M1 D2HP: TU4 Immunopathology and hematologic dysregulations

Clinical and biological diagnosis of autoimmune diseases

January 10th, 2025

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Outline

- **INTRODUCTION**
  - **Reminders**
  - **AID: Diagnosis objectives and strategy**
  - **Therapeutic strategies**

- **DIAGNOSIS OF AID**
  - **Clinical signs**
  - **Biological diagnosis**

- **DIAGNOSIS OF SYSTEMIC AUTOIMMUNE DISEASES: EXAMPLE OF THE LUPUS**

- **DIAGNOSIS ORGAN SPECIFIC AUTOIMMUNE DISEASES : EXAMPLE OF AUTOIMMUNE ENDOCRINOPATHIES AND OF MULTIPLE SCLEROSIS**

A bit further

This symbol means the slide or part of the slide is very detailed and if it is a lot for you, you should only remember the key message

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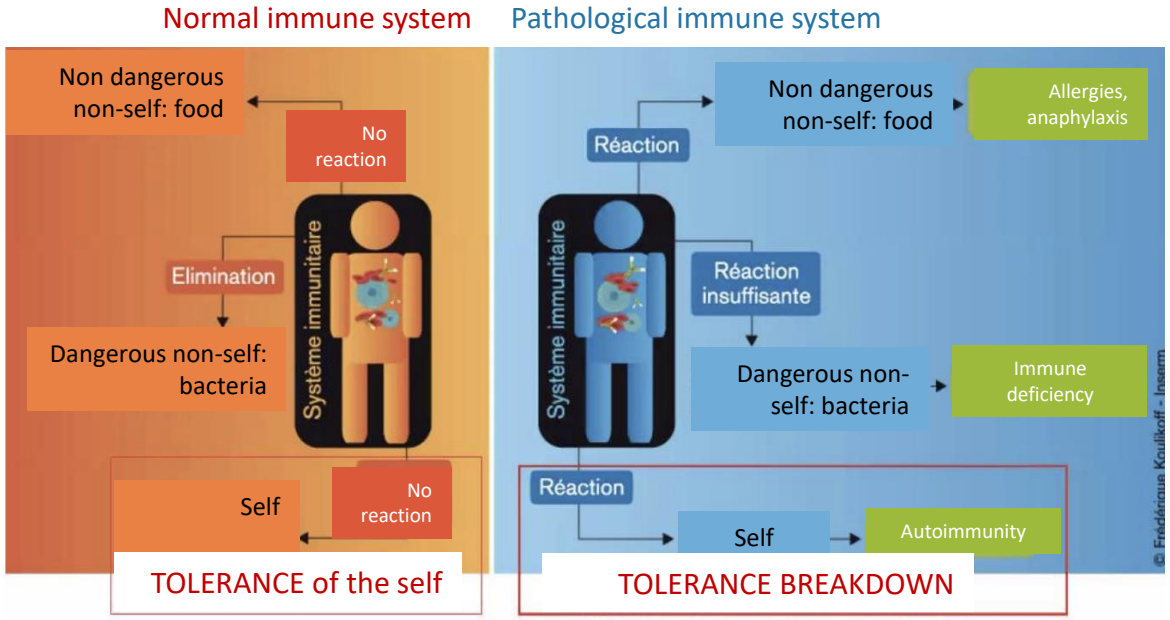
Reminders on Autoimmunity

- **Detection of self and non-self** allows for the destruction of foreign antigens

→ **Protection**

- If this **distinction is dysfunctionnal**

→ **Destruction of self antigens**



AUTOIMMUNITY : Clinical consequences of the activation of an individual's immune system against one or more of its constituents (Self)

Reminders on Autoimmune diseases (AID)

Main effectors involved in tissue damage: autoantibodies and/or autoreactive T lymphocytes

- **Autoantibodies**
  - Activating/blocking
    - TSH receptor : Grave's disease
    - Acetylcholine receptor : myasthenia
  - Haemolytic : autoimmune anemia
- **Immune complexes** : SLE

Auto antibodies mediated effects

Can be detected for the biological diagnosis

IgG isotype: transplacental passage and risk of obstetrical complications

- **CD4 and CD8 T cells**
  - Infiltration of thyroid : Hashimoto's disease
  - Myelin auto-reactive CD4 T cells in multiple sclerosis
- **Cytokines production**
  - TNFalpha in Crohn's disease and rhumatoid arthritis

Auto reactive cells mediated effects

Cytotoxicity and cell death dependent or not on autoantibodies

Inflammation associated with cytokine production: main target of treatment

Reminders on Autoimmune diseases (AID)

Auto antibodies mediated effects

Can be detected for the biological diagnosis

IgG isotype: transplacental passage and risk of obstetrical complications

Auto reactive cells mediated effects

Cytotoxicity and cell death dependent or not on autoantibodies

Inflammation associated with cytokine production

Consequences: Tissue destruction and/ or inflammation associated with remodelling of tissues (fibrosis, granuloma)
Causes functional limitations, poor quality of life and risk for the patients life
Chronic diseases

Reminders on Autoimmune diseases (AID): Classification based on target

NON-ORGAN SPECIFIC DISORDERS

Auto-antigen present in multiple organs

CONNECTIVE TISSUE DISEASES

Common clinical symptoms : arthralgy, fever, cutaneous symptoms

- Systemic lupus erythematous
- Rheumatoid arthritis
- Antiphospholipids syndrome
- Systemic sclerosis
- Sjögren's syndrome
- Myositis

VASCULITIS

Blood vessels damage

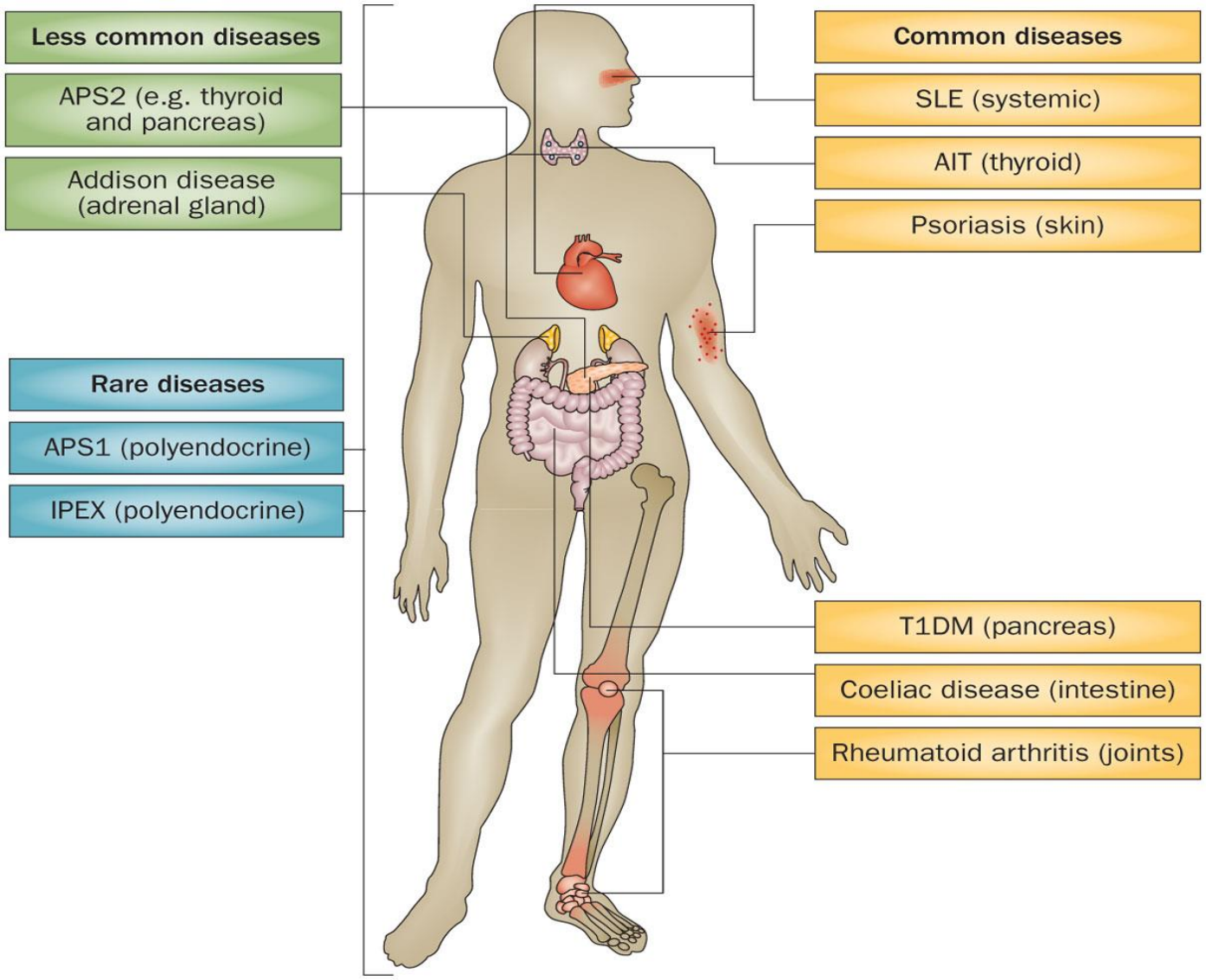
- ANCA-associated vasculitis
  - Microscopic polyangeitis
  - Granulomatosis with polyangeitis
    - (ex Wegener)

ORGAN SPECIFIC DISORDERS

Target of auto-antibodies localized in one organ

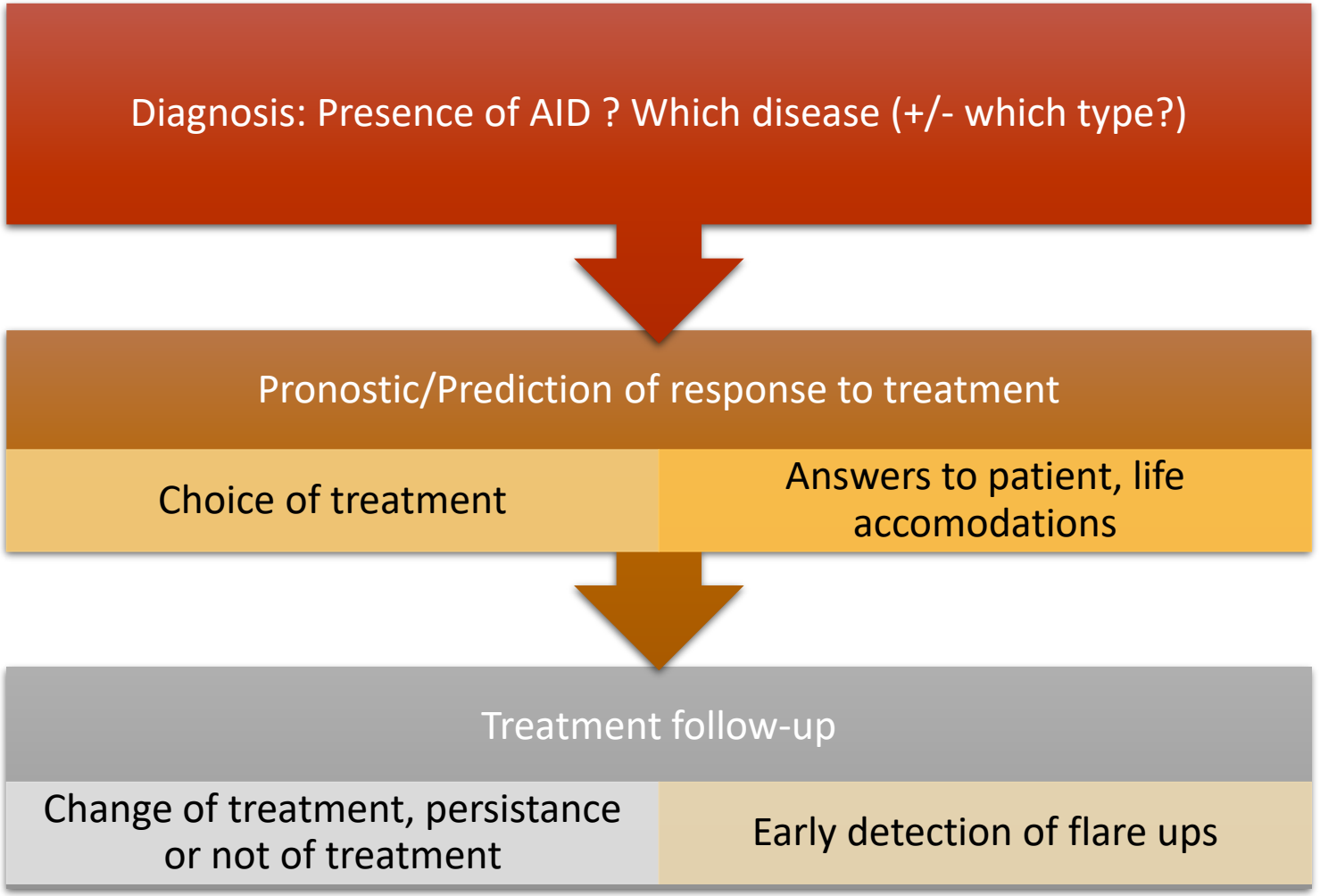
Target	Disease	Autoantigenes
Thyroid	Hashimoto's disease Grave's disease	TG, TPO, TSH receptor
Intestin	Celiac disease Crohn's disease	Gliadin, transglutaminase, endomysium Microbiota
Liver	Autoimmune hepatitis Primary biliary cholangitis	LKM1, actin, type 2 mitochondria
Pancreas	T1 diabetes	GAD, IA2, β islets of Langerhans
Skin	Bullous pemphigoid Pemphigus vulgaris	BP180, BP230 Desmoglein
Stomach	Autoimmune gastritis	Parietal cells, IF
PNS	Autoimmune neuropathy	MAG, ganglioside
CNS	Multiple sclerosis	Myelin
Muscles	Myasthenia	Acetylcholin receptor

