

Sepsis and Septic Shock

DRIP 3

December 15, 2021

Instructor: Dr. Christopher G. Byers, DVM, DACVECC,
DACVIM (SAIM), CVJ

© 2021 Drip Learning Technologies LLC.

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without permission in writing from the copyright owner. Printed in the United States of America

Be advised this document is here to enhance your learning experience and is a cumulative of the slides and transcript & area for your notes. You are welcome to take your notes electronically or print then use it to supplement your learning while watching the drip

Neutrophils



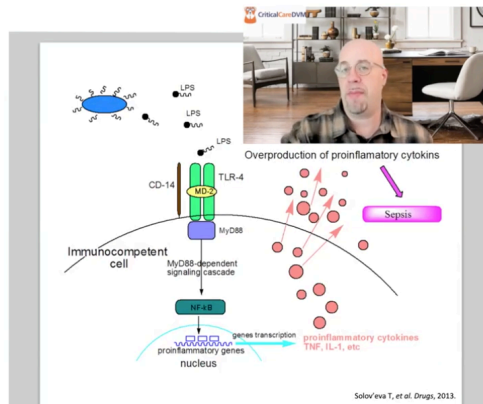
NETs

- Composed of filamentous DNA, histones, granular antimicrobial proteins, proteases
- Trap/kill pathogens – oxidative vs. non-oxidative mechanisms
- Activate factor XII via their negative charge
- DNA & histones involved in fibrin formation
- Inhibit fibrinolysis through blockade of plasminogen activator binding sites

Express TF

Neutrophils are really unique cells. And so through a process that we call NETs osis, these neutrophils shootout strands of DNA, and histones, that can trap and kill pathogens through oxidative and non-oxidative means. But these NETs contribute to pro coagulation and hyperfibrinolysis through activation of factor XII, through fibrin information itself. And through inhibition of fibrinolysis.

- LPS released & binds to LPS binding protein (via lipid A portion)
- LPS recognized by cell surface receptor (i.e.: CD14)
 - Epithelial cells, macrophages, neutrophils, endothelial cells
- CD14 transfers LPS to TLR-4 and MD-2 for cellular activation
- LPS binding to cell surface receptor activates cell
- Most common organisms:
 - *Escherichia coli*



So let's take a practical example, gram negative sepsis, a gram negative bacteria. Remember they have lipopolysaccharide in their outer membrane. In circulation, LPS, lipopolysaccharide binds to the lipopolysaccharide binding protein. And this complex gets recognized by a cell surface receptor called CD14. CD14 transfers that complex to toll-like receptor 4, TLR-- in that process, that step, activates the cell.



Gram Positive Sepsis

Peptidoglycan

- Contains lipoteichoic acid
- Less potent than endotoxin
- Causes release of proinflammatory cytokines

May be derived from

- Skin
- Soft tissue
- IV catheters

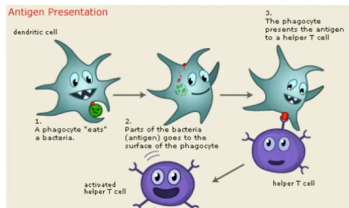
Most common organisms

- *Enterococcus* spp.
- *Staphylococcus* spp.
- *Streptococcus* spp.

Now obviously gram positive bacteria, can cause sepsis too, but lipopolysaccharide is obviously not involved. But we do have some of the other bacterial components involved like lipoteichoic acid. But gram positive bacteria interact with their own toll-like receptors. Then interacting typically with toll-like receptor 4, they have their own and that stimulation will trigger a similar cascade of pro-inflammatory events.

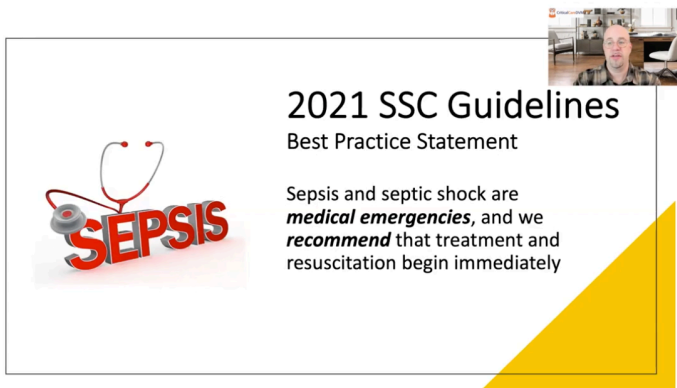
Adaptive Immunity

- Antigen-presenting cells ingest pathogen
- Naive T cells proliferate
- Effector cells are generated
 - Th1 - TNF, IL-2, IL-12, IFN- γ
 - Th17 - IL-17A
 - Th2 - IL-4, IL-5, IL-9, IL-10, IL-13



And so we have activation of cytokine production. We have initiation of inflammatory response, but we also ultimately will stimulate adaptive immunity. So dendritic cells ingest pathogens by recognizing those PAMPs. And then once a pathogen gets phagocytosed, there's an upregulation in expression of those MHC class II molecules that we learned about in immunology.

