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ACQUIRED HEMOPHILIA A: CURRENT CONCEPTS IN EPIDEMIOLOGY, PATHOGENESIS, DIAGNOSIS, AND MANAGEMENT IN THE EMICIZUMAB ERA

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ABSTRACT

Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder caused by neutralizing autoantibodies against factor VIII, most often affecting older adults without a prior bleeding history. This narrative review summarizes current knowledge on its epidemiology, pathogenesis, diagnosis, and management, with special attention to emicizumab. A selective PubMed/MEDLINE search of English-language literature published from 2005 to 2025 was performed, prioritizing international guidelines, reviews, registry studies, and clinically relevant cohort reports. AHA typically presents as a hematologic emergency with soft-tissue and mucosal bleeding, isolated prolongation of activated partial thromboplastin time, low factor VIII activity, and a detectable factor VIII inhibitor. Management requires two parallel goals: rapid bleeding control with bypassing agents or recombinant porcine factor VIII, and inhibitor eradication using individualized immunosuppressive therapy. Although remission rates of 70–80% are achievable, mortality remains significant because of both severe bleeding and treatment-related toxicity in elderly, multimorbid patients. Emerging evidence suggests that emicizumab may reduce bleeding burden, limit exposure to intensive bypass therapy, and support safer treatment strategies in selected cases. Earlier recognition, standardized diagnostic pathways, and careful integration of emicizumab may improve outcomes in AHA.

KEYWORDS

Acquired Hemophilia A, Factor VIII Inhibitor, Autoimmune Bleeding Disorder, Emicizumab, Immunosuppression, Bypassing Agents

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Introduction

Acquired hemophilia A (AHA) is a rare but potentially life-threatening autoimmune bleeding disorder characterized by neutralizing autoantibodies against endogenous coagulation factor VIII (FVIII) (Franchini et al., 2005; Kruse-Jarres et al., 2017). In contrast to congenital hemophilia A, which is an inherited X-linked deficiency predominantly affecting males and typically presenting early in life, AHA affects both sexes and most commonly occurs in older adults without a prior history of bleeding, often in the setting of multimorbidity (Collins et al., 2007; Mingot-Castellano et al., 2017).

In AHA, spontaneous autoantibody formation produces an acquired defect in secondary hemostasis, frequently associated with aging, immune dysregulation, malignancy, autoimmune disease, pregnancy, or drug exposure, although approximately half of cases remain idiopathic (Franchini et al., 2005; Mingot-Castellano et al., 2022). The annual incidence is estimated at approximately 1 to 1.5 cases per million persons, but registry and population-based data suggest that the disease remains underdiagnosed and is often recognized late in the clinical course (Collins et al., 2007; Kruse-Jarres et al., 2017; Knoebl et al., 2012; Tian et al., 2023).

Clinically, patients present with sudden and often severe spontaneous or post-procedural bleeding, most commonly involving the skin, muscles, and mucosal surfaces rather than hemarthroses. Laboratory evaluation typically reveals isolated prolongation of activated partial thromboplastin time (aPTT), low FVIII activity, and a detectable FVIII inhibitor (Franchini et al., 2005; Mingot-Castellano et al., 2017; Huth-Kühne et al., 2009; Collins et al., 2010). Over the last two decades, improved awareness, laboratory algorithms, registry-based observations, and international recommendations have led to more standardized diagnostic and therapeutic pathways (Kruse-Jarres et al., 2017; Knoebl et al., 2012; Huth-Kühne et al., 2009).

Despite advances in hemostatic and immunosuppressive therapy, AHA remains associated with substantial morbidity and mortality driven by bleeding and treatment-related toxicity, particularly in elderly patients (Mingot-Castellano et al., 2022; Kruse-Jarres et al., 2017; Poston & Kruse-Jarres, 2022; Rungjirajittranon et al., 2024). Emicizumab, a bispecific FVIII-mimetic antibody, has emerged as a promising

option for bleeding control and may reduce exposure to intensive immunosuppression in selected cases, although evidence is still limited (Alcedo Andrade et al., 2024; Poston & Kruse-Jarres, 2023; Knoebl et al., 2021; Tiede et al., 2023; Pfrepper et al., 2024; Ghachem et al., 2024).

