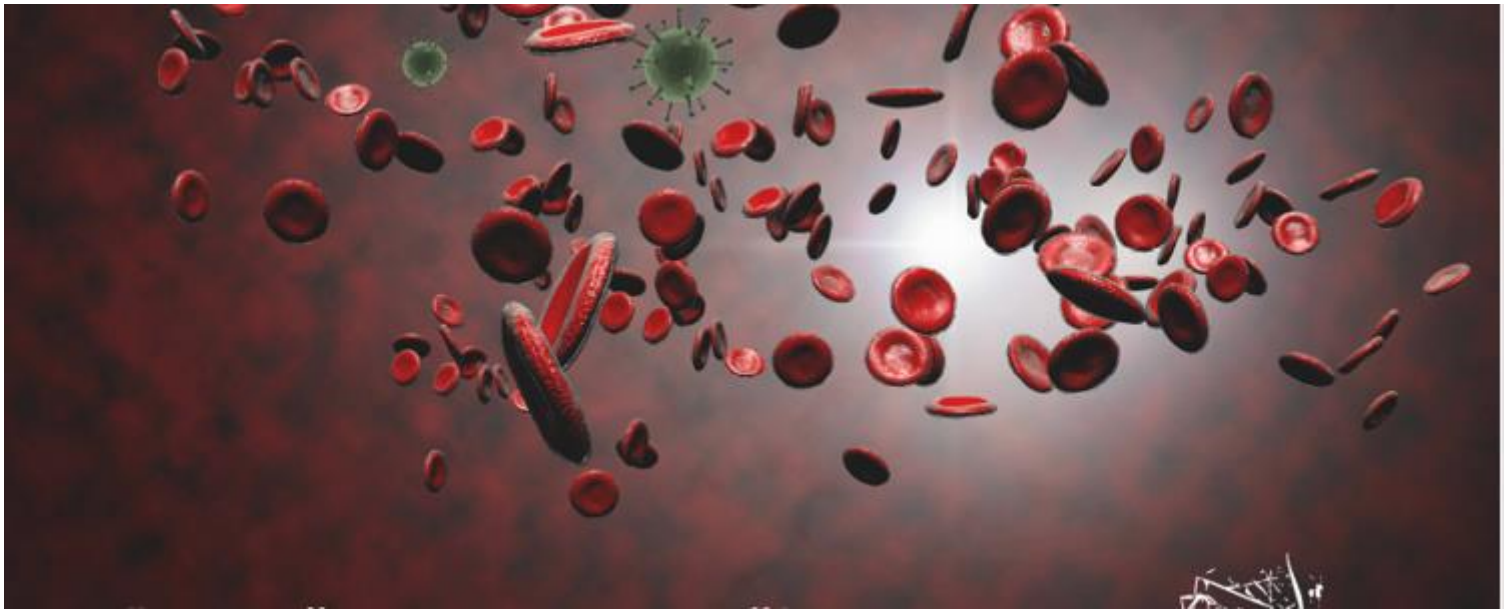
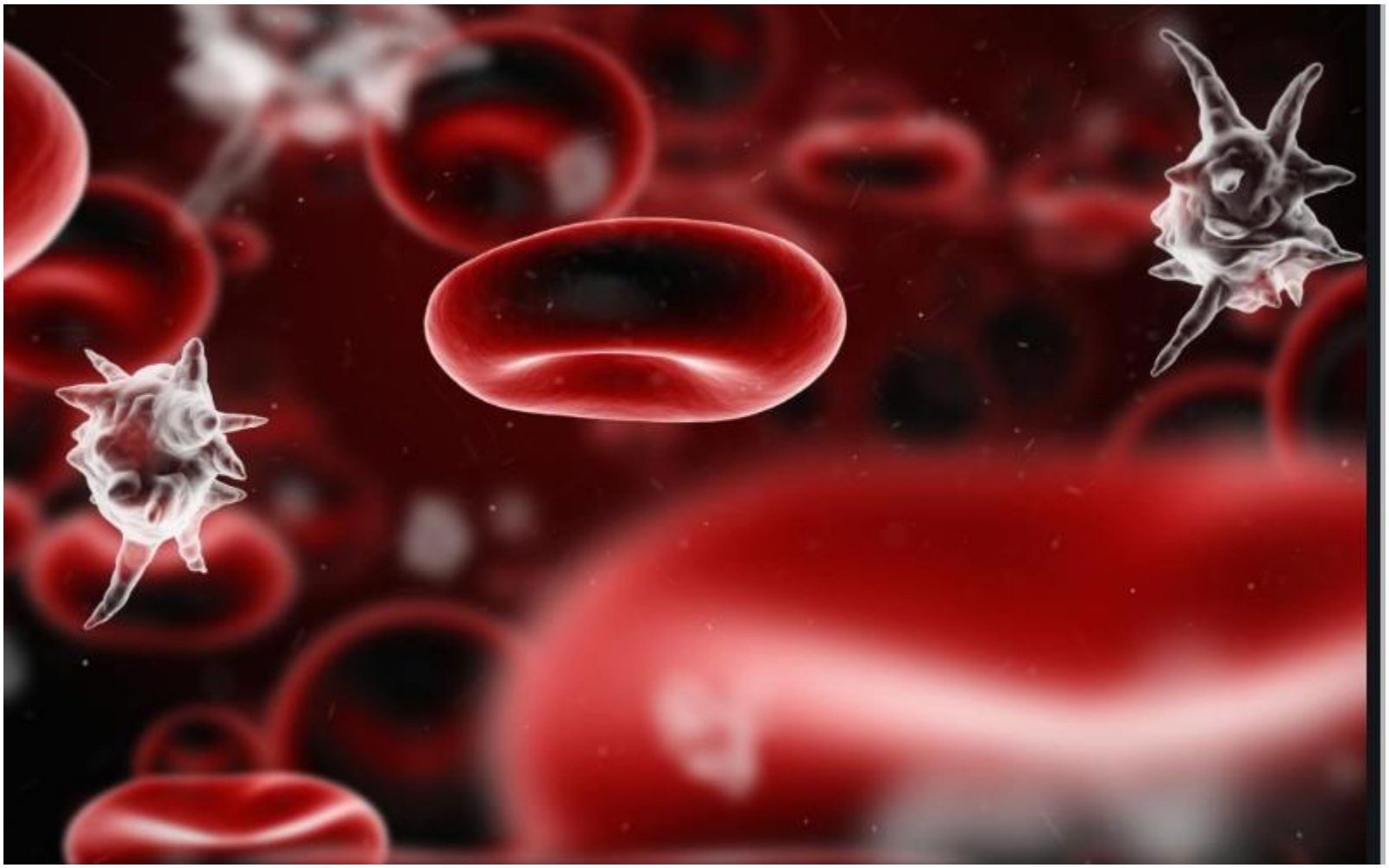


Sepsisde Güncel Bilgiler

Prof Dr Meral SÖNMEZOĞLU

Yeditepe Üniversitesi Hastanesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji ABD



- "Sepsisi Önle, Hayatı Kurtar"
- "Sepsisi Tanı, Hayatı Kurtar"

SEPSİS

- Sepsis; enfeksiyona vücudun oluşturduğu düzensiz cevap ile gelişen karmaşık bir klinik durumdur,
- organ fonksiyonlarında bozukluk/yetmezliklerle ilerler
- yüksek ölüm riski taşır
- farkındalık artışı, erken tanıma ve erken tedavi gerektiren bir enfeksiyon acilidir

SEPSİS

- Dünya Sağlık Örgütü 2017 de sepsisi "Küresel Sağlık Önceliğine" almıştır
- Bu çabalara rağmen dünyada insidansı ve mortalitesi artmaktadır

The World Health Assembly Has Adopted a Resolution on Sepsis

Posted on May 26, 2017

SEVENTIETH WORLD HEALTH ASSEMBLY **WHA70.7**

Agenda item 12.2 **29 May 2017**

Improving the prevention, diagnosis and clinical management of sepsis

Sepsisin halk sağlığı üzerindeki etkilerine dikkat çekmek üzere DSÖ Başkanından talepler

- 2018 sonuna kadar sepsis ve onun global sonuçları hakkında bir rapor hazırlaması
- Üye ülkeleri yeterince desteklemesi
- Diğer Birleşmiş Milletler organizasyonları ile iş birliği yapılması
- Kararın uygulanması ile alakalı 2020 yılındaki WHA'ye rapor hazırlanması

SEPSİS SIKLIĞI

Assessment of Global Incidence and Mortality of Hospital-treated Sepsis

Current Estimates and Limitations

Carolin Fleischmann[1,2], André Scherag[3], Neill K. J. Adhikari[4], Christiane S. Hartog[1,2], Thomas Tsaganos[5], Peter Schlattmann[6], Derek C. Angus[7*], and Konrad Reinhart[1,2*]; on behalf of the International Forum of Acute Care Trialists

- 1,553 rapor; 1979- 2015
- 45 çalışma
- 27 yüksek gelir düzeyi ülkelerden meta-analiz

- Hastanede sepsis mortalitesi %17 ve ağır sepsisde %26
- Dünyada yılda 31.5 milyon sepsis
- 19.4 milyon ağır sepsis
- 5.3 milyon ölüm tahmin ediliyor

Am J Respir Crit Care Med Vol 193, Iss 3, pp 259–272, Feb 1, 2016

SEPSİS SIKLIĞI

World map of included studies on sepsis and severe sepsis
Fleischmann, Scherag, Adhikari, et al.: Global Sepsis Incidence and Mortality

SEPSİS SIKLIĞI

Vincent et al. Critical Care (2019) 23:196
https://doi.org/10.1186/s13054-019-2478-6

Critical Care

RESEARCH Open Access

Frequency and mortality of septic shock in Europe and North America: a systematic review and meta-analysis

Jean-Louis Vincent[1*], Gabriel Jones[2], Sholto David[2], Elena Olariu[2] and Kevin K. Cadwell[2]

- 71 makaleden 6291 kayıt incelenmiş
- Septik şok sıklığı %10.4
- YBÜ mortalitesi %37.3,
- Hastane mortalitesi %39.0
- 28-/30-gün mortalitesi %36.7

SEPSİS SIKLIĞI

Baykara *et al. Critical Care* (2018) 22:93
https://doi.org/10.1186/s13054-018-2013-1

Critical Care

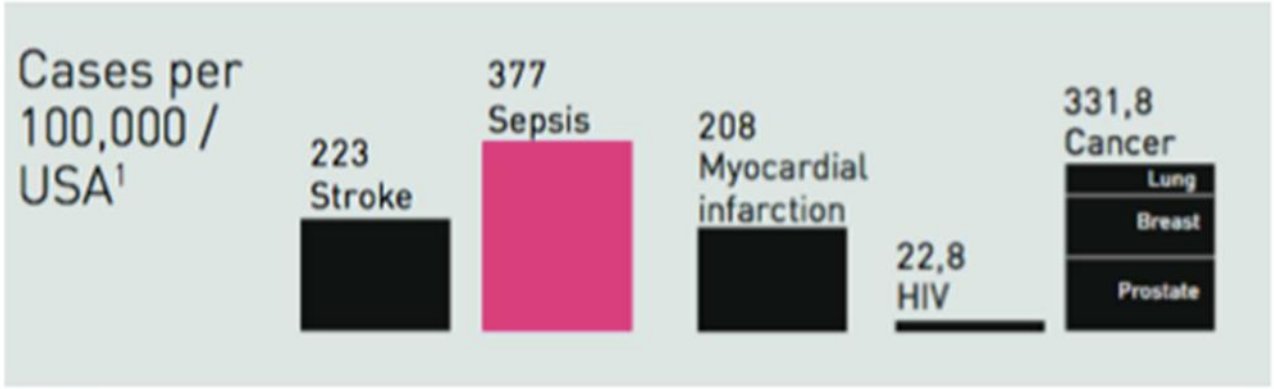
RESEARCH Open Access

Epidemiology of sepsis in intensive care units in Turkey: a multicenter, point-prevalence study

Nur Baykara[1*], Halis Akalın[2], Mustafa Kemal Arslantaş[3], Volkan Hancı[4], Çiğdem Çağlayan[5], Ferda Kahveci[6], Kubilay Demirağ[7], Canan Baydemir[8], Necmettin Ünal[9] and Sepsis Study Group

- 1499 hasta analizi (132 YBÜ/ 94 hastanede)
- 237 (% 15.8) SIRS olmayan enfeksiyon
- 163 (%10.8) SIRS ve enfeksiyon ⟶ %24.8
- 260 (%17.3) ağır sepsis (şok olmayan) → %55.7
- 203 (%13.5) septik şok ⟶ % 70.4
- Mortalite oranı ağır sepsisde %55.7, septik şokta % 70.4 , sadece enfeksiyon olanda %24.8

SEPSİS: Kıyaslamalı Sıklık



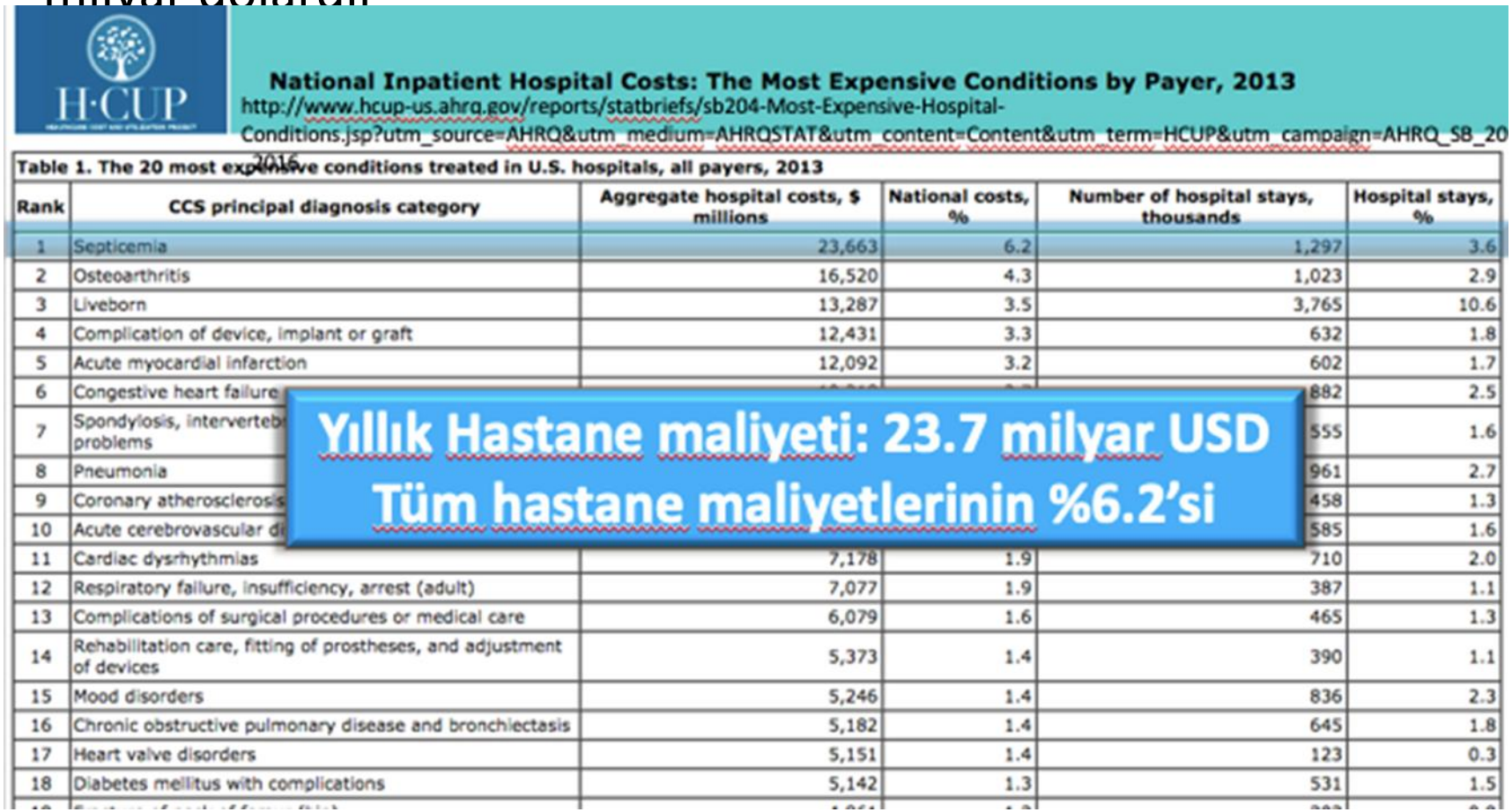
ABD: Yıllık(2011) araştırma bütçesi (milyon USD)	317	91	1.236	2.900	2.277

En sık karşılaşılan hastalık

En az araştırılan hastalık

SEPSİS MALİYETİ

- ABD'de en pahalı sağlık bakım problemidir ve yıllık maliyeti 23.7 milyar dolardır



National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013

http://www.hcup-us.ahrq.gov/reports/statbriefs/sb204-Most-Expensive-Hospital-Conditions.jsp?utm_source=AHRQ&utm_medium=AHRQSTAT&utm_content=Content&utm_term=HCUP&utm_campaign=AHRQ_SB_2016

