

ESGIE PGEC, Rome 2013

Sepsis presentation in the elderly

Mical Paul

Rambam Health Care Center, Haifa

Tel-Aviv University, Israel



Goya - From the Black Paintings
Museo del Prado, Madrid, Spain
ecweems.com/goya

Sepsis presentation
comparing the
elderly to younger
adults

ESCMID Online Lecture Library
© by author

Bacteremia I

- France, 1992. Prospective study
- Comparing bacteremia presentation in elderly patients (>65 years) hospitalized in a geriatric medicine unit vs. younger patients hospitalized in an internal medicine unit, with community-onset or hospital-acquired infections
- Defined data set collected at the time bacteremia was diagnosed

TABLE III**Clinical Indication of the Source of Infection**

Source of Infection	Group 1	Group 3
Genitourinary tract	23	8
Respiratory tract	12	3
Bowel and biliary tract	7	2
Skin and soft tissue	8	8
Ear, nose, throat	2	3
Others	8	8
Number of sources suspected	60	32

Group 1: Elderly >65

Group 3: Young <65

TABLE V**Blood Culture Isolates (n = 105) in Bacteremic Elderly (Group 1) and Bacteremic Young (Group 3)**

Organism	Group 1	Group 3
<i>Escherichia coli</i>	34	4
<i>Staphylococcus aureus</i> and others	10	12
<i>Streptococcus pneumoniae</i>	14	9
Enterococci	3	0
Gram-negative bacilli (<i>E coli</i> excluded)	7	7
Anaerobes	3	0
Total	71	34*

*Two additional polymicrobial infections.

TABLE IV

**Frequency and Comparison of Studied Parameters
Between Bacteremic Elderly (Group 1) and
Bacteremic Young (Group 3)**

Parameter	Group 1 Frequency %	Group 3 Frequency %	P Value*
Rapid onset of infection	50	35	NS
Fever	80	91	NS
Fever spike	61	79	NS
Hypothermia	1.5	2	NS
Shaking and chills	33	88	<0.0001
Sweating	25	52	<0.01
Altered general state	57	79	<0.05
Tachycardia	28	38	NS
Splenomegaly	4.2	8	NS
Altered mental status	12	33	<0.01
Underlying disorders	57	67	NS
Leucocytosis	66	79	NS
Leucopenia	9.8	6	NS
Erythrocyte sedimentation rate >30 mm/h	71	89	NS
Lymphopenia	26	51	<0.05
Clinical indication of source of infection	77	79	NS

*P value for comparison between these two groups.

NS = not significant.

Group 1: Elderly >65

N=71

Group 3: Young <65

N=34

Fever: several controlled rectal temperatures readings above 38.5°C; temperature was taken twice a day)

Fever spike: one temperature reading at least 1.5°C higher than the previous and following measures
 Mean number of positive findings:
 Group 1: 7.07 ± 2.2 vs
 Group 3: 9.4 ± 1.7, P<0.01

Hypothermia: controlled rectal temperature readings below 36°C

Bacteremia II

- 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 (≥ 85 years), elderly (65-84 years) and adults (< 65 years)

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

	A> Adult (n = 415) No. (%)	B> Elderly (n = 406) No. (%)	C> Oldest Old (n = 69) No. (%)	ANOVA p Value
Urinary tract infection	93 (22.4)	<u>126 (31.0)*</u>	<u>19 (27.5)</u>	0.020
Primary bacteremia [†]	87 (21.0)	<u>55 (13.5)[†]</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 (11.3)	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 [§]	16 (3.9)	15 (3.7)	1 (1.4)	0.604
Infective endocarditis	26 (6.3)	<u>13 (3.2)[†]</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 ($p < 0.05$).

[†]Significantly lower frequency compared with the adult group ($p < 0.05$).

[‡]Sources of unknown origin.

[§]Including hollow organ perforation, peritonitis, appendicitis, pancreatitis, neutropenic enterocolitis, and diverticulitis.

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

	A> Adult (n = 415) No. (%)	B> Elderly (n = 406) No. (%)	C> Oldest Old (n = 69) No. (%)	ANOVA p Value
Tachycardia	343 (82.7)	293 (72.2) [†]	57 (82.6)	0.001
Fever (tympanic temperature >38.5 °C)	359 (86.5)	349 (86.0)	53 (76.8) [†]	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 ³)	50 (12.0)	43 (10.6)	7 (10.1)	0.769
Leukocytosis (WBC ≥12,000/mm ³)	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).