This narrative review summarizes current concepts in the epidemiology, pathogenesis, diagnosis, and management of AHA, with particular attention to the emerging role of emicizumab.

Methodology

This article is a narrative literature review of acquired hemophilia A structured around the major clinical domains relevant to internal medicine and hematology (Franchini et al., 2005; Kruse-Jarres et al., 2017). Literature was identified through targeted searches of PubMed/MEDLINE for English-language publications from January 1, 2005, to December 31, 2025.

Priority was given to international recommendations, review articles, registry studies, and clinically informative cohort reports (Mingot-Castellano et al., 2022; Kruse-Jarres et al., 2017; Knoebl et al., 2012; Tian et al., 2023; Huth-Kühne et al., 2009; Collins et al., 2010). Landmark studies published before 2005 were included selectively when they provided important mechanistic or historical context (Franchini et al., 2005; Collins et al., 2007). The search focused on five domains: epidemiology, pathogenesis, diagnostic approach, hemostatic management, and inhibitor eradication, with additional emphasis on recent publications addressing emicizumab (Alcedo Andrade et al., 2024; Poston & Kruse-Jarres, 2023; Knoebl et al., 2021; Tiede et al., 2023; Pfrepper et al., 2024; Ghachem et al., 2024).

Where multiple articles reported overlapping cohorts or registry data, the most comprehensive or recent publication was preferentially used (Knoebl et al., 2012; Tian et al., 2023; Rungjirajittranon et al., 2024). Because this is a narrative review, no formal risk-of-bias assessment, protocol registration, or statistical pooling was performed. Findings were synthesized qualitatively and organized thematically, with attention to concordance between guidelines and real-world data (Mingot-Castellano et al., 2022; Kruse-Jarres et al., 2017; Knoebl et al., 2012; Huth-Kühne et al., 2009; Ghachem et al., 2024; Iarossi & Hermans, 2024; Rungjirajittranon et al., 2024).

Ethical approval was not required for this article, as it is a narrative literature review based exclusively on previously published, publicly available sources and did not involve the collection of new primary data from human or animal subjects.

Results

Epidemiology and patient profile

Across population-based studies, registries, and large case series, acquired hemophilia A consistently appears as a rare but clinically important bleeding disorder. The largest prospective source of demographic data, the European Acquired Haemophilia Registry (EACH2), enrolled 501 patients (266 men, 235 women) from 117 centers in 13 European countries between 2003 and 2008, and remains the most comprehensive dataset assembled to date (Knoebl et al., 2012). In this cohort, the median age at diagnosis was 73.9 years, and the disease was idiopathic in 51.9% of cases, while malignancy (11.8%) and autoimmune disorders (11.6%) accounted for most of the remaining identifiable causes (Knoebl et al., 2012). Population-based surveillance corroborates these findings: a 2-year national study in the United Kingdom identified 172 unselected patients with a median age of 78 years and an annual incidence of 1.48 cases per million, with fewer than one in six patients younger than 65 years at diagnosis (Collins et al., 2007). More recently, a 15-year population-based review from Manitoba, Canada, identified 34 patients between 2006 and 2021, corresponding to an incidence of 1.78 cases per million per year, closely matching earlier European and British estimates (Tian et al., 2023). Together, these registries support the characterization of AHA as a disease of older adults, with reviews increasingly emphasizing it as a condition of the elderly population, in whom multimorbidity substantially complicates both diagnosis and treatment (Poston & Kruse-Jarres, 2022).

In contrast to congenital hemophilia A, which is X-linked and confined almost exclusively to males, AHA shows essentially no sex predilection outside the reproductive years: in the EACH2 registry, men and women were nearly equally represented, aside from a distinct subgroup of women who develop the disorder in the postpartum period (Knoebl et al., 2012; Collins et al., 2007). Etiologically, approximately half of all cases remain idiopathic despite thorough investigation, while the remainder are distributed across malignant, autoimmune, infectious, pregnancy-related, and drug-associated causes, a pattern repeatedly confirmed across independent cohorts and reviews (Franchini et al., 2005; Mingot-Castellano et al., 2017; Mingot-Castellano et al., 2022).

