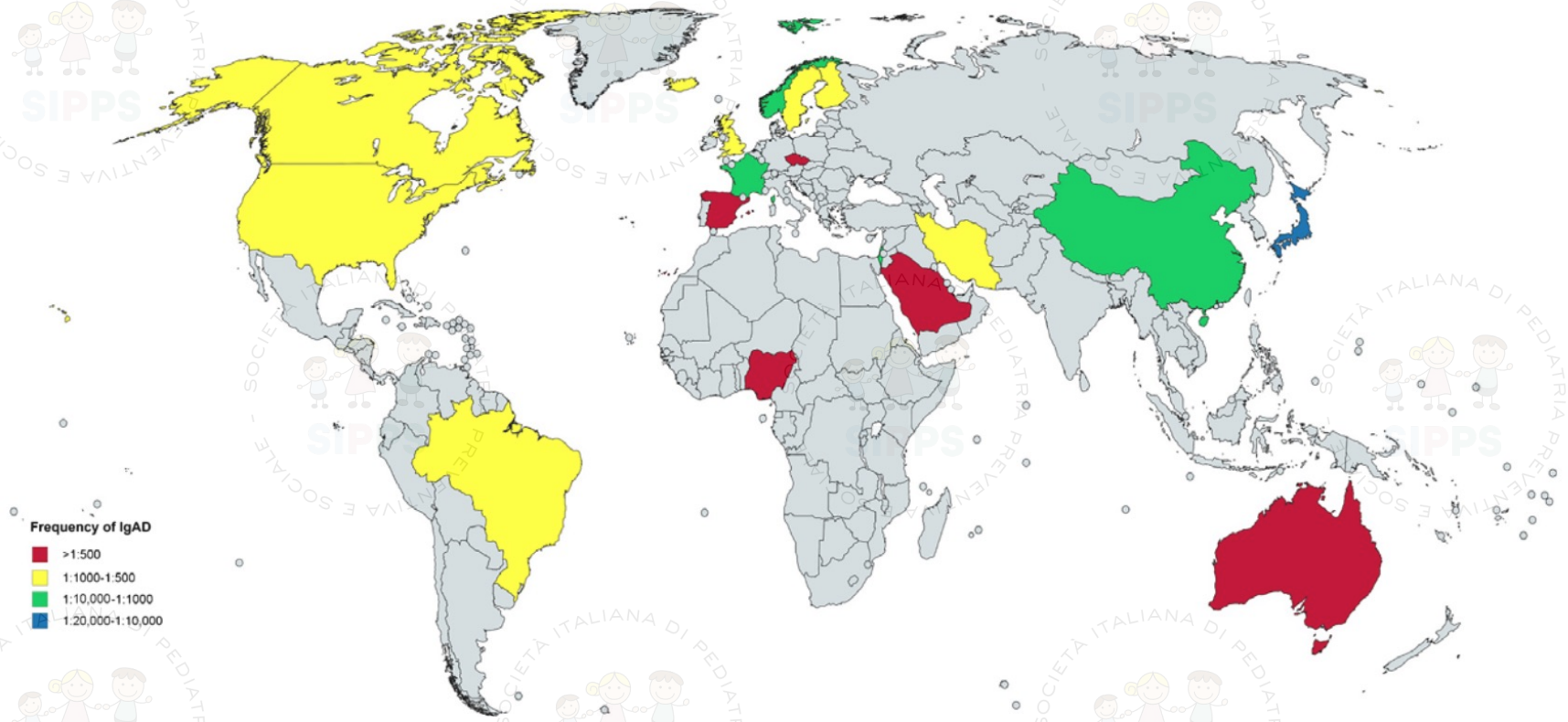
METANALISI GWSA: 5 GENI ASSOCIATI A SIGAD E AUTOIMMUNITA’
PIU’ GENI COINVOLTI NELLA PATOGENESI SIGAD

Non raro

Prevalenza in EU: 1: 400

"Convenzionale"

Asintomatico in ca 80% casi



Jeffrey Modell Foundation prevalenza variabile→1/400-1/600 popolazione caucasica

Dati universalmente sottostimati perché i pz sono spesso asintomatici (diagnosi screening routine o donatori sangue)

NON programma di screening e non studi su larga scala utili a chiarire patogenesi e management

Yazdani et al. Scand J Immunol 2017; 85:3,12

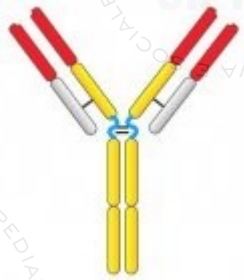
IgA

75% della produzione anticorpale giornaliera, con una emivita di 6 giorni.
due sottoclassi in base catena pesante: le IgA1, prevalenti nel siero e le IgA2 a livello mucosale.

IgA sieriche

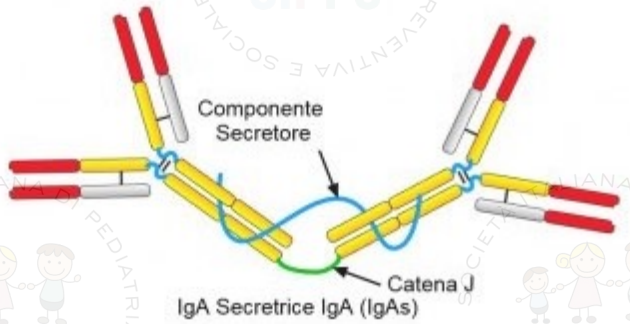
- **secondo isotipo per concentrazione**,
- range 37-348 mg/dl
- Soprattutto monomeriche
- IgA1

.



IgA secretorie (SIgA)

- a livello mucosale,saliva, lacrime, colostro
- Soprattutto forma dimerica
- IgA2



I livelli di IgA nel plasma sono il migliore surrogato, pur non riflettendo i reali livelli delle IgA sulle mucose

Abbas AK et al., Cellular and molecular immunology, *8th ed. Philadelphia, W.B Saunders Company 2015.*

The Heterogeneous Pathogenesis of Selective Immunoglobulin A Deficiency

Patogenesi di SIgAD è ancora da definire → più meccanismi possono essere coinvolti, **giustificandone l'eterogeneità clinica**

-Difetto intrinseco nella maturazione delle cellule B con ridotte cellule B switched

