STM JOURNALS

Research & Reviews: A Journal of
Medicine

https://journals.stmjournals.com/rrjom/

ISSN: 2249-8648 (Online)
ISSN: 2348-7917 (Print)
Volume 16, Issue 2, 2026
May–August
DOI (Journal): 10.37591/RRJOM

Review RRJOM

Exploring the Relationship Between Disseminated Intravascular Coagulation and Waterhouse–Friderichsen Syndrome

Deepa Narayan Naik[1,*], Juliet Dsouza[1]

Abstract

Waterhouse–Friderichsen syndrome was first identified as a distinct clinical entity by Little in 1901. He described four cases from his own observations and, after examining existing literature, identified eight additional cases that he considered previously unclassified. One case in his report may have involved purpura resulting from a different cause. The knowledge of this unusual disorder developed slowly from several significant clinical observations and case reports during the first two decades of the 20th century. In 1911, William Waterhouse published a report detailing an additional case in England, as well as a review of 15 cases that had been previously published. Waterhouse's review is regarded as one of the first comprehensive descriptions of the clinical features, pathological changes, and progression of this syndrome, contributing to the recognition of it as a separate medical condition. Then in 1918, Dr. M. Friderichsen published another two cases from Germany and provided an extensive analysis of the cases previously published by Dr. E. Little, in addition to sixteen other cases found in the medical literature. Dr. Friderichsen's research contributed to a greater understanding at that time of the clinical features and pathological basis of this syndrome. In 1934, Dr. V. Bamatter published a detailed review of 38 cases, including two cases that he had seen in his own practice. This comprehensive review of the literature provided additional information on the syndrome and provided a more solid foundation for its diagnosis and clinical recognition.

Keywords: Waterhouse–Friderichsen syndrome, bilateral adrenal haemorrhage, meningococcal infection, medical malpractice, Clinical features

INTRODUCTION

Waterhouse–Friderichsen syndrome (WFS), also referred to as purpura fulminans, is a severe septic condition associated with a high risk of mortality [1, 2]. It most commonly affects the pediatric population, particularly infants and young children. The syndrome is characterized by acute and extensive hemorrhagic necrosis of the adrenal glands, often resulting from meningococcal infection. More than 80% of cases are linked to infection by Meningococcal disease through the bacterium Neisseria meningitidis [3, 4]. However, other microorganisms, including gonococci, streptococci, and pneumococci, have also been identified as causative agents. These organisms can produce severe septic shock, like WFS, by stimulating excessive cytokine release [5, 6].

***Author for Correspondence**
Deepa Narayan Naik
E-mail: naikd5783@gmail.com

[1]Assistant Lecturer, Department of Nursing, R.N.S College of Nursing, Mavalli, Karnataka, India

Received Date: May 25, 2026
Accepted Date: June 08, 2026
Published Date: July 16, 2026

Citation: Deepa Narayan Naik, Juliet Dsouza. Exploring The Relationship Between Disseminated Intravascular Coagulation and Waterhouse–Friderichsen Syndrome. Research & Reviews: A Journal of Medicine. 2026; 16(2): 45–49p.

Sepsis with patchy purpura and associated bilateral haemorrhagic necrosis of the adrenals are key findings for the diagnosis of WFS [7]. However, cases with only one adrenal haemorrhage have also been reported [8]. In fact, when only adrenal haemorrhagic necrosis is present, other

causes must be considered (for example, trauma, coagulopathies, anticoagulation therapy, hypotensive events, complicated pregnancies, etc.) [9]. The adrenal necrosis as well as the generalized rash of the skin have been attributed to coagulation abnormalities and intravascular changes consistent with disseminated intravascular coagulation (DIC) and consumption of clotting factors caused by endotoxins, hypotension and clinical adrenal insufficiency [5].