Table 1. The 20 most expensive conditions treated in U.S. hospitals, all payers, 2013

Rank	CCS principal diagnosis category	Aggregate hospital costs, $ millions	National costs, %	Number of hospital stays, thousands	Hospital stays, %
1	Septicemia	23,663	6.2	1,297	3.6
2	Osteoarthritis	16,520	4.3	1,023	2.9
3	Liveborn	13,287	3.5	3,765	10.6
4	Complication of device, implant or graft	12,431	3.3	632	1.8
5	Acute myocardial infarction	12,092	3.2	602	1.7
6	Congestive heart failure			882	2.5
7	Spondylosis, intervertebral problems			555	1.6
8	Pneumonia			961	2.7
9	Coronary atherosclerosis			458	1.3
10	Acute cerebrovascular disease			585	1.6
11	Cardiac dysrhythmias	7,178	1.9	710	2.0
12	Respiratory failure, insufficiency, arrest (adult)	7,077	1.9	387	1.1
13	Complications of surgical procedures or medical care	6,079	1.6	465	1.3
14	Rehabilitation care, fitting of prostheses, and adjustment of devices	5,373	1.4	390	1.1
15	Mood disorders	5,246	1.4	836	2.3
16	Chronic obstructive pulmonary disease and bronchiectasis	5,182	1.4	645	1.8
17	Heart valve disorders	5,151	1.4	123	0.3
18	Diabetes mellitus with complications	5,142	1.3	531	1.5

Yıllık Hastane maliyeti: 23.7 milyar USD

Tüm hastane maliyetlerinin %6.2'si

SEPSİS MALİYETİ

Amerikada 27 Milyar Dolarlık Sepsis Krizi

https://www.bloomberg.com/news/articles/2017-07-14/america-has-a-27-billion-sepsis-crisis

SEPSİS MORTALİTESİ

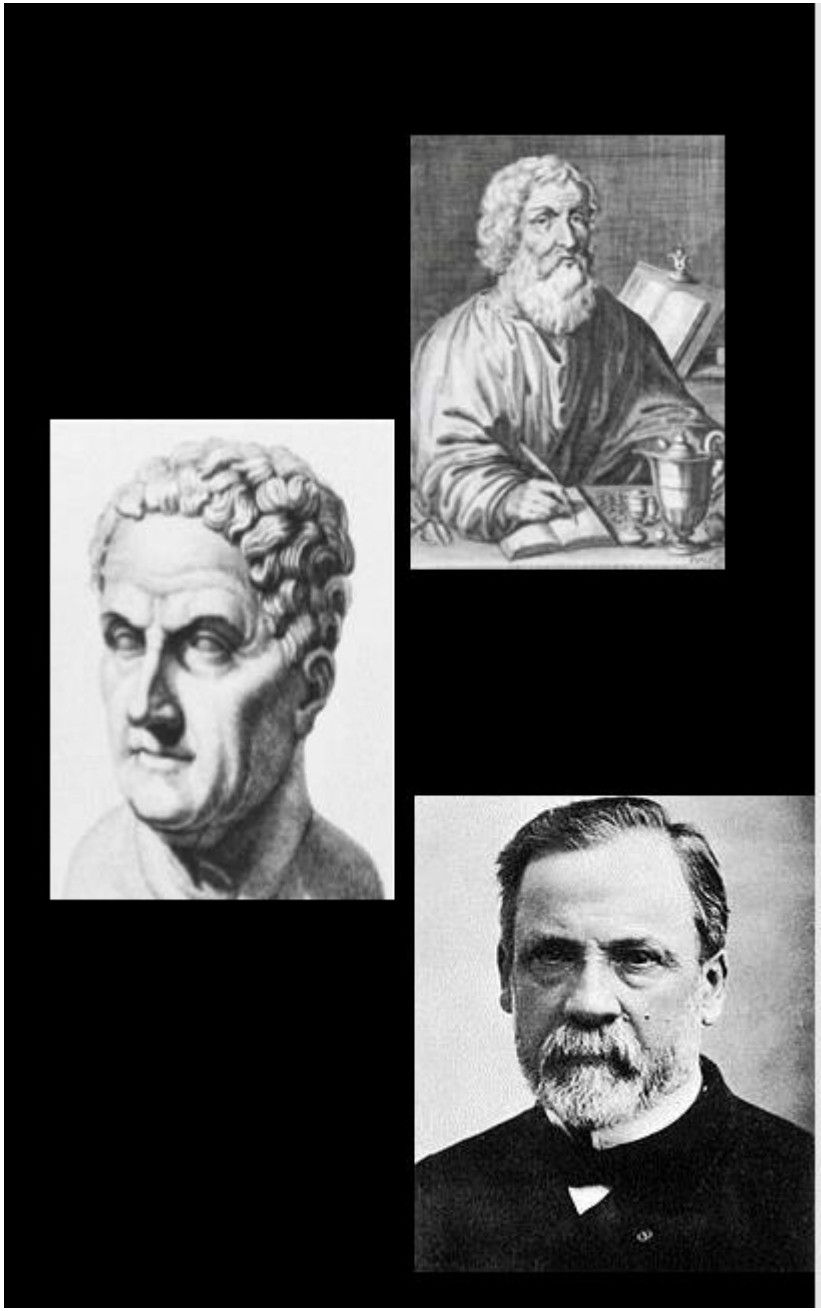
	Dünya Nüfusu ($x10^3$)	Toplam Ölüm ($x10^3$)	Enfeksiyonlar ($x10^3$)	Kardiovasküler Hastalıklar ($x10^3$)	Maligniteler ($x10^3$)	Yaralanma ($x10^3$)
2004	6.436.826	59.000	13.777 (%23)	17.073 (%29)	7.424 (%13)	5784 (%10)
2012	6.938.255	56.000	10.066 (%18)	16.586 (%30)	7870 (%14)	4971 (%9)
2015	7.349.472	56.441	5.706 (%10,1)	17.689 (%31.3)	8.763 (%15.5)	3527 (%8.8)

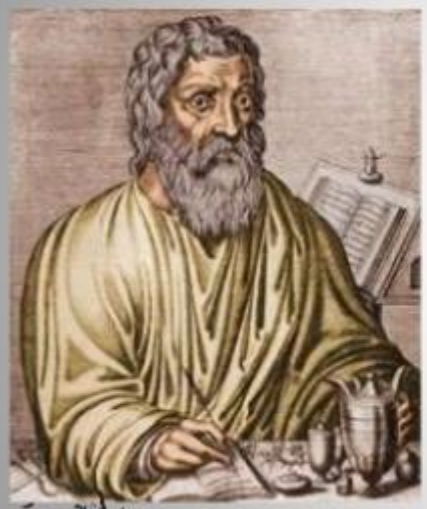
SAĞLIK İSTATİSTİKLERİ YILLIĞI 2015

ICD-10 Ana Tanı Kodları	2012	2013	2014	2015
Bazı Enfeksiyöz ve Paraziter Hastalıklar	1.67	1.77	1.78	2.11

SEPSİS TANIMI

- Eti çürüten, pis kokular ve irinli yaralar süreci (ση΄ψις) Hipokrat
- Yara iyileşmesi için gerekli, övgüye değer bir olay Galen
- “Kan zehirlenmesi” Pasteur





stop
sepsis
save
lives

HIPPOCRATES (460-370 BC)

Greek word: ***sipsis*** = make rotten

pepsis = good digestion

IBN SINA (Avicenna)
(979-1037 BC)

Noticed the coincidence of blood putrefaction (septicemia) and fever

stop sepsis save lives

Circa 1904

Sir William Osler

in "The Evolution of Modern Medicine"-1904

"Except on few occasions, the patient appears to die from the body's response to infection rather than from it."

HUGO SCHOTTMULLER
(1867-1936)
Germany

- ***Modern definition of sepsis (1914):***

"Sepsis is present if a focus has developed from which pathogenic bacteria, constantly or periodically, invade the blood stream in such a way that this causes subjective and objective symptoms."

- "Therapy should not be directed against bacteria in the blood but against the released bacterial toxins"

1991

ROGER C. BONE (1941-1997)
US

Helped develop the multi-disciplinary subspecialty of modern Critical Care Medicine

Promoted evidence-based approach to sepsis

Sepsis Tanımlamaları Tarihçesi

Sepsis = Çürüme, Kokuşma

\- Hipokrat

1991

Sepsis 1.

Sepsis = Enfeksiyon+SIRS

2001

Sepsis 2.

Sepsis = Belirti ve bulguların komplex topluluğu

2016

Sepsis 3.

Sepsis = Enfeksiyon+Organ disfonksiyonu

Terminology	SSC Definitions[9, 13]	Sepsis-3 Definitions[1]
SIRS	The presence of at least two of the following clinical criteria: • Temperature, < 36°C or > 38.3°C • Heart rate, > 90 bpm • Respiratory rate, > 20 bpm, or $PaCO_2$, < 32 mmHg • WBC count, < 4,000 mm^3 or > 12,000 mm^3	Not part of the definition
Sepsis	The presence of at least two SIRS criteria and known or suspected infection	• Sepsis is a life-threatening organ dysfunction caused by a dysregulated patient response to infection. • In lay terms, sepsis is a life-threatening condition that arises when the body's response to infection causes injury to itself and its organs.
Severe Sepsis	• Sepsis-induced hypotension • SBP, < 90 mmHg • MAP, < 70 mmHg, or an SBP reduction of 40 mmHg from baseline • Serum lactate, > 2 mmol/L • Signs of organ dysfunction (acute oliguria, for example)	Not part of the definition
Septic Shock	Sepsis-induced hypotension that persists despite adequate fluid resuscitation and requires vasopressors to support perfusion	Septic shock is seen in patients with sepsis who develop underlying circulatory and metabolic abnormalities resulting in hypotension that require vasopressors to maintain a MAP of ≥ 65 mmHg and having a serum lactate level of ≥ 2 mmol/L despite adequate volume resuscitation, resulting in a higher risk of mortality.

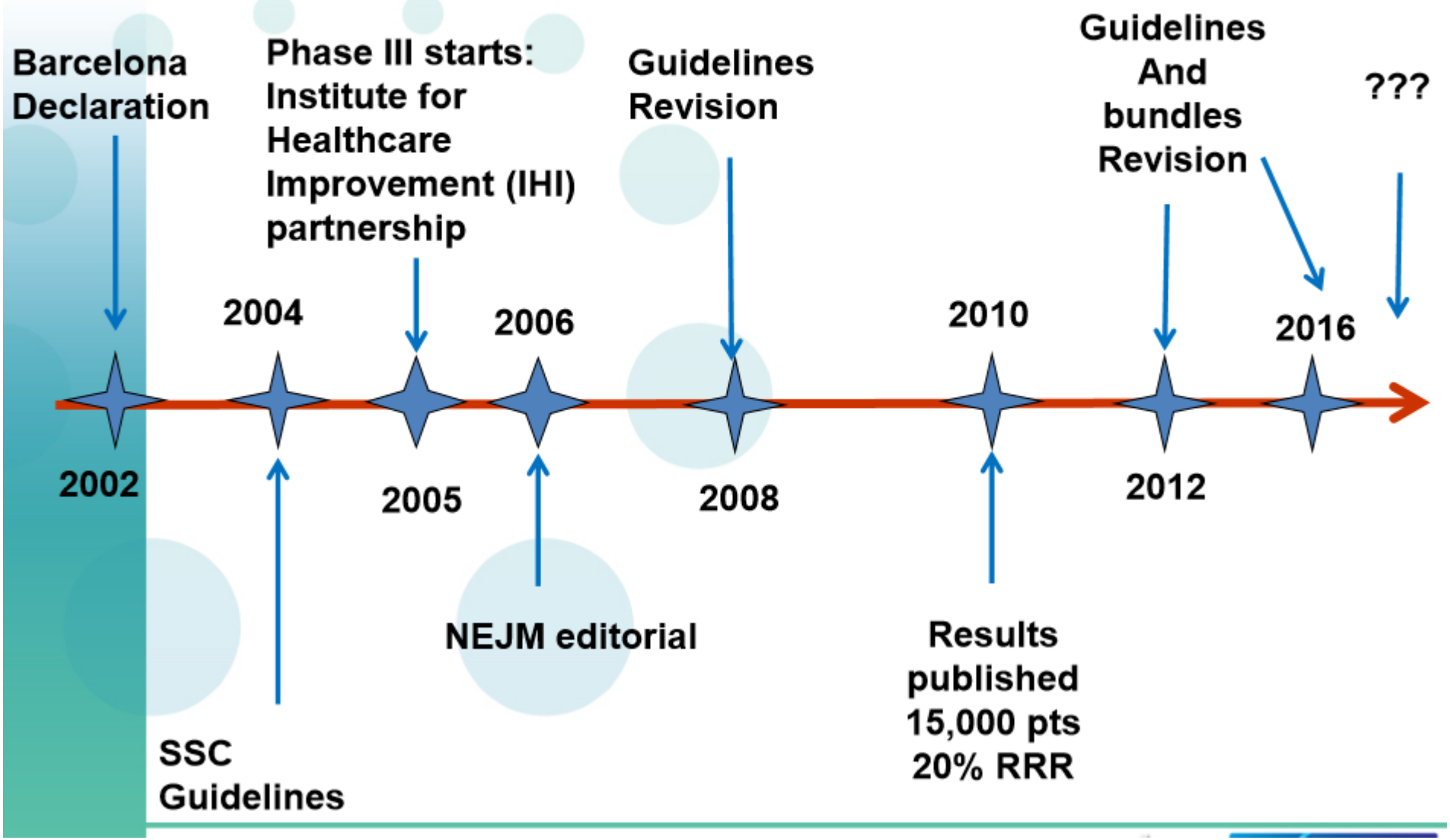
MAP = mean arterial pressure; $PaCO_2$ = partial pressure of arterial carbon dioxide; SBP = systolic blood pressure; Sepsis-3 = Third International Consensus Definitions for Sepsis and Septic Shock; SIRS = systemic inflammatory response syndrome; SSC = Surviving Sepsis Campaign; WBC = white blood cell.

Table 1. Definitions of sepsis.

Sepsis 1 (1991)[6]	**Sepsis 2 (2001)**[7]	**Sepsis 3 (2016)**[8]
Systemic inflammatory response syndrome (SIRS): systemic inflammatory response to a variety of severe clinical insults: Temperature >38°C or <36°C; heart rate > 90 beats per min; respiratory rate > 20 breaths per min or $PaCO_2$ < 32 mmHg; and white blood cell count > 12,000/cu mm, <4000/cu mm, or >10% immature (band) forms Sepsis is a systemic response to infection, manifested by two or more of the SIRS criteria as a result of infection. Severe sepsis: Sepsis associated with organ dysfunction, hypoperfusion, or hypotension; hypoperfusion and perfusion abnormalities may include, but not limited to, lactic acidosis, oliguria, or an acute alteration in mental status Septic shock: Sepsis-induced, with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but not limited to, lactic acidosis, oliguria, or an acute alteration in mental status; patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.	Infection: Documented or suspected and some of the following: **General parameters:** Fever (core temperature > 38.3°C); hypothermia (core temperature < 36°C); heart rate > 90 beats per min or > 2 SD above the normal value for age; tachypnea: respiratory rate > 30 breaths per min; altered mental status; significant edema or positive fluid balance (>20 mL kg^{-1} over 24 h) Hyperglycemia (plasma glucose > 110 mg dL^{-1} or 7.7 mM L^{-1}) in the absence of diabetes **Inflammatory parameters:** Leukocytosis (white blood cell count > 12,000/μL); leukopenia (white blood cell count < 4000/μL); normal white blood cell count with > 10% immature forms; plasma C-reactive protein > 2 SD above the normal value; and plasma procalcitonin > 2 SD above the normal value **Hemodynamic parameters:** Arterial hypotension (systolic blood pressure < 90 mmHg, MAP < 70 mmHg, or a systolic blood pressure decrease > 40 mmHg in adults or < 2 SD below normal for age, mixed venous oxygen saturation > 70%, cardiac index > 3.5 L min^{-1} m^{-2}) Organ dysfunction parameters: Arterial hypoxemia (PaO_2/FIO_2 < 300); acute oliguria (urine output < 0.5 mL kg^{-1} h^{-1} or 45 mM L^{-1} for at least 2 h); creatinine increase ≥ 0.5 mg dL^{-1}; coagulation abnormalities (international normalized ratio > 1.5 or activated partial thromboplastin time > 60 s); ileus (absent bowel sounds); thrombocytopenia (platelet count < 100,000 μL^{-1}) Hyperbilirubinemia (plasma total bilirubin > 4 mg dL^{-1} or 70 mmol L^{-1}) **Tissue perfusion parameters:** Hyperlactatemia (>3 mmol L^{-1}); decreased capillary refill or mottling	Sepsis is a life-threatening organ dysfunction caused by dysregulated host response to infection. **Clinical criteria for sepsis:** Suspected or documented infection and an acute increase of ≥2 SOFA points (Table 2) The task force considered that positive qSOFA (quick SOFA) criteria should also prompt consideration of possible infection in patients not previously recognized as infected. qSOFA criteria: Altered mental status (GCS score < 15); systolic blood pressure < 100 mmHg; respiratory rate > 22 breaths per min Septic shock is defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality. Septic shock can be identified with a clinical construct of sepsis with persisting hypotension, requiring vasopressor therapy to elevate MAP ≥ 65 mm Hg and lactate > 2 mmol L^{-1} (18 mg dL^{-1}) despite adequate fluid resuscitation

Surviving Sepsis Campaign

Surviving Sepsis Campaign: Timeline



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Sepsis is a systemic response to infection, manifested by two or more of the SIRS criteria as a result of infection.
Severe sepsis: Sepsis associated with organ dysfunction, hypoperfusion, or hypotension; hypoperfusion and perfusion abnormalities may include, but not limited to, lactic acidosis, oliguria, or an acute alteration in mental status

Septic shock: Sepsis-induced, with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but not limited to, lactic acidosis, oliguria, or an acute alteration in mental status; patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.