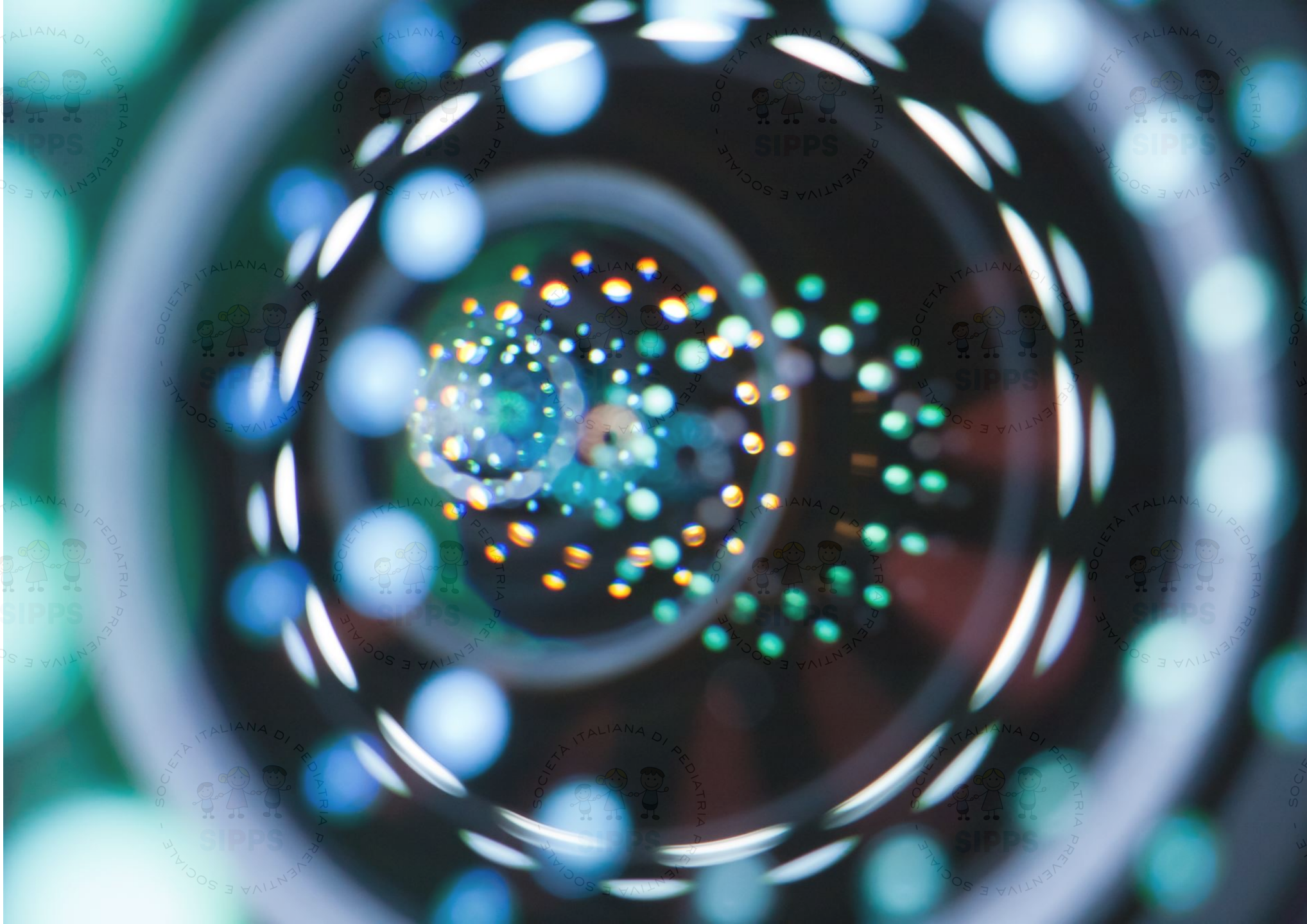
-Alterata F citochine: Bassi livelli sierici TGF-β coinvolto nella differenziazione dei linfociti B in plasmacellule che secernono IgA

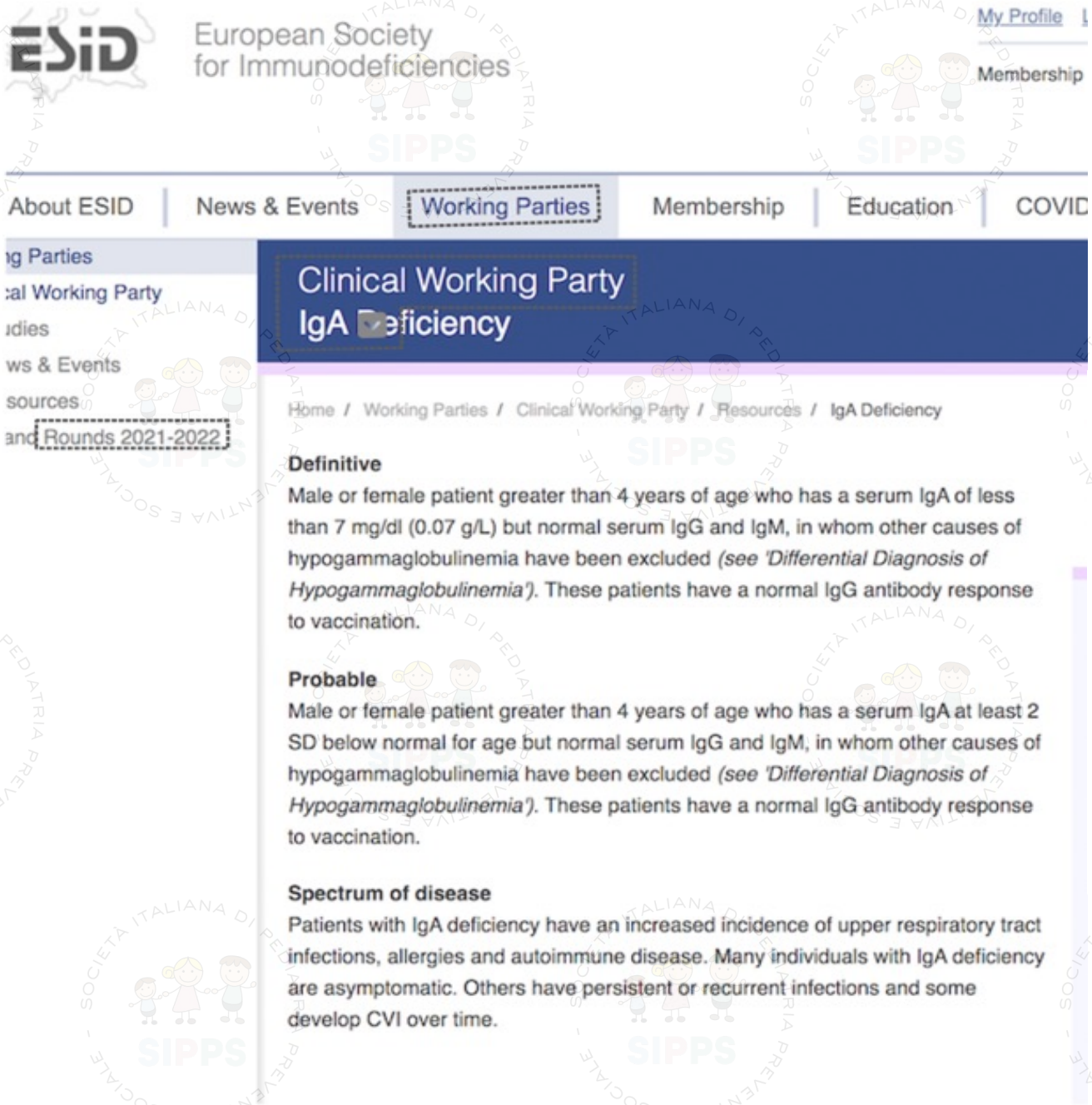
-Alterato N o funzione cellule T helper

-Ridotto n cellule T regolatorie FoxP3 (Tregs) → autoimmunità

sIgAd

Luci?





Il riscontro occasionale di ridotti livelli di IgA necessita sempre conferma del dato e indagini per conferma sIgAd assoluto

Perchè 4 anni?

