



CPC 16Th January

A 65-year old woman admitted to IM ward with edema, abdominal distension, mild fever, and progressive renal failure



RESULTS

Second Part: Results

Cryoglobulins **POSITIVE**

Hypogamaglobulinemia



Determinación	Resultado	Unidades	Margenes de normalidad
Complemento C3	51.5	mg/dL	79.0 - 152.0
Complemento C4	<1.67	mg/dL	16.0 - 38.0
Properdina Factor B del Complem.	18.7	mg/dL	19.0 - 50.0
Antiestreptolisina O en suero	<25.0	UI/mL	0.0 - 116.0

ESTUDIO DE CRIOGLOBULINAS
Validado por: DR. JUAN JOSE RODRIGUEZ

Determinación	Resultado	Unidades	Margenes de normalidad
Crioglobulinas	Positiva		
Criocrito	7.5	%	
IgG en sobrenadante	185.0	mg/dL	IgG: 750-1500
IgA en sobrenadante	142.0	mg/dL	IgA: 80-450
IgM en sobrenadante	64.3	mg/dL	IgM: 40-300
F. reumatoide en sobrenadante	287.0	UI/mL	
IgG en crioprecipitado	10.70	mg/dL	
IgA en crioprecipitado	<1.11	mg/dL	
IgM en crioprecipitado	23.60	mg/dL	
F reumatoide en crioprecipitado	324.0	UI/mL	
Informe Crioglobulinas	Crioglobulina mixta monoclonal IgM-kappa		

Cryoglobulins are immunoglobulins with the peculiarity crystallize at low temperatures and dissolve after rewarming.

Clinical Diagnosis

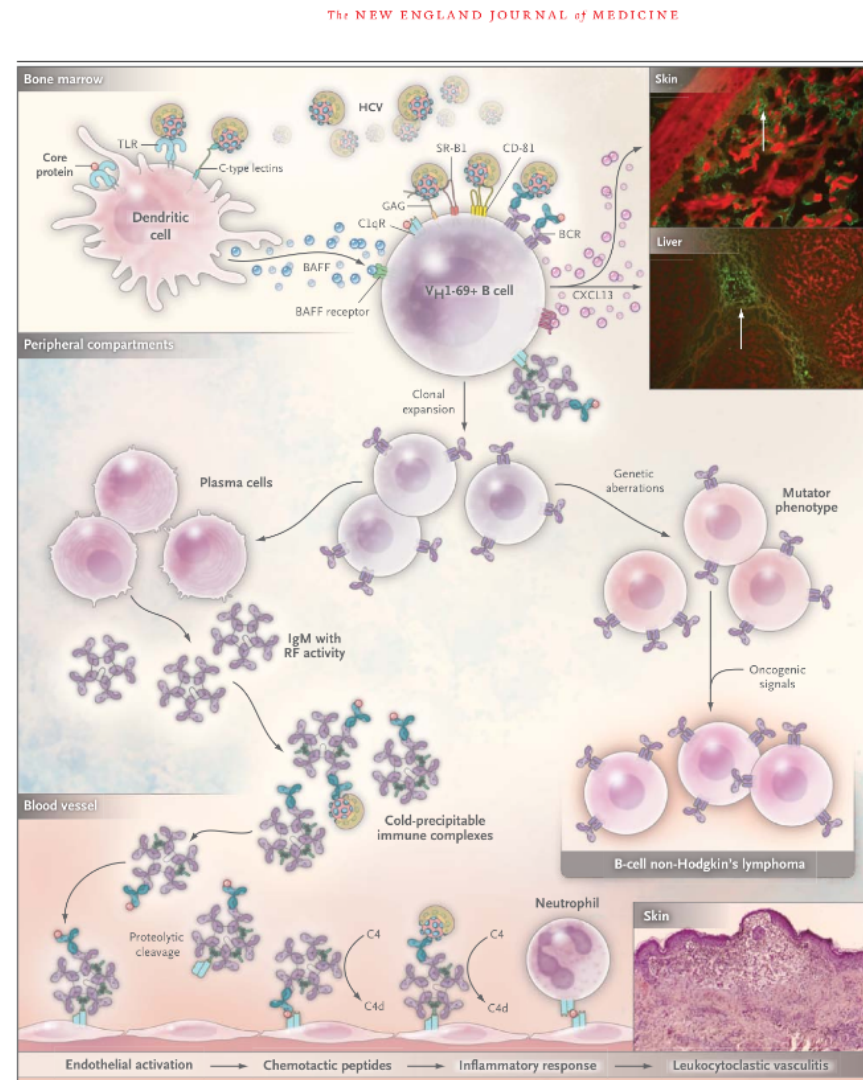
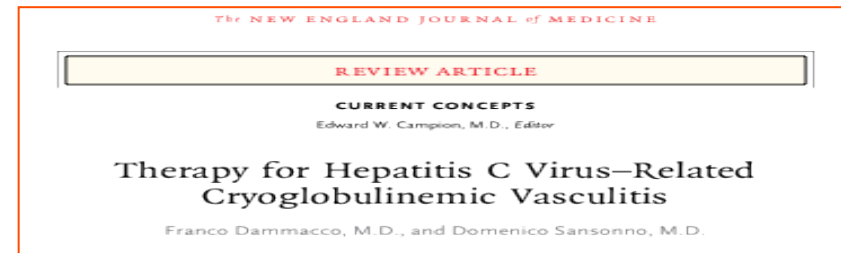
- Hepatitis virus C ¿subclínical?
- Crioglobulin mixed tipo II (Rheum. Factor +)
- Hypogammaglobulinemia ¿Lymphoma?
- ARDS severe.
- Herpes simple infection (Pneumonia)
- Heart Failure. Renal Failure

