



What's up, What's down? Identifying signs of sepsis

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Disclosure belangen spreker	
(potentiële) Belangenverstrengeling	Geen / Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven¹	Bedrijfsnamen
• Sponsoring of onderzoeksgeld² ☐ Honorarium of andere (financiële) vergoeding³ ☐ Aandeelhouder⁴ ☐ Andere relatie, namelijk ...⁵	-Adviesraad: Boehringer Ingelheim, Vifor Pharma -Spreker: Pfizer



Wat gaan we bespreken?

- Vroegtijdig identificeren van patiënten at risk
- Vroegtijdig herkennen van sepsis
- Toepassingen van de sepsis richtlijnen (bij kankerpatiënten)
- Behandelen van sepsis of septische shock
- Nieuwe definities van sepsis
 - Waarom definitie verandering?
 - Wat is er veranderd?





CANCER IS A FIGHT.
DON'T LET THE FLU KNOCK YOU DOWN.

EMERGENCY ROOM PERSONNE

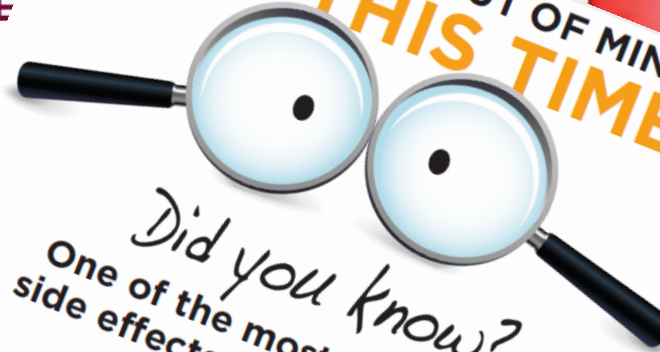
This is especially true for a cancer patient undergoing chemotherapy who develops a fever.

Get the full picture about people with cancer who are receiving chemotherapy.

If they have a fever, remember—

1. A fever may be the only sign of infection and should be treated as an emergency.
2. Developing an infection is a life-threatening complication.
3. A minor infection can turn serious fast. Quick action can save a life.

OUT OF SIGHT, OUT OF MIND...
NOT THIS TIME!



Did you know?
One of the most dangerous side effects of chemotherapy cannot be seen?

That's right, a low white blood cell count, or neutropenia, puts cancer patients at a higher risk for getting an infection.

An infection in people with cancer is an emergency. Be prepared, and remember the following three things during chemotherapy:

1. Treat a fever as an emergency, and call your doctor right away if you develop a fever.
2. Find out from your doctor when your white blood cell count will be the lowest because this is when you are most at risk for infection.
3. If you have to go to the emergency room, it's important that you tell the person checking you in that you have cancer and are receiving chemotherapy. If you have an infection you should not sit in the waiting room for a long time. Infections can get very serious in a short amount of time.

National Center for Chronic Disease Prevention and Health Promotion
Division of Cancer Prevention and Control
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Learn more at: www.cdc.gov/cancer/preventinfections



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IT BACK!
OUR FLU SHOT

on to protect yourself against the flu,
n focus on the fight that matters most.

s for people who have cancer,
e-two punch this season:

t—not the nasal spray vaccine.

a people you live with or who care for you
not too.

*shot is your best protection
against the flu this season.*



Learn more at: www.cdc.gov/cancer/preventinfections

National Center for Chronic Disease Prevention and Health Promotion
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This program was made possible through a CDC Foundation partnership with, and funding from, Amgen.

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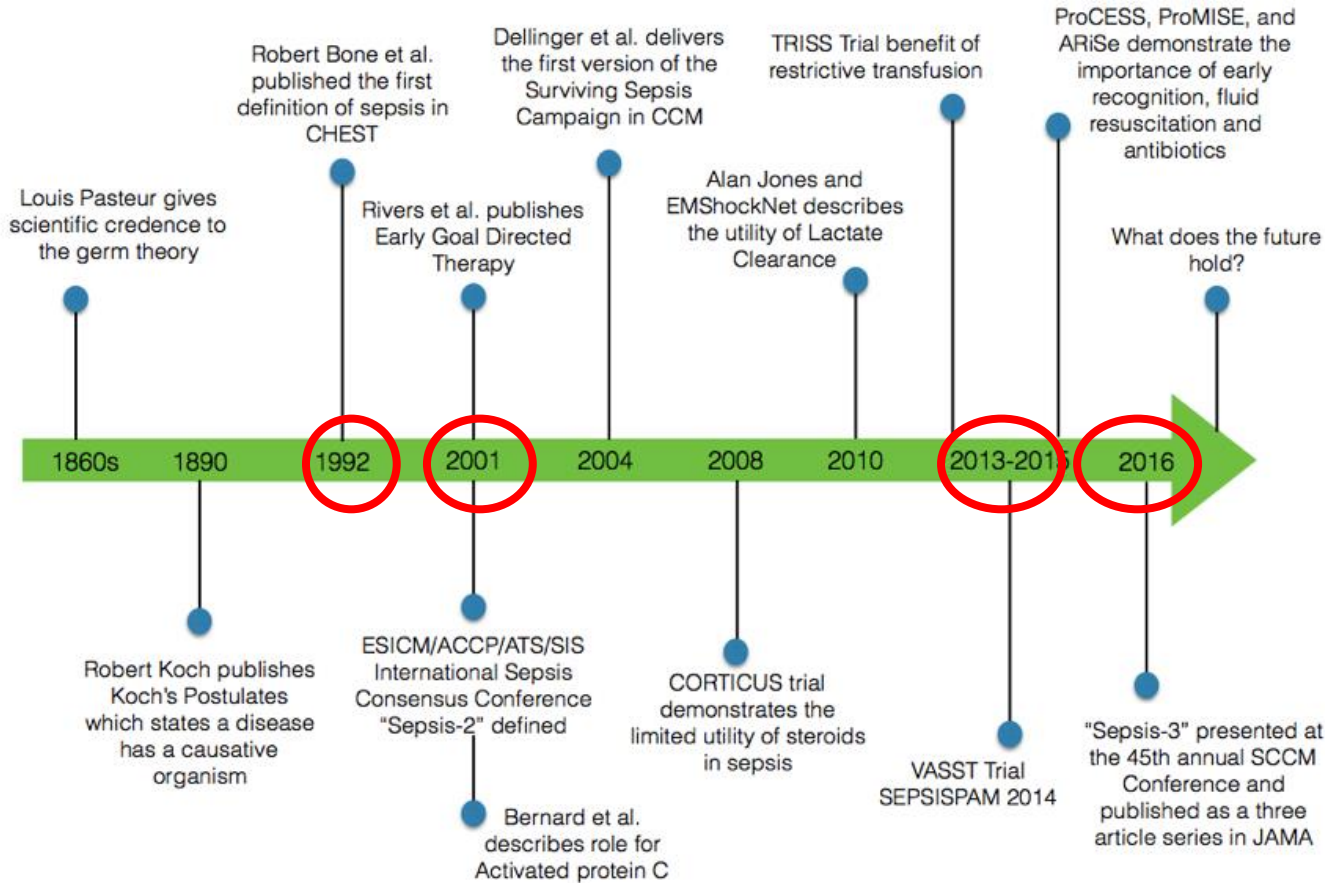