Reminders on AID: Classification based on frequency



Zhernakova, Nat Review, 2013

Diagnosis objectives



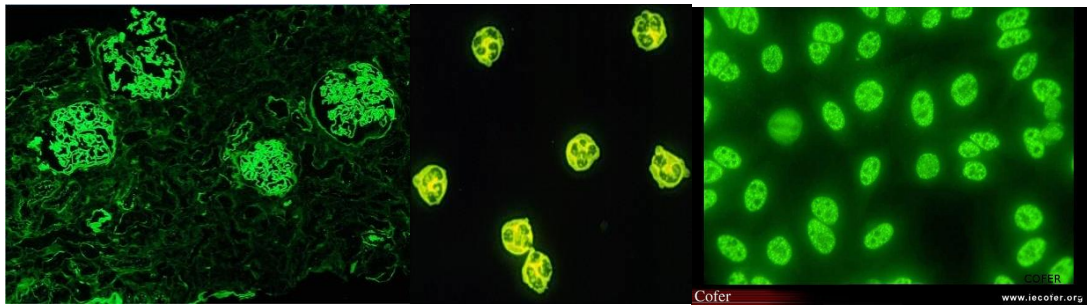
Diagnosis strategy

Diagnosis: Presence of AID ? Which disease (+/- which type?)

Pronostic/Prediction of response to treatment

Set of clinico-biological arguments, sometimes supplemented by genetics and imaging data

Autoantibodies detection: Autoantibodies highlighting, chimiluminescence, immunodots, …



Function of the targeted organ or markers of destruction: hormones, enzymes in liver cells, …

Markers of inflammation: CRP, cytokines, total antibody production

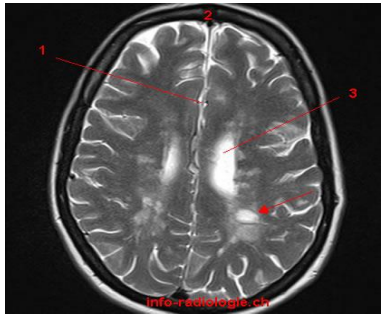
Genetics associated with a risk for a specific AID, ex: HLAB27 in ankylosing spondylitis

Clinical triad of connective tissue diseases:

Clinical triad: skin, joints and altered general condition (fever, asthenia, anorexia)

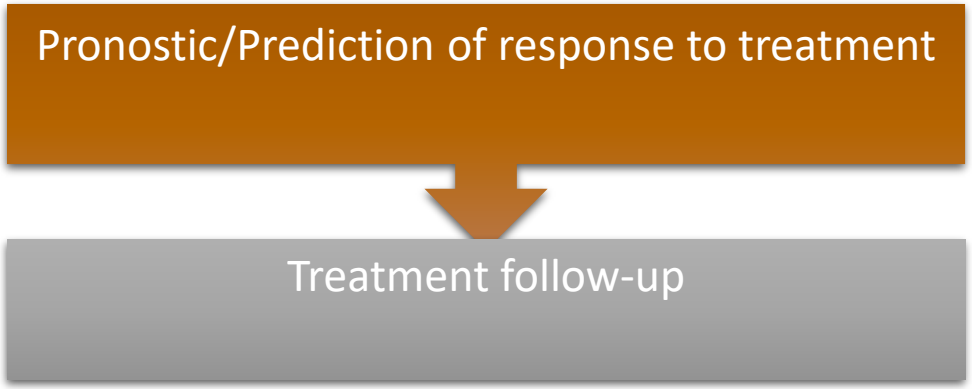
Clinical signs of an altered organ

Imaging data on the altered organ



Brain MRI in MS

Therapeutic strategies



Clinical or biological markers reflecting the activity of the diseases

Inflammation markers and cytokins, autoantibodies, hormones, …

1- Control the inflammatory relapse and the acute tissue destruction

- Symptomatic anti-inflammatory and analgesic treatment
- Immunomodulatory treatments: corticosteroids, immunosuppressors, therapeutic monoclonal antibodies, polyvalent Immunoglobulins (regulation of autoantibody production)
- Plasmapheresis: elimination of pathogenic autoantibodies from the plasma by filtration of the blood

2- Limit the occurrence of new relapses and the progression of the disease

- Long-term maintenance, not curative treatment
- Immunomodulatory treatments: corticosteroids, immunosuppressors, therapeutic monoclonal antibodies
- AID-specific preventive approach: ex Gluten-free diet and celiac diseas

3- Compensation of the destroyed tissues/organ:

- Insulinotherapy and diabetes
- Synthetic thyroid hormones and hypothyroiditis……..

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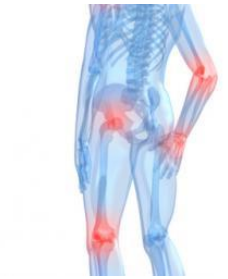
CLINICAL DIAGNOSIS OF AID: WHICH SYMPTOMS SHOULD EVOQUE A SYSTEMIC AUTOIMMUNE DISEASE ?

A bit further

The details of clinical signs do not have to be known

Altered general condition

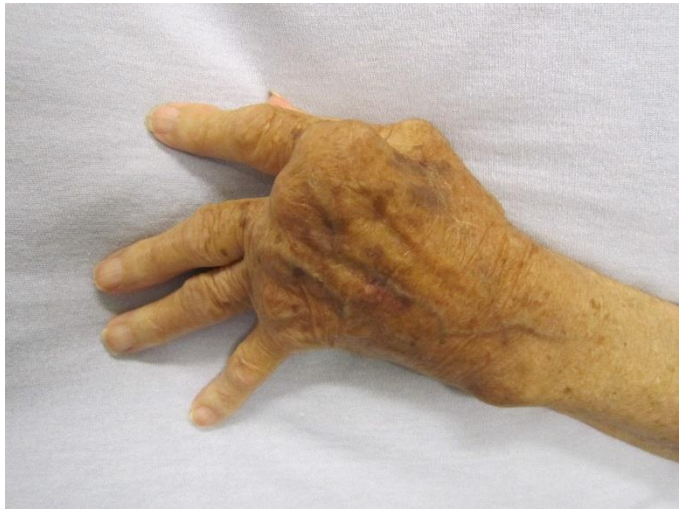
Joint damage: arthritis and arthralgia; +/- symetrical; +/- erosive and deforming

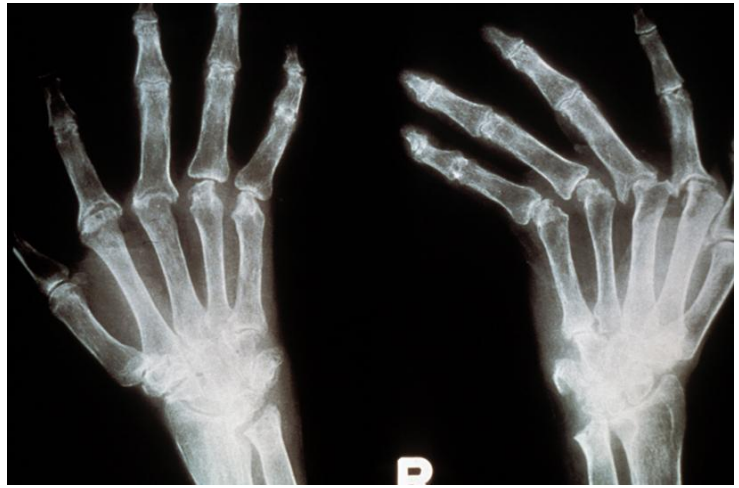


Asthenia

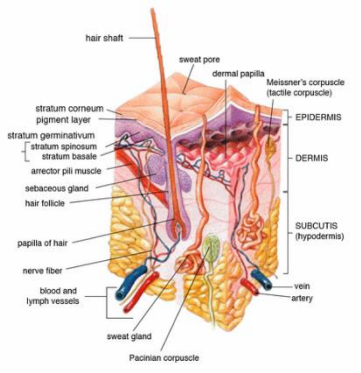
Recurrent fever, night perspiration

Anorexia



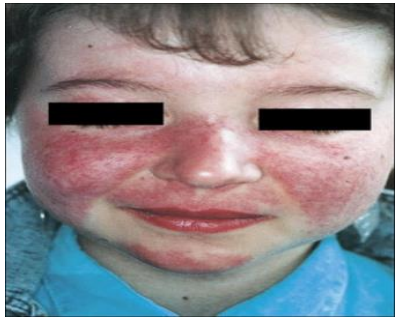


Joint deformity in rhumatoid arthritis

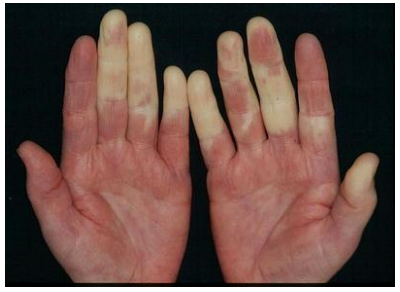


Skin lesions

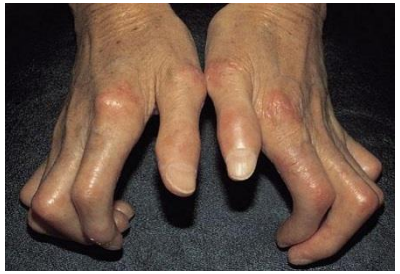
Vespertilio: bilateral non-itchy rash of the wings of the nose and cheeks (SLE)



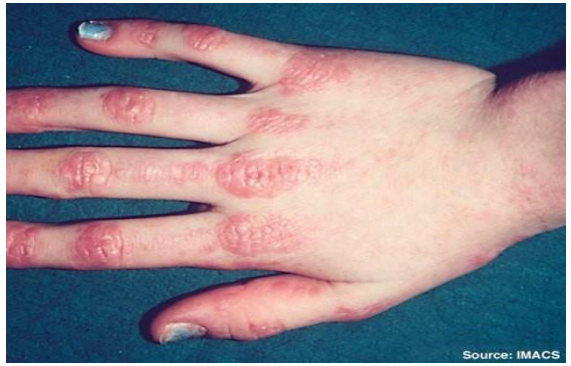
Raynaud syndrome : reversible acute ischemic attack triggered by cold and emotions, secondary to arterial wall damage or a change in the vascular tone of the arteries (SLE, sclerodermia)



