Il Lupus Eritematoso Sistemico

Prof. Raffaella Scorza

Unità di Allergologia e Immunologia Clinica
&
Centro di Riferimento per le Patologie Autoimmuni Sistemiche

Università di Milano
Fondazione IRCCS Ospedale Policlinico, Mangiagalli e Regina Elena

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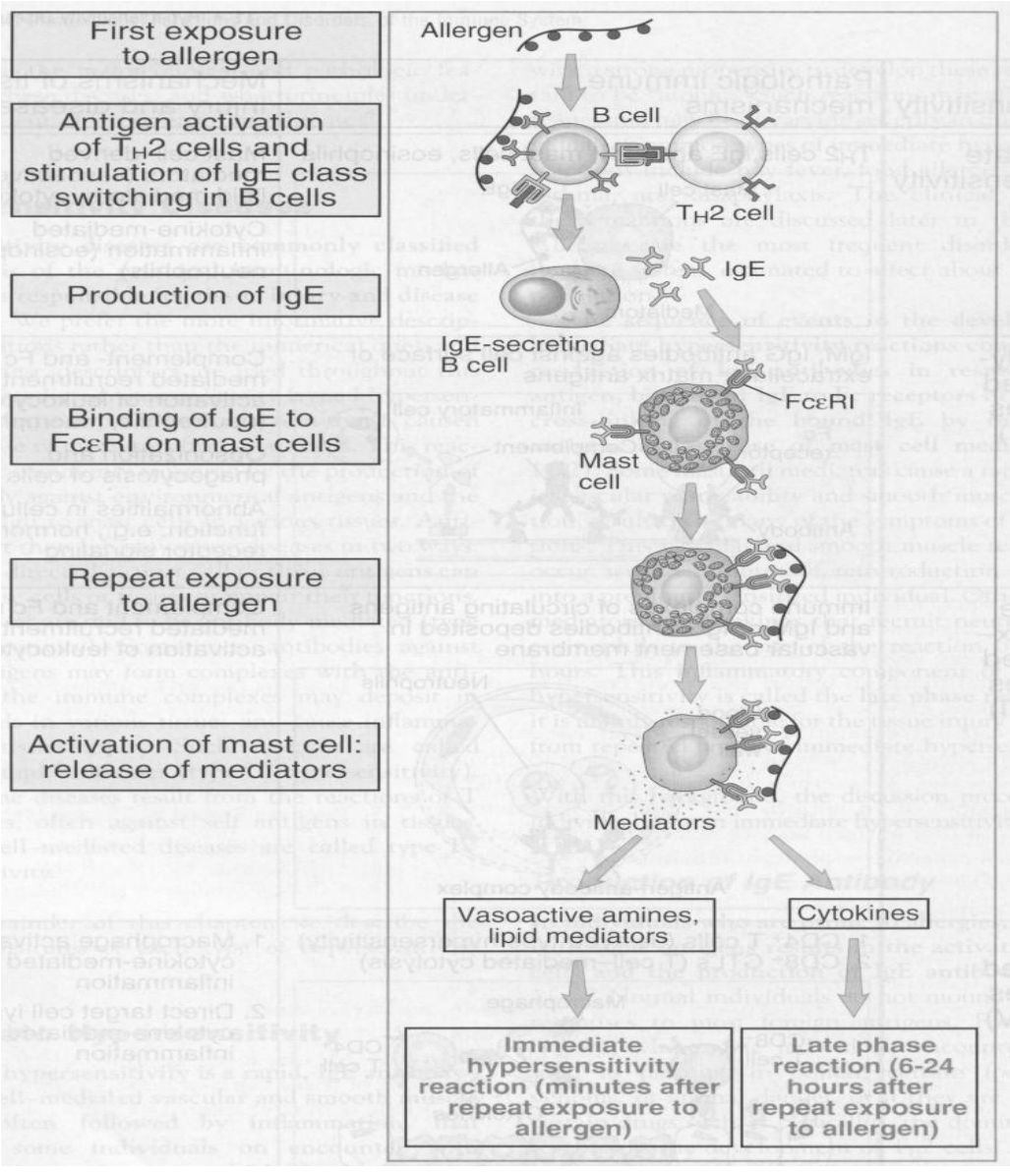
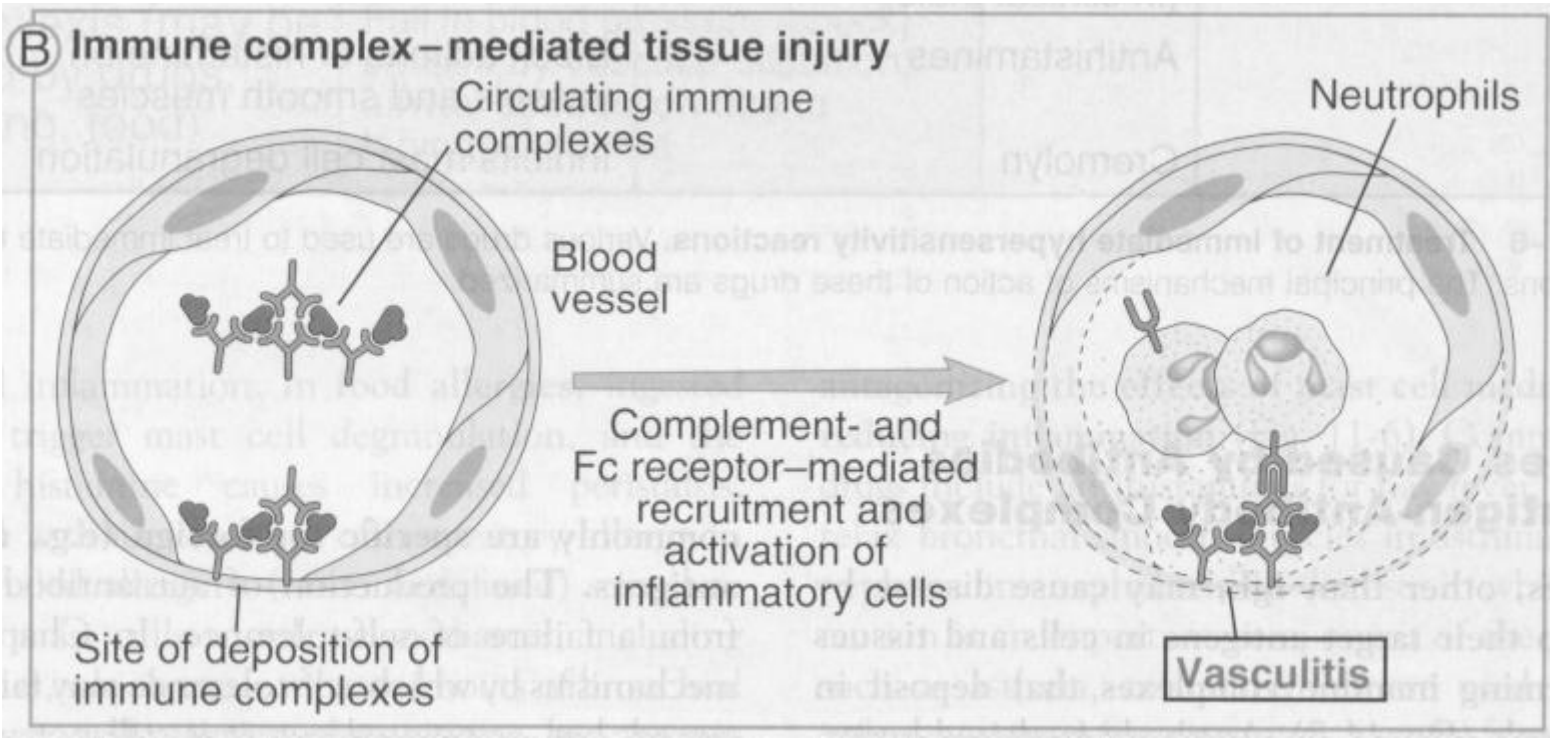
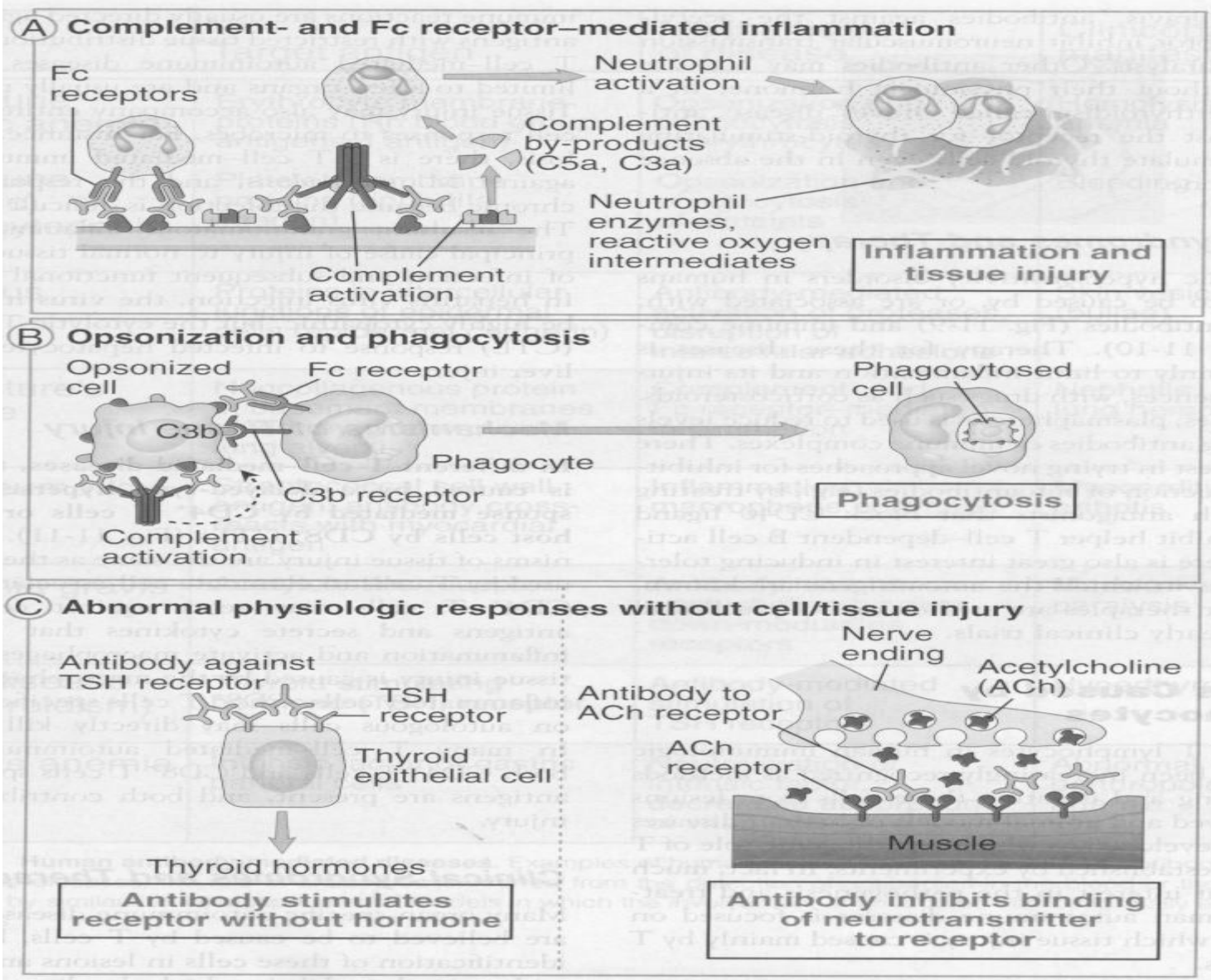
Ipersensibilità Tipo I