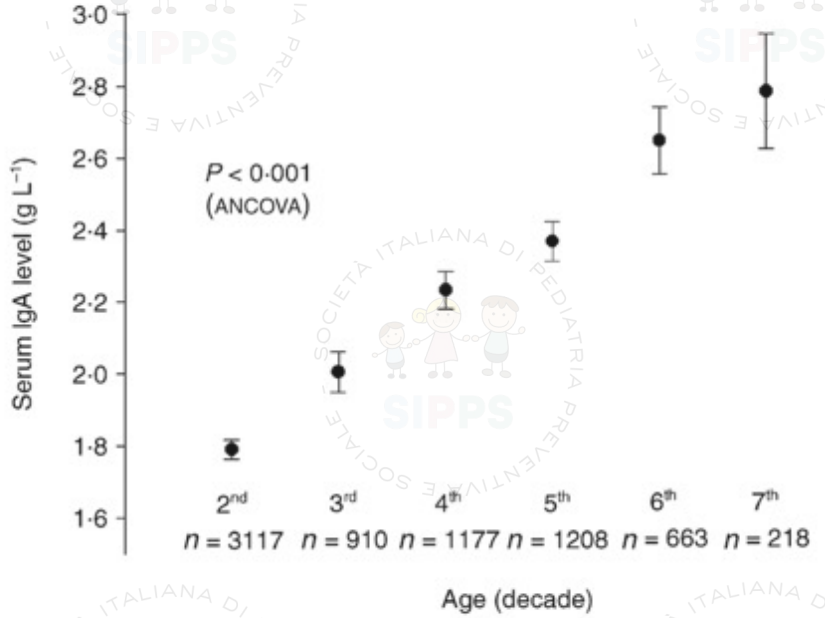
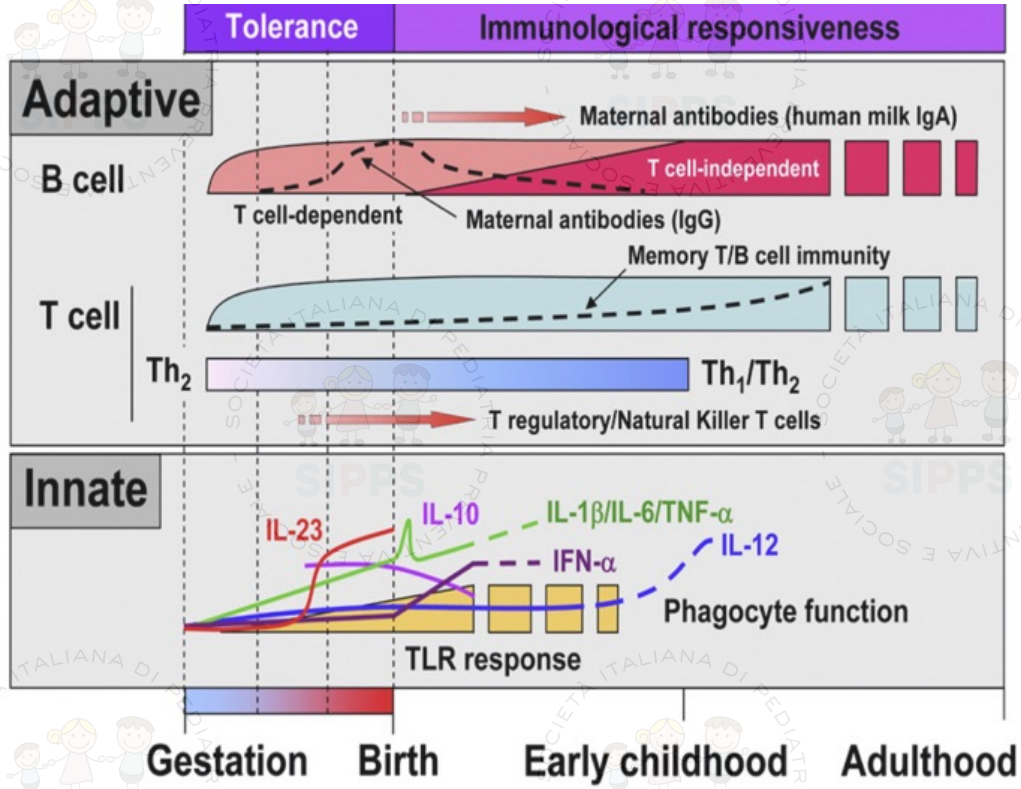


Figure 2 Relation between age (decades of life) and serum IgA levels in 7293 subjects is shown (mean; 95% CI). Serum immunoglobulin A (SIgA) levels increase with age on average by



Kollmann et al. 2013

Perché dosaggio IgG + IgM ?

Perché Ig sieriche e titoli anticorpali a vaccinazioni

Escludono altri errori congeniti dell'immunità (CVID)

Escludere difetto secondario di IgA

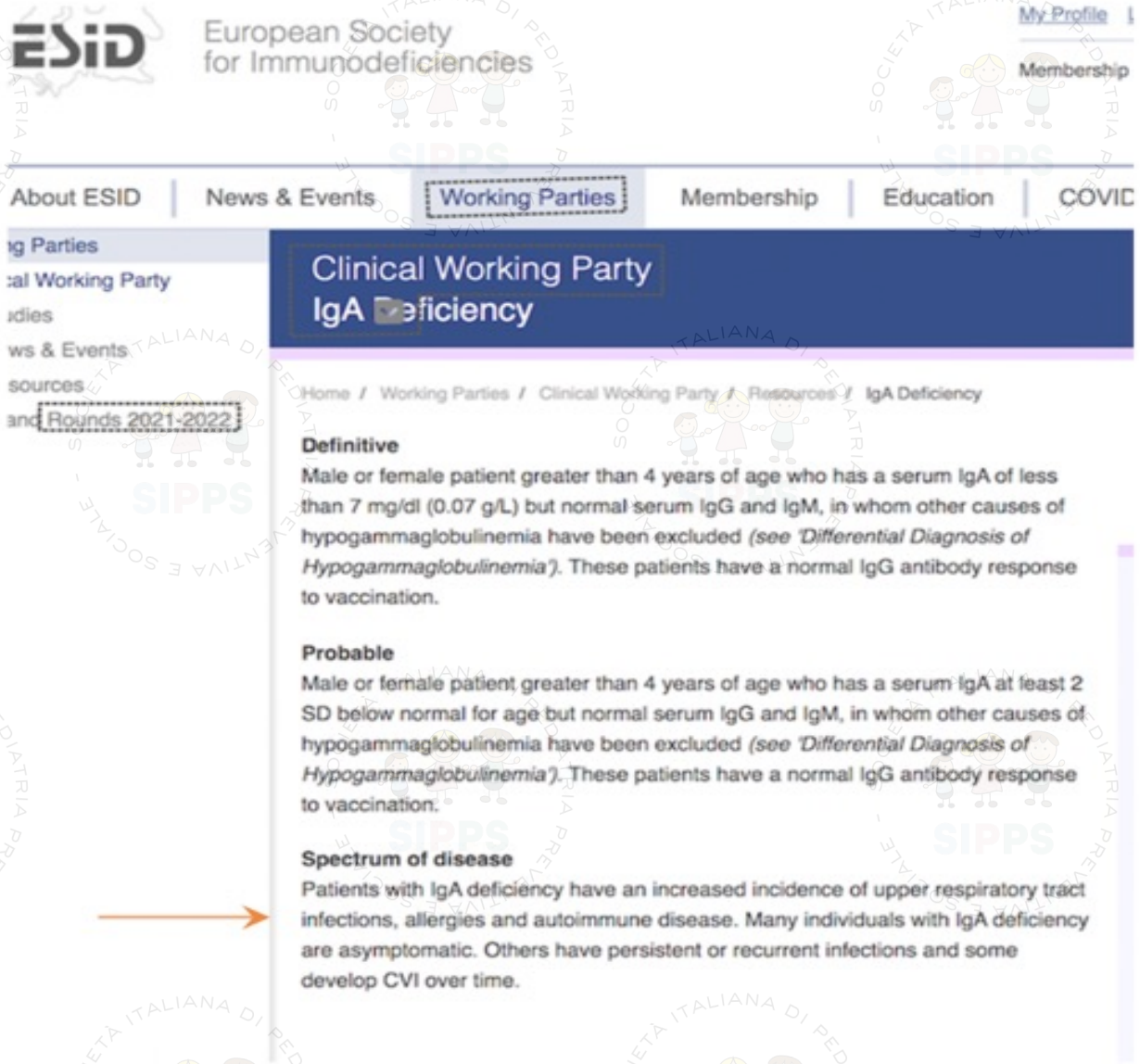
Cause secondarie di deficit di IgA

Malattie monogeniche	Atassia-teleangectasia
	Deficit di transcobalamina II e ipogammaglobulinemia
	Sindrome di Wiskott-Aldrich
	Disordini linfoproliferativi X-linked (associati a EBV)
Anomalie cromosomiche	Sindrome da delezione del cromosoma 18q
	Monosomia 22
	Trisomia 8
	Trisomia 22
Esposizione ambientale	
Indotta da farmaci	Farmaci antimalarici
	Captopril
	Carbamazepina
	Glucocorticoidi
	Fenclofenac
	Sali d'oro
	Penicillamina
	Fenitoina
	Sulfasalazina
Infezioni	Rosolia congenita
	Infezione congenita da *Citomegalovirus*
	Infezione congenita da *Toxoplasma gondii*
	Virus di *Epstein-Barr*
	Virus dell'immunodeficienza umana

https://esid.org/Education/Differential-Diagnosis-of-Hypogammaglobulinemia


Ombre

Follow up del bambino con sIgAd



IRR e/o allergia e/o autoimmunità evoluzione a CVID

Review Article

Immunoglobulin A deficiency in children, an undervalued clinical issue

M.H. (Mischa) Koenen[a,**], J.M. (Joris) van Montfrans[a], E.A.M. (Elisabeth) Sanders[a,b], D. (Debby) Bogaert[a,c], L.M. (Lilly) Verhagen[a,*]

….SIgAD can be challenging for physicians in determining which patients require closer monitoring and possibly treatment

inadeguato PC ..