Sepsis statistieken

- In NL op IC: doodsoorzaak nr. 1
- < 1^e 4 uur behandeld: overlevingspercentage >50%. Daarna daalt de overlevingskans snel.
- 3^e oorzaak van overlijden in de wereld, meest gangbare oorzaak van niet-maligne dood in de oncologie^{1,2}
- Komt bij 14% van de kankerpatiënten voor^{1,3,4}
- Mortaliteit bij kankerpatiënten 30-40%, hoger dan bij andere populaties
- 22% ongeplande opnames (SKCCC John Hopkins in Baltimore)

1. Baden, R., Swaminathan, S., Angarone, M., Blouin, G., Camins, B.C., Casper, C., ... Wilson, J.W. (2017). *Prevention and treatment of cancer-related infections, version 2.2017*, Retrieved from www.nccn.org, on February 28, 2017. 2. Mariotte, E., Canet, E., Debrumetz, A., Lemiale, V., Seguin, A., Darmon, M., Schlemmer, B., & Azoulay, E. (2012). *Survival in neutropenic patients with severe sepsis or septic shock*. *Critical Care Medicine*, 40(1), 43-49. 3. Mokart, D., Saillard, C., Sannini, A., Chow-Chine, L., Brun, J.P., Faucher, M., Blache, J.L., Blaise, D., Leone, M. (2014). *Neutropenic cancer patients with severe sepsis: need for antibiotics in the first hour*. *Intensive Care Med*, 40 (8), 1173-1174. 4. Young, R.S., Gobel, B.H., Schumacher, M., Lee, J., Weaver, C., Weitzman, S. (2014). *Use of the modified early warning score and serum lactate to prevent cardiopulmonary arrest in hematology-oncology patients: a quality improvement study*. *American Journal Medical Quality*, 29(6), 530-53.

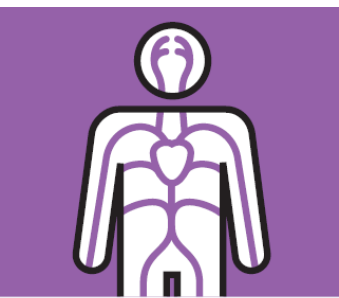
Het verleden



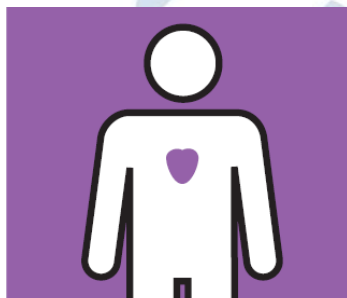
Vroegtijdig herkennen van patiënten at risk.



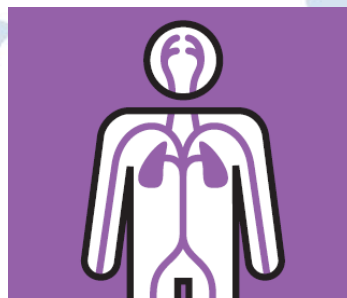
- Systemic Inflammatory Response Syndrome (SIRS) is two or more of the following: Temp $>38.3^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, HR >90 , RR >20 , WBC >12 or <4 K/cu mm or $>10\%$ bands



Systolische bloeddruk <90 en >200 mmHg



Hartritm <40 en >130 slagen per minuut



Zuurstofsaturatie $<90\%$



Ademhalingsfrequentie <8 en >30 per minuut



Bewustzijnsverandering



Oude definitie: sepsis

Sepsis: ≥ 2 SIRS-verschijnselen met verdenking op of aanwijzing voor infectie.

SEPSIS

- Two SIRS criteria PLUS a known or suspected bacterial, viral, or fungal infection





Oude definitie: ernstige sepsis

Hiervan is sprake, wanneer naast sepsis ook nog aanwijzingen zijn voor een acute stoornis in de functie van één of meerdere organen zoals:

- Hypoxie
- Hypotensie (systolische bloeddruk < 90 mm Hg, MAP < 70 mm Hg of een daling van de systolische bloeddruk met meer dan 40 mm Hg ten opzichte van de vorige waarde of een systolische bloeddruk $< 10^{\text{de}}$ percentiel voor de leeftijd)
- Tekenen van hypoperfusie (lactatacidose, oligurie, veranderd bewustzijn)

SEVERE SEPSIS

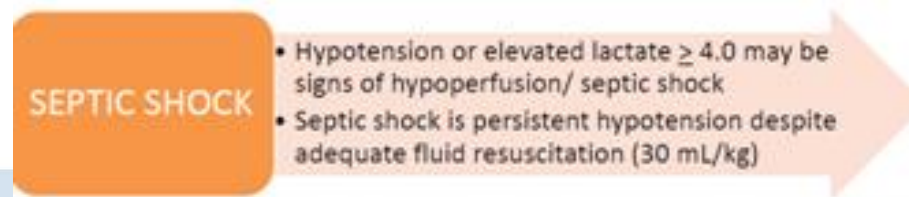
- Sepsis + at least one sign of end organ dysfunction- altered mental status, decreased urinary output, thrombocytopenia, lactate > 2.0 , systolic blood pressure (SBP) < 90 or mean arterial pressure (MAP) < 65 , prior to fluid resuscitation





Oude definitie: Septische shock

- Sepsis geassocieerd met hypoperfusie, orgaanfalen of hypotensie die niet herstelt na volumetoediening, zodat er voor de behandeling vasopressoren nodig zijn.