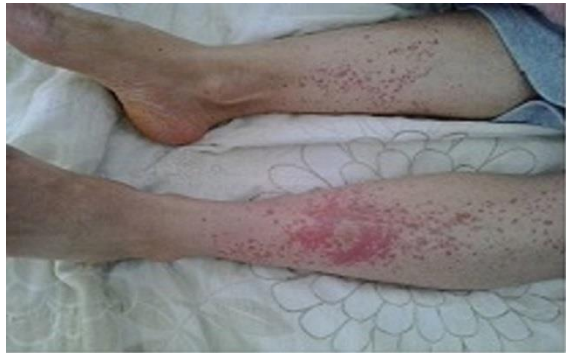
Sclerosis: fibrous remodelling of the subcutaneous tissue with retraction and thickening of the skin (sclerodermia)



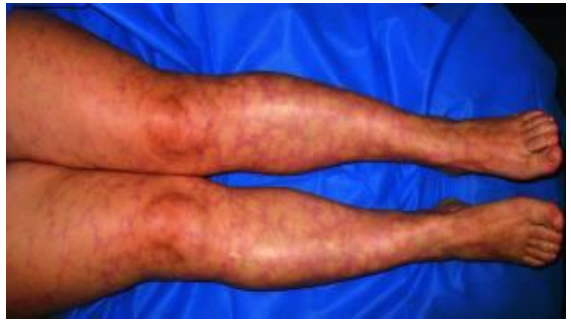
Gottron's papules : purple infiltrated papules on the back of the finger joints. Erythematous lesions along the tendon sheaths (Dermatomyositis)



Vascular purpura: vessels' inflammation of the lower limbs (lupus vasculitis)



Livedo: purplish erythema, mesh appearance (APLS, vasculitis)



Other disorders

Dry syndrome: lymphoid infiltrate of the salivary and lacrimal glands → drying up of secretions (SS)

Cardiovascular lesions :

- Pericarditis, heart failure, endocarditis (SLE)
- Deep vein thrombosis (APLS)
- Multiple infarctions (vasculitis)

Lung lesions :

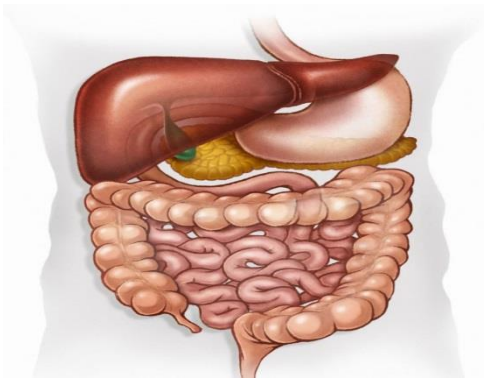
- Pleurisy (SLE, AR)
- Late severe asthma (vasculitis :eosinophilic granulomatosis with polyangitis)
- Fibrosis (RA)
- Pulmonary arterial hypertension (scleroderma)

Neurological disorders: strokes ; psychiatric disorders (APLS; SLE)

Kidney disorders: diffuse oedema, proteinuria, hematuria (SLE)

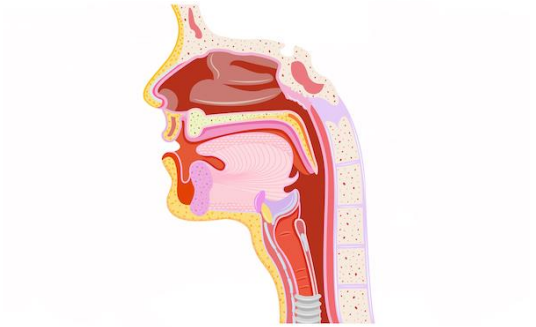
Intestinal lesions : Diarrhea +/- blood

Malabsorption syndrome: chronic diarrhea, weight loss, vitamin B12 deficiency…(Biermer syndrom)



Obstetrical complications : multiple miscarriage (APLS)

ORL symptoms : recurrent rhinitis, sinusitis, otitis (vasculitis)



CLINICAL DIAGNOSIS OF AID: WHICH SYMPTOMS SHOULD EVOQUE AN ORGAN SPECIFIC AUTOIMMUNE DISEASE ?

Altered general condition

+/- Joint damage

+/- Skin lesions

Altered organ function *(non exhaustive)*

Neurological disorders: strokes ; psychiatric disorders

Peripheral nervous disorders : motor or sensory deficiencies (MS)

Ophtalmological symptoms : diplopia (Graves' disease); retrobulbar optic nevritis (MS)

Liver disorders : cholestasis/ictere (primary biliary cholangitis, AIH)

Intestinal lesions : rectal bleeding (ulcerative colitis),

anal ulcerations (Crohn)

Diarrhea +/- blood

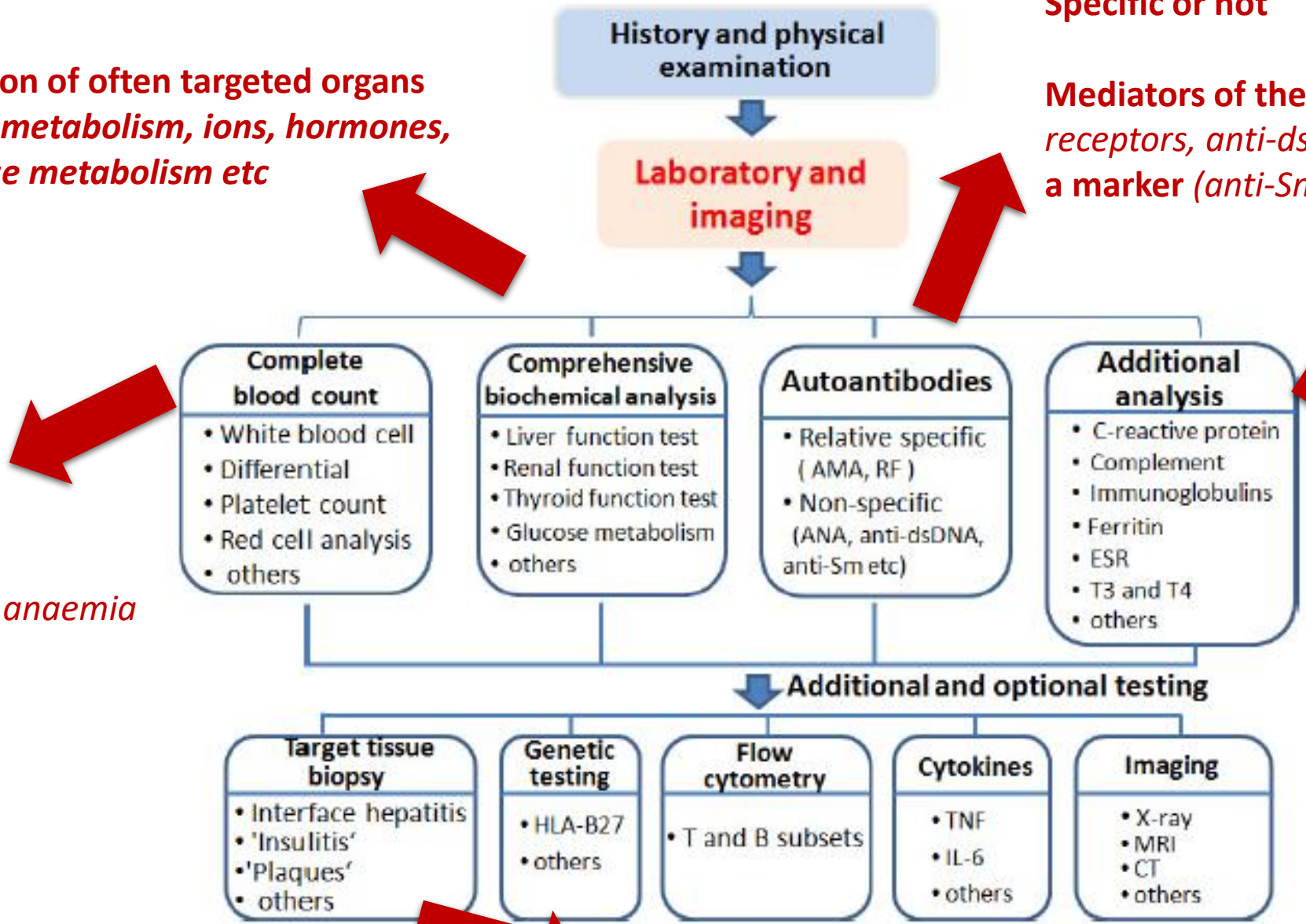
Malabsorption syndrome: chronic diarrhea, weight loss, vitamin B12 deficiency…(celiac disease)

BIOLOGICAL DIAGNOSIS OF AID: FROM LESS TO MOST SPECIFIC

Function of often targeted organs
Lipids metabolism, ions, hormones, glucose metabolism etc

Specific or not

Mediators of the disease *(anti-thyroid receptors, anti-dsDNA, anti-SSA)* **or just a marker** *(anti-Sm)*



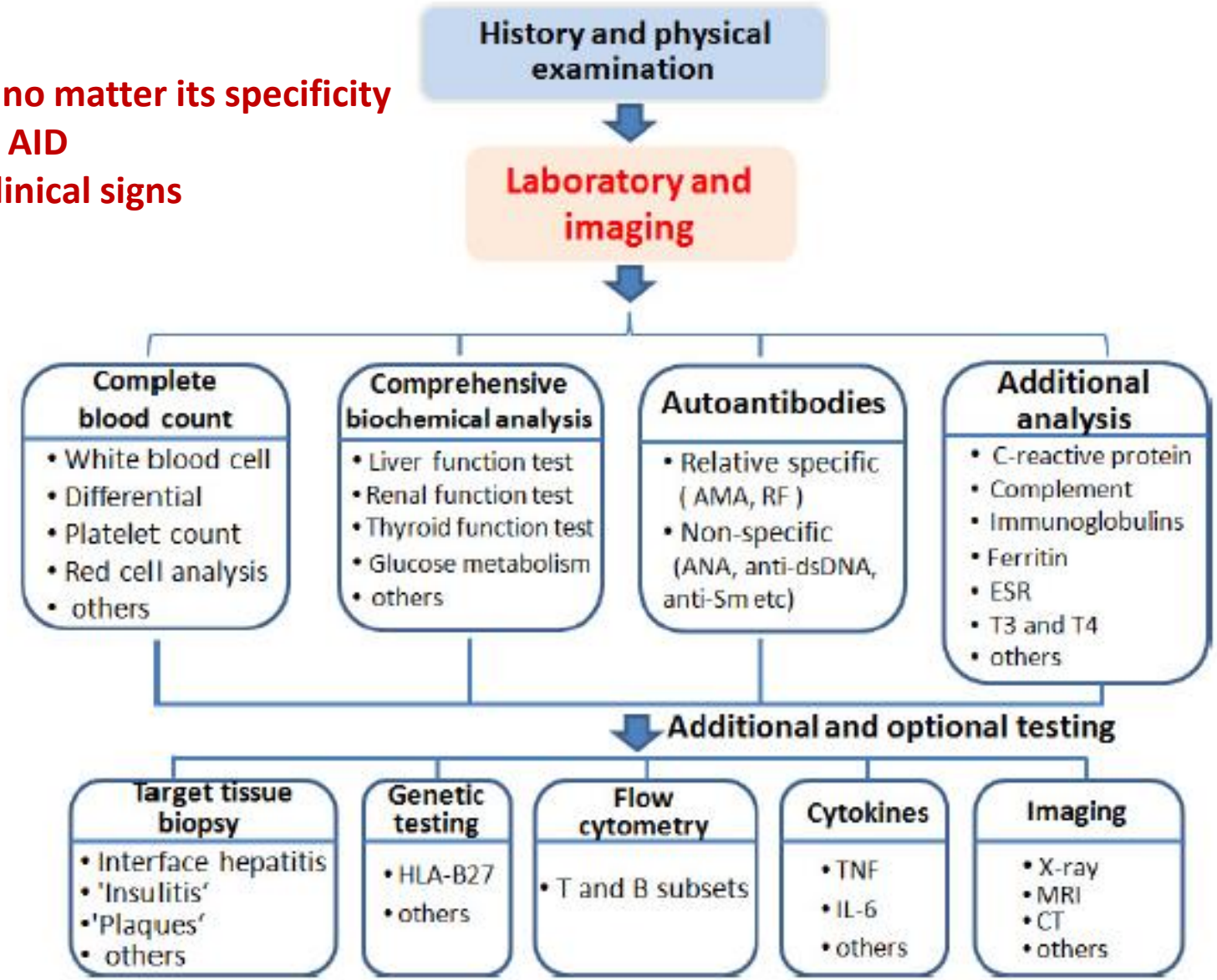
Inflammation?
Leukocytosis, thromobocytosis, anaemia
Destruction?
Anaemia