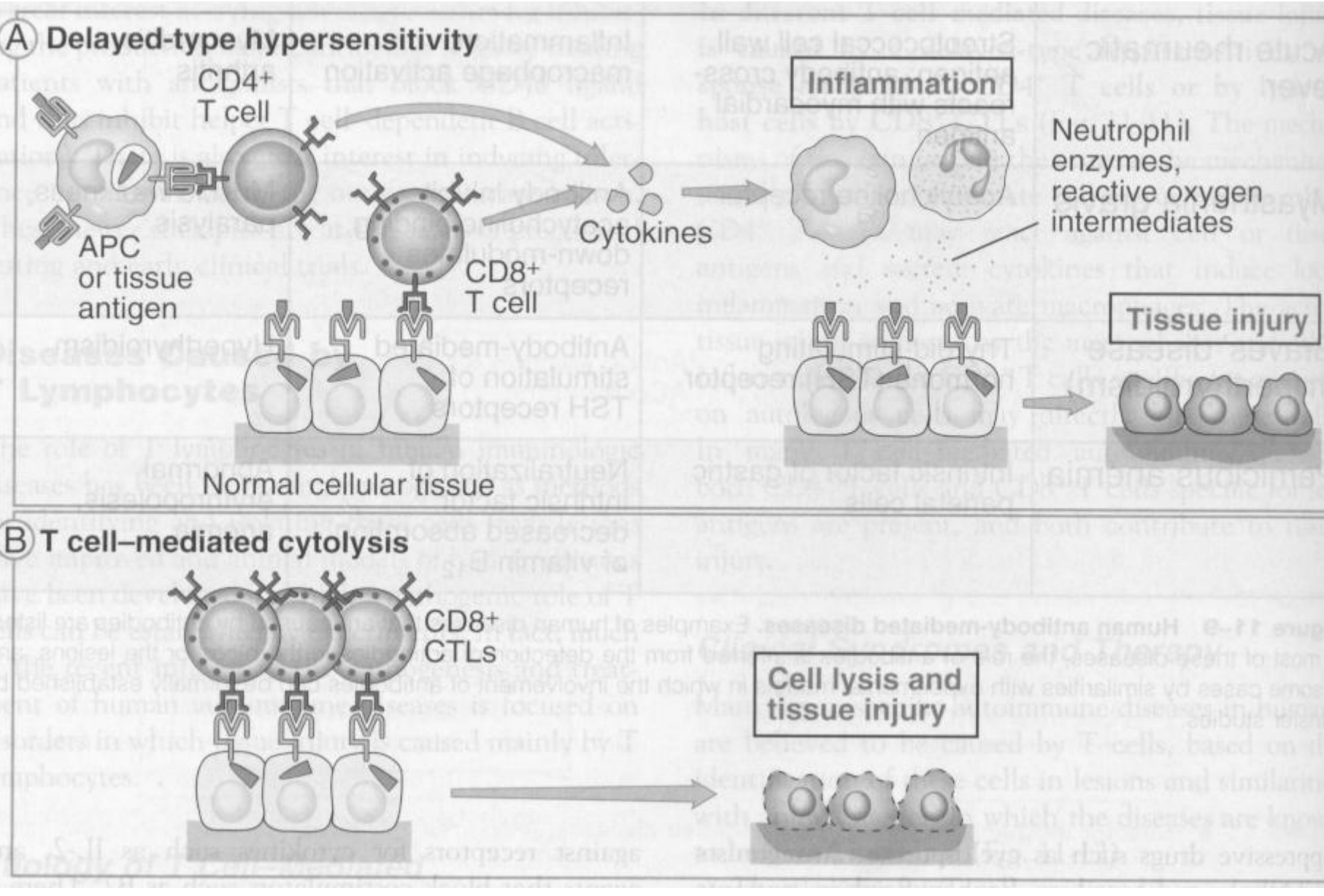
Clinical syndrome	Clinical and pathologic manifestations
Allergic rhinitis, sinusitis (hay fever)	Increased mucus secretion; inflammation of upper airways, sinuses
Food allergies	Increased peristalsis due to contraction of intestinal muscles
Bronchial asthma	Bronchial hyper-responsiveness caused by smooth muscle contraction; inflammation and tissue injury caused by late phase reaction
Anaphylaxis (may be caused by drugs, bee sting, food)	Fall in blood pressure (shock) caused by vascular dilatation; airway obstruction due to laryngeal edema



Disease	Antibody specificity	Mechanisms of disease	Clinicopathologi manifestations
Systemic lupus erythematosus	DNA, nucleoproteins, others	Complement- and Fc receptor–mediated inflammation	Nephritis, arthritis, vasculitis
Polyarteritis nodosa	Hepatitis B virus surface antigen	Complement- and Fc receptor–mediated inflammation	Vasculitis
Post-streptococcal glomerulonephritis	Streptococcal cell wall antigen(s)	Complement- and Fc receptor–mediated inflammation	Nephritis


A Complement- and Fc receptor–mediated inflammation
Fc receptors
Neutrophil activation
Complement by-products (C5a, C3a)
Neutrophil enzymes, reactive oxygen intermediates
Inflammation and tissue injury
Complement activation
B Opsonization and phagocytosis
Opsonized cell
Fc receptor
C3b
Phagocyte
C3b receptor
Complement activation
Phagocytosed cell
Phagocytosis
C Abnormal physiologic responses without cell/tissue injury
Antibody against TSH receptor
TSH receptor
Thyroid epithelial cell
Thyroid hormones
Antibody stimulates receptor without hormone
Nerve ending
Acetylcholine (ACh)
Antibody to ACh receptor
ACh receptor
Muscle
Antibody inhibits binding of neurotransmitter to receptor

Disease	Target antigen	Mechanisms of disease	Clinicopathologi manifestations
Autoimmune hemolytic anemia	Erythrocyte membrane proteins (Rh blood group antigens, I antigen)	Opsonization and phagocytosis of erythrocytes	Hemolysis, anemia
Autoimmune (idiopathic) thrombocytopenic purpura	Platelet membrane proteins (gpIIb:IIIa integrin)	Opsonization and phagocytosis of platelets	Bleeding
Pemphigus vulgaris	Proteins in intercellular junctions of epidermal cells (epidermal cadherin)	Antibody-mediated activation of proteases, disruption of intercellular adhesions	Skin vesicles (bullae)
Goodpasture's syndrome	Noncollagenous protein in basement membranes of kidney glomeruli and lung alveoli	Complement- and Fc receptor–mediated inflammation	Nephritis, lung hemorrhages
Acute rheumatic fever	Streptococcal cell wall antigen; antibody cross-reacts with myocardial antigen	Inflammation, macrophage activation	Myocarditis, arthritis
Myasthenia gravis	Acetylcholine receptor	Antibody inhibits acetycholine binding, down-modulates receptors	Muscle weakness, paralysis
Graves' disease (hyperthyroidism)	Thyroid-stimulating hormone (TSH) receptor	Antibody-mediated stimulation of TSH receptors	Hyperthyroidism
Pernicious anemia	Intrinsic factor of gastric parietal cells	Neutralization of intrinsic factor, decreased absorption of vitamin B_{12}	Abnormal erythropoiesis, anemia

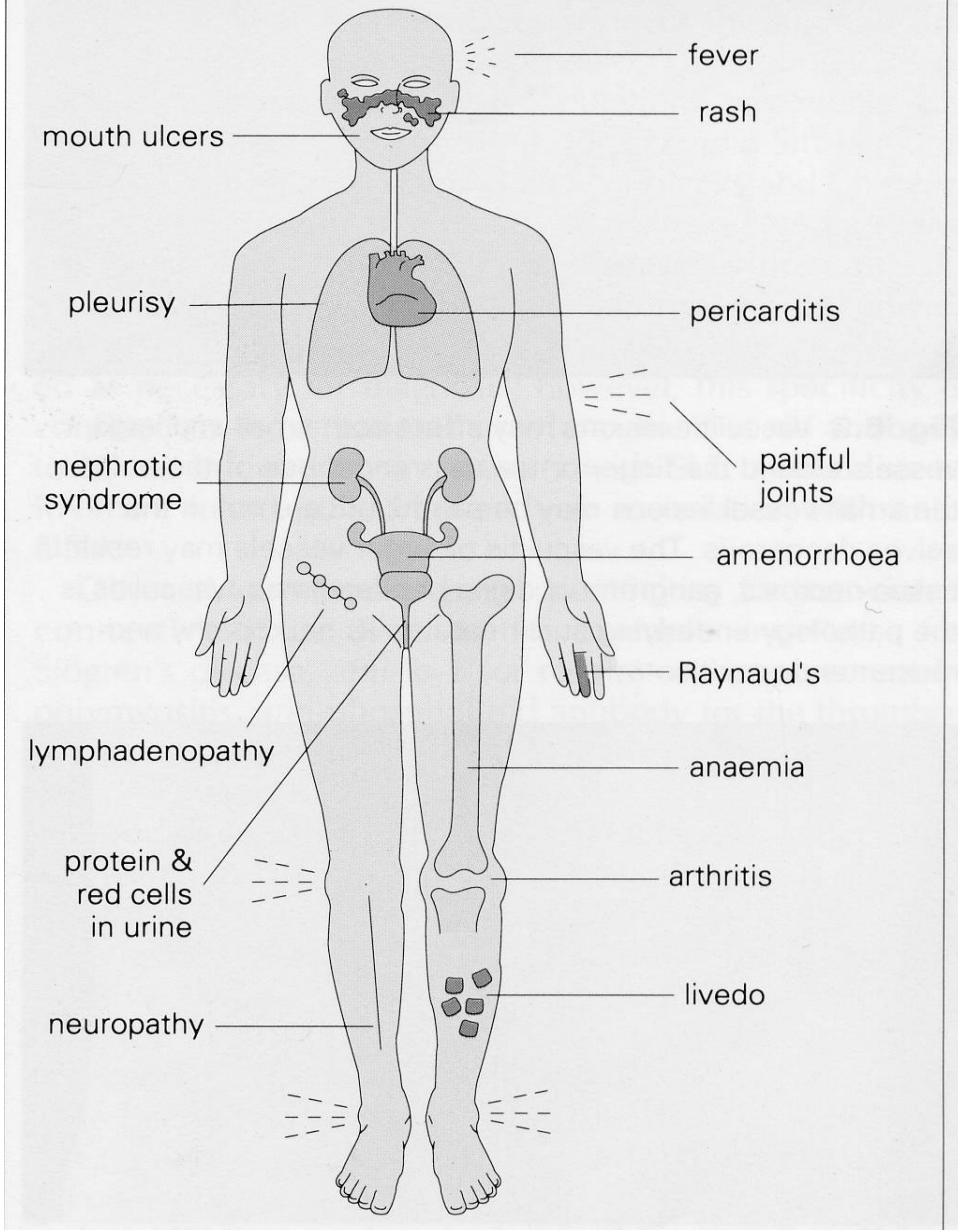

A Delayed-type hypersensitivity
CD4+
T cell
APC
or tissue
antigen
CD8+
T cell
Cytokines
Inflammation
Neutrophil
enzymes,
reactive oxygen
intermediates
Tissue injury
Normal cellular tissue
B T cell–mediated cytolysis
CD8+
CTLs
Cell lysis and
tissue injury

Disease	Specificity of pathogenic T cells	Human disease	Animal models
Insulin-dependent (type I) diabetes mellitus	Islet cell antigens (insulin, glutamic acid decarboxylase, others)	Specificity of T cells not established	NOD mouse, BB rat, transgenic mouse models
Rheumatoid arthritis	Unknown antigen in joint synovium	Specificity of T cells and role of antibody not established	Collagen-induced arthritis, others
Experimental allergic encephalomyelitis	Myelin basic protein, proteolipid protein	Postulated: multiple sclerosis	Induced by immunization by CNS myelin antigens; transgenic mouse models
Inflammatory bowel disease	Unknown, ? role of intestinal microbes	Specificity of T cells not established	Induced by IL-2 or IL-10 gene knockout or lack of regulatory T cells

Il lupus eritematoso sistemico (LES) è una malattia infiammatoria cronica caratterizzata da:

- Presenza di autoanticorpi diretti contro antigeni nucleari e, in maniera caratteristica da anticorpi anti-dsDNA
- Presenza di immunocomplessi circolanti e altri segni di attivazione del sistema immunitario
- Interessamento multiorgano

The classical SLE patient

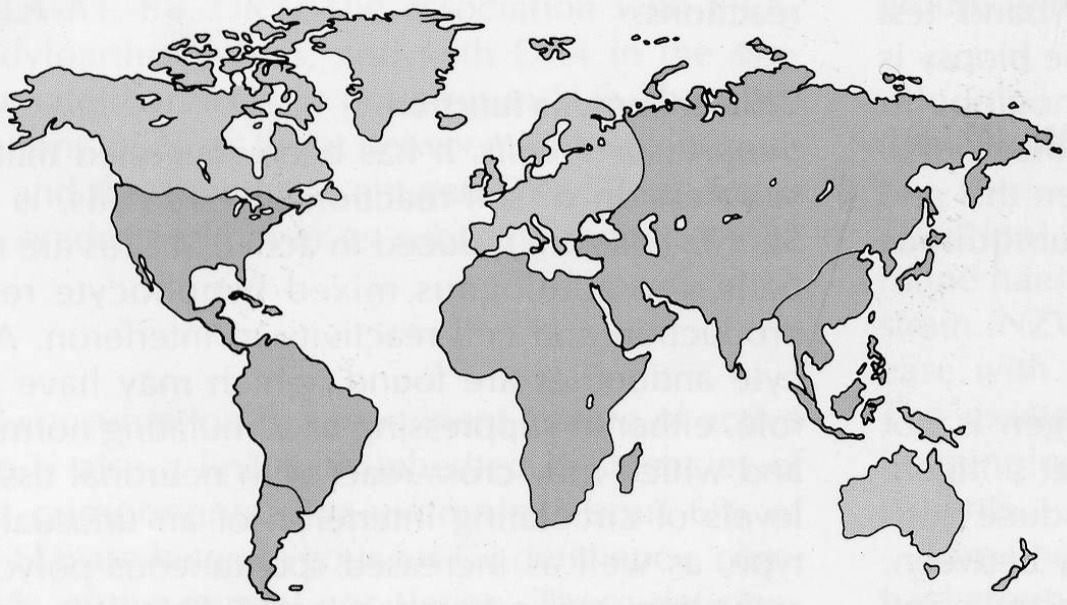


Caratteristiche epidemiologiche

Prevalenza: 180-500 casi/milione di abitanti

F:M = 9:1

Worldwide prevalence of SLE



high (in population/ major sub–populations)

low

uncertain

Clustering of autoimmune diseases in families of 268 Italian SLE patients

reported disorder	affected siblings	F:M ratio
SLE	1.2% (n=6)*	5:1
other systemic auotoimmune disease	0.6% (n=3)	3:0
organ specific autoimmune diseases	1.9 (n=10)	5:5
photosensitivity	1.3% (n=7)	4:3
Raynaud's phenomenon	1.2% (n=6)	4:2