Orgaandysfunctie

Signs & symptoms

- Veranderde mentale status
- Verminderde urineproductie
- Capp refill > 3 sec.
- Vlekken
- Toename gewicht >20 ml/kg
(ongeveer 2 kg in 2 voorgaande dagen)

Labwaarden

- Bilirubin > 2 mg/dl
- Creatinine > 2.0 mg/dl
- Glucose > 140 mg/dl w/o diabetes
- Hypoxemia requiring BiPAP
- INR ≥ 1.5
- Lactate > 2.0 mmol
- Platelets < 100,000/mm³



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Labwaarden

- Bilirubine

Lactaat is een marker voor de mate van weefseloxygenatie. Bij zuurstoftekort zal er veel lactaat gevormd worden.



Where does febrile neutropenia fit?

Even though this uses 38.3°C, oncology resources^{1,6} recommend 38.0°C X 2 within one hour

SIRS

- Temp >38.3 C or <36 C, HR >90, RR >20, WBC >12 or <4 K/cu mm or >10% bands

SEPSIS

- SIRS + Infection

SEVERE SEPSIS

- Sepsis + End Organ Damage or SBP <90 or MAP <65, prior to fluid resuscitation

SEPTIC SHOCK

- Severe Sepsis Hypotension refractory to fluids

Patients with neutropenia are escalated to at least sepsis

Definitie: Leukopene koorts

- Sepsis bij hematologische/oncologische patiënten met :
 - leukopenie $< 1 \times 10^9/l$ en/of granulocyten $< 0,5 \times 10^9/l$.
 - $T > 38.3$
- De meest voorkomende verwekkers (bij adequate SDD) zijn:
 - grampositieve micro-organismen (60-70%); stafylokokken, streptokokken, enterokokken en *Corynebacteria*.
 - Soms gisten (*Candida*), schimmels (*Aspergillus*), opportunisten
 - gramnegatieve bacteriën, zoals *Pseudomonas spp.*, *E. coli*, *Klebsiella-spp.*
- Mucositis en i.v.-of Port-A-Cath-katheter zijn sterk predisponerende factoren.
- Hematologische patiënten hebben meestal SDD, oncologische patiënten hebben meestal geen infectieprofylaxe.

Screeningsinstrumenten

Screening Ernstige Sepsis

3 keer "JA" is ernstige sepsis:

- 1 Is er verdenking op een (nieuwe) infectie?
 - 2 Zijn ≥ 2 symptomen aanwezig?
 - a. Ademfrequentie $> 20/\text{min}$ (of $\text{pCO}_2 < 4,3 \text{ kPa}$)
 - b. Hartfrequentie $> 90/\text{min}$
 - c. Veranderd bewustzijn/delirium
 - d. Temperatuur $> 38,0$ of $< 36,0 \text{ }^\circ\text{C}$
 - e. Koude rillingen
 - f. Leukocyten > 12 of $< 4 \times 10^9/\text{l}$
 - g. Glucose $> 6,8 \text{ mmol/l}$ in afwezigheid van diabetes
 - 3 Is orgaanfunctie aanwezig (en niet chronisch bestaand)?
 - a. Zuurstofbehoefte 5 Ltr O_2 of meer om $\text{SaO}_2 > 90\%$ te houden
 - b. Bloeddruk (syst) $< 90 \text{ mmHg}$ of $> 40 \text{ mmHg}$ gedaald
 - c. Lactaat $> 2 \text{ mmol/l}$
 - d. PT $> 20 \text{ sec}$ of APTT $> 60 \text{ sec}$
 - e. Trombocyten $< 100 \times 10^9/\text{l}$
 - f. Bilirubine $> 35 \text{ } \mu\text{mol/l}$
 - g. Kreatinine $> 150 \text{ } \mu\text{mol/l}$ of diurese $< 0,5 \text{ ml/kg/u}$
- Overleg met zaalarts; informeer zo nodig het MET
 - Start zo snel mogelijk met de resuscitatiebundel en registreer de uitvoering hiervan op het sepsisformulier.

Resuscitatiebundel Ernstige Sepsis

- Meet lactaat (als dat nog niet gedaan is)
- Neem direct 2 bloedkweeken af en kweek andere verdachte foci
- Geef antibiotica ($< 1 \text{ uur}$) volgens beleid Radboudumc
- Geef bij hypotensie / lactaat $> 4 \text{ mmol/l}$: fluid challenge (b.v. $500-1000 \text{ ml NaCl } 0,9\%$ in 30 min.)
- Streef na:
 - bloeddruk (syst) $> 90 \text{ mmHg}$,
 - diurese $> 0,5 \text{ ml/kg/u}$,
 - $\text{SaO}_2 > 90\%$

december 2014_v2.4

Modified Early Warning Score (MEWS) en referentiewaarden

Alarmsignalen bij vitaal bedreigde patiënt

Score		3	2	1	0	1	2	3
A	O ₂ -toediening				buitenlucht	< 5l O ₂ /min	≥ 5l O ₂ /min	
	SaO ₂ %	≤ 91	92-93	94-95	≥ 96			
B	Ademfrequentie	≤ 8		9-11	12-20		21-24	≥ 25
C	Hartfrequentie	≤ 40		41-50	51-90	91-110	111-130	≥ 131
	Bloeddruk (syst)	≤ 90	91-100	101-110	111-219			≥ 220
D	Bewustzijn				A		delirium	V/P/U
E	Temperatuur	≤ 35,0		35,1-36,0	36,1-38,0	38,1-39,0	≥ 39,1	

- MEWS 0,1 of 2 : controleer vitale waarden 1 x per 8 uur.
- MEWS 3,4,5 of ongerust : controleer vitale waarden 1 x per 4 uur . Overleg met collega verpleegkundige/zaalarts
- MEWS 6 of meer : controleer vitale waarden 1 x per uur, overweeg continue monitoring. Overleg met zaalarts $< 10 \text{ min.}$ Informeer zo nodig het MET

A = alert V = reactie op aanspreken P = reactie op pijn U = geen reactie Denk aan sepsis z.o.z.

MET (Medical Emergency Team) - toestel 77777, b.g.g. 90000

Radboudumc

Risicoscore Febriële Neutropenie

MASCC score

Tabel 1. Risicofratiatiemodell van 'The Multinational Association for Supportive Care in Cancer'.¹⁵

Kenmerk	Punten
leeftijd <60 jaar	2
poliklinische behandeling	3
klinische status bij presentatie: • geen of milde klachten • matig ernstige klachten	5 3
geen hypotensie (systolische bloeddruk >90 mmHg)	5
geen dehydratie (waarvoor intraveneuze suppletie)	3
co-morbiditeit • geen COPD • solide maligniteit of hematologische maligniteit zonder voorgaande invasieve schimmel- of gistinfectie	4 4
Indien een kenmerk aanwezig is, worden punten toegekend. Bij een totaalscore >20 geldt de patiënt als laag risico (<10%) op het ontwikkelen van ernstige medische complicaties gedurende de neutropene fase.	
COPD=chronic obstructive pulmonary disease.	

