

# Sepsis in the elderly: clinical considerations

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# What are the frequent questions we encounter when managing an old person with a suspected infection?

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- Does this person have a bacterial infection?
    - are signs, symptoms and lab results less sensitive or specific in the old?
  - Is the distribution of the sites of infection or pathogens different in old patients?
  - Should I treat this patient differently?
  - Is the prognosis affected by age?
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Signs, symptoms, lab findings:

Yahav D. Presentation of infection in older patients. *Ann Med*. 2015 Apr 9: 1-5. [Epub ahead of print]

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- ❑ Prospectively collected database on presentation of infection in 4308 patients.
  - ❑ Compared the presentation of elderly patients ( $\geq 75$  years) versus adults ( $< 75$  years).
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# Inclusion criteria

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- With systemic inflammatory response syndrome
  - Suspected focus of a bacterial infection
  - Septic shock
  - Febrile neutropenia
  - Prescribed antibiotics (not for prophylaxis)
  - Patients from whom blood cultures were drawn
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# Vital signs (elderly, n=1891; adults, n=2250)

Parameter	Older patients Median (IQR)	Adults Median (IQR)
Fever	38.3 (37.4–39.0)	38.4 (37.3–39.0)
HR	90.0 (80.0–109.0)	95.0 (78.0–100.0)
SBP	126.0 (108.0–145.0)	120.0 (105.0–138.0)
DBP	67.0 (58.0–77.0)	70.0 (61.0–79.0)

Percentage of hypothermic and of febrile similar.

# Vital signs, bacteremic patients

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Parameter	Older patients Median (IQR)	Adults Median (IQR)
Fever	38.7 (38.0–39.1)	38.7 (38.0–39.4)
HR	91.0 (80.0–106.0)	101.0 (89.5–116.0)
SBP	120.0 (100.0–138.0)	114.0 (98.0–137.0)
DBP	69.0 (52.0–75.0)	64.0 (56.0–75.0)

# Presentation:

All patients

Older patients

Adults

Consciousness	1029 (54.6)	1898 (85.2)
Dyspnea	608 (35.8)	462 (22.3)
Septic shock	81 (4.4)	59 (2.7)
Acute renal failure	388 (21.1)	241 (11.2)
Chills	257 (16.7)	458 (23.5)
Vomiting	177 (9.3)	292 (12.6)

# Presentation, bacteremic patients:

	Older patients	Adults
Consciousness	117 (50.9)	172 (77.5)
Dyspnea	58 (27.9)	40 (19.7)
Septic shock	25 (11.3)	10 (4.6)
Acute renal failure	86 (38.7)	41 (18.6)
Chills	68 (34.9)	73 (37.4)
Vomiting	21 (9.1)	35 (15.3)



# Lab values, all patients

Value	Older patients Median (IQR)	Adults Median (IQR)
Leukocytes ( $\times 10^3/\text{microl.}$ )	11.6 (8.3–15.7)	10.8 (7.5–15.0)
Creatinine (mg/dl)	1.1 (0.8–1.6)	0.9 (0.7–1.2)
Urea (mg/dl)	55.0 (39.0–85.0)	35.0 (24.0–54.0)
Glucose (mg/dl)	130.0 (108.0–177.0)	118.0 (99.0–157.0)
Sodium (mmol/L)	137.0 (133.0–140.0)	136.0 (133.0–139.0)
Platelets ( $\times 10^3/\text{microL}$ )	228.0 (167.5–310.0)	237.0 (176.0–315.0)

# Final diagnosis

Type of infection	Older patients <i>n</i> (%)	Adults <i>n</i> (%)
All	1933 (100%)	2375 (100%)
Lower respiratory tract	454 (23.5%)	370 (15.6%)
Urinary tract	344 (17.8%)	260 (10.9%)
Abdominal	87 (4.5%)	191 (8.0%)
Soft tissue, bone	142 (7.3%)	209 (8.8%)
Upper respiratory	22 (1.1%)	36 (1.5%)
Endovascular	36 (1.9%)	38 (1.6%)
Neutropenic fever	32 (1.7%)	78 (3.8%)
Other bacterial	178 (9.2%)	233 (9.8%)
Non-bacterial infection	71 (3.7%)	163 (6.9%)
Indefinite	172 (8.9%)	216 (9.1%)
Unknown	212 (11%)	285 (12%)
Non-infectious	182 (9.4%)	238 (10%)
Missing	0 (0%)	42 (1.7%)