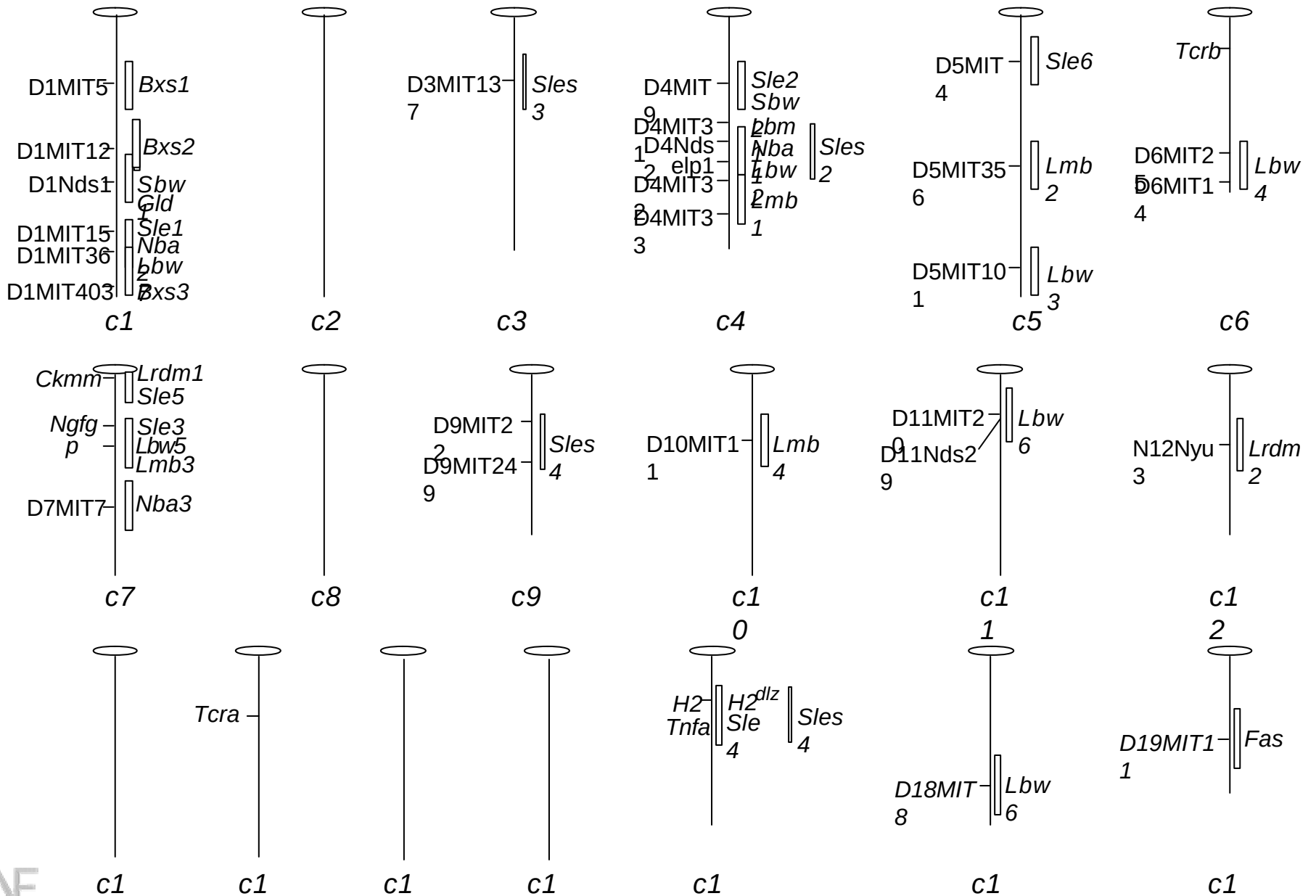
* Compared with population prevalence: p=0.000; λ_s=30

Della Bella et al.

CONCORDANZA PER ALTERAZIONI CLINICHE E BIOUMORALI IN COPPIE DI GEMELLI MONOZIGOTI AFFETTI DA LES

Carattere	Livello di concordanza
Ipergammaglobulinemia	100%
Anticorpi anti-nucleo	100%
Fotosensibilità	80-90%
Eritema a farfalla	80-90%
LED	50%
Alopecia	50%
Sierosite	50%
Proteinuria	50%
Wasserman falsamente positiva	25%

Murine lupus					
Strain	**Predominant manifestations**	**Influence of gender**	**Genes**	**Immunology**	**Survival (50%)**
NZB	haemolytic anaemia (glomerulonephritis) (reticulum sarcoma)	slight	polygenic	anti-RBC IgM hyperglobulinaemia immune complexes +	8 months
NZB/W F1	glomerulonephritis Sjögren's syndrome (haemolytic anaemia)	oestrogens accelerate, androgens retard	polygenic	anti-DNA (ds & ss) -RNA -gp70 -Sm antibodies immune complexes ++	8 months (F)
MRL lpr/lpr	glomerulonephritis lymphoproliferation periarthritis vasculitis Sjögren's syndrome	some androgen protection	lpr major accelerator	anti-DNA (ds & ss), -Sm, -thymocyte, -globulin (RFs) antibodies cryoglobulins T cell dysregulation hyperglobulinaemia	12–14 months
BxSB	severe proliferative glomerulonephritis	males worse	—	anti-DNA, -RBC -globulin, -thymocyte antibodies	6 months (M+F)


D1MIT5
Bxs1
D1MIT12
Bxs2
D1Nds1
Sbw1
Gld1
D1MIT15
Sle1
D1MIT36
Nba2
Lbw2
D1MIT403
Bxs3
c1
c2
D3MIT137
Sles3
c3
D4MIT9
Sle2
Sbw1
D4MIT31
Lbm2
D4Nds2
Nba1
elp1
Lbw1
D4MIT32
Lmb1
D4MIT33
Sles2
c4
D5MIT4
Sle6
D5MIT356
Lmb2
D5MIT101
Lbw3
c5
Tcrb
D6MIT25
D6MIT14
Lbw4
c6
Ckmm
Lrdm1
Sle5
Ngfgp
Sle3
Lbw5
Lmb3
D7MIT7
Nba3
c7
c8
D9MIT22
D9MIT249
Sles4
c9
D10MIT11
Lmb4
c10
D11MIT20
D11Nds29
Lbw6
c11
N12Nyu3
Lrdm2
c12
Tcra
c13
c14
c15
H2Tnfa
H2dlzSle4
Sles4
c16
D18MIT8
Lbw6
c17
D19MIT11
Fas
c18

