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Overview of Temperature-Sensitive Acquired Autoimmune Hemolytic Anemia (TS-AIHA)

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Temperature-Sensitive Acquired Autoimmune Hemolytic Anemias

- **Patients with temperature-sensitive acquired autoimmune hemolytic anemias (TS-AIHA) are currently coded under D59.1 Other autoimmune hemolytic anemia**

- **The diagnosis, disease course and treatment approach for the three types of TS-AIHA have significant differences**

- **ICD-10-CM codes for each type will enable *better identification of the type of TS-AIHA at diagnosis leading to improved patient management including new treatments in development, and facilitate tracking of the morbidity, mortality, and health outcomes of the different diseases***

- **The American Society of Hematology supports the creation of new codes under D59.1 to further define the three types of TS-AIHA, and the proposed coding changes for TS-AIHA align with the ICD-11 beta code set being developed by the World Heath Organization (WHO)**

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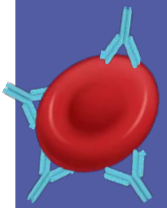
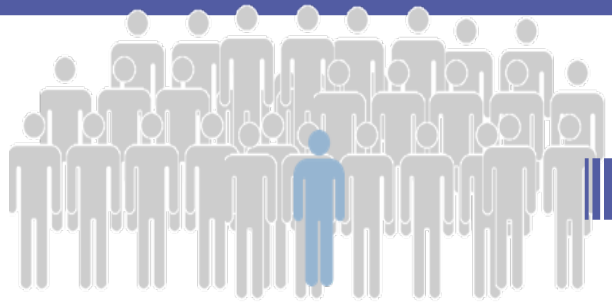
ICD-10-CM, International Classification of Disease, Tenth Revision, Clinical Modification.

TS-AIHA: Disease Overview



Patients' own antibodies destroy red blood cells and induce anemia based on a *triggering temperature*

Prevalence of TS-AIHA: 17 cases per 100,000[2]



~56,000 cases in the US

AIHA can be:

- Warm-type
- Cold-type (CAD)
- Mixed-type

based on the type of autoantibody mediating the hemolysis[7]

Serious consequences: Acute crisis with life-threatening anemia and transfusion need, thrombosis, myocardial infarction, stroke, poor quality of life

1. Go RS, et al. Blood. 2017;129(22):2971-2979
2. Bass GF, et al. Autoimmun Rev. 2014;13(4-5):560-564.

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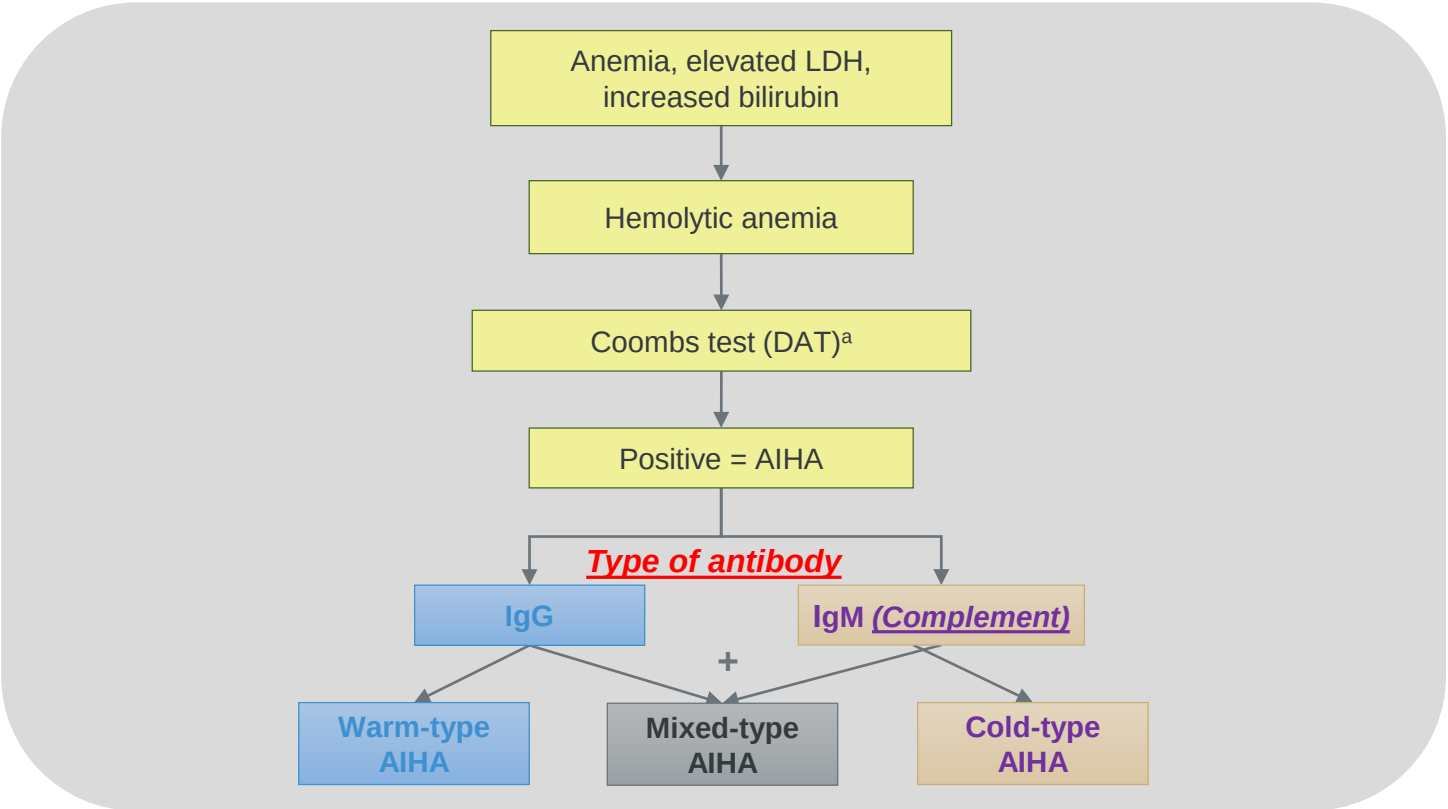
Diagnostic Algorithm for TS-AIHA



AIHA, autoimmune hemolytic anemia; C3d, complement 3d; DAT, direct antiglobulin test; Ig, immunoglobulin; LDH, lactate dehydrogenase.
[a]In patients with suspected cold agglutinin disease, specimen should be kept at 37°C until serum has been separated.