# Conclusions:

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- ❑ Elevated fever and leukocytosis were found to be at least equally common in older patients compared to younger adults as part of the presentation of infection.
  - ❑ Presentation with septic shock, acute renal failure, and reduced consciousness was significantly more common in older patients.
  - ❑ **'Non-specific' presentation was rare and** equally uncommon in old patients and in adults.
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# Bacteremia

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- Taiwan, 2001-2002. Prospective study
- Patients admitted to ED and evaluated for sepsis or with clinical indications of infection, in whom a clinically significant bacteremia was diagnosed. Only community-onset infections included
- **Comparison between the oldest old ( $\geq 85$  years), elderly (65-84 years) and adults ( $< 65$  years)**

**TABLE 3. Source of Bloodstream Infection, by Age-Group**

	<b>A&gt; Adult</b> (n = 415) No. (%)	<b>B&gt; Elderly</b> (n = 406) No. (%)	<b>C&gt; Oldest Old</b> (n = 69) No. (%)	<b>ANOVA</b> p Value
Urinary tract infection	93 (22.4)	<u>126 (31.0)*</u>	<u>19 (27.5)</u>	0.020
Primary bacteremia <sup>†</sup>	87 (21.0)	<u>55 (13.5)<sup>†</sup></u>	<u>12 (17.4)</u>	0.019
Biliary tract infection	55 (13.3)	73 (18.0)	13 (18.8)	0.158
Lower respiratory tract infection	23 (5.5)	32 (7.9)	<u>13 (18.8)*</u>	0.001
Skin and musculoskeletal infection	47 (11.39)	39 (9.6)	6 (8.7)	0.647
Spontaneous bacterial peritonitis	24 (5.4)	16 (3.8)	0 (0)	0.119
Liver abscess	23 (5.5)	17 (4.2)	1 (1.4)	0.119
Catheter-related infection	13 (3.1)	16 (3.9)	1 (1.4)	0.533
Intra-abdominal infection <sup>§</sup>	16 (3.9)	15 (3.7)	1 (1.4)	0.604
Infective endocarditis	26 (6.3)	<u>13 (3.2)<sup>†</sup></u>	1 (1.4)	0.047
Polymicrobial infection	42 (9.5)	42 (9.9)	<u>12 (17.4)*</u>	0.010
Gram-negative bacteria	295 (71.1)	290 (71.4)	49 (71.0)	0.993
Gram-positive bacteria	114 (27.5)	109 (26.8)	19 (27.5)	0.978
Anaerobic bacteria	23 (5.5)	21 (5.2)	6 (8.7)	0.499

\*Significantly higher frequency compared with the adult group (p < 0.05).

<sup>†</sup>Significantly lower frequency compared with the adult group (p < 0.05).

<sup>‡</sup>Sources of unknown origin.

<sup>§</sup>Including hollow organ perforation, peritonitis, appendicitis, pancreatitis, neutropenic enterocolitis, and diverticulitis.

