

Life After Sepsis

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Surviving Sepsis: What is Next?

What Sepsis Survivors Need to Know?



Surviving Sepsis

- Each year, more than 19 million individuals develop sepsis, defined as a life-threatening acute organ dysfunction secondary to infection.
- Approximately 14 million survive to hospital discharge and their prognosis varies. Half of patients recover, one-third die during the following year, and one-sixth have severe persistent impairments.
 - Impairments include development of an average of 1 to 2 new functional limitations (eg, inability to bathe or dress independently),
 - A 3-fold increase in prevalence of moderate to severe cognitive impairment (from 6.1% before hospitalization to 16.7% after hospitalization)
 - High prevalence of mental health problems, including anxiety (32% of patients who survive), depression (29%), or posttraumatic stress disorder (44%).

Prescott et al. Enhancing Recovery From Sepsis: A Review. 2018 Jan 2;319(1):62-75

Surviving Sepsis

- About 40% of patients are re-hospitalized within 90 days of discharge, often for conditions that are potentially treatable in the outpatient setting
 - Such as infection (11.9%) and exacerbation of heart failure (5.5%).
- Compared with patients hospitalized for other diagnoses, those who survive sepsis (11.9%) are at increased risk of recurrent infection than matched patients (8.0%) matched patients ($P < .001$), acute renal failure (3.3% vs 1.2%, $P < .001$), and new cardiovascular events (adjusted hazard ratio [HR] range, 1.1-1.4).

Surviving Sepsis

- Objectives
 - What causes sepsis?
 - Once an individual recovers from sepsis, what will life be like?
 - How will an individual feel after going home?
 - What will be the recovery process?
 - Long term side effects of sepsis?
 - Is it possible to have sepsis again?

Definition

Normal Response to Infection:

- Host responds to an infection when immune cells (mainly macrophages) recognize and bind microbial components
- Causative pathogen replicates and releases microbial components such as endotoxin, exotoxin, and DNA, known as pathogen-associated molecular patterns
- The pathogen-associated molecular patterns bind the surface of host immune cells

Definition

Sepsis:

- Release of proinflammatory mediators in response to an infection exceeds the boundaries of the local environment
- Excessive proinflammatory cytokines spill into the bloodstream, causing the progression from normal host response of infection *to sepsis*
 - Results in cellular injury, tissue injury, and organ dysfunction
 - Example: respiratory failure, acute liver injury

Life After Sepsis

Survivors can expect a wide range of short or long-term effects:

- **Short term:** weakness, fatigue, kidney injury (could be long-term if renal function not improving, requiring dialysis)
- **Long term:** breathing difficulties if there is lung injury which is irreversible, cognitive changes, panic attacks/depression, amputation of limbs if there is disruption of blood flow

After going home expect:

- Weakness
- Easily fatigued
- Tired from even conversations
- Difficulty sleeping
- Nightmares
- Mood swings
- Feeling of wanting to be alone
- Angered quickly
- Feeling hopeless, anxious and depressed

These are normal responses to severe illness or trauma:

- Subside over time
- Ask the hospital, if there is support staff in a clinic to help after discharge

Recovery From Sepsis

In the months after hospital discharge for sepsis, management should focus on:

- Identifying new physical, mental, and cognitive problems and referring for appropriate treatment
- Reviewing and adjusting long-term medications
- Evaluating for treatable conditions that commonly result in hospitalization, such as infection, heart failure, renal failure, and aspiration.
 - For patients with poor or declining health prior to sepsis who experience further deterioration after sepsis, consider palliative care

Long Term Side Effects of Sepsis

Advances in intensive care medicine and goal-directed interventions, early 30-day sepsis mortality has diminished:

- There is a “steady escalation” in mortality after recovery from acute events
 - Due to alterations in cellular immune functions
 - Sepsis alters innate and adaptive responses, leading to immune suppression and chronic inflammation, which eventually leads to infectious complications, ultimately resulting in hospital re-admission

What needs to be done?

- More thorough and rigorous patient stratification and selection
- Strategic and thoughtful long-term monitoring of immune function
- Goal-directed immune modulatory therapy will, over time, provide optimal clinical benefit to those surviving initial sepsis.