A recurrent and clinically important theme across the literature is delayed recognition. In the EACH2 registry, the interval between symptom onset and diagnosis meaningfully affected the timing of treatment initiation in approximately one-third of patients, and hemostatic therapy was ultimately required in about 70% of the cohort because of bleeding episodes (Knoebl et al., 2012). This pattern of diagnostic delay, often preceded by weeks to months of unexplained bruising or soft-tissue bleeding, is consistently described as a preventable contributor to morbidity and is attributed to limited awareness of AHA outside specialized hematology centers (Mingot-Castellano et al., 2022; Tian et al., 2023).

Clinical presentation and diagnosis

AHA presents with a distinctive bleeding phenotype that differs sharply from that of congenital hemophilia A. Patients most often develop extensive subcutaneous ecchymoses, deep intramuscular hematomas, mucosal bleeding, retroperitoneal hemorrhage, or bleeding after minor procedures, frequently disproportionate in severity to the inciting event (Franchini et al., 2005; Kruse-Jarres et al., 2017). Hemarthrosis, the hallmark bleeding pattern of congenital hemophilia A, is comparatively uncommon in AHA, and its absence in a patient with a bleeding diathesis is repeatedly described as a useful diagnostic clue that should raise suspicion for an acquired rather than inherited coagulopathy (Mingot-Castellano et al., 2017; Kruse-Jarres et al., 2017).

The laboratory signature of AHA is highly characteristic and, when recognized, allows rapid triage toward the correct diagnosis. Typical findings include an isolated prolongation of the aPTT with a normal prothrombin time, markedly reduced FVIII activity, and a time- and temperature-dependent FVIII inhibitor demonstrable on Bethesda- or Nijmegen-modified assays (Collins et al., 2007; Collins et al., 2010). Because the aPTT prolongation is isolated and the patient typically has no personal or family bleeding history, international recommendations consistently emphasize that this laboratory pattern in an older adult—particularly before a planned invasive procedure—should trigger urgent evaluation for AHA and prompt hematology referral rather than being dismissed as a pre-analytical artifact (Huth-Kühne et al., 2009; Collins et al., 2010).

Hemostatic management

Acute hemostatic management in AHA is guided by the principle that the FVIII-dependent step of coagulation must be bypassed or substituted with a form of FVIII resistant to inhibition. Activated prothrombin complex concentrate (aPCC) and recombinant activated factor VII (rFVIIa) remain the most widely used first-line bypassing agents in registries and consensus guidance, while recombinant porcine FVIII offers a further option, particularly for patients with very high inhibitor titers who might otherwise not respond adequately to bypassing therapy (Kruse-Jarres et al., 2017; Huth-Kühne et al., 2009; Collins et al., 2010). In the EACH2 registry, hemostatic therapy was required in roughly seven of every ten enrolled patients because of a bleeding episode at or shortly after diagnosis, underscoring how frequently acute intervention is necessary rather than optional in this population (Knoebl et al., 2012).

Standard human FVIII concentrates are generally considered inadequate in the presence of high-titer inhibitors, since the infused factor is rapidly neutralized, but they may still have a role in carefully selected patients with low-titer inhibitors under close laboratory monitoring (Franchini et al., 2005; Collins et al., 2007). Across guidelines and registry-based experience, the choice among available hemostatic agents is shaped less by superiority of one agent over another and more by local availability, clinician familiarity, and the patient's comorbidity profile, including renal function, thrombotic risk, and prior exposure to blood products (Mingot-Castellano et al., 2022; Tian et al., 2023). The consistent message across international recommendations is that bleeding control in AHA constitutes a hematologic emergency, and that patients should be transferred to, or managed in close collaboration with, centers experienced in inhibitor-related bleeding disorders whenever feasible (Kruse-Jarres et al., 2017; Huth-Kühne et al., 2009).

Inhibitor eradication and outcomes

Parallel to hemostatic control, eradication of the FVIII autoantibody is essential to achieve durable remission and reduce the risk of recurrent bleeding. First-line immunosuppressive regimens most commonly combine corticosteroids with cyclophosphamide, with rituximab-based regimens used either upfront in selected patients or as second-line therapy for those with persistent or relapsing inhibitors (Kruse-Jarres et al., 2017; Huth-Kühne et al., 2009; Collins et al., 2010).