**TABLE 2. Clinical and Laboratory Manifestations of Community-Acquired Bacteremia, by Age-Group**

	<b>A&gt; Adult</b> (n = 415) No. (%)	<b>B&gt; Elderly</b> (n = 406) No. (%)	<b>C&gt; Oldest Old</b> (n = 69) No. (%)	<b>ANOVA</b> <b>p Value</b>
Tachycardia	343 (82.7)	293 (72.2) <sup>†</sup>	57 (82.6)	0.001
Fever (tympanic temperature >38.5 °C)	359 (86.5)	349 (86.0)	53 (76.8) <sup>†</sup>	0.07
Hypothermia	12 (2.9)	16 (3.9)	1 (1.4)	0.434
Acute respiratory distress	25 (6.0)	50 (12.3)*	12 (17.4)*	0.001
Altered consciousness	54 (13.0)	58 (14.3)	18 (26.1)*	0.017
Acute renal failure	30 (7.0)	51 (12.6)*	13 (18.8)*	0.002
Septic shock	96 (23.1)	106 (26.1)	27 (39.1)*	0.019
Leukopenia (WBC ≤4000/mm <sup>3</sup> )	50 (12.0)	43 (10.6)	7 (10.1)	0.769
Leukocytosis (WBC ≥12,000/mm <sup>3</sup> )	164 (39.5)	181 (44.6)	37 (53.6)*	0.05
Left-shift leukocytosis (Band and Seg ≥90%)	206 (49.6)	217 (53.4)	45 (65.2)*	0.049
Anemia (Hb ≤10 mg/dL)	91 (21.9)	106 (26.1)	22 (31.9)	0.131
Bandemia (Band ≥10%)	50 (12.0)	61 (15.0)	13 (18.8)	0.221
Inappropriate use of antibiotics	107 (25.8)	98 (24.1)	21 (30.4)	0.185

Abbreviations: WBC = white blood cells, Hb = hemoglobin.

\*Significantly higher frequency compared with the adult group (p < 0.05).

<sup>†</sup>Significantly lower frequency compared with the adult group (p < 0.05).

# Sepsis

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- ❑ Australia, 2004-2007. Retrospective study
- ❑ Patients admitted to the intensive care unit with a diagnosis of sepsis
- ❑ Data on the first 24 hours of sepsis presentation and outcomes collected from the ICU database
- ❑ Comparison between patients >65 years and younger patients

<b>Variable</b>	<b>&lt;= 65 years (n = 67)</b>	<b>&gt; 65 years (n = 108)</b>	<b>P Value</b>
PaO <sub>2</sub> (torr)	93 (67-126)	101 (73.7-172.7)	0.25
PaCO <sub>2</sub> (torr)	41 (34-50)	39 (32-49)	0.59
HCO <sub>3</sub> (mmol/L)*	2056 (4.09)	17.97 (5.38)	<0.01
pH	7.32 (7.25-7.41)	7.29 (7.15-7.37)	0.02
Heart rate	110 (99-128)	105 (88.5-120)	0.02
Systolic blood pressure (mmHg)	120 (95.5-141)	138 (113.5-152)	<0.01
Diastolic blood pressure (mmHg)	65 (51-72)	62 (50-74)	0.77
Mean blood pressure(mmHg)	84 (67-95)	87 (77-98)	0.13
Temperature (degree Celsius)	37.8 (37-38.5)	37.2 (36.5-37.9)	<0.01
Respiratory rate	26 (18.5-32.5)	26 (20-30)	0.28
Number of organs failed on admission	1 (0-2)	1 (0-2)	0.10
<i>Laboratory variables</i>			
Sodium (mmol/L)	142 (138.2-145.7)	142 (139-145)	0.71
Potassium (mmol/L)	4.25 (0.84)	4.50 (0.78)	0.04
Urea (mmol/L)	9 (5.2-15.8)	14.5 (9.2-22.5)	<0.01
Creatinine (umol/L)	80.5 (51.7-147.5)	160 (100-250)	<0.01
Bilirubin (umol/L)	14 (8.25-27)	15.5 (8-27.5)	0.93
Albumin (g/L)	28.85 (7.39)	29.27 (5.87)	0.69
Blood sugar (mmol/L)	7.8 (6.1-12.2)	9.4 (6.7-12.2)	0.23

Contd.



Contd.