Editorials

IgA deficiency: what we should—or should not—be doing

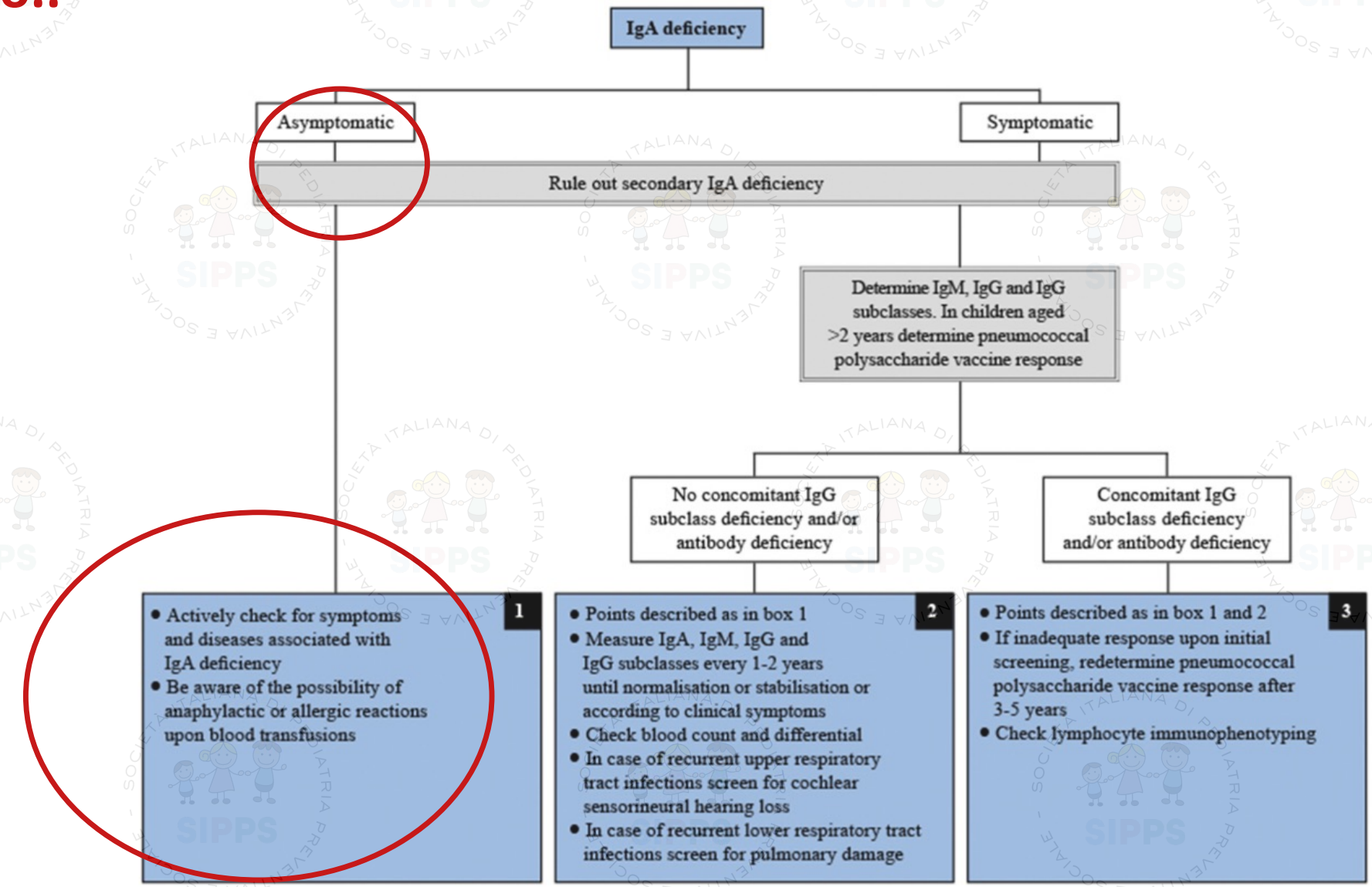
Although IgA deficiency (IgAD) is currently recognised as the most frequent immunodeficiency in humans,[1] individuals with IgAD are largely considered to be healthy and when discovered are usually not investigated further or followed up.[2] The rare occasion when IgAD is a cause for

How frequently are anti-IgA antibodies found

One of the most important issues regarding IgA recognition that some patients lacking IgA will serious, life threatening adverse reactions upon blood or blood products containing IgA, and th reactions are in many cases associated with

J Clin Pathol 2001;54:337–338 337

Ma 18 anni dopo..



E un anno dopo…

IgA DEFICIENCY

(Medico e Bambino 2020;39:365-369)

Key words

IgA deficiency, Primary immunodeficiency, Immunoglobulins, Recurrent infections

Summary

IgA deficiency (D-IgA) in the p
tests performed for other reas
not suspected. D-IgA is the mo
valence according to ethnicity,
IgA should be dosed twice in a
defined by the presence of ser
should always be dosed. Mos
low-up (85% are asymptomatic
20 times more frequent in pati
current infections (mainly affec
nal tract), signs and symptoms
pes of primary immunodeficie
which, although rarely, can be
adolescents and adults, have a
toimmune diseases. The family
fic laboratory evaluations are not necessary. Four clinical cases are presented: an occasional finding of D-IgA in a healthy child, the association with coeliac disease, the association with juvenile idiopathic arthritis, and IgA deficiency in a patient with an immunodeficiency disorder (ataxia-telangectasia).

CHI È DI SOLITO IL BAMBINO CON DEFICIT DI IgA?

L'85% dei bambini con D-IgA è perfettamente sano e il riscontro di tale deficit avviene, come detto, nella maggior parte dei casi incidentalmente nel corso di esami eseguiti per altri motivi.

DIFETTO SELETTIVO DI IGA

Raccomandazioni diagnostiche e terapeutiche

Versione definitiva 16 Dicembre 2010

- **Alla diagnosi:**

Emocromo completo Ig sieriche Sottoclassi IgG Tipizzazione linfocitaria (CD3, CD4, CD8, CD19) Ab anti-transglutaminasi (IgG) ANA Ab anti tireoglobulina, anti perossidasi IgE totali

- **Ogni 12 mesi:**

Controllo clinico

- **Ogni 3 anni:**

Emocromo completo Ig sieriche Sottoclassi IgG Tipizzazione linfocitaria (CD3, CD4, CD8, CD19) Ab anti-transglutaminasi (IgG) ANA Ab anti tireoglobulina, anti perossidasi IgE totali

In base all'andamento clinico individuare la comparsa di problemi autoimmuni, allergici o tumorali con accertamenti diagnostici specifici caso per caso.

sIgAd
80 F(44%) 104 M(56%),
22aa FU (1989 – 2011)

Clinical and Laboratory Features of 184 Italian Pediatric Patients Affected with Selective IgA Deficiency (SIgAD): a Longitudinal Single-Center Study

Table 1 Clinical and familial features of 184 patients affected with SIgAD at diagnosis

Patients' features	Numbers (percentages)
Sex (M:F)	104:80 (56% vs 44%)
Recurrent URTI	114/184 (62)
Pneumonia	3/184 (2)
Growth delay/Celiac disease suspicion	16/184 (9)
Articular pain	7/184 (4)
Allergies	42/184 (23)
Positive family history	
SIgAD	24/184 (13)
CVID	5/184 (3)
Celiac disease	10/184 (5)
Allergies	106/184 (58)
Psoriasis	13/184 (7)
Vitiligo	4/184 (2)
Thyroid disease	14/184 (8)

Table 2 Patients' clinical features during follow-up

Infections during follow-up	
Incidence of URTI/year	3.1 episodes (mean)
Incidence of pneumonia/year	0.4 episodes (mean)
Gastrointestinal infections	50/184 patients (27%)
Diagnosis during follow-up	Numbers (percentages)
Celiac disease	20/184 (11%)
Autoimmune manifestations	12/184 (7%)
Allergies	30/184 (16%)
Adenotonsillectomy	37/184 (20%)