[†]Significantly lower frequency compared with the adult group (p < 0.05).

Sepsis

- 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

<i>Variable</i>	<i><= 65 years (n = 67)</i>	<i>> 65 years (n = 108)</i>	<i>P Value</i>
PaO ₂ (torr)	93 (67-126)	101 (73.7-172.7)	0.25
PaCO ₂ (torr)	41 (34-50)	39 (32-49)	0.59
HCO ₃ (mmol/L)*	20.56 (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.

Variable	<= 65 years (n = 67)	> 65 years (n = 108)	P Value
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
Scores			
APACHE III	67 (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

Sepsis, intra-abdominal

- US, 1987-1990. Retrospective study
- Review of records for patients discharged with a diagnosis of microbiologically-documented intra-abdominal infection
- Comparison between patients >65 years or younger, with respect to disease presentation and outcomes

Sources of infection

	Elderly N=43	Younger N=88
Appendicitis	28%	61%
Diverticulitis	28%	6%
Cholangitis	12%	8%
Cholecystitis	12%	2%
Intra-abdominal abscess	9%	16%
Perforated viscus	0%	5%
Biliary/ pancreatic	28%	10%

	Younger N=88	Elderly N=43	P-value
Nausea	64%	37%	<0.005
Vomiting	58%	28%	<0.001
Diarrhea	36%	16%	<0.01
Fever	60%	33%	<0.001
Hypothermia <36	3%	14%	<0.05
Mean temperature	38.2°C	37.5°C	<0.001
Duration of symptoms before presentation	4 days	9.1 days	<0.05
Presenting diagnosis unknown or extra- abdominal	9%	23%	<0.05
Leukopenia <2000/mm ³	5%	16%	<0.005

No significant differences in physical findings, including abdominal tenderness, peritoneal signs, and lethargy and other hematologic parameters

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

- 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



... Studies focusing on specific infections

Specific diagnoses

Author	Journal, year	Population	Epidemiology		Results
Terpenning et al.	Am J Med 1987	53 >60 yrs. vs. 55 <60 with endocarditis	Different pathogens. More nosocomial in the elderly	↓	Symptoms
				↓	Febrile response
				↑	Error in diagnosis (68%)
Werner et al.	Am J Med 1996	28 <50 yrs. vs. 58: 50-70 vs. 20 >70 yrs. with endocarditis	Different predisposition	↓	Fever
				↓	Leukocytosis
				↓	Vegetation size
Marrie et al.	J Am Geriatr Soc 1985	81 >65 yrs vs. 57 <65 yrs. hospitalized with CAP	Different pathogens	↓	Febrile response (57 vs. 26%)

Specific pathogens

Author	Journal, year	Population	Epidemiology		Results
Finklestein et al.	J Am Geriatr Soc 1983	> 65 yrs. vs. younger (total 187) with pneumococcal bacteremia	NS	↓	Fever
				—	Leukocytes
				—	Heart rate
Paul et al.	Unpublished	463 >80 yrs. vs. 652: 65-80 vs. 550 <65 yrs. with <i>S. aureus</i> bacteremia	Less CVC-related and post-op in all elderly, less HA in the very old	↓	Fever
				↑	Leukocytes
				↑	Septic shock

Staphylococcus aureus bacteremia

- Israel, 2008-2010. Retrospective study
- *S. aureus* bacteremia and sepsis

	<65 yrs. N=550	65-80 yrs. N=652	>80 yrs. N=463	ANOVA p
Fever at onset <37.5	24%, 540	31%, 635	33%, 452	0.001
Leukocytes <10 K/mm ³	42%, 543	38%, 640	30%, 457	<0.001
Shock at onset	10%, 550	14%, 652	16%, 463	0.006
Thrombocytes/mm ³	234.9	226.5	240.9	NS
Creatinine mg/dl	1.6	2.2	3.0	NS
Urea mg/dl	53.3	76.0	93.1	<0.001
Albumin mg/dl	3.0	2.8	2.8	<0.001

Summary of sepsis presentation studies

- Mostly retrospective studies, conducted many years ago, mostly small

Sepsis presentation in the elderly	n/N studies
Less fever	4/6
Altered mental status	2/2
Shock	2/3
Respiratory distress	1 /2
Leukocytosis	3/6
Renal failure	2/3

Is the question important?