A recent 25-year cohort study paired with a network meta-analysis provides some of the most detailed comparative data available on this question (Rungjirajittranon et al., 2024). In this analysis, the combination of cyclophosphamide and prednisolone was the most frequently used first-line regimen, and lower inhibitor titers at presentation were significantly associated with higher rates of complete remission (86.8% versus

62.2% in patients with higher titers; odds ratio 0.26), while median relapse-free survival extended to over three years (37.1 months) and was significantly prolonged by cyclophosphamide-based therapy (hazard ratio 0.24) (Rungjirajittranon et al., 2024). Pooling data across studies through network meta-analysis, both cyclophosphamide-based and rituximab-based regimens significantly outperformed corticosteroid monotherapy in achieving complete remission and reducing relapse, without a clear advantage of one over the other, positioning cyclophosphamide-based therapy as a reasonable first-line option, particularly where access to rituximab is limited (Rungjirajittranon et al., 2024).

These findings are broadly consistent with earlier registry-based experience, in which the large majority of patients who received immunosuppression—approximately three-quarters of the EACH2 cohort—achieved complete remission, though the time required to do so varied considerably between regimens and individual patients (Knoebl et al., 2012). Importantly, remission rates in the 70–80% range achievable with immunosuppression must be weighed against the substantial toxicity of the treatment itself: infections, cytopenias, and other complications of intensive immunosuppression in older, frail patients remain a leading driver of mortality, and several reviews caution that harms related to treatment can rival or exceed those directly attributable to bleeding (Poston & Kruse-Jarres, 2022; Mingot-Castellano et al., 2022). This tension between efficacy and toxicity underlies the growing interest in strategies, such as emicizumab, that might allow effective bleeding control while permitting a less intensive or delayed immunosuppressive approach (Rungjirajittranon et al., 2024).

Emerging role of emicizumab

The emergence of emicizumab, a bispecific monoclonal antibody that bridges activated factor IX and factor X to reconstitute FVIII-like enzymatic function independent of FVIII inhibitors, has introduced a genuinely new therapeutic option in AHA (Alcedo Andrade et al., 2024). Because its hemostatic activity is unaffected by autoantibodies directed against FVIII, emicizumab offers the theoretical advantage of providing sustained bleeding protection without reliance on repeated intravenous bypassing-agent infusions.

Early clinical experience came from case series describing off-label use in patients with active or refractory bleeding. In one of the more detailed reports, twelve patients with AHA (six men, six women; median age 74 years) who had an insufficient hemostatic response to bypassing agents were switched to emicizumab: after the first dose, the aPTT normalized within one to three days, hemostatic efficacy allowing discontinuation of bypassing therapy was achieved after a median of 1.5 days, and no breakthrough bleeding occurred following the first injection in any patient; complete remission, defined by recovery of FVIII activity above 50%, was reached after a median of 115 days, and emicizumab itself was discontinued after a median of 31 days, with a median of only five injections required per patient (Knoebl et al., 2021). All patients in this series continued to receive concomitant immunosuppression with steroids and/or rituximab, and no patient died from bleeding or thromboembolism (Knoebl et al., 2021).

This early experience has since been extended by the first prospective clinical trial in this population, the German-Austrian GTH-AHA-EMI phase 2 study, which enrolled 47 treatment-naïve patients with AHA across 16 centers and administered emicizumab as monotherapy (6 mg/kg on day 1, 3 mg/kg on day 2, then 1.5 mg/kg weekly) for 12 weeks before immunosuppression was introduced (Tiede et al., 2023). The median age of participants was 76 years, reflecting the typical AHA population, and the trial's primary endpoint—clinically relevant bleeds per patient-week—was met with a mean rate of 0.04, well below the pre-specified efficacy threshold of 0.15 bleeds per patient-week derived from historical cohorts treated with bypassing agents and immunosuppression (Tiede et al., 2023). Seventy percent of patients experienced no bleeding events at all during the 12-week prophylaxis period, and adverse events of grade 3 or higher were limited to a small number of infections, an acute kidney injury, and a single stroke, with no treatment-related deaths reported (Tiede et al., 2023). These results directly informed subsequent consensus dosing recommendations from the German, Austrian, and Swiss GTH working group, which formalized the loading and maintenance schedule used in the trial and provided structured guidance on monitoring and the timing of transition to, or avoidance of, immunosuppression in eligible patients (Pfrepper et al., 2024).