Table 5 Comparison of clinical features in reported pediatric cohorts of patients with selective IgA deficiency

	Index study	Shkalim et al. [9]	Aytakin et al. [10]	Moschese et al. [11]
Number of patients	184	63	118	53
Country	Italy	Israel	Turkey	Italy
Recurrent URTI	Yes	Yes	Yes	Yes
Recurrent LRTI	No	Yes	Yes	No
Celiac disease	Yes (14%)*	Yes (3%)	Yes (6%)	Yes (6%)
Gastrointestinal symptoms	Yes (27%)	NA	Yes (7%)	Yes (11%)
Allergies	Yes (39%)	Yes (32%)	Yes (43%)	Yes (36%)
Autoimmune diseases	Yes (8%)	Yes (21%)	Yes (17%)	Yes (8%)
Progression to CVID	Yes (2%)	No	No	NA
Malignancy	No	Yes (5%)	No	No
Positive family history for humoral immunodeficiency	Yes (16%)	NA	NA	Yes (10%)

NA, not available

Percentages in parentheses indicate the percentage of patients presenting the indicated complication

Prevalenza di allergia/ autoimmunità/ IRR è > rispetto alla popolaazione generale

«these findings underline the importance of a regular follow-up for SIgAD patients with periodic clinical and laboratory evaluations»

Familiarità per IEI o autoimmunità→ segno di allarme per sIgAd (e IEI in generale)

Follow-up necessario → autoimmunità o progressione a CVID

Infezioni ricorrenti: motivo principale di indagine

IR

- Haemophilus influenzae,
- Streptococcus pneumoniae
- SARS- CoV2

GI

- Giardia lamblia,
- Salmonella,
- Campylobacter

Malattie allergiche nel sIgad: talora unica manifestazione clinica

Journal of *Clinical Medicine*

MI

Review

The Epidemiology and Clinical Presentations of Atopic Diseases in Selective IgA Deficiency

Izabela Morawska [1], Sara Kurkowska [2], Dominika Bębnowska [3], Rafał Hrynkiewicz [3], Rafał Becht [4], Adam Michalski [1], Hanna Piwowarska-Bilska [2], Bożena Birkenfeld [2], Katarzyna Załuska-Ogryzek [5], Ewelina Grywalska [1], Jacek Roliński [1] and Paulina Niedźwiedzka-Rystwej [3,*]

Immunoglobulin deficiency in patients with chronic rhinosinusitis: Systematic review of the literature and meta-analysis

Adrien J.-P. Schwitzguébel, MD,[a] Peter Jandus, MD,[a] Jean-Silvain Lacroix, MD,[b] Jörg D. Seebach, MD,[a]* and

neva, Switzerland

Clinical immunology

DOI: https://doi.org/10.5114/ceji.2020.97907

Study of selective immunoglobulin A deficiency among Egyptian patients with food allergy

RASHA YOUSSEF SHAHIN[1], FAWZIA HASSAN ABO ALI[1], NERMINE ABDEL NOUR MELEK[1], ISLAM ADEL ABD ELATEEF[2], MOHAMED YOUSSEF ATTIA[3]

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[3]Immunology Laboratory, Ain Shams University Hospital, Cairo, Egypt

Quali malattie autoimmuni?

Citopenie:neutropenia, trombocitopenia

IBD e morbo celiaco

LES, AIG

Tiroidite, DM1

La prevalenza della malattia celiaca è 35 volte superiore nei pazienti con IgAD, mentre la prevalenza di LES e DM1 è 10 volte superiore vs popolazione generale

Progression of Selective IgA Deficiency to Common Variable Immunodeficiency

CVID difetto umorale

Ipogammaglobulinemia + immunodisregolazione

Condivide manifestazioni cliniche con sIgAD.

Base genetica condivisa per IgAD e CVID (membri differenti dello stesso albero genealogico)

Possibile patogenesi comune (disordine differenziativo dei linfociti B (non maturano in plasmacellule che secernono IgA)

In 3-5% casi sIgAd segnalata progressione a CVID

Table 2. Characteristics of reported IgAD patients who progressed to CVID

Case	Sex	Interval of progression years	Characteristics of individual patients				Ref.
			clinical finding	immunological abnormalities	genetic association	family history	
P1	F	27	sinusitis, dermatitis, oral candidiasis, ITP, vitiligo	HIV infection, CD4 lymphopenia	18q deletion	–	12
P2	F	6	weight loss, chronic active hepatitis, vitiligo	NA	HLA A11,24, B38,39, DR3,4	–	11
P3	F	1	respiratory infection, systemic lupus erythematosus	ANA, anti-dsDNA, Antihiston, antimicrosomal	HLA A3,26, B18,51, DR1,4	–	11
P4	F	12	respiratory and gastrointestinal infections	IgG2 deficiency	NA	–	11
P5	M	5	recurrent pneumonia and tonsillitis	IgG2 and IgG4 deficiency	NA	NA	13
P6	M	4	recurrent infections	CD4 lymphopenia	NA	NA	13
P7	F	9	pneumonia, diabetes mellitus, thyroiditis	IgG2 and IgG3 deficiency	18q deletion	NA	32
P8	F	5	recurrent infections, ITP, autoimmune hemolytic anemia, Sjogren's syndrome	CD4 deficiency	NA	NA	29
P9	M	1.5	recurrent pneumonia	CD4/CD8 decreased	NA	+	30
P10	F	4	respiratory infections, diarrhea, alopecia	NA	NA	NA	31
P11	F	–	recurrent infections, chronic ITP	IgG2 and IgG4 deficiency	NA	+	33
P12	M	8	recurrent sinusitis	IgG2 and IgG4 deficiency	HLA A1, B8, DR3,4	+	34
P13	M	2	recurrent sinusitis, otitis media	IgG2 and IgG4 deficiency	HLA A1,31, B7,8, DR2,3	NA	34
P14	F	15	sinusitis, otitis media, bronchitis	NA	HLA A1,2, B44,49, DR7,13	–	34
P15	M	7 months	ulcerative colitis, amyloid changes, non-A/non-B hepatitis, bronchopneumonia, lichen planus	low B cells; defect in B and T cells	ND	–	35
P16	M	11	sarcoidosis, respiratory tract infection, bronchopneumonia	low B cells	HLA B7,40, DR4,4, DQ3,3	NA	35
P17	M	4	respiratory tract infection, measles, pneumonia, diarrhea	B cell defect; decreased number of CD20 cells; IgG1, 2, 3, 4 deficiency		NA	34
P18	M	7	ITP	IgG subclass deficiency and low isohemaglutinins; nonreactive DHST, transient antithyroid and antiplatelet Ab	–	NA	28
P19	F	15	respiratory tract infection, nephrotic syndrome	IgG subclass deficiency and low isohemaglutinins; nonreactive DHST, transient antithyroid and antiplatelet Ab	–	NA	28
P20	F	7	pneumonia, JRA, thyroiditis	IgG subclass deficiency and low isohemaglutinins; nonreactive DHST, transient antithyroid and antiplatelet Ab	–	NA	28

ITP = Idiopathic thrombocytopenic purpura; ANA = antinuclear antibody; DHST = delayed hypersensitivity skin test; ND = not determined; Ab = antibody; JRA = juvenile rheumatoid arthritis; NA = not available.

Progression of Selective IgA Deficiency to Common Variable Immunodeficiency

A Rischio per progressione a CVID

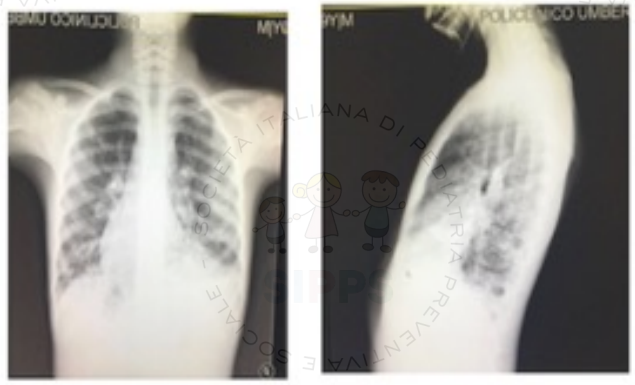
- Pazienti sIgAd con associato difetto sottoclassi IgG
- Autoimmunità
- Familiarità per sIgAd /CVID e/o autoimmunità

- Diagnosi precoce CVID → IvIg per prevenire infezioni gravi, IR..

