DIE WELT DER PNEUMOKOKKEN

AMBULANT ERWORBENE PNEUMONIE

F L O R I A N T H A L H A M M E R

FACHARZT FÜR INNERE MEDIZIN & INFEKTIOLOGIE/TROPENMEDIZIN

UNIVERSITÄTSKLINIK FÜR UROLOGIE – UNIVERSITÄTSKLINIKUM & MEDIZINISCHE UNIVERSITÄT WIEN

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Minimed.at 27.03.2022 12:10

AMBULANT ERWORB PNEUMONIE
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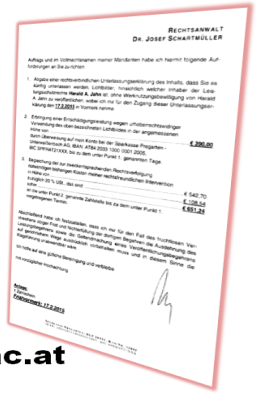

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MEDIZINISCHE UNIVERSITÄT WIEN

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Florian Thalhammer

MEDIZINISCHE UNIVERSITÄT WIEN

AMBULANT ERWORB PNEUMONIE

Leben & Sterben

TREATMENT OF PNEUMONIA WITH 2-(*p*-AMINOBENZENESULPHONAMIDO) PYRIDINE

By G. M. Evans, M.D. Birm., M.R.C.P. Lond.

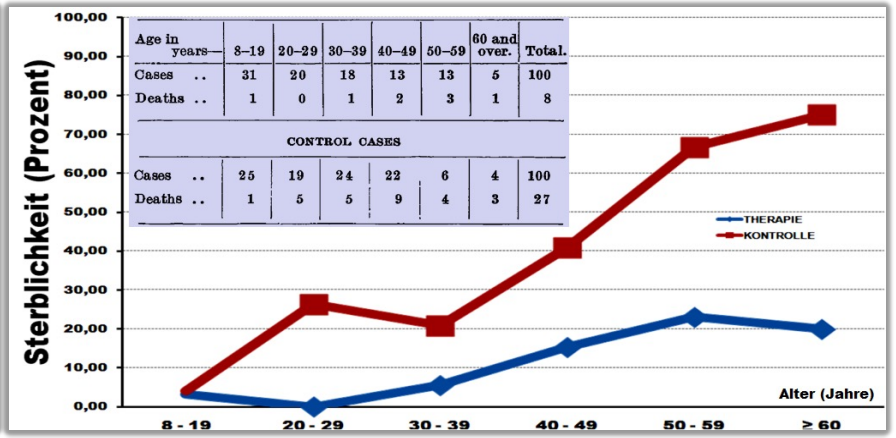
AND

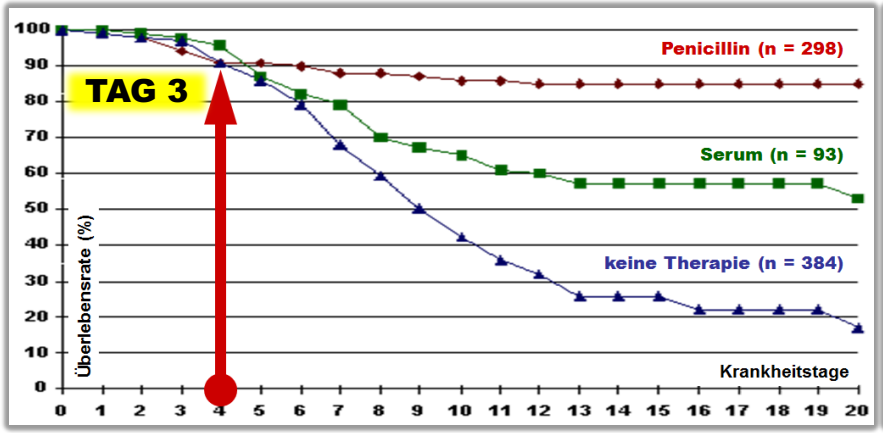
Wilfrid F. Gaisford, M.D., M.R.C.P. Lond.

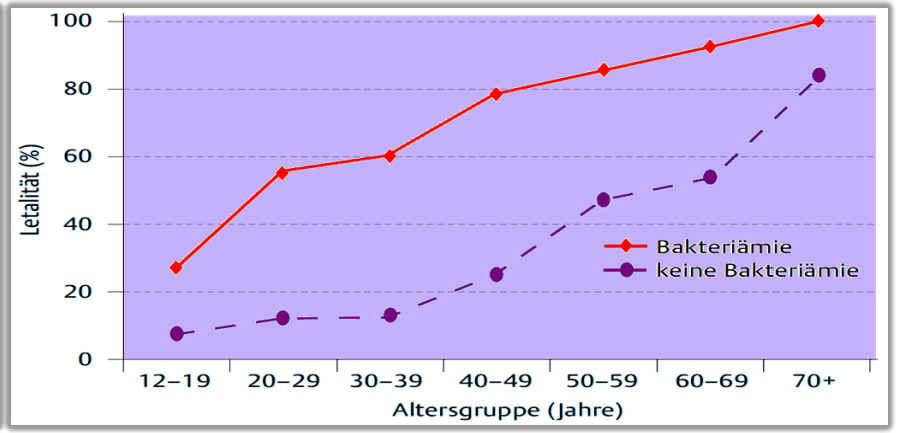
PHYSICIANS TO DUDLEY ROAD HOSPITAL, BIRMINGHAM

LETZTE PLACEBO-KONTROLLIERTE CAP-STUDIE

Age in years—	8–19	20–29	30–39	40–49	50–59	60 and over.	Total.
Cases ..	31	20	18	13	13	5	100
Deaths ..	1	0	1	2	3	1	8
CONTROL CASES							
Cases ..	25	19	24	22	6	4	100
Deaths ..	1	5	5	9	4	3	27

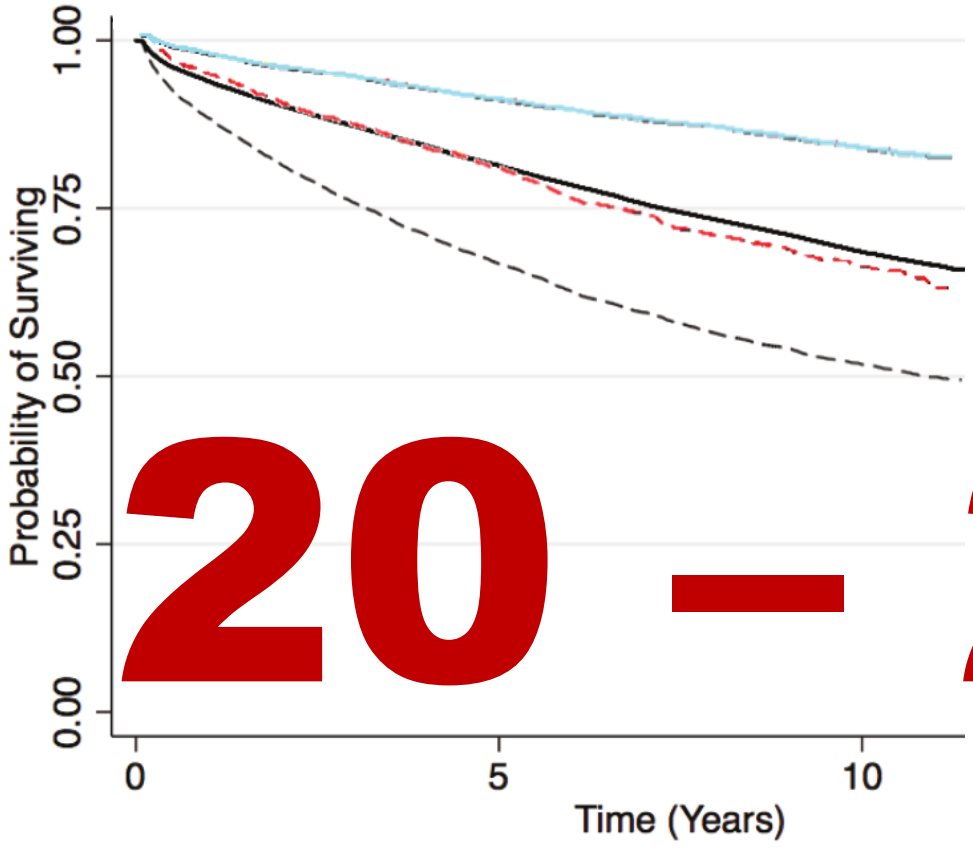






Tilghman, Ann Intern Med 1937 – Evans, Lancet 1938 – Austrian, Ann Int Med 1964 – Welte, Pneumologie 2010