A systematic review pooling 32 studies and 171 patients treated with emicizumab for AHA—including both retrospective case-based experience and the emerging trial data—found that bleeding was well controlled in essentially all reported cases, with no major recurrent bleeding episodes; reported adverse events were infrequent but included three cases of deep vein thrombosis, two strokes, and two instances of anti-emicizumab antibody development in patients with pre-existing thromboembolic risk factors (Ghachem et al., 2024). Complementary narrative reviews have proposed that, in appropriately selected patients, emicizumab could be considered from the time of diagnosis as first-line prophylaxis against bleeding, potentially allowing

immunosuppression to be deferred until the patient's overall clinical status has stabilized (Poston & Kruse-Jarres, 2023; Iarossi & Hermans, 2024).

Despite these encouraging findings, several important caveats persist. The evidence base remains dominated by observational data, small case series, and, to date, only two prospective single-arm trials without a randomized comparator; dosing strategies and the timing of concomitant immunosuppression remain heterogeneous across published experience (Alcedo Andrade et al., 2024; Poston & Kruse-Jarres, 2023; Knoebl et al., 2021; Tiede et al., 2023). No large randomized controlled trial comparing emicizumab-based strategies against standard bypassing-agent-and-immunosuppression pathways has yet been completed, and questions remain regarding optimal treatment duration, long-term thromboembolic risk in an elderly and often multimorbid population, and cost-effectiveness relative to established therapy (Alcedo Andrade et al., 2024; Ghachem et al., 2024). Emicizumab should therefore currently be regarded as a promising and increasingly evidence-supported adjunct rather than a wholesale replacement for established hemostatic and immunosuppressive management, with its use best confined, for now, to centers with expertise in both AHA and emicizumab therapy (Pfrepper et al., 2024; Tiede et al., 2023).

Discussion

This narrative review confirms that AHA, though epidemiologically rare, is a clinically disproportionate contributor to morbidity and mortality in internal medicine and hematology. Registry data from Europe, the United Kingdom, and North America converge on an annual incidence in the range of 1 to 1.8 cases per million, a median age at diagnosis in the mid-to-late seventies, and a strikingly consistent finding that roughly half of all cases remain idiopathic despite thorough investigation (Knoebl et al., 2012; Collins et al., 2007; Tian et al., 2023). This convergence across geographically and temporally distinct cohorts—spanning a UK national surveillance study conducted in the mid-2000s, a pan-European registry recruiting through the late 2000s, and a Canadian population-based review extending into the 2020s—provides reassuring evidence that the epidemiological profile of AHA has remained stable over nearly two decades, even as diagnostic awareness and treatment options have evolved substantially (Collins et al., 2007; Knoebl et al., 2012; Tian et al., 2023).

Despite this consistency, the reviewed data show that diagnostic delay remains a persistent and largely unresolved problem. In the EACH2 registry, delayed diagnosis measurably affected the timing of treatment initiation in roughly one-third of patients, a proportion that has not been shown to have meaningfully improved in more recent cohorts (Knoebl et al., 2012; Tian et al., 2023). This delay most plausibly reflects the rarity of the condition relative to far more common causes of bruising and bleeding in older adults, such as anticoagulant use, vasculopathy, or thrombocytopenia, combined with limited familiarity with AHA outside specialized hematology services (Mingot-Castellano et al., 2022). The practical implication for internists, surgeons, and emergency physicians is direct: an isolated, otherwise unexplained prolongation of the aPTT in an older adult without a personal or family bleeding history—especially when identified incidentally before an invasive procedure—should be treated as a potential hematologic emergency rather than a laboratory artifact, and should prompt urgent hematology consultation and factor VIII/inhibitor testing rather than repeat testing or observation alone (Huth-Kühne et al., 2009; Collins et al., 2010; Haider & Anwer, 2022). Embedding a simple decision rule of this kind into hospital coagulation-testing protocols and pre-operative pathways—for example, automatic hematology notification for any unexplained isolated aPTT prolongation before elective surgery—could meaningfully shorten the time to diagnosis without requiring substantial new resources (Huth-Kühne et al., 2009).