Individui suscettibili

Sle1
Sap
C1q

Pathway 1: perdita della tolleranza verso gli antigeni nucleari

2-4% della popolazione ANA positiva

Sle2
Sle3
Fas
Lyn
SHP-1

Pathway 2: disregolazione del sistema immunitario

Pathway 3: coinvolgimento degli organi bersaglio

Autoimmunità patogenetica

Sle6
Fcγ RIII

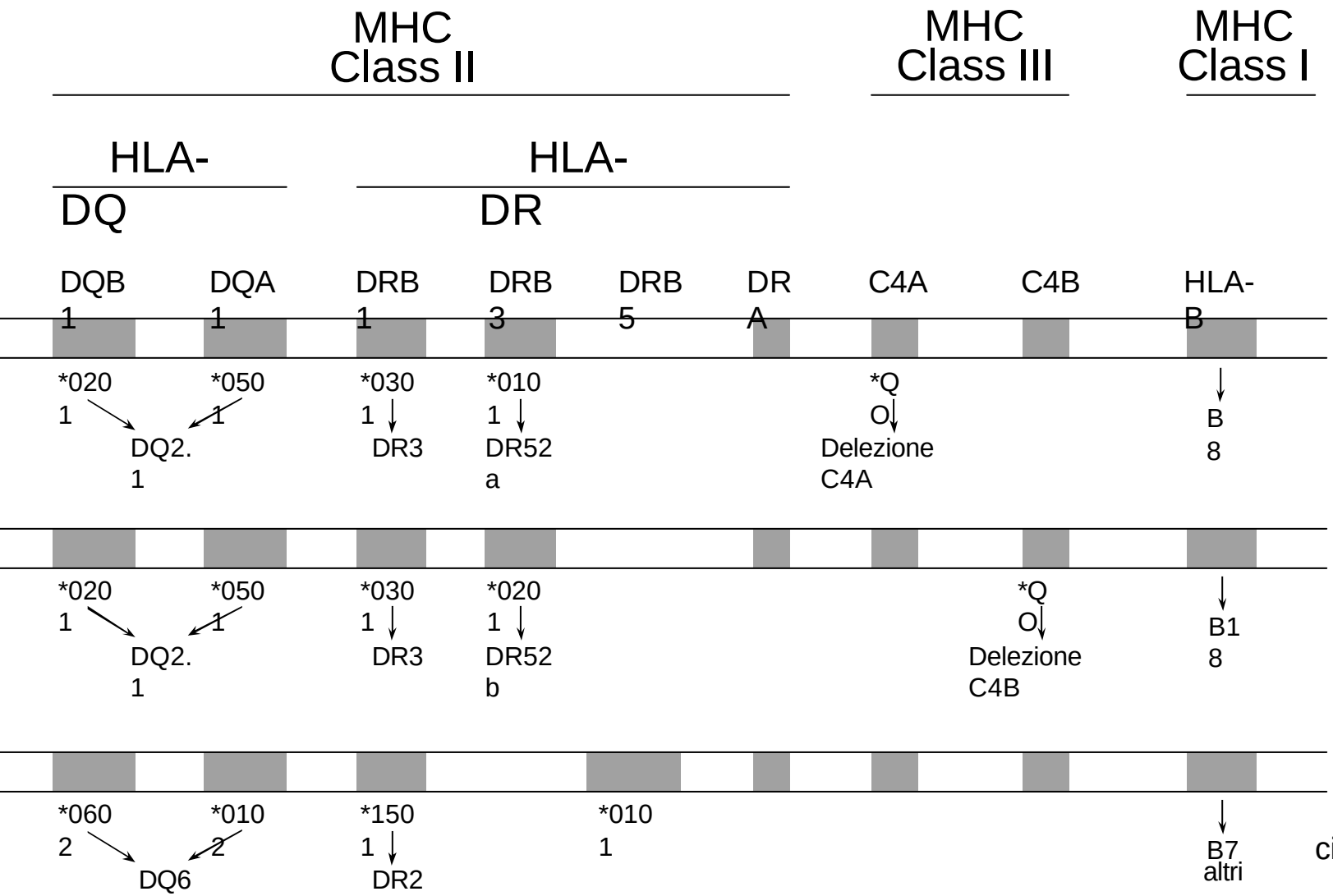
Disordini neurologici

Nefrite

Artrite

Vasculite

Aplotipi HLA associati al LES



Gruppi etnici

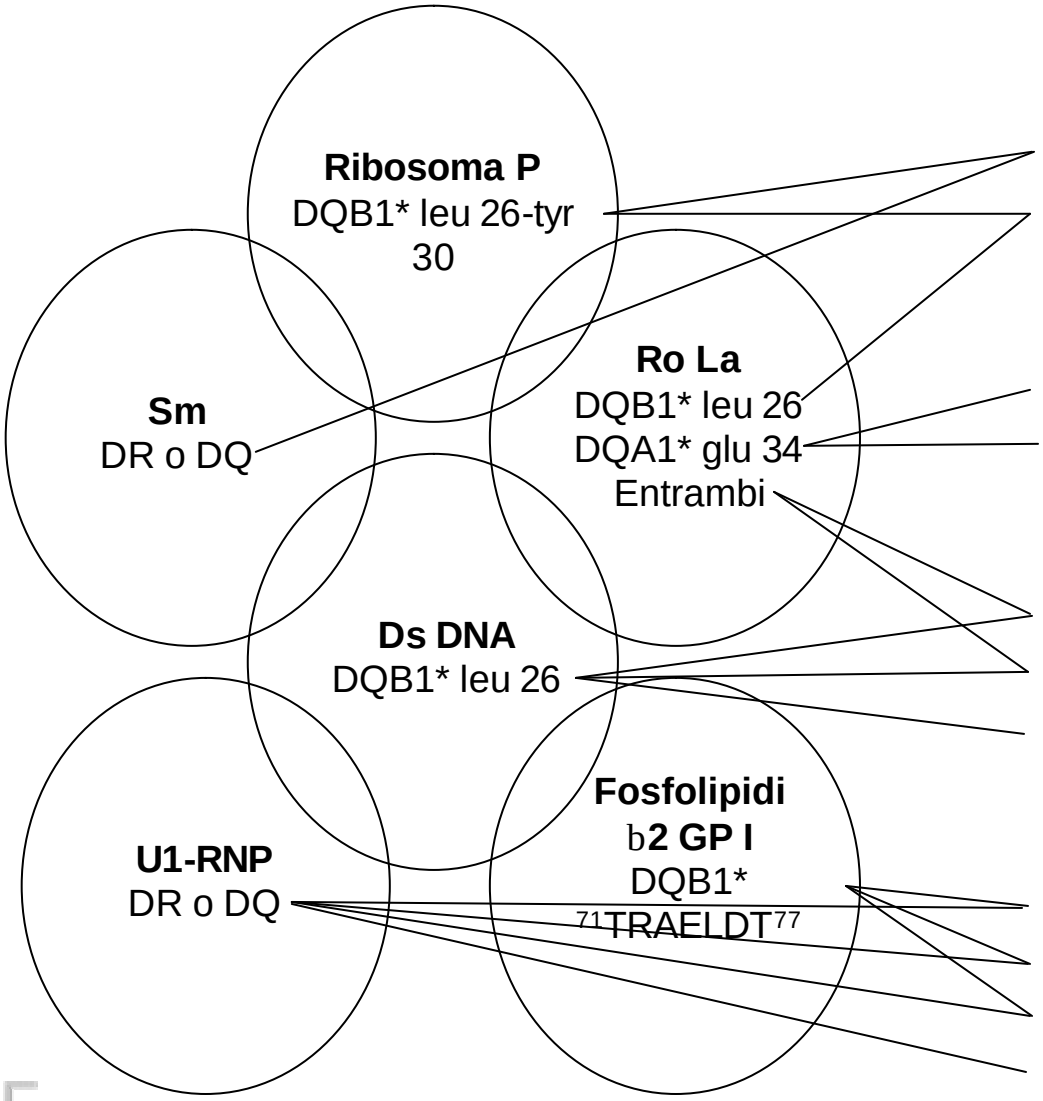
Caucasoid
Europei settentriona
e occidenta

Caucasoid
Europei meridionali
e messican

Caucasoid
Europei occidentali,
giapponesi
cinesi, corean
africani
(DRB1*1503

* Nella popolazione italiana RR=12.76 *Scorza et al.*

Associazioni HLA – autoanticorpi nel LES



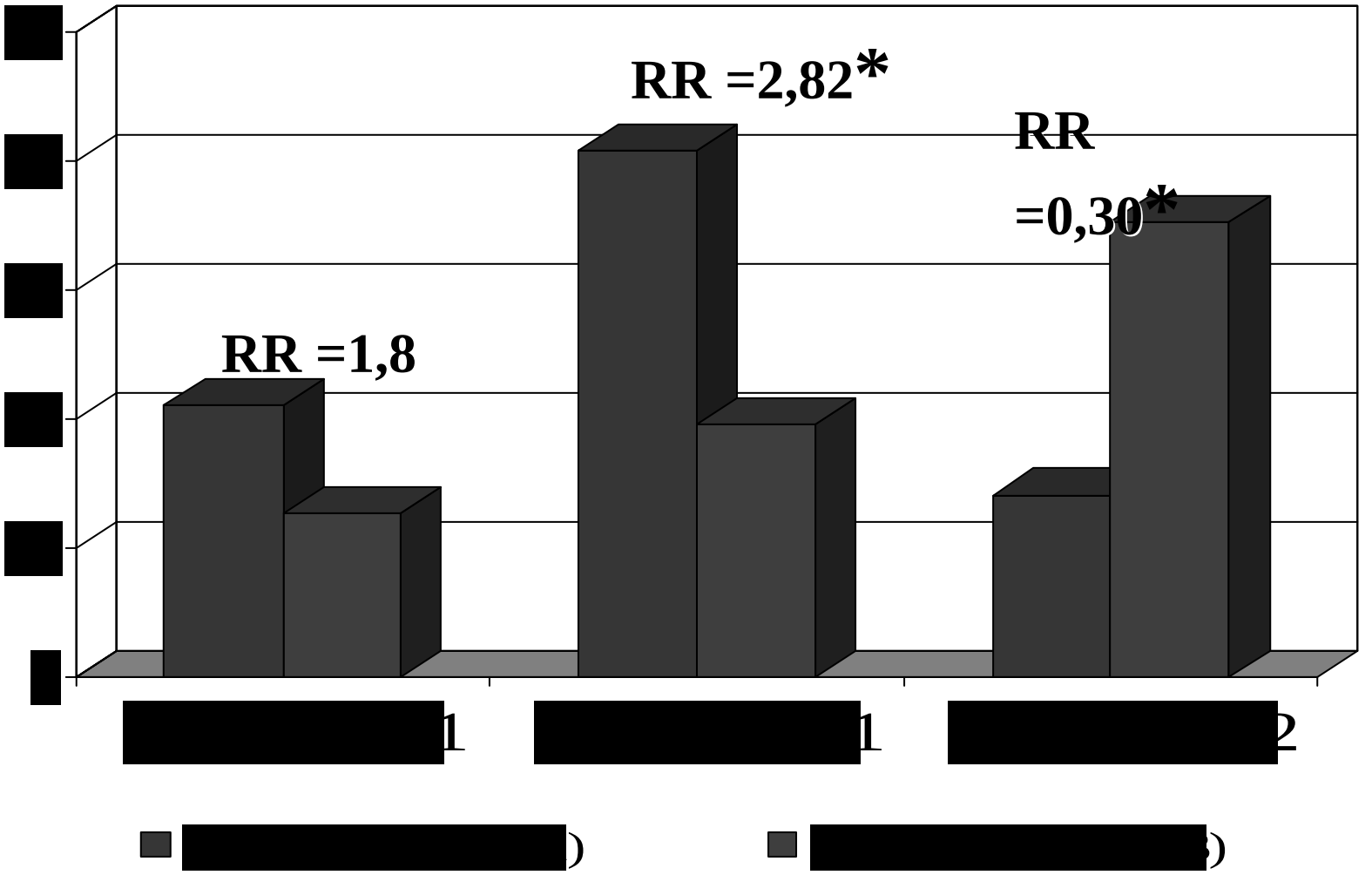
DQ6 (**DQB1*0602**) – DR2 (***1501/*1503**)
DQ8 (**DQB1*0302**) – DR4

DQ7 (**DQA1*0501**) – DR5, DR4
DQ4 (**DQA1*0401**) – DR8, DR3 (***0302**)

DQ2.1 (**DQB1*0201**) – DR3 (***0301**)
DQ6 (**DQB1*0601**) – DR2, DR13
DQ8 (**DQB1*0302**) – DR4

DQ7 (**DQB1*0301**), DR5, DR4
DQ8 (**DQB1*0302**), DR4

Distribution of relevant HLA-Class II alleles in SLE patients with and without lupus nephritis



Scorza et al.

Opposite influences by HLA-DQA1*01 alleles on the DR15- associated lupus nephritis

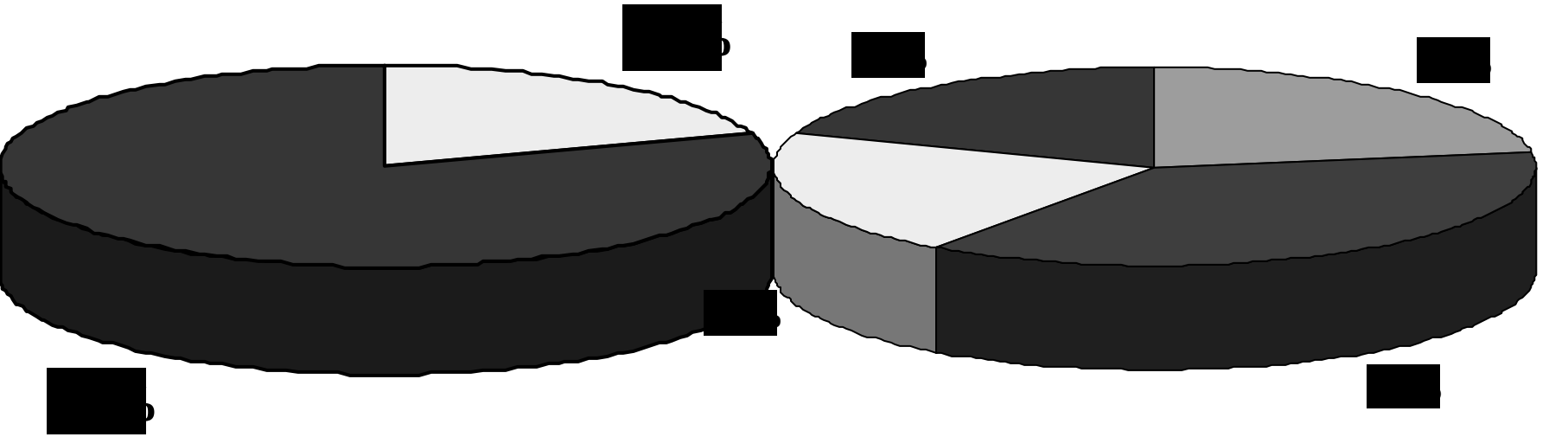
	nephritis +ve (n)	nephritis –ve (n)	RR	*p*
RB1*1501, QA1*0101		0	65,9	<0,001
RB1*1501, QA1*0102	1	21	0,1	<0,001
RB1*1501, QA1*0103	3	1	7,6	0,138

Scorza et al.

Distribution of different glomerulonephritis patterns (WHO classes) in SLE patients by HLA-DR 15 bearing haplotypes