Inflammation?
CRP, Ferritin
Activation of specific (or not) par of the immune system?
Ig, Complement
Function?
Hormones

Associated with specific diseases to once you know what to look for

J Intern Med 2015; Wang L et al

Any biological marker alone, no matter its specificity is not enough to diagnose an AID
You aways need associated clinical signs



J Intern Med 2015; Wang L et al

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Diagnosis of systemic AID: Example of lupus

Systemic chronique autoimmune disease with a multi organ involvement

Leads to a broad spectrum of clinical manifestations

Sex ratio : 1 man /9 women

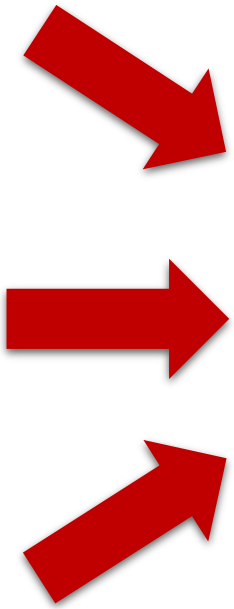
Age at diagnosis: 15-45 years (for women: peak at puberty and pregnancy)

Incidence: 5,6/100 000 persons-year

Chronic disease

Invalidating symptoms: pain, asthenia, psychological disorders

Life endangering symptoms



High societal and individual burden

Diagnosis of systemic AID: Example of lupus

« Benign » cutaneous lupus

« Severe » systemic lupus erythematosus with renal, pulmonary, neurologic disorders…

Diagnosis: Presence of AID ? Which disease (+/- which type?)

Pronostic/Prediction of response to treatment

Classification criteria

American College of Rhumatology (ACR) 1997

Systemic Lupus International Collaborating Clinics (SLICC) 2012

European League Against Rheumatism (EULAR) / ACR 2019

Diagnosis of systemic AID: Example of lupus

Example of the chronology of lupus in a woman diagnosed during puberty

Flare up with lupus nephritis

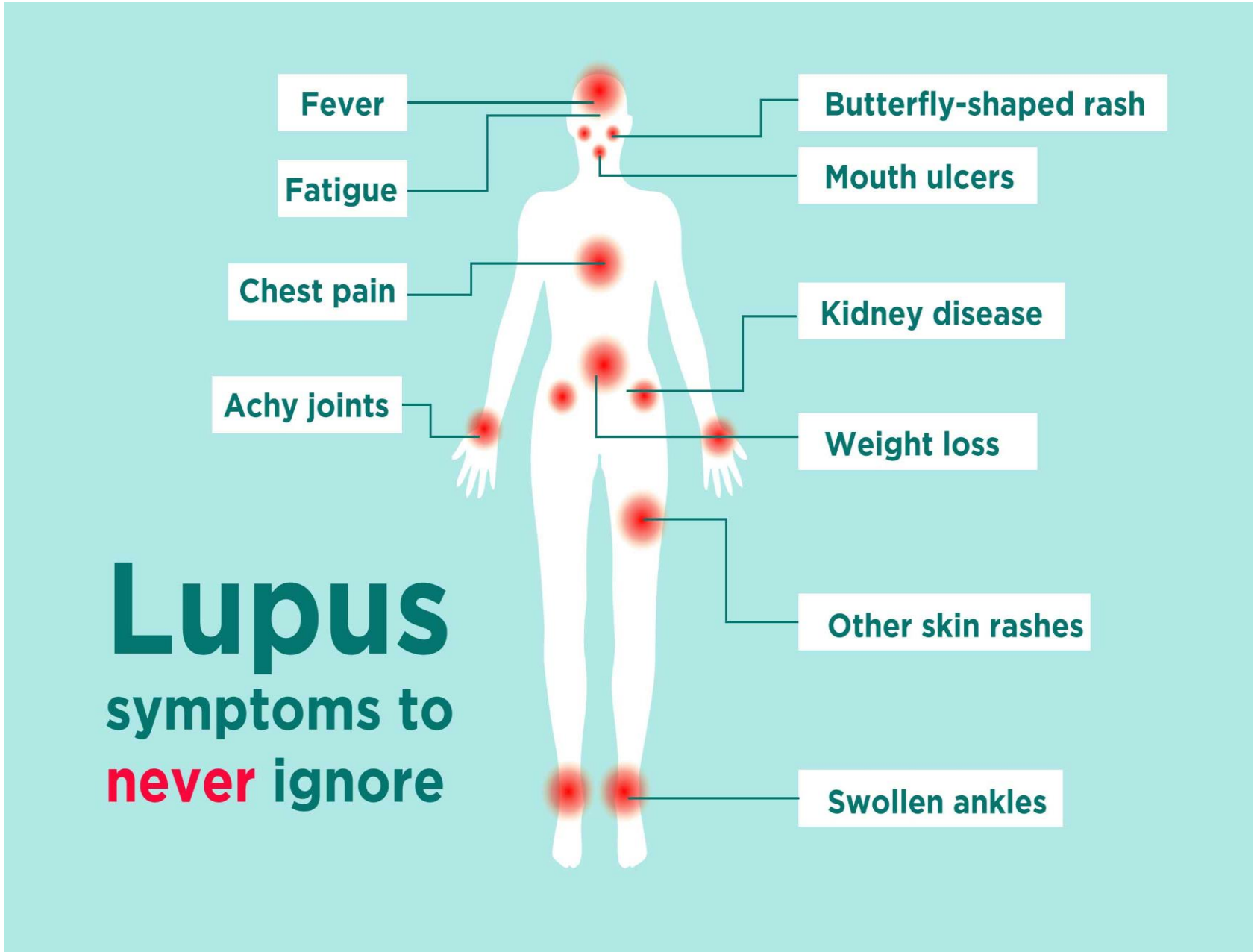
Pregnancy: Adapted treatment, reinforced surveillance, risk evaluation for fetal heartblock

Pronostic/Prediction of response to treatment

Treatment follow-up

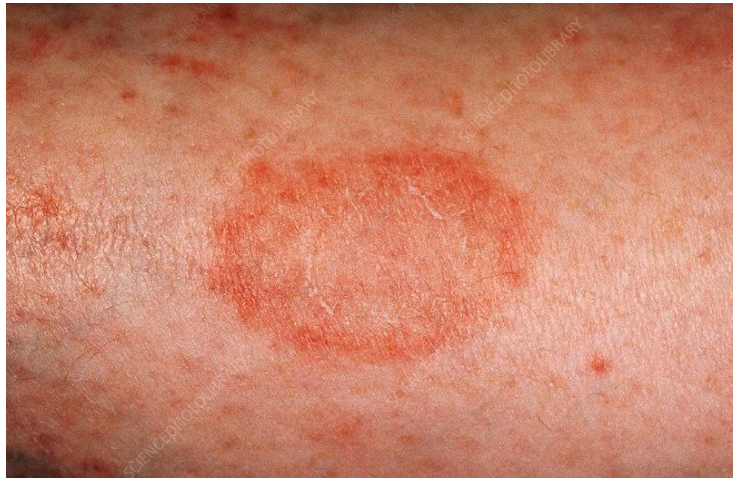
Lupus is a chronic disease with flare up that can be monitored biologically and which are strongly impacted by the environment and hormones

Lupus: Clinical diagnosis

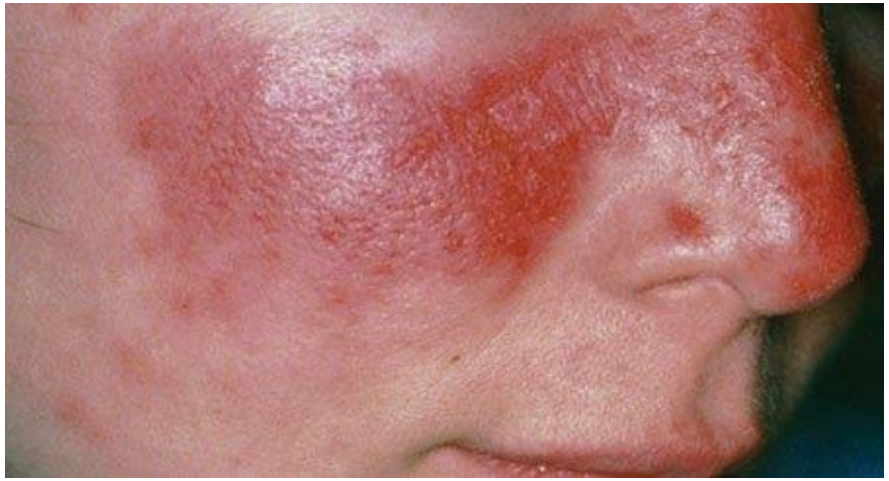


Lupus: Clinical diagnosis

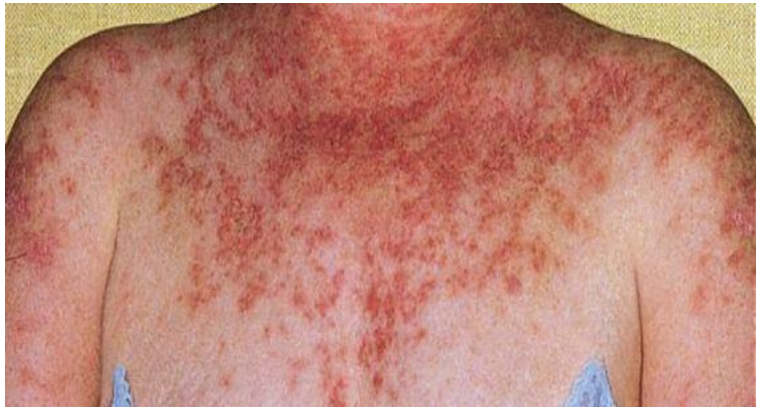
Skin damage



Discoid lupus (annular lesion)



Vespertilio

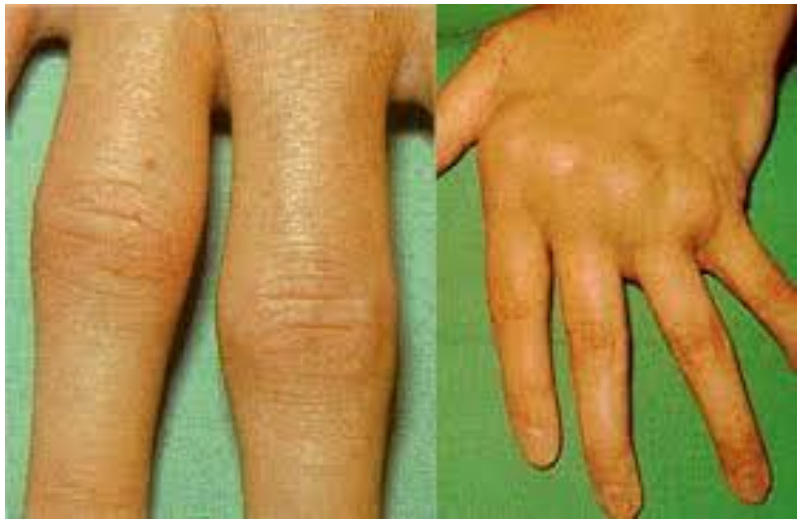


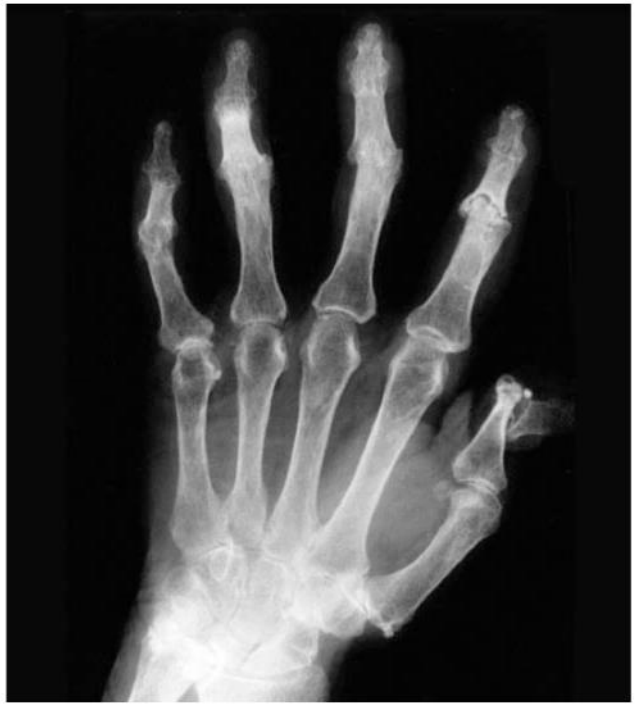
Photosensibility

Skin involvement : > 80% of patients
Erythematous rash
Topographic location: areas exposed to the sun, butterfly shape on nose and cheeks (lupus mask)

Lupus: Clinical diagnosis

Joint damage





Painful joints : 90% of patients
Non-erosive and non-deforming small joint arthritis

Lupus: Clinical diagnosis

Other symptoms

Moderate forms not involving the vital and functional prognosis of patients

Pleurisy

Pericarditis

Inflammatory anemia

Autoimmune hemolytic anemia

Thrombocytopenia

Nervous system damage

neuropsychiatric disorders, epilepsy, ischemic stroke….