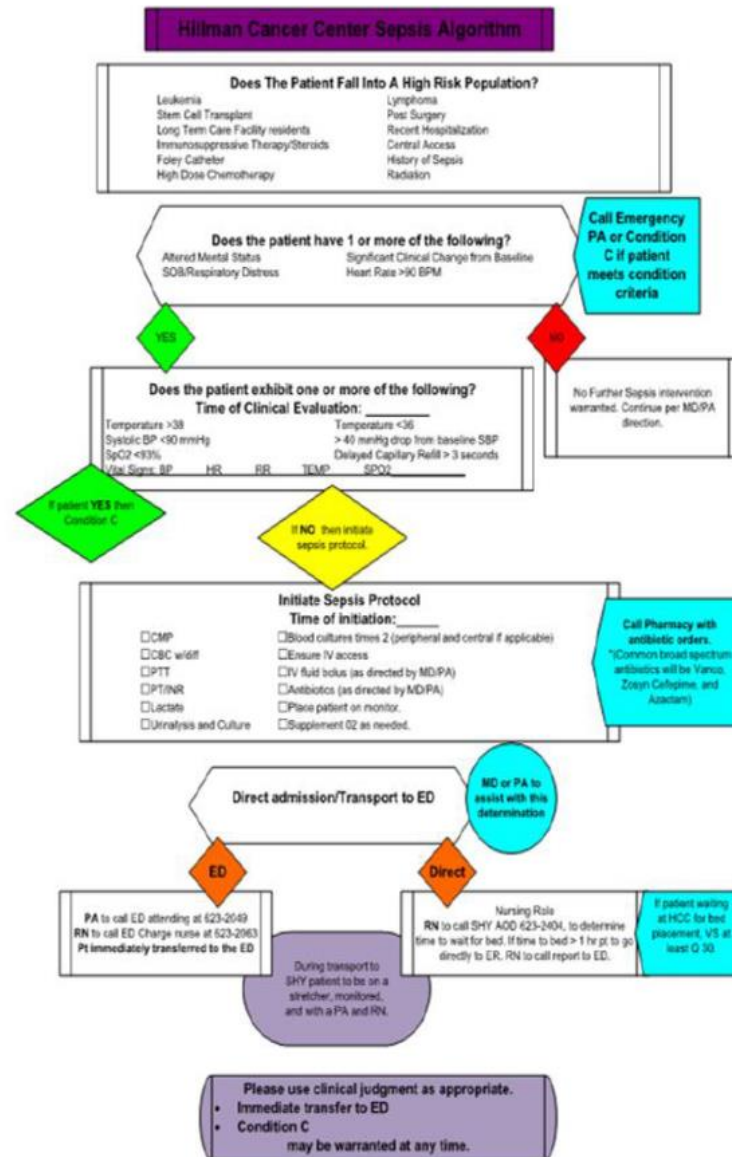


Overzichtstabel aangaande risico op febrile neutropenie bij chemotherapie behandeling

Febrile neutropenie (%)	Graad 3-4 neutropenie (%)	Schema (mg/m ² , tenzij anders aangegeven)	Chemotherapie	Referentie nr.
Borstkanker				
2	—	600/(40/600) ¹¹⁻⁸ Q3W	CMF	2
0-2	25-84	500/90-100/500 Q3W	FEC 90/100	4,5
9-14	86-94	(500/60) ¹¹⁻⁸ /75 ¹¹⁻¹⁴ Q4W	FEC 120	3,6
10-20	—	60/600 Q3W	AC	7
16-17	77	100 Q3W	Doc	7,8,9
25	> 88	(60/600-100) Q3W	AC-T	7,10
33-48	61-97	50/75 Q3W	A doc	11,12
21-32	89-91	60/125-200 Q3W	AT	7,13,14
25	66	75/50/500 Q3W	TAC	7,15
Lymfomen				
4	19	(25/10/6/375) ¹¹⁻¹⁵ Q4W	ABVD HD	16
20.8	—	375/(750/50/1.4) ¹⁵ /100 mg ¹⁵⁻⁷ Q3W	R-CHOP-21 NHL	38
31	> 53	100/2 x 2,000 ¹² /40 mg ¹¹⁻⁴ Q3W-Q4W	DHAP NHL	7,18
Niet-kleincellig longkanker				
5-11	69-75	75/75 Q3W	Doc/Cis	19,26
1-7	17-64	1.250 ¹¹⁻⁸ /75-100 Q3W	Gem/Cis	20,21
1-10	43-81	25 ¹⁰ /100 Q4W	Vin/Cis	21,22,23
< 5	14-63	175-225/AUC6 Q3W	Pac/Cb	21,24,26
16	75	135/75 ¹² Q3W	Pac/Cis	7,26
26	> 73	75/AUC6 Q3W	Doc/Cb	7,27
54	86	(200/35) ¹¹⁻³ Q4W	Etop/Cis	28
Kleincellig longkanker				
9	47	200/AUC6 Q3W	Pac/Cb	29
10-20	—	100 ¹¹⁻³ /300 Q3W	Etop/Cb	7
19	76	0,75 ¹¹⁻⁵ /60 Q3W	Top/Cis	7,30
57	—	50/1,000/120 ¹¹⁻³ Q3W	ACE (=CDE)	7,31
28	88	1,5 ¹¹⁻⁵ Q3W	Top	7,32
Ovariumkanker				
3-8	37-72	175-185/AUC5-6 Q3W	Pac/Cb	33,34
10-18	82-97	1,5 ¹¹⁻⁵ Q3W	Top	7,35,36,37
33	78	135 Q3W	Pac	7,39

• (R-)CHOP-14 dient altijd ondersteund te worden met G-CSF (Neulasta®)

VS: sepsis algoritme





Surviving Sepsis Campaign

Johns Hopkins in Baltimore



Dellinger, R.P., Levy, M.M., Rhodes, A., Annane, D., Gerlach, H., Opal, S.M..... The Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. (2013). Surviving Sepsis Campaign: **International Guidelines for management of severe sepsis and septic shock, 2012.** *Intensive Care Medicine*, 39, 165-228.





Implementeren richtlijnen sepsis bij kankerpatiënten: een uitdaging!