Main Facts

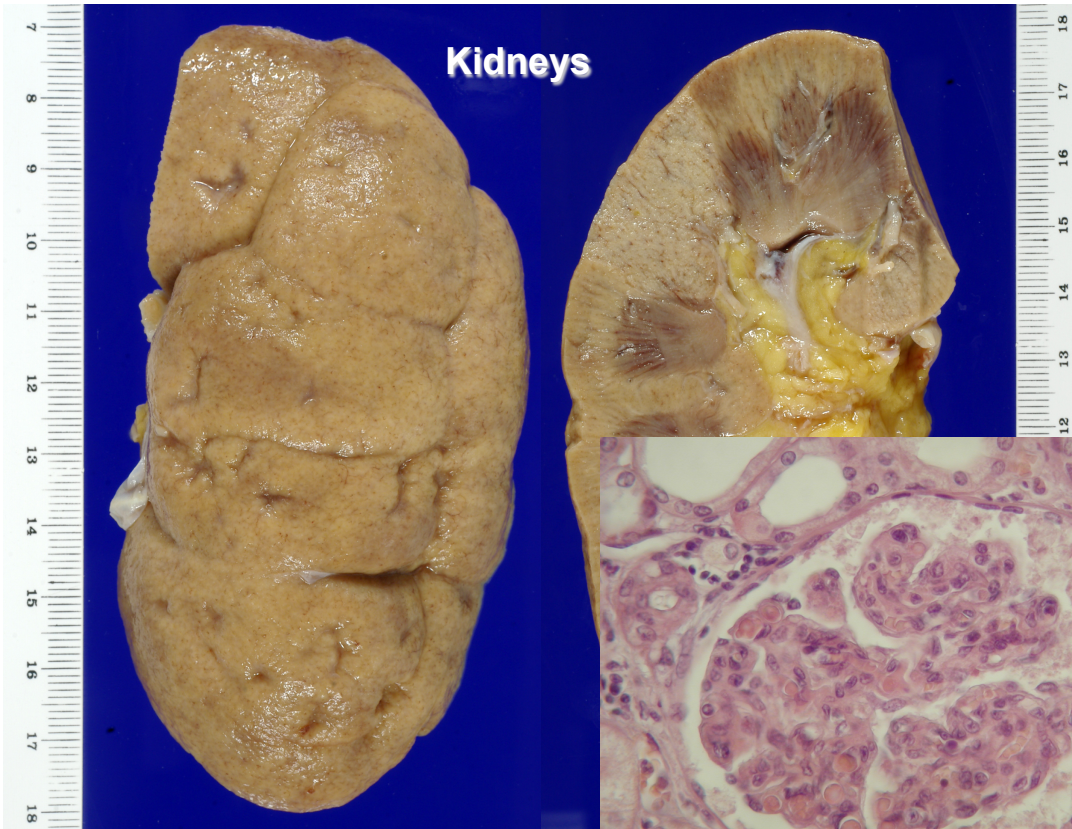
✓ **Cryoglobulins** are classified as either:
type I (single monoclonal Ig)
type II mixed (2 or more Ig types)
type III, without a M component

✓ **90%** of patient with mixed CB are infected by Virus C

✓ **Cryoglobulins can be detected in 25-30% of HCV positive patients** but cryoglobulinemic vasculitis appears in a minority (**10-15%**) from mild purpura to life-threatening disease



Post Mortem Findings

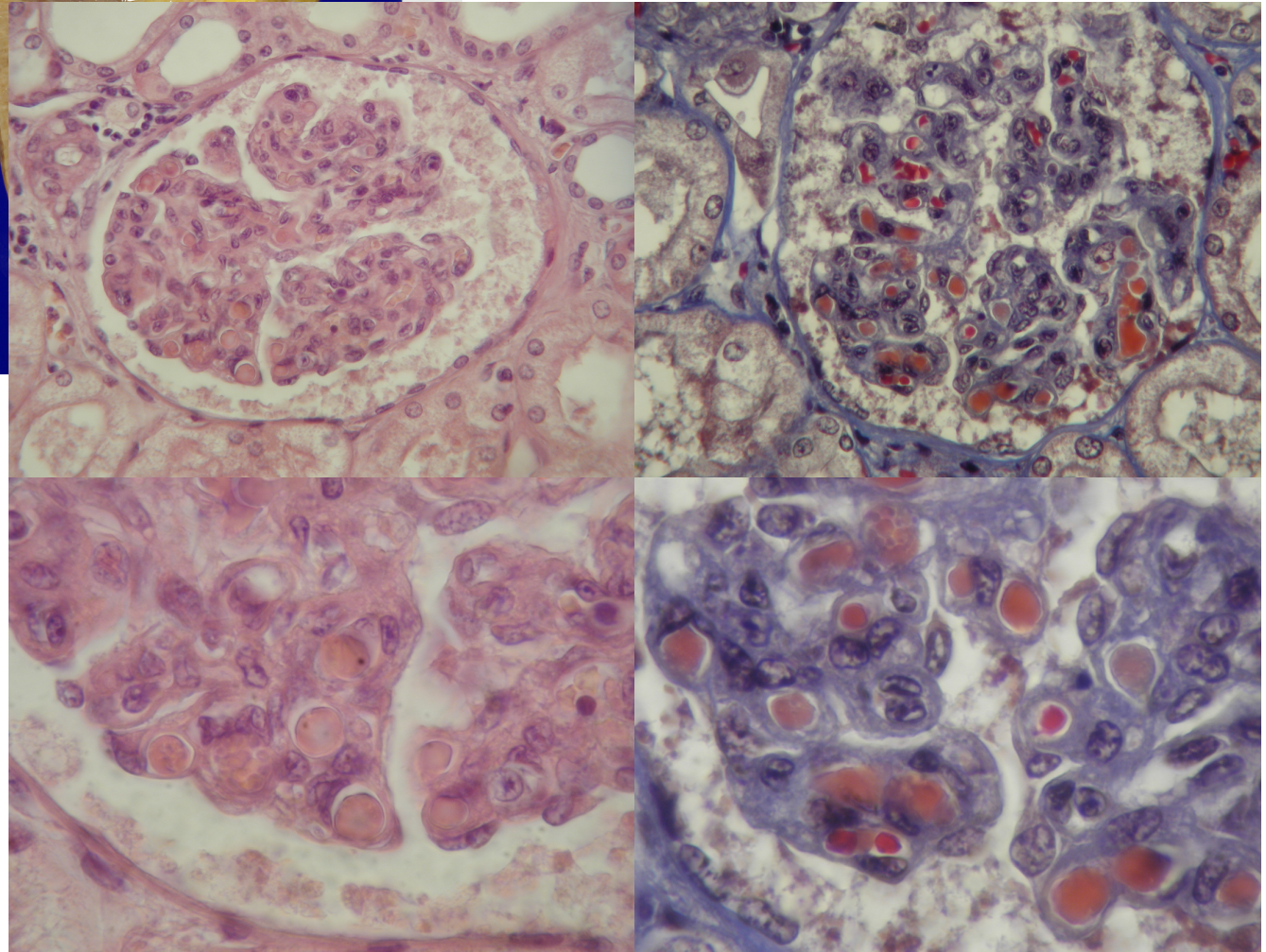


Massive infiltration of glomeruli by activated monocytes and macrophages with intracapillary deposits IgM and IgG typical of cryoglobulin precipitates with pseudothrombi