AMBULANT ERWORB PNEUMONIE
Lebenserwartung



Kontrollpatienten – 46 – 65 Jahre

Kontrollpatienten – alle Altersklassen

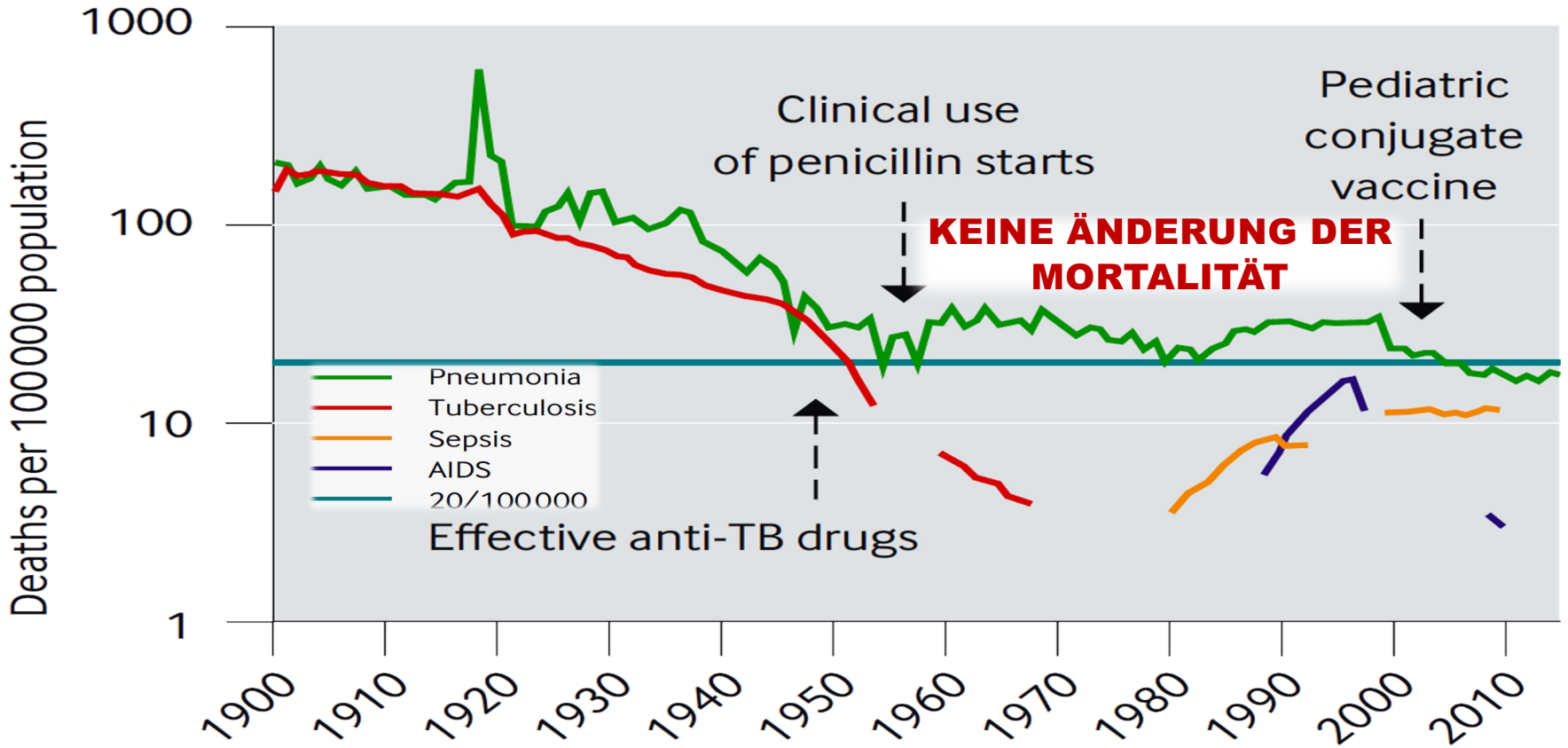
CAP-Patienten – 46 – 65 Jahre

CAP-Patienten – alle Altersklassen

20 – 25%

Eurcih, Am J Respir Crit Care Med 2015

AMBULANT ERWORB PNEUMONIE
Mortalität im Laufe der Jahrzehnte



Wunderink, BMJ 2017

AMBULANT ERWORB PNEUMONIE
Schweregradeinteilung

- **Gruppe 1a**
  - gute bis ausreichende Funktionalität
  - Bettlägerigkeit <50% des Tages
  - CRB-65 Score Stratefizierung
- **Gruppe 1b**
  - NHAP bzw. schlechte Funktionalität
  - Bettlägerigkeit >50% des Tages
  - (CRB-65 Score Stratefizierung)
- **Gruppe 2**
  - schwere Komorbidität
  - infauste Prognose
  - Palliation als Therapieziel

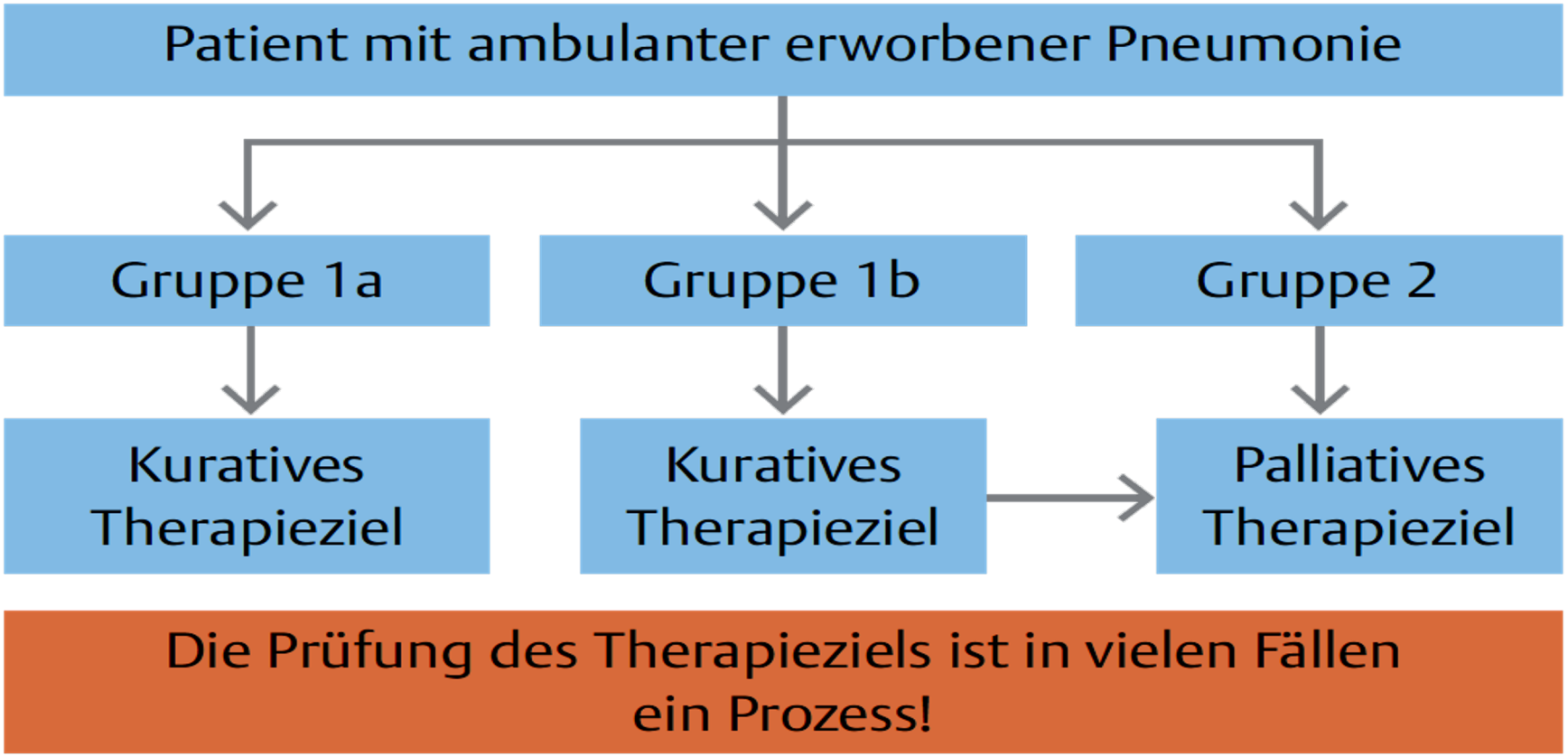
Prüfung auf das Vorliegen folgender Kriterien
1) Atemfrequenz ≥ 30/min
2) diastolischer Blutdruck ≤ 60 mmHg oder systolischer Blutdruck < 90 mmHg
3) Bewusstseinstrübung
4) Alter ≥ 65 Jahre

Zusatzkriterien KH-Aufnahme
- Oxygenierung
- (instabile) Komorbidität
- Multiresistenz

KEINE IMMUNSUPPRESSION
- Nephropathie
- Hepatopathie
- Diabetes mellitus
- strukturelle Lungenerkrankung ohne systemische Steroidtherapie
- Tumorerkrankungen ohne Neutropenie

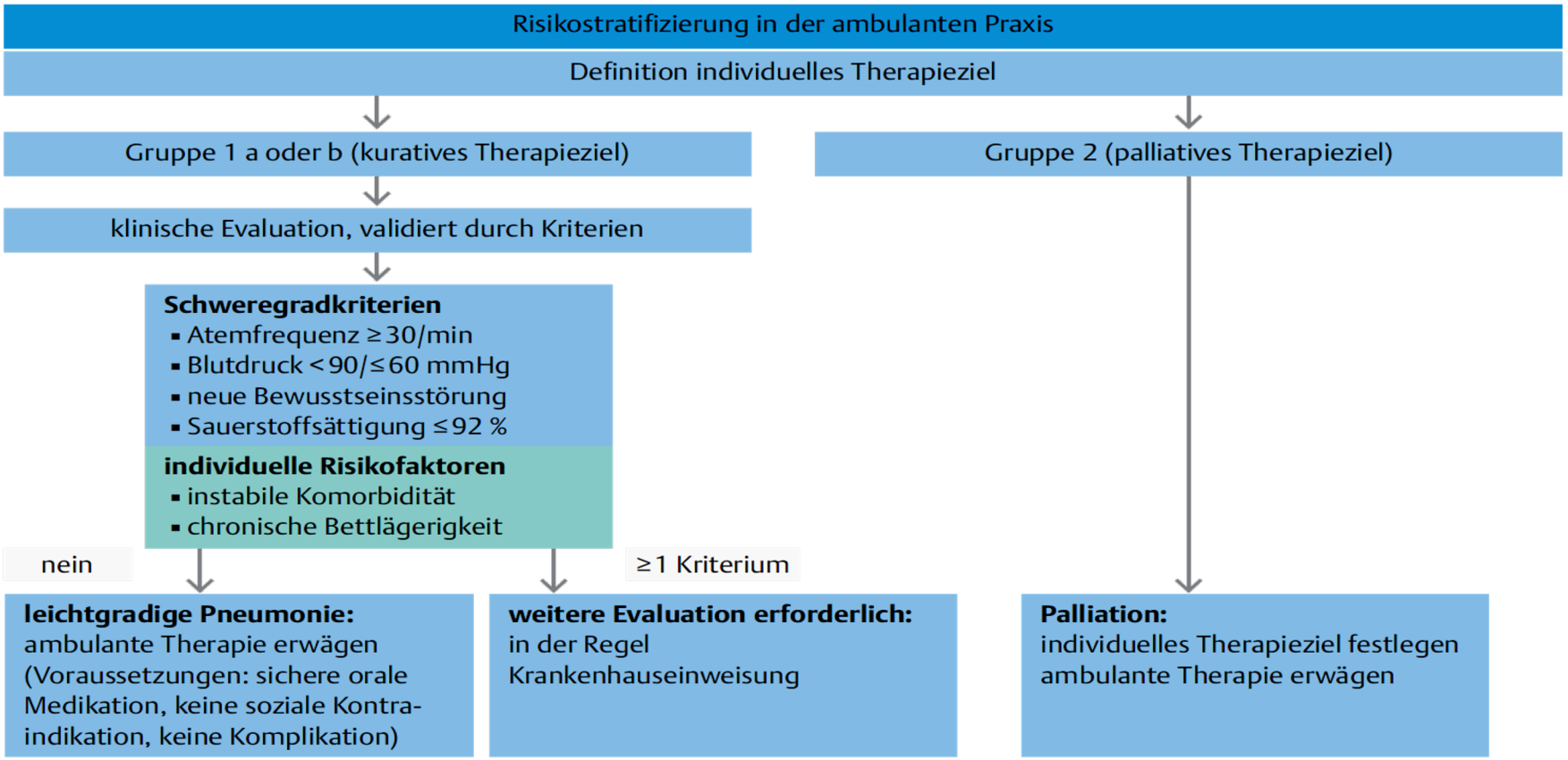
Bauer, J Intern Med 2006 – Ewig, Thorax 2009 – Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE
Therapieziel