- Exclusie bij meeste studies
 - Kanker
 - CHF
- Variabiliteit in meten
- Meerdere verstoringen lactaat
 - Maligniteit
 - Dehydratie of hypoperfusie
- 7% -15% mortaliteit reductie
- Patiënten ontvangen niet overal dezelfde zorg
 - ‘Time zero’ is moeilijk vast te stellen
 - Niet overal goede sepsis management
 - Tijdig starten
ANTIBIOTICUM is lastig





Surviving Sepsis Recommendations

1^e 6 uur

3 uur

- Screen for sepsis- first encounter/ triage, defined intervals
- Blood cultures + lactate if positive screen
- Assess organ function
- First antimicrobial dose within 60 min of triage
- Oxygen if O₂ sat < 90%
- Fluid bolus *at least 30 mL/kg if hypotensive*

6 uur

- Assessment of source
- MAP $\geq$ 65 mm Hg
- Vasopressors initiated within 6 hr if persistent hypotension
- CVP line- goal 8-12 mm Hg
- Central venous oxygen saturation (ScvO₂) $\geq$ 70%
- Urine output $\geq$ 0.5 mL/kg/hr





Sepsis aanbevelingen

1^e 24 uur

- Indications:
 - Severe sepsis or septic shock OR
 - Persistent hypotension OR
 - hyperlactemia (≥ 4.0 mmol/L)
- Low volume ventilation/plateau pressures < 30 mm
- Glucose goal < 180 mg/dl
- Gastric Ulcer prophylaxis
- Venous thromboembolism (VTE) prophylaxis
- Low dose steroids for patients with hypotension*



Hoe richtlijn te implementeren

Strategy	Pro	Con
Focused Education ¹⁸	Easy answer Easy to perform	Knowledge retention inconsistent Staff turnover
Protocols, policies, algorithms ¹⁹⁻²⁴	Summarization complex literature Familiar structure	Accessibility when and where needed Complexity
Structured pre-printed or electronic orders ^{17,19-28}	Guide prescribers to choose correct EBP interventions	Requires recognition of need to activate May lead to over-treatment
Unit based Champions/ super-users ²⁹	Solutions within the unit culture Peer to peer influence	Labor-intensive Champions may not always be present/available
Rapid Response activation with protocols ²¹	High activation rates (crying wolf) Standardization/frequent usage	Resource intensive
Combined interventions ^{23,30-35}	Proven most effective Targets different learning styles/ locus of motivation	Resource intensive for integration

Largest Threat to Effective Implementation

Recognizing the
septic patient early

BUT...

Oncology may require
revised screening processes
OR anticipate many false
positive alerts



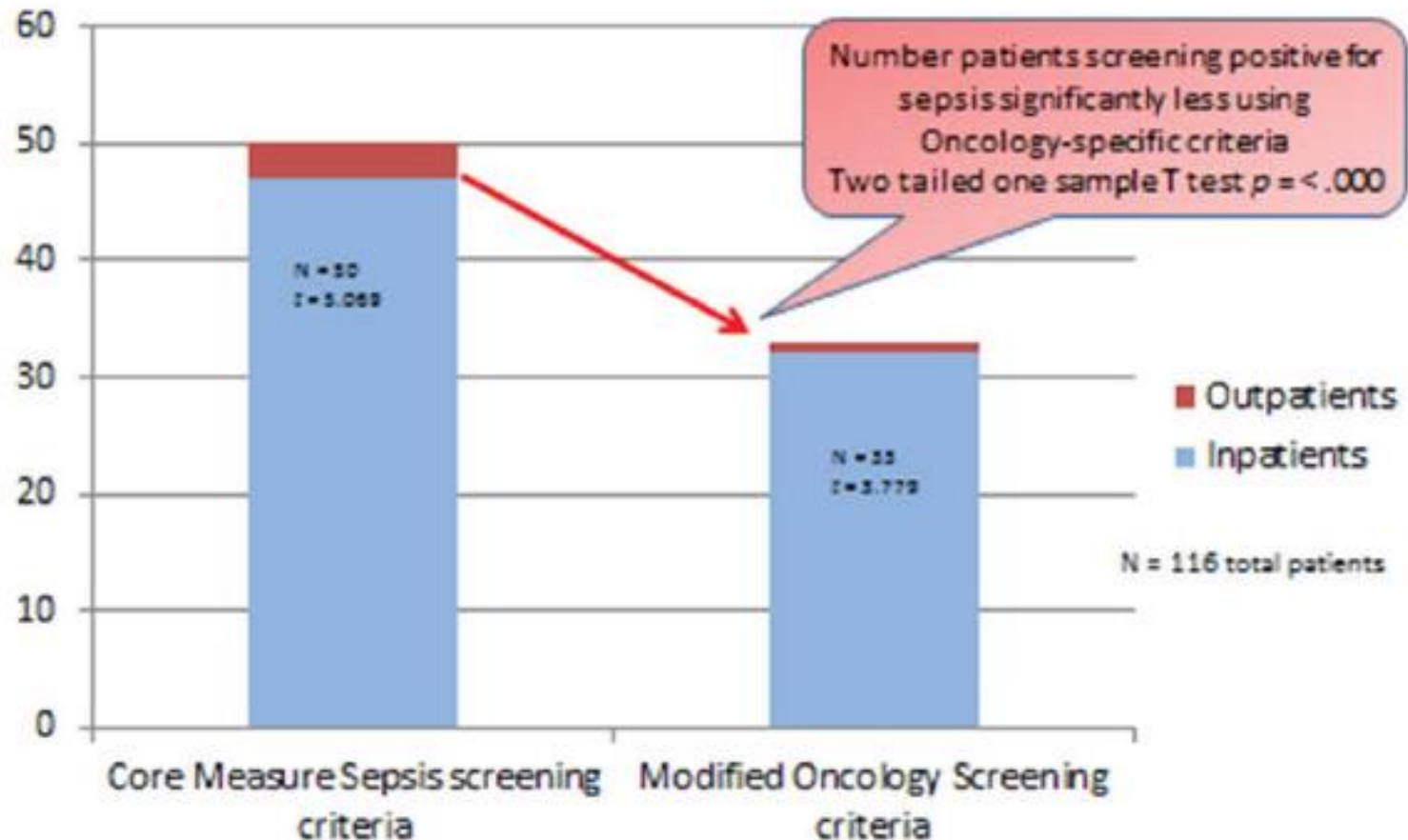
Johns Hopkins Baltimore

Revised sepsis criteria

Parameter	Surviving sepsis	JHH
Temperature (T)	T < 36.0C or > 38.3C	T < 35.5C (without symptoms) or > 38.0C ^{1,36,37}
Heart rate (HR)	HR > 90/min	HR > 100/min ^{37,38}
Respirations (RR)	RR > 20/min	RR > 20/min
Blood pressure (BP)	Systolic BP < 90 mm or > 40 mm drop from baseline, OR MAP < 65 mm	Systolic BP < 90 mm or > 40 mm drop from baseline, OR MAP < 65 mm
WBC	< 4000/mm ³ or > 12,000/mm ³ , or > 10% bands	< 4000/mm ³ or > 12,000/mm ³ , or > 10% bands neutropenia ^{1,38}
Other	None	Glucose > 140 mg/dl in absence of diabetes ^{5,36} Altered mental status ^{5,36,38,39} Mottling ^{5,36-38}