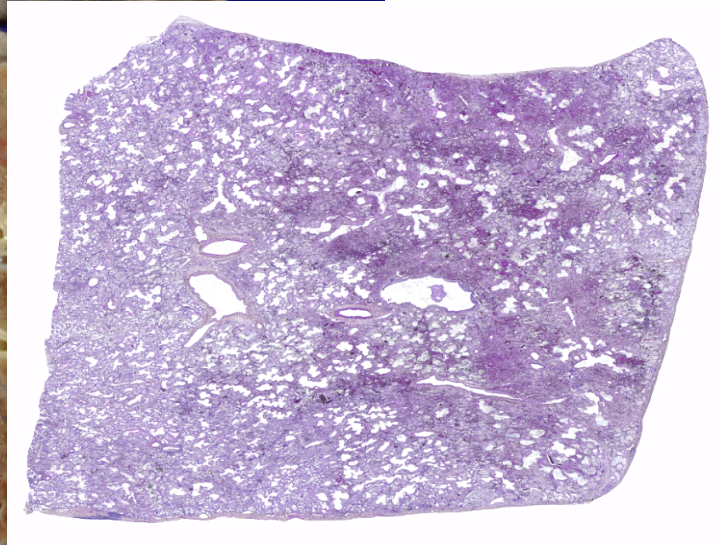
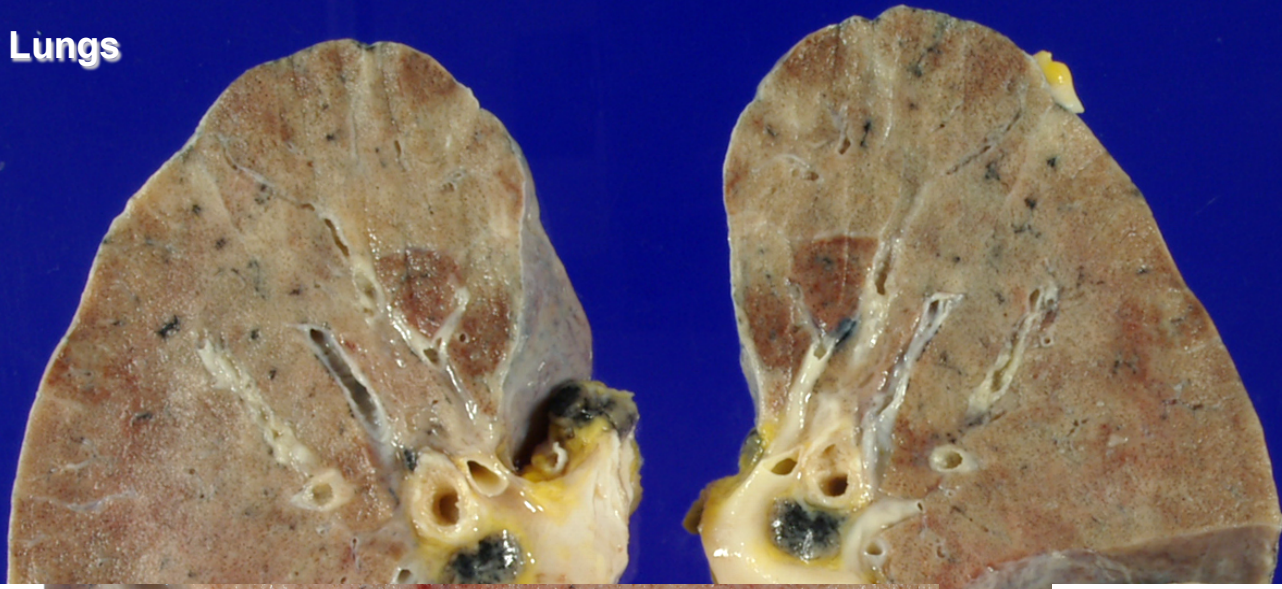
Membranoproliferative glomerulonephritis

Compatible with type II cryoglobulinemia

Small vessel vasculitis



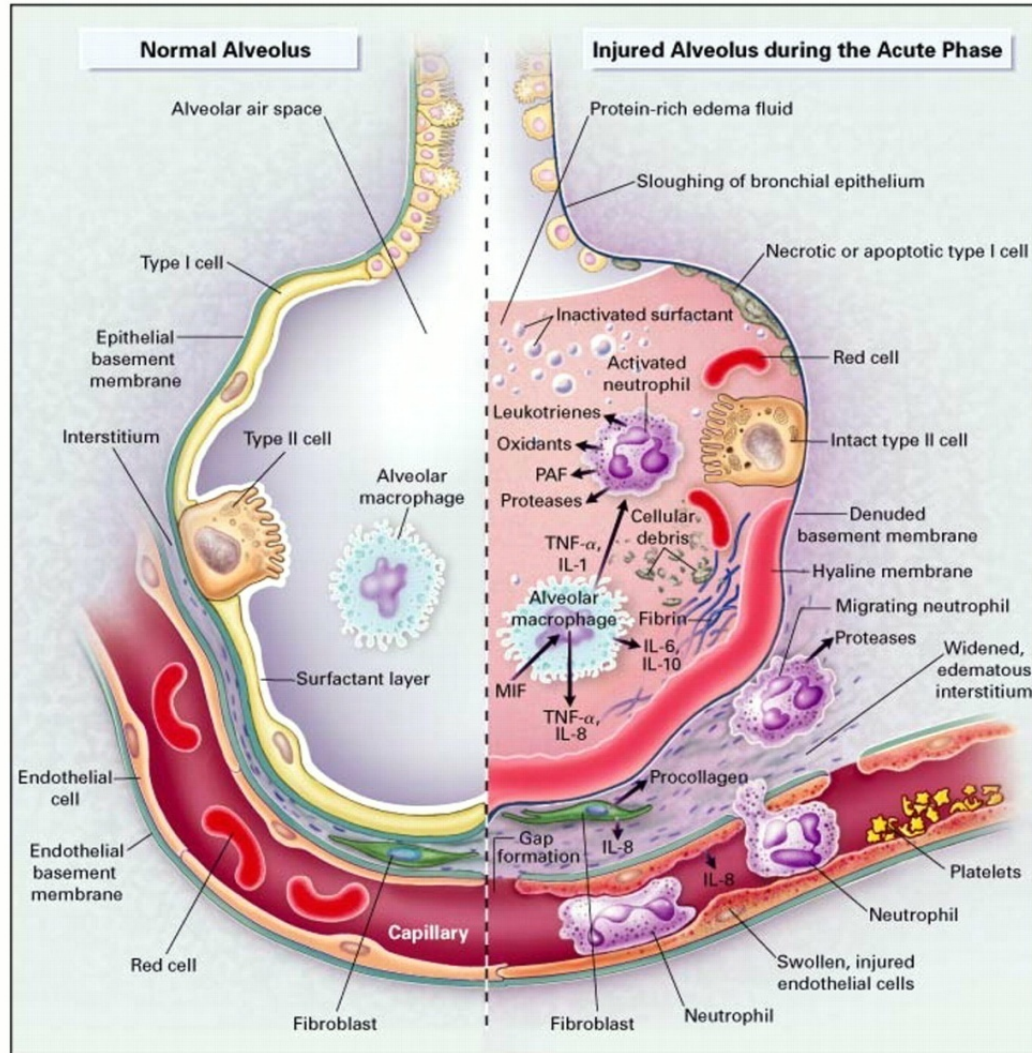
Lungs



Data of acute distress respiratory syndrome with haemorrhagic necrosis and signs of inflammation

Lung Injury and the Acute Respiratory Distress Syndrome.

Normal Alveolus



Injured Alveolus

TABLE 2. CLINICAL DISORDERS ASSOCIATED WITH THE DEVELOPMENT OF THE ACUTE RESPIRATORY DISTRESS SYNDROME.