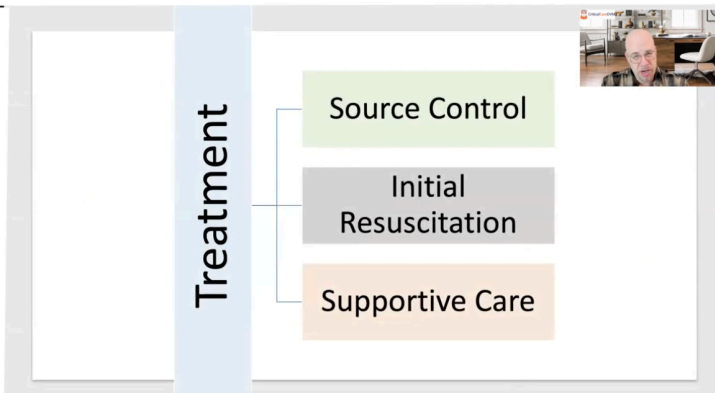
But we also get upregulation of several co-stimulatory molecules that are required for T cell activation. Things like CD40 and B7. The dendritic cells fully mature, and they move from the tissue to lymph nodes. What do they do there? They encounter and activate T cells.



The slide features a graphic on the left with a red stethoscope and the word "SEPSIS" in large, bold, red 3D letters. To the right, the text reads: "2021 SSC Guidelines Best Practice Statement" followed by "Sepsis and septic shock are **medical emergencies**, and we **recommend** that treatment and resuscitation begin immediately". A small video inset in the top right corner shows a man speaking. A yellow triangle is in the bottom right corner of the slide.

So that's it for about the physiology. Now we get to move on to the stuff that you've been waiting for, which is treating a patients, hopefully so that we can get them home to their families. And no matter any of the details about which we're going to discuss, we have to keep in mind two very simple basic premises.

Number 1, sepsis and septic shock are true medical emergencies. You drop everything and you start intervening with them, no matter how inconvenient it is, because to it is imperative-- that we begin treating these patients immediately and appropriately.



And when I think about treating my septic patients, I categorize my interventions as source control, initial resuscitation. And lastly, all the other important supportive interventions that these patients need to maximize the likelihood of a positive outcome.

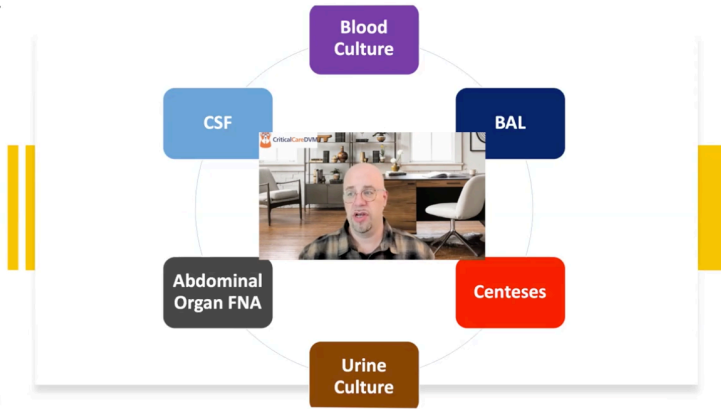
Source Control



- A specific anatomic diagnosis of infection should be identified or excluded as rapidly as possible
- Implement ASAP after the diagnosis is made
- Appropriate routine microbiologic cultures should be obtained before starting antimicrobial therapy
 - Doing so should not delay start of antimicrobial

Remember the first step is, source control. Find out the origin of your patient's problem. Is it the urinary tract? Is it a bacterial translocation event from the gastrointestinal tract? Wherever it is, figure it out as soon as possible.

And as soon as you suspect or have confirmed you have a septic patient or one in septic shock, find the source and control it. Get those culture samples before starting antimicrobial therapy. As long as taking that step, doesn't delay antimicrobial therapy meaningfully.



And sometimes you're going to have to think outside the box. You're going to have to do more than a urine culture. You may have to sample third space fluids. You may have to evaluate through the spinal fluid, or fluid from the lungs.

Most of the time, sampling is going to be non-invasive or minimally invasive. But I would be negligent if I didn't tell you every once in a while. You're going to have to use invasive techniques to figure out the source of infection and control it.

Usefulness of whole blood, plasma, peritoneal fluid, and peritoneal fluid supernatant glucose concentrations obtained by a veterinary point-of-care glucometer to identify septic peritonitis in dogs with peritoneal effusion

2015 *J Am Vet Med Assoc* prospective study of 39 dogs (Koenig A, *et al*)

POC glucometer used to evaluate heparinized whole blood (WB), plasma (P), peritoneal fluid (PF), & peritoneal fluid supernatant (PFS)

• WB-PF vs. P-PF vs. P-PFS

>20 mg/dL difference for WB-PF was insensitive (sens: 41.2%, spec 100%)

P-PF & P-PFS were more sensitive (88.2% & 82.4%, respectively) but had lower specificity (80%, 77.8%, respectively)

Cut-off = 38 mg/dL resulted in improved specificity, positive predictive value, and accuracy of P-PF & P-

Now classic example, is gastrointestinal sepsis. That's caused peritoneal effusion. And so you can very simply measure and compare glucose in both the peritoneal fluid and blood. And based on this more recent study out of the University of Georgia, by Koenig and colleagues.

Using plasma and a cutoff value of 38 milligrams per deciliter-- not 20 but 38, had the highest sensitivity.

SSC 2021 Guidelines – Best Practice Statement

For adults with suspected sepsis or septic shock but unconfirmed infection, we **recommend** continuously re-evaluating and searching for alternative diagnoses and discontinuing empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected

For adults with sepsis or septic shock, we **recommend** rapidly identifying or excluding a specific anatomical diagnosis of infection that requires emergent source control and implementing any required source control as soon as medically and logistically practical.



So again, here from the most recent surviving sepsis guidelines, best practice statements are essentially summarized by find the source and control it as quickly as possible.



POLL QUESTION #2

True or false-- patients with sepsis and septic shock, should never be taken to surgery for source control?