Sepsis 2 (2001)[7]

Infection: Documented or suspected and some of the following:
General parameters:
Fever (core temperature > 38.3°C); hypothermia (core temperature < 36°C); heart rate > 90 beats per min or > 2 SD above the normal value for age; tachypnea: respiratory rate > 30 breaths per min; altered mental status; significant edema or positive fluid balance (>20 mL kg^{-1} over 24 h)
Hyperglycemia (plasma glucose > 110 mg dL^{-1} or 7.7 mM L^{-1}) in the absence of diabetes
Inflammatory parameters:
Leukocytosis (white blood cell count > 12,000/μL); leukopenia (white blood cell count < 4000/μL); normal white blood cell count with > 10% immature forms; plasma C-reactive protein > 2 SD above the normal value; and plasma procalcitonin > 2 SD above the normal value
Hemodynamic parameters:
Arterial hypotension (systolic blood pressure < 90 mmHg, MAP < 70 mmHg, or a systolic blood pressure decrease > 40 mmHg in adults or < 2 SD below normal for age, mixed venous oxygen saturation > 70%, cardiac index > 3.5 L min^{-1} m^{-2})
Organ dysfunction parameters:
Arterial hypoxemia (PaO_2/FIO_2 < 300); acute oliguria (urine output < 0.5 mL kg^{-1} h^{-1} or 45 mM L^{-1} for at least 2 h); creatinine increase ≥ 0.5 mg dL^{-1};
coagulation abnormalities (international normalized ratio > 1.5 or activated partial thromboplastin time > 60 s);
ileus (absent bowel sounds);
thrombocytopenia (platelet count < 100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin > 4 mg dL^{-1} or 70 mmol L^{-1})

Tissue perfusion parameters:
Hyperlactatemia (>3 mmol L^{-1}); decreased capillary refill or mottling

Sepsis 3 (2016)[8]

Sepsis is a life-threatening organ dysfunction caused by dysregulated host response to infection.

Clinical criteria for sepsis:
Suspected or documented infection and an acute increase of ≥2 SOFA points (Table 2)

The task force considered that positive qSOFA (quick SOFA) criteria should also prompt consideration of possible infection in patients not previously recognized as infected.

qSOFA criteria:
Altered mental status (GCS score < 15);
systolic blood pressure < 100 mmHg;
respiratory rate > 22 breaths per min
Septic shock is defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality.

Septic shock can be identified with a clinical construct of sepsis with persisting hypotension, requiring vasopressor therapy to elevate MAP ≥ 65 mm
Hg and lactate > 2 mmol L^{-1} (18 mg dL^{-1}) despite adequate fluid resuscitation

SOFA SKORLAMA SİSTEMİ

Sequential [Sepsis-Related] Organ Failure Assessment Score

	Skor				
Sistem	0	1	2	3	4
Solunum					
PaO_2/FIO_2, mm Hg	≥400	<400	<300	<200 solunum desteği varlığında	<100 solunum desteği varlığında
Koagülasyon					
Trombosit $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Karaciğer					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Kardiyovasküler	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (herhangi)[b]	Dopamine 5.1-15 veya epinephrine ≤0.1 veya norepinephrine ≤0.1[b]	Dopamine >15 veya epinephrine >0.1 veya norepinephrine >0.1[b]
MSS					
Glasgow Koma Skalası skoru	15	13-14	10-12	6-9	<6
Böbrekl					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
İdrar debisi, mL/d				<500	<200

[b] Katekolamin dozları μg/kg/dak'dır ve en az 1 H uygulanmıştır

Vincent JL. Intensive Care Medicine 1996; 22 (7): 707-10
Singer M. JAMA. 2016;315(8):801-810

Sequential Organ Failure Assessment (SOFA) Score ☆

Predicts ICU mortality based on lab results and clinical data.

INSTRUCTIONS

Welcome Sepsis-3 readers! We've also added the qSOFA Score with a summary of the new definitions and recommendations.

Use the worst value in a 24-hour period.

When to Use ⌄ | Pearls/Pitfalls ⌄ | Why Use ⌄

PaO_2	Norm: 10 - 13,3	kPa ⇋
FiO_2		%
On mechanical ventilation Including CPAP	No / Yes	
Platelets, $\times 10^3/\mu L$	≥150	0
	100-150	+1
	50-99	+2
	20-49	+3
	<20	+4
Glasgow Coma Scale If on sedatives, estimate assumed GCS off sedatives	15	0
	13-14	+1
	10-12	+2
	6-9	+3
	<6	+4

Bilirubin, mg/dL (µmol/L)	**<1.2 (<20)**	**0**
	1.2–1.9 (20-32)	+1
	2.0–5.9 (33-101)	+2
	6.0–11.9 (102-204)	+3
	≥12.0 (>204)	+4
Mean arterial pressure OR administration of vasoactive agents required Listed doses are in units of mcg/kg/min	**No hypotension**	**0**
	MAP <70 mmHg	+1
	DOPamine ≤5 or DOBUTamine (any dose)	+2
	DOPamine >5, EPINEPHrine ≤0.1, or norEPINEPHrine ≤0.1	+3
	DOPamine >15, EPINEPHrine >0.1, or norEPINEPHrine >0.1	+4
Creatinine, mg/dL (µmol/L) (or urine output)	**<1.2 (<110)**	**0**
	1.2–1.9 (110-170)	+1
	2.0–3.4 (171-299)	+2
	3.5–4.9 (300-440) or UOP <500 mL/day	+3
	≥5.0 (>440) or UOP <200 mL/day	+4

Result:

Mortality	SOFA score
<10%	0-6
15-20%	7-9
40-50%	10-12
50-60%	13-14
>80%	15
>90%	15-24

Mortality	Score trend (First 48 hrs)
>50%	Increasing
27-35%	Unchanged
<27%	Decreasing

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

JAMA. 2016;315(8):801-810

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM;

SOFA Skoru:

Kan testi yapmayı gerektirir

Külfetlidir

ICU dışında uygulanamaz

YBÜ dışındaki hastada ölüm riski artışı

YBÜ de kalış süresi uzaması (>3 gün)

ICU dışında ve yeterli kaynak olmadığında daha basit sistemlere gereksinim vardır

ICU DIŞINDA SEPSİS OLASILIĞININ TARANMASI

Quick SOFA (qSOFA)

- Solunum Hızı≥ 22/dak
- Şuur Değişikliği
- Sistolik Kan Basıncı ≤ 100 mmHg

3 klinik kriterden 2'sinin varlığı

qSOFA

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

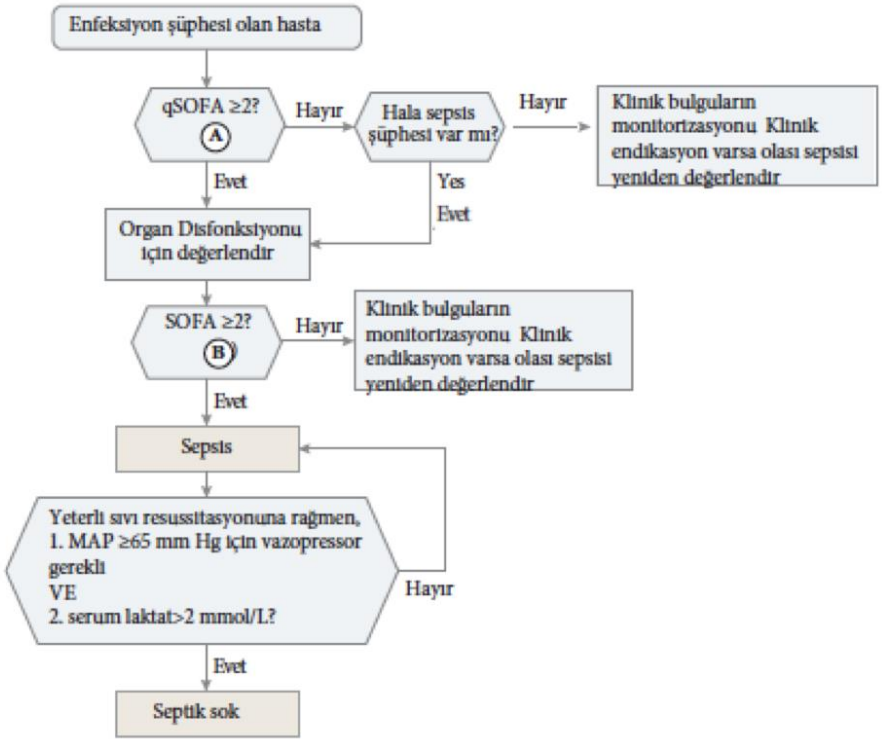
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM;

JAMA. 2016;315(8):801-810

stop sepsis save lives

Sepsis ve Septik Şoklu Hastaların Ayırt Edilmesi için Klinik Kriterler



Türk Yoğun Bakım Derneği

(A) qSOFA değişkenleri
- Solunum hızı
- Mental durum
- Sistolik kan basıncı

(B) SOFA değişkenleri
- PaO_2/FiO_2
- GKS
- MAP
- Vazopressor uygulaması (tipi ve infüzyon dozu)
- Serum kreatinin veya idrar debisi
- Bilirubin
- Trombosit sayısı

Enfeksiyon başlamadan önce hastada bilinen organ disfonksiyonu (Akut veya Kronik) yok ise bazal SOFA skoru sıfır olarak kabul edilmelidir.

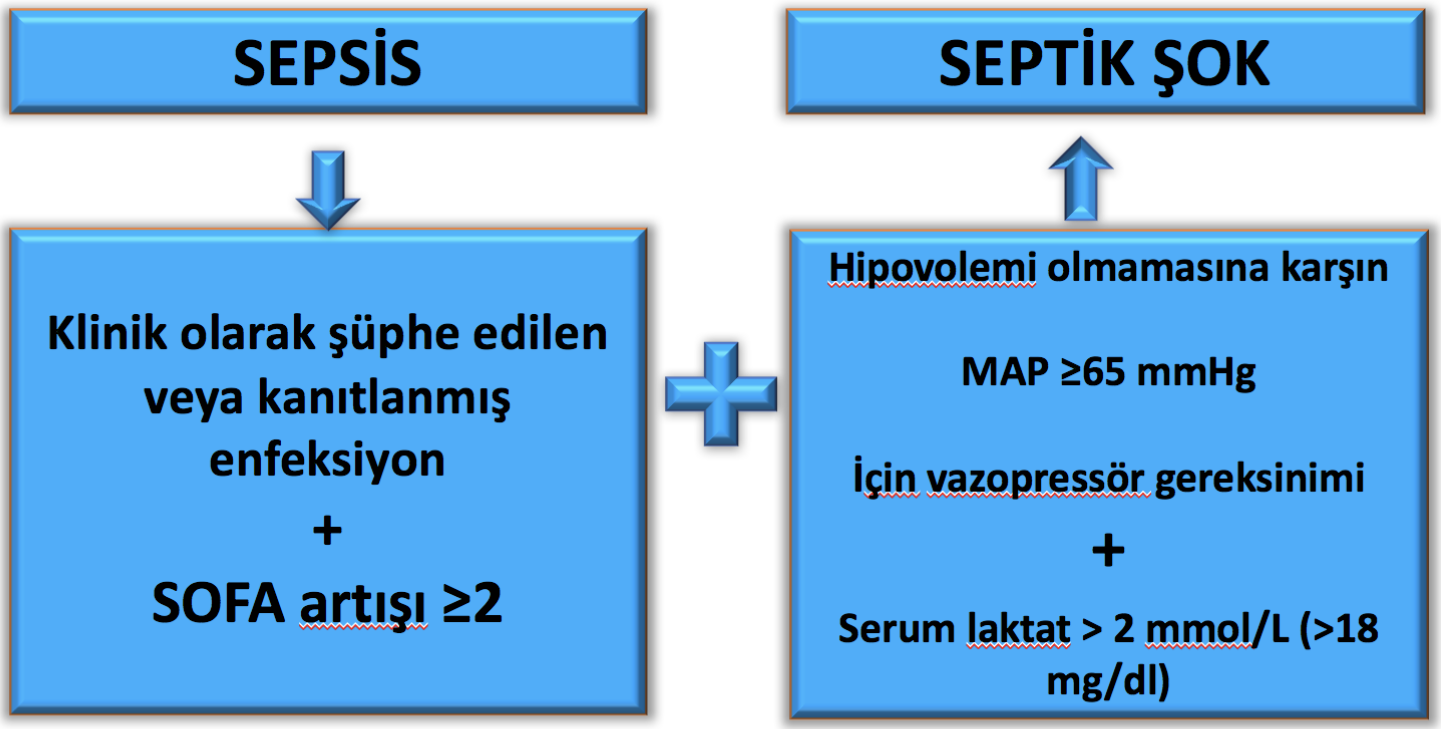
SEPSİS-3 TANIMLARI

- Sepsis “enfeksiyona karşı düzensiz konak cevabı ile oluşan hayatı tehdit eden organ disfonksiyonu”

- Septik şok hipovolemi olmadan laktat seviyesinin 2 mmol L üzerine çıkması ve ortalama arter basıncının 65 mmHg üzerinde tutulması için vazopressör başlanması gereken durum

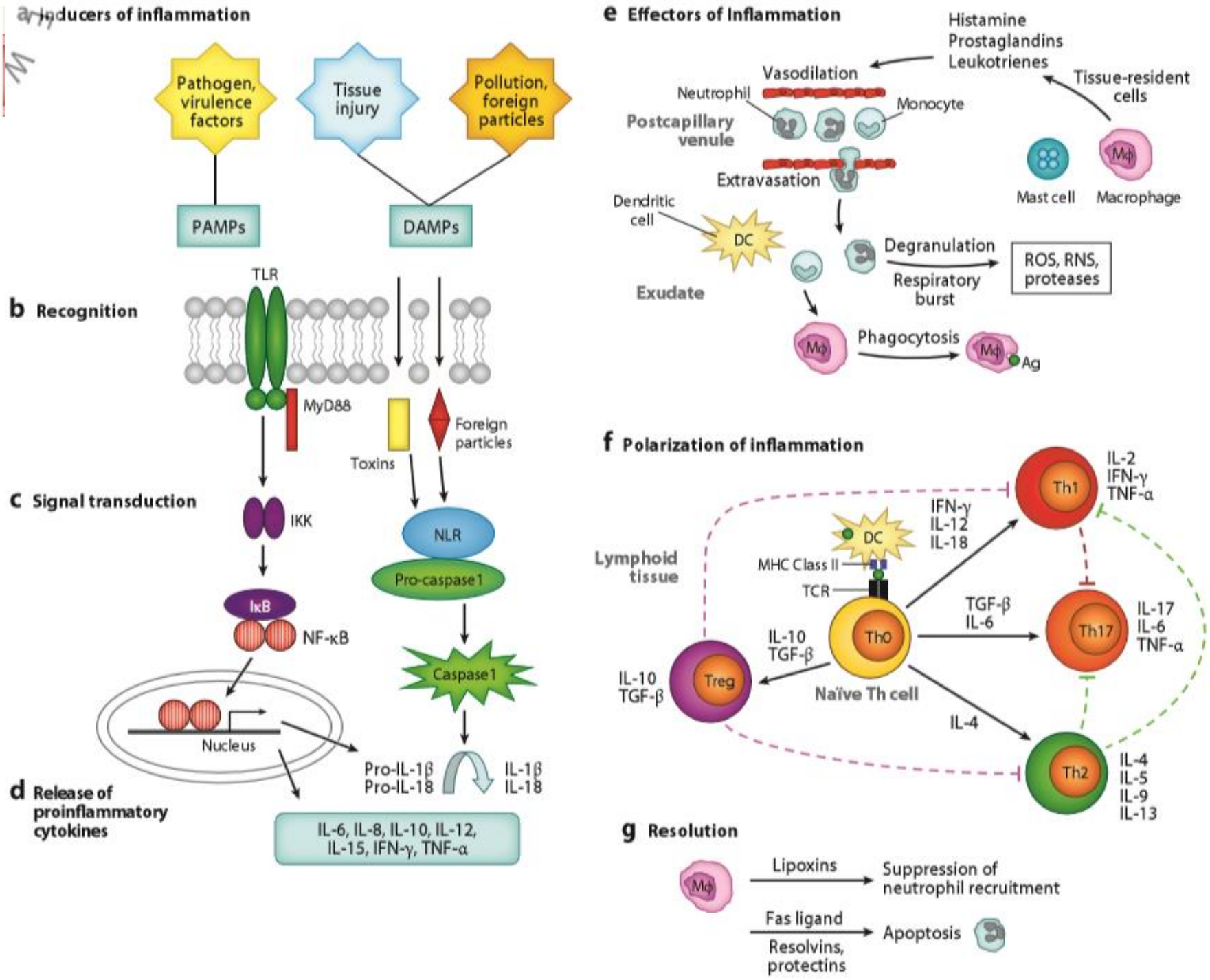
- Önceki rehberlerde geçen şiddetli sepsis tanımı kaldırıldı.