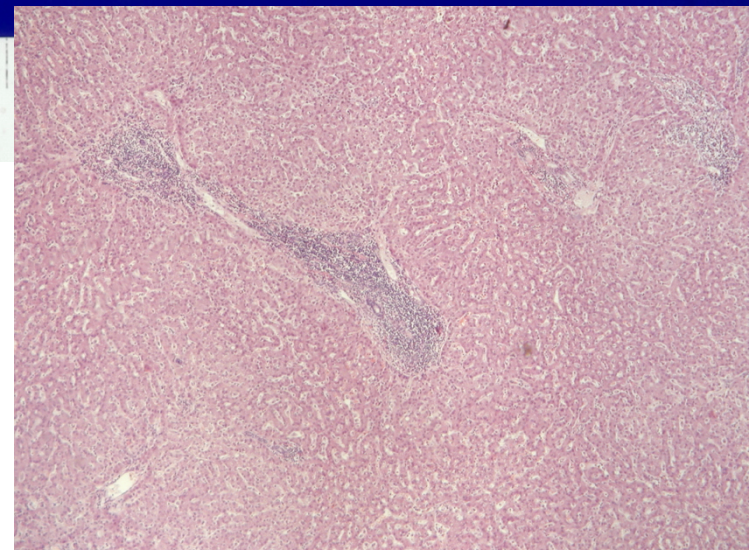
DIRECT LUNG INJURY	INDIRECT LUNG INJURY
Common causes	Common causes
Pneumonia	Sepsis
Aspiration of gastric contents	Severe trauma with shock and multiple transfusions
Less common causes	Less common causes
Pulmonary contusion	Cardiopulmonary bypass
Fat emboli	Drug overdose
Near-drowning	Acute pancreatitis
Inhalational injury	Transfusions of blood products
Reperfusion pulmonary edema after lung transplantation or pulmonary embolectomy	

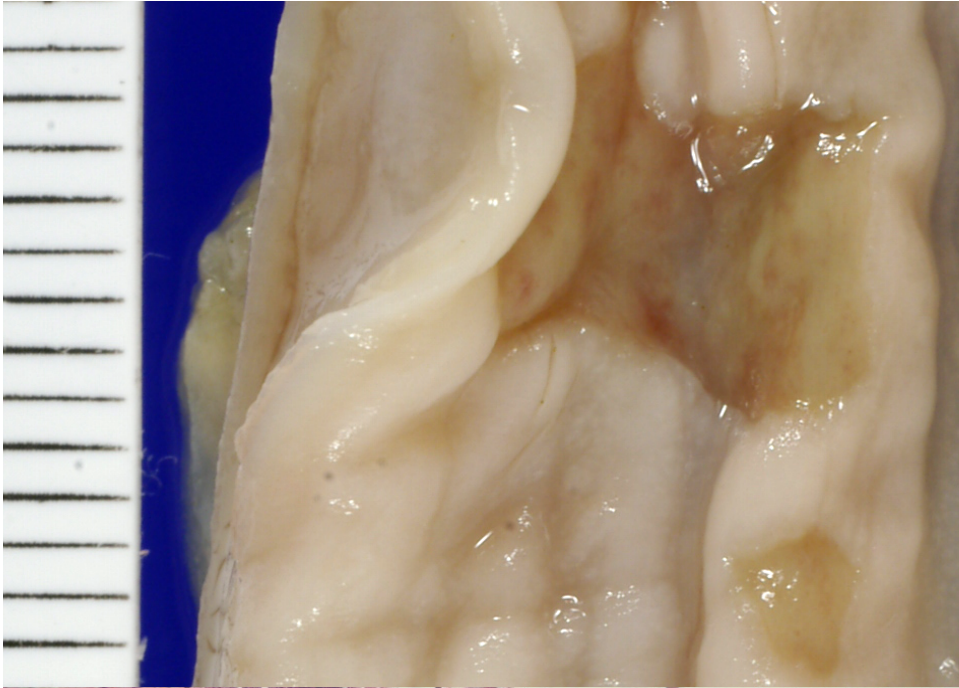
Liver



**Compatible with a active chronic hepatitis
related to virus C**

(mainly with portal and lobular inflammation)





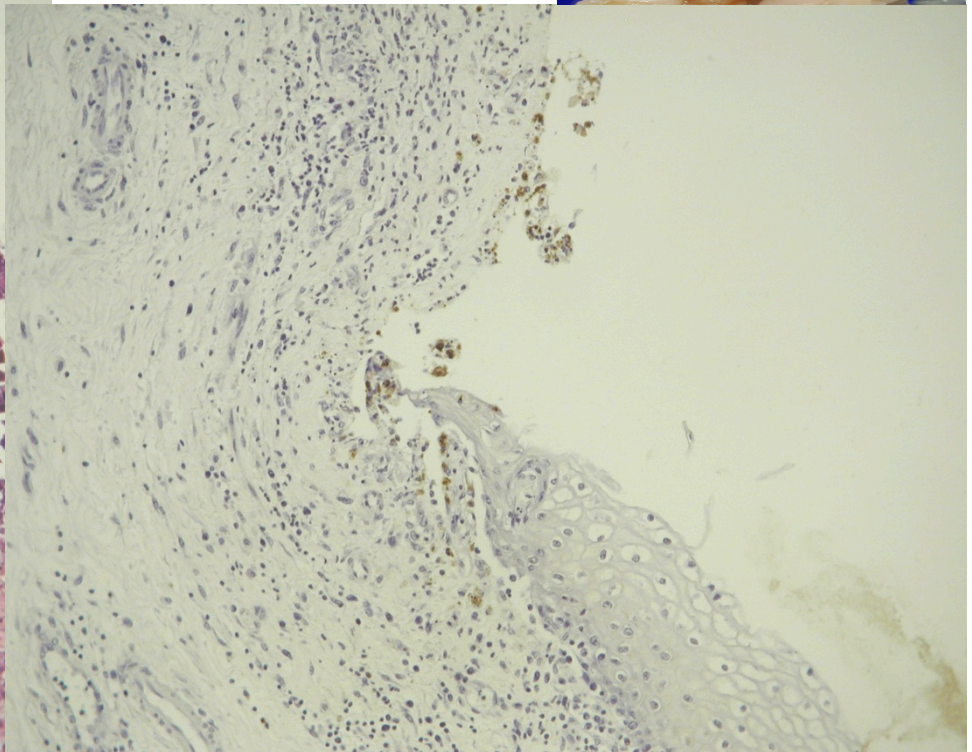
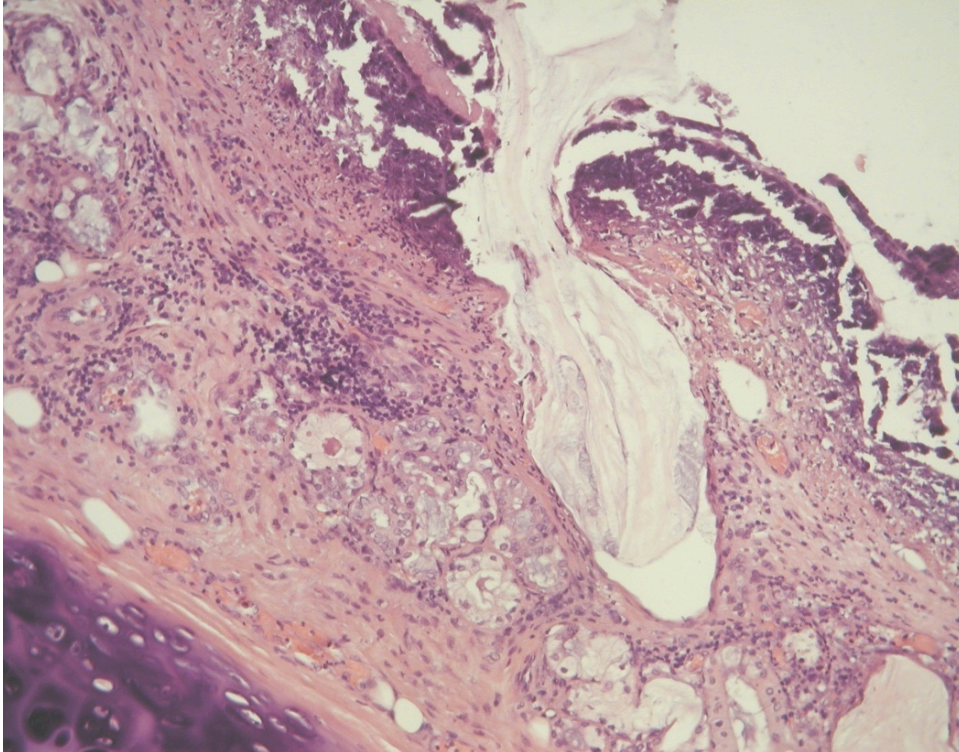
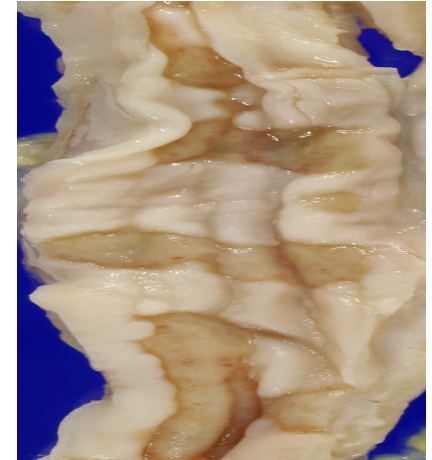
Acute necrotizing tracheobronchitis