Immunomodulators in Sepsis

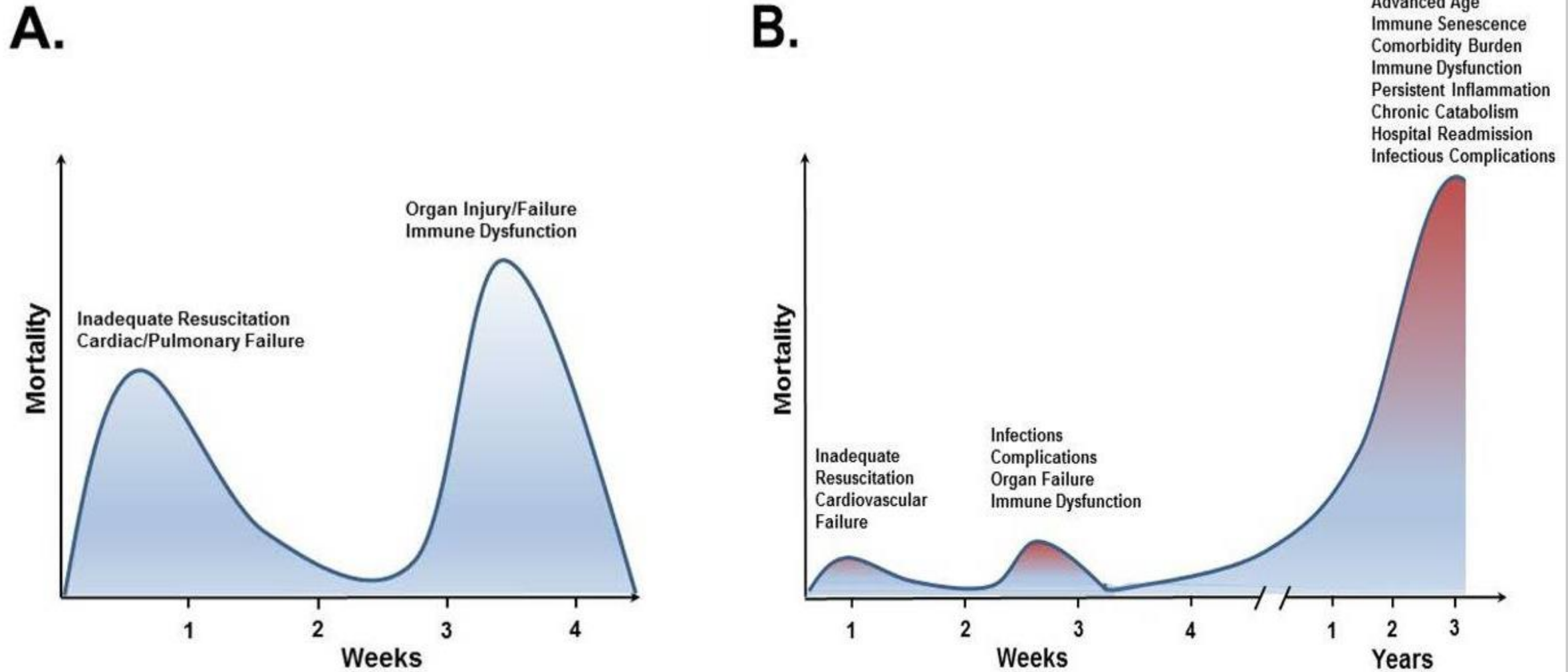
Immune Modulator	G-CSF	GM-CSF	IFN γ	PD-1 and PD-L1	IL-3	IL-7	IL-15
Cellular Benefit	Improve neutrophil and monocyte production and release	Improve neutrophil and monocyte production and function	Improve monocyte HLA-DR expression and function	Biomarker to identify candidates for immune modulatory therapy	Promote stem cell and progenitor development	Increase T cell proliferation and recruitment	Decrease NK, T cell, and NKT cell apoptosis
	Improve myelopoiesis and granulopoiesis	Enhance monocyte and lymphocyte cytotoxicity	Reduce infection and related complications	Reverse T cell exhaustion	Enhance lymphopoiesis in combination with IL-7	Decrease lymphocyte apoptosis	Increase NK, T cell, and NKT cell proliferation and activation
		Augment T cell responses	Improve immunity against fungal infections	Promote lymphocyte proliferation		Increase T cell IFN γ secretion	