Lupus: Clinical diagnosis

Kidney damage: lupus nephritis

About 50 % of patients
Main factor of poor prognosis

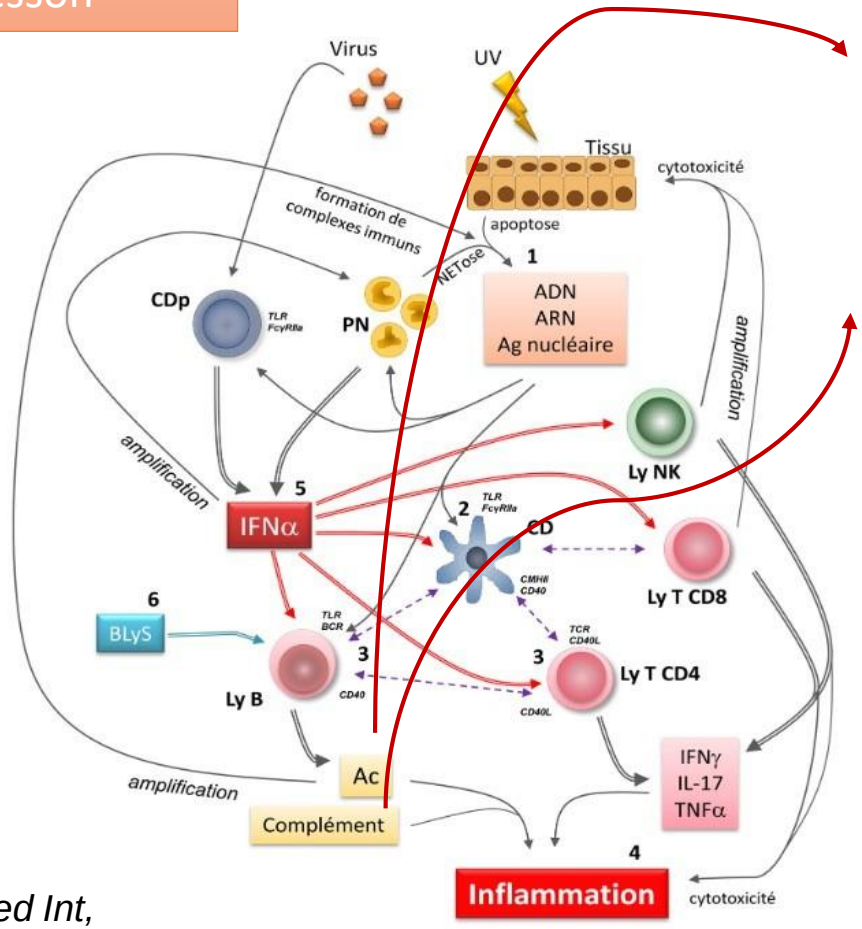
Inaugural symptom or most often occurring within the first 5 years after diagnosis

Nephrotic syndrome with or without hematuria and high blood pressure that can progress to true renal failure requiring kidney transplantation

Lupus: Biological diagnosis

See pathophyiology of lupus in G. Schlecht-Louf lesson

Mainly auto-andibodies mediated AID: Diagnosis with autoantibodies mainly

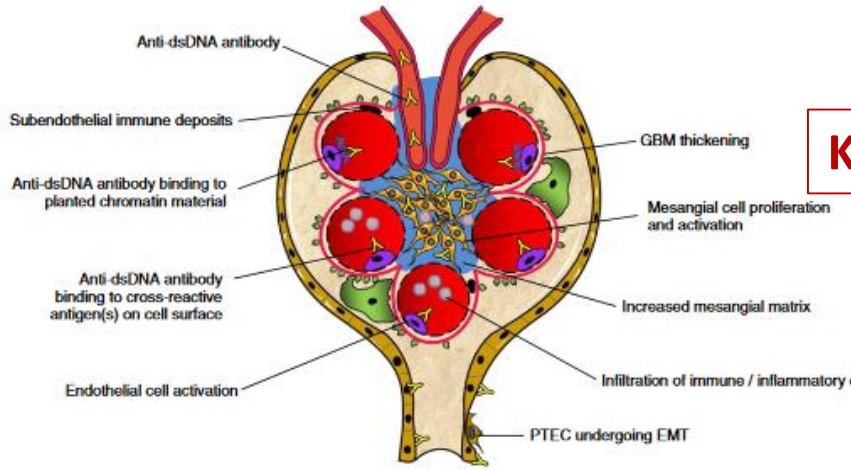


Mathian, Rev Med Int, 2014

Autoantibodies: antinuclear antibodies

The complement system

Kidney damage: lupus nephritis
Strongly associated with prognosis

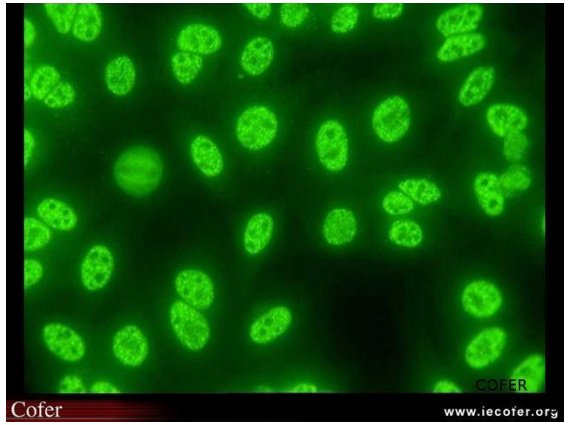


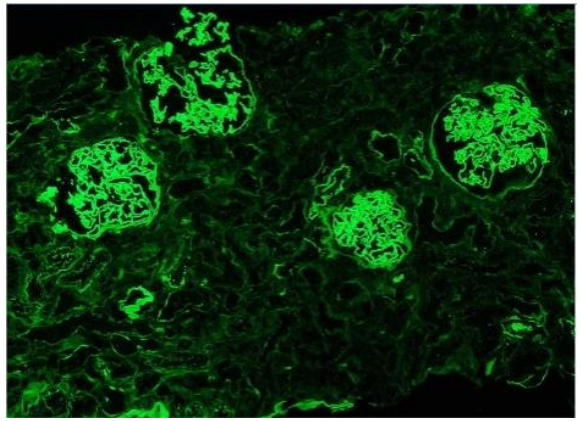
Kidney exploration

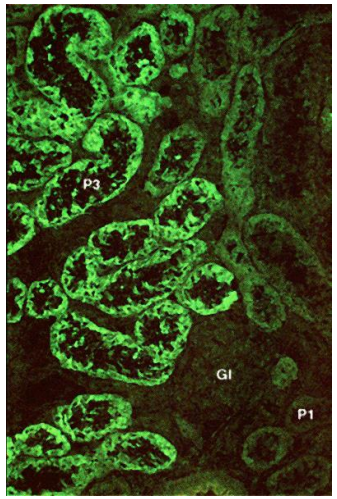
Biological diagnosis: Autoantibodies

Step 1: Non specific screening strategy

Immunofluorescence







Target autoantigens in native conformation on sections tissue or cell smear: specificity +++

Biological diagnosis: Autoantibodies

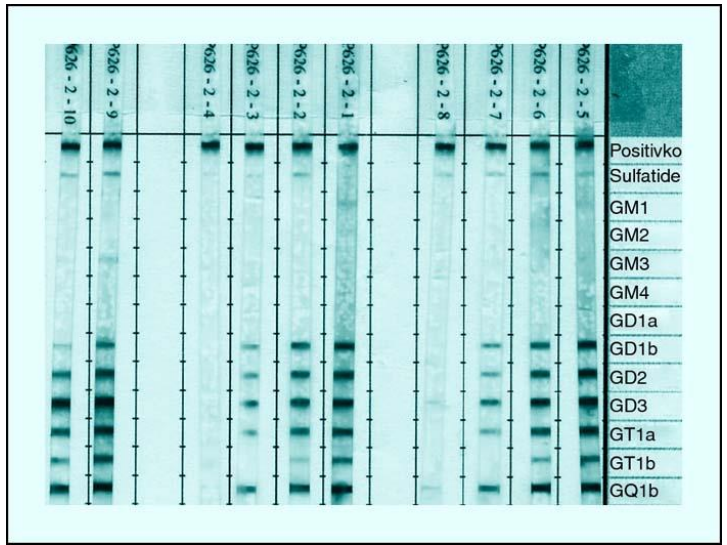
Step 2: Specific identification

Target autoantigens fixed on a support: nitrocellulose, microplate, beads...

Varied antigenic nature: purified or recombinant protein, synthetic peptide….

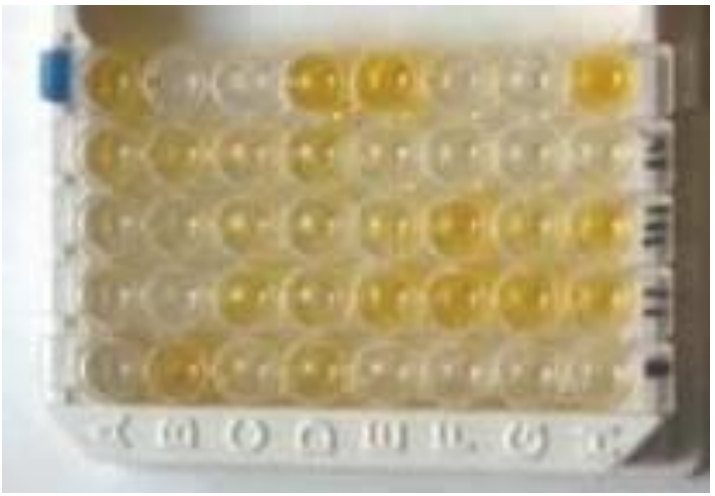
Less specific but highly sensitive methods

Immunodot Blotting analysis



Automated immunoanalyses

ELISA



Biological diagnosis: Autoantibodies

Antinuclear antibodies diagnostic strategy

Step 1
Non specific screening

Total antinuclear antibodies

Negative

Positive

Step 2
Identification

Anti-ribonucleoproteins
antibodies (anti-SSA, SSB, Sm, RNP…..)