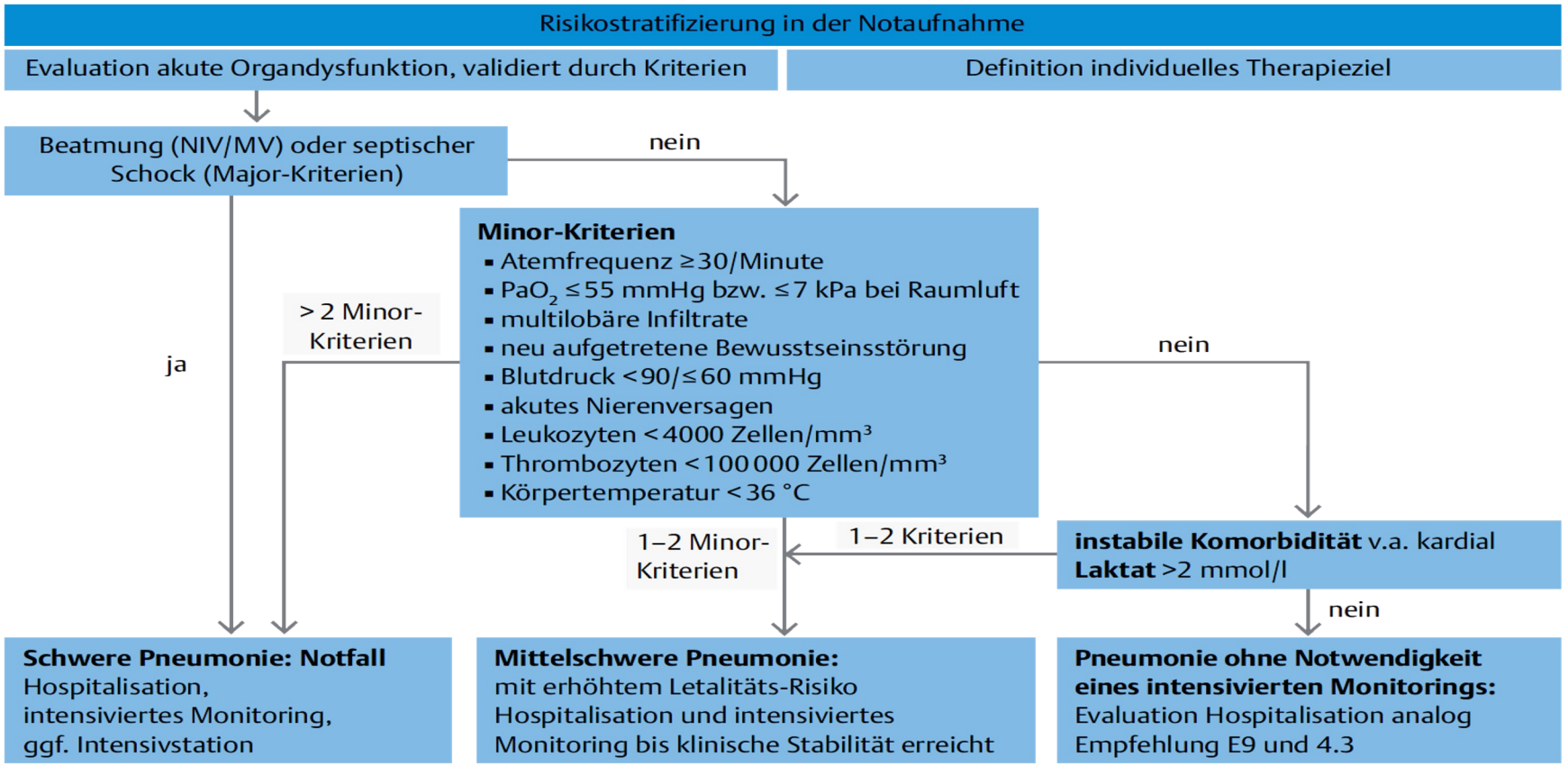
Ewig, Pneumologie 2021

AMBULANT ERWORB PNEUMONIE
Risikostratifizierung & Therapieziel



Ewig, Pneumologie 2021

AMBULANT ERWORB PNEUMONIE
Risikostratifizierung NFA



Ewig, Pneumologie 2021

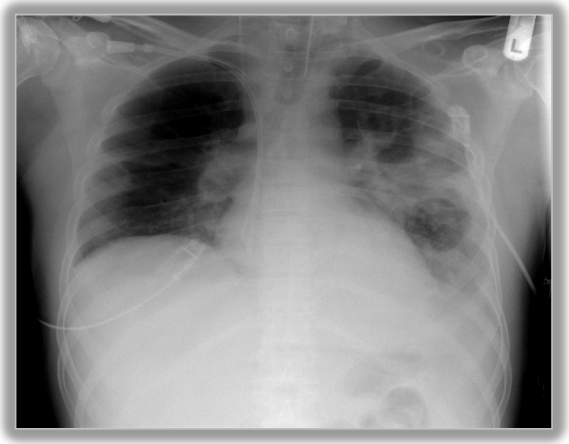
AMBULANT ERWORB PNEUMONIE
Klinische Symptome

- **Atemwegssymptome**
  - Husten mit oder ohne Auswurf
  - Dyspnoe
  - atemabhängige thorakale Schmerzen
- **Allgemeinsymptome**
  - Fieber oder Hypothermie
  - allgem Krankheitsgefühl ("malaise")
  - "grippale" Symptome: Myalgien, Arthralgien, Cephalgien, Palpitationen, Kreislaufbeschwerden, Diarrhöen
- **Neurologische Symptome**
  - Desorientiertheit ("confusion")

PPV <50%

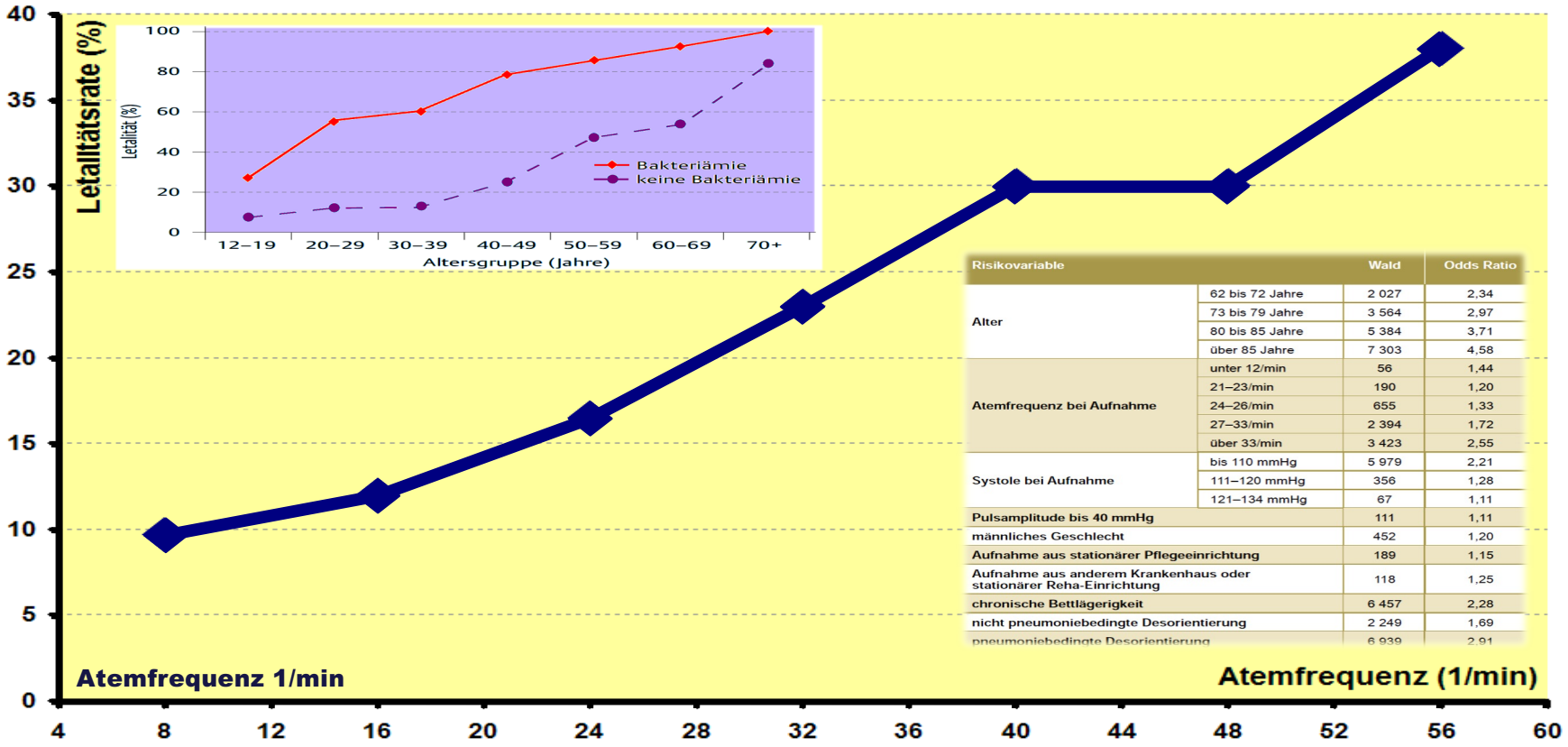
NPV hoch

OLIGOSYMPTOMATIK
bei älteren PatientInnen



Mittl, Am J Respir Crit Care Med 1994 – Metlay, Arch Int Med 2007 – Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE
Atemfrequenz, Bakteriämie & Letalität