- IgAd associato a deficit di sottoclassi IgG2 e/o IgG4 infezioni ricorrenti piu frequenti e spesso di gravità maggiore, talora terapia sostitutiva Ig

Stefano

- 9 anni, febbre e e tosse
- RX torace: focolai di **addensamento parailare dx**, ili adenopatici, **opacità base polmane sin, formazioni macronodulari subpleuriche**



AF Zia paterna LES
APP 3 ricoveri per broncopolmonite basale destra in 12 m, alvo diarroico

-Mantoux (-), virologici incluso HIV (-), broncoscopia con BAL (pos per Hemophilus <10.000 CFU)
- **IgA e IgM indosabili, IgG= 620 mg/dl**
- TC torace (linfoadenopatie mediastiniche ascellari lomboaortiche…
- Biopsia polmonare **LIP**

Biopsia linfonadale: non alterazioni morfologiche ed istochimiche della popolazione linfoide sospette per linfoma
Colonscopia: colite microscopica

- eziologia **non infettiva, non neoplastica** della **linfadenopatia**
- **LIP**
- **diarrea cronica** /colite microscopica/collagena
- **Progressiva Ipogammaglobulinemia**

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REPORT

Patients with LRBA deficiency show CTLA4 loss and immune dysregulation responsive to abatacept therapy

BERNICE LO , KEJIAN ZHANG , WEI LU, LIXIN ZHENG, QIAN ZHANG, CHRYSI KANELLOPOULOU, YU ZHANG, ZHIDUO LIU, JILL M. FRITZ, [...], AND MICHAEL B. JORDAN

+23 authors Authors Info & Affiliations

personal data

SIgAd quadro d'esordio →LRBAdef

personal data

Follow up sIGAd

Autoimmunità e progressione a IEIs (anche molti anni dopo la diagnosi)

Ripetere laboratorio periodicamente!

Lab completo di Ig sieriche , sottoclassi IgG, pannello autoanticorpale..

Prognosi?

IgA Deficiency & Mortality: A Population-Based Cohort Study

J. F. Ludvigsson · M. Neovius · L. Hammarström

IgA Deficiency and Risk of Cancer: A Population-Based Matched Cohort Study

Jonas F. Ludvigsson · Martin Neovius · Weimin Ye · Lennart Hammarström

- SIgA d > Rischio mortalità vs popolazione generale
- Causa mortalità piu frequente neoplasie: k gastrico e linfoproliferative

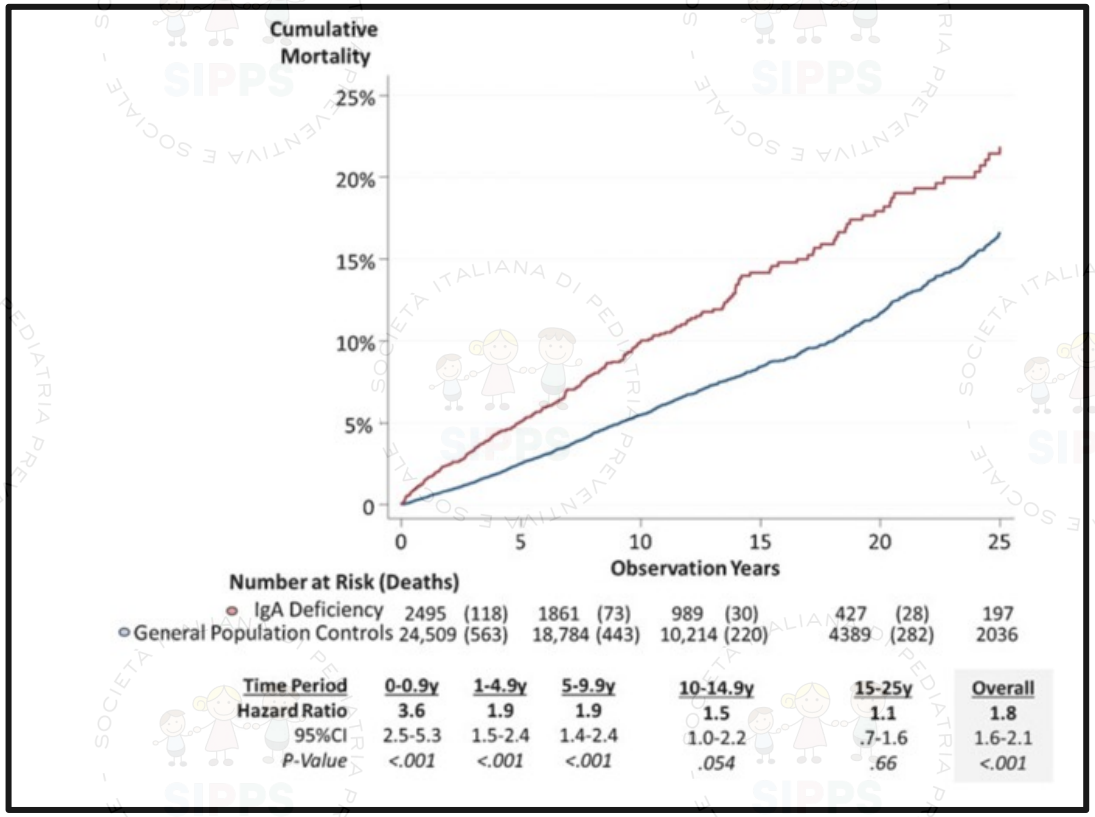


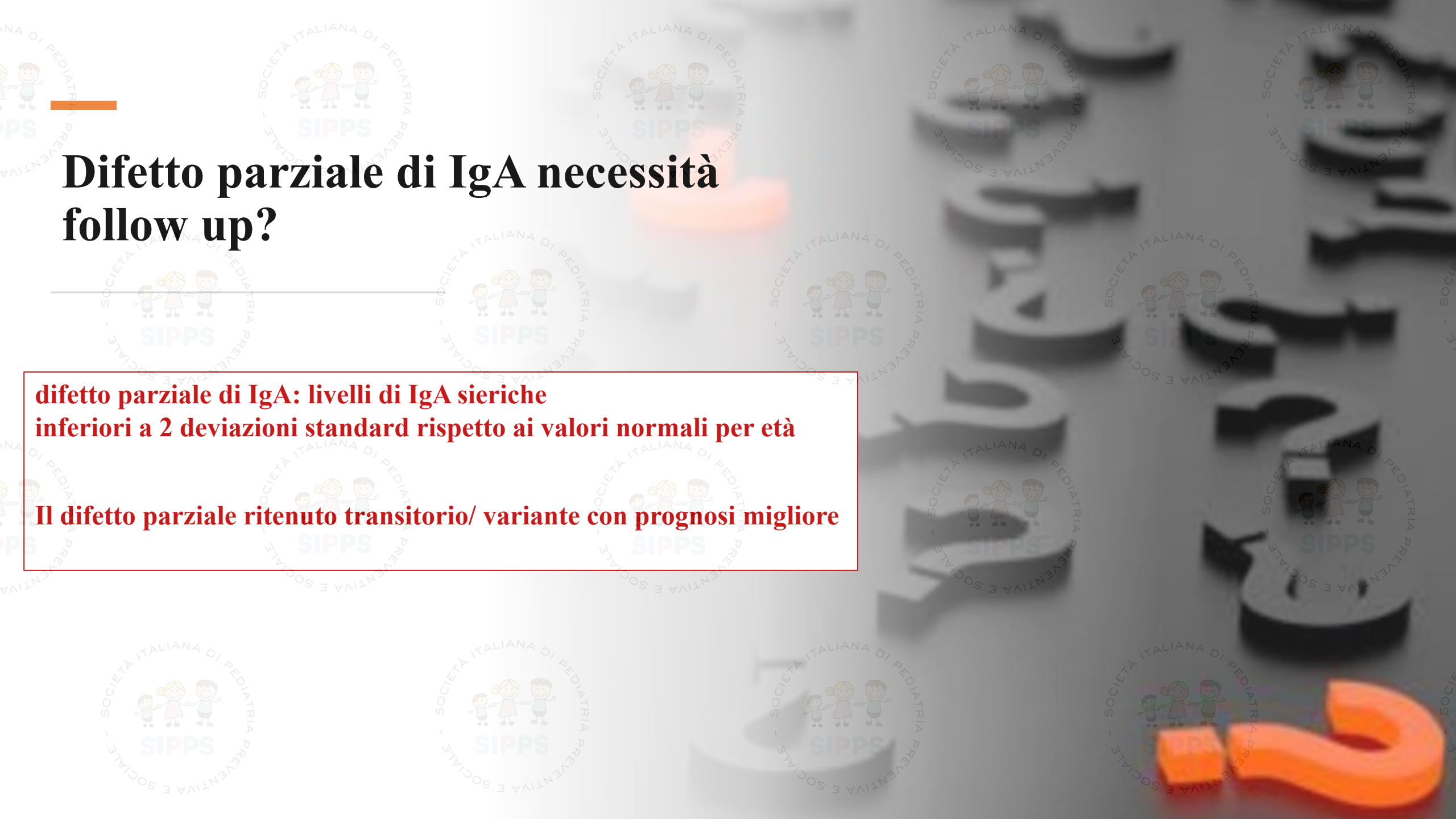
Table II Person-years of observation and deaths