DR15+ve patients n=15

DR15-ve patients n=57



Class II: mesangial

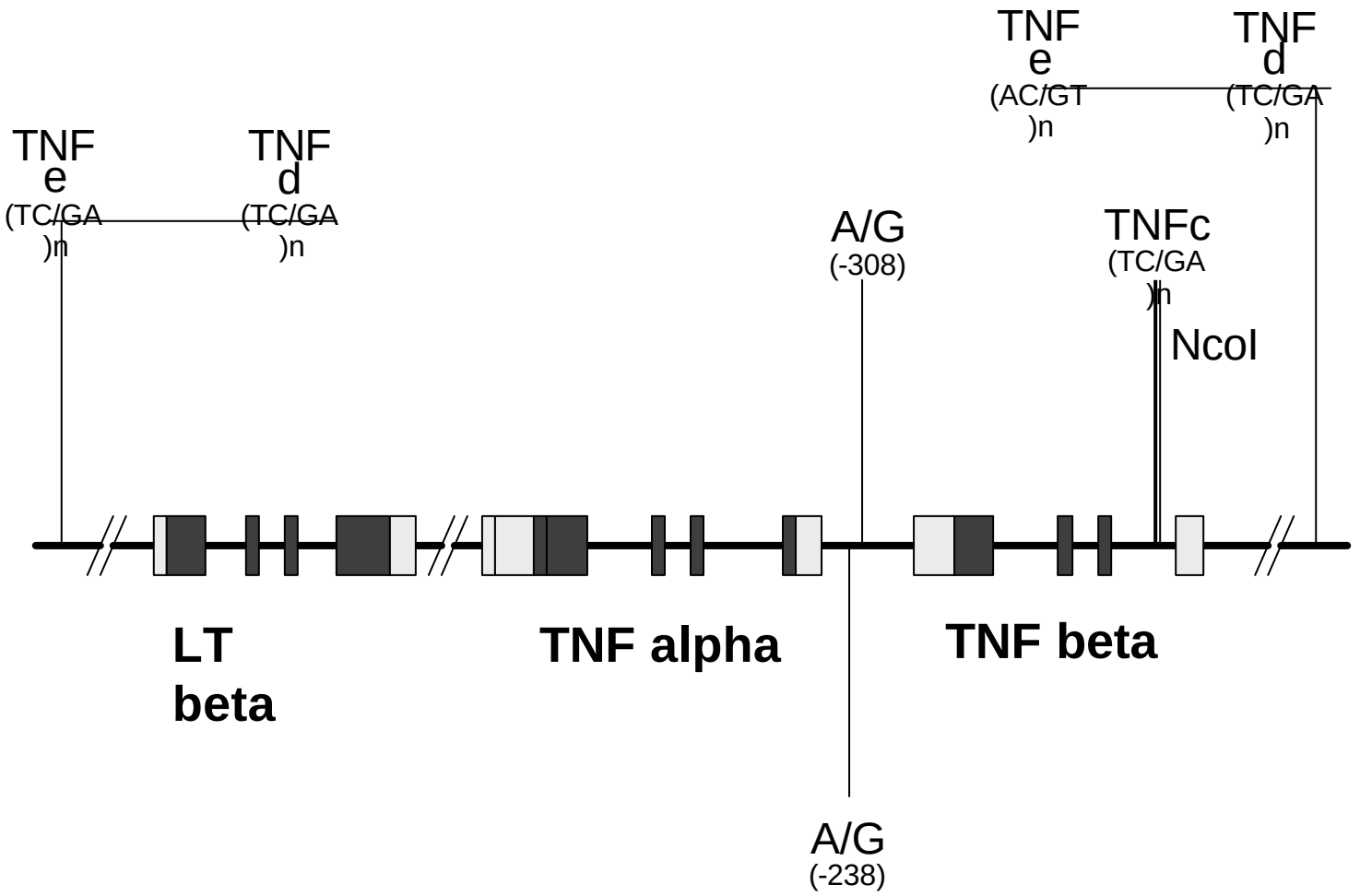
Class III: focal proliferative

Class V: membranouse

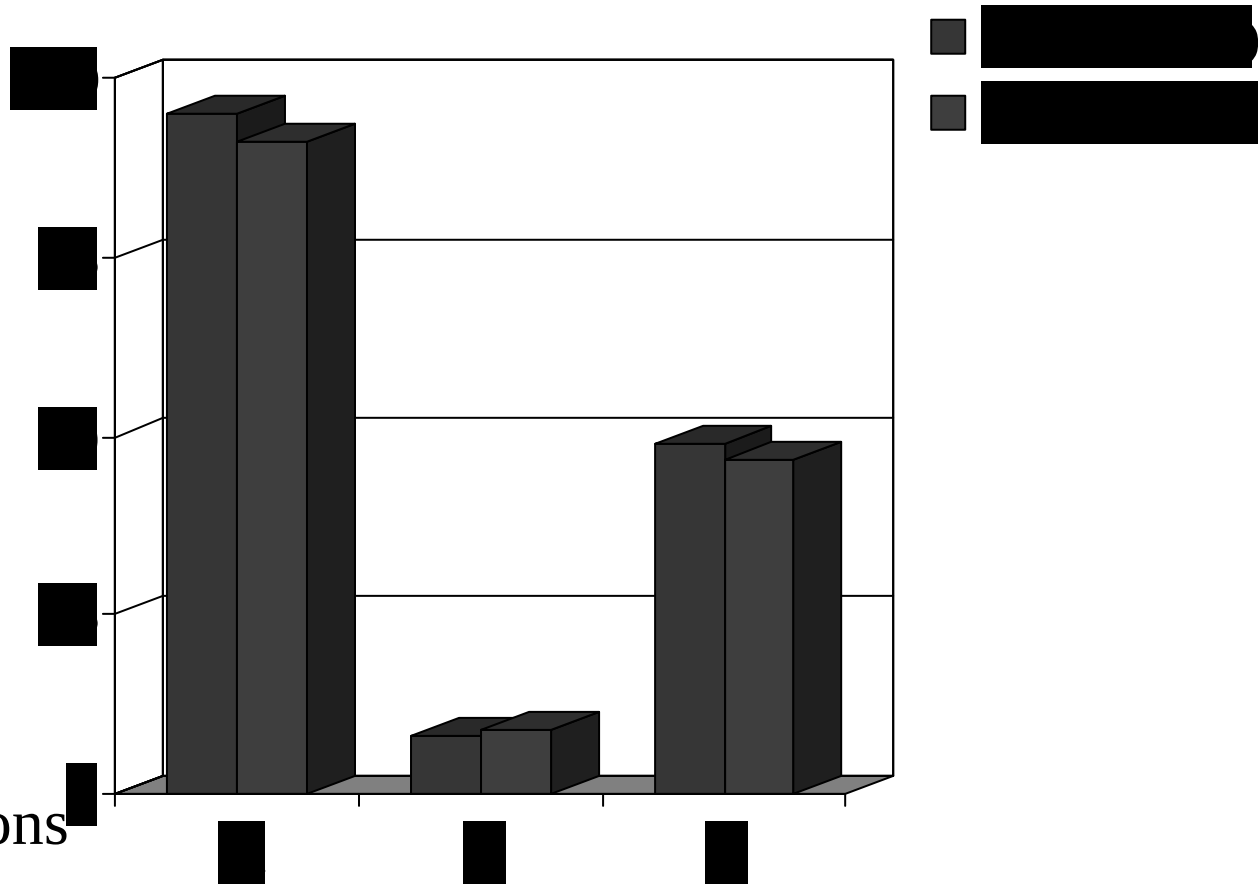
Class IV: diffuse proliferative

Scorza et al.

Polimorfismo nella regione TNF



Fas polymorphism is not associated to SLE in Italian population



Nucleotide positions

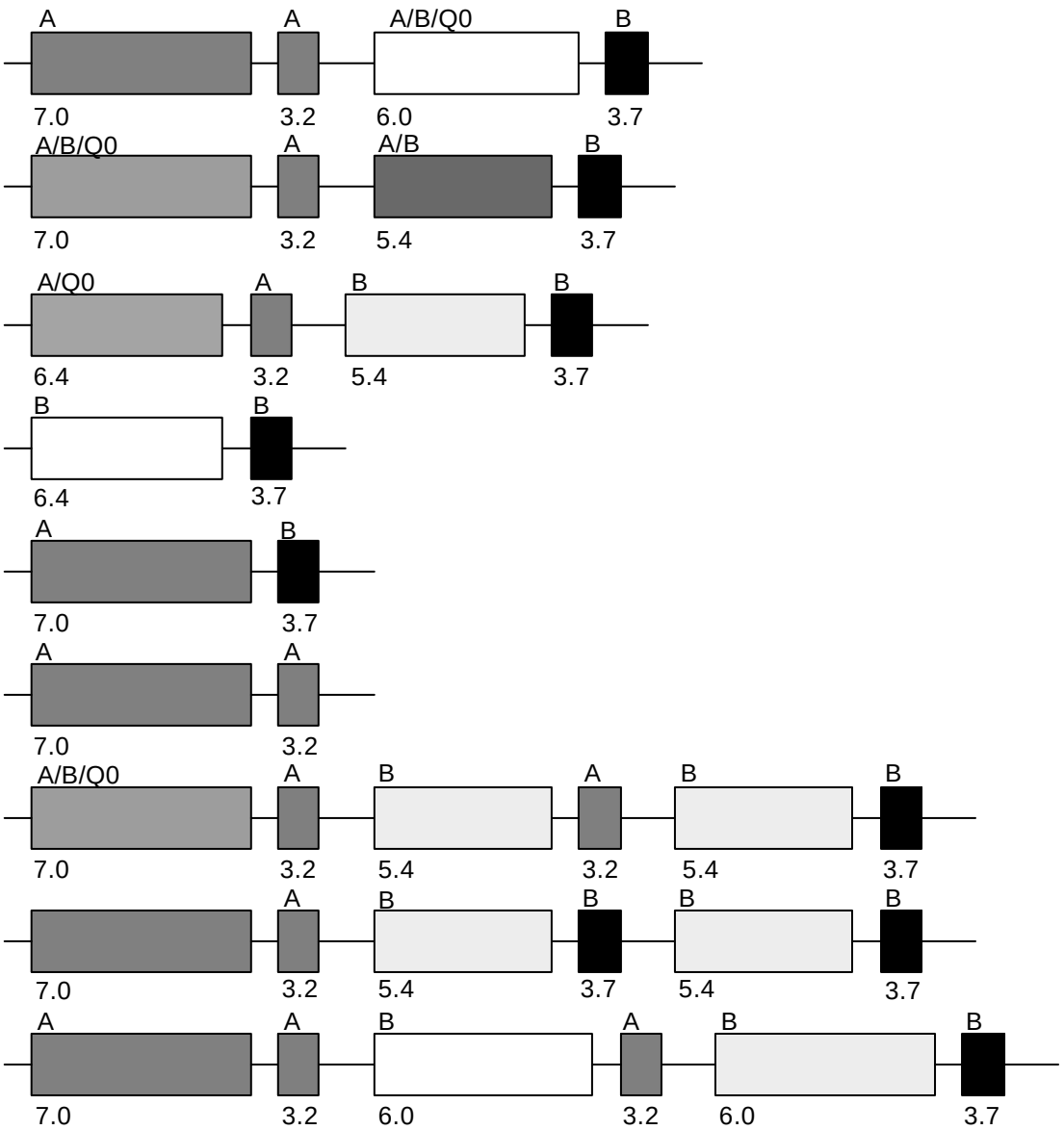
416 (exon 3)	A	G	A
836 (exon 7)	C	C	T

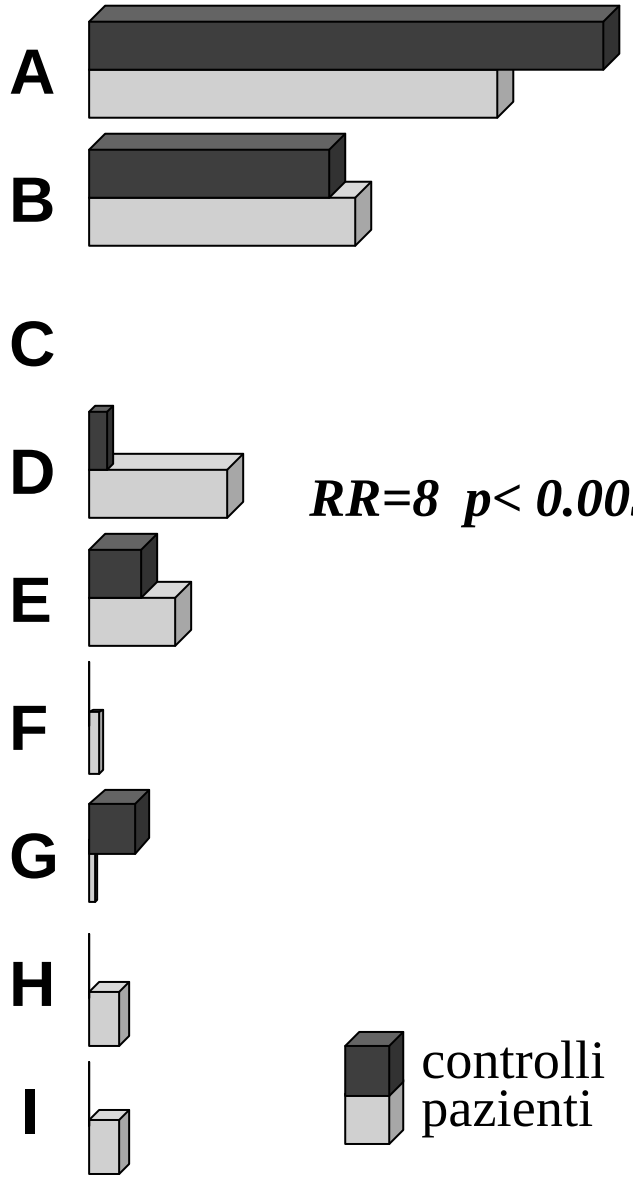
Ruberti et al.

Ruolo dell’aplotipo HLA-DRB1*03011 e dell’anti-52kd nello sviluppo del Blocco di conduzione cardiaco del neonato

DRB1*03011	Anti-52-kd anticorpo	Madri con CCHB (%) n=11	Madri con LES e SS (%) n=30
+	+	64	10
+	-	18	33
-	+	18	27
-	-	0	30

Pattern RFLP dei geni C4 e 21OH in 88 pazienti con LES e 55 controlli

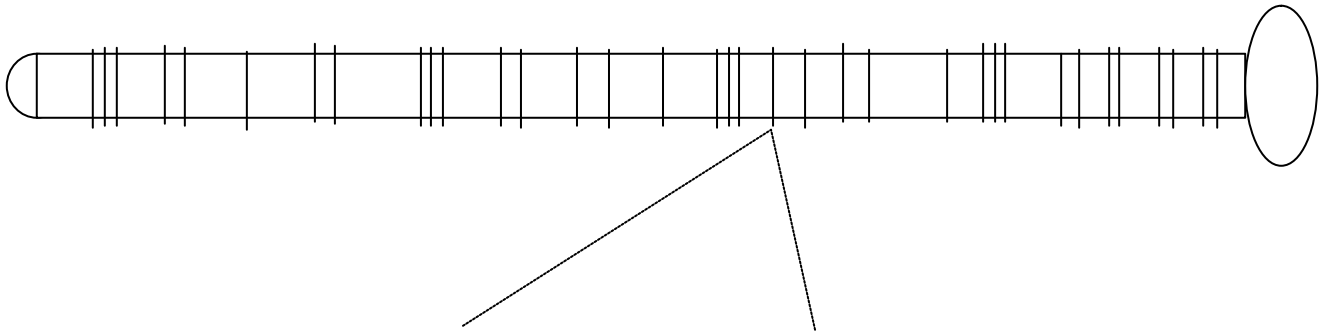




RR=8 p< 0.005

Scorza et al.