Yes

- Do an appropriate study, adjusting for design-related bias
 - Uniform and broad criteria for sepsis evaluation
 - Uniform diagnostic algorithm (rectal fever)
 - Analysis by pathogen/diagnosis

No

- Focus on appropriate and superfluous antibiotic treatment
 - Define infections where empirical treatment in the elderly has an effect
 - Accurately predict infections and rule out no infection



Prediction of infections in the elderly

Bacteremia I

- Switzerland, 1988-1990. Prospective study
- All women >62 years and men >65 years who had blood cultured in hospital during the defined period were included (average age 83.8 ± 6.5 years)
- Pre-coded protocol completed within 24 hours by the resident who had requested the blood cultures
- Physician's subjective assessment of the probability of bacteremia

Potential Predictors of Bacteremia ¹¹	Prevalence in All Episodes (%)	Sensitivity (%)	Specificity (%)	Positive Predict. Value (%)	Relative Risk
Alcoholism	8.1	10.9	92.2	11.1	1.44
Malnutrition	19.2	23.9	81.3	10.3	1.36
Dehydration	13.4	21.7	87.3	13.7	1.91
Bladder catheter	17.7	26.1	83.0	12.1	1.72
Bladder catheter removal	6.6	23.9	94.9	29.7	<u>5.87</u>
Diabetes mellitus	14.2	17.4	86.1	10.1	1.31
Malignant diseases	14.5	15.2	85.5	8.6	1.06
Congestive heart failure	32.4	37.0	68.0	9.4	1.24
Neuropsychiatric disorders	31.4	39.1	69.3	10.3	1.45
Fever (38°5C)	74.2	<u>87.0</u>	27.0	9.7	<u>2.46</u>
Functional decline	11.8	13.0	88.3	9.1	1.13
Confusion	21.5	30.4	79.3	11.7	1.68
Fall	9.7	13.0	<u>90.6</u>	11.1	1.45
Rigors	14.3	39.1	87.9	22.5	<u>4.67</u>
Shock	1.4	6.5	<u>99.0</u>	37.5	<u>7.07</u>
WBC 10,000/mm ³	40.9	43.5	59.4	8.8	1.12
Total band count 1500/mm ³	13.4	34.8	88.7	23.5	4.19
Lymphocytes count 1000/mm ³	38.4	67.4	64.4	15.6	<u>3.74</u>

46 elderly patients with bacteremia and 512 without bacteremia
Prediction score based on variables with highest RRs

Score performance

Risk Score per Episode	Bacteremia rate (n = 558)
0	4.2
1	2.0
2	7.5
3	29.8
4	54.5
5	100.0
All Episodes	8.2

Predictors included: fever ($\geq 38.5^{\circ}\text{C}$), rigors, shock, total band count ($\geq 1500/\text{mm}^3$), lymphocyte count ($\leq 1000/\text{mm}^3$) and bladder catheter removal

ROC 0.792 ± 0.041

Bacteremia II

- US, 1998. Retrospective study
- Record review of all elderly (>65 years) evaluated in the ER, blood cultures were taken and hospitalized for suspected infection
- Comparison between bacteremic and non-bacteremic patients
- Record reviewer blinded to bacteremia status

Symptoms, signs, WBC count, laboratory findings, and admitting impression in bacteremic and nonbacteremic patients

	Bacteremic	Nonbacteremic	P	Odds ratio	95% CI
	(79)	(136)			
	No. (%)	No. (%)			
Symptoms					
Fever	13 (16.5)	19 (14.0)	NS		
Chills	28 (35.4)	30 (22.1)	.04	1.94	1.00 to 3.75
Respiratory symptoms (cough, dyspnea, sputum)	35 (44.3)	75 (55.1)	NS		
Vomiting	18 (22.8)	14 (10.3)	.007	2.57	1.21 to 6.37
Abdominal pain, diarrhea	32 (40.5)	43 (31.6)	NS		
Urinary symptoms (frequency, urgency, dysuria)	14 (17.7)	11 (8.1)	NS		
Signs					
Blood pressure < 100 mm Hg	16 (20.3)	10 (7.4)	.005	3.20	1.28 to 8.11
Pulse rate > 100/min	48 (60.8)	71 (52.2)	NS		
Respirations > 20/min	51 (64.5)	95 (69.8)	NS		
Temperature (C)					
< 36.1	8 (10.1)	8 (6.0)	NS		
36.1 to 37.2	11 (13.9)	36 (26.9)	NS		
37.2 to 38.3	31 (39.2)	50 (37.3)	NS		
38.3 to 39.4	22 (27.8)	31 (23.1)	NS		
> 39.4	7 (8.9)	9 (6.7)	NS		
Mental status change (confusion, lethargy, coma)	41 (51.9)	43 (31.6)	.003	2.33	1.27 to 4.30
Abdominal tenderness	13 (16.5)	19 (14.0)	NS		
Skin lesions (cellulitis, erythema)	10 (12.7)	20 (14.7)	NS		