Vershil in screen Positive patiënt

No missed cases true sepsis



Critical sepsis intervention tracking

To be done within 3 hours of Time Zero			
Vitals: Increase frequency of VS to Q2hrs x 3, unless ordered more frequently			
			
Lactate level collected within 3 hours of start time	Cultures obtained before giving antibiotics	Fluid bolus (30 mL/kg) given as ordered if hypotensive or lactating > 4 mmol/L	Antibiotics infused
Time collected:		Within 1 Hour After Infusion: BP#1 _____ Time _____ BP#2 _____ Time _____	Abx name: Time hung:
Check if done ☐	Check if done ☐	Check if done ☐	

To be done within 6 hours of Time Zero

Vitals: Increase frequency for level of care

		
Repeat lactate within 5 hours of Time Zero, if first lactate is > 2	If hypotensive after fluid bolus, remind provider to complete <u>Septic Shock Reassessment Note</u>	Vasopressors if persistent hypotension
Check if done ☐	Check if done ☐	Check if done ☐

Start Antibiotica <1 uur

Citation	Methods	Results
Gaieski, Pines, Band, Mikkelsen, Massone, Furia, Shofer, Goyal, 2010 ⁴⁶	Single center, retrospective cohort, 161 pts with severe sepsis and septic shock from 2005-2006	Median time to antimicrobials was 119 min. Strong association between antimicrobial initiation > 1 hr to increased mortality. <u>Increased 7.6% for every hour delay in antimicrobial initiation</u>
Fletcher, Hodgkiss, Zhang, Browning, Hadden, Hoffman, Winick, M, 2013 ⁴⁷	Single center, retrospective cohort, 652 pts	1.1%, 0.7% mortality, 4.7% PICU. Adverse outcomes > 60 min antimicrobial
Ali, Baqir, Hamid, Khurshid, 2013 ⁴⁸	Single center, retrospective cohort, 200 pts	Median time to antimicrobials was 45 min. <u>Time to antimicrobial > 60 min, and included the incidence of severe sepsis</u>
Ko, Ahn, Lee, Kim, Lee, 2015 ⁴⁹	Single center, retrospective cohort, 118 pts	Median time to antimicrobials was 140 min. <u>Time to antimicrobial did NOT influence incidence of severe sepsis, septic shock or mortality</u>
Mokart, Saillard, Sannini, Chow-Chine, Brun, Faucher, Blache, Blaise, Leone, 2014 ³	Single center, retrospective cohort, 118 pts	<u>Multivariate analysis showed most important predictor for mortality was time to antibiotic greater than 1 hr</u>

Elk uur wachten na het eerste uur, verhoogd mortaliteit met 7,6%.



Time zero

Time zero is wanneer patiënt aan onderstaande criteria voldoet

- 2 of meer SIRS criteria met EN verdenking op infectie EN orgaan dysfunctie aangetoond in lab/ lactaat > 2 mmol/ L
OR
- Hypotensie en/of lactaat ≥ 4 mmol/L



Fever order set

John Hopkins

(for Fevers that are unrelated to blood product transfusion)

Goal: Administration of a broad-spectrum antibiotic within 60 minutes.

"New" fever - a patient that has been previously treated for a fever and remains afebrile for 48 hours but later develops fever. This is to be treated as a "new" fever.

If patient has a NEW temperature $\geq 38^{\circ}\text{C}$ then proceed with the following:		
NURSING INTERVENTIONS		Time Done
v Inform a medical officer or consultant to assess the patient immediately		Initial (RN)
v IV access (if not already initiated)		
v FBC, SPI and 2 sets of blood cultures (2 peripheral or 1 peripheral and 1 via central line if in place). <i>If obtaining 2 sets of blood cultures will delay administration of antibiotic by ≥ 60 minutes, initiate antibiotic after 1st set of blood cultures and then proceed to obtain second set</i>		
v Urine FEME and culture		
v Monitor vital signs every hour for 4 hours or until stable then per routine		
v If patient is hypotensive (systolic blood pressure less than 90) or tachycardic (heart rate greater than 125), then monitor vital signs every 15 minutes for 1 hour until stable and then as above		
v Place Intra nasal O_2 at 2L/min if O_2 saturation is less than 93% or in respiratory distress		
PHYSICIAN ORDERS		
☐	Portable Chest X-ray	
IV fluids (if required)		(Continuous infusion: order on MAR)
☐	Normal Saline bolus 500ml	
☐	Normal Saline bolus 1000ml	
☐	Other:	
Antibiotics (to be administered within 60 minutes)		
(All orders are one-time orders - routine antibiotics should be ordered on MAR)		
Allergies:	☐ NKA Other:	
	Reaction Type:	
*For hemodynamically unstable or suspected neutropenic patients, consider antibiotics in bold		
☐	*Piperacillin/Tazobactam 4.5g IV	
☐	*Cefepime 1 or 2 (circle) gram IV	
☐	*Meropenem 1 gram IV	
☐	*Imipenem 750 mg IV	
☐	Cefazidime 1 gram IV	
☐	If Penicillin allergy, Aztreonam 1 gram IV & Amikacin 15 mg/kg IV	
☐	Other:	
Other Laboratory Tests		
☐	PT/PTT	
☐	D-dimer	
☐	Sputum Gram Stain and culture	
☐	Other	





Overige interventies

**Unclear if CVP
measurements or
CVP guided therapy
enhances outcomes.**





Overige interventies

No established best practice for steroid use in sepsis despite recommendations from Surviving Resuscitation.