TANIMLAMA

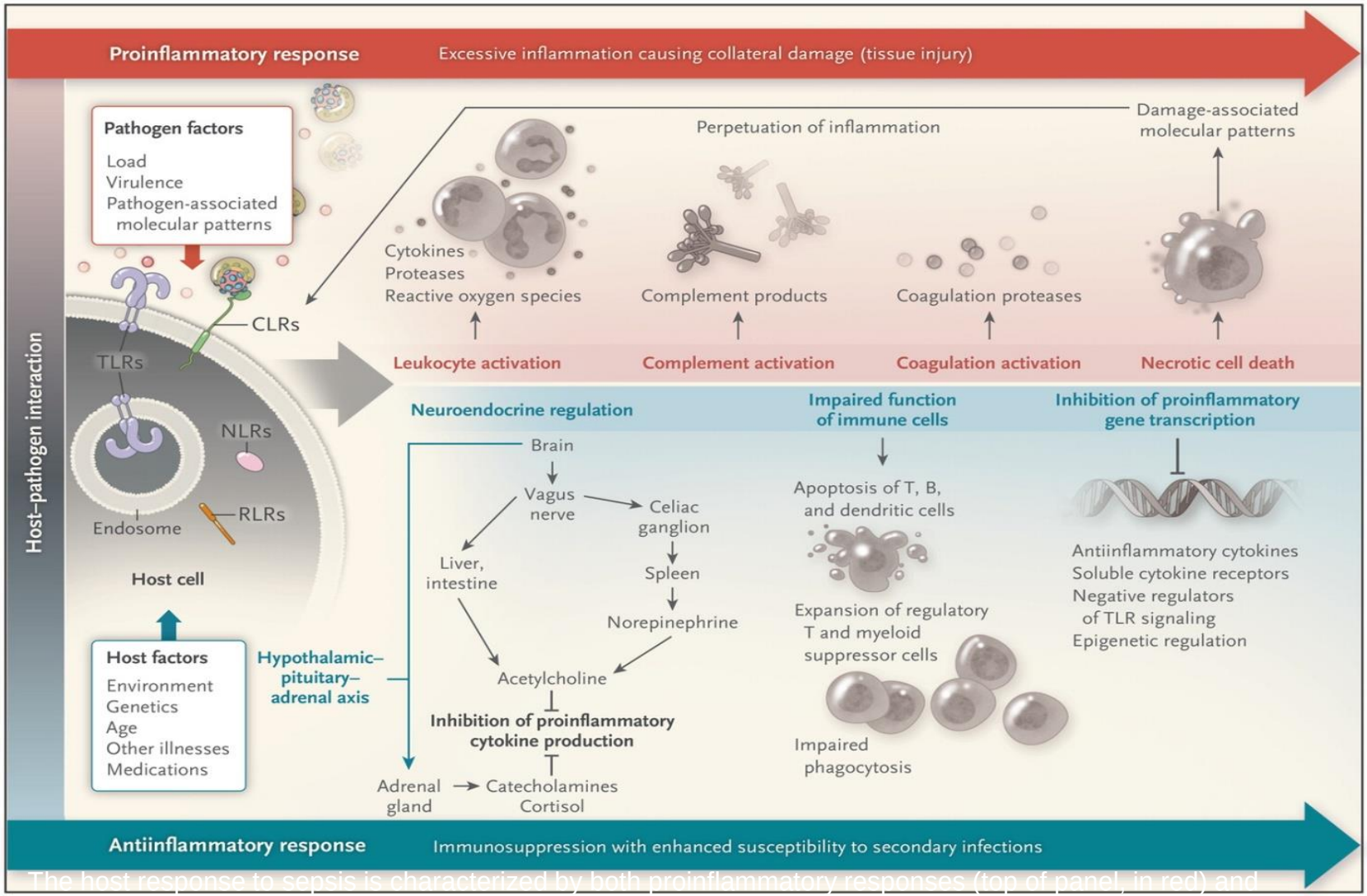


Hastane mortalitesi>%10

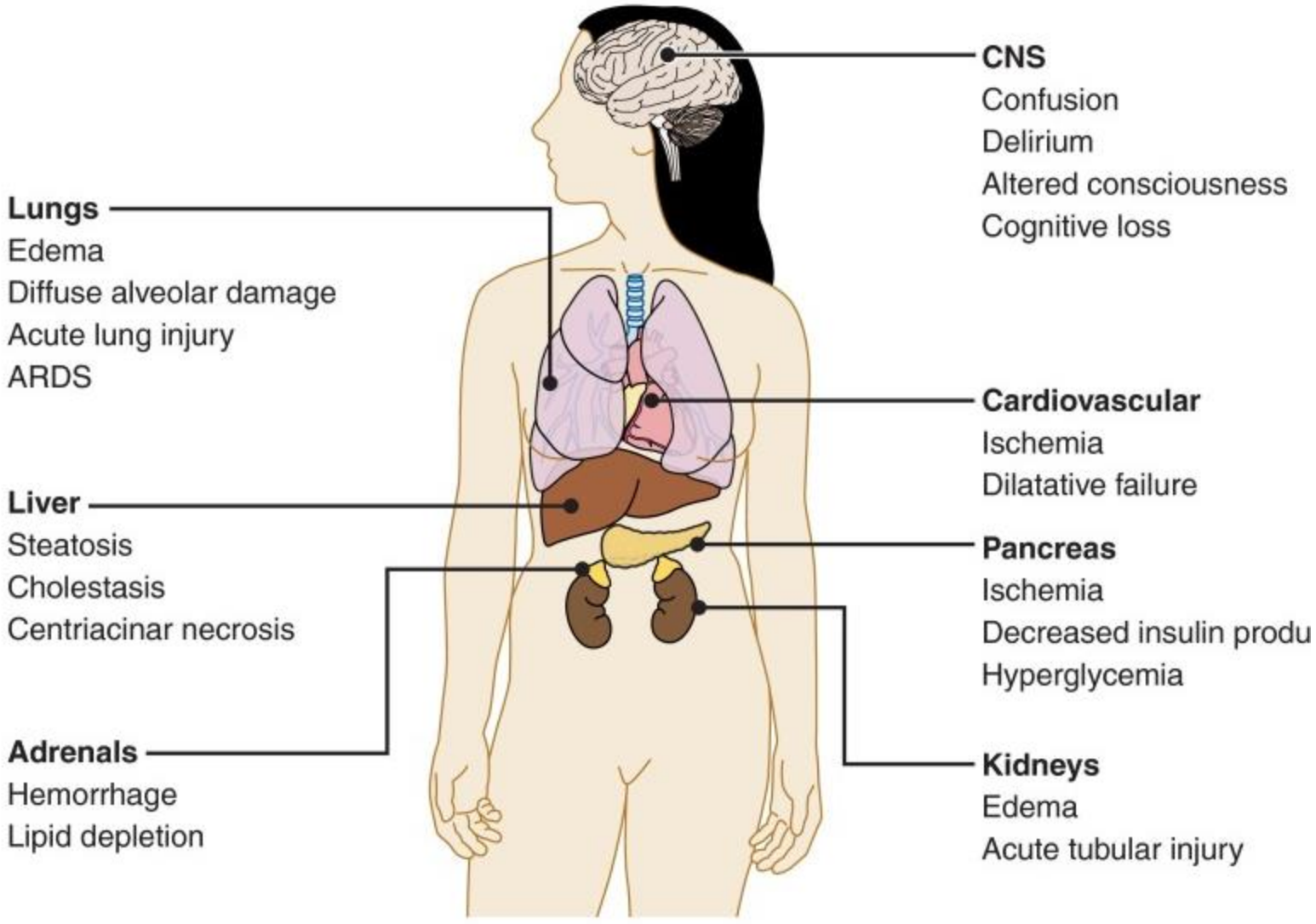
Hastane mortalitesi>%40


a Inducers of inflammation
Pathogen, virulence factors
Tissue injury
Pollution, foreign particles
PAMPs
DAMPs
b Recognition
TLR
MyD88
Toxins
Foreign particles
c Signal transduction
IKK
NLR
Pro-caspase1
IκB
NF-κB
Caspase1
Nucleus
Pro-IL-1β
Pro-IL-18
IL-1β
IL-18
d Release of proinflammatory cytokines
IL-6, IL-8, IL-10, IL-12, IL-15, IFN-γ, TNF-α
e Effectors of Inflammation
Histamine
Prostaglandins
Leukotrienes
Vasodilation
Neutrophil
Monocyte
Postcapillary venule
Extravasation
Tissue-resident cells
Mast cell
Macrophage
Dendritic cell
DC
Degranulation
Respiratory burst
ROS, RNS, proteases
Exudate
Phagocytosis
Ag
f Polarization of inflammation
Lymphoid tissue
DC
MHC Class II
TCR
IFN-γ
IL-12
IL-18
Th1
IL-2
IFN-γ
TNF-α
TGF-β
IL-6
Th17
IL-17
IL-6
TNF-α
IL-10
TGF-β
Th0
Treg
IL-10
TGF-β
Naïve Th cell
IL-4
Th2
IL-4
IL-5
IL-9
IL-13
g Resolution
Lipoxins
Suppression of neutrophil recruitment
Fas ligand
Resolvins, protectins
Apoptosis

Sepsis Patogenezi



The host response to sepsis is characterized by both proinflammatory responses (top of panel, in red) and



End Organ Damage in Sepsis

SEPSİS YÖNETİMİ


Sepsis ve Septik Şok Yönetimi
Başlangıç Resüsitasyon
Tanı
Antibiyotik Tedavisi
Kaynak Kontrolü
Sıvı Tedavisi
Vazopresörler
Kortikosteroid
Kan Ürünü
Glukoz Kontrolü
Bikarbonat Tedavisi
Mekanik Ventilasyon
Antikoagülanlar
Venöz Tromboemboli Profilaksisi
Stres Ülser Profilaksisi
İmmunoglobulinler
Renal Replasman Tedavisi
Nütrisyon
Sepsis Rehberi 2016

Tedavi Başlama Zamanı

- Hastane mortalitesi:%20-60
  - İlk 1 saatte başlanırsa %20
  - 6 saatten sonra başlanırsa %70

Kumar A. Critical Care Medicine 2006; 34: 1589–96.
Angus DC. Crit Care Med, 2001. 29(7): p. 1303-10.
Engel C, Intensive Care Med, 2007. 33(4): p. 606-18.
Angus DC. JAMA, 2010. 304(16): p. 1833-4.

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes, MB BS, MD(Res) (Co-chair)[1]; Laura E. Evans, MD, MSc, FCCM (Co-chair)[2]; Waleed Alhazzani, MD, MSc, FRCPC (methodology chair)[3]; Mitchell M. Levy, MD, MCCM[4];

stop sepsis save lives

89 Öneri

- 32 **Güçlü Öneri**

EİU

- 18 En iyi uygulama bildirimi

- 39 **Zayıf Öneri**

SEPSİS YÖNETİMİ

- Sepsis tedavisinde demet kullanımı, en iyi kanıt temelinde kullanılmaya başlanan bir grup tedavidir.
- Sepsis Sağkalım Kampanyası 2012 rehberinde “şiddetli sepsis 3 saatlik resüssitasyon demeti” ve “6 saatlik septik şok demeti” önerilmişti.
- Ancak 2018 yılında iki demet bir saatlik demette birleştirildi

Sepsis tedavisinde ilk bir saatte yapılması gerekenler

Sepsis Sağkalım Kampanyası İlk 1 saat Paketi	
İlk 1 saatte yapılması gerekenler	**Öneri Gücü ve Kanıt Düzeyi.**
Laktat düzeyini ölç. İlk laktat >2mmol/L ise tekrar ölç.	Zayıf öneri, düşük kanıt kalitesi.
Antibiyotik vermeden önce kan kültürlerini al.	En iyi uygulama (BPS).
Geniş spektrumlu antibiyotik ver.	Güçlü öneri, orta kanıt kalitesi.
Hipotansiyon veya laktat düzeyi >4mmol/L için hızla 30ml/kg kristalloid başla.	Güçlü öneri, düşük kanıt kalitesi.
Hasta sıvı resüsitasyonu süresince veya resüsitasyon sonrasında hipotansif ise >65mmHg ortalama kan basıncı (MAP) değerine ulaşmak amacıyla vazopressör ver.	Güçlü öneri, orta kanıt kalitesi.

Hour-1 Bundle

Initial Resuscitation for Sepsis and Septic Shock

Surviving Sepsis Campaign

MEDICAL EMERGENCY

Initiate bundle upon recognition of sepsis/septic shock.

May not complete all bundle elements within one hour of recognition.

1 Measure lactate level.

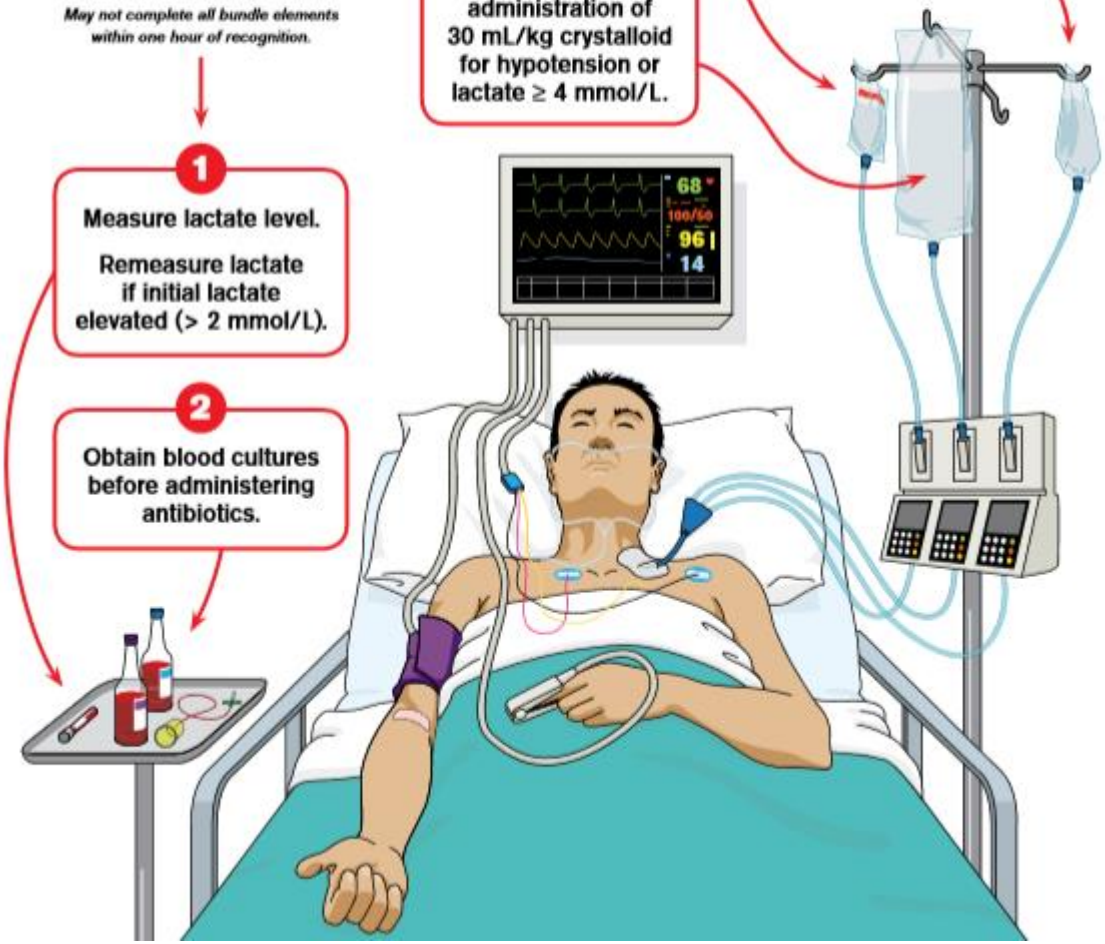
Remeasure lactate if initial lactate elevated (> 2 mmol/L).