<b>Variable</b>	<b>&lt;= 65 years (n = 67)</b>	<b>&gt; 65 years (n = 108)</b>	<b>P Value</b>
C reactive protein (mg/L)	197.6 (91.4-274.3)	168.7 (62.3-253.5)	0.28
Lactate (mmol/L)	2.1 (1.4-4.3)	2.8 (1.5-6.1)	0.29
White cell count ( $\times 10^9/L$ )	16.2 (11.3-20.9)	15.2 (10.2-24)	0.98
Hematocrit (%)	0.30 (0.26-0.33)	0.31 (0.27-0.35)	0.10
Positive culture in the first 24 hours (%)	40.3	44.6	0.62
<b>Scores</b>			
APACHE III	57 (41.2-70.2)	77 (58.5-93)	<0.01
APACHE III without age component	48 (36-65)	57.5 (40.2-77.7)	0.03
SAPS II	34.5 (26.7-42)	47 (39-56.5)	<0.01
SAPS II without age component	27 (20-34)	31 (22-41.5)	0.01

# Possible bias in estimation of 'atypical' sepsis presentation in the elderly

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- Observational studies portray real life and in real life physicians work under the assumption that sepsis presents atypically in the elderly and thus bias results towards fewer sepsis signs in the elderly
    - Referral to the hospital
    - Blood culture sampling
    - Diagnosing infections
  - Presentation different because pathogens and diagnoses are different
  - Oral/ axillary temperature measurements unreliable in the elderly
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# My conclusions (1):

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- ❑ Atypical presentation is rare in the elderly
  - ❑ **'Deterioration' should not be counted as the** single presentation of a bacterial infection.
  - ❑ Fever by itself is no more in favor of a bacterial infection than in adults.
  - ❑ And almost the same with fever and leukocyturia (because asymptomatic bacteriuria is so common in the old).
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## My conclusions (2):

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- ❑ UTI and lower respiratory tract infections more common in the old.
  - ❑ Neutropenic fever and bacterial endocarditis less common.
  - ❑ Clostridium difficile related diarrhea more common
  - ❑ In bacteremic patients, more polymicrobial infections.
  - ❑ In bacteremic pneumonia a slightly higher percentage of Gram (-) bacteria, but probably not enough to change practice.
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Table 3. Mean Participant Age in Randomized Controlled Trials (RCTs) and Observational Studies

Pneumonia Classification	RCT	Observational	P-Value
	Mean ± SD (n)		
CAP all trials <sup>a</sup>	54.0 ± 9.6 (23)	66.2 ± 8.1 (113)	<.001
CAP—ambulatory	45 ± 4.2 (2)	58.2 ± 17.5 (1)	NA
CAP—ambulatory/hospitalized	45.6 ± 1.6 (3)	63.7 ± 7.04 (11)	.001
CAP—hospitalized	55.0 ± 9.1 (16)	65.3 ± 8.2 (81)	.001
CAP—hospitalized, HCAP included	68.0 ± 3.5 (2)	65.3 ± 7.5 (20)	.62
Hospitalized, all	56.4 ± 9.5 (18)	66.2 ± 8.14 (101)	.001
HCAP	84.4 ± 2.2 (3)	71.5 ± 11 (9)	.08
HCAP and CAP—hospitalized included	77.9 ± 9.3 (5)	66.2 ± 8.3 (29)	.08
HAP/ventilator-acquired pneumonia	57.4 ± 9.3 (13)	62.9 ± 9.7 (61)	.06

# Long –term consequences:

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- ❑ Long term decrements in sepsis patients' QoL scores compared to population norms (Winters BD et al. Crit Care Med 2010; 38: 1276-83).
  - ❑ Lower BMI than controls, or then expected from their own pre-sepsis trajectory (Iwashyna TJ et al. Am J Respir Crit Care Med 2012; 185: 835-41).
  - ❑ Cognitive impairment increased from 6% before the sepsis to 17% after severe sepsis, deterioration higher than in patients hospitalized for other reasons (Iwashyna TJ et al. JAMA 2010; 304: 1787-94).
  - ❑ Long term significant deterioration in functions of daily living (idem).
  - ❑ High medical care charges for the years following sepsis (Weycker D et al. Crit Care Med 2003; 31: 2316-23).
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# Practical implications:

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- ❑ Elderly survivors of severe infections should be carefully assessed whether they need intermediate care for recuperation and re-conditioning when leaving the hospital.
  - ❑ Survivors of sepsis are a large and growing group, and the additional resources demanded to take care of long-term consequences of sepsis should be explicitly taken into account.
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# Ethical dilemmas:

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- ❑ Can we decide that in a given situation patients have such a limited life expectancy that antibiotic treatment can be given up?
  - ❑ Can we decide that in a given situation patients have such a low quality of life that antibiotic treatment can be given up?
  - ❑ Can we decide that in patients with extreme **dementia antibiotic treatment won't be** offered?
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# Factual solutions:

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- Encourage living wills; with detailed lists of interventions; that allow discussion with patients or care-takers; if the local laws and mores allow it.
  - Define (to a fine resolution) groups that do not benefit from antibiotic treatment:
    - From empirical antibiotic treatment
    - From any antibiotic treatment
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# Results

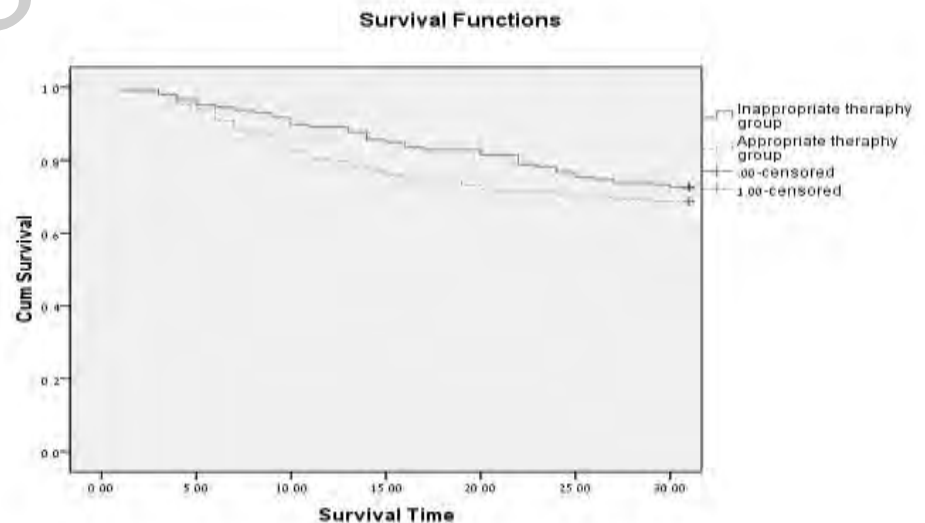
- 51% (153/299) received appropriate empiric antibiotic treatment.

- 30 day mortality rate:

- Appropriate initial treatment- 31.3% (48/153)
- Inappropriate initial treatment- 27.4% (40/146)

Survival curve for patients who receive appropriate initial antibiotic therapy compared to those who received inappropriate therapy:

Log Rank (Mantel-Cox)-sig 0.338



Tanya B, ECCMID 2014, Barcelona-Clinical Microbiology and infectious diseases congress.

# Conclusions (1):

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- ❑ Signs and symptoms and common lab determinations in bacterial sepsis are probably similar in adults and in the elderly.
  - ❑ **'General deterioration'** or refusal to eat or other non-specific observations should not be treated with antibiotics (even in the presence of leukocyturia).
  - ❑ Presentation of bacterial infections with septic shock and renal failure are more common in the elderly.
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## Conclusions (2):

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- ❑ Distribution of pathogens is not different enough to mandate different empirical antibiotic treatment.
  - ❑ I have not touched on the question of dosing (pharmacokinetics/pharmacodynamics).
  - ❑ The base of evidence might be weak.
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## Conclusions (3):

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- ❑ Sepsis/severe infections have long term consequences, especially in the elderly.
  - ❑ Elderly survivors of severe infections should be carefully assessed whether they need intermediate care for recuperation and re-conditioning when leaving the hospital.
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## Conclusions (4):

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- Given the resistance to antibiotics crisis, we should ask explicit questions about futile antibiotic treatment.

Thank you

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