Concerns for Implementation in Resource-limited settings



Concern	Response
Screening criteria sensitive, many false positives	New recommended qSOFA criteria are simpler with better predictability for poor outcomes ^{39,41}
Time sensitivity of recommendations	Studies show benefit even with less than optimal implementation ⁴⁸⁻⁵⁰
Availability of lactate measurement	Hypotension paired with other clinical signs of hypoperfusion (urine out, mottling) may be equally predictive ^{14,35}
Perfusion evaluation requiring technology	Latest recommendations no longer suggest central venous catheter or central venous oxygen saturation. Physical evaluation of perfusion acceptable ^{39,51}



Discussie

- Sepsis core measure has a clinical impact upon workload.
- Hospital-wide efforts to detect and intervene in sepsis should be tailored to the population
 - Cancer-specific sepsis triggers missed with universal screening
 - Oncology-specific criteria require more robust evaluation.
 - Pilot data suggest that modified screening criteria reduces workload without sacrificing sensitivity of screening.
- Accurate and streamlined early screening for sepsis permits more time for recommended three-hour interventions.





Samenvattend – het verleden

- SIRS lijkt niet meer te voldoen
- Er is geen gouden standaard voor sepsis of septische shock
- Er is behoefte aan meer uniformiteit
- De huidige definitie geeft te weinig uniformiteit
- Ernstige sepsis lijkt een overbodige term
- Is sepsis en septische shock niet voldoende?

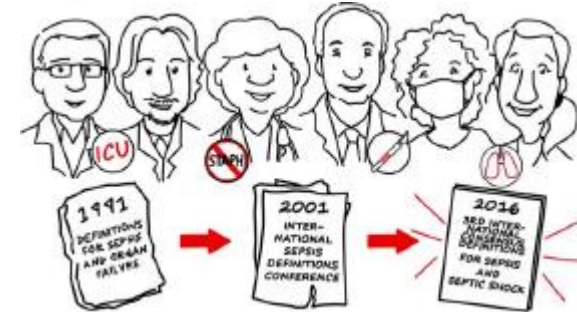
Waarom moeilijk bij oncologie patiënten?



Tijd voor verandering



- Task force SCCM/ESICM



Special Communication | Caring for the Critically Ill Patient

FREE

February 23, 2016

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP¹; Clifford S. Deutschman, MD, MS²; Christopher Warren Seymour, MD, MSc³; et al

» [Author Affiliations](#) | [Article Information](#)

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287





SIRS

- 1:8 ptn met een ernstige sepsis is SIRS negatief
- Geen duidelijke cut-off bij 2 SIRS criteria
- >2 SIRS criteria = goede sensitiviteit, maar lage specificiteit

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTI

Incidence and Prognostic Value of the Systemic Inflammatory Response Syndrome and Organ Dysfunctions in Ward Patients

Matthew M. Churpek¹, Frank J. Zadewicz¹, Christopher Winslow², Michael D. Howell¹, and Dana P. Edison¹
Department of Medicine, University of Chicago, Chicago, Illinois, and ²Department of Medicine, NorthShore University HealthSystem, Evanston, Illinois

ORIGINAL ARTICLE

Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

Kirsi-Maija Kaukonen, M.D., Ph.D., Michael Bailey, Ph.D., David Pilcher, F.C.I.C.M., D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.



Key points

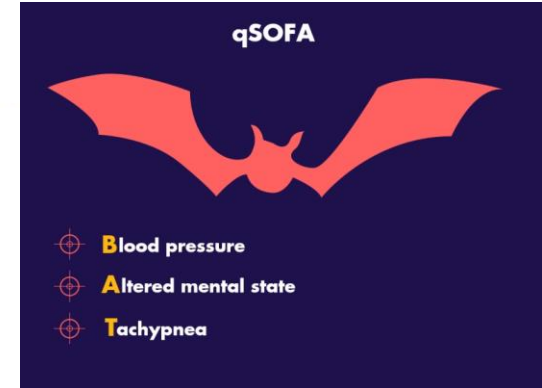
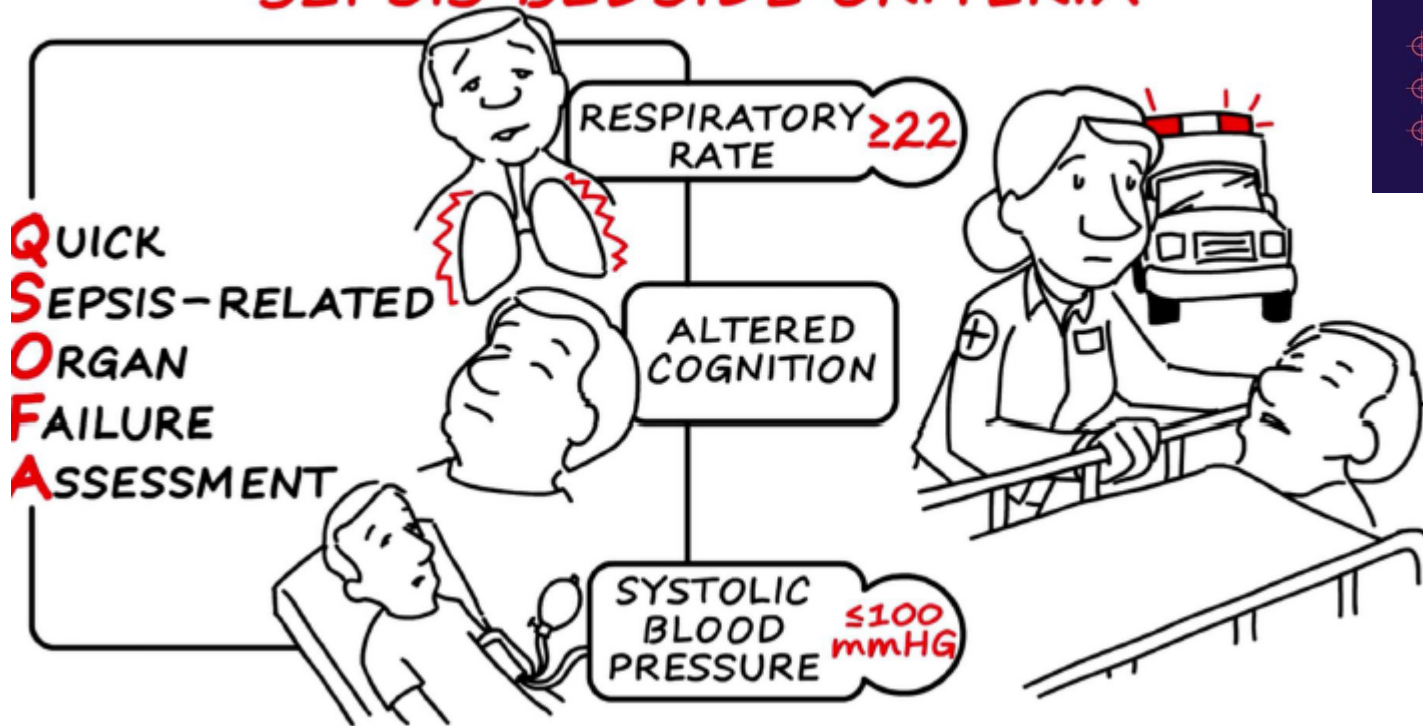
- Na 15 jaar is in 2016 een update van de sepsis definities verschenen
- SIRS wordt al jaren bekritiseerd door de matige specificiteit maar ook sensitiviteit en is uit de definities gehaald.
- SIRS dwingt wel tot nadenken: waarom vertoont mijn patiënt deze abnormale parameters?
- Nieuw in de definities is de quick SOFA (qSOFA) score