Immunomodulators in Sepsis

Immune Modulator	Propranolol	Oxandrolone	Dronabinol
Benefit	Reduce inflammatory cytokine production Diminish muscle protein catabolism Improve 30 day survival	Improve weight loss Protect muscle mass, Reduce length of stay Minimize cachectic metabolism	Improve gut transit, Increase appetite Reduce TNF α production Reduce nitric oxide generation

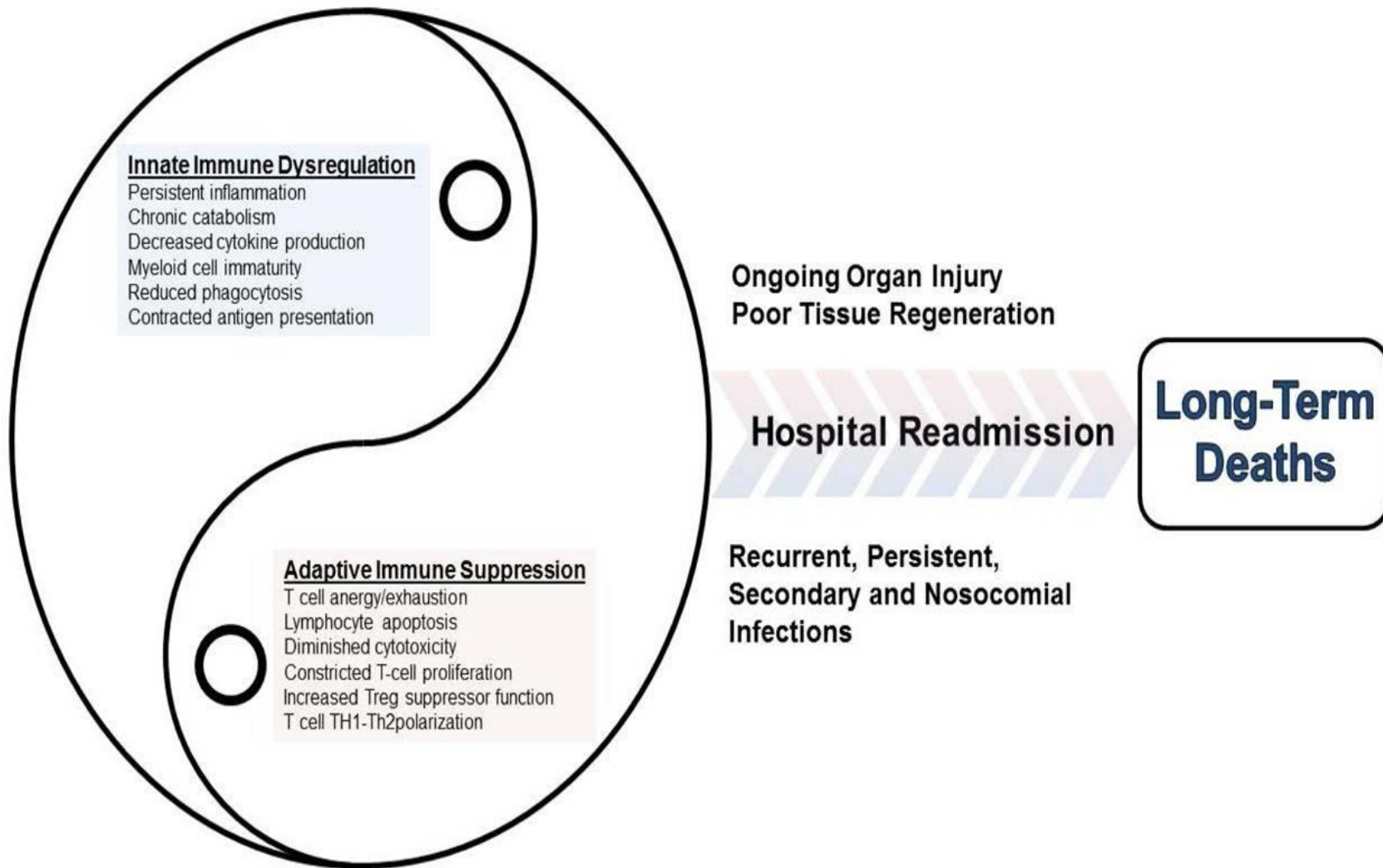
Delano et al. The Immune System's Role in Sepsis Progression, Resolution and Long-Term Outcome. [Immunol Rev.](#) 2016 Nov; 274(1): 330–353

