

CYTOKINE RELEASE SYNDROME is a systemic inflammatory condition that may occur after treatment with some types of immunotherapy.

RISK FACTORS

- Adoptive T-cell therapies
- High disease burden
- High dosage
- Pediatric population
- Other high-risk drugs (e.g., monoclonal antibodies, interferons, interleukins)



CAUSES/PATHOPHYSIOLOGY

- Large, rapid release of cytokines into the bloodstream from immune cells affected by certain types of immunotherapy



SIGNS & SYMPTOMS

- Mild: general flu-like symptoms, fevers (days to weeks), hypotension, tachycardia, chills, nausea, anorexia, swelling of the tongue, itching, rash (during or several hours after infusion), myalgia
- Life-threatening: respiratory distress, cardiotoxicity (including capillary leak syndrome)
- Some patients develop neurotoxicity after administration of T-cell therapies. Signs and symptoms include the following:
 - Mild confusion with word-finding difficulty
 - Headaches and hallucinations to aphasia
 - Hemiparesis
 - Cranial nerve palsies
 - Seizures
 - Somnolence



DIAGNOSTIC CRITERIA

- Cytokine release syndrome (CRS) can be challenging to diagnose because the presentation can mimic other inflammatory disorders. It is important to rule out other causes, such as sepsis or tumor lysis syndrome, because some will require different treatment or could be detrimental if treated incorrectly.
- Laboratory changes you might see include the following:
 - Cytopenias
 - Elevated creatinine and liver enzymes
 - Deranged coagulation parameters
 - High C-reactive protein



INTERVENTIONS

- Early recognition and prompt intervention can help prevent progression of CRS.
- Specific premedication and dosing schedules are recommended or required.
- In its most fatal state, CRS is called a "cytokine storm."
- Early interventions are determined based on the symptoms and would be supportive in nature.
 - Moderate: could include ruling out sepsis if the patient is neutropenic; antipyretics; low-flow oxygen therapy; vasopressors
 - Moderate to severe: may need high-flow oxygen therapy, anticytokine therapy, such as tocilizumab (anti-IL-6 monoclonal antibody), corticosteroids, or mechanical ventilation



ADDITIONAL RESOURCES

Eisenberg, S. (2018). Infusion reactions, extravasation, and transfusion reactions. In M. Kaplan (Ed.), *Understanding and managing oncologic emergencies: A resource for nurses* (3rd ed., pp. 327–396). Oncology Nursing Society.

Olsen, M., LeFebvre, K., & Brassil, K. (Eds.). (2019). *Chemotherapy and immunotherapy guidelines and recommendations for practice*. Oncology Nursing Society.

Shimabukuro-Vornhagen, A., Gödel, P., Subklewe, M., Stemmler, H. J., SchlöBer, H. A., Schlaak, M. . . . Kochanek, M. (2018). Cytokine release syndrome. *Journal of Immunotherapy of Cancer*, 6, 56. <https://doi.org/10.1186/s40425-018-0343-9>