Sepsis Mortality at the NIH Clinical Center

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Sepsis

- Life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs.

- 30-day mortality rates range from 35-50% in published literature

- Disease burden is high - severe sepsis contributes to more than 200,000 deaths annually in the US.

- Globally it is the most common cause of death in people who have been hospitalized.

Sviri,S. *J Crit Care 2014*
Rhodes A. *Crit Care Med 2016*

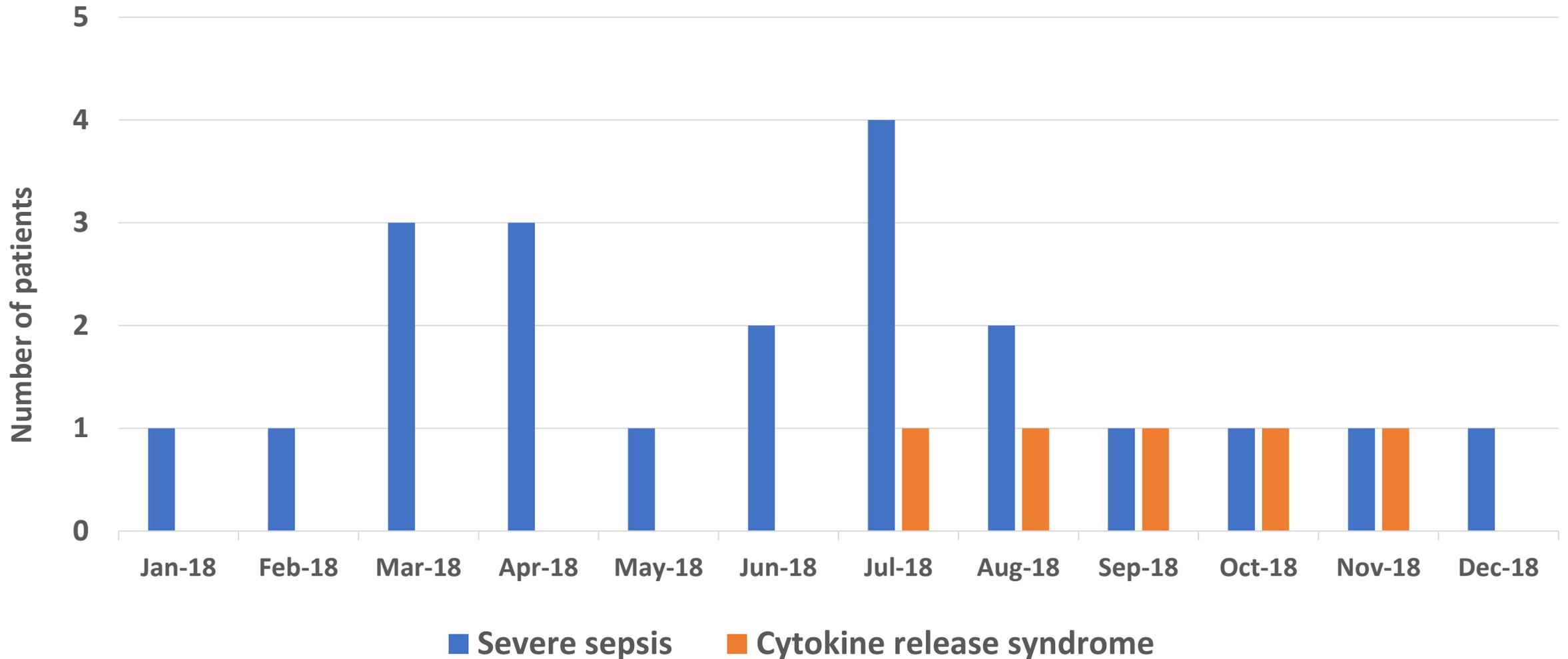# Signs and Symptoms of Severe Sepsis

- Hypotension (systolic blood pressure < 90 mm Hg, mean arterial pressure <70 mm Hg, or a decrease in SBP by > 40 mm Hg)

- Elevated lactate (above upper limit of normal)

- Decreased urine output (<0.5 ml/kg/hr for more than 2 hours despite fluid resuscitation)

- Acute lung injury / ARDS (if no pneumonia present: $PaO_2/FiO_2 < 250$; if pneumonia present: $PaO_2/FiO_2 < 200$)

- Creatinine > 2 mg/dL

- Total Bilirubin > 2 mg/dL

- Thrombocytopenia (platelet count < 100,000)

- Coagulopathy (INR > 1.5)

Cytokine Release Syndrome (CRS)

- Cytokine release syndrome is a side effect of CAR T-cell therapy (CAR = Chimeric Antigen Receptor)

- CAR T-cells are a form of immunotherapy that uses specially engineered white blood cells to fight specific types of cancer.

- T-cells release chemical immune messengers, cytokines. When the immune response is extremely vigorous, cytokine release can be overwhelming, and cause high fever and low blood pressure.

- ***CRS can look just like sepsis***!

Severe Sepsis and Cytokine Release Syndrome at the NIH Clinical Center ICU, 2018

What is the 30-day crude mortality rate for severe sepsis in the NIH Clinical Center?

Methods

- Looked back over 1 year (Jan-Dec 2018) using Biomedical Translational Research Informatics (BTRIS)

- Used vasopressor requirement as a surrogate marker for severe hypotension

- 514 patients admitted to the ICU, identified 63 cases requiring vasopressor therapy

- Chart review conducted to determine if severe hypotension was sepsis or something else

- 21 cases of severe sepsis; 5 deaths within 30 days

- 23% all-cause 30-day mortality

Deaths from Severe Sepsis

- Patient with metastatic cancer and progression of disease, admitted to ICU for hypotension after weeks in hospital. Received broad spectrum antibiotics and CPR. Family changed goals of care to comfort and patient expired in the ICU.

- Patient with lymphoma, stem cell transplant complicated by graft vs. host disease. Transferred to ICU for multiple infections, organ failure, after weeks in hospital. Developed hypotension and became vasopressor dependent. Family made patient DNR and patient expired in the ICU.

- Patient with extensive lymphoma that precluded transplant due to hepatic obstruction. Presented to ICU for hypotension and bacterial bloodstream infection. Hypotension resolved and patient was discharged from the ICU. Patient returned to his home country for hospice care.

Deaths from Severe Sepsis, Cont.

- Patient with metastatic cancer found to have pneumonia during his screening evaluation. Admitted to the ICU after weeks in hospital with hypotension and hypoxemia, and expired despite maximal treatment.

- Patient with HIV/AIDS and AIDS-related malignancies. After weeks in hospital, admitted to the ICU for septic shock with a fungal bloodstream infection. Shock resolved and the patient expired in hospice care.

Cytokine Release Syndrome

- CRS can look just like sepsis, and can also be fatal.

- None of the five cases in 2018 were fatal.

- CRS is treated with tocilizumab, which blocks IL-6, a cytokine that is abundant in CRS.

- Additional cases occurred in 2018 following immunotherapy with other agents.

- Take home message: We will likely see more cases of CRS and similar conditions as the use of cell therapy expands.

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