Anti-DNA antibodies
Dosage

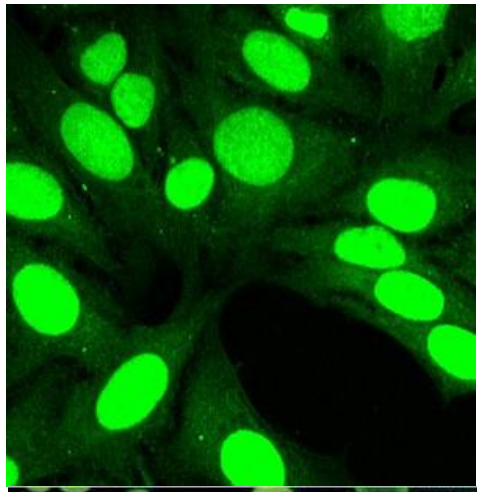
A bit further

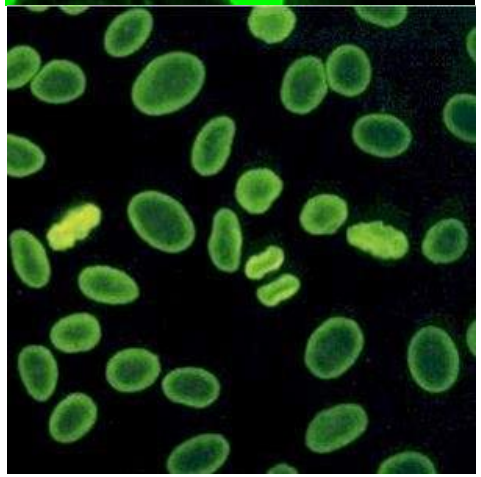
Biological diagnosis: Autoantibodies

Immunofluorescence on HEp-2 cells for identification of antinuclear antibodies

HOMOGENOUS

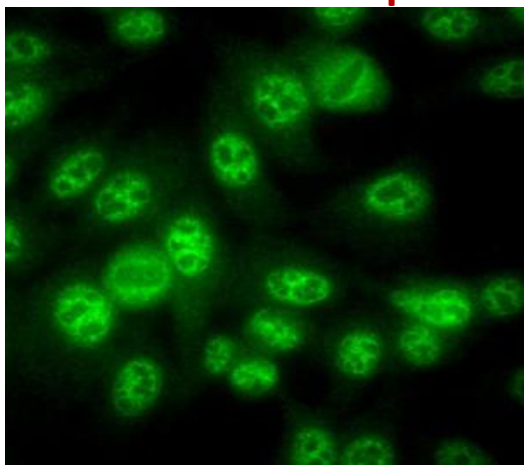
Found in lupus

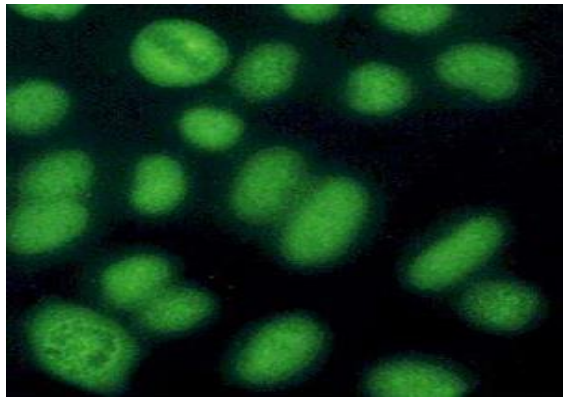




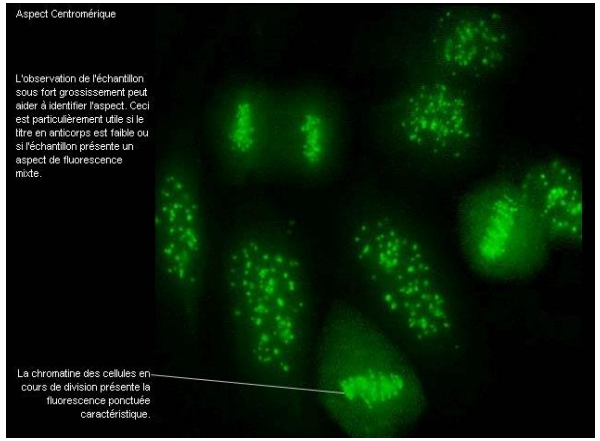
SPECKLED

Found in lupus

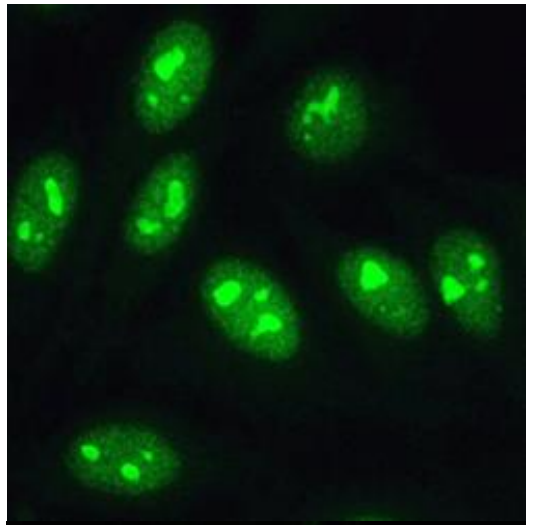


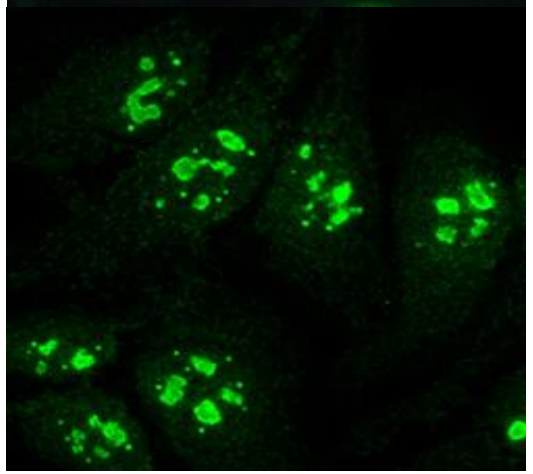


CENTROMERIC



NUCLEOLAR





Biological diagnosis: Autoantibodies

Antinuclear antibodies are mostly present at high titers in SLE and usually keep being positive during follow up

Their presence and titers have no link with disease activity

They can be positive in other auto-immune diseases or other contexts

In other auto-immune diseases, their presence is variable

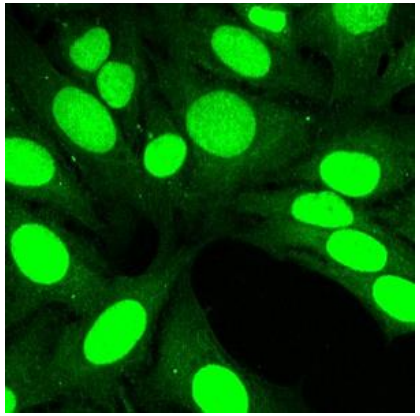
Diseases	Frequency (%)
SLE	≈ 100%
RA	35
SS	60
Sclerodermia	80
Myositis	30
MTCD	100
Autoimmune hepatitis	70
Infections	40
Hemopathies	10
Healthy subjects > 60 ans	20
Healthy subjects < 60 ans	10

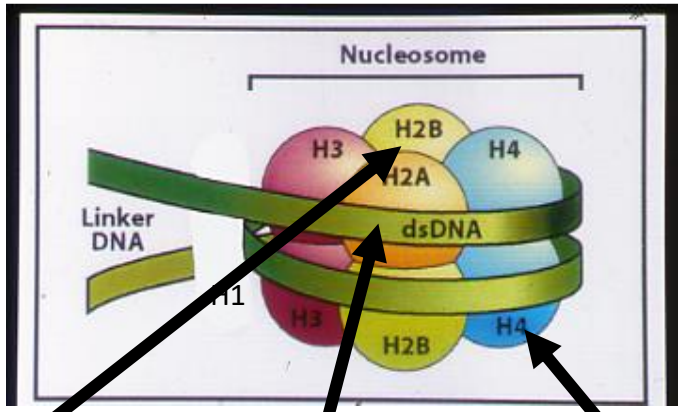
Biological diagnosis: Autoantibodies

Specific identification of antinuclear antibodies

Anti-chromatine antibodies

HOMOGENOUS





anti-nucleosome

anti-histone

anti-DNA

Anti-DNA:

- **Highly specific for SLE**

Diagnosis

- **The most involved in tissue damage**

Prognosis

- **Levels tend to reflect disease severity**

Follow up

Positivity of anti-ADN is not enough to diagnose an AID

You aways need associated clinical signs

Biological diagnosis: Autoantibodies

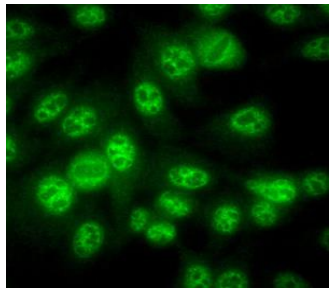
Specific identification of antinuclear antibodies

Anti-ribonucleoprotein antibodies

Cutaneous lupus: increase risk of photosensitive rash

Increased risk of obstetrical complications (fetal heart block)

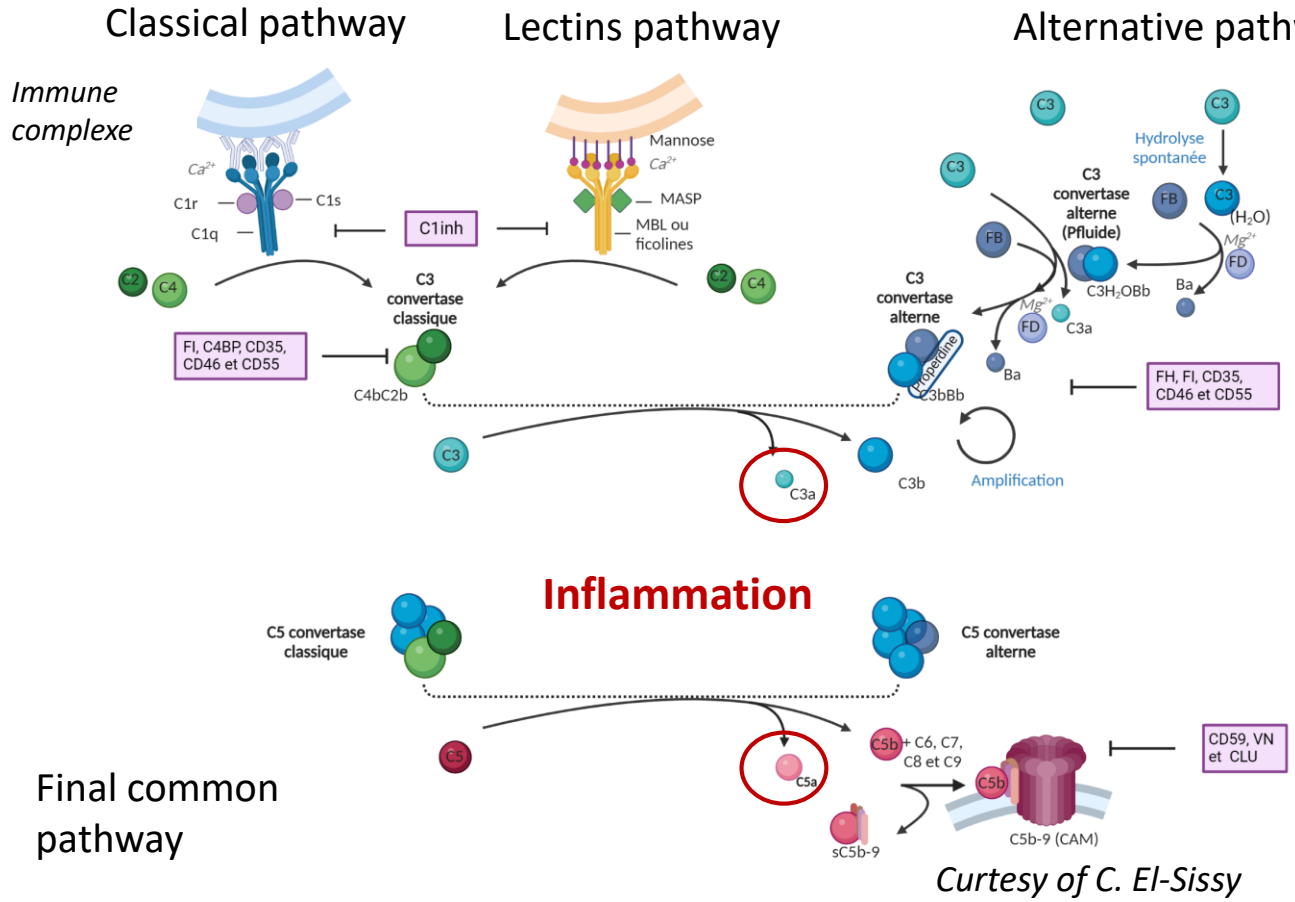
SPECKLED



Positivity of anti-Sm is not enough to diagnose an AID
You aways need associated clinical signs