Risikovariable		Wald	Odds Ratio
Alter	62 bis 72 Jahre	2 027	2,34
	73 bis 79 Jahre	3 564	2,97
	80 bis 85 Jahre	5 384	3,71
	über 85 Jahre	7 303	4,58
Atemfrequenz bei Aufnahme	unter 12/min	56	1,44
	21–23/min	190	1,20
	24–26/min	655	1,33
	27–33/min	2 394	1,72
	über 33/min	3 423	2,55
Systole bei Aufnahme	bis 110 mmHg	5 979	2,21
	111–120 mmHg	356	1,28
	121–134 mmHg	67	1,11
Pulsamplitude bis 40 mmHg		111	1,11
männliches Geschlecht		452	1,20
Aufnahme aus stationärer Pflegeeinrichtung		189	1,15
Aufnahme aus anderem Krankenhaus oder stationärer Reha-Einrichtung		118	1,25
chronische Bettlägerigkeit		6 457	2,28
nicht pneumoniebedingte Desorientierung		2 249	1,69
pneumoniebedingte Desorientierung		6 939	2,91

Tilghman, Ann Intern Med 1937 – Welte, ÖGP-Kongress 2008 – Welte, Pneumologie 2010 – Strauß, Dtsch Arztebl Int 2014

AMBULANT ERWORB PNEUMONIE
Radiologische Befunde

Type	Pathogen	Lobar Consolidation	Reticulonodular Opacities	Peribronchial Cuffing	Pleural Effusion	Notes
Nonzoonotic	*M pneumoniae*	+	+++	+++	+	Possible to have effusions or adenopathy
	L pneumoniae	+++	–	–	+++	Unilateral pleural effusions are common
	C pneumoniae	++	+	–	+	Typically unilobar involvement, with patchy consolidation in lower lobes
Zoonotic	*F tularensis*	++	++	–	++	Variable appearance; can have single consolidations that resemble lung cancer
	C psittaci	++	+	–	–	Favors lower lobes
	C burnetii	++	++	–	–	Variable appearance; conflicting data on upper versus lower lobe predominance
Viral (general population)	Influenza	++	++	–	–	Bilateral opacities, with or without focal areas of consolidation
	Parainfluenza	++	++	–	–	Nonspecific; unilateral or bilateral consolidations
	RSV	++	+++	+	+	Nonspecific; can appear normal
	Adenovirus	++	+	+	–	Can resemble findings of bacterial pneumonia
	HMPV	++	+++	+	–	Variable depending on severity of infection
Viral (outbreaks)	Avian influenza	+++	++	–	+	Extensive pneumonic consolidation, mostly located in lower zones
	SARS-CoV-1	++	++	–	–	Findings can be unilateral or bilateral
	MERS-CoV	++	++	–	–	Predominance in periphery of lungs
	SARS–CoV-2	++	++	–	–	Subpleural areas of consolidation

Auskultation

Röntgen

▪ zur Aufnahme	innerhalb von 24 – 36 Std.
▪ zur Entlassung	
▪ Abschlußröntgen	4 – 6 Wochen nach der Entlassung
✓ C/P p.a. & seitlich	Standard
✓ C/P Seitenlage	Pleuraerguß? Punktion?

Mittl, Am J Respir Crit Care Med 1994 – van Vugt, Eur Respir J 2013 – Dueck, RadioGraphics 2021

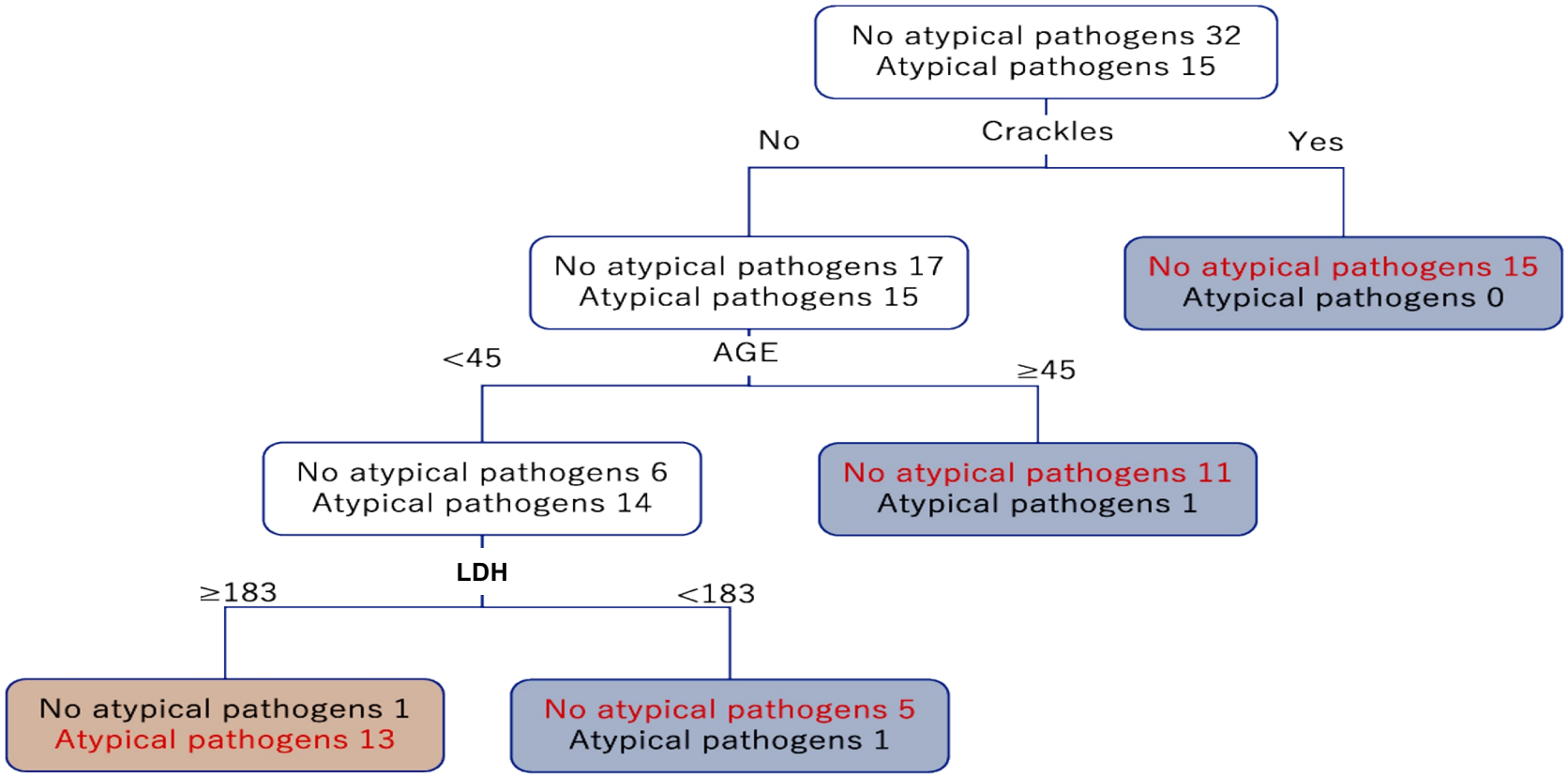
AMBULANT ERWORB PNEUMONIE

Symptome & Labor bei atyp Pneumonie

Erreger	Häufige extrapulmonale Symptome	Wegweisende Laborbefunde	Diagnostik
Legionella pneumophila	Verwirrtheit, abdominelle Schmerzen, Diarrhö, Hypotension/Schock, relative Bradykardie, starke Kopf- und Muskelschmerzen, pleuritische Schmerzen, Hämoptysen	Elektrolytstörung (Hyponaträmie, Hypophosphatämie), erhöhte Transaminasen, erhöhte Kreatinkinase (CK), ggf. Mikrohämaturie	— Antigentest im Urin (nur Serotyp 01) — PCR (respiratorisches Material) — Kultur auf Spezialmedien (respiratorisches Material, Lungengewebe, Pleuraflüssigkeit) — direkte Immunofluoreszenz (Lungengewebe)
Mycoplasma pneumoniae	Diarrhö, nicht-exsudative Pharyngitis, Rhinitis, zervikale Adenopathie, Otitis media, Enzephalitis, aseptische Meningitis, Muskelschmerzen, Hauterscheinungen (Erythema multiforme, kutane leukozytoklastische Vaskulitis), Myokarditis, Perikarditis, neue Blockbildung im EKG	erhöhte Kälteagglutinine ($\geq$ 1:64)	— Serologie (4-facher IgG-Titeranstig oder Serokonversion im Verlauf) — PCR — ggf. Kultur auf Spezialmedien (respiratorisches Material)
Chlamydophila pneumoniae	Nicht-exsudative Pharyngitis, Rhinitis, Muskelschmerzen, Otitis media	normale Leukozytenzahl, erhöhte Transaminasen	— Serologie (4-facher IgG- oder IgA-Titeranstieg oder Serokonversion im Verlauf; IgM-Titer > 1:16) — Kultur auf Spezialmedien (respiratorisches Material)
Francisella tularensis	Grippeähnliche Symptome, Lymphadenopathie, Erythema multiforme oder nodosum, je nach Infektionsweg: Hautulzerationen (nach Hautkontakt mit dem Erreger), Stomatitis, Pharyngitis, Tonsillitis (nach Aufnahme von kontaminiertem Wasser oder Lebensmittel), Übelkeit, Erbrechen, Bauchschmerzen		— PCR — Antigennachweis — Kultur auf Spezialmedien — ggf. Serologie
Coxiella burnetii	Hohes Fieber, Schüttelfrost, Myalgie, Cephalgie, Hepatitis, seltener Myokarditis, Perikarditis, Endokarditis oder Meningoenzephalitis, Hautausschlag	erhöhte Transaminasen	— Serologie: Antikörper gegen Coxiellen-Ag (Phase II und ggf. Phase I) — ggf. Kultur — ggf. PCR — ggf. Immunfluoreszenz oder Elektronenmikroskopie auf Biopsiematerial
Chlamydophila psittaci	Grippeähnliche Symptome, Fieber, Cephalgie, Exanthem, Splenomegalie, Bradykardie	Leukozytopenie und Linksverschiebung, mäßig beschleunigte BSG	— Kultur (selten) — PCR (nicht standardisiert) — Serologie: IgM $\geq$ 1:16, IgG-Differenz $\geq$ 1:32 in > 2 Wochen