The hemostatic management data reviewed here reinforce a now well-established principle: bypassing agents and recombinant porcine FVIII, rather than standard human FVIII concentrates, should be the default choice for active bleeding in patients with high-titer inhibitors, and initiation of therapy should not be delayed while awaiting confirmatory Bethesda assay results in a patient with a compatible clinical and laboratory picture (Kruse-Jarres et al., 2017; Huth-Kühne et al., 2009; Collins et al., 2010). At the same time, the finding that roughly seven in ten patients in the largest available registry required hemostatic intervention underscores that AHA is rarely a purely laboratory diagnosis managed expectantly; active bleeding is the rule rather than the exception at presentation, which has direct implications for triage and resource planning in centers that see even occasional AHA cases (Knoebl et al., 2012).

The comparative data on immunosuppressive regimens add useful precision to what has historically been a highly individualized, experience-based decision. The recent network meta-analysis reviewed here demonstrates a measurable and statistically significant advantage of cyclophosphamide-based and rituximab-based regimens over corticosteroid monotherapy, with no clear superiority between the two more intensive approaches, and identifies

inhibitor titer at presentation as an independent predictor of remission (Rungjirajittranon et al., 2024). This has two important implications for practice. First, it provides a stronger evidence basis than previously available for favoring combination immunosuppression over steroids alone as first-line therapy in most patients, tempered by the physician's judgment regarding infection risk and frailty. Second, together with the tension identified across multiple registries and reviews between achievable remission rates of 70–80% and substantial mortality driven by treatment-related toxicity, it strengthens the case for individualized regimen selection that explicitly weighs a patient's comorbidity burden, infection risk, and functional status against the modest additional efficacy gained from more intensive immunosuppression (Rungjirajittranon et al., 2024; Poston & Kruse-Jarres, 2022; Mingot-Castellano et al., 2022; Knoebl et al., 2012).

It is in this context that the emerging data on emicizumab appear most consequential. The GTH-AHA-EMI trial is, to date, the strongest available evidence that a treatment strategy other than immunosuppression can independently and effectively prevent bleeding in AHA, achieving a mean bleeding rate roughly one-quarter of the pre-specified historical benchmark and leaving 70% of enrolled patients entirely free of bleeding during the 12-week prophylaxis period (Tiede et al., 2023). Combined with case-series evidence that emicizumab can rapidly normalize hemostatic parameters and permit early discontinuation of bypassing agents even in patients with an inadequate response to conventional therapy (Knoebl et al., 2021), and systematic review data confirming a favorable bleeding-control profile across 171 pooled patients (Ghachem et al., 2024), these findings support a genuine shift in how AHA might be approached: rather than immunosuppression and bypassing therapy proceeding simultaneously from diagnosis, emicizumab could allow bleeding protection to be established first, with immunosuppression introduced once the patient is clinically stable or deferred altogether in selected cases where spontaneous or treatment-induced remission is anticipated (Tiede et al., 2023; Pfrepper et al., 2024; Poston & Kruse-Jarres, 2023). For an elderly, multimorbid population in whom immunosuppression-related toxicity is a leading cause of death, the possibility of decoupling bleeding control from immediate high-intensity immunosuppression, even partially, represents a meaningful potential improvement in the risk-benefit balance of AHA management (Poston & Kruse-Jarres, 2022; Rungjirajittranon et al., 2024).

At the same time, several caveats temper enthusiasm for emicizumab as a default first-line strategy. Both prospective studies to date are single-arm and open-label, and while the historical comparator used in the GTH-AHA-EMI trial was derived from a well-characterized cohort, this design cannot fully account for temporal changes in supportive care or referral patterns that might independently have improved outcomes (Tiede et al., 2023). Reported thromboembolic events, while infrequent, occurred across nearly every dataset reviewed, including deep vein thrombosis, stroke, and, in the systematic review, the development of anti-drug antibodies in patients with pre-existing thromboembolic risk factors, and require ongoing vigilance, particularly given the elderly, often hospitalized, and frequently multimorbid nature of the AHA population (Knoebl et al., 2021; Ghachem et al., 2024; Tiede et al., 2023). Consensus dosing recommendations now exist to standardize practice (Pfrepper et al., 2024), but questions regarding optimal treatment duration, criteria for safely discontinuing emicizumab, and its role relative to immunosuppression in patients who fail to spontaneously remit remain incompletely resolved (Alcedo Andrade et al., 2024; Poston & Kruse-Jarres, 2023).