Waterhouse–Friderichsen syndrome (WFS) is associated with a very high mortality rate, estimated at approximately 95%, and is characterized by a sudden appearance of symptoms, rapid progression of the disease, and the possibility of unexpected death. These features create important medico-legal concerns regarding the determination of the cause of death and issues related to possible medical negligence. Delays in diagnosis may result in fatal outcomes and can also hinder timely preventive measures for close contacts. In many situations, family members of affected individuals may question the clinical decisions of the first healthcare providers such as general practitioners or pediatricians. Consequently, emergency physicians and healthcare professionals may face legal liability if delayed recognition or treatment is believed to have contributed to the patient's death. Such concerns are commonly examined during civil and criminal investigations involving unexpected deaths. Nevertheless, establishing a clinical diagnosis of WFS remains highly challenging due to its rapid and complex presentation [10–12].

EPIDEMIOLOGY

Waterhouse–Friderichsen syndrome (WFS) is an uncommon condition that occurs more frequently in children than in adults. Evidence suggests that the occurrence of WFS in the United States may be declining, likely due to a reduction in meningococcal infections. The frequency of meningococcal disease differs across geographic regions, with the highest rates reported in Sub-Saharan Africa. In the United States, the incidence of meningococcal disease has previously been reported to reach approximately 1.7 cases per 100,000 population [13].

AETIOLOGY

Waterhouse–Friderichsen syndrome was initially identified in association with septic infections caused by *Neisseria meningitidis*. Subsequently, a variety of bacterial and viral pathogens have also been recognized as potential causes of the syndrome [14].

- *Streptococcus pneumonia.*
- *Hemophilus influenzae.*
- *Escherichia coli.*
- *Staphylococcus aureus.*
- Group A beta-hemolytic Streptococcus.
- *Capnocytophaga canimorsus.*
- *Enterobacter cloacae.*
- *Pasteurella multocida.*
- *Plesiomonas shigelloides.*
- *Neisseria gonorrhoeae.*
- *Moraxella duplex.*
- Bilateral adrenal hemorrhage has also been reported with *Rickettsia rickettsii.*
- *Bacillus anthracis.*
- *Treponema pallidum.*
- *Legionella pneumophila.*

Viral Infections Including

- Cytomegalovirus.
- Parvovirus B19.
- Epstein–Barr virus.
- Varicella.

Signs and Symptoms

- Patients commonly present with nonspecific symptoms, including sudden onset of headache, fever, generalized weakness, fatigue, abdominal or flank discomfort, loss of appetite, nausea, vomiting, confusion, or altered mental status.
- Physical examination of the abdomen may reveal findings such as tenderness, abdominal rigidity, or rebound tenderness.
- When WFS occurs with meningococcemia, characteristic features may include petechial skin eruptions, Disseminated Intravascular Coagulation (DIC), purpura fulminans, and neurological signs commonly associated with meningitis.
- Petechial lesions typically appear first on the trunk and lower extremities, although they may also involve mucosal surfaces. These lesions can merge and progress into larger purpuric areas and ecchymoses. The appearance and severity of petechiae are often associated with the degree of thrombocytopenia. Therefore, careful assessment of these skin manifestations is important, as they may indicate an increased risk of bleeding complications related to DIC.
- Diagnosis of WFS can be difficult, particularly in patients with active sepsis, because its clinical presentation may resemble septic shock. Additionally, hypotension develops before shock in only about half of affected patients, which may further complicate early recognition (Figure 1) [15].

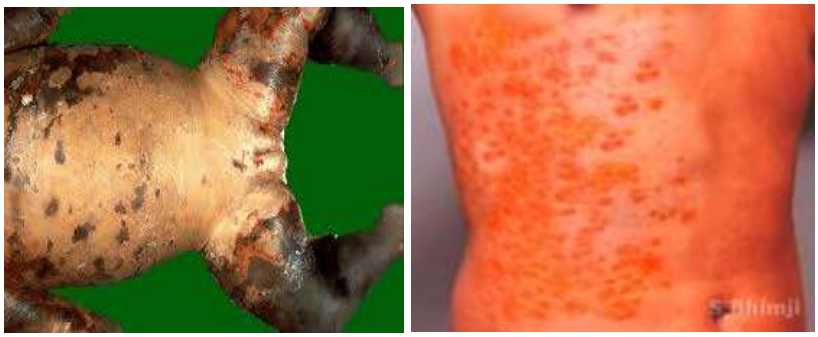

Figure 1. Purpuric rash in WFS (image courtesy S Bhimji MD).