1. Hill QA, et al. *Br J Haematol*. 2017;176(3):395-411.

Characteristics of TS-AIHA Subtypes

	Warm-type AIHA[1–5]	Cold-type AIHA (Cold Agglutinin Disease)[4]	Mixed-type AIHA[1–4]
Percentage of AIHA cases	65%–75%	15%–25%	5%
Autoantibodies present	IgG	IgM (cold agglutinins)	IgG and IgM
Temperature for red blood cell destruction	37°C	As low as 4°C	4°C–37°C
Patient population	Children and adults	Middle-aged to elderly	Primarily adults, incidence rises with age

AIHA, autoimmune hemolytic anemia; C3, complement 3; DAT, direct antiglobulin test; Ig, immunoglobulin; RBC, red blood cell.

1. Hill QA, et al. *Br J Haematol*. 2017;176(3):395-411. 2. Guidice V, et al. *Open Med (Wars)*. 2016;11(1):374-380. 3. Bass GF, et al. *Autoimmun Rev*. 2014;13(4-5):560-564. 4. Berentsen S. *Br J Haematol*. 2018;181(3):320-330. 5. Mickel M. *Presse Med*. 2014;43(4 Pt 2):e97-e104.

Characteristics of TS-AIHA Subtypes

	Warm-type AIHA	Cold-type AIHA	Mixed-type AIHA
Anemia symptoms[1]	Yes	Yes	Yes
Circulatory symptoms	None	70-90% of patients[2,3] Cold-induced Debilitating pain Discoloration of hands and feet	None
Disease onset	Acute presentation and more rapid resolution[4]	Insidious onset and chronic (life-long) [2]	Acute presentation[4]
Risk of thromboembolism	15%–20% in 2 case series[5]	31% in claims-database analysis	Data not available
Mortality/survival	8%–16% mortality [7,8]	61% survival probability vs 82% in general population (first 5 years after diagnosis)[9]	Data not available

AIHA, autoimmune hemolytic anemia; KM, Kaplan-Meier.

1. Hill QA, et al. *Br J Haematol*. 2017;176(3):395-411. 2. Swiecicki PL, et al. *Blood*. 2013;122(7):1114-1121. 3. Berentsen S. *Br J Haematol*. 2018;181(3):320-330. 4. Barcellini W, et al. *Disease Markers*. 2015;2015:635670. 5. Lecouffe-Desprets M, et al. *Autoimmun Rev.* 2015;14(11):1023-1028. 6. Broome C, et al. *Blood*. 2017;130(Suppl 1):928. 7. Roumier M, et al. *Am J Hematol*. 2014;89(9):E150-E155. 8. Rattarittamrong E, et al. *Hematology*. 2016;21(6):368-374. 9. Bylsma LC, et al. EHA 2018. Poster PS1131.

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Treatment Approach for TS-AIHA

Treatment	Warm-type AIHA[1–3]	Cold-type AIHA[1,4–6]	Mixed-type AIHA[1–3]
Lifestyle changes	No	Yes (eg, cold avoidance)	No
Transfusions	Yes	Yes In-line blood warmer required Blood samples should be warmed	Yes
Pharmacologic or surgical	Corticosteroids • 80% response	Corticosteroids not indicated	Corticosteroids with variable responses (may require addition of rituximab)
	Splenectomy • Response 50%–85%;	Splenectomy not indicated	Response unclear
	Rituximab • Refractory treatment only • Response: 79%–100% • Relapse: 14-25%	Rituximab • Upfront treatment • Response: 45%–58% • Relapse: 57%–89% Chemotherapy agents added as first or second line	Rituximab with variable responses (may require addition of steroids)

AIHA, autoimmune hemolytic anemia; CR, complete response; RR, response rate.

1. Hill QA, et al. *Br J Haematol*. 2017;176(3):395-411. 2. Go RS, et al. *Blood*. 2017;129(22):2971-2979. 3. Guidice V, et al. *Open Med (Wars)*. 2016;11(1):374-380. 4 Swiecicki PL, et al. *Blood*. 2013;122(7):1114-1121. 5. Berentsen S. *Br J Haematol.* 2018;181(3):320-330. 6. Mullins M et al. *Blood Adv.*2017;1(13):839-848.

TS-AIHA: Conclusions

Given the significant differences among these three conditions, new ICD-10 CM codes by type of TS-AIHA are warranted in order to:

- **Help providers tailor diagnosis and treatment including the use of new therapies in development to the specific type of TS-AIHA**
- **Document and track the significantly varied morbidity and mortality seen in patients with TS-AIHA**
- **Assist public health researchers in contrasting outcomes and impact on healthcare utilization among TS-AIHA types**

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AIHA, autoimmune hemolytic anemia; RBC, red blood cell.

1. Go RS, et al. *Blood*. 2017;129(22):2971-2979. 2. Hill QA, et al. *Br J Haematol*. 2017;176(3):395-411.