Mikolajewska, MMW Fortschr Med 2021

AMBULANT ERWORB PNEUMONIE
atypisch vs typisch



Ishimaru, Intern Emerg Med 2021

AMBULANT ERWORB PNEUMONIE
Procalcitonin

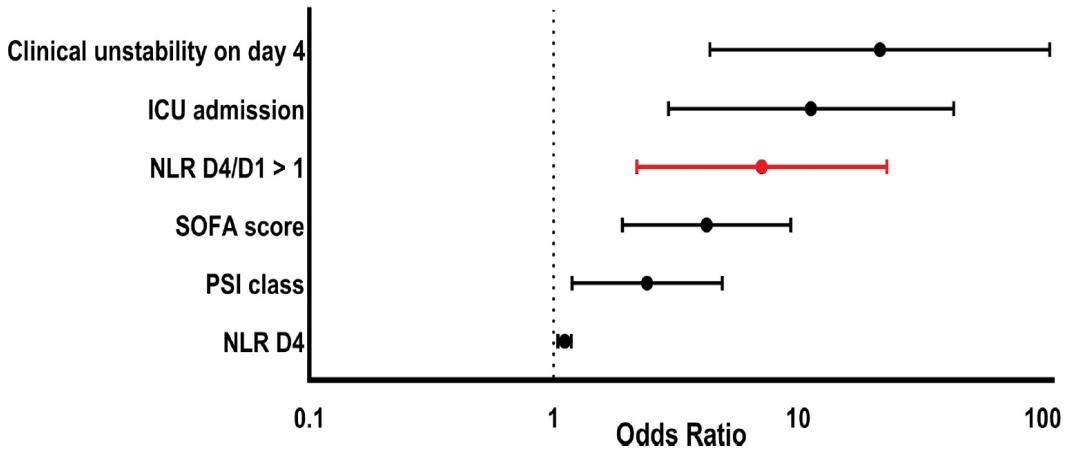
- **selten erhöhte Werte**
  - bei M. pneumoniae oder L. pneumophilia
- **schlechte Sensitivität**
  - bei bakteriell-viralen Mischinfektionen
- **insuffiziente Daten**
  - um Therapie hintanzuhalten
- **irreführende Aussagen**
  - Reduktion der Therapiedauer nur in Studien mit langer Therapiedauer
- **unklare Daten**
  - schlechter Outcome besser als mit CURB-65 vorhergesagt

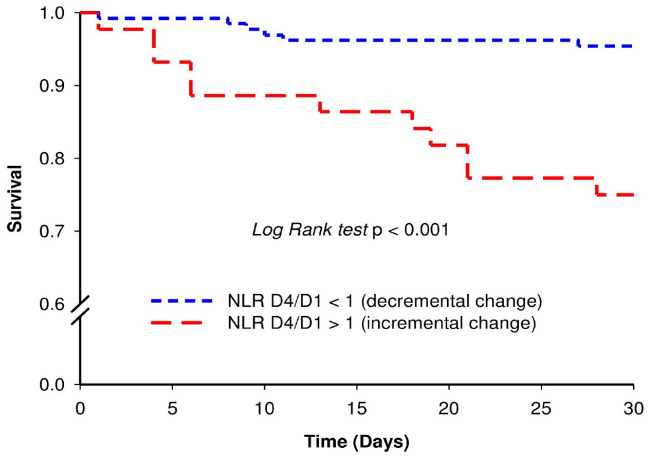
Wunderink, BMJ 2017

AMBULANT ERWORB PNEUMONIE
Neutrophile-Lymphozyten-Ratio [NLR]

- **NLR: Neutrophile abs geteilt durch Lymphozyten abs**

	All patients (n = 175)	Survivors (n = 158)	Non-survivors (n = 17)	*P* value
NLR				
D1	10.1 (5.6–18.8)	9.9 (5.5–19.4)	11.5 (5.4–15.3)	0.964
D4	5.9 (3.3–10.5)	5.4 (3.2–9.8)	11.1 (7.8–25.5)	<0.001
D4/D1	0.62 (0.30–1.02)	0.55 (0.30–0.91)	1.29 (0.61–2.72)	0.001
D4/D1 > 1	44 (25.1)	33 (20.9)	11 (64.7)	<0.001
CRP, mg/dL				
D1	11.9 (6.3–22.7)	11.4 (6.1–22.6)	19.8 (12.0–23.8)	0.054
D4	7.2 (3.0–13.1)	6.7 (2.9–11.9)	15.9 (5.1–21.3)	0.005
D4/D1	0.61 (0.35–1.04)	0.61 (0.34–0.97)	0.77 (0.47–1.16)	0.244
D4/D1 > 1	46 (26.3)	39 (24.7)	7 (41.2)	0.121
PCT, ng/mL				
D1	0.95 (0.32–3.59)	0.99 (0.36–3.51)	0.84 (0.23–21.6)	0.854
D4	0.44 (0.15–1.59)	0.41 (0.14–1.44)	0.71 (0.35–8.01)	0.104
D4/D1	0.43 (0.20–0.98)	0.37 (0.19–0.92)	0.74 (0.40–1.09)	0.084
D4/D1 > 1	22 (20.4)	18 (19.4)	4 (26.7)	0.363





Yoon, Ann Lab Med 2013 – Lee, PLoS One 2021 – Cury, PLoS One 2021

AMBULANT ERWORB PNEUMONIE

Pleuraempyem

Klassifikation parapneumonischer Pleuraergüsse/Empyeme			
	Unkomplizierter PPE	**Komplizierter PPE**	**Empyem**
pleurale Morphologie	dünn, permeabel	Fibrinexsudation, Septierungen	verdickt, Granulationsgewebe, Septen und Kammern
Pleurapunktat	klar	trüb	eitrig
pH	>7,3	7,1–7,2 (7,3)	<7,1
Laktathydrogenase	<500	>1000	>1000
Glukose mg/dL	>60	<40	<40
Zytologie	PMN +	PMN + +	PMN + + +
Mikrobiologie	steriles Punktat	gelegentlich positiv (mikroskopisch und kulturell)	häufig positiv (mikroskopisch und kulturell)

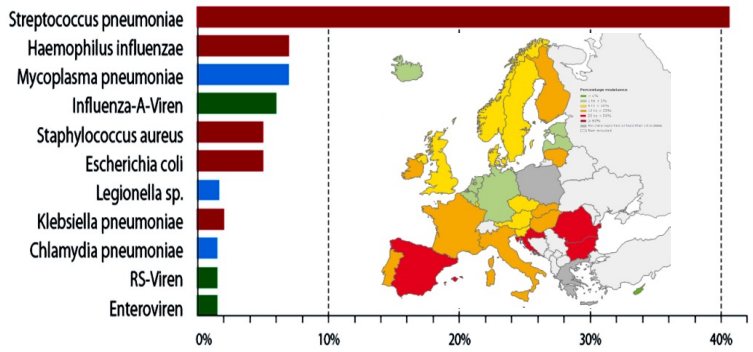
PUNKTION

- ... bei fehlender Besserung unter Antibiotikatherapie
- ... pH-Wert <7.2 im Erguss ist ein Hinweis auf Empyem

Ewig, Pneumologie 2021

AMBULANT ERWORB PNEUMONIE
Erregerspektrum

CAP



KEINE RELEVANZ

Bakterien und Pilze der oropharyngealen Standortflora ohne therapeutische Relevanz bei nosokomialer Pneumonie.

- Corynebacterium spp.
- Enterococcus spp.
- Neisseria spp.
- α-hämolysierende (vergrünende) Streptokokken
- Koagulase-negative Staphylokokken
- Candida spp.

NAP & VAP

Infektionserreger bei nosokomialer Pneumonie, Patienten ohne Risikofaktoren für multiresistente Erreger (MRE).

- Enterobacteriaceae
  - Escherichia coli
  - Klebsiella spp.
  - Enterobacter spp.
- Haemophilus influenzae
- Staphylococcus aureus (MSSA)
- Streptococcus pneumoniae

Infektionserreger bei nosokomialer Pneumonie, Patienten mit Risikofaktoren für multiresistente Erreger (MRE).