Analisi di polimorfismi della lunghezza di semplici sequenze di microsatelliti



Ceppo A CAGTACTACGGTTTTCACACACACAGACTGGCTTTATCCCG

Ceppo B CAGTACTACGGTTTTC~~ACA~~ CAGACTGGCTTTATCCCG

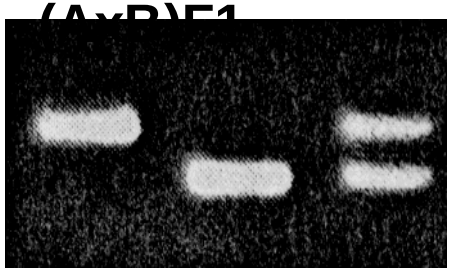
Primer L

Primer R

A B

(AxB)F1

Prodotti di PCR con primer L e R



Search for genetic susceptibilty factors to Systemic Lupus Erythematosus (SLE)

Gene	Gene location	Marker type	Polymorphic site	N alleles	Associated allele Reported	Associated allele This study
Bcl-2	18q21.3	SNP	nt 21, (exon 2)	2	nd	ns
CTLA-4	2q33.1	SNP	nt 49, (exon 1)	2	nd	ns
TNFR II	1p36.22	(CA)n	IVS 4	6	nd	ns
IL1RN	2q14.2	VNTR, 86 bp	IVS 2	3	2	ns
FcgRIIa	1q24.1	SNP	nt 131	2	R	ns
CD 19	16p11.2	(dinucleotide)n	from nt 1815	6	nd	ns
IL-10	1q32.1	(CA)n	from nt -1193	16	9,13	11

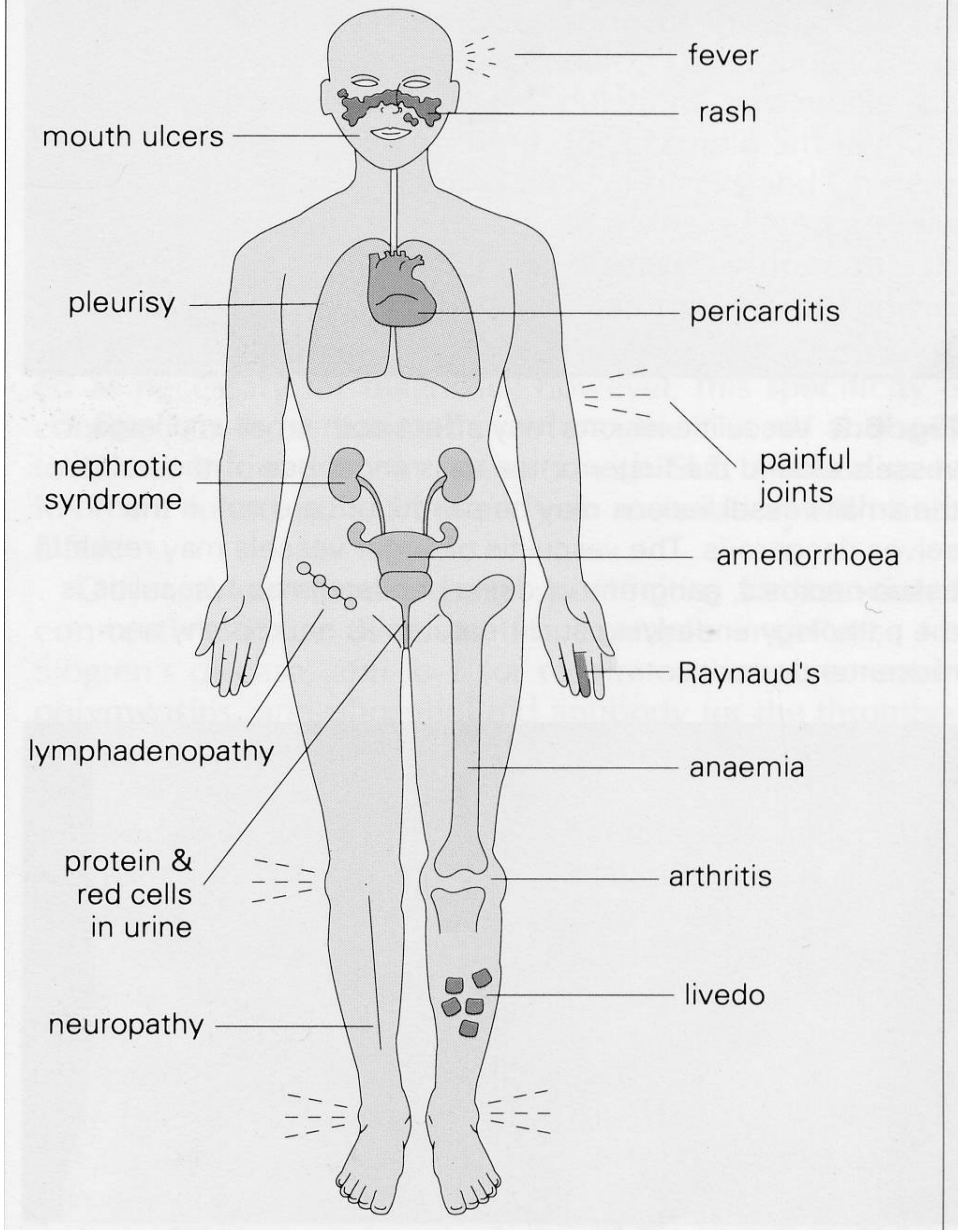
D'Alfonso et al.

Phenotype and gene frequency of TNF alleles in controls and patients

TNF alleles Microsatellite	Controls n=86	Patients n=89
a1	5.8	11.2
a2	39.5	44.9
a3	2.3	4.5
a4	11.6	10.1
a5	14.0	11.2
a6	20.9	15.7
a7	22.1	18.0
a8	2.3	2.2
a9	3.5	5.6
a10	27.9	33.6
a11	20.9	19.1
a12	0	0
a13	11.6	11.2
TNFA promoter -238	n=199	n=123
A	12.6	13.8
G	100	97.5
TNFA promoter -308		
1	97.1	98.4
2	25.3	28.5

D'Alfonso et al.199

The classical SLE patient



Clinical Associations of Autoantibodies in SLE		
Antigen specificity	**Clinical associations**	**Prevalence**
dsDna	Marker for active disease, titers fluctuates with disease activity, correlates best with renal disease	40-60 percent
ssDNA	Nonspecific, no clinical utility	70 percent
Ro/SSA	Subacute cutaneous lupus (75%), photosensitivity, neonatal lupus, complement deficiencies	40 percent
RNP (U1-RNP)	SLE generally in conjunction with Sm; in MCTD, required for diagnosis	30-40 percent
La/SSB	With La, low prevalence of renal disease Neonatal lupus (75%)	10-15 percent
Sm	Marker for disease, not generally useful in management; May be associated with CNS disease	About 20 percent
Phospholipids	Hypercoagulable state in some patients. No Clinical significance in others. Thrombocytopenia, later trimester abortions	30 percent
Histones	>95% in drug-related lupus. Also present in RA, SLE, reported in systemic sclerosis with pulmonary fibrosis	
Ribosomal P	Initially associated with psychosis in SLE, more recently with depression	10-40 percent
KU	SLE, MCTD (European, American population) Scleroderma/myositis overlap (Japanese population)	≤19 percent, ≤39 percent
PCNA		3 percent

†Rates vary depending on technique used

Frequency of Symptoms of Systemic Lupus Erythematosus[†]

Symptoms	Percent at onset	Percent at anytime
Fatigue	50	74-100
Fever	36	40-80+
Weight loss	21	44-60+
Arthritis or arthralgia	62-67	83-95
Skin	73	80-91
Butterfly rash	28-38	48-50+
Photosensitivity	29	≤60
Mucuous membrane lesion	10-21	27-52
Alopecia	32	55-71
Raynaud's phenomenon	17-33	30-71
Purpura	10	15-34
Uticaria	1	4-8
Renal	16-38	50-73
Nephrosis	5	11-18
Gastrointestinal	18	38-44
Pulmonary	2-12	24-98
Pleurisy	17	30-45
Effusion		24
Pneumonia		29
Cardiac	15	20-46
Pericarditis	8	8-48
Murmurs		23
ECG changes		34-70
Lymphadenopathy	7-16	31-50
Splenomegaly	5	9-20
Hepatomegaly	2	7-25
Central nervous system	12-21	25-75
Functional		Most
Psychosis	1	5-52
Convulsions	0.5	2-20

[†]Adapted from Von Feldt, JM, Postgrad Med 1995; 97:79.

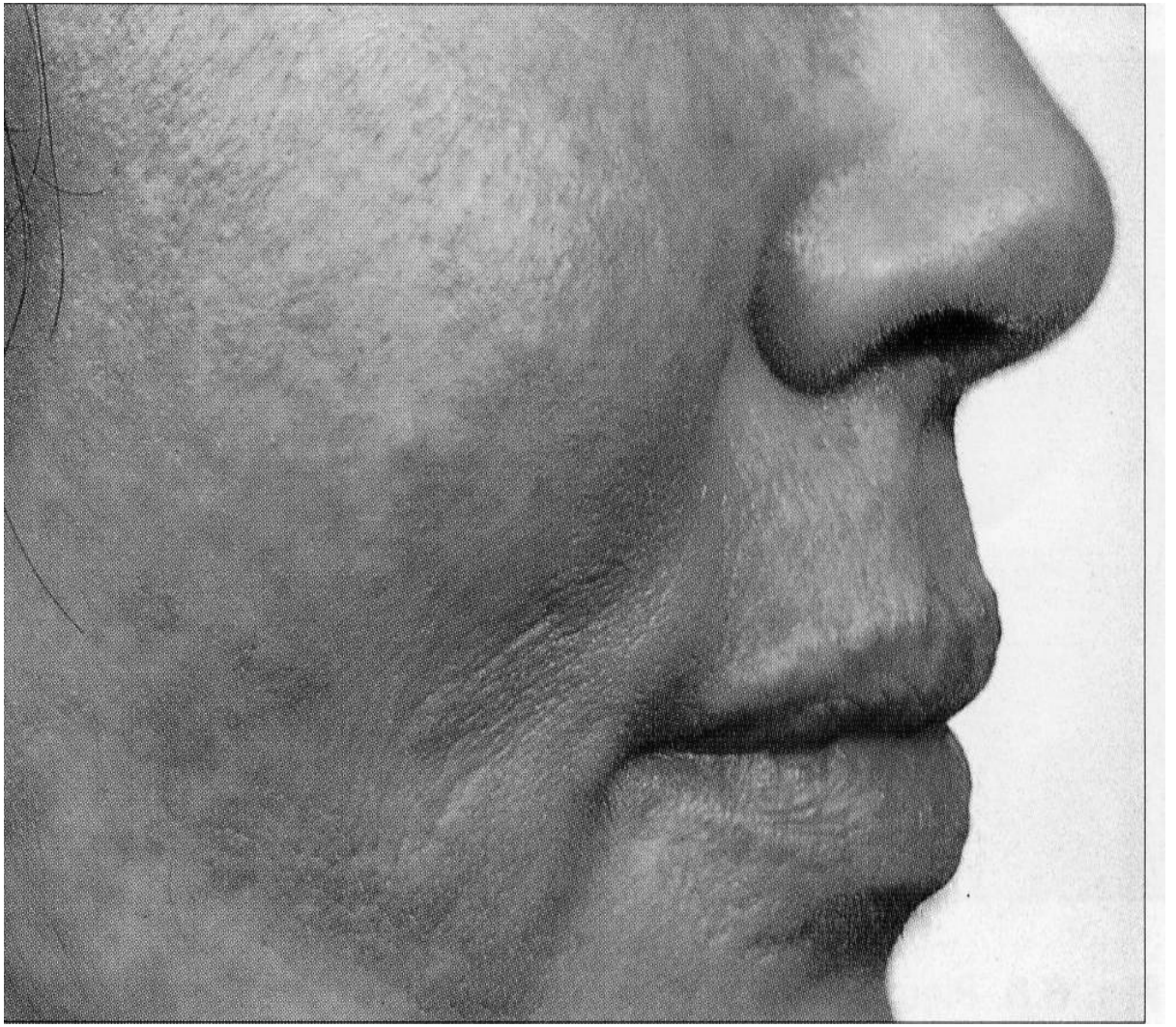
Lupus eritematoso sistemico: criteri ARA 1982, aggiornati sec. Hochberg 1997