Taken together, the evidence synthesized in this review points to several concrete priorities for the field. Clinically, there is a continued need to raise awareness of AHA's distinctive presentation among non-hematology specialists and to embed simple, low-cost diagnostic triggers—such as mandatory hematology consultation for unexplained isolated aPTT prolongation—into routine hospital and pre-operative pathways (Huth-Kühne et al., 2009; Knoebl et al., 2012; Tian et al., 2023). Therapeutically, the combination of more precise comparative data on immunosuppressive regimens and increasingly robust prospective evidence for emicizumab creates an opportunity to move away from a one-size-fits-all approach toward individualized strategies that explicitly balance bleeding risk, inhibitor titer, comorbidity burden, and treatment-related toxicity for each patient (Rungjirajittranon et al., 2024; Tiede et al., 2023; Pfrepper et al., 2024). At the research level, the field would benefit substantially from randomized comparative trials of emicizumab-based versus conventional bypassing-agent-and-immunosuppression strategies, from longer-term thromboembolic safety data in elderly cohorts, and from prospective validation of risk-stratification tools that could identify patients most likely to benefit from lower-intensity immunosuppression (Poston & Kruse-Jarres, 2022; Ghachem et al., 2024; Iarossi & Hermans, 2024; Rungjirajittranon et al., 2024). For internists and hematologists managing this rare but high-stakes disease, the convergence of better-characterized epidemiology, sharper comparative immunosuppression data, and a rapidly maturing emicizumab evidence base offers a realistic pathway toward measurably better outcomes for a patient population that has historically been underserved by standardized, low-toxicity care pathways (Kruse-Jarres et al., 2017; Knoebl et al., 2012; Poston & Kruse-Jarres, 2022; Tiede et al., 2023).

Conclusions

Acquired hemophilia A is a rare but potentially life-threatening autoimmune bleeding disorder that predominantly affects older adults and remains underdiagnosed despite a characteristic clinical and laboratory profile (Collins et al., 2007; Mingot-Castellano et al., 2022; Kruse-Jarres et al., 2017; Knoebl et al., 2012; Tian et al., 2023; Poston & Kruse-Jarres, 2022). Early recognition based on isolated prolongation of aPTT, atypical soft-tissue bleeding, and the presence of a factor VIII inhibitor is essential and requires a high index of suspicion from internists, surgeons, and hematologists (Franchini et al., 2005; Collins et al., 2007; Mingot-Castellano et al., 2017; Huth-Kühne et al., 2009; Collins et al., 2010; Haider & Anwer, 2022).

Acute bleeding control with bypassing agents or recombinant porcine FVIII, together with immunosuppressive therapy aimed at inhibitor eradication, remains the cornerstone of treatment (Kruse-Jarres et al., 2017; Huth-Kühne et al., 2009; Collins et al., 2010). However, toxicity from intensive immunosuppression narrows the therapeutic safety margin in elderly patients and requires individualized strategies (Mingot-Castellano et al., 2022; Kruse-Jarres et al., 2017; Knoebl et al., 2012; Tian et al., 2023; Poston & Kruse-Jarres, 2022; Rungjirajittranon et al., 2024).

Emerging data on emicizumab suggest the possibility of more stable bleeding prophylaxis and reduced exposure to aggressive treatment, but current evidence remains limited and largely derived from observational case series and early expert consensus (Alcedo Andrade et al., 2024; Poston & Kruse-Jarres, 2023; Knoebl et al., 2021; Tiede et al., 2023; Pfrepper et al., 2024; Iarossi & Hermans, 2024). In practice, improved outcomes in AHA depend on heightened awareness among non-hematology physicians, standardized diagnostic and therapeutic pathways, and prospective studies that define the optimal role of emicizumab (Mingot-Castellano et al., 2022; Kruse-Jarres et al., 2017; Knoebl et al., 2012; Huth-Kühne et al., 2009; Ghachem et al., 2024; Iarossi & Hermans, 2024; Rungjirajittranon et al., 2024). For internists and hematologists, AHA remains a major challenge, but also an area where system-level interventions can translate into meaningful gains for a high-risk patient population (Kruse-Jarres et al., 2017; Knoebl et al., 2012; Tian et al., 2023; Poston & Kruse-Jarres, 2022; Alcedo Andrade et al., 2024; Poston & Kruse-Jarres, 2023; Knoebl et al., 2021; Tiede et al., 2023; Pfrepper et al., 2024).

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