- *zusätzlich:*
- Methicillinresistente Staphylococcus aureus (MRSA)
- ESBL-bildende Enterobacteriaceae
- Pseudomonas aeruginosa
- Acinetobacter baumannii
- Stenotrophomonas maltophilia

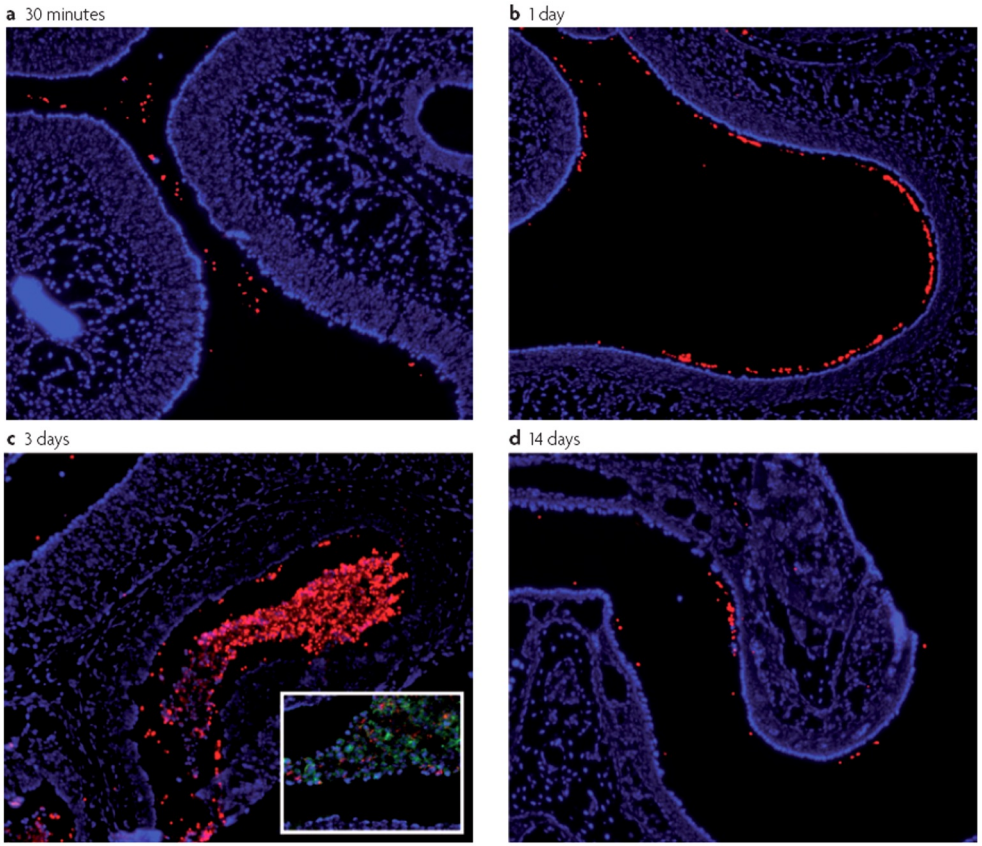
Welte, Med Klinik 2006 – Welte, Thorax 2010 – Dalhoff, Pneumologie 2012 – AURES 2014

AMBULANT ERWORB PNEUMONIE
Erreger, Anamnese & Diagnostik

Erreger	Typische Anamnese	Verfahren
Bakterien		
Mycoplasma pneumoniae	junger Patient, ambulant, manchmal Ausbrüche, epidemiologische Situation	NAT Serologie (IgM)
Legionella pneumophila	epidemiologische Situation, Reisen mit Hotelaufenthalt	Urinantigen NAT
Chlamydophila psittaci	Tierkontakt (Papageien, Sittiche, Tauben)	NAT Serologie
Coxiella burnetii	epidemiologische Situation, Tier (Schaf)-Kontakte	NAT Serologie
Burkholderia pseudomallei	Reisen nach Südostasien (Melioidose)	Kultur
Respiratorische Viren		
Influenza A/B	epidemiologische Situation (Saison, Epidemie, Pandemie)	NAT
Parainfluenzaviren Adenoviren RSV Metapneumovirus	epidemiologische Situation	NAT
SARS-CoV-1, MERS	epidemiologische Situation, Kontakt zu Infizierten	NAT
SARS-CoV-2	epidemiologische Situation, Kontakt zu Infizierten	NAT
Pilze		
Coccidioidomykose (Coccidioidis immitis)	Aufenthalt in trockenen Zonen/Regionen der südl. USA, Mittel- und Südamerika	kulturell Serologie NAT
Histoplasmose (Histoplasma capsulatum)	Aufenthalt in gefährdeten Regionen der USA (Ohio, entlang der Flüsse Mississippi und Missouri und St. Lawrence River) und Mittelamerika	kulturell Serologie NAT
Cryptococcus neoformans var. gattii	endemisch auf Vancouver Island; gehäuft im Nordwesten der USA, in Australien, Südamerika, China	kulturell Antigen-Test NAT

Ewig, Pneumologie 2021

AMBULANT ERWORB PNEUMONIE
Kolonisation

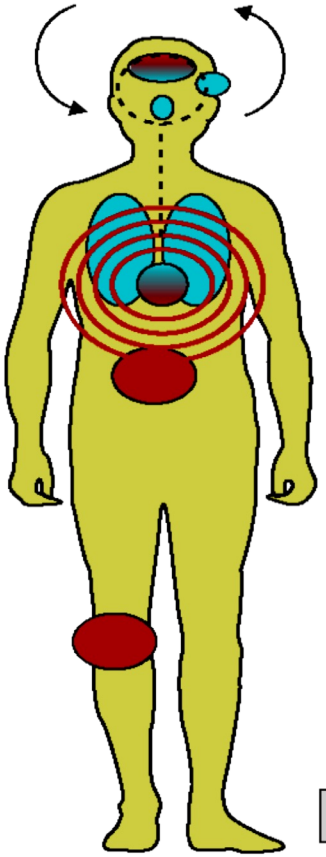


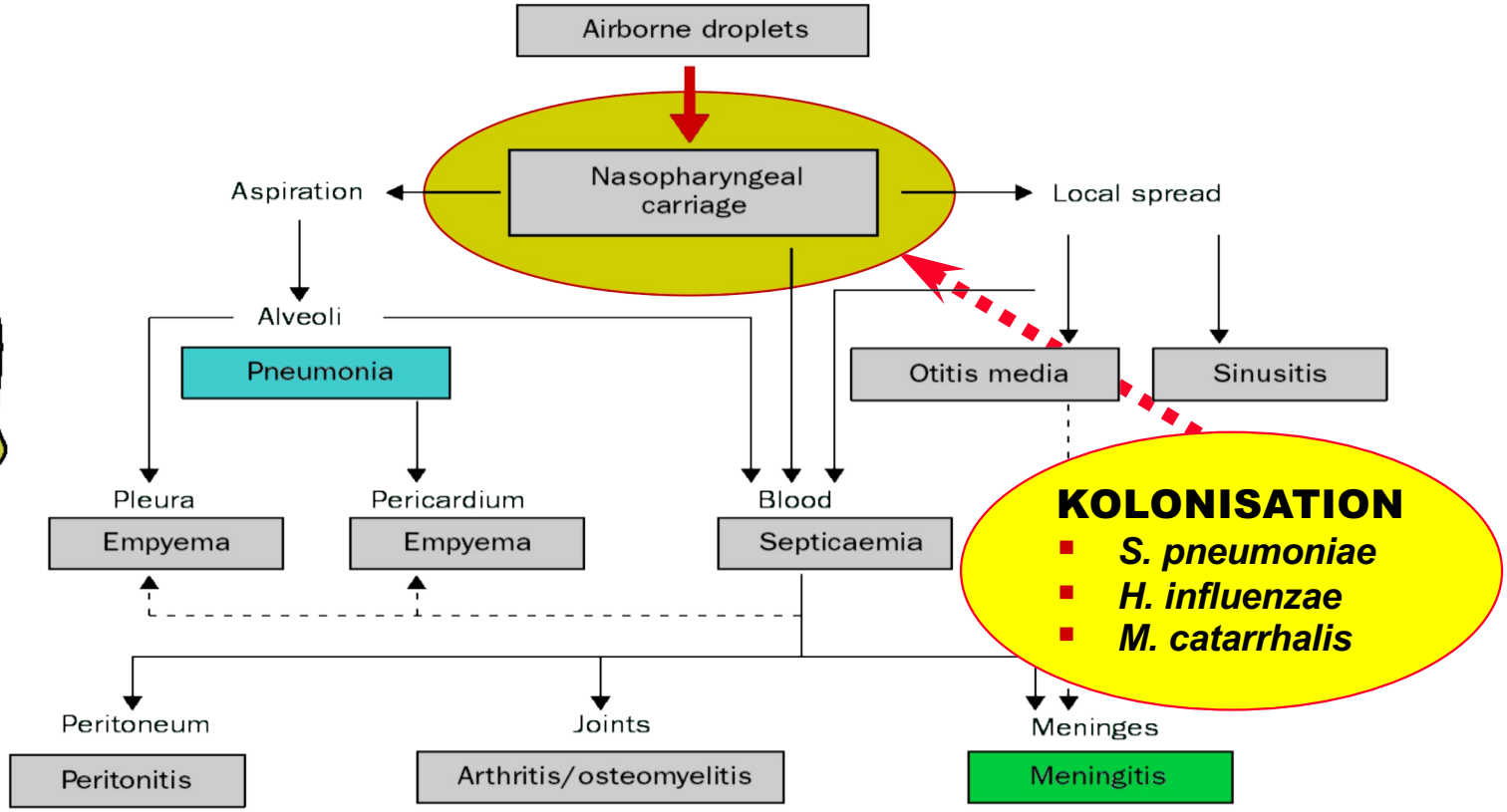
- **JEDE** Pneumokokken-erkrankung beginnt mit nasaler Kolonisation
- **Carrier-Status**
  - Wochen bis Monate
  - bes. Kleinkindern bis 40%
  - Erwachsene bis 10%
  - impfen > Herdimmunität
- **Mensch-zu-Mensch**
  - Übertragung durch direkten Sekretkontakt

Kadioglu, Nat Rev Microbiol 2008

AMBULANT ERWORB PNEUMONIE

Pathophysiologie





Bogaert, Lancet Infect Dis 2004

AMBULANT ERWORB PNEUMONIE
Streptococcus pneumoniae

Methode	nachgewiese Komponente	Probentyp	Sensitivität	Spezifität	erforderliche Zeit
Binax NOW	**Antigen**	**Urin**	**86 %[1]**	**94 %**	**15 Minuten**
Blutkultur	Organismus	Blut	10 % - 30 % [2]	> 95 %	24 - 48 Stunden
Sputum Kultur	Organismus	Sputum	50 % - 60 %	50 % - 85 %	24 - 48 Stunden
Sputum Gram	Antikörper	Sputum	50 % - 88 %	50 % - 80 %	15 Minuten

- **Harn-Antigen**
  - **positiv bei bakteriämischer und nicht-bakteriämischer Pneumokokkenpneumonie**
  - **falsch positive Ergebnisse**
    - **nasopharyngeale Kolonisation**
      - **20 – 40% gesunder Kinder**
      - **5 – 10% gesunder Erwachsener**
    - **bis 48 Stunden nach Pneumokokkenimpfung, daher bis 5 Tage nach Vaccination kein Urin-Antigentest**
- **Blutkultur**