Long-Term Side Effects of Sepsis



Delano et al. The Immune System's Role in Sepsis Progression, Resolution and Long-Term Outcome. *Immunol Rev.* 2016 Nov; 274(1): 330–353

Long-Term Side Effects of Sepsis



The perpetual state of immunologic yin and yang is thought to drive ongoing inflammation, facilitate organ injury, and enable infectious complications that all preclude durable sepsis survival.

Delano et al. The Immune System's Role in Sepsis Progression, Resolution and Long-Term Outcome. [Immunol Rev. 2016 Nov; 274\(1\): 330–353](#)

Is It Possible To Have Sepsis Again?

Yes! Due to immune dysregulation

More research underway how to balance the inflammatory and anti-inflammatory processes

Measures To Prevent Recurrence Of Sepsis

Improved Post-Discharge Processes:

- Sepsis readmissions are on the increase as more people survive sepsis
 - However, there are no existing standardized guidelines for the care of post-sepsis patient after discharge
- Physicians and others involved in the emergency care of sepsis patients must build post-discharge processes to reduce readmissions
 - For example, Philadelphia based Penn Medicine partnered with both home health services and skilled nursing facilities to ensure that patients safely transition from urgent care to post-acute care before returning home

<https://www.infectiousdiseaseadvisor.com/features/sepsis-recovery-requires-an-all-hands-approach>

Measures To Prevent Recurrence Of Sepsis

All Hands Approach to Post-Sepsis Care:

- Post-sepsis patients benefit most from a post-discharge protocol that combines follow-up appointments with both a physician and a nurse
- Patients who saw both a doctor and a home health nurse after sepsis were significantly less likely to need to be readmitted to the hospital
- Home health nurses were more likely than doctors to spot potential complications triggered by conflicting medications, signs of infections, or problems in the home environment before they had begun to seriously impact the patient's health

Measures To Prevent Recurrence Of Sepsis

Better Education on Sepsis for Patients and Caregivers:

- Patients and caregivers need to be made aware that an individual who had sepsis is susceptible to recurring or new infections which can rapidly become serious

Measures To Prevent Recurrence Of Sepsis

Rehabilitation Referrals:

- An observational study of 30,000 sepsis cases conducted by the University of Michigan and the University of Pennsylvania revealed that a referral to rehabilitation within 90 days of discharge from the hospital was correlated with a *lower 10-year mortality risk*
- Physical therapy and other rehabilitative treatments not only help keep patients alive; they also help to identify and treat the many serious side effects of sepsis in the weeks and months post-discharge
 - Sepsis survivors may experience severe cognitive impairment, anxiety, depression, and PTSD, as well as physical symptoms such as recurring infections and exacerbated heart failure
 - A study suggests that many of these symptoms could be effectively treated without the need for hospitalization if caught early enough by a rehabilitation treatment program

Physical therapy could also help patients recover functional mobility more quickly, reduce the risk of falls caused by cognitive impairment, and help patients deal with the day-to-day activities affected by post-sepsis complications.

Thank you and any questions!



References

- Delano et al. The Immune System's Role in Sepsis Progression, Resolution and Long-Term Outcome. [Immunol Rev.](#) 2016 Nov; 274(1): 330–353.
- <https://www.endsepsis.org/what-is-sepsis/surviving-sepsis>
- Long-term mortality and quality of life after septic shock: a follow-up observational study. Nessler N, Defontaine A, Launey Y, Morcet J, Mallédant Y, Seguin P . Intensive Care Med. 2013 May;39(5):881-8. Epub 2013 Jan 29.
- Prescott et al. Enhancing Recovery From Sepsis: A Review. 2018 Jan 2;319(1):62-75
- Wang et al. Subsequent Infections in Survivors of Sepsis: Epidemiology and Outcomes. [J Intensive Care Med.](#) 2014 Mar-Apr; 29(2): 87–95.