OASIS DERMATOLOGY GROUP

Ph: (956) 971 - 0404
www.oasisderm.com

# DRESS Syndrome

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a rare, potentially life-threatening hypersensitivity reaction to specific medications, characterized by severe systemic symptoms, a distinctive skin rash, and organ involvement. While the condition is uncommon, it carries a significant mortality rate, with estimates ranging between 10% and 20% depending on the severity and timing of diagnosis.

DRESS can affect both adults and children, with no strong gender preference, although the condition's incidence and severity may vary according to ethnicity and the offending drug. The overall incidence is relatively rare, estimated at 1 in 1,000 to 1 in 10,000 drug exposures, although certain drugs, such as phenytoin, are associated with a higher incidence of 2.3-4.5 per 10,000.

**Etiology and Pathophysiology**

DRESS syndrome is a complex immune-mediated reaction, typically triggered by drugs that provoke an exaggerated immune response. The pathophysiology of DRESS is not fully understood, but it is believed to involve both cellular and humoral immune mechanisms, with a strong T-cell response to the offending drug. This reaction leads to widespread inflammation and subsequent organ involvement. A key feature of DRESS is the reactivation of latent viruses, particularly from the herpesvirus family, including human herpesvirus 6 (HHV-6), which has been implicated in approximately 40% of cases . Additionally, certain genetic factors, particularly the presence of specific human leukocyte antigen haplotypes, have been shown to predispose individuals to DRESS, particularly in response to drugs like anticonvulsants and sulfonamides.

**Clinical Presentation**

The hallmark symptoms of DRESS syndrome include a distinctive skin rash, fever, eosinophilia, and systemic organ involvement. The cutaneous manifestations typically begin 2 to 6 weeks after exposure to the triggering drug and often start as a morbilliform (measles-like) rash. The rash gradually becomes more generalized and confluent, often with a characteristic erythematous and scaly appearance. The lesions may affect more than 90% of the body surface area in severe cases.

In addition to the rash, patients often present with systemic symptoms, including fever, lymphadenopathy, facial edema, and involvement of multiple organs such as the liver, lungs, kidneys, and heart. Organ-specific manifestations can range from mild hepatitis to severe liver failure, interstitial pneumonia, pleural effusion, myocarditis, and renal impairment. Blood tests typically reveal elevated eosinophil counts (often >1,500/μL), elevated liver enzymes, and a shift in white blood cell counts, including the presence of atypical lymphocytes.

**Diagnosis**

The diagnosis of DRESS syndrome is challenging and often requires a high index of suspicion, as the symptoms overlap with other serious conditions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, systemic lupus erythematosus, and viral exanthems. The key distinguishing features include a combination of the following:

- ***Latency***: Symptoms typically arise 2 to 6 weeks after the introduction of the causative drug.
- ***Skin Findings*****:** A rose-red, confluent rash that may progress to exfoliative dermatitis.
- ***Systemic Symptoms*****:** Fever, lymphadenopathy, eosinophilia, and elevated liver enzymes.
- ***Organ Involvement*****:** Multisystem involvement including hepatitis, interstitial pneumonia, and renal failure.
- ***Reactivation of HHV-6*****:** Detection of reactivated herpesviruses in some cases.

A skin biopsy may reveal lymphocytic infiltration near blood vessels and may help differentiate DRESS from other dermatologic conditions. Scoring systems, such as the one proposed by Kardaun et al, can aid in assessing the likelihood of DRESS based on clinical features, eosinophil counts, and organ involvement (see Table 1). However, no single diagnostic test can definitively diagnose DRESS, making clinical judgment critical.

**Table 1: Clinical Features of DRESS Syndrome**

| History | Skin Findings | Systemic Symptoms | Organ Involvement |
|---|---|---|---|
| Drug exposure 2–6 weeks prior (e.g., anticonvulsants, sulfonamides, allopurinol) | Diffuse, erythematous rash, often confluent | Fever, lymphadenopathy, eosinophilia | Hepatitis, interstitial pneumonia, pleural effusion, myocarditis, renal failure |
| Itching or fever preceding rash | Exfoliative dermatitis >90% BSA | Blood: Elevated eosinophils, atypical lymphocytes, monocytes | Re-activation of HHV-6 or other herpesviruses |

**Management**

The cornerstone of management for DRESS syndrome is the immediate discontinuation of the causative drug, which is essential to halt the progression of the syndrome and prevent further organ damage. Systemic corticosteroids are often required, particularly in severe cases with significant organ involvement, such as hepatic failure, respiratory distress, or renal insufficiency. For less severe skin involvement, high-potency topical corticosteroids may be used.

In severe cases, hospitalization may be required for supportive care, including fluid and electrolyte management, as well as close monitoring of organ function. The management of organ-specific manifestations, such as interstitial pneumonia or hepatitis, may involve additional therapies like immunosuppressive agents (e.g., tacrolimus or cyclophosphamide) in refractory cases.

## Prognosis

The prognosis of DRESS syndrome largely depends on the severity of the systemic involvement, the speed of diagnosis, and the promptness of treatment. Early recognition and discontinuation of the offending drug are critical to improving outcomes. While skin manifestations often improve with appropriate therapy, recovery from internal organ involvement may take weeks to months, and in severe cases, permanent organ damage or death can occur.

Preventive measures are important for individuals at high risk, particularly those with known genetic predispositions or prior history of DRESS. Drug substitution or modification of therapy should be considered in patients with known risk factors.

## Conclusion

DRESS syndrome is a rare but serious drug-induced hypersensitivity reaction characterized by widespread skin involvement, eosinophilia, and systemic organ dysfunction. The diagnosis is clinical and involves recognizing the hallmark symptoms in the context of recent drug exposure. Management focuses on the early discontinuation of the causative drug and the use of systemic corticosteroids to manage severe symptoms. Close monitoring of organ function and supportive care is critical to prevent long-term complications. Given the potentially life-threatening nature of the syndrome, early recognition, and intervention are essential for improving outcomes.

## References

- Hernandez, A. D., Wong, C. K., & Lee, M. P. (2021). Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: An update on diagnosis, pathophysiology, and management. *Journal of Clinical Dermatology*, 46(2), 104-111. https://doi.org/10.1016/j.jcd.2020.11.003
- Kardaun, S. H., Sidoroff, A., Valeyrie-Allanore, L., et al. (2007). Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? *British Journal of Dermatology*, 156(3), 609-611. https://doi.org/10.1111/j.1365-2133.2007.07875.x
- Schneider, M., Garbe, C., & Pföhler, C. (2021). The pathogenesis, diagnosis, and management of DRESS syndrome. *Journal of the European Academy of Dermatology and Venereology*, 35(3), 491-502. https://doi.org/10.1111/jdv.16810
- Shiohara, T., & Kaneko, F. (2019). Drug-induced hypersensitivity syndrome (DRESS): Pathophysiology, diagnosis, and management. *The Journal of Dermatology*, 46(6), 587-594. https://doi.org/10.1111/1346-8138.14659