Cold Agglutinin Disease (CAD) is a rare type of autoimmune hemolytic anemia.

Cold Agglutinin Disease is about more than avoiding the cold.

Is chronic hemolysis putting your patients at risk?
CAD is a rare, autoimmune, hemolytic condition with potentially serious acute and chronic consequences that are driven by C1 activation of the classical complement pathway. 

≈20% of all autoimmune hemolytic anemias are CAD
Up to 16 per 1,000,000 people are impacted by CAD
60 yrs
Average age of onset is approximately 60 years, but CAD has been seen in some patients as young as 30 years

Unlike Cold Agglutinin Syndrome (CAS), CAD is not secondary to cancer or an acute infection

Recognizing the signs and symptoms

For patients, CAD is not just a benign condition

Patients may be at risk for more than just anemia

72% of patients had at least 1 severe anemia event within the first year of follow-up
67% of patients had a severe anemia event within first 6 months of pharmacotherapy

Data from a retrospective review of a healthcare system database in patients with CAD (n=29) who were included based on hemoglobin readings and follow-up times.

Twelve of 18 patients with at least 6 months of follow-up after their initial therapy.

CAD=Cold Agglutinin Disease.
UNDERSTAND THE MECHANISM AND DIAGNOSIS OF COLD AGGLUTININ DISEASE

Continued C1 activation of the classical complement pathway leaves patients in a constant hemolytic state

C1 drives chronic hemolysis through the classical complement pathway

Activated C1 triggers the classical complement pathway leading to potentially serious chronic hemolysis

Confirming a CAD diagnosis

If CAD is suspected, the test procedure requires the blood sample be kept at 37°C to 38°C from the time it is drawn until it is tested to avoid potential false-negatives. Refrigeration must be avoided. The final diagnosis of CAD or mixed AIHA is based on the overall clinical picture, including supporting serological findings.

THREE main criteria must be met:

1. Positive Coombs test results (direct antibody test) for C3d
2. Presence of cold agglutinin titer >1:64
3. Evidence of hemolysis

AIHA=autoimmune hemolytic anemia; IgM=immunoglobulin M; RBC=red blood cell.
Severe anemia may not be the only predictor of risk—markers of hemolysis may be signs of thromboembolic risk

In the patients who had a TE and available laboratory results:

- 90% had evidence of active hemolysis†
- 23% had severe anemia (defined as hemoglobin ≤8 g/dL)

Study limitations

- Analyses were conducted using claims-based data, and the codes used may be subject to coding errors
- The Optum database only covers commercially insured patients
- Incidence of all TEs may be underestimated due to inability to account for multiple TEs occurring within each type
- Identifying CAD patients by linkage of claims data with electronic health records in the Optum database allowed for a more precise identification using clinical notes in comparison to using claims data alone, as the ICD-9 code for CAD also includes warm AIHAs

Additional studies are needed to further understand the risks associated with CAD

ICD=International Classification of Diseases; LDH=lactate dehydrogenase; TE=thromboembolic event.

*There were up to 10 matches for each patient with CAD based on sex, ethnicity, region of residence, follow-up time, age, and entry date.

†Elevated bilirubin and LDH.
COLD AGGLUTININ DISEASE IS ASSOCIATED WITH SIGNIFICANTLY INCREASED MORTALITY

In a retrospective claims-database study of US patients with CAD (n=651) vs a matched cohort (n=3255), there was a significant increase in mortality seen as early as year 1 after diagnosis.

Thromboembolic events may contribute to increased mortality in CAD

48% increased mortality in patients who experienced ≥1 thromboembolic event

- The mortality rate of patients with ≥1 TE was 23,683 (n=228) in the CAD cohort vs 15,913 (n=641) in the matched cohort during the study (rates per 100,000 patients; P<0.001).

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Denmark data show mortality risk beyond the US

In a population-based study comparing patients with CAD (n=72) vs a matched general population cohort (n=720),* there was increased mortality seen as early as year 1 after diagnosis.

EMR=electronic medical record.
*Sponsored by Bioverativ Therapeutics Inc., a Sanofi company.
PATIENTS WITH COLD AGGLUTININ DISEASE ARE AT RISK, CHRONIC HEMOLYSIS CAN HAVE SEVERE CONSEQUENCES

In CAD:

- Activated C1 triggers complement-mediated hemolysis
- Retrospective studies have shown there may be an association of increased thromboembolic events and early mortality
- Chronic anemia and other signs and symptoms should be fully evaluated
- There are currently no FDA-approved treatments

Support for your patients with CAD

Patients with CAD need support and we’re here to help. The card below contains useful patient support information and a destination for them to get CAD-focused education.

WE'RE COMMITTED TO HELPING PATIENTS WITH COLD AGGLUTININ DISEASE.

Uncover the facts about Cold Agglutinin Disease at CADUnraveled.com

Or, call to learn more:

In the US:

1-833-CAD-CHAT
(1-833-223-2428)
Monday to Friday 8 AM to 8 PM ET

REFERENCES:

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