2 Obtain blood cultures before administering antibiotics.

3 Administer broad-spectrum antibiotics.

4 Begin rapid administration of 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L.

5 Apply vasopressors if hypotensive during or after fluid resuscitation to maintain a mean arterial pressure ≥ 65 mm Hg.

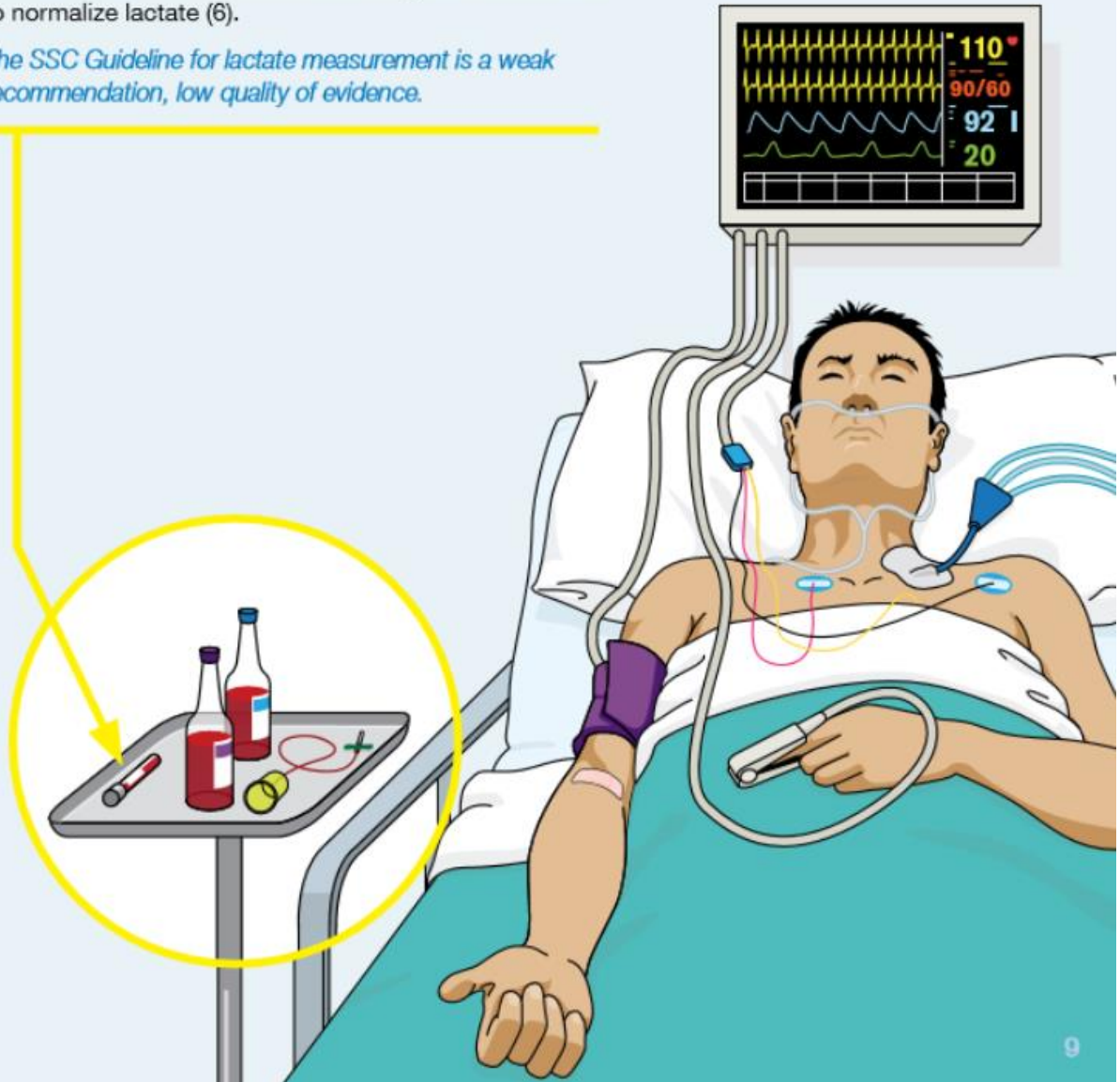


1. Measure Lactate Level

Serum lactate can be a surrogate for tissue perfusion (4,5). Studies have shown a significant reduction in mortality via lactate-guided resuscitation (6-10).

If initial lactate is >2mmol/L, the guidelines recommend remeasurement within 2 to 4 hours to guide resuscitation to normalize lactate (6).

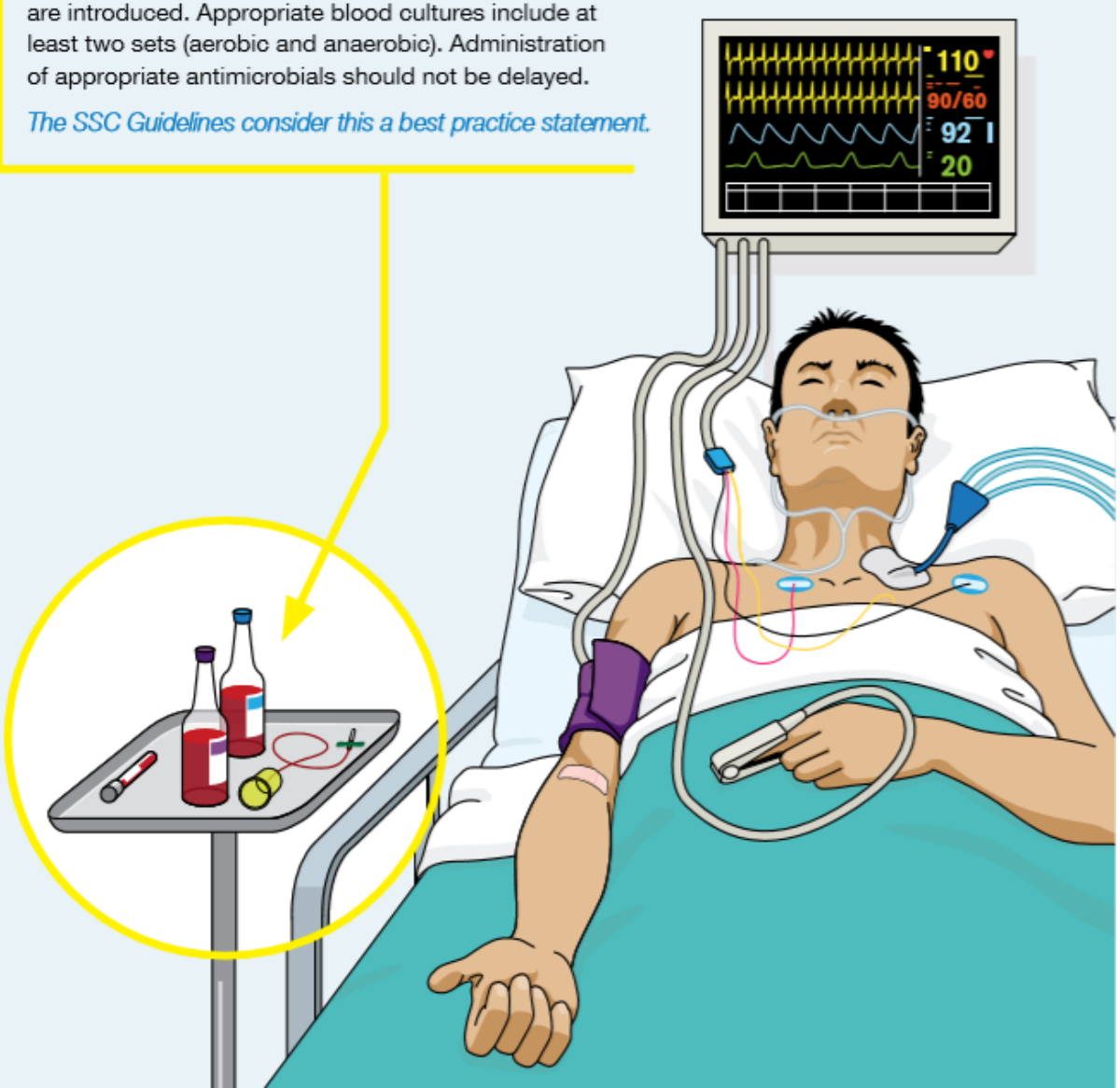
The SSC Guideline for lactate measurement is a weak recommendation, low quality of evidence.



2. Obtain Blood Cultures Before Administering Antibiotics

Optimizing the identification of pathogens to improve outcomes is crucial. Because cultures can be sterilized within minutes of delivery of the appropriate antimicrobial (11,12), cultures should be drawn before antimicrobials are introduced. Appropriate blood cultures include at least two sets (aerobic and anaerobic). Administration of appropriate antimicrobials should not be delayed.

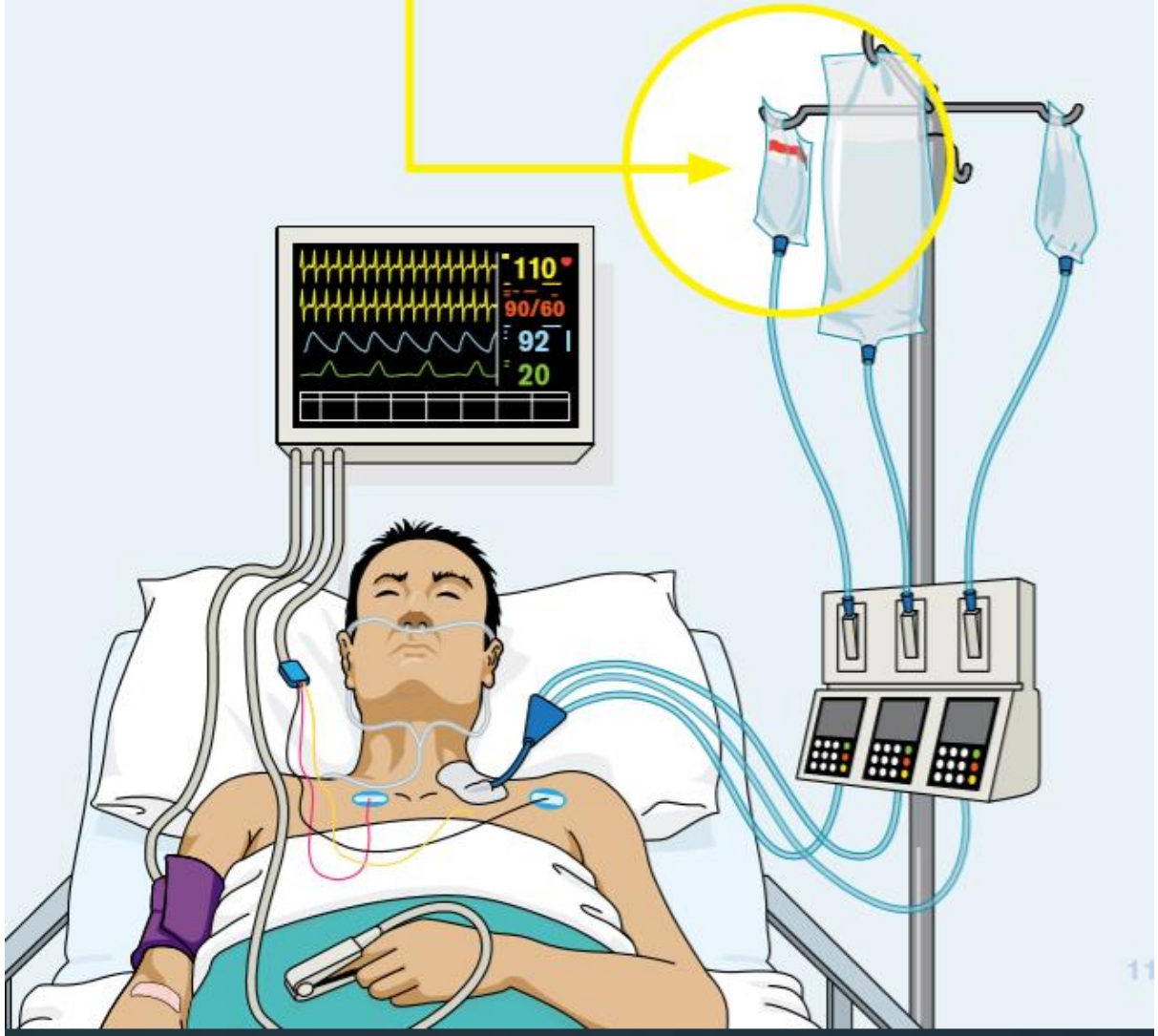
The SSC Guidelines consider this a best practice statement.



3. Administer Broad-Spectrum Antibiotics

One or more intravenous antimicrobials should be started immediately (13). Once pathogen identification and sensitivities are established, empiric antimicrobial therapy should be narrowed or discontinued if the patient does not have an infection. The consideration of early administration of antibiotics for suspected infection and antibiotic stewardship are essential to high-quality sepsis management.

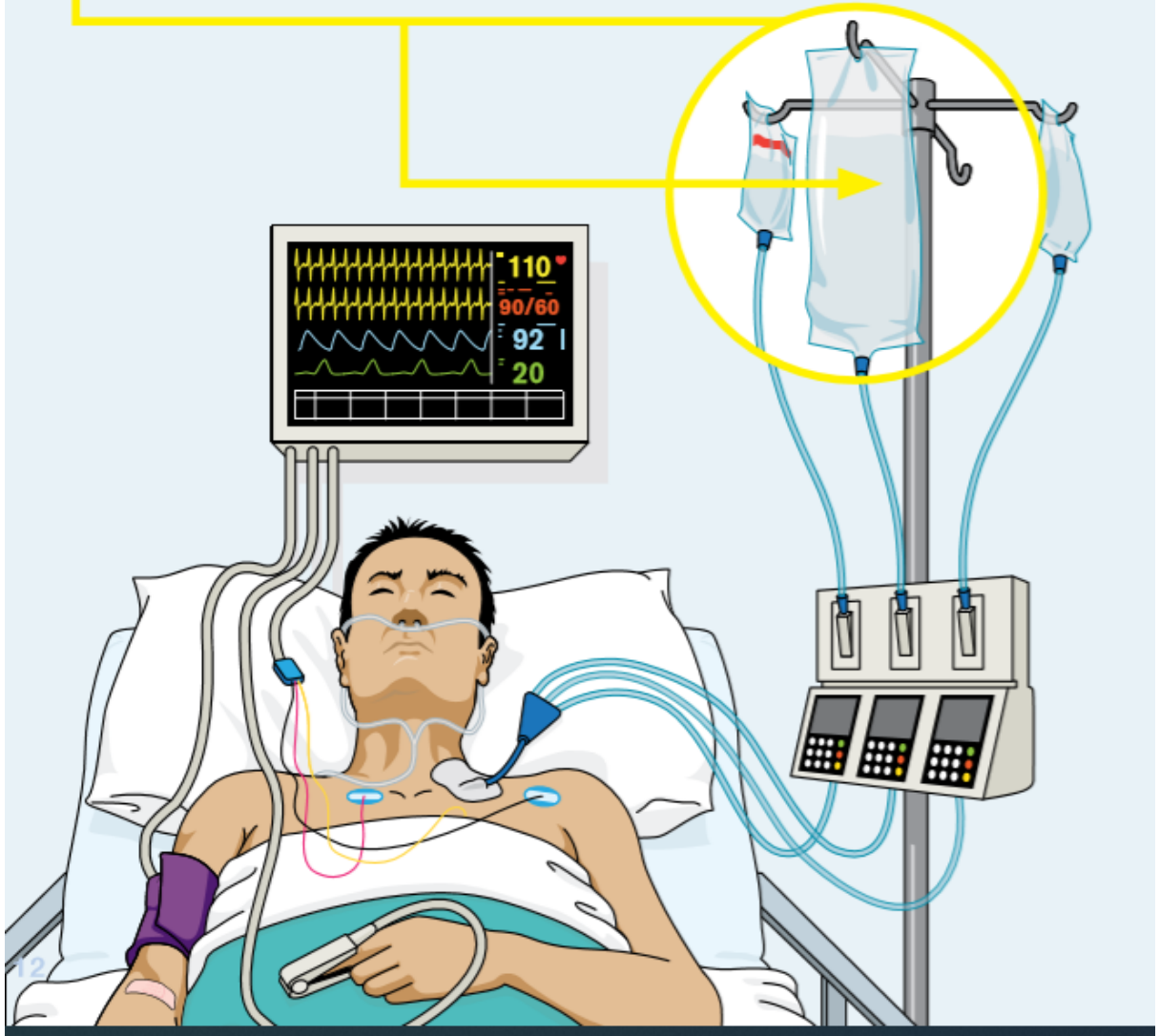
The SSC Guideline is a strong recommendation, moderate quality of evidence.



4. Administer IV Fluid

Initial fluid resuscitation should begin immediately upon recognizing a patient with sepsis and/or hypotension and elevated lactate. The guidelines recommend a minimum of 30 mL/kg of intravenous crystalloid fluid to be completed within 3 hours of recognition. Observational evidence supports this volume (1,14). Fluid administration beyond initial resuscitation should be carefully monitored to ensure that the patient remains fluid responsive.