**Herpes Simplex infection
(virus cytopathic inclusions)**

Multiple ulcers in:

Trachea

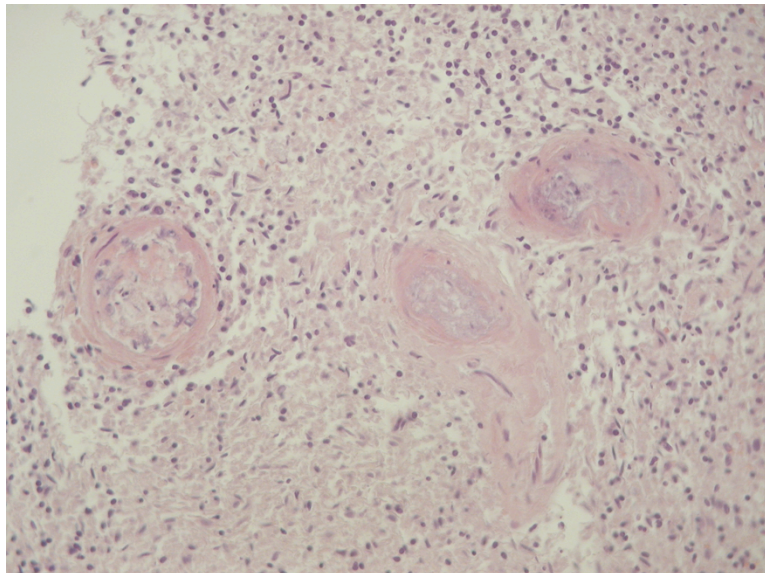
Esophagus



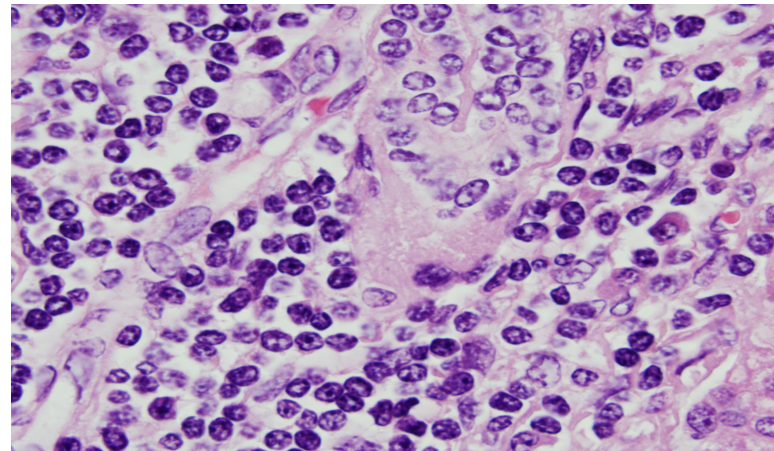
Spleen:



Small vasculitis with recent infarcts.



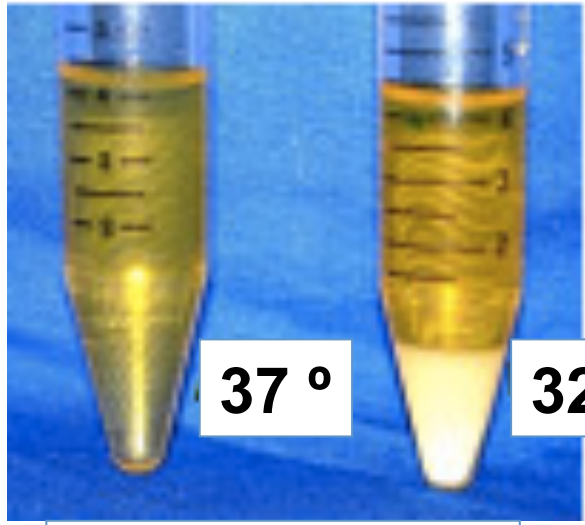
Lymphoproliferation B cells in marginal zone



Pathology

Final and Main diagnosis:

- Cryoglobulin mixed tipo II (Rheum. Factor +) associated to chronic C Virus hepatitis
- Spleen Lymphoma (type B, cryptic, marginal zone, associated to Virus C)
- Herpes simplex Pneumonia (with ulcers of Trachea and Esophagus)
- Multiorgan failure with severe ARDS