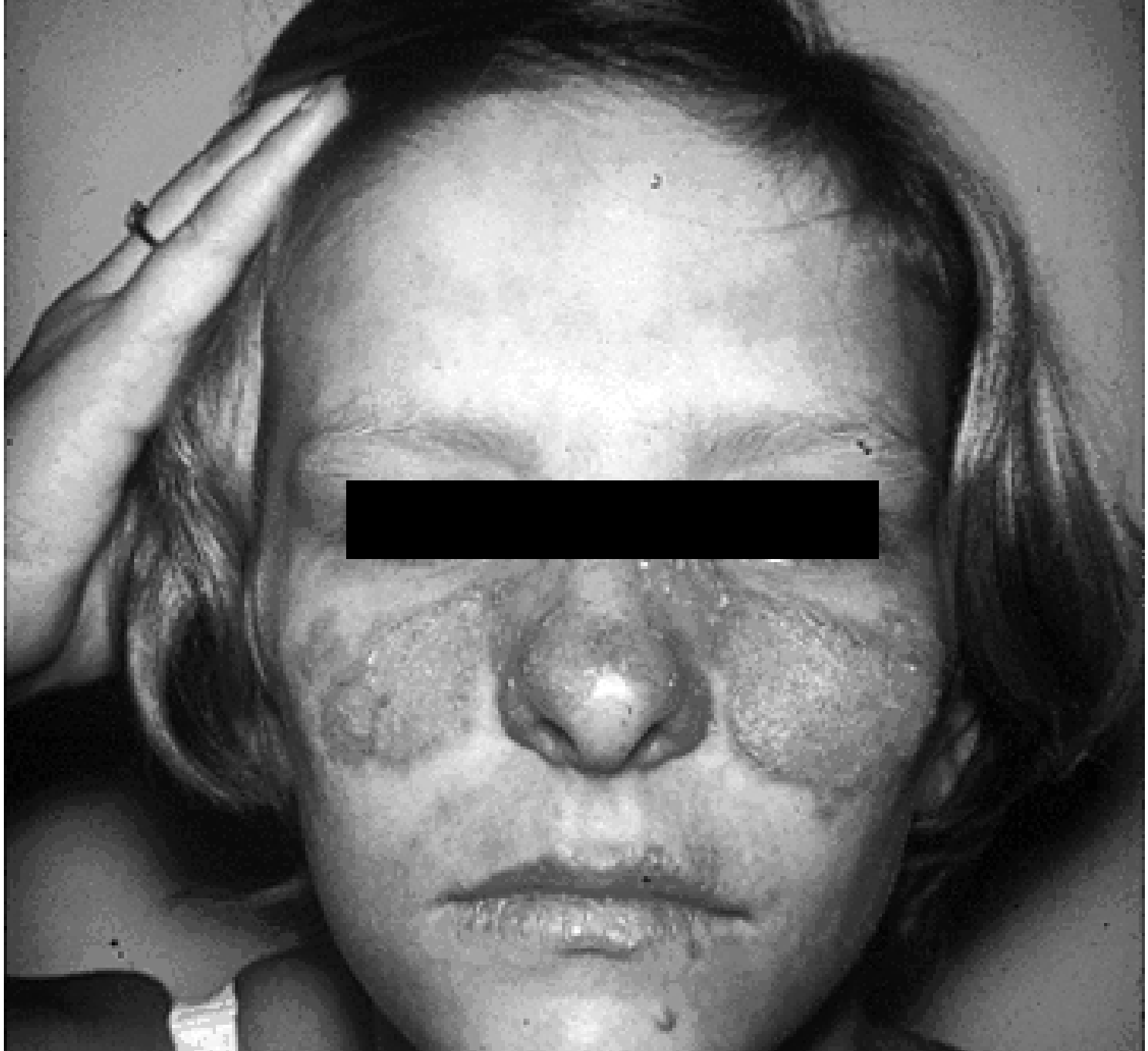
1. ***Eruzione malare***	eritema fisso, piano o rilevato, agli zigomi, tendente a risparmiare le pieghe naso-labiali
2. ***Eruzione discoide***	placche eritematose rilevate con ipercheratosi e ostruzione dei follicoli; nelle lesioni di più vecchia data possono osservarsi cicatrici atrofiche
3. ***Fotosensibilità***	rash cutaneo come risultato di una abnorme reazione alla luce solare, descritto dal paziente in passato, o osservato da un medico
4. ***Ulcere orali***	ulcerazioni orali o nasofaringee, solitamente non dolorose, osservate da un medico
5. ***Artrite***	artrite non erosiva a carico di due o più articolazioni periferiche, caratterizzata da dolorabilità, tumefazione, o versamento
6. ***Sierosite***	pleurite - anamnesi tipica di dolore pleuritico o sfregamenti uditi da un medico o dimostrazione di versamento pleurico; oppure pericardite - documentata dall'ECG o sfregamenti o dall'evidenza di versamento pericardico
7. ***Alterazioni renali***	proteinuria persistente > 0,5 g/die o maggiore di +++ se il dosaggio non è stato eseguito; oppure cilindri cellulari - possono essere eritrocitari, emoglobinici, granulari, tubulari o misti
8. ***Alterazioni neurologiche***	convulsioni - in assenza di farmaci responsabili o di alterazioni metaboliche note, per es. uremia, chetoacidosi, squilibrio elettrolitico; oppure psicosi - in assenza di farmaci responsabili o di alterazioni metaboliche note, per es. uremia, chetoacidosi, squilibrio elettrolitico
9. ***Alterazioni ematologiche***	anemia emolitica - con reticolocitosi; oppure leucopenia <4000/mmc in due o più occasioni; oppure linfopenia <1500/mmc in due o più occasioni; oppure piastrinopenia <100000/mmc in assenza di farmaci responsabili
10. ***Alterazioni immunologiche***	fenomeno LE positivo; oppure anticorpi anti-DNA nativo a titolo abnorme; oppure presenza di anticorpi contro l'antigene nucleare Sm; oppure positività per anticorpi antifosfolipidi, basata sulla presenza di livelli sierici abnormi di anticorpi anticardiolipina IgG o IgM, o sulla presenza dell'anticoagulante lupico, o su una reazione sierologica falsamente positiva per la sifilide per almeno 6 mesi, verificata con i test di immobilizzazione del Treponema pallidum o di assorbimento degli anticorpi specifici
11. ***Anticorpi antinucleari***	un titolo abnorme di anticorpi antinucleari dimostrati con immunofluorescenza o test equivalente, in qualunque momento del decorso, e in assenza di farmaci noti per la loro associazione con la sindrome del "lupus da farmaci"

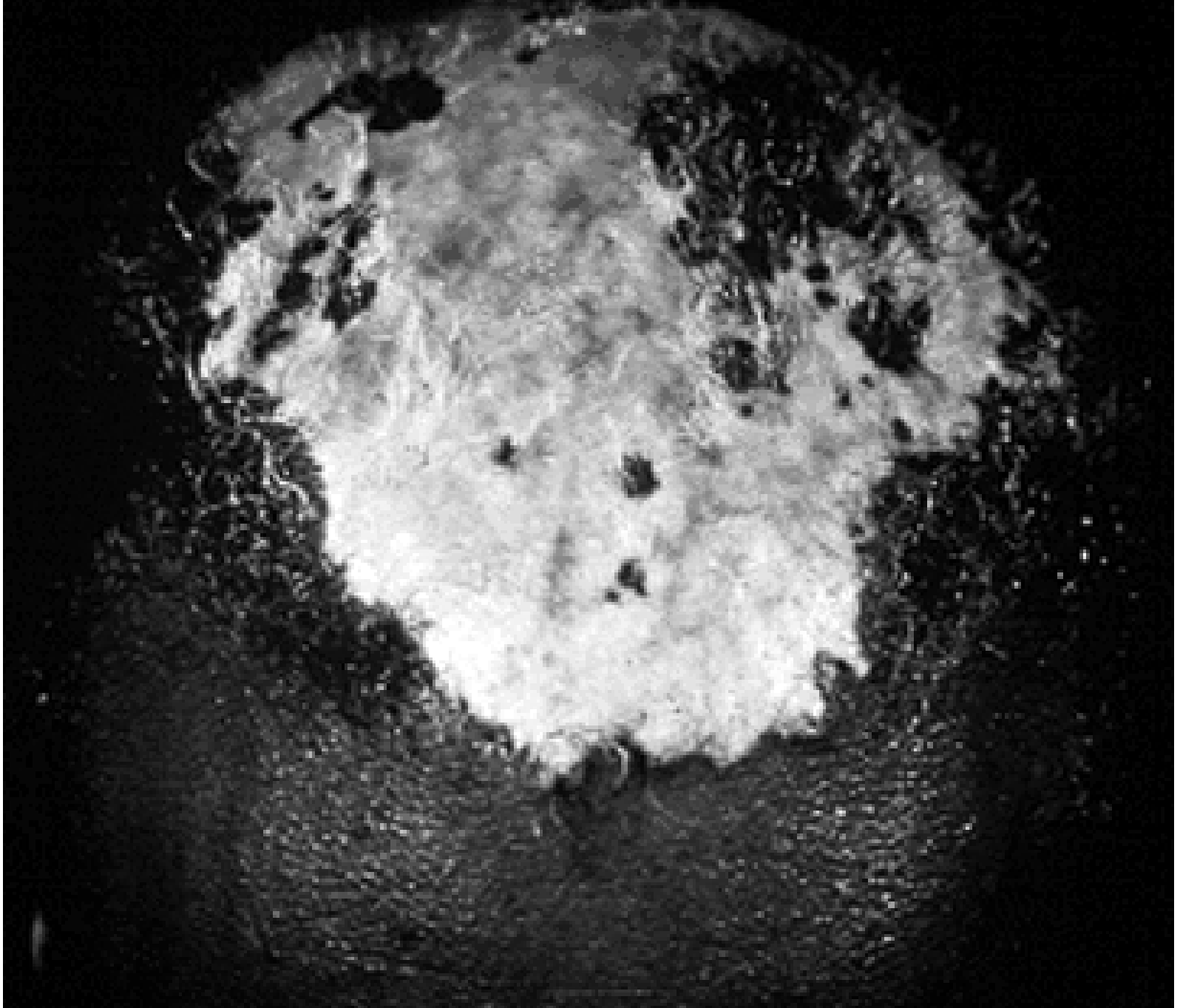
A scopo diagnostico-classificativo è richiesta la presenza successiva o contemporanea di almeno 4 criteri.

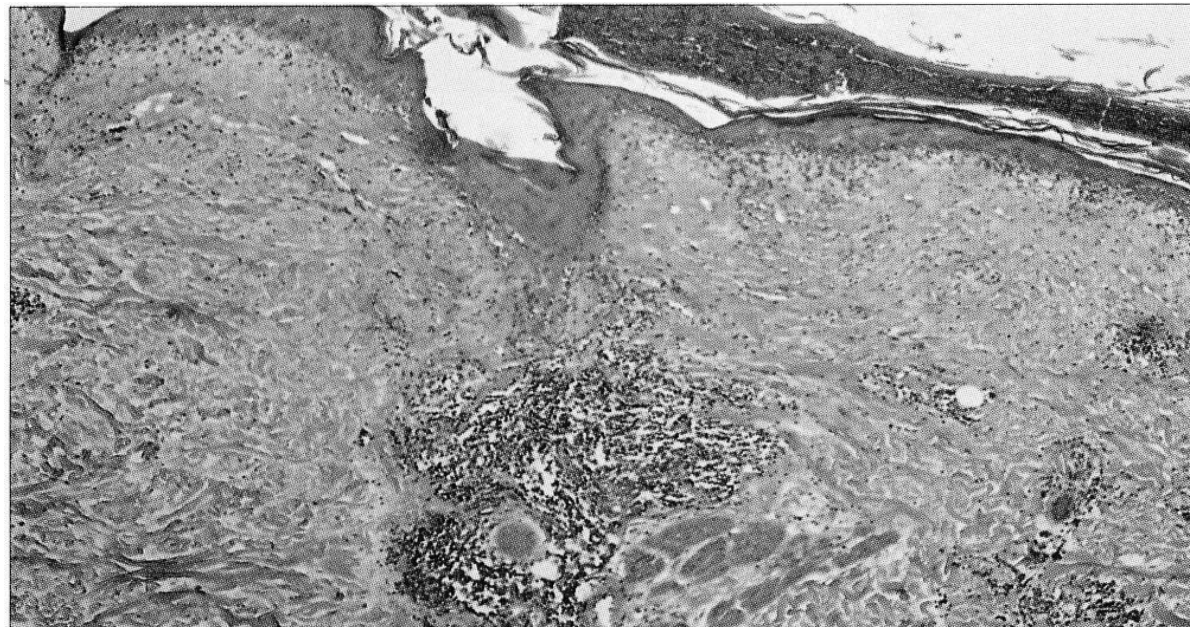
Sindrome da antifosfolipidi

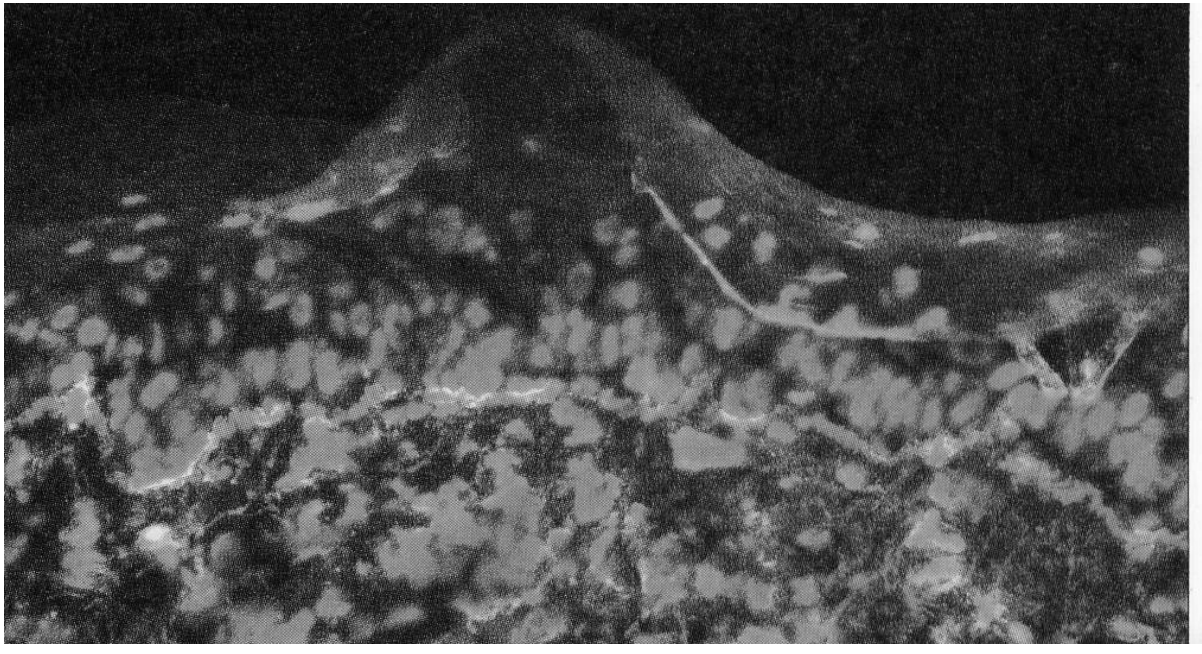
- Poliabortività
- Trombosi venose
- Trombosi arteriose