AMBULANT ERWORB PNEUMONIE
Haemophilus influenzae

- **CAPNETZ 2004 ► 2016**
  - **S. pneumoniae 58.0% ► 37.5%**
  - **H. influenzae 12.2% ► 20.8%**

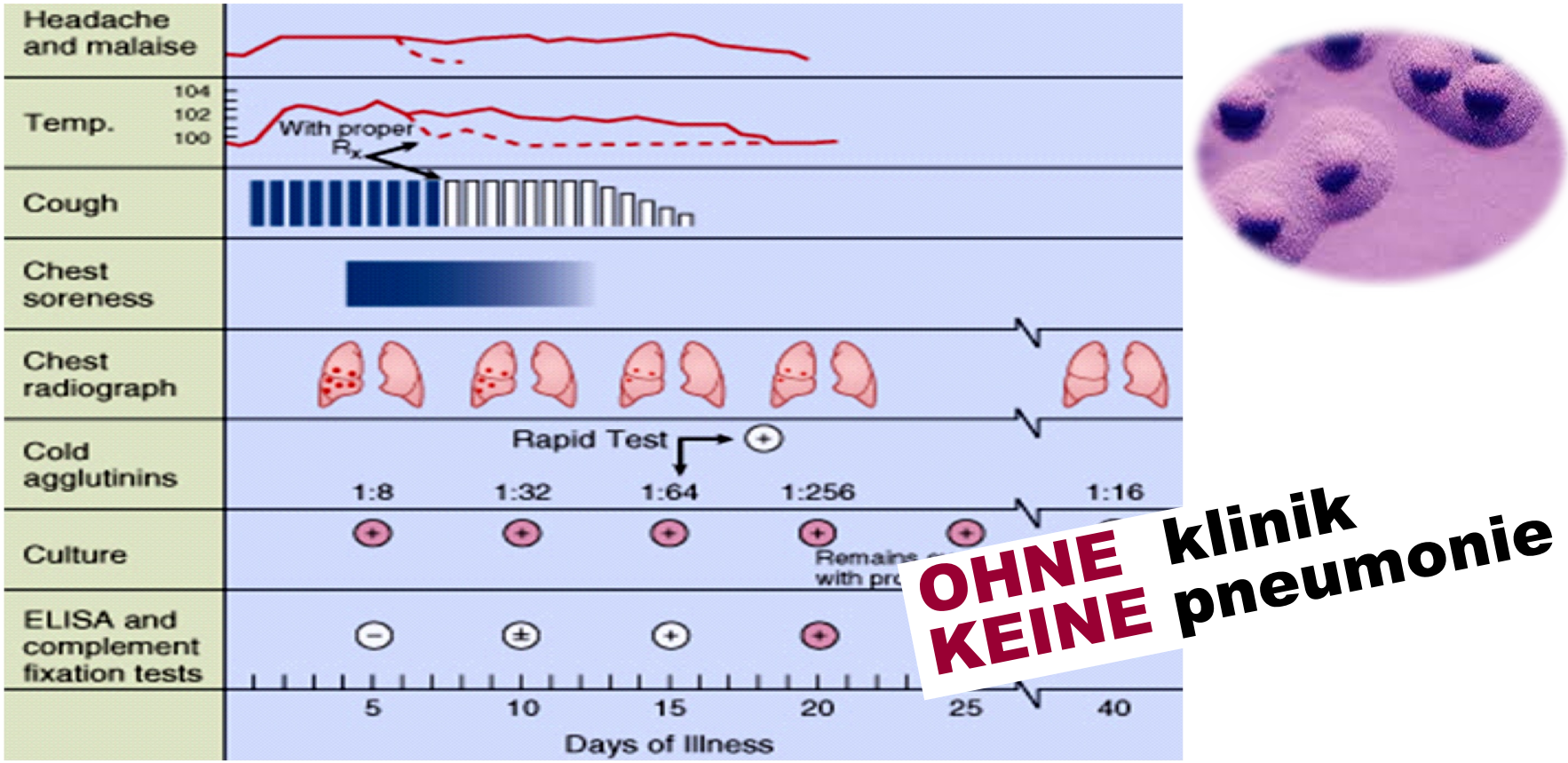
	H. influenzae (n = 33)	*S. pneumoniae* (n = 36)	*P*
Shock	0	13.9	.03
Admission to ICU	15.2	16.7	.9
PORT score	92 [81–118]	100.5 [86–130.75]	.2
Pneumonia Severity Index	4 [3–4]	4 [3–4]	.1
ATS/IDSA severe pneumonia	18.2	16.7	.9
qSOFA ≥2	3	13.9	.1
In-hospital mortality	0	11.1	.05
30-d mortality	0	13.9	.02

- **EUCAST 2018**
  - **Makrolide im Antibiogramm wegen unzureichender Aktivität nicht angeben**

Shoar, Open Forum Infect Dis 2021 – Braeken, Infection 2021

AMBULANT ERWORB PNEUMONIE

Mycoplasma pneumoniae



OHNE klinik
KEINE pneumonie

Mandell, Principle and Practice of Infectious Diseases

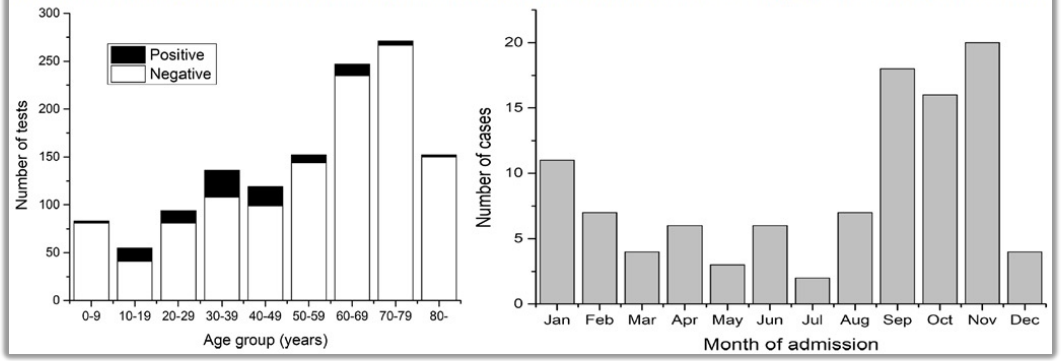
AMBULANT ERWORB PNEUMONIE

Mycoplasma pneumoniae

Macrolide-Resistant *Mycoplasma pneumoniae* Infections in Children, Ohio, USA

- protrahierter Verlauf
- höhere Morbidität
- Makrolidresistenzen
  - 88.3% China
  - 49.4% – 83.3% Japan
  - 70.3% Korea
  - 20.0% Italien
  - 3.1% Deutschland
  - 2.8% – 10.0% USA
  - 3.1% Deutschland

85% of the patients had a triad of typical symptoms: fever, cough and shortness of breath. Symptoms in the upper respiratory tract were rare. In 91% of the cases, *M. pneumoniae* was the only pathogen found. The highest incidence was found in the age group of 30–40 years, and 68% of the patients did not have any underlying diseases. Most patients were initially empirically treated with beta-lactam antibiotics and needed 2–4 changes in their treatment. Only 6% were discharged without an antibiotic effective against *M. pneumoniae*. This study shows that *M. pneumoniae* often led to hospitalisation and that patients needed appropriate antimicrobial treatment to recover. Mixed infections were rare, and situations that could be interpreted as carriage did not occur.



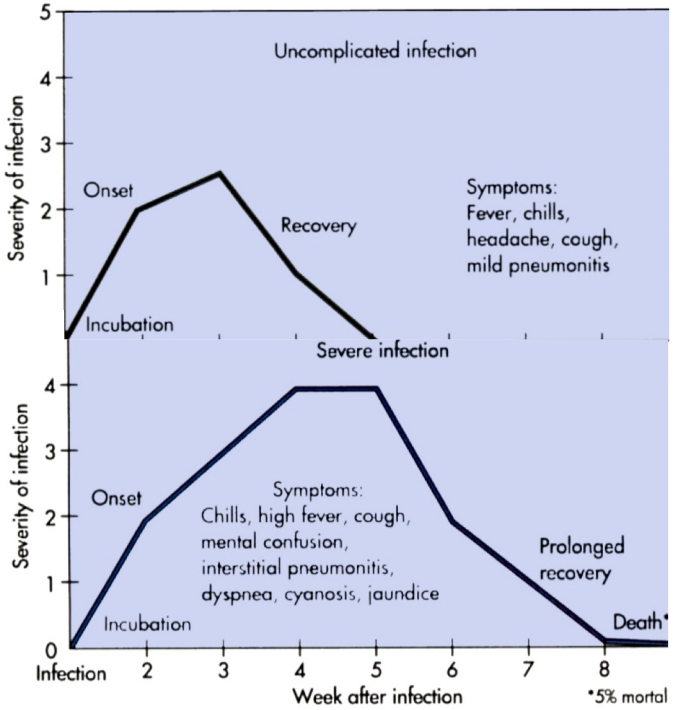
Emergence of Macrolide-Resistant *Mycoplasma pneumoniae* during an Outbreak in a Primary School

Lanata, Emerg Infect Dis 2021 – Ishimaru, Intern Emerg Med 2021 – Hubert, Pathogens 2021