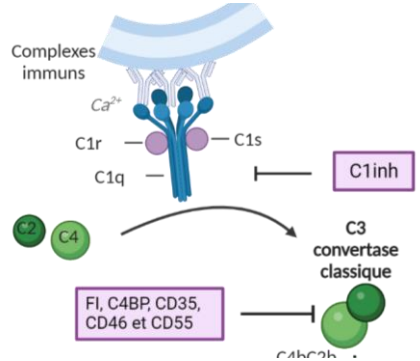
Autoantibodies	Associated-diseases
Anti-SSA **Prognostic marker**	70%SS 30% lupus
Anti-SSB	70% SS 10% lupus
Anti-RNP	100% MTCD 30% lupus 15% RA, sclerodermia
Anti-Sm **Diagnostic marker**	10-20 % lupus

Biological diagnosis: The complement system

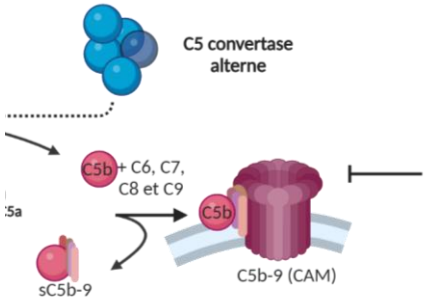


Final common pathway

Curtesy of C. El-Sissy



In lupus: Immune complexe with autoantibodies



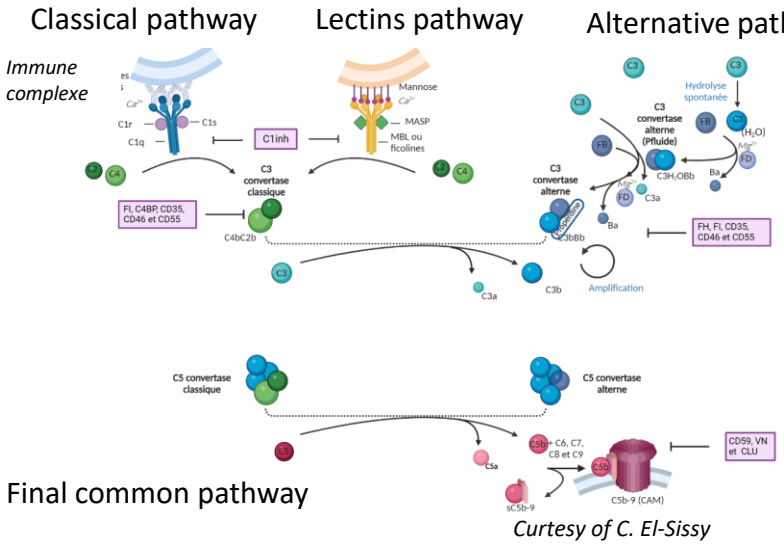
In lupus: Membrane attack complexe (MAC) on tissue cells *(role +++ in lupus nephritis)*

Activation leads to a decrease in components: consumption. After a flare up: Back to normal

Inflammation is associated with increased C3 and C4

Hereditary deficiency of proteins of the classical pathway (C1, C2, C4) is associated with lupus

Biological diagnosis: The complement system

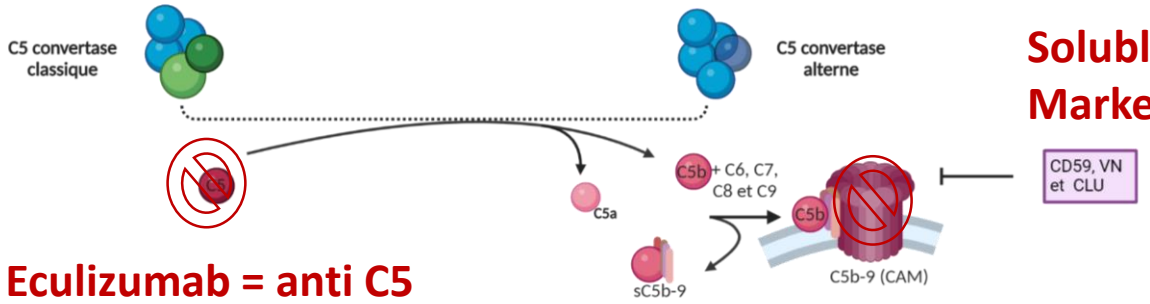


Curtesy of C. El-Sissy

Activation leads to a decrease in components: consumption. After a flare up: Back to normal

Inflammation is associated with increased C3 and C4

= Decreased C4 with normal or elevated C3 is a diagnosis and activity (flares) of lupus



Soluble C5b-9 can be measured :
Marker fo treatment follow up

Eculizumab = anti C5

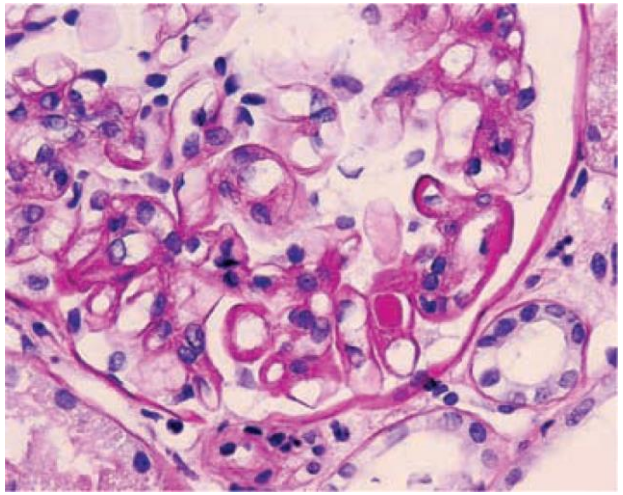
Decreases kidney tissue destruction during lupus nephritis

Biological diagnosis: Kidney damage

The main predictor of morbidity and mortality in SLE

Glomerulonephritis
A quarter of patients progress to renal failure

- Urinary strip to evaluate proteinuria or hematuria
- Plasma creatinine increase
- To be discussed according to the results of the renal biochemical assessment : renal biopsy to evaluate the histologic stage of glomerulonephritis for therapeutic monitoring



Aringer M, *et al*. *Ann Rheum Dis* 2019

Entry criterion

Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0.5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Immunology domains and criteria	Weight
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR	
Anti-β2GP1 antibodies OR	
Lupus anticoagulant	2
Complement proteins	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody* OR	
Anti-Smith antibody	6

Total score:

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

Differential diagnosis with other connective tissue diseases

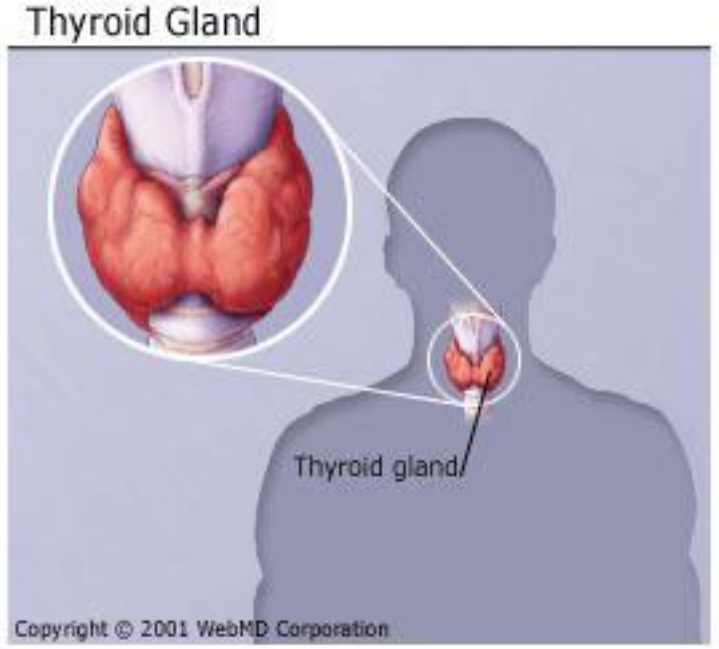
A bit further

Clinical and biological signs	SLE	Rhumatoid Arthritis	Sclerodermia	Myopathies
Joints	+++	+++	++	++
Skin	+++	-	+++	+++
Lung	+	-	++	++
Kidney	++	-	++	-
Antinuclear antibodies	+++	+	++	++
Anti-DNA Anti-Sm Anti-Scl70 Anti-JO1	+++ + - -	- - - -	- - + -	- - - +
Rhumatoid factors	++	+++	+	+
Anti-citrullinated proteins	-	+++	-	-

Outline

- INTRODUCTION
  - Reminders
  - AID: Diagnosis objectives and strategy
  - Therapeutic strategies
- DIAGNOSIS OF AID
  - Clinical signs
  - Biological diagnosis
- DIAGNOSIS OF SYSTEMIC AUTOIMMUNE DISEASES: EXAMPLE OF THE LUPUS
- **DIAGNOSIS ORGAN SPECIFIC AUTOIMMUNE DISEASES : EXAMPLE OF AUTOIMMUNE ENDOCRINOPATHIES AND OF MULTIPLE SCLEROSIS**

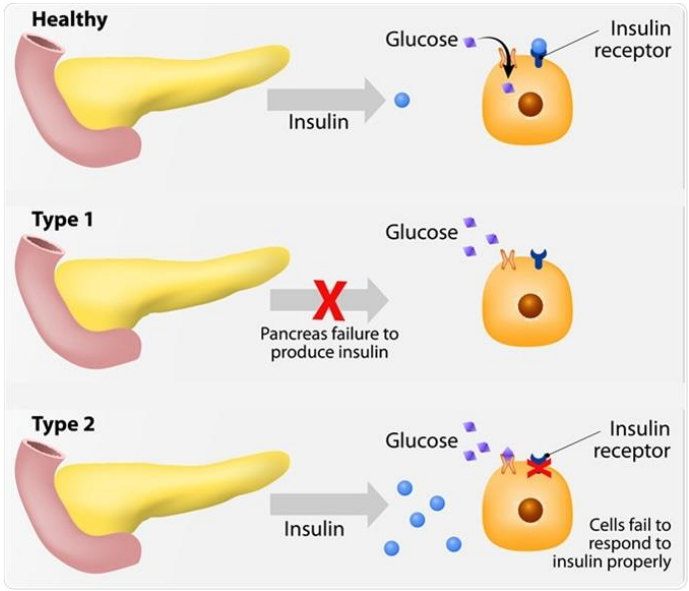
Diagnosis of organ specific AID: Example of Autoimmune endocrinopathies



Autoimmune thyroiditis

Autoantibodies targeting antigens in the thyroid gland: destruction of tissue or activation of receptors

Mainly cell autoantibody mediated autoimmunity



Diabetes

Type 1 diabetes: Aberrant immune response to specific pancreatic β-cell autoantigens resulting in insulin deficiency

Mainly cell mediated autoimmunity: infiltration of lymphocytes in pancreatic islets

Autoimmune endocrinopathies: Clinical diagnosis

Autoimmune thyroiditis

Graves' disease	Hashimoto's disease
Hyperthyroiditis	Hypothyroiditis
Goiter	Goiter
Exophtalmia	/
Tachycardia	Bradycardia
Nervousness	/
Asthenia	Asthenia
Sleep disorders : insomnia	/
Accelaration of transit	Constipation
Rapid loss of weight	Moderate loss of weight
Excessive sweating	Hoarsely, cramps, myalgia…

Type 1 Diabetes

10% of diabetes

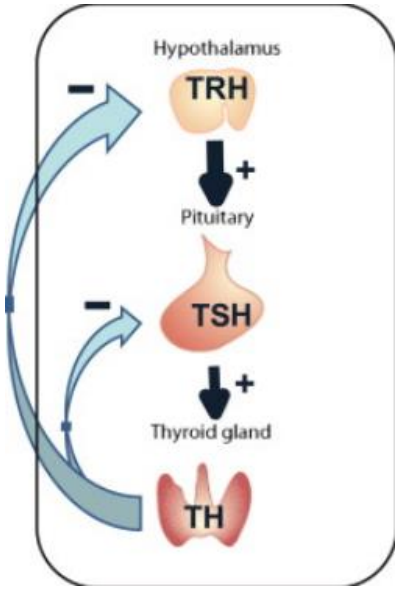
Onset of diagnosis : < 35 years old

HLA DR3/DR4 genetic background

Triad of symptoms : polyuria, polydypsia and loss of weight

Complications : renal, vision, cardiovascular…

Autoimmune endocrinopathies: Biological diagnosis



Autoimmune thyroiditis

Graves' disease	Hashimoto's disease
Decrease in TSH	Increase in TSH
Increase in T4 and T3 hormones	Decrease in T3 and T4 hormones
Anti-TSH Receptor antibodies +++	- Anti-thyroperoxydase (TPO) antibodies +++ - Anti-thyroglobulin (Tg) antibodies +