Diagnostic Evaluation

- Gram staining of cerebrospinal fluid (CSF) is considered a valuable and rapid method for the early identification of the causative organism.
- Culture of samples obtained from CSF or a skin lesion biopsy remains the gold standard for confirming the diagnosis.
- Blood culture testing may also identify the responsible microorganism in certain cases [16].

TREATMENT/MANAGEMENT

- Management of WFS primarily focuses on supportive treatment of sepsis, including fluid resuscitation, administration of appropriate antibiotics, vasopressor support to maintain adequate organ perfusion, and other necessary supportive measures.
- An initial fluid bolus of D5 normal saline (5% dextrose with 0.9% normal saline) at 20 mL/kg over one hour may be administered to restore circulatory volume while also correcting associated hypoglycemia.
- In patients with persistent shock, normal saline infusion may be repeated, with a cumulative dose of up to 60 mL/kg within one hour if clinically indicated.
- Hypoglycemia can be corrected by administering 25% dextrose at a dose of 2–4 mL/kg as an intravenous bolus.
- Glucocorticoid replacement therapy commonly involves hydrocortisone, given at a dose of 50–100 mg/m² as an initial bolus.
- Age-based hydrocortisone dosing generally includes 25 mg for children younger than 3 years, 50 mg for children aged 3–12 years, and 100 mg for individuals older than 12 years.

- The same hydrocortisone dose may subsequently be administered over 24 hours, either as a continuous infusion or divided into four separate doses [17].
- Immediate mineralocorticoid replacement therapy is generally unnecessary because its sodium-retaining effects require more time to become clinically effective.
- Administration of hydrocortisone combined with normal saline therapy may contribute to correction of hyponatremia, partly by influencing antidiuretic hormone activity.
- In many cases, hyperkalemia improves following fluid therapy and hydrocortisone treatment. In severe symptomatic cases, additional interventions, such as insulin with glucose administration, may be required.
- Continuous assessment of electrolyte levels and fluid balance is essential during treatment. After stabilization of the acute phase, long-term maintenance therapy with glucocorticoids and mineralocorticoids may be initiated as appropriate.
- Conservative treatment is generally preferred for traumatic adrenal hemorrhage when there is no evidence of ongoing bleeding. Such management includes supportive care, regular monitoring of hematocrit levels, and blood transfusion if necessary.
- In patients managed non-operatively, follow-up imaging studies are important to evaluate resolution of adrenal hematoma and to distinguish benign hematoma from adrenal masses that may require surgical intervention.
- If bleeding continues despite conservative measures, interventional procedures, such as angioembolization of adrenal vessels, may be required for hemorrhage control. Surgical intervention is reserved for selected cases of traumatic adrenal hemorrhage [18].

CONCLUSION

The presence of bilateral adrenal haemorrhage during autopsy is considered a characteristic finding of Waterhouse–Friderichsen syndrome, a condition commonly linked with severe and rapidly progressing meningococcal septicaemia. Furthermore, the close genetic similarity observed among three isolated strains of *Staphylococcus aureus* – including one methicillin-sensitive strain and two methicillin-resistant strains – highlights the strong association between highly virulent methicillin-susceptible and methicillin-resistant strains currently circulating within the community.