	IgA (n=2495)	Matched controls (n=24,509)
Observation years		
Sum	25,367	257,219
Median	8.3	8.6
Deaths, n	260	1599
Cancer	70 (27 %)	470 (29 %)
Cardiovascular causes	66 (25 %)	531 (33 %)
Respiratory causes	21 (8 %)	99 (6 %)
Other causes	103 (40 %)	499 (31 %)
Death rate (per 10,000 person-years)	102	62
Death rate difference (95%CI)	40 (28–53)	
P-value	*P<.001*	
Attributable death fraction (95%CI)	39 % (31–47 %)	

Difetto parziale di IgA necessità follow up?

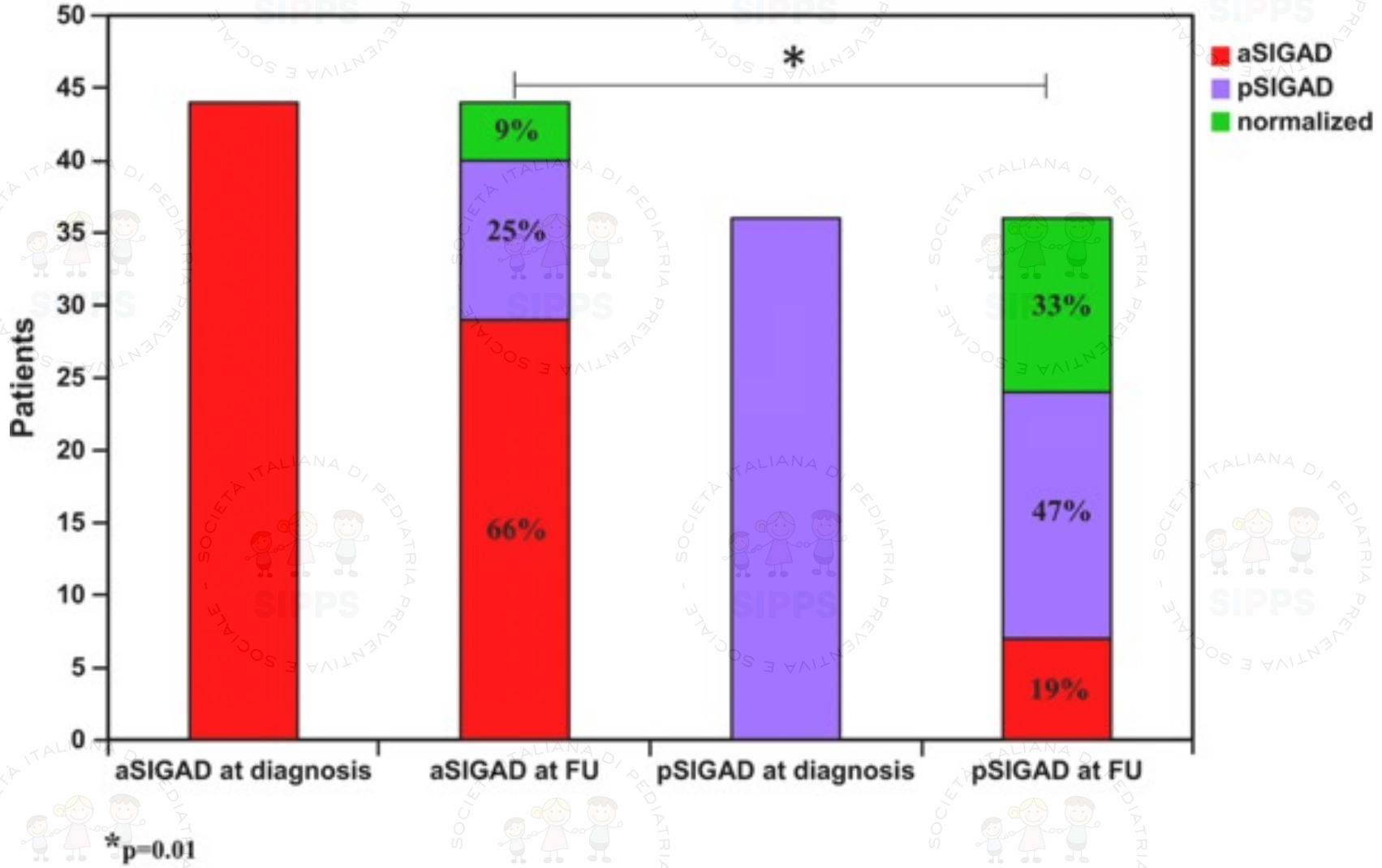
difetto parziale di IgA: livelli di IgA sieriche inferiori a 2 deviazioni standard rispetto ai valori normali per età