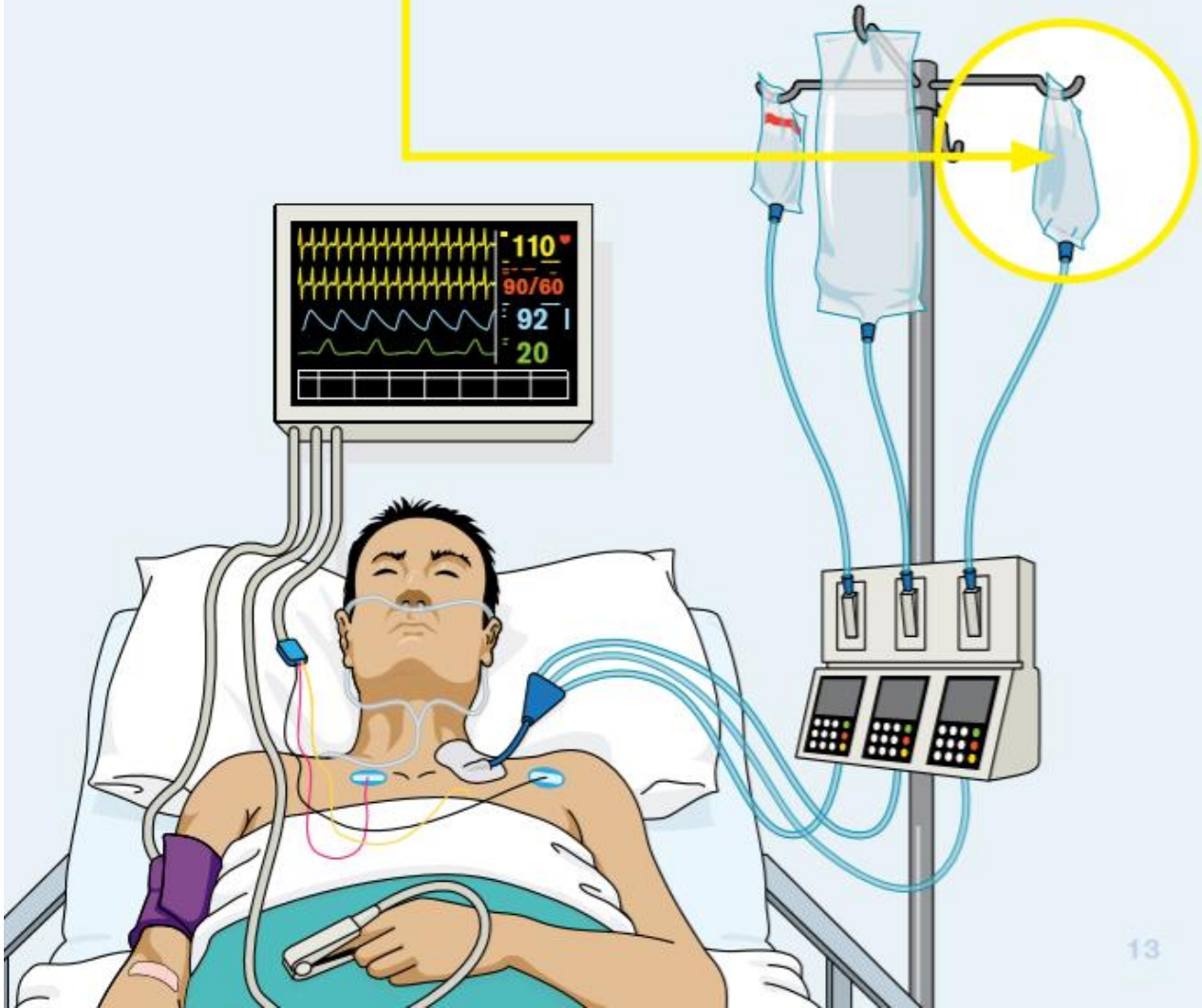
The SSC Guideline is a strong recommendation, low quality of evidence.



5. Apply Vasopressors

Restoration of adequate perfusion pressure to the vital organs is essential. Vasopressors should be started within the first hour to achieve MAP of ≥ 65 mm Hg if initial fluid resuscitation is not adequate.

The SSC Guideline is a strong recommendation, moderate quality of evidence.



Laktat Ölçülmesi

- Serum laktat seviyesi doku perfüzyonunun dolaylı bir göstergesidir.
- Laktat artışı; doku hipoksisi, aşırı beta-adrenarjik uyarının arttırdığı hızlanmış aerobik glikoliz veya daha kötü sonlanımlar ile ilişkili diğer nedenlerin göstergesi olabilmektedir
- İlk bakılan laktat > 2 mmol/L ise, 2-4 saat içerisinde tekrar ölçülüp başlanmış olan resüsitasyon buna göre yönlendirilmelidir

Enfeksiyon Kontrolü

- Sepsisin başlangıç tedavisinin en önemli parçası kaynak kontrolü ve uygun antibiyotik başlanmasıdır.
- Uygun antibiyotik seçimi; önceki enfeksiyonlar, kullanılan antibiyotikler, lokal antibiyotik paterni, antibiyotik duyarlılıkları, major klinik komorbiditeler ve altta yatan sendromlar gibi çok sayıda etkene bağlıdır.
- Her saat gecikmenin mortaliteyi yaklaşık %7 artırdığı gösterilmiş.
- İlk saatte başlanan antibiyotik ile sağkalım oranı %80 lere çıkmaktadır
- Antibiyotik verilmeden önce kültürler alınmalıdır.

Kaynak Kontrolü

- Enfeksiyon kaynağının bulunması ve tedavisi çok önemlidir.
- Enfekte sıvı birikiminin drene edilmesi,
- potansiyel enfekte aletin çıkarılması (santral venöz katater gibi)
- perfore barsak rezeksiyon ve anastomozu gibi işlemlerin geciktirilmeden yapılması gerekir

Antibiyotik

- Tanı konur konmaz 1 saat içinde başlanır
- Olası tüm patojenleri kapsayan geniş spektrumlu antb
- Kültür sonuçlarına göre günlük gözden geçirilir
- Rutin kombinasyon gerekli değildir, başlanırsa 3-5 günü geçmez
- Kültür alınamıyorsa antibiyotik geciktirilmez
- Septik şok başlangıç tedavisine olası patojenleri kapsayan geniş spektrumlu ve kombine antibiyotik tedavisi ampirik başlanır
- Antibiyotik dozları farmakodinamik ve farmakokinetik prensiplere göre düzenlenir.
- Antibiyotik süresi 7-10 günü geçmez

International Study of the Prevalence and Outcomes of Infection in Intensive Care Units

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Claude D. Martin, MD
Rui Moreno, MD, PhD
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Charles Gomersall, MD
Yasser Sakr, MD, PhD
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for the EPIC II Group of Investigators

Context Infection is a major cause of morbidity and mortality in intensive care units (ICUs) worldwide. However, relatively little information is available about the global epidemiology of such infections.

Objective To provide an up-to-date, international picture of the extent and patterns of infection in ICUs.

Design, Setting, and Patients The Extended Prevalence of Infection in Intensive Care (EPIC II) study, a 1-day, prospective, point prevalence study with follow-up conducted on May 8, 2007. Demographic, physiological, bacteriological, therapeutic, and outcome data were collected for 14 414 patients in 1265 participating ICUs from 75 countries on the study day. Analyses focused on the data from the 13 796 adult (>18 years) patients.

Results On the day of the study, 7087 of 13 796 patients (51%) were considered infected; 9084 (71%) were receiving antibiotics. The infection was of respiratory origin in 4503 (64%), and microbiological culture results were positive in 4947 (70%) of the infected patients; 62% of the positive isolates were gram-negative organisms, 47% were gram-positive, and 19% were fungi. Patients who had longer ICU stays prior to the study day had higher rates of infection, especially infections due to resistant staphylococci, *Acinetobacter*, *Pseudomonas* species, and *Candida* species. The ICU mortality rate of infected patients was more than twice that of noninfected patients (25% [1688/6659] vs 11% [682/6352], respectively; $P<.001$), as was the hospital mortality rate (33% [2201/6659] vs 15% [942/6352], respectively; $P<.001$) (adjusted odds ratio for risk of hospital mortality, 1.51; 95% confidence interval, 1.36-1.68; $P<.001$).

Conclusions Infections are common in patients in contemporary ICUs, and risk of infection increases with duration of ICU stay. In this large cohort, infection was independently associated with an increased risk of hospital death.

JAMA. 2009;302(21):2323-2329 www.jama.com

INFECTION IS A COMMON PROBLEM FOR patients in intensive care units (ICUs) and is associated with considerable morbidity, mortality, and costs.[1-4] Infection and related sepsis are the leading cause of death in noncardiac ICUs, with mortality rates that reach 60% and account for approximately 40% of total ICU expenditures.[1,5] Importantly, the incidence of sepsis is increas-

YBÜ Enfeksiyonları

- 75 ülkeden 1265 YBÜ 14,414 hasta.
- 13 796 yetişkin hastanın 7087 (% 51) enfekte
- Hastaların %71 i antibiyotik alıyor

YBÜ Enfeksiyonları

- Enfeksiyonların %64 ü (4503) solunum sistemi kaynaklı,
- Enfekte hastaların % 70 inde kültür pozitif;
- İzolatların % 62 gram-negatif organizmalar,
- %47 gram-pozitif,
- % 19 mantar.

	No. (%)[a]					
	All	Western Europe	Eastern Europe	Central/ South America	North America	
No. (%)	7087 (51.4)	3683 (49)	426 (56.4)	1290 (60.3)	607 (48.4)	2
Site of infection						
Respiratory tract	4503 (63.5)	2332 (63.3)	305 (71.6)[b]	851 (66)	345 (56.8)[b]	1
Abdominal	1392 (19.6)	778 (21.1)	93 (21.8)	228 (17.7)[b]	101 (16.6)	
Bloodstream	1071 (15.1)	546 (14.8)	53 (12.4)	139 (10.8)[b]	157 (25.9)[b]	
Renal/urinary tract	1011 (14.3)	411 (11.2)	84 (19.7)[b]	222 (17.2)[b]	135 (22.2)[b]	
Skin	467 (6.6)	242 (6.6)	37 (8.7)	73 (5.7)	26 (4.3)	
Catheter-related	332 (4.7)	171 (4.6)	21 (4.9)	73 (5.7)	16 (2.6)	
CNS	208 (2.9)	100 (2.7)	20 (4.7)	40 (3.1)	14 (2.3)	
Others	540 (7.6)	289 (7.8)	31 (7.3)	87 (6.7)	62 (10.2)	
Microorganisms						
Positive isolates	4947 (69.8)	2678 (72.7)	357 (83.8)[b]	719 (55.7)[b]	457 (75.3)	2
Gram-positive	2315 (46.8)	1311 (49.0)	185 (51.8)	273 (38.0)[b]	252 (55.1)	1
Staphylococcus aureus	1012 (20.5)	525 (19.6)	77 (21.6)	138 (19.2)	123 (26.9)[b]	
MRSA	507 (10.2)	233 (8.7)	37 (10.4)	79 (11.0)	80 (17.5)[b]	
S epidermidis	535 (10.8)	301 (11.2)	43 (12)	67 (9.3)	56 (12.3)	
Streptococcus pneumoniae	203 (4.1)	127 (4.7)	16 (4.5)	24 (3.3)	20 (4.4)	
VSE	352 (7.1)	250 (9.3)	35 (9.8)	17 (2.4)[b]	24 (5.3)[b]	
VRE	186 (3.8)	113 (4.2)	16 (4.5)	15 (2.1)[b]	22 (4.8)	
Other	319 (6.4)	184 (6.9)	15 (4.2)	29 (4.0)[b]	48 (10.5)	
Gram-negative	3077 (62.2)	1573 (58.7)	258 (72.3)[b]	510 (70.9)[b]	228 (49.9)[b]	1

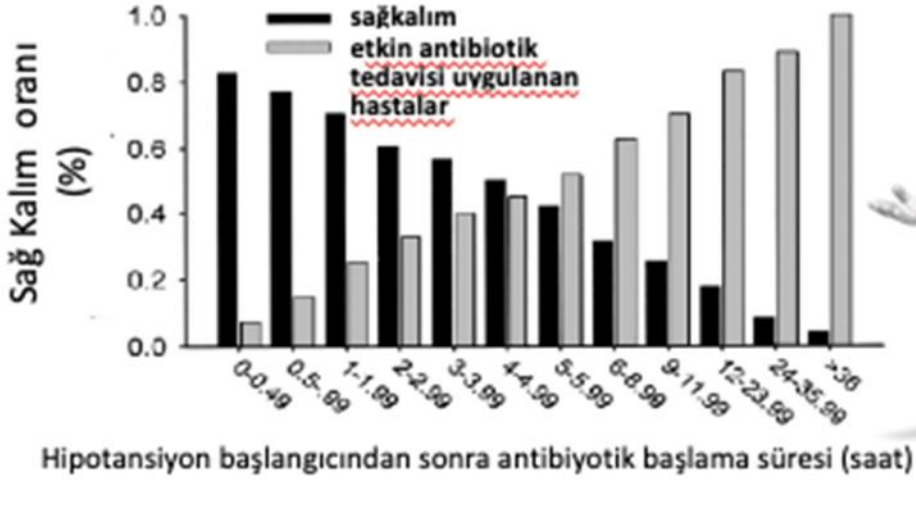
Bloodstream	1071 (15.1)	546 (14.8)	53 (12.4)	139 (10.8)	157 (23.9)	49 (17.2)	16 (18)	111 (15.7)
Renal/urinary tract	1011 (14.3)	411 (11.2)	84 (19.7)[b]	222 (17.2)[b]	135 (22.2)[b]	33 (11.6)	15 (16.9)	111 (15.7)[b]
Skin	467 (6.6)	242 (6.6)	37 (8.7)	73 (5.7)	26 (4.3)	30 (10.5)	8 (9.0)	51 (7.2)
Catheter-related	332 (4.7)	171 (4.6)	21 (4.9)	73 (5.7)	16 (2.6)	15 (5.3)	4 (4.5)	32 (4.5)
CNS	208 (2.9)	100 (2.7)	20 (4.7)	40 (3.1)	14 (2.3)	11 (3.9)	4 (4.5)	19 (2.7)
Others	540 (7.6)	289 (7.8)	31 (7.3)	87 (6.7)	62 (10.2)	22 (7.7)	14 (15.7)[b]	35 (5.0)[b]
Microorganisms								
Positive isolates	4947 (69.8)	2678 (72.7)	357 (83.8)[b]	719 (55.7)[b]	457 (75.3)	204 (71.6)	54 (60.7)	478 (67.6)[b]
Gram-positive	2315 (46.8)	1311 (49.0)	185 (51.8)	273 (38.0)[b]	252 (55.1)	104 (51.0)	27 (50.0)	163 (34.1)[b]
Staphylococcus aureus	1012 (20.5)	525 (19.6)	77 (21.6)	138 (19.2)	123 (26.9)[b]	56 (27.5)[b]	16 (29.6)	77 (16.1)
MRSA	507 (10.2)	233 (8.7)	37 (10.4)	79 (11.0)	80 (17.5)[b]	19 (9.3)	11 (20.4)[b]	48 (10.0)
S epidermidis	535 (10.8)	301 (11.2)	43 (12)	67 (9.3)	56 (12.3)	17 (8.3)	8 (14.8)	43 (9.0)
Streptococcus pneumoniae	203 (4.1)	127 (4.7)	16 (4.5)	24 (3.3)	20 (4.4)	5 (2.5)	3 (5.6)	8 (1.7)[b]
VSE	352 (7.1)	250 (9.3)	35 (9.8)	17 (2.4)[b]	24 (5.3)[b]	9 (4.4)	0[b]	17 (3.6)[b]
VRE	186 (3.8)	113 (4.2)	16 (4.5)	15 (2.1)[b]	22 (4.8)	10 (4.9)	0	10 (2.1)
Other	319 (6.4)	184 (6.9)	15 (4.2)	29 (4.0)[b]	48 (10.5)	19 (9.3)	4 (7.4)	20 (4.2)
Gram-negative	3077 (62.2)	1573 (58.7)	258 (72.3)[b]	510 (70.9)[b]	228 (49.9)[b]	122 (59.8)	31 (57.4)	355 (74.3)[b]
Escherichia coli	792 (16.0)	458 (17.1)	53 (14.8)	103 (14.3)	65 (14.2)	27 (13.2)	6 (11.1)	80 (16.7)
Enterobacter	345 (7.0)	184 (6.9)	29 (8.1)	62 (8.6)	37 (8.1)	7 (3.4)	4 (7.4)	22 (4.6)
Klebsiella species	627 (12.7)	261 (9.7)	76 (21.3)[b]	116 (16.1)[b]	41 (9)	24 (11.8)	10 (18.5)	99 (20.7)[b]
Pseudomonas species	984 (19.9)	458 (17.1)	103 (28.9)[b]	189 (26.3)[b]	59 (12.9)	30 (14.7)	8 (14.8)	137 (28.7)[b]
Acinetobacter species	435 (8.8)	149 (5.6)	61 (17.1)[b]	99 (13.8)[b]	17 (3.7)	9 (4.4)	8 (14.8)[b]	92 (19.2)[b]
Other	840 (17.0)	487 (18.2)	54 (15.1)	121 (16.8)	52 (11.4)[b]	42 (20.6)	11 (20.4)	73 (15.3)
ESBL-producing	93 (1.9)	47 (1.8)	7 (2.0)	21 (2.9)	1 (0.2)[b]	0	1 (1.9)	16 (3.3)
Anaerobes	222 (4.5)	142 (5.3)	12 (3.4)	10 (1.4)[b]	36 (7.9)	7 (3.4)	1 (1.9)	14 (2.9)
Other bacteria	76 (1.5)	33 (1.2)	7 (2.0)	14 (1.9)	4 (0.9)	4 (2.0)	3 (5.6)	11 (2.3)
Fungi								
Candida	843 (17)	495 (18.5)	66 (18.5)	92 (12.8)[b]	83 (18.2)	26 (12.7)	6 (11.1)	75 (15.7)
Aspergillus	70 (1.4)	44 (1.6)	1 (0.3)	5 (0.7)	12 (2.6)	3 (1.5)	0	5 (1)
Other	50 (1)	22 (0.8)	5 (1.4)	7 (1)	10 (2.2)	2 (1)	0	4 (0.8)
Parasites	34 (0.7)	18 (0.7)	2 (0.6)	6 (0.8)	3 (0.7)	2 (1)	0	3 (0.6)
Other organisms	192 (3.9)	122 (4.6)	9 (2.5)	15 (2.1)[b]	22 (4.8)	8 (3.9)	2 (3.7)	14 (2.9)

Abbreviations: CNS, central nervous system; ESBL, extended-spectrum β-lactamases; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus;* VSE, vancomycin-sensitive *Enterococcus.*

[a]Percentages do not necessarily equal 100, because patients may have had more than 1 type of infection or microorganism.