Contd.

Symptoms, signs, WBC count, laboratory findings, and admitting impression in bacteremic and nonbacteremic patients

	Bacteremic (79) No. (%)	Nonbacteremic (136) No. (%)	P	Odds ratio	95% CI
WBC Count					
< 5000 mm ³	7 (9.0)	2 (1.5)	.02	2.23	1.50 to 3.31
5,000 to 10,000	13 (16.7)	40 (30.1)	NS		
10,000 to 15,000	18 (23.1)	36 (27.1)	NS		
15,000 to 20,000	15 (19.2)	31 (23.3)	NS		
> 20,000	25 (32.1)	24 (18.0)	.03	2.16	1.08 to 4.34
Segmented WBC > 80	30 (38.0)	58 (42.6)	NS		
> 6% Band forms	53 (67.1)	58 (42.6)	.001	2.74	1.48 to 5.11
Total bands > 1,000	46 (59.0)	42 (31.6)	.0001	3.12	1.69 to 5.79
Selected Laboratory Studies					
Hemoglobin < 10 g/dL (< 100 g/L)	15 (19.0)	12 (9.0)	NS		
Urea nitrogen > 26 mg/dL (> 9.75 mmol/L)	30 (38.0)	77 (56.0)	NS		
Creatinine > 2.0 mg/dL (> 176.8 μmol/L)	30 (38.0)	35 (26.7)	NS		
Urinalysis—WBC > 10 hpf	34 (43.0)	65 (47.8)	NS		
pH < 7.30*	3/25 (12.0)	2/49 (4.1)	NS		
pO ₂ < 60*	10/25 (40.0)	19/49 (38.8)	NS		

Independent predictors by stepwise logistic regression analysis:

- Altered mental status : OR=2.88; 95% CI, 1.52 to 5.50
- vomiting : OR=2.63; 95% CI, 1.16 to 6.15
- WBC band forms of more than 6% (0.06): OR= 3.50; 95% CI, 1.58 to 5.27.

Bacteremia III

- France, 1992. Prospective study
- Examining predictors of bacteremia in elderly patients (>65 years) hospitalized in a geriatric medicine unit and comparing them to elderly patients with suspicion of bacteremia, but negative blood cultures
- Defined data set collected at the time bacteremia was diagnosed, consisting of history, presenting signs and symptoms and laboratory data

TABLE II**Sensitivity and Specificity of Parameters
in the Bacteremic Elderly**

Parameter	Sensitivity %	Specificity %
Rapid onset of infection	50	70
Fever	80	45
Fever spike	61	50
Hypothermia	1.5	89
Shaking and chills	33	81
Sweating	25	81
Altered general state	57	67
Tachycardia	28	77
Splenomegaly	4.2	98
Altered mental status	12	93
Underlying disorders	57	45
Leukocytosis	66	48
Leukopenia	9.8	88
Erythrocyte sedimentation rate > 30 mm/h	71	49.7
Lymphopenia	26	82
Clinical indication of the source of infection	77	47

Four variables were significantly and independently associated in an elderly patient with bacteremia.