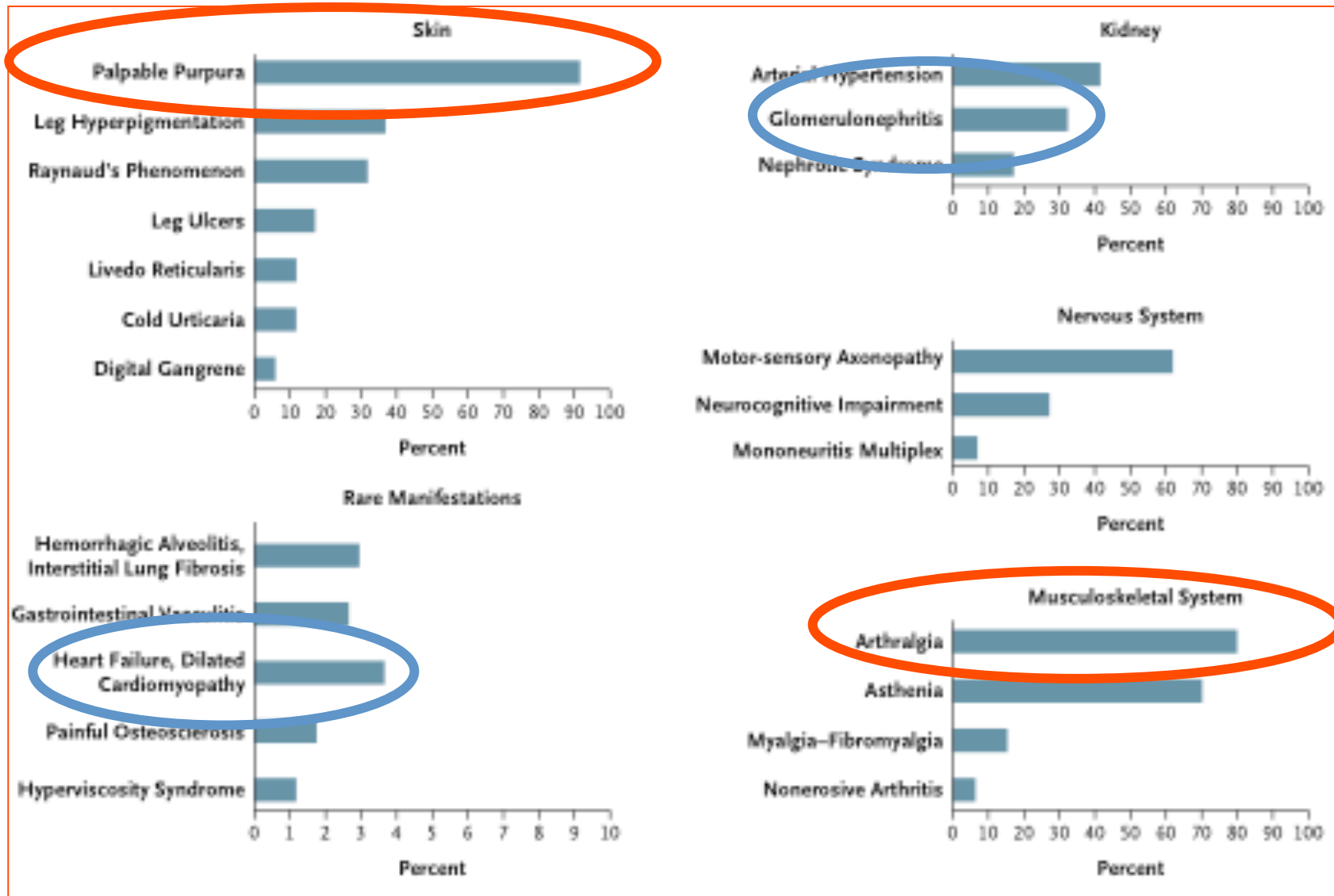
Cryoglobulins



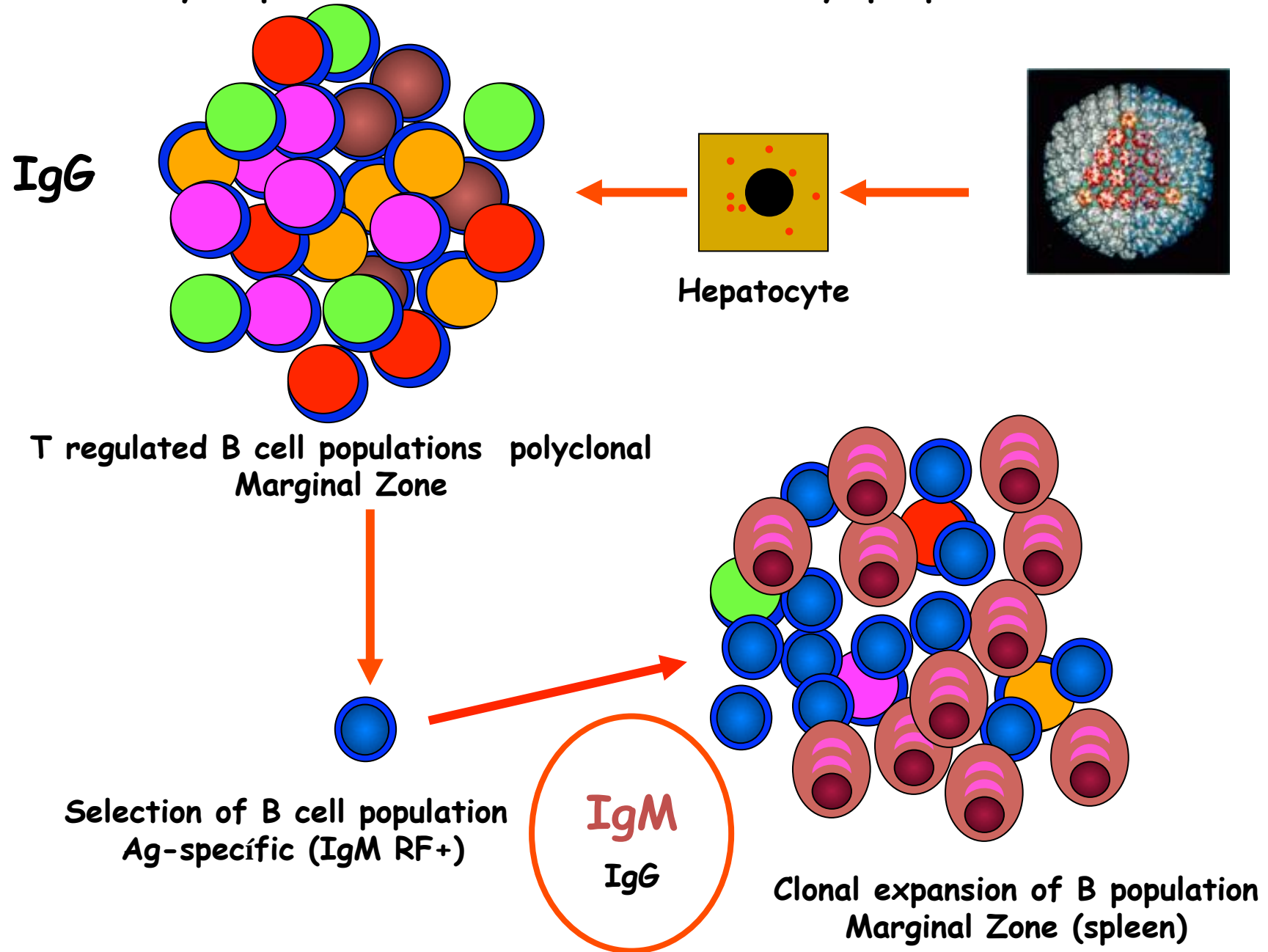
Clinical Manifestation of Cryoglobulinemic Vasculitis virus C Hepatitis related

- Skin lesions (**88%-100%**)
- Arthralgia (**50%-90%**),
- Weakness (67%-100%),
- Liver alterations (62%-88%),
- Renal failure (8%-54%)
- Neurological (peripheral nerve: 30%).

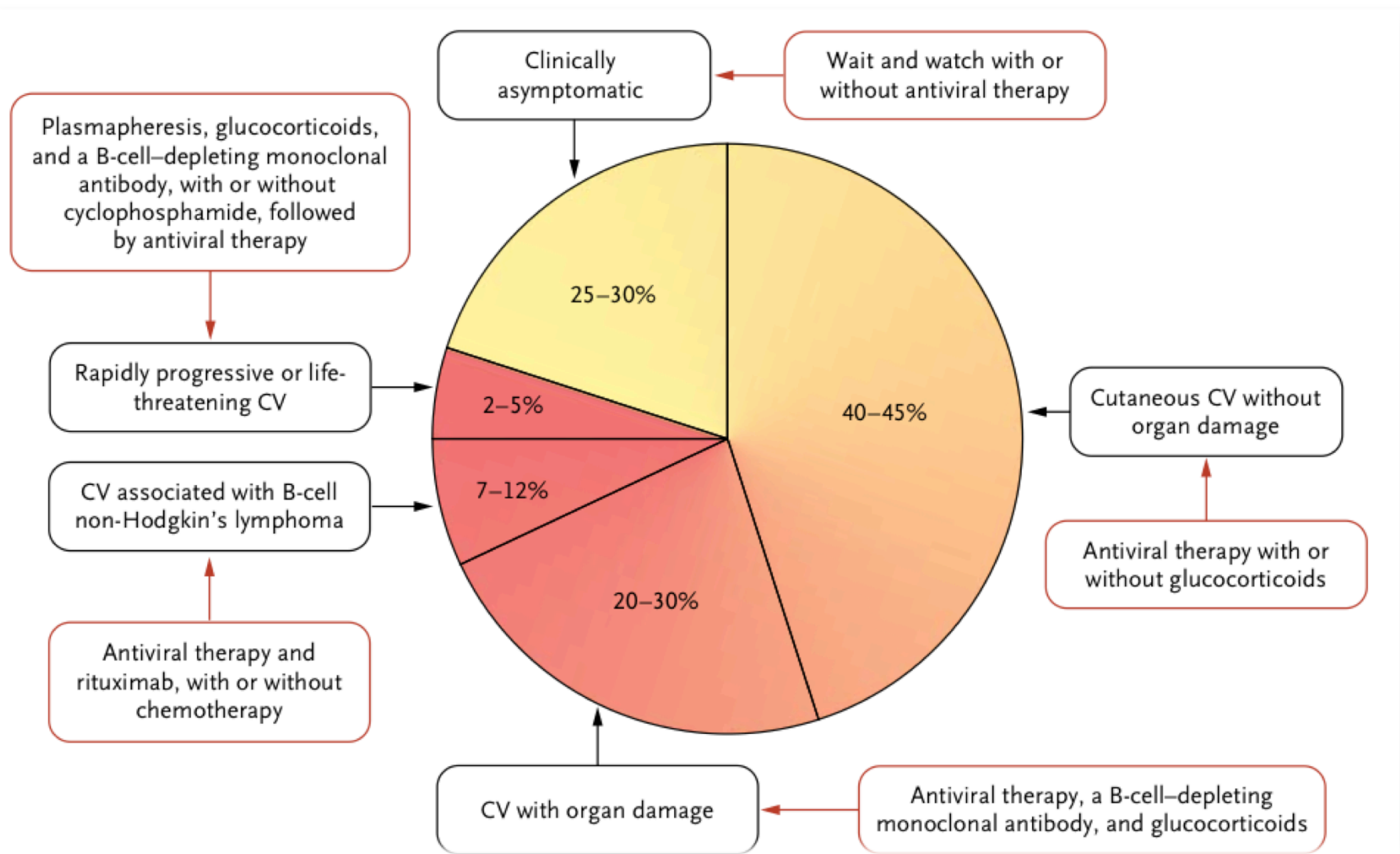
Clinical Manifestation of Cryoglobulinemic Vasculitis virus C Hepatitis related



¿Why Hepatitis C Virus could facilitate lymphoproliferation?



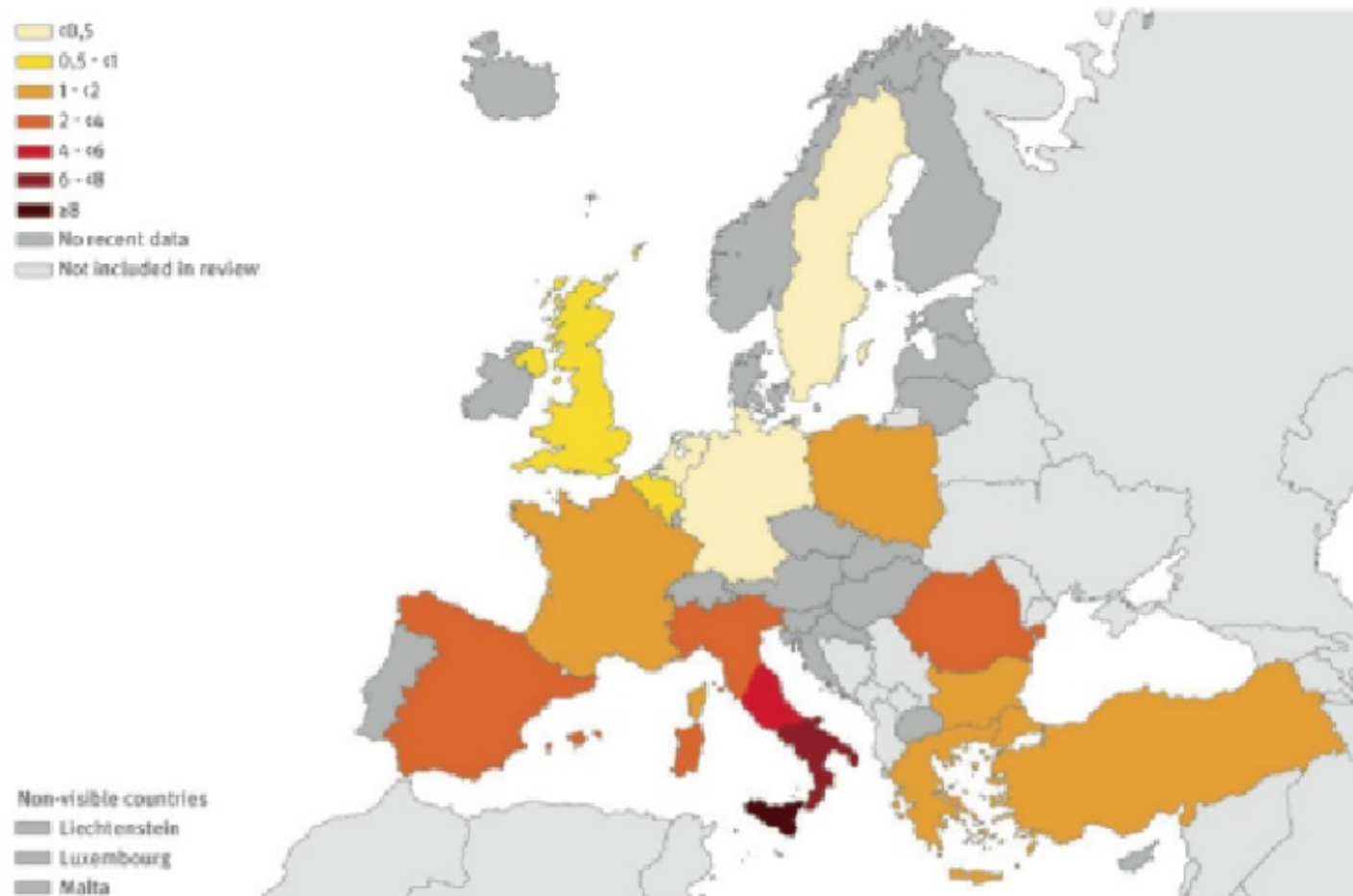
Proposed Therapeutic Algorithm for HCV-Related Cryoglobulinemic Vasculitis (CV)



Seven ideas to conclude...

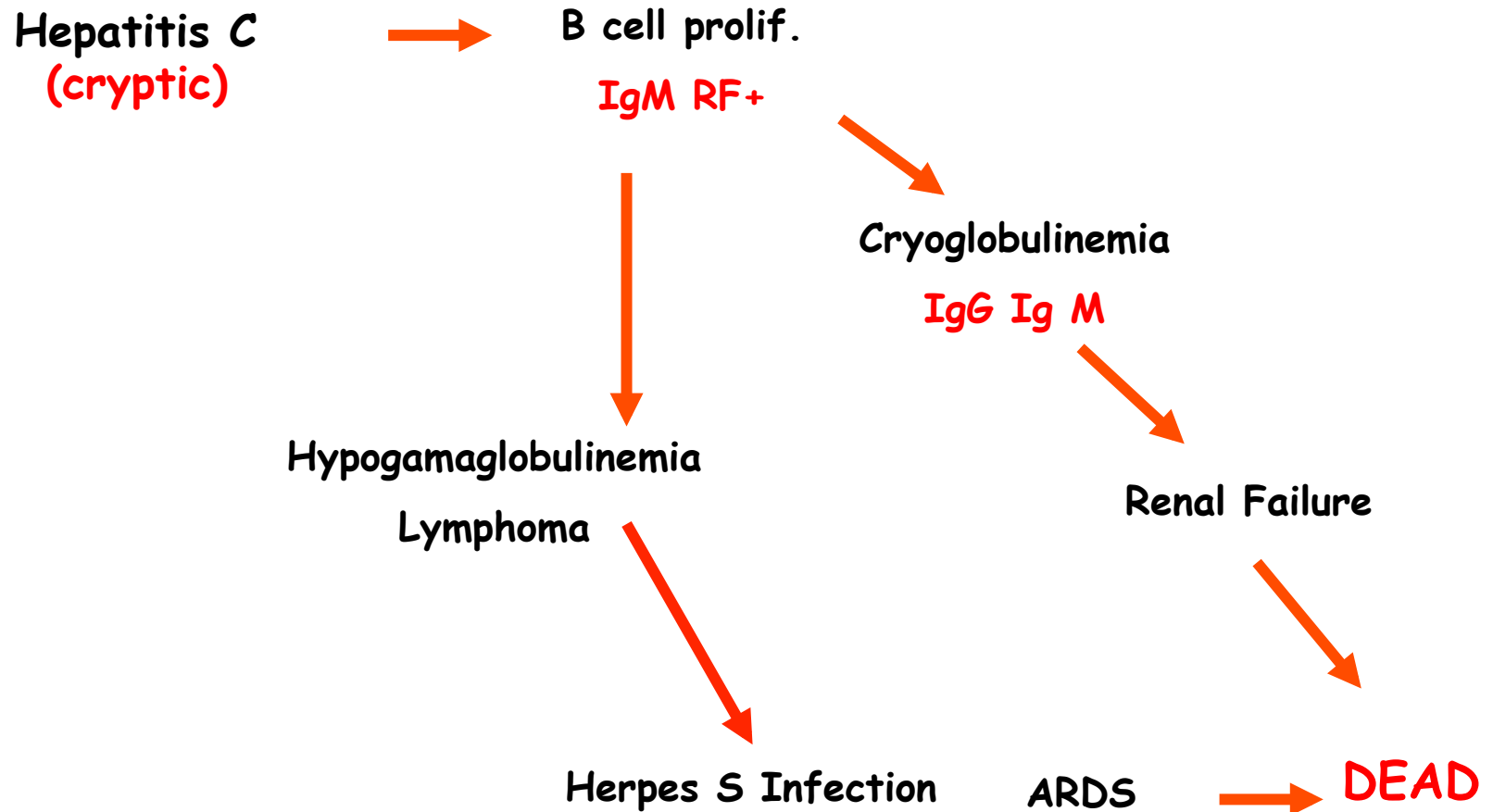
- 1.-Cryoglobulin (CG) consists of immunoglobulins (Ig) and complement components and precipitates upon refrigeration of serum. (mind transport!)**
- 2.-The majority of people with CG are asymptomatic.**
- 3.-In type II CG syndrome there is a mixture of polyclonal IgG in association with a monoclonal IgM, with Rheumatoid Factor activity.**
- 4.- Mixed CG is most often due to chronic HCV infection.**
- 5.- Some patients with CG may have little or no clinical evidence of active hepatitis at the time of presentation.**
- 6.- Most common manifestation are skin lesions (purpura), arthralgias, lymphadenopathy, hepatosplenomegaly and peripheral neuropathy.**
- 7.-Renal disease occurs in 20 to 60 percent of patients with CG type II (marker of higher mortality)**

European prevalence of hepatitis C infection



2010

A global view of our patient ("being an internist")





Thanks