[b]Significant at 5% (with Bonferroni correction) vs Western Europe.

Sepsiste erken tedavinin önemi



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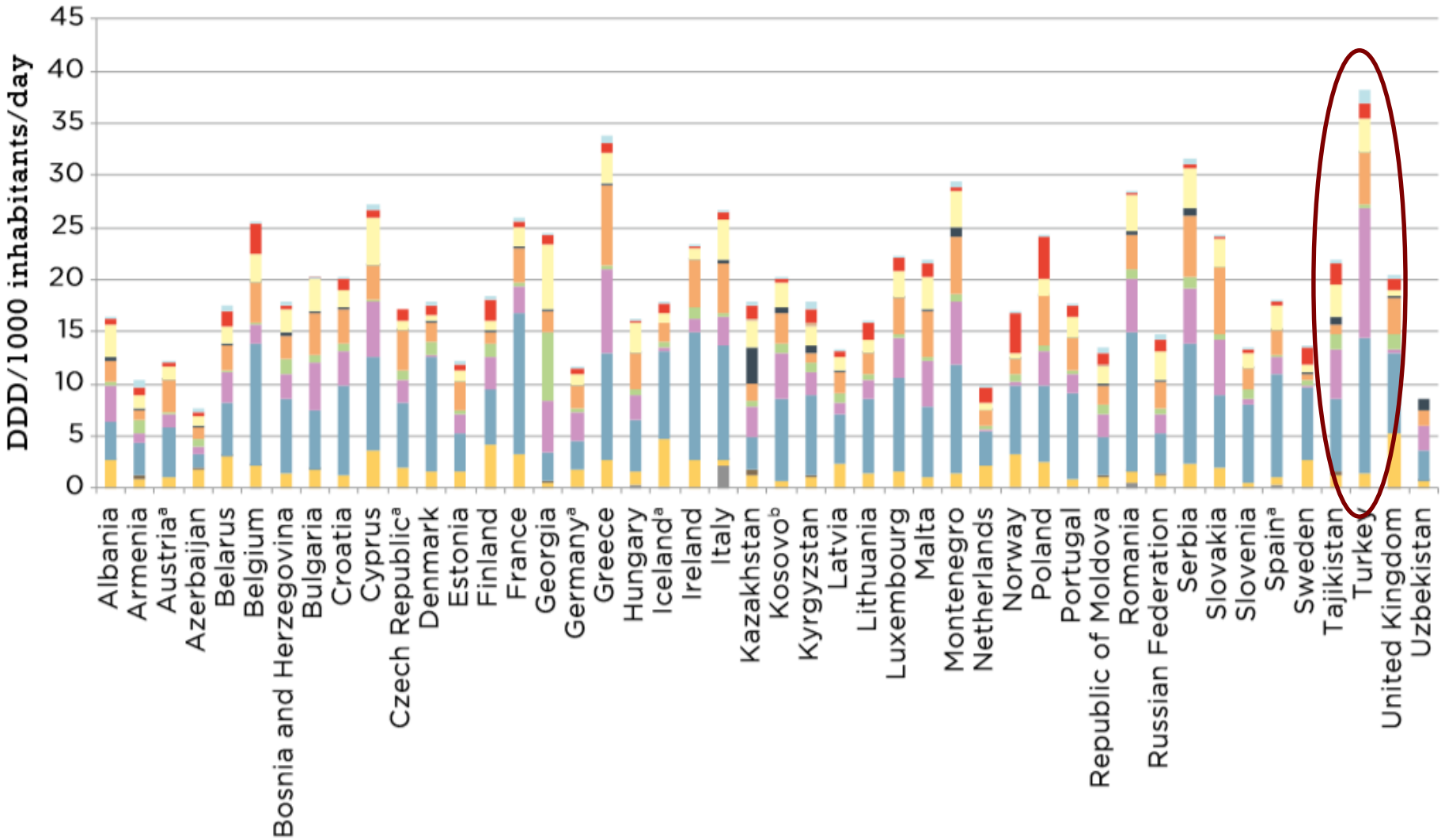
- WSD_Sepsisburden_2015.pdf

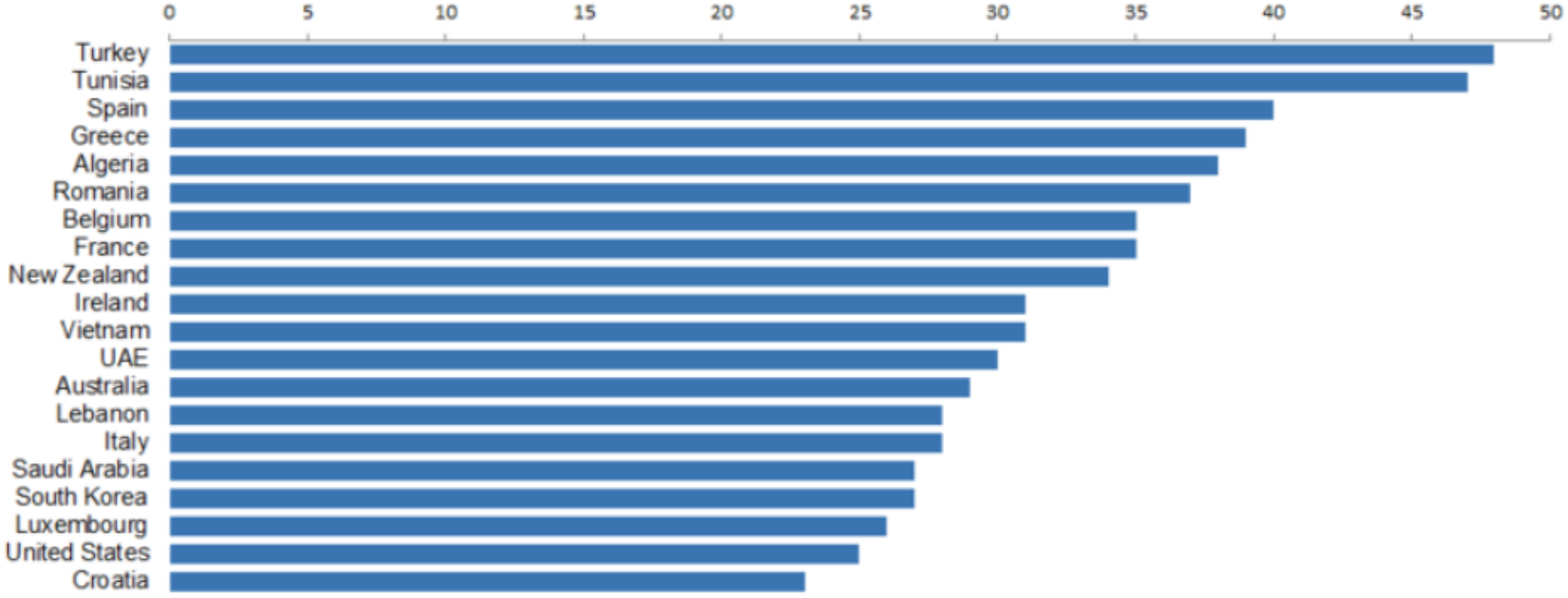
- **Antibiyotik tedavisinde her saat gecikme = yaşam şansını %7.6 oranında azalma.**
- **Ortalama Antibiyotik başlama süresi = 6 saat**

Fig. 4.6 Consumption of antibiotics (DDD per 1000 inhabitants per day) by pharmacological subgroup in 45 countries and Kosovo[3] of the European Region, 2015



Global antibiotic use by country

Daily dose per 1,000 inhabitants in 2015 (with global average at 15 per day)



Source: IQVIA MIDAS

Sıvı resüssitasyonu

- Sepsisle oluşan doku perfüzyon azalması akut organ fonksiyon bozukluğu veya başlangıç sıvı tedavisine ragmen dirençli hipotansiyon veya kan laktat düzeyinin $\geqslant$ 4 mmol L olmasıdır.
- Bu nedenle erken agresif sıvı resüssitasyonu şiddetli sepsis/septik şoklu hastanın stabilize edilmesinin temelini oluşturur.
- Doku perfüzyon bozukluğu olan sepsisde başlangıç sıvı tedavisi kristaloidlerle ve ilk 3 saatte 30 mL/ kg ile yapılır
- Kolloidlerin kristaloidlere göre ek bir fayda sağlamadığından ve albüminin getirdiği ek maliyet nedeni ile öncelikli olarak kristaloidler ile sıvı resüsitasyonu önerilmektedir
- Albumin ve Hidroksietil nişasta (HES) önerilmemektedir

Vazopressör kullanımı

- Septik şok tedavisinde en kritik olan doku perfüzyonunu düzeltmek ve korumaktır.
- Bu sadece kardiyak output düzelterek ve ortalama arter basıncını (MAP) uygun aralığa getirerek olabilir.
- Başlangıç sıvı tedavisi hipotansiyonu düzeltemezse vazopresör kullanılması gerekir. MAP >65mmHg hedefini sağlamak için ilk 1 saatte vazopressör başlanmalıdır.
- Septik şokta en sık kullanılan vazopressörler norepinefrindir.

Steroid kullanımı

- İki mekanizma ile etki eder:
  - immün modülasyon ve
  - kardiyovasküler modülasyon
- Eğer uygun sıvı resüssitasyonu ve vasopressör tedavi ile hastanın hemodinamik stabilitesi sağlanamıyorsa günde 200 mg iv hidrokortizon eklenebilir

The NEW ENGLAND JOURNAL
ESTABLISHED IN 1812

Adjunctive Glucocorti
with Se

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhanda
M. Harward, C. Joyce, Q. Li, C. McArthur, A. Pern
for the ADRENAL Trial Investigators and the Australian

- 90 günlük mortalitede fark yok
- Transfüzyon ihtiyacı azalmış

Table 3. Adverse Events.*

Adverse Event	Hydrocortisone (N=1835)	Placebo (N=1829)
No. of patients with event	21	6
No. of events		
Total adverse events	27	6
Hyperglycemia	6	3
Hypernatremia	3	0
Hyperchloremia	1	0
Hypertension	3	0
Bleeding	2	1†
Encephalopathy	3	0
Leukocytosis	2	0
Myopathy‡	3†	0
Septic arthritis	1	0
Ischemic bowel	1†	0
Abdominal-wound dehiscence	0	1†
Circulatory shock	1†	0
Thrombocytopenia	1	0
Miscellaneous	0	1

CLINICAL FOCUS REVIEW

Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M., Editor

Adjunctive Corticosteroid Treatment in Septic Shock

Jeremy Cohen, M.D., Ph.D., Balasubramanian Venkatesh, M.D.

OLUMLU

- YBÜ kalış süresi kısalmış
- Eritropoeze olumlu etki ile kan transfüzyon ihtiyacı azalmış
- Şoku düzeltmeye katkısı ile sıvı resüssitasyonu miktarı azalmış

OLUMSUZ

- Hiperglisemi ve hipernatremi
- GI kanama
- Nöromuskuler zayıflama
- İmmünsüpresyon

Anesthesiology August 2019, Vol.131, 410-419

CLINICAL FOCUS REVIEW

Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M., Editor

Adjunctive Corticosteroid Treatment in Septic Shock

Jeremy Cohen, M.D., Ph.D., Balasubramanian Venkatesh, M.D.

- Hidrokortizon 200 mg tek doz ve yedi gün kullanılabilir. Bolus ve infüzyon
- Vazopressöre yanıt olmazsa gecikmeden başlanabilir
- Azaltarak kesmeye gerek yoktur.
- Kortikotropin testine gerek yoktur
- Ek fludrokortizona gerek yoktur.

Glisemi kontrolü ve nütrisyon desteği

- Glukoz kontrolünün 180 mg/dL altında olması
- Enteral beslenmeyi tolere eden hastalara sepsis veya septik şokda erken enteral beslenme
- Hem trofik (500 kcal/günlük limit) hemde tam enteral beslenme hasta değerlendirilerek uygulanabilir.
- Sepsis ve septik şokda erken dönemde tam enteral beslenmeden kaçınma artık önerilmiyor.
- 2016 kılavuzunda rutin gastrik rezidü kontrolü önerilmiyor. Sadece aspirasyon riski olan hastalarda öneriliyor.
- Yine 2016 kılavuzunda yeni olan öneri; beslenmeyi tolere edemeyen hastalara prokinetik ajan kullanımı ve postpilorik pozisyonda beslenme tüpü yerleştirmektir.

Kan transfüzyonu

- Hasta septik şok kliniğinde stabilize olduğunda ES transfüzyon sadece hemoglobin düzeyi <7 g/dL olduğunda uygulanmalıdır.
- İstisnaları dirençli ciddi hipoksemi, miyokardiyal iskemi, akut kanama veya aktif iskemik kalp hastalığıdır
- TDP sadece kanama ve invazif girişimlerde
- Trombosit süspansiyonu, aktif kanama, cerrahi girişim veya invazif girişimlerde

YENİLİKLER

1. Tiamin, askorbik asit

- Tiamin (B1 vitamini) ve askorbik asit (C vitamini) son yıllarda sepsis tedavisinde kombine olarak kullanılmaktadır.
- Suda eriyebilen C vitamini serbest oksijen radikalleri için avcıdır, ayrıca demir ve bakır içeren enzimler için kofaktördür. C vitamininin antienflamatuar etkileri gösterilmiştir. Katakolamin ve kortizol sentezini artırır ve endotel bütünlüğünü korur
- Tiamin de hücresel metabolizmanın çok önemli parçasıdır. Doku oksidatif hasarına karşı koruyucudur

2. Anjiyotensin II

- Vazokonstriksiyon ve sıvı retansiyonunu renin-anjiyotensin-aldosteron sistemi üzerinden sağlayan bir ajandır.
- Tromboembolik olay, deliryum, hipokalemi, asidoz ve periferik iskemi plasebo grubundan daha fazla görülmüştür.

[Original Research **Critical Care**]

CHEST

Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock

A Retrospective Before-After Study

PODCAST

Paul E. Marik, MD, FCCP; Vikramjit Khangoora, MD; Racquel Rivera, PharmD; Michael H. Hooper, MD; and John Catravas, PhD, FCCP

BACKGROUND: The global burden of sepsis is estimated as 15 to 19 million cases annually, with a mortality rate approaching 60% in low-income countries.

METHODS: In this retrospective before-after clinical study, we compared the outcome and clinical course of consecutive septic patients treated with intravenous vitamin C, hydrocortisone, and thiamine during a 7-month period (treatment group) with a control group treated in our ICU during the preceding 7 months. The primary outcome was hospital survival. A propensity score was generated to adjust the primary outcome.