AMBULANT ERWORB PNEUMONIE
Chlamydophila psittaci

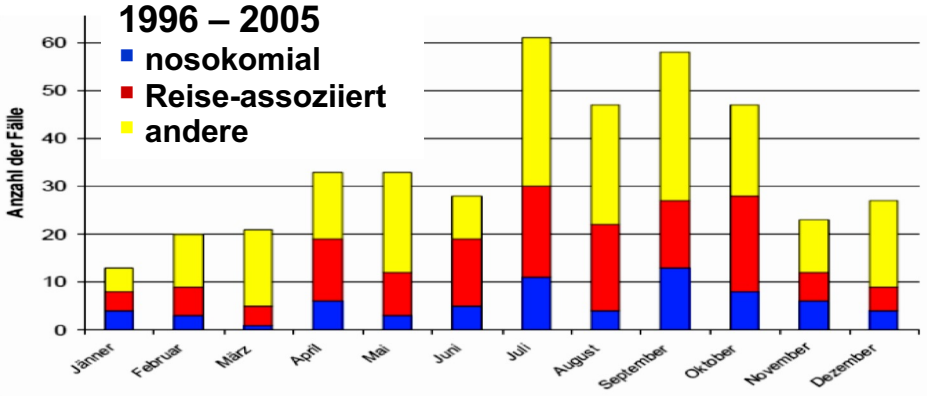
PSITTAKOSE

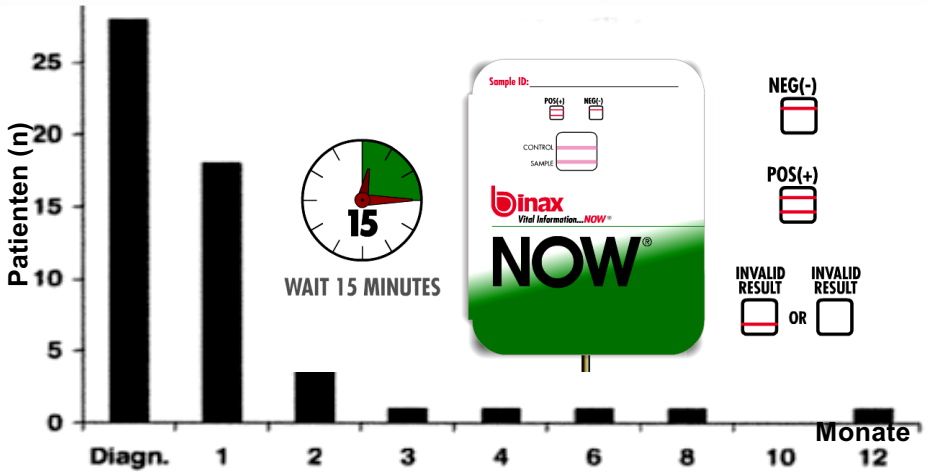
- gattungsspezifische Ak erfasst
- KBR, PCR



AMBULANT ERWORB PNEUMONIE
Legionellen pneumophila

- *Legionella pneumophila*
  - Nachweis der Serotype 1
  - Sens. >90%
  - Spez. 99 – 100%
  - Dauer 15 min
- Nativharn
  - < 24h RT
  - bis 14 d 4°C
- ab Tag 3 positiv
- **kein** Einfluss des Antibiotikums auf Testergebnis





Ewig, Pneumologie 2002 – Sopena, Eur J Clin Microbiol Infect Dis 2002 – Roigl, J Antimicrob Chemother 2003 – AGES 2006

AMBULANT ERWORB PNEUMONIE
Legionellen pneumophila

	Legionella-Pneumonie	Pontiac-Fieber	Extrarespiratorische Manifestation	Inapparente Serokonversion
Häufigkeit	1–5% (bis 30%) aller Pneumonien	Geschätzt 10-mal häufiger als Pneumonie	?	Geschätzt 100-mal häufiger als Pneumonie
Manifestationsrate	1–5%			
Inkubationszeit	4–10 (–20) Tage			
Krankheitsdauer	2–3 Wochen und länger			
Klinik	Allgemeininfektion mit Pneumonie, Pleuritis, ZNS- und anderen extrapulmonalen Symptomen			
Letalität	2–10% (bis 80%)			
Chemotherapie	Makrolide Fluorchinolone (Rifampicin)	Nicht erforderlich	Chirurgische Sanierung, Chemotherapie wie bei Pneumonie	

	Percentage means		
Pathogen	**Outpatient**	**Hospital**	**Intensive care unit**
S pneumoniae	38	27	28
M pneumoniae	8	5	2
H influenzae	13	6	7
Chlamydophila pneumoniae	21	11	4
Staphylococcus aureus	1.5	3	9
Enterobacteriaceae	0	4	9
Pseudomonas aeruginosa	1	3	4
Legionella spp.	0	5	12
C burnetii	1	4	7
Respiratory viruses	17	12	3
Unclear	50	41	45

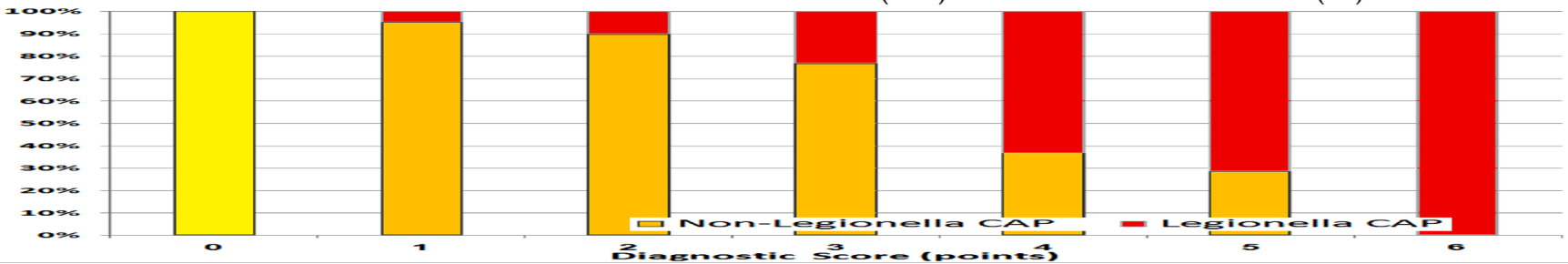
30 – 50%
Durchfall

Lück, Bundesgesundheitsbl - Gesundheitsforsch -Gesundheitsschutz 2006
Welte, Thorax 2010

AMBULANT ERWORB PNEUMONIE
Legionellen-CAP-Score

Parameter	AUC	95% CI*	*P-value*	Optimal cut off	Sensitivity	Specificity
Combined Score	0.86	0.81–0.90	-	< 2	78.0	78.8
Temperature	0.74	0.63–0.78	*<0.0001*	> 39.4	48.1	84.4
No sputum	0.68	0.61–0.74	*<0.0001*	-	-	-
Sodium	0.71	0.63–0.78	*<0.0001*	< 133	64.6	70.8
Lactate dehydrogenase	0.62	0.53–0.71	*<0.0001*	> 225	67.1	58.1
C-reactive protein	0.76	0.70–0.82	*<0.0001*	> 187	71.6	64.7
Platelet counts	0.71	0.64–0.78	*<0.0001*	< 171	45.7	83.6

Points	Sensitivity	Specificity	*Legionella* CAP	Non-*Legionella* CAP
≥ 0	100	-	0 (0%)	70 (19.0%)
≥ 1	92.7	50.3	6 (7.3%)	115 (31.3%)
≥ 2	78.0	78.8	12 (14.6%)	105 (28.5%)
≥ 3	58.5	93.2	16 (19.5%)	53 (14.4%)
≥ 4	14.6	98.9	36 (43.9%)	21 (5.7%)
≥ 5	2.4	100	10 (12.2%)	4 (1.1%)
6	-	100	2 (2.4%)	0 (0%)



Fiumefreddo, BMC Pulmonary Medicine 2009

AMBULANT ERWORB PNEUMONIE
Therapiefragen

- **mono** oder **kombi**
- **Aminopen** oder **Ceph3**
- **Chinolone – ja** oder **nein**
- **peroral** oder **intravenös**
- **Kortison – inhalativ** oder **systemisch**
- **Therapiedauer – kurz** oder **lang**

AMBULANT ERWORB PNEUMONIE

Erregerspezifische Therapie

Zurück **Pneumonie (CAP)**

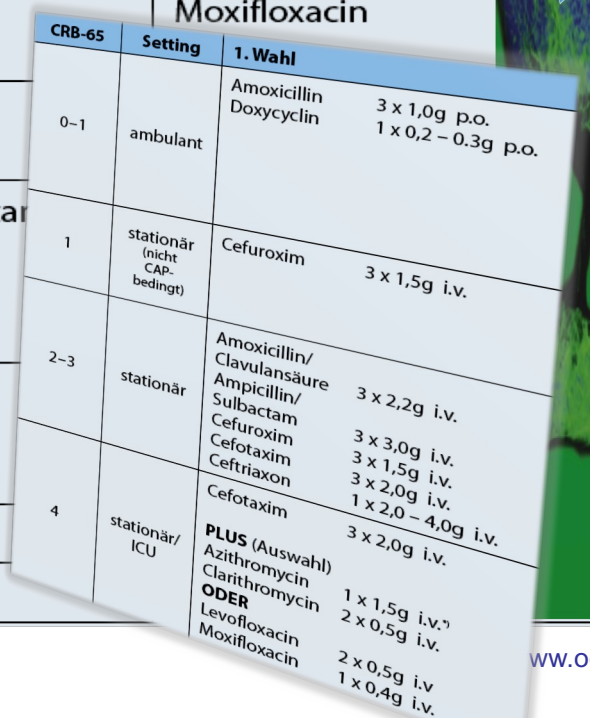
Handelsnamen | Wirkstoff

Therapie	Wirkstoff	Tage
M	Cefotaxim	5 - 7
R	Ceftarolin	5 - 7
M	Ceftriaxon	5 - 7
M	Cefuroxim	5 - 7
M	Clarithromycin	5 - 7
M	Doxycyclin	5 - 7
M	Levofloxacin	5 - 7
M	Moxifloxacin	5 - 7
M	Penicillin G	

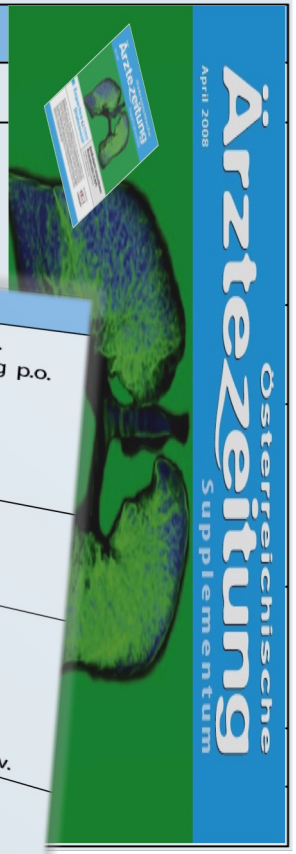
keine Angaben | geeignet | Reserve
Mittel der letