

Organizado por:



Clínica
Universidad
de Navarra

PUESTA AL DÍA
HEMATOLOGÍA
EN 48H [LO QUE DEBES
CONOCER PARA TU
PRÁCTICA CLÍNICA]
X EDICIÓN



Diagnóstico y tratamiento de las anemias hemolíticas autoinmunes

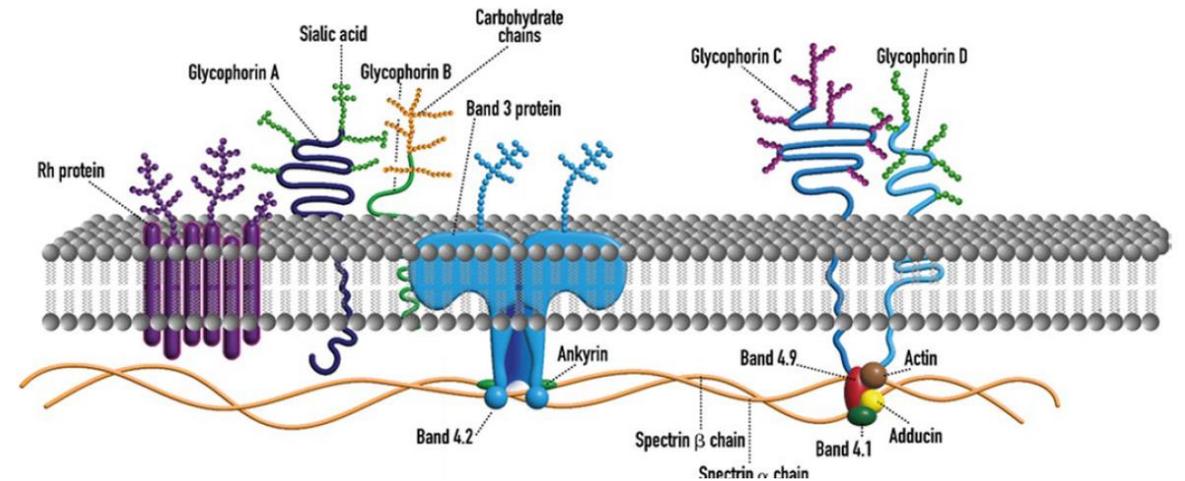
Pilar Solves Alcaina

Hospital Universitari i Politècnic La Fe, Valencia

AHAI

Características

- ✓ Hemólisis adquirida por autoanticuerpos anti-eritrocitarios
- ✓ Incidencia: 1-10:100000 personas y año
- ✓ Heterogeneidad clínica
- ✓ Primarias o secundarias
- ✓ Por autoAcs calientes o fríos y fármacos



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Diagnóstico

✓ Anemia (7-10 g/dl) hemolítica (**LDH y haptoglobina**)



✓ Prueba de la antiglobulina directa positiva (CD)



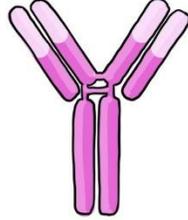
✓ Exclusión de otras causas (hemólisis post-transfusión)

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Clasificación

WARM
AUTOIMMUNE
HEMOLYTIC
ANEMIA

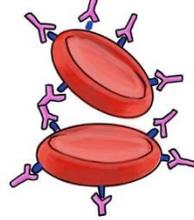
IgG ANTIBODY:



OPTIMAL TEMPERATURE
FOR REACTIVITY:

37°C

IgG REACTS AGAINST
PROTEIN ANTIGEN ON RED
BLOOD CELL SURFACE

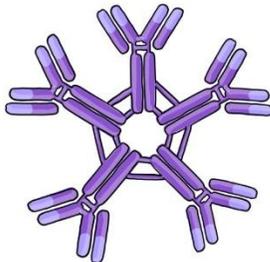


SPHEROCYTES



COLD
AGGLUTININ-
MEDIATED AUTO-
IMMUNE HEMOLYTIC
ANEMIA

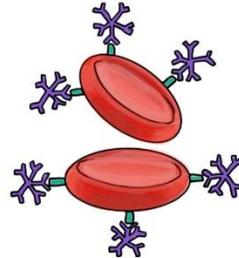
IgM ANTIBODY:



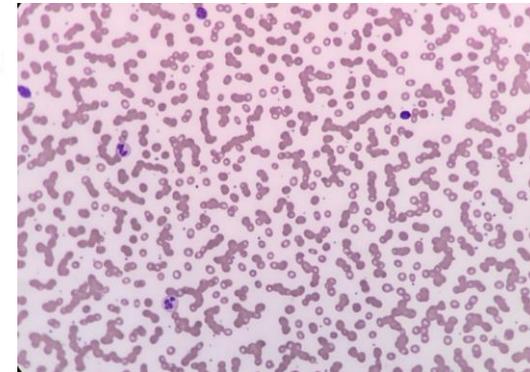
OPTIMAL TEMPERATURE
FOR REACTIVITY:

<30°C

IgM REACTS AGAINST
POLYSACCHARIDE ANTIGEN

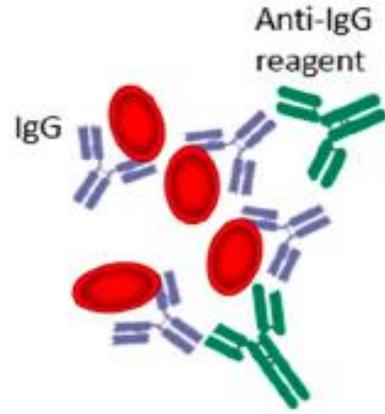


RED CELL AGGLUTINATES



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Fisiopatología

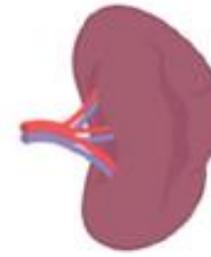


IgG auto Abs weakly activate complement, do not agglutinate spontaneously

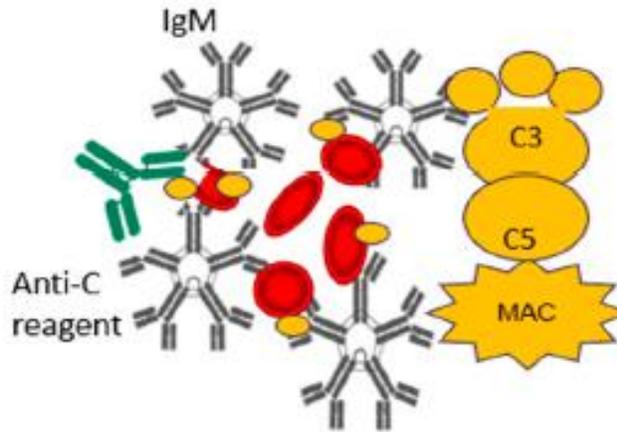
Agglutination occurs with anti-IgG reagent



DAT + IgG



extravascular hemolysis by phagocytosis of IgG-opsionized RBC in the spleen (wAIHA)

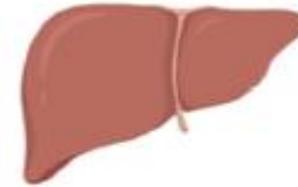


IgM auto Abs agglutinate RBC and strongly activate complement, Spontaneously agglutinate RBC



DAT + C

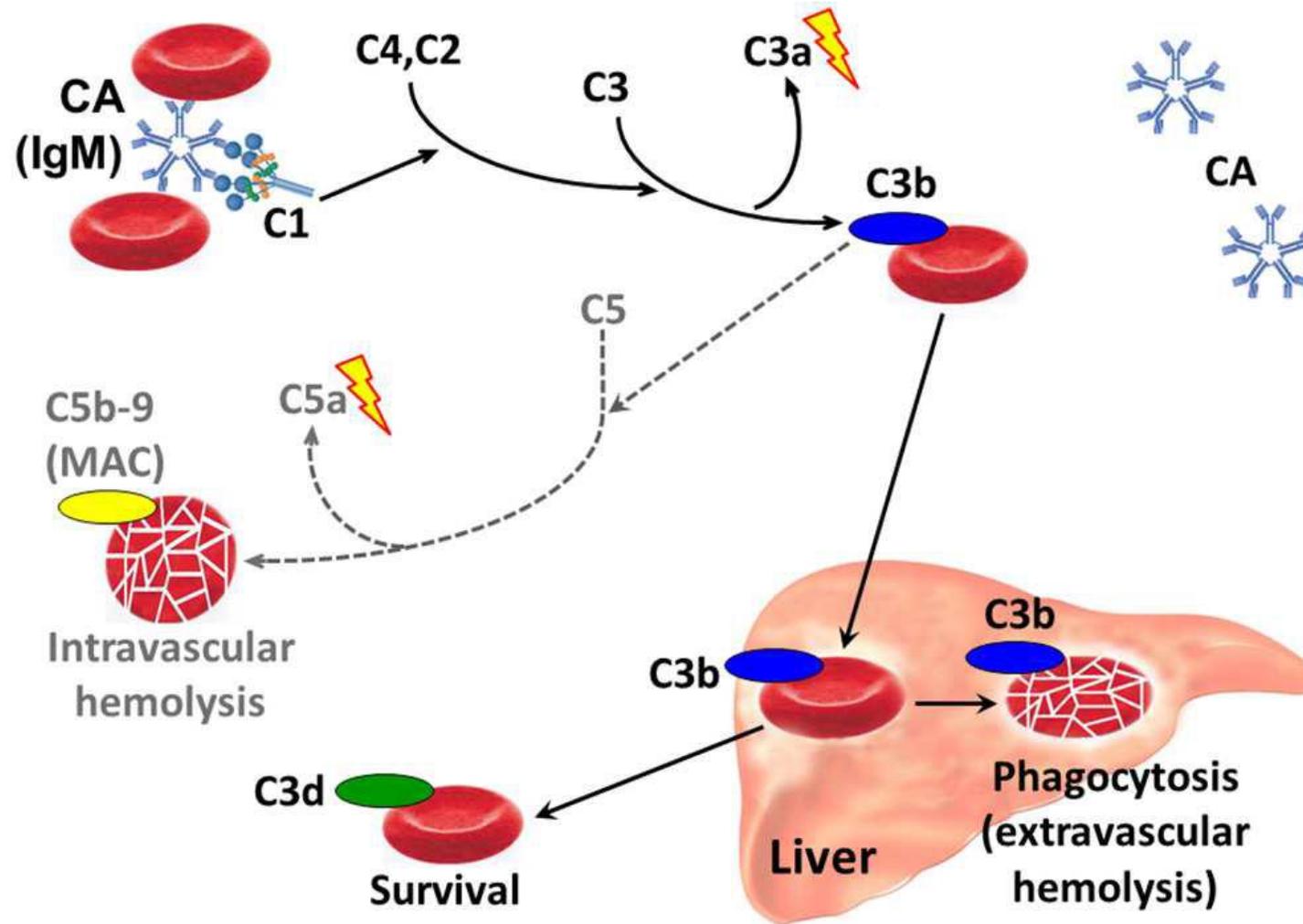
intravascular hemolysis by membrane attack complex (MAC)



extravascular hemolysis by phagocytosis of C3b-opsionized RBC in the liver (CAD)

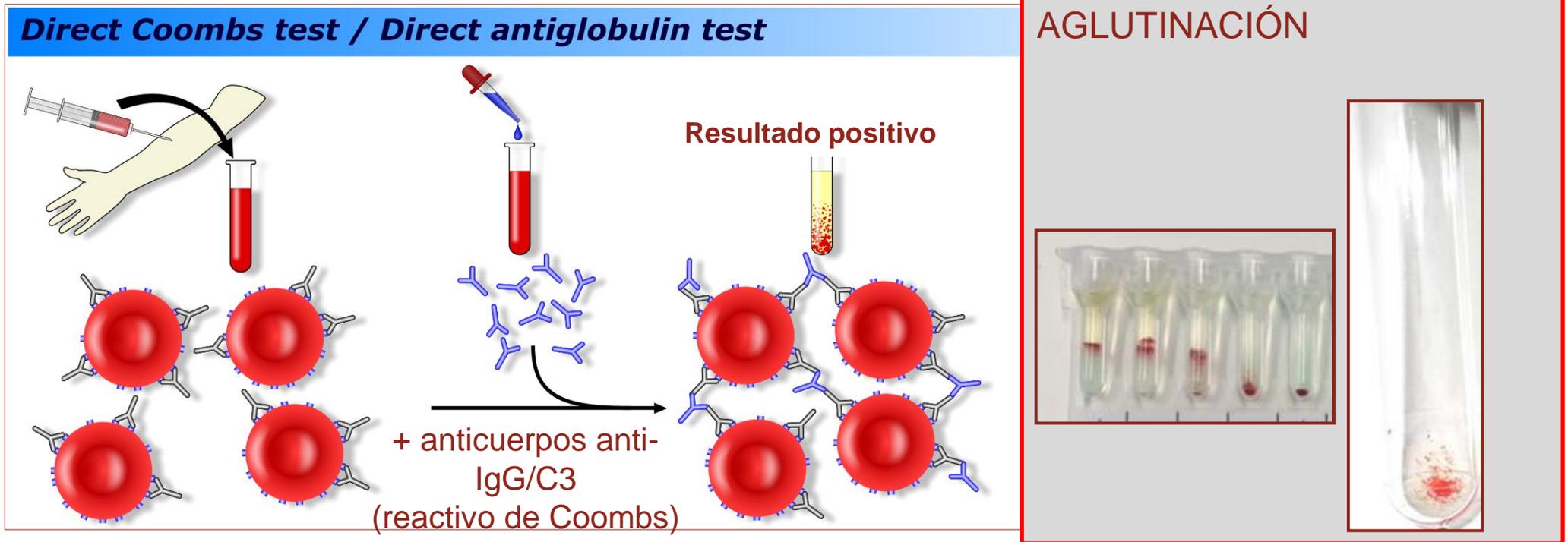
AHAI Acs fríos

Fisiopatología



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Prueba de la antiglobulina directa (Coombs directo)

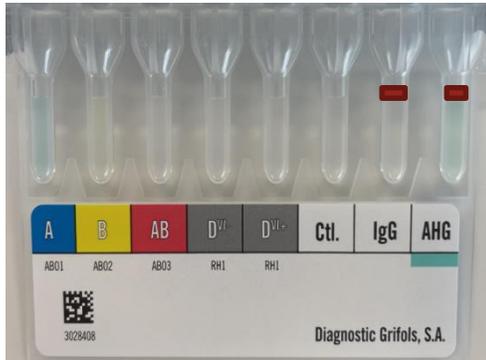


Anticuerpos unidos a los hematíes *in vivo*

El CD detecta hematíes sensibilizados a IgG y/o complemento *in vivo*

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Prueba de la antiglobulina directa poliespecífica y mono-específica



AutoAc caliente



AutoAc frío

DAT and eluate results	Conclusions
C3 only	Immune complex, cold agglutinin disease, cold agglutinin syndrome
IgG, negative eluate	Drug, absorbed IgG
IgG, eluate specific	Alloimmune
IgG, eluate binds all RBCs	wAIHA, drug
IgG, +/- C3, eluate binds all RBCs	wAIHA

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Diagnóstico serológico

Características	AHAI Ac calientes	AHAI Ac fríos	HPF
T^a de reacción (rango)	37°C (0-40)	4°C (4-34)	Reacciona a 4°C y hemoliza a 37°C
Tipo de Ig	IgG	IgM	IgG
PAD	IgG (raro) IgG + C3d (67%)	C3	C3
Eluído	Panaglutinina	No reactivo	No reactivo
Especificidad auto-anticuerpo	Anti-Rh	Anti-I	Anti-P
Hemólisis in vivo	Extravasacular	Intravasacular/extravasacular	Intravasacular

AHAI Ac fríos (15-20 %)

CAD

CAS

HPF

- CD C3d
- Críoaglutinina ≥ 64 a 4°C

- CD C3d
- Donath-Landsteiner

Linfoproliferativo B monoclonal en sangre y/o médula sin evidencia clínica ni radiológica de malignidad

Asociado a otra enfermedad: infecciosa, autoimmune, linfoma
evidencia clínica y radiológica de malignidad

Niños, asociado a infecciones víricas

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Estudio de las crioaglutininas

- ✓ **Prueba de crioaglutininas:** Demostrar la presencia del autoanticuerpo frío en plasma/suero (4°C)
 - ✓ Título, amplitud térmica, especificidad
- ✓ **Prueba de Donath-Landsteiner (HPF):** Demostrar la presencia de la hemolisina bifásica

El estudio de crioaglutininas debe realizarse en muestra extraída y mantenida a 37°C

Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting

- Cold agglutinin disease (CAD) AIHA, a monospecific DAT strongly positive for C3d (and negative or weakly positive with IgG) and a cold agglutinin (CA) titer of 64 or greater at 4°C. We recognize that there may be occasional cases with CA titer < 64. Patients may have a B-cell clonal lymphoproliferative disorder detectable in blood or marrow but no clinical or radiological evidence of malignancy.
- Cold agglutinin syndrome (CAS) AIHA, a monospecific DAT strongly positive for C3d (and negative or weakly positive with IgG) and a CA titer of 64 or greater at 4°C. Patients have an associated condition, for example infection, autoimmune disorder, overt evidence of a B-cell lymphoma (clinical or radiological), or other malignancy.

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Autoanticuerpos calientes

Review

Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting

Warm AIHA (wAIHA)

wAIHA is diagnosed in patients lacking cold associated symptoms with a DAT positive for IgG, IgA (rarely), or C3d \pm IgG when a clinically significant cold reactive antibody has been excluded.

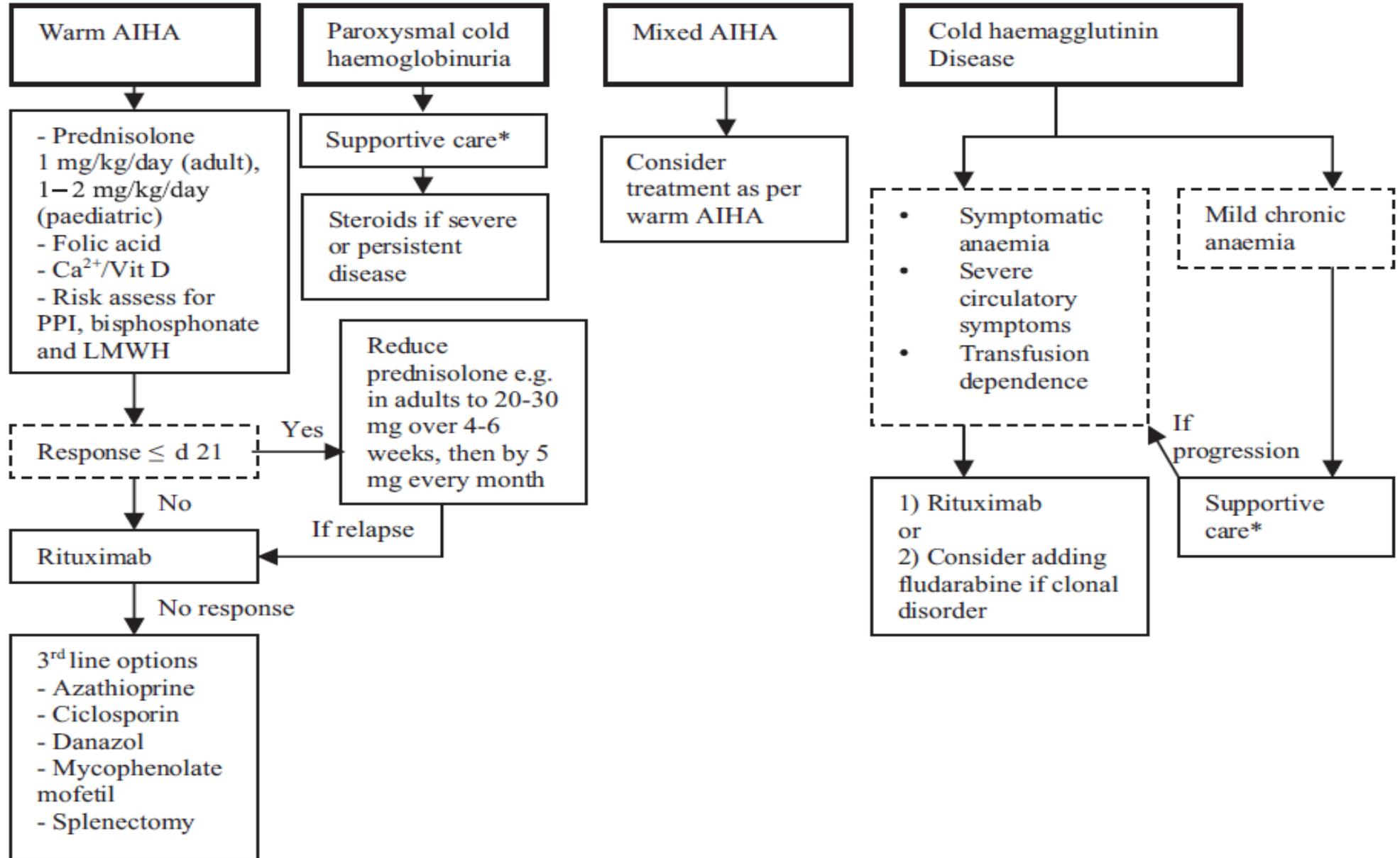
Table 4

Recommendations for the diagnosis of secondary wAIHA in adults.

Disease or condition	Tests to be performed in every patient
SLE and other autoimmune diseases	. Antinuclear Abs (ANA) and if + with titer > 1/80 : anti-dsDNA Abs and other specificities
Lymphoma and solid tumors	. Serum protein electrophoresis . Immunoelectrophoresis . Immunophenotyping of B-lymphocytes from peripheral blood . ^a CT scan (chest/abdomen/pelvis)
Primary immunodeficiency	. IgG, IgA and IgM levels
Infections	. HIV, HCV and (HBV) ^b tests

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Tratamiento



AHAI Acs calientes

Tratamiento

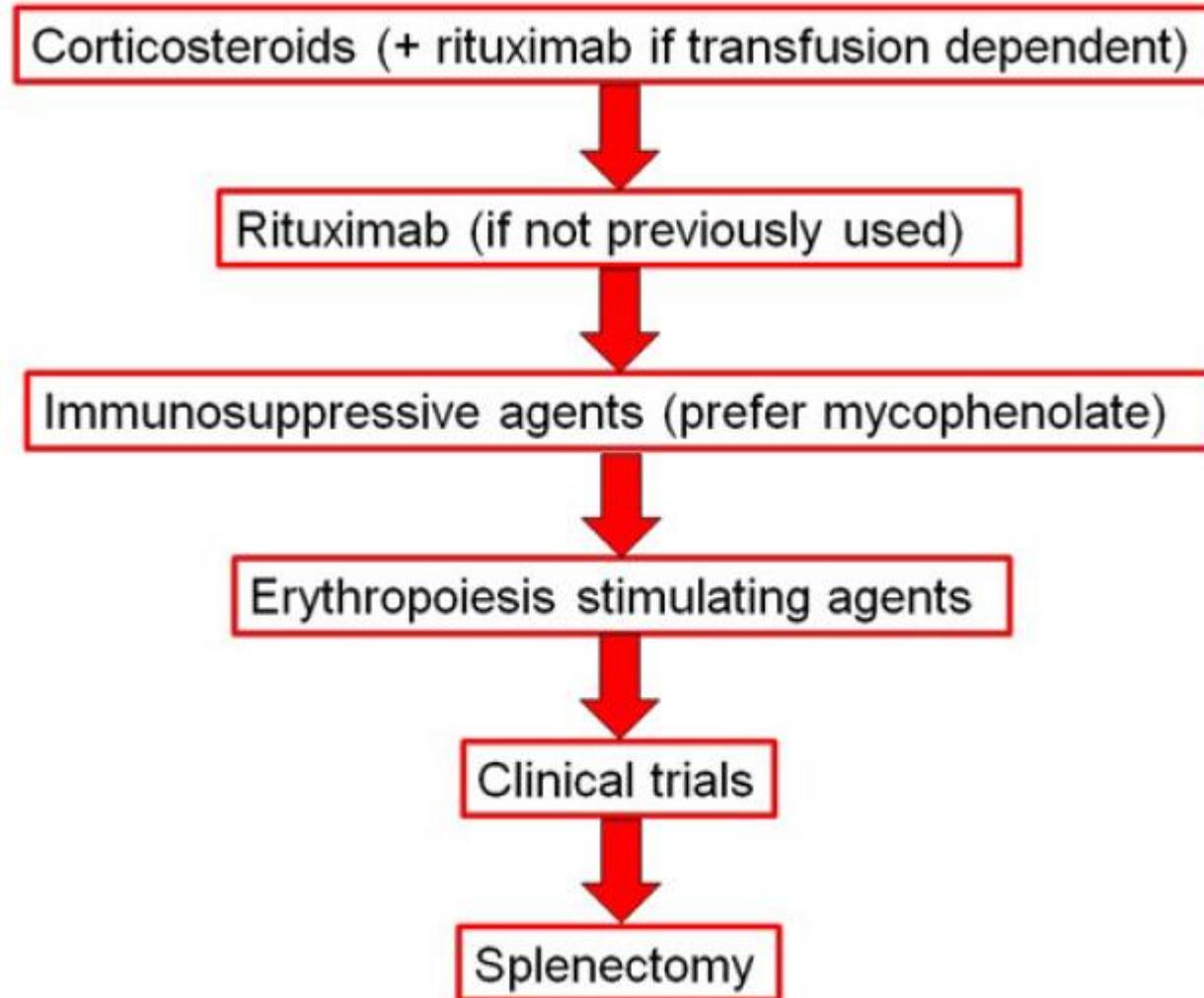
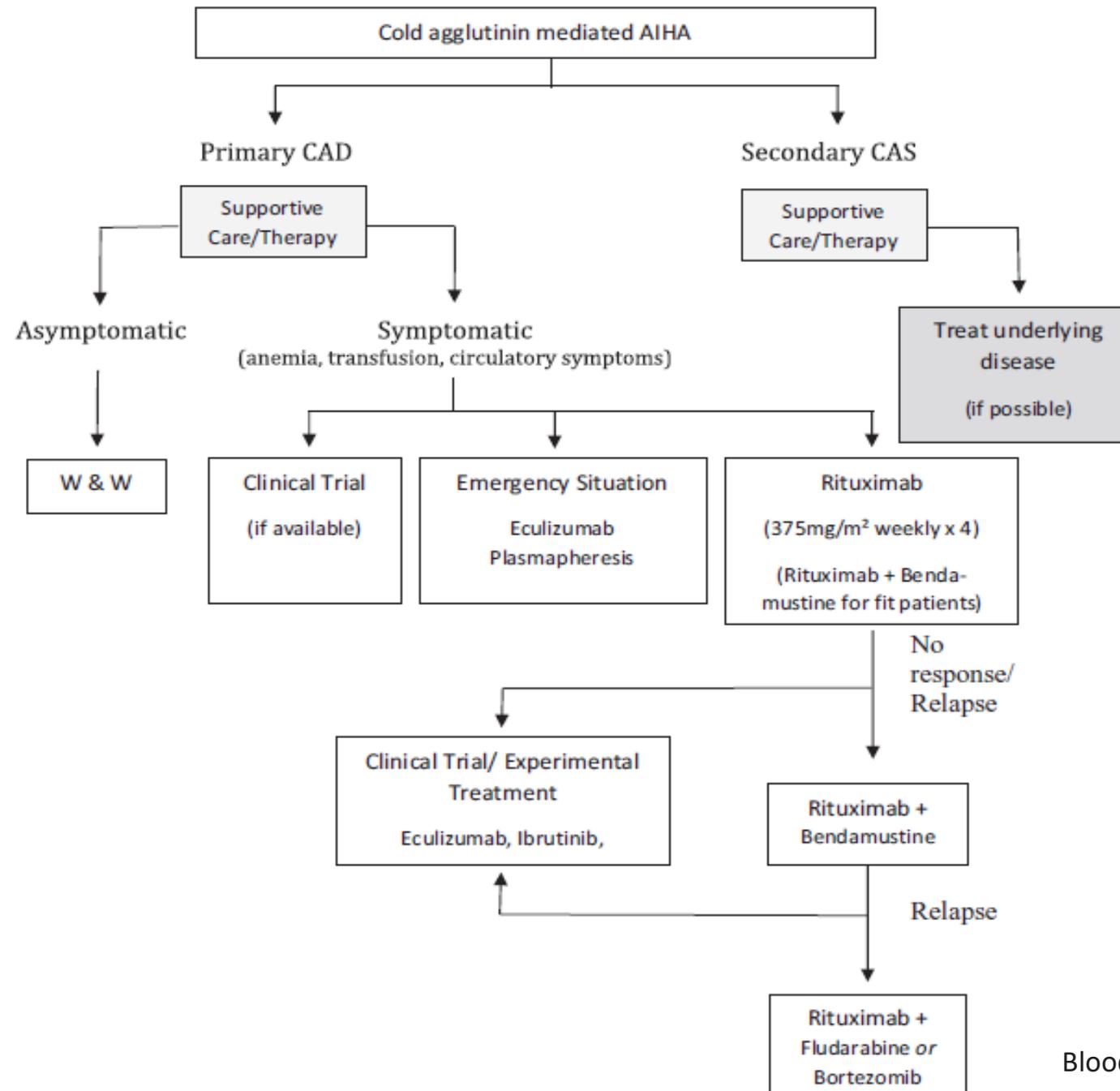


Figure 4. Proposed treatment algorithm for wAIHA.

AHAI Acs fríos

Tratamiento



- ✓ Ácido fólico/vitamina B12/Hierro
- ✓ Profilaxis antitrombótica
- ✓ Bifosfonatos/calcio
- ✓ EPO
- ✓ Profilaxis pneumocistis
- ✓ Inhibidores de la bomba de protones

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Tratamiento de la AHAI

Acs calientes severa

Acute and very severe onset

- Hb < 6 g/dL and/or hemodynamic instability

- methylprednisolone 100-200 mg/day for 7-10 days or 250 to 1000 mg/day for 1-3 days, then follow the oral schedule of predniso(lo)ne (right panel)
- Transfusion 1 blood unit/day, monitor post transfusion Hb and hemolysis
- IvIg 0.4 g/kg/d x 5 d, particularly if infection is present
- early rituximab 375 mg/kg/wk for 4 wk in case of no response in 1 wk
- Consider PEX in case of no response in 7-10 days
- Test endogenous EPO if reticulocytopenia
- LMWH prophylaxis if no contraindications

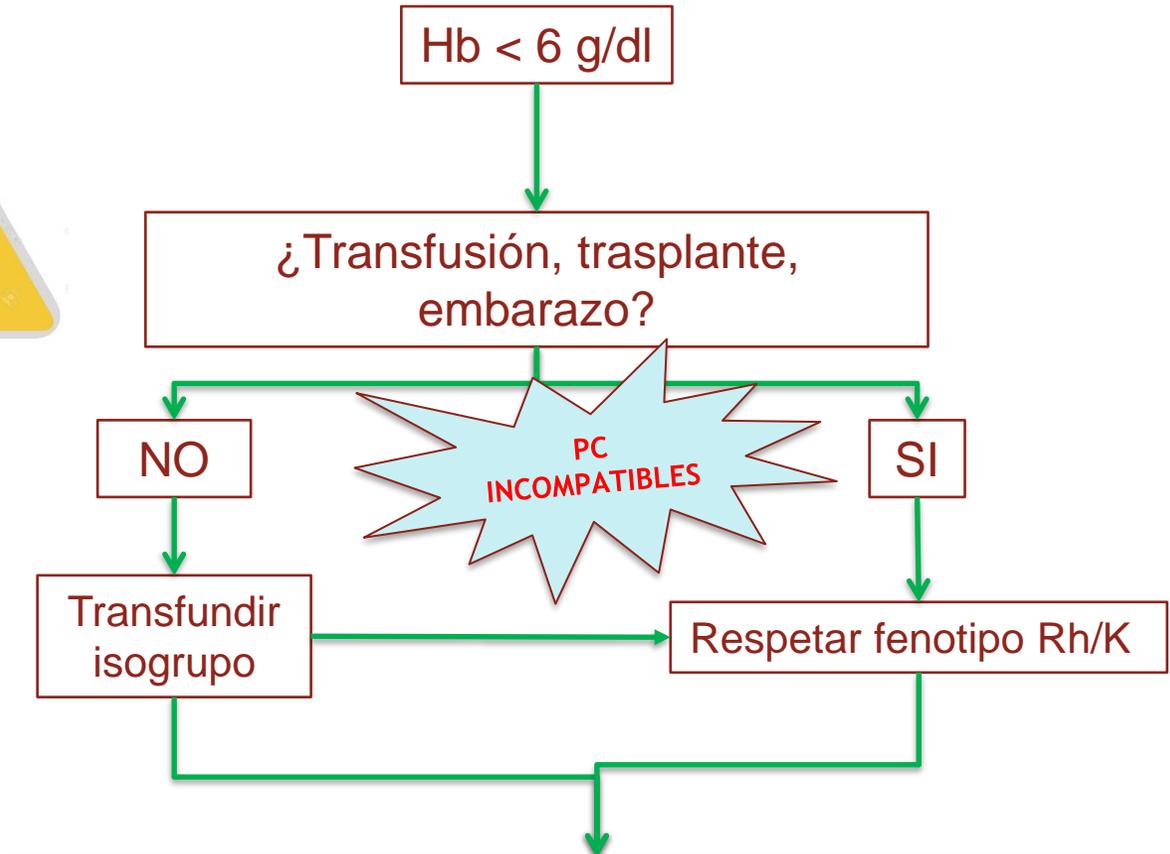
RBC transfusions

In medically unstable, symptomatic patients, particularly those with Hgb levels lower than 6g/dL, RBC transfusion is indicated. Appropriately crossmatched blood may not be immediately available because of the panagglutinin, and therefore type-specific blood is used. In general, worsening of hemolysis is more likely to occur with alloimmune antibodies than with autoantibodies.



AHAI

Transfusión



- Transfundir 20 ml, esperar 5-10 minutos, continuar
- Transfundir en bomba de perfusión durante 4 horas
- Utilizar calentador en AHAI por Ac fríos



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A destacar

- El diagnóstico inmunohematológico es crucial
- Es una enfermedad crónica, con recaídas frecuentes
- La transfusión es segura

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ACTUALÍZATE



48 HORAS

Muchas gracias por vuestra atención