1. Singer M, Deutschman CS, Seymour CW, et al. [The Third International Consensus Definitions for Sepsis and Septic Shock \(Sepsis-3\)](#). JAMA. 2016;315(8):801-810.
2. Seymour CW, Liu VX, Iwashyna TJ, et al. [Assessment of Clinical Criteria for Sepsis For the Third International Consensus Definitions for Sepsis and Septic Shock \(Sepsis-3\)](#). JAMA. 2016;315(8):762-774.
3. Shankar-Hari, M, Phillips GS, Levy ML, et al. [Criteria for Septic Shock For the Third International Consensus Definitions for Sepsis and Septic Shock \(Sepsis-3\)](#). JAMA. 2016;315(8):775-787.

Q SOFA

SEPSIS BEDSIDE CRITERIA



Nieuwe definitie: Sepsis

- Sepsis is een levensbedreigend orgaanfalen veroorzaakt door een gedysreguleerde host respons op een infectie
- Criteria: infectie + stijging *Sepsis related organ failure assessment* $\text{SOFA} \geq 2$
 - Op afdeling/ extern: infectie + stijging $\text{qSOFA} \geq 2$



Sepsis = oude ernstige sepsis

Gereguleerde host respons = normale response op infectie.

February 23, 2016

Assessment of Clinical Criteria for Sepsis
: For the Third International Consensus Definitions
for Sepsis and Septic Shock (Sepsis-3)

Christopher W. Seymour, MD, MSc^{1,2}; Vincent X. Liu, MD, MSc³; Theodore J. Iwashyna, MD, PhD^{4,5,6}; et al.



Nieuwe definitie: septische shock

- Septische shock:
 - een onderdeel van sepsis waarin uitgesproken circulatoire, cellulaire en metabole afwijkingen geassocieerd zijn met een hoger mortaliteitsrisico dan sepsis alleen.
- Klinische criteria septische shock:
 - Circulatoire dysfunctie: aanhoudende hypotensie, waarbij vasopressoren nodig zijn om een MAP ≥ 65 mmHg te verkrijgen én
 - Metabole en cellulaire afwijkingen: serum lactaat ≥ 2 mmol/L ondanks adequate volumeresuscitatie.

Met deze criteria ligt de *in-hospital* mortaliteit boven de **40%**.

- Septische shock verschilt van sepsis in mortaliteit.



Kijkje in de toekomst

- Waar q SOFA je op dit moment mee kan helpen, is risicostratificatie. Wat is het risico op overlijden of langdurige IC-opname?
- Wat zal het worden? Definities aan de hand van biomarkers? (een patiënt heeft sepsis bij CRP > 100, een PCT van > 10 en een verhoogde IL-1, IL-6 en TNF- α ?)



Informatie voor de patiënt

SYMPTOMS can include **ANY**
of the above infection symptoms, plus the following:



**Shivering, fever,
or very cold**



**Extreme pain
or discomfort**



**Clammy, or
sweaty skin**



**Confusion or
disorientation**



Short of breath



High heart rate

CANCER, INFECTION AND SEPSIS FACT SHEET

A POTENTIALLY DEADLY COMBINATION EVERY CANCER PATIENT SHOULD KNOW ABOUT

Why does cancer put me at risk for developing an infection and sepsis?
Having cancer and undergoing certain treatments for cancer, such as chemotherapy, can make your body unable to fight off infections the way it normally would.

What is the difference between infection and sepsis?
An **INFECTION** occurs when germs enter a person's body and multiply, causing illness, organ and tissue damage, or disease. For cancer patients, an infection can turn serious, or even deadly, very fast.
SEPSIS is a complication caused by the body's overwhelming and life-threatening response to infection which can lead to tissue damage, organ failure, and death. For a person with cancer, any infection that is anywhere in your body can lead to sepsis.

How does chemotherapy increase my risk for infection and sepsis?
Chemotherapy works by killing the fastest-growing cells in your body—both good and bad. This means that along with killing cancer cells, chemo also kills your infection-fighting white blood cells.

Is there a specific time I may be more likely to get an infection?
An infection or sepsis can happen at any time. However, when your body has very low levels of a certain type of white blood cell (neutrophils), your risk of getting an infection that can lead to sepsis increases. This condition is a common side effect of chemo called **neutropenia**.

How will I know if I have neutropenia?
Your doctor will routinely test for neutropenia by checking the level of your white blood cells (neutrophils).

How can I prevent an infection?
In addition to receiving treatment from your doctor, the following suggestions can help reduce your risk for getting an infection:

- Wash your hands often and ask others around you to do the same.
- Avoid crowded places and people who are sick.
- Talk to your doctor about getting a flu shot or other vaccinations.
- Take a bath or shower every day (unless told otherwise).
- Use an unscented lotion to try to keep your skin from getting dry or cracked.
- Clean your teeth and gums with a soft toothbrush.
- Use a mouthwash to prevent mouth sores (if your doctor recommends one), as toothbrushes.
- Cook meat and eggs all the way through to kill any germs.
- Carefully wash raw fruits and vegetables.
- Protect your skin from direct contact with pet bodily waste (urine or feces).
- Wash your hands immediately after touching an animal or removing its waste, even after wearing gloves.
- Use gloves for gardening.

 Centers for Disease Control and Prevention
Division of Cancer Treatment and Diagnosis
National Cancer Institute

Take home message

- Bij 'time 'zero' begint het sepsis management en is lastig vast te stellen
- < 1 uur start antibiotica!
- Lactaat een voorspeller?
- QSOFA → ook voor oncologiepatiënten?