Il difetto parziale ritenuto transitorio/ variante con prognosi migliore



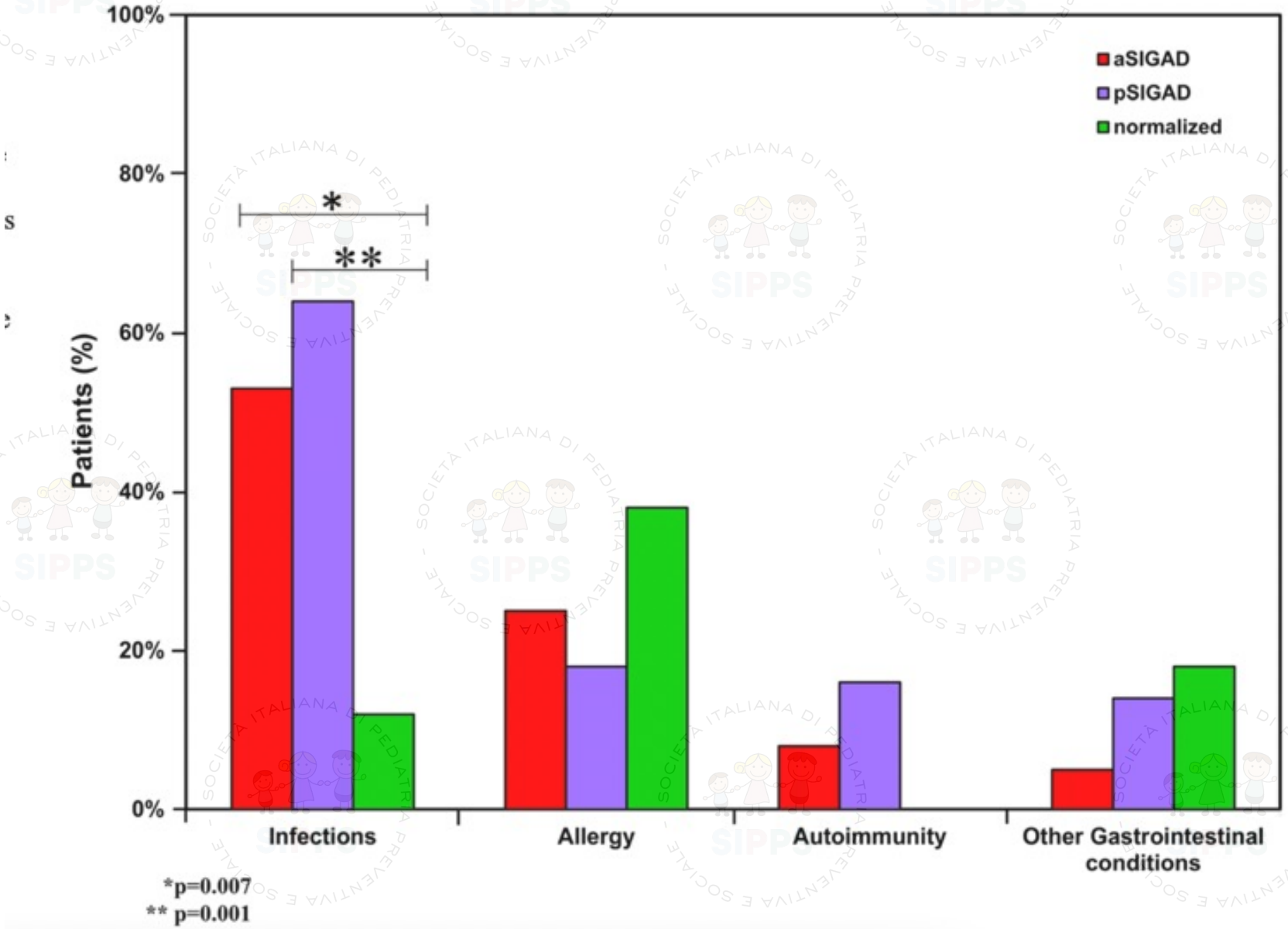
SIgAd sintomatico: Progressione di malattia in 5 aa.

fenotipo clinico 103 pz sIGAd
sintomatici alla diagnosi
53 assoluto, 50 parziale
4-18aa
FU 5 aa



Moschese V et al. Eur J Pediatr. 2019 Jan;178(1):51-60.

SIgAd sintomatico: fenotipo clinico a 5 aa



Difetto parziale di IgA necessita FU clinico e di laboratorio come il sIgAd assoluto

Conclusions: Regardless of a diagnosis of absolute or partial defect, monitoring of symptomatic patients with selective IgA deficiency is recommended overtime for prompt identification and treatment of associated diseases. Further, diagnostic workup protocols should be revisited in children with IgA deficiency.

What is Known:

- *Selective IgA Deficiency is the most common primary immunodeficiency and is usually asymptomatic.*
- *Symptomatic pediatric patients with selective IgA deficiency mostly suffer with respiratory and gastrointestinal infections.*

What is New:

- *Symptomatic children with partial IgA defect may have similar clinical, immunological, and genetic features than symptomatic children with absolute IgA deficiency.*
- *Symptomatic children with partial IgA deficiency deserve accurate monitoring for associated diseases as per children with absolute IgA deficiency.*

Abbagli

MEDICAL INTELLIGENCE ARCHIVE

Anaphylactic Reactions after Gamma Globulin Administration in Patients with Hypogammaglobulinemia

Arvil Wesley Burks, M.D., Hugh A. Sampson, M.D., and Rebecca H. Buckley, M.D.

Article Figures/Media

February 27, 1986
N Engl J Med 1986; 314:560-564
DOI: 10.1056/NEJM198602273140907

Autoanticorpi organo e non organo specifici sono presenti nel 40% dei pazienti; anche se asintomatici

20-40% pz sIgAd produzione anticorpi (IgG, IgM , IgE) anti IgA con reazioni avverse/anafilattiche, talvolta gravi, se trasfusioni con sangue o emoderivati contenenti IgA

.

THE JOURNAL OF AABB
transfusion.org
TRANSFUSION

COMMENTARY

The entity of immunoglobulin A–related anaphylactic transfusion reactions is not evidence based

- **Rara possibilità di sviluppo di anticorpi IgE anti-IgA in pazienti con sIgAd**
- Rara anafilassi in corso di somministrati di emoderivati contenenti IgA.
- In attesa di ulteriori studi per di conferma SIgAD /reazioni trasfusionali anafilattiche, cautela nel somministrare sangue contenente IgA a soggetti con deficit di IgA

Case Report

Persistent Hyper IgA as a Marker of Immune Deficiency: A Case Report

Russell J. Hopp * and Hana B. Niebur

IgA sieriche in età pediatrica superiori a **368 mg/dL** sono spesso associati a:

malattie reumatologici,

malattie infiammatorie croniche intestinali,

Immunodeficienza

Conclusioni

Non raro ma non trascurabile!!!

Riscontro sIgAd asintomatico richiede work up immunologico per confermare la diagnosi

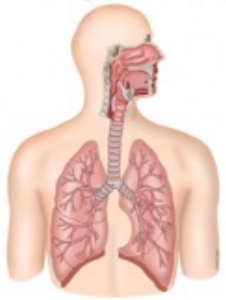
Follow up necessario anche negli asintomatici e nel difetto parziale (concordato con pediatra immunologo)

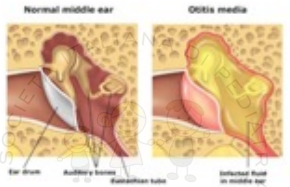
sIgAd manifestazione iniziale di CVID o altre IEI

Conclusioni

casi asintomatici alla diagnosi necessitano FU

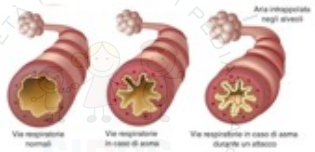
IRR (50-80%)

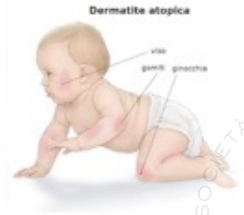




Maggiore frequenza se si associa deficit sottoclassi IgG (IgG2 e IgG4)

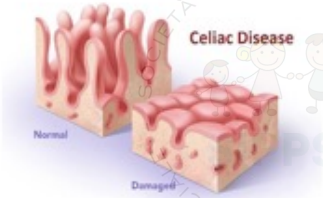
Atopia(20-50%)

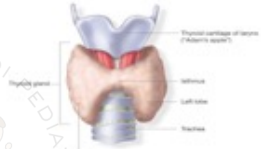




Rare reazioni (anche anafilassi) a seguito di trasfusioni di emoderivati (pz con anti IgA)

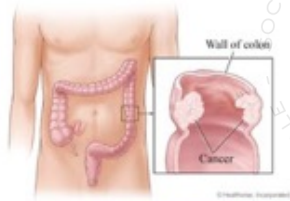
Autoimmunità (10-30%)

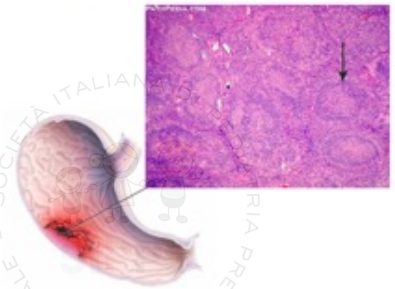




Autoimmunità popolazione generale 5%

K gastrocolon, Linfoprolif. (2-7%)





Yazdani et al. Scand J Immunol 2017; 85:3,12

SIPPS

SOCIETÀ ITALIANA DI PEDIATRIA PREVENTIVA E SOCIALE

Challenge sIgAD: determinare quali pazienti richiedono monitoraggio

Revisione sistematica della letteratura: quesiti specifici

Valutazione delle informazioni disponibili (storia naturale, fenotipi clinici, prevalenza patologie associate, criteri diagnosi e FU e monitoraggio dei livelli di assistenza erogati)