Type 1 Diabetes

Fasting blood glucose concentration

Hyperglycaemia : >1.26 g/L , in 2 different occasions
Glycated haemoglobin (HbA1c) > 7%

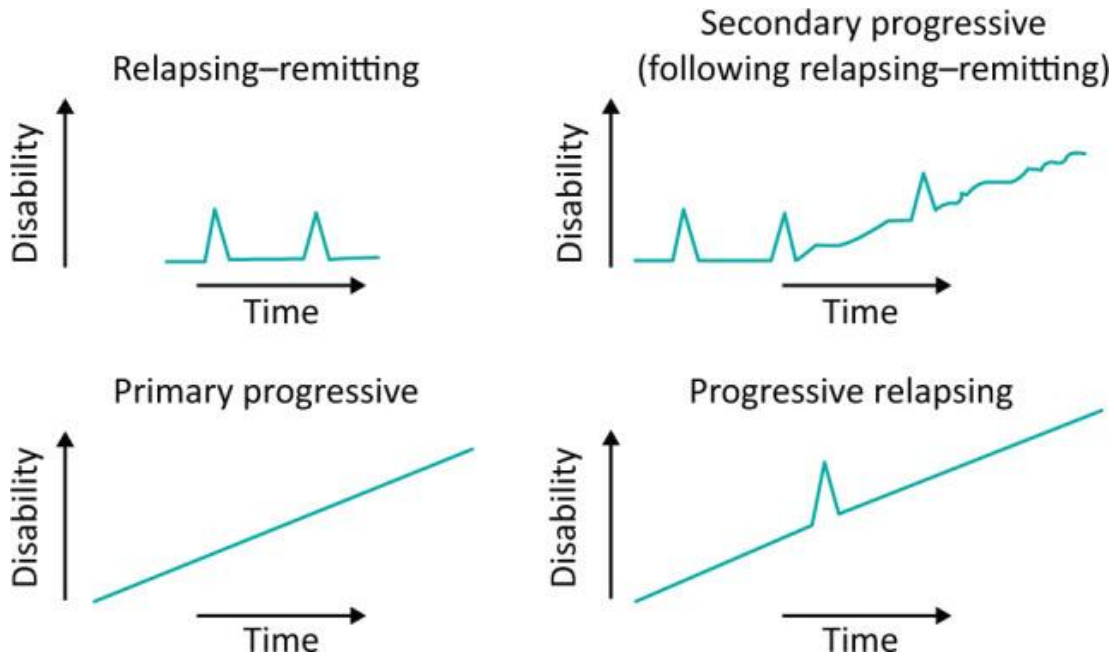
Autoantibodies

Anti-pancreatic islet cells (ICA)
Anti-pancreatic glutamic acid decarboxylase (GAD)
Anti-pancreatic tyrosine phosphatase (IA2)
Anti-insulin

Diagnosis with clinical signs and hormone levels +/- autoantibodies

Diagnosis of systemic AID: Example of Multiple sclerosis

Chronic inflammatory, demyelinating and neurodegenerative disease of the central nervous system



Ford H.Clin Med (Lond). 2020

Not always easy to diagnose outside of relapses

See pathophysiology of MS in G. Schlecht-Louf lesson

Diagnosis of systemic AID: Example of Multiple sclerosis

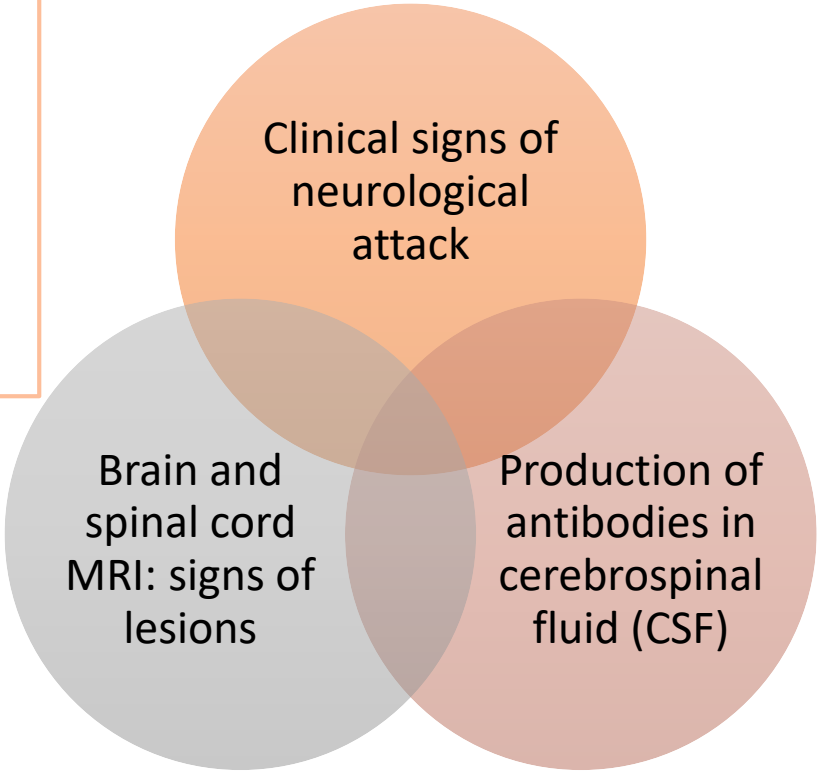
At least 24 hours in the absence of fever or infection

Visual loss or impairment, nystagmus, sensitive or motor dysfunction, facial sensory loss, veritgo, dysarthria, …

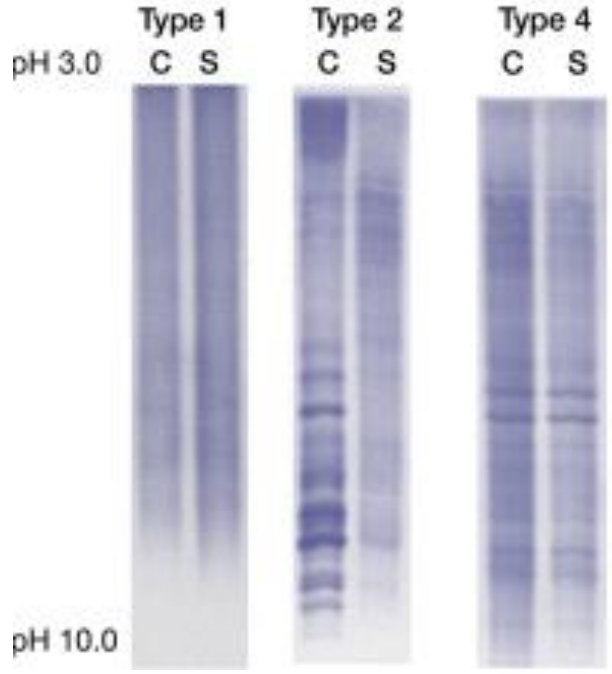
More evocative if disseminated in time and space (= different parts of the body)

Allow or evidence of dissemination in time and space

2017 MacDonalds Criteria



Oligoclonal bands in the CSF not found in the serum

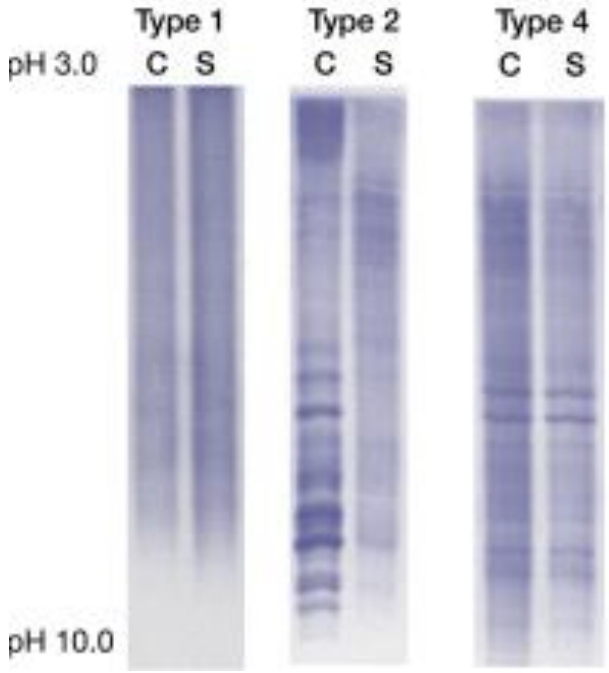


+/- elevated CSF proteins and pleiocytosis (surrogate for antibodies production)

Mainly cell mediated AID: Diagnosis with signs of lesions at imagery

Diagnosis of systemic AID: Example of Multiple sclerosis

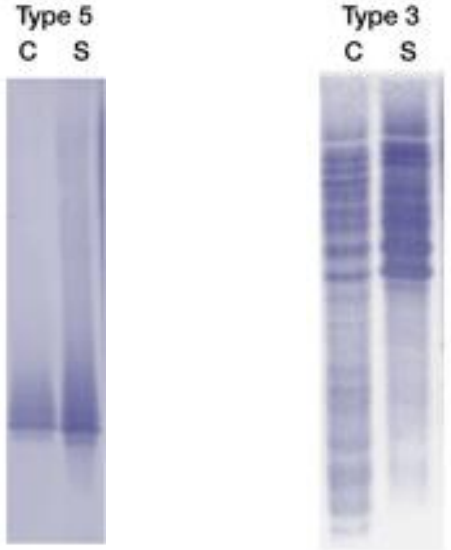
Oligoclonal bands in the CSF not found in the serum



Normal MS CNS inflammation

Possible observer-dependant variability

Hardships in interpretation



Monoclonal IgG passing through in CSF

CNS inflammation (serum IgG passing through to CSF) + oligoclonal bands = **MS**

Calls to include KFLC ratio in Mac Donald Criteria

New marker: Kappa free light chains (KFLC) ratio from CSF to serum

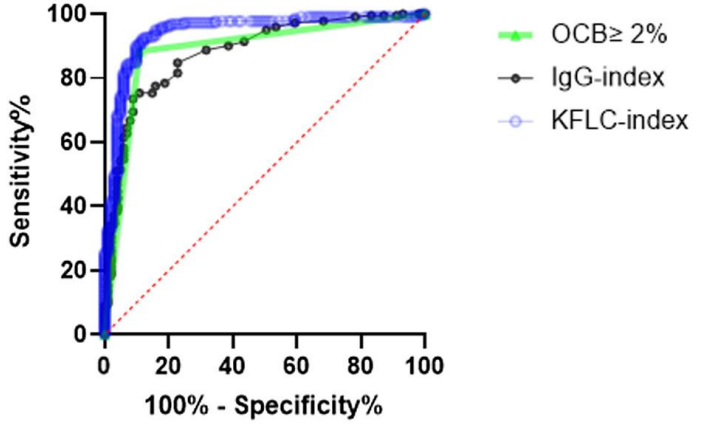
Free light chains are synthetized as the same time as Ig by B cells

$$(KFLC_{CSF}/KFLC_{serum})/(Albumin_{CSF}/Albumin_{serum})$$

- Result is not subjected to interpretation
- Surrogate for intrathecal Ig production

- Good performances in real life settings:

(a) ROC of KFLC-index, IgG-index and OCBs≥ 2 in CIS/RIS/MS vs. controls



Rosenstein I, *et al*. J Neurochem. 2021

TAKE HOME MESSAGES

Clinical diagnosis of AID is not always specific and symptoms can be inconstant outside of relapses/flare up but without clincial symptoms there is no AID

Biological diagnosis of AID depends on the pathophysiology of the disease (mainly cell or antibodies mediated?), the systemic or organ dependant aspect and wether the involved organ function can be assessed

Biological diagnosis allows for diagnosis, pronostic and predictive/follow up markers
It should be sequential from less to more specific