Il coinvolgimento renale nel LES

- Riscontrabile all'autopsia nel 90% dei pazienti
- Presente in forma clinicamente evidente nel 30 - 75% dei pazienti in tutto il decorso della malattia
- Presente in forma clinicamente evidente nel 10 - 35% dei pazienti all'esordio della malattia
- La prevalenza all'esordio è più elevata nel LES che insorge prima dei 20 anni
- L' evoluzione verso l' isufficienza renale è del 2-30% dei pazienti
- Manifestazioni cliniche: proteinuria (80%), ematuria/piuria (40-50%)

Types of Renal Disease Associated with SLE

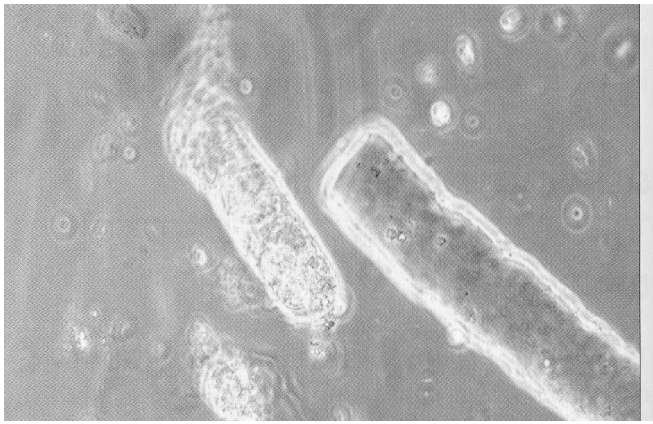
- Immune complex glomerular disease
  - Mesangial
  - Focal proliferative
  - Diffuse proliferative and membranoproliferative
  - Membranous
- Tubulointerstitial nephritis
- Vascular disease
  - Immune complex deposition
  - Thrombotic microangiopathy, including lupus anticoagulant
  - Renal vein thrombosis
- Pauci-immune necrotizing glomerulonephritis
- Drug-induced lupus
- Nonsteroidal antiinflammatory drugs

Table 55.1. WHO Classification of Lupus Nephritis

Patterns	Immunofluorescence		Electron Microscopy		
	Mesangial	Peripheral	Mesangial	Subendothelial	Subepithelial
I Normal	0	0	0	0	0
IIA Mesangial Deposits	+	0	+	0	0
IIB Mesangial Hypercellularity	+	0	+	0	0
III Focal-Segmental GN (<50%)	++	+	++	+	+
IV Diffuse GN (>50%)	++	++	++	++	+
V Membranous GN	+	++	+	+	++

L’esistenza di infiammazione a livello renale si evidenzia precocemente per la presenza nelle urine di:

- Ematuria
- Leucocituria
- Cilindruria
- Proteinuria



Il sedimento caleidoscopico fa sospettare una glomerulo- nefrite proliferativa diffusa

Prevalenza / milione di abitanti delle principali malattie autoimmuni sistemiche

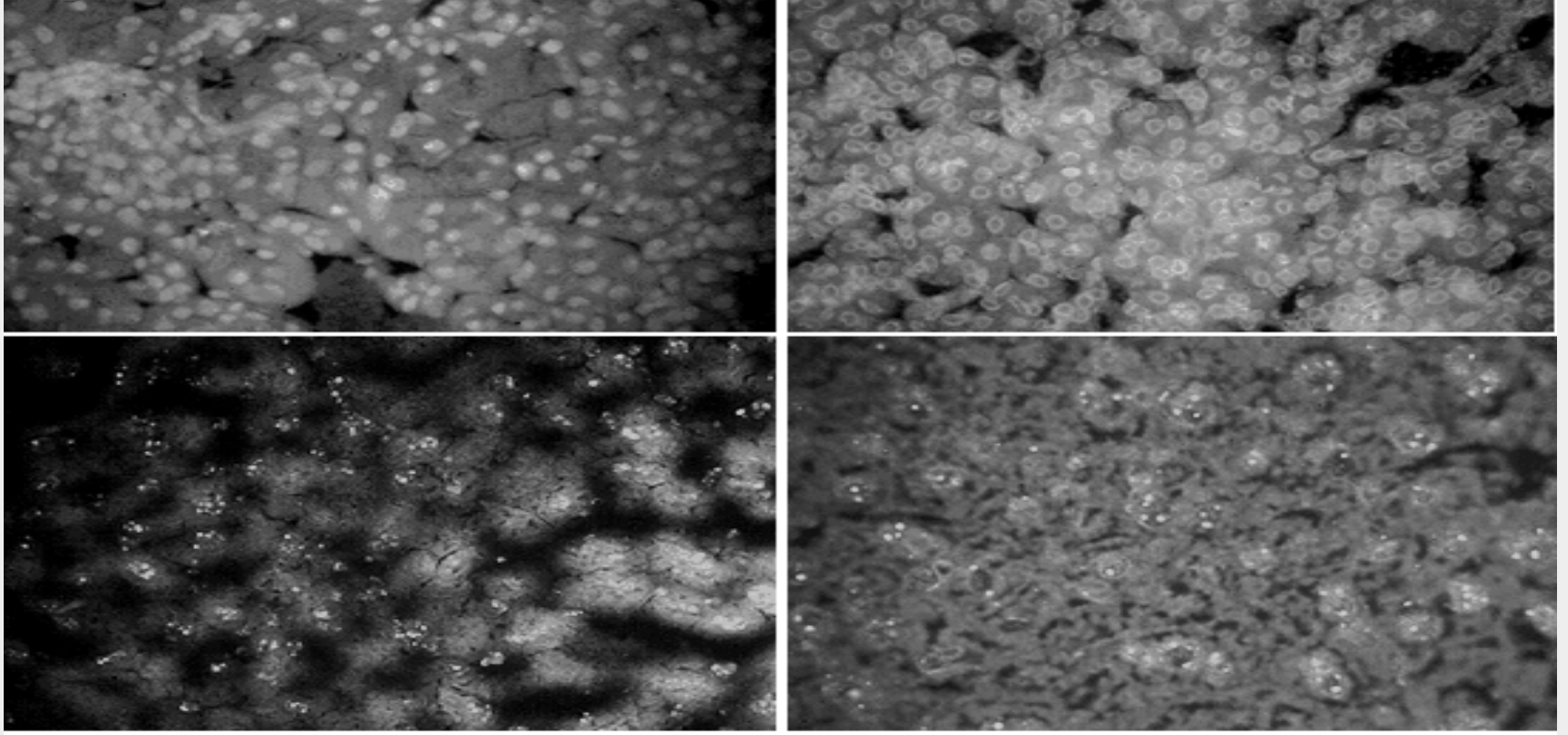
- **Artrite Reumatoide: 2000-5000**
- **Lupus eritematoso sistemico: 180-500**
- **Sindrome di Sjogren: 100 – 250**
- **Sclerosi Sistemica: 500-800**
- **Polimiosite/dermatomiosite: 80-100**
- **Vasculiti primitive: 300-700**

Connettiviti: malattie infiammatorie croniche, a patogenesi immunitaria, caratterizzate dalla presenza di anticorpi diretti contro antigeni del nucleo cellulare

- Artrite Reumatoide
- Lupus eritematoso sistemico
- Sindrome di Sjogren
- Sclerosi Sistemica
- Polimiosite/dermatomiosite
- Connettivite mista
- Connettivite indifferenziata
- Sindromi da overlap

Connettiviti: aspetti clinici

	LES	dcSSc	lcSSc	PM/DM	MCTD	SS	AR
Febbre	+++	±	±	+++	+++	±	+++
Artromialgie	+++	+	±	+++	+++	++	+++
Artrite	+++	±	-	±	+++	++	+++
Miosite	±	±	-	+++	++	-	±
Fenomeno di Raynaud	++	+++	+++	±	+++	±	±
Ulcere digitali	±	+++	+++	±	+++	±	±
Vasculite cutanea	+++	±	-	+	±	±	+
Eruzioni cutanee	+++	±	±	++	++	±	±
Sindrome sicca	±	+	+	-	+	+++	++
Sierositi	+++	++	-	-	++	++	++
Interessamento polmonare	+	+++	++	-	+	+	+
Interessamento renale	+++	+	±	-	±	±	-
Interessamento digerente	±	+++	+++	-	+++	+	-
Interessamento SNC	+++	-	-	-	++	+	-
Interessamento di SNP	++	++	++	-	+	±	++



ANA staining patterns Antinuclear staining patterns on mouse liver by immunofluorescence which have lower sensitivity and specificity for specific diseases than previously considered. Top left panel: There is homogeneous or diffuse staining of the nuclei. The pattern is strongly associated with antibodies to nucleoprotein (NP), nucleosomes, and single-stranded DNA. It is seen in patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and drug-induced lupus. Top right panel: The peripheral (also called rim or shaggy) pattern, in which the periphery of the nucleus reacts with the patient's serum. This pattern correlates strongly with antibodies to double-stranded DNA (dsDNA) and is highly suggestive of SLE. Bottom left panel: The speckled pattern in which there may be few or many speckles, and small or large speckles. The pattern represents antibodies to the components of extractable nuclear antigen, eg, Sm, RNP, Ro (SSA), La (SSB) and probably other nuclear antigens. The pattern may be seen in patients with SLE, Sjögren's syndrome, scleroderma, infectious mononucleosis and other conditions, and in normal subjects (especially in low titer). Bottom right panel: There is a nucleolar pattern, in which the patient's serum only reacts with the nucleoli. This pattern

Sensitivity, Specificity, and Predictive Value of Different Antinuclear Antibodies

	Antibody							
	ds DNA	ss DNA	Histone	Nucleoprotein	Sm	RNP	Ro	La
SLE								
Sen	70 percent	80	30-80	58	25-30	50	25-35	15
Spec	95 percent		50	mod	mod	99	87-94	
Pre	95 percent	50	mod	mod	97	46-85		
Drug LE								
Sen		80	95	50	1%		low	low
Spec	1-5 percent	50	high	mod				
Pre	1-5 percent	50	high	mod				
RA								
Sen		mod	low	25	1%	47	low	low
Spec	1 percent	mod		low				
Pre	1 percent	mod		low				
Scleroderma								
Sen			<1 percent	<1 percent	<1 percent	20		
Spec	<1 percent	low						
Pre	<1 percent	low						
PM/DM								
Sen			<1 percent	<1 percent	<1 percent		low	
Spec	<1 percent	low						
Pre	<1 percent	low						
Sjögren's								
Sen		mod	low	mod	1-5 percent	5-60	8-70	14-60
Spec	1-5 percent	mod	low	mod			87	94
Pre	1-5 percent	mod	low	mod			5-48	26-41

Sen: sensitivity; Spec: specificity; Pre: predictive value
Other associations: RNP: MCTD; Ro: SCLE, 1° biliary cirrhosis, vasculitis, CHB

Sensitivity, Specificity, and Predictive Value of Different Antinuclear Antibodies

	Antibody							
	PCNA	Scl-70	PM-1	Mi-1	Jo-1	Ku	Nucleoli	Centromere
SLE								
Sen	5				low	low	26	
Spec	95							
Pre	95							
Drug LE								
Sen	low				low			
Spec								
Pre								
RA								
Sen	low				low			
Spec								
Pre								
Scleroderma								
Sen	low	15-20	low		low		54	25-30
Spec		high						
Pre		high						
PM/DM								
Sen	low	lo	30-50	low	30-50			
Spec								
Pre								
Sjögren's								
Sen		5			low			
Spec								
Pre								

Sen: sensitivity; Spec: specificity; Pre: predictive value
Other associations: Centromere: CREST