RESULTS: There were 47 patients in both treatment and control groups, with no significant differences in baseline characteristics between the two groups. The hospital mortality was 8.5% (4 of 47) in the treatment group compared with 40.4% (19 of 47) in the control group ($P < .001$). The propensity adjusted odds of mortality in the patients treated with the vitamin C protocol was 0.13 (95% CI, 0.04-0.48; $P = .002$). The Sepsis-Related Organ Failure

Moskowitz et al. Critical Care (2018) 22:283
https://doi.org/10.1186/s13054-018-2217-4

Critical Care

REVIEW Open Access

Ascorbic acid, corticosteroids, and thiamine in sepsis: a review of the biologic rationale and the present state of clinical evaluation

Ari Moskowitz[1], Lars W. Andersen[2,3,4], David T. Huang[5,6], Katherine M. Berg[1], Anne V. Grossestreuer[2], Paul E. Marik[7], Robert L. Sherwin[8], Peter C. Hou[9], Lance B. Becker[10,11], Michael N. Cocchi[2,12], Pratik Doshi[13], Jonathan Gong[14], Ayan Sen[15] and Michael W. Donnino[1,2,16*]

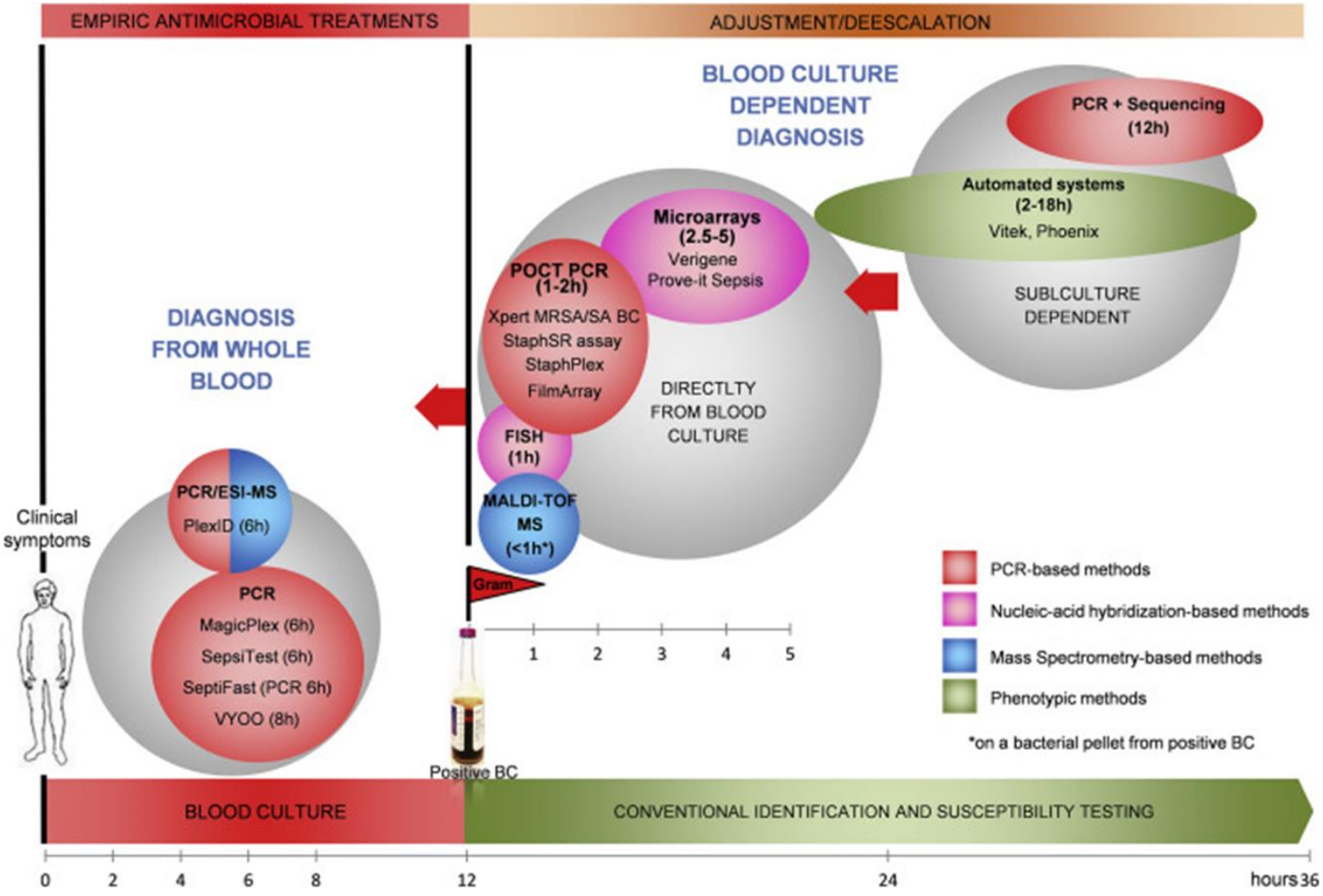
Abstract

The combination of thiamine, ascorbic acid, and hydrocortisone has recently emerged as a potential adjunctive therapy to antibiotics, infectious source control, and supportive care for patients with sepsis and septic shock. In the present manuscript, we provide a comprehensive review of the pathophysiologic basis and supporting research for each element of the thiamine, ascorbic acid, and hydrocortisone drug combination in sepsis. In addition, we describe potential areas of synergy between these therapies and discuss the strengths/weaknesses of the two studies to date which have evaluated the drug combination in patients with severe infection. Finally, we describe the current state of current clinical practice as it relates to the thiamine, ascorbic acid, and hydrocortisone combination and present an overview of the randomized, placebo-controlled, multi-center Ascorbic acid, Corticosteroids, and Thiamine in Sepsis (ACTS) trial and other planned/ongoing randomized clinical trials.

Keywords: Thiamine, Ascorbic acid, Corticosteroids, Metabolic resuscitation, Sepsis

Sepsis yönetiminde gelecekte beklenenler

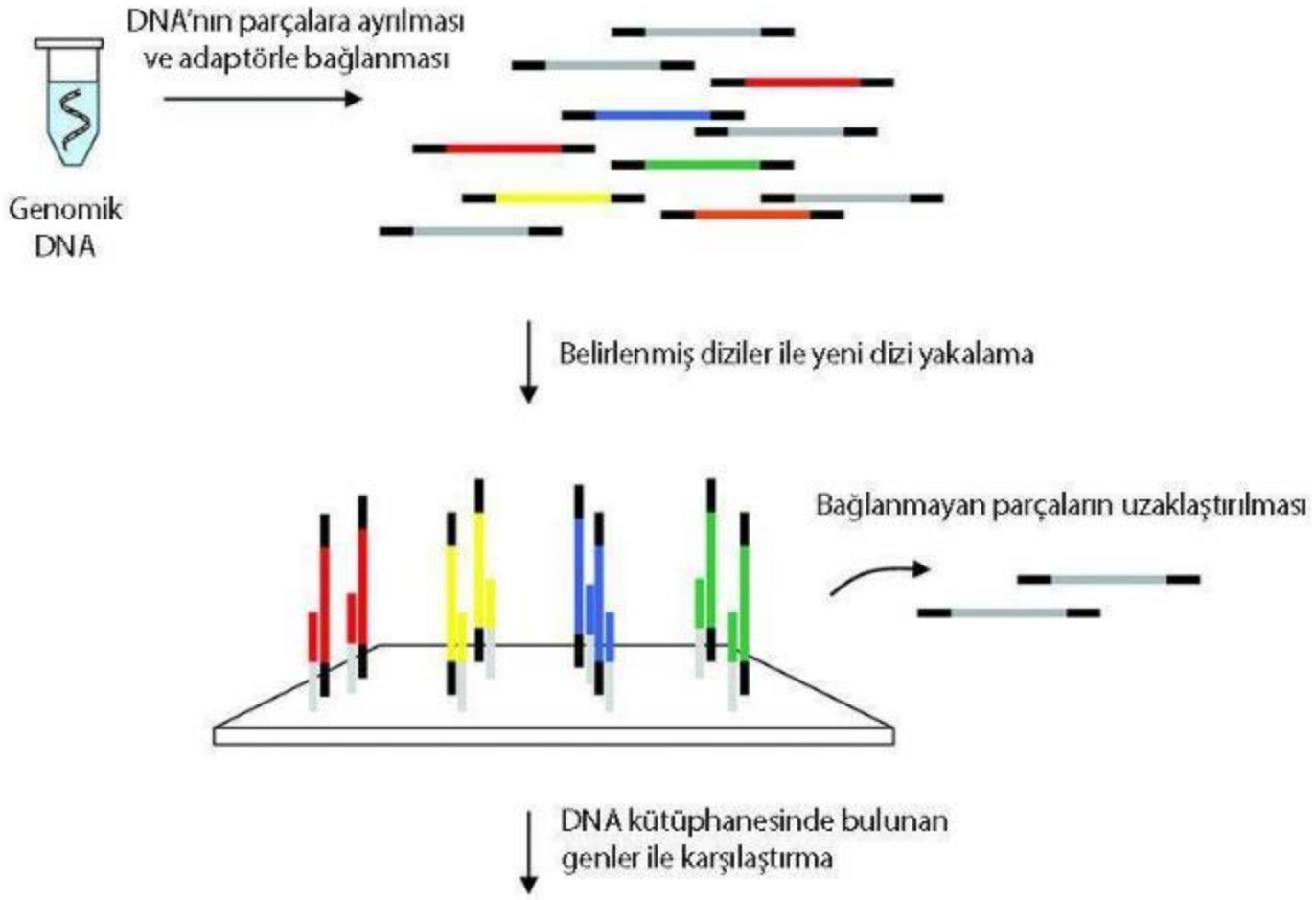
- Farkındalığı artıracak tek bir tanım olması
- Yeni sepsis kriterleri için moleküler indikatörler geliştirilmesi
- Sepsisin erken tanısı koymak için patojenlerin erken saptanmasını sağlayacak hızlı testler geliştirilmesi



(Matriks assisted laser desorption ionization time of flight mass spectrometry)

Güvenliği artırmak için yapılanlar II

- Multiplex Test Teknolojileri
- Mass spektrometre-dayalı sistemler
- Direk klinik örnekten nükleik asit ve proteinlerin moleküler ağırlığına bağlı
- Nükleik asit ve protein microarray testleri
- DNA oligonükleotid probları kullanılarak
- Massive parallel next-generation sequencing (NGS)- yeni nesil dizileme
  - NGS teknolojileri ile bir çalışmada tüm genom, transkriptom veya daha küçük hedef bölgelerdeki milyonlarca DNA parçası dizilenebilmektedir



Yeni Nesil Dizileme (Next-Generation Sequencing, NGS)

Yeni testler

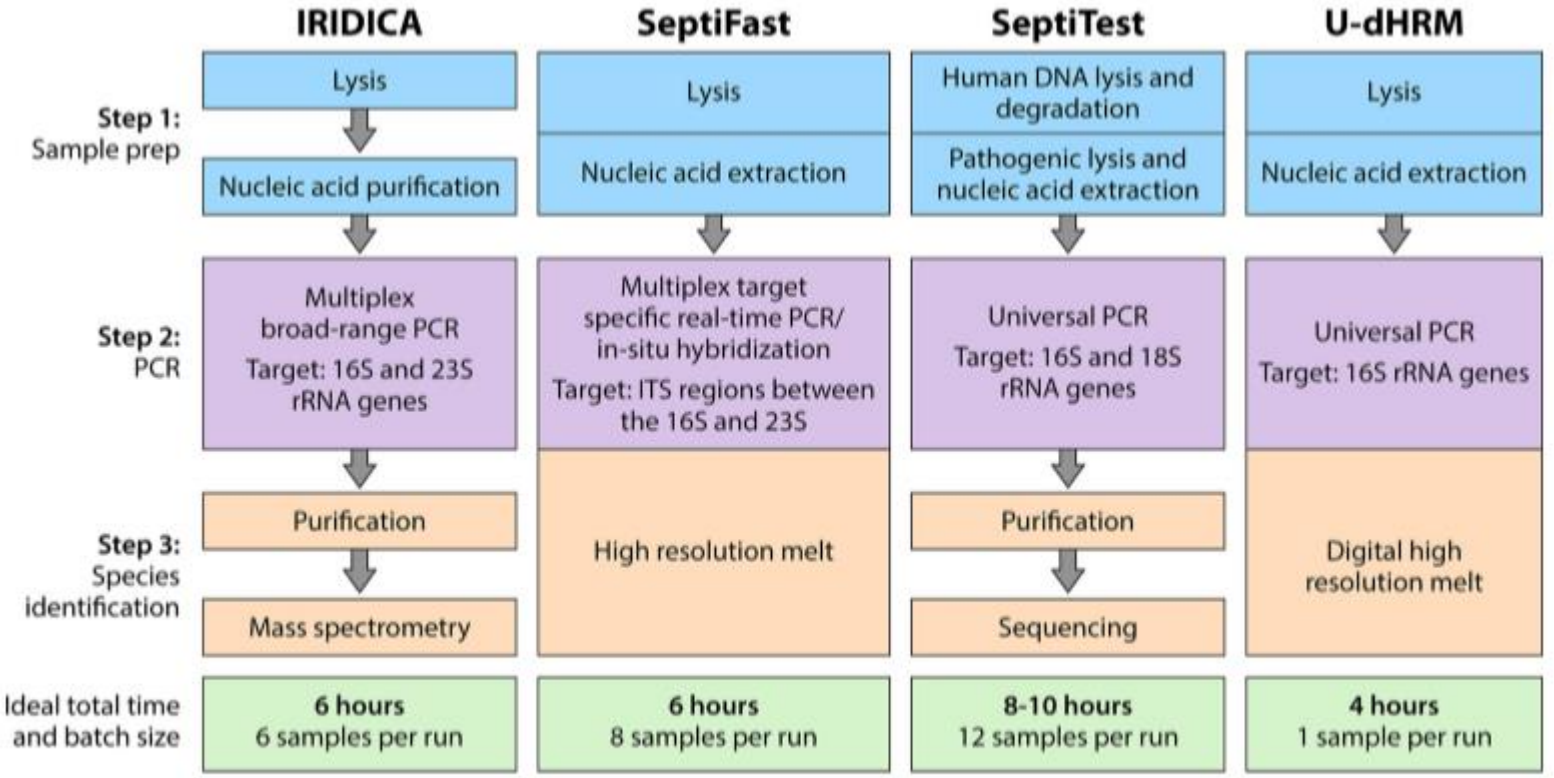


FIG 1 Workflow for the analysis of a single whole-blood specimen for pathogen identification. Even though U-dHRM shows promise as the fastest technology, it could benefit from parallelizing for multiple loads in the future.

SinhaM,JupeJ,MackH,ColemanTP, LawrenceSM, FraleySI. Emerging technologies for molecular diagnosis of sepsis CMR 2018

Yeni testler

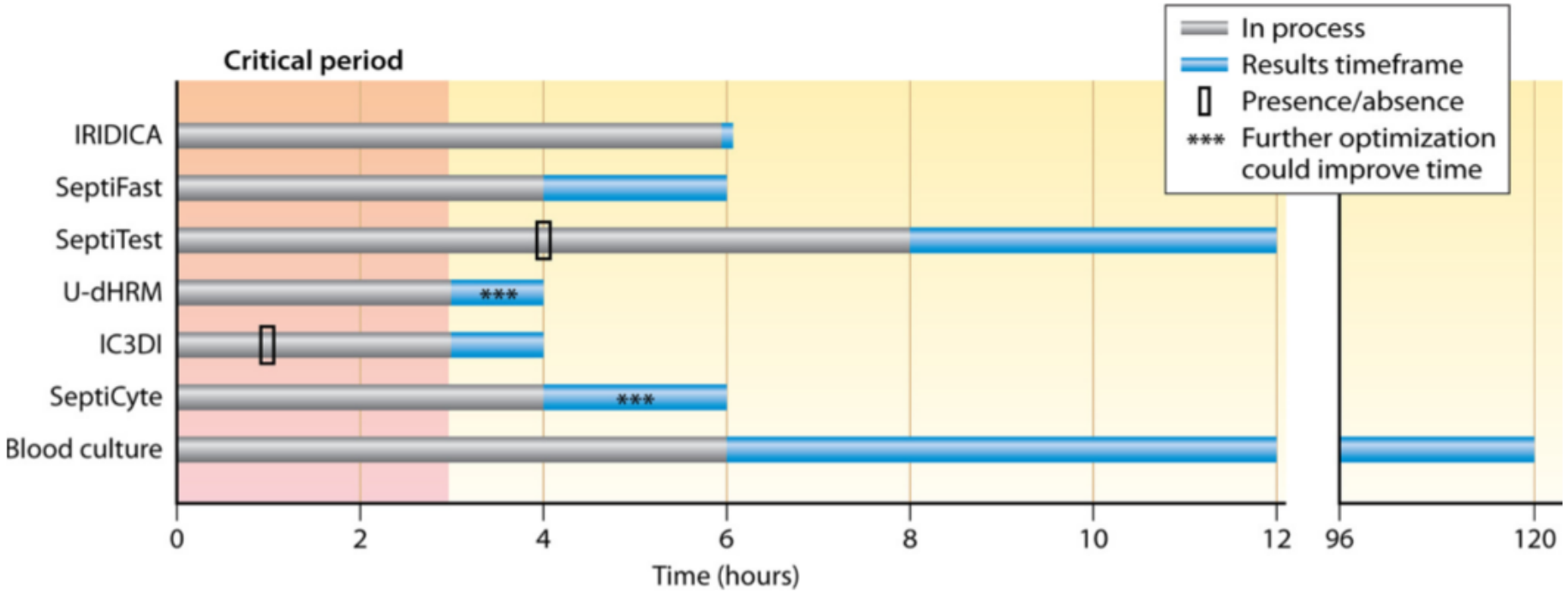


FIG 4 Timeline of sepsis technologies and where they fall compared to the gold standard of blood culture and the 1- to 3-h critical time for affecting clinical decision-making. SeptiCyte and U-dHRM may be further optimized to provide results in a shorter time frame.

SinhaM,JupeJ,MackH,ColemanTP, LawrenceSM, FraleySI. Emerging technologies for molecular diagnosis of sepsis CMR 2018

Türk Yoğun Bakım Derneği

DÜNYA SEPSİS GÜNÜ
13 EYLÜL

T.C. Sağlık Bakanlığı

TEŞEKKÜR EDERİM