- Rapid onset of infection (P <0.04), OR=2.1
- Fever (P<0.005), OR=3.1
- Altered general state (P <0.03), OR=2.9
- Clinical indication of the source of infection (P <0.002), OR=3.4

Summary of studies predicting bacteremia in the elderly

- Few studies, heterogeneous. None evaluated a similar set of variables
 - Fever, chills, mental or general status change, urinary catheter, falls, shock, vomiting, focus of infection, rapid onset, leukocytosis
- Prediction models compared bacteremic to non-bacteremic patients; however non-bacteremic patients might also have severe infections
- None with internal or external validation
 - Sensitivity and specificity of models unclear

ESCMID Online Lecture Library
© by author

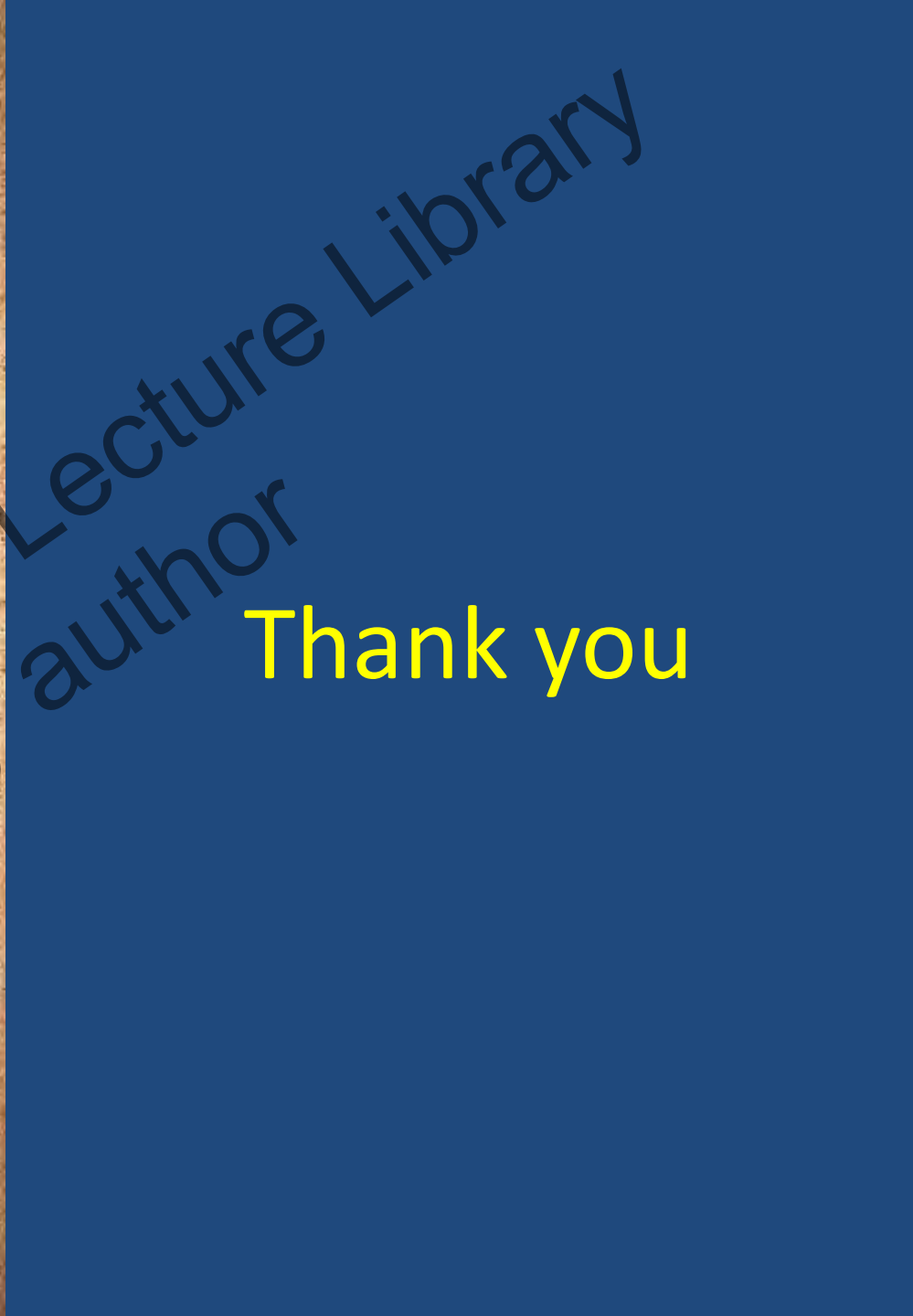


Studies needed

- Prediction of specific infections and bacteremia in the elderly
 - Decision support systems based on complex models
 - Better diagnostics
- Defining clinical scenarios where empirical antibiotic treatment has no benefit
- What did Goya think about old age?



ESCMIID Online Lecture Library
© by author



Thank you