REFERENCES

1. Aegerter EE. The Waterhouse-Friderichsen syndrome: Review of the literature and a report of two cases. JAMA. 1936;106(20):1715–1719.
2. Tsokos M. Postmortem measurement of serum procalcitonin concentration in Waterhouse-Friderichsen syndrome. Virchows Arch. 2002;441(6):629–631. doi: 10.1007/s00428-002-0710-5.
3. Böhm N. Adrenal, cutaneous and myocardial lesions in fulminating endotoxinemia (Waterhouse-Friderichsen syndrome). Pathol Res Pract. 1982;174(1–2):92–105. doi: 10.1016/S0344-0338(82)80063-3.
4. Garland J, Tse R, Cala AD. Neisseria meningitidis isolated in postmortem vitreous humor in a death due to meningococcal sepsis. Am J Forensic Med Pathol. 2016;37(4):233–235. doi: 10.1097/PAF.0000000000000263.
5. Varon J, Chen K, Sternbach GL. Rupert Waterhouse and Carl Friderichsen: Adrenal apoplexy. J Emerg Med. 1998;16(4):643–647. doi: 10.1016/S0736-4679(98)00059-3.
6. Ryan CA, Wenman W, Henningsen C, Tse S. Fatal childhood pneumococcal Waterhouse-Friderichsen syndrome. Pediatr Infect Dis J. 1993;12(3):250–251.
7. Harris P, Bennett A. Waterhouse-Friderichsen syndrome. N Engl J Med. 2001;345(11):841. doi: 10.1056/NEJM200109133451116.
8. Mühlig K, Theile J, Dalitz E. Einseitige Nebennierenblutung – ein Waterhouse-Friderichsen-Syndrom? Ultraschall Med. 1995;16(6):293–296.
9. Tormos LM, Schandl CA. The significance of adrenal hemorrhage: Undiagnosed Waterhouse-Friderichsen syndrome, a case series. J Forensic Sci. 2013;58(4):1071–1074. doi: 10.1111/1556-4029.12149.
10. Gentile G, Amadasi A, Bailo P, Boracchi M, Maciocco F, Marchesi M, et al. The importance of the postmortem interval for the diagnosis of Waterhouse-Friderichsen syndrome by Neisseria

meningitidis in a series of forensic cases. Autops Case Rep. 2019;9(3):e2019103. doi: 10.4322/acr.2019.103.
11. Mok Q, Butt W. The outcome of children admitted to intensive care with meningococcal septicaemia. Intensive Care Med. 1996;22(3):259–263. doi: 10.1007/BF01712249.
12. Ventura F, Bonsignore A, Portunato F, Orcioni GF, Varnier OE, De Stefano F. A fatal case of streptococcal and meningococcal meningitis in a 2-year-old child occurring as Waterhouse-Friderichsen syndrome. J Forensic Leg Med. 2013;20(6):678–682. doi: 10.1016/j.jflm.2013.03.020.
13. Rijal R, Kandel K, Aryal BB, Asija A, Shrestha DB, Sedhai YR. Waterhouse-Friderichsen syndrome, septic adrenal apoplexy. In: Litwack G, editor. Vitamins and Hormones. Vol. 124. Cambridge (MA): Academic Press; 2024. p. 449–461. doi: 10.1016/bs.vh.2023.10.013.
14. Karki BR, Sedhai YR, Syed. Waterhouse-Friderichsen Syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551510/
15. Rao RH, Vagnucci AH, Amico JA. Bilateral massive adrenal hemorrhage: Early recognition and treatment. Ann Intern Med. 1989;110(3):227–235. doi: 10.7326/0003-4819-110-3-227.
16. Sonavane A, Baradkar V, Salunkhe P, Kumar S. Waterhouse-Friderichsen syndrome in an adult patient with meningococcal meningitis. Indian J Dermatol. 2011;56(3):326–328. doi: 10.4103/0019-5154.82496.
17. Udobi KF, Childs EW. Adrenal crisis after traumatic bilateral adrenal hemorrhage. J Trauma. 2001;51(3):597–600. doi: 10.1097/00005373-200109000-00030.
18. Ikeda O, Urata J, Araki Y, Kume S, Torigoe Y, et al. Acute adrenal hemorrhage after blunt trauma. Abdom Imaging. 2007;32(2):248–252. doi: 10.1007/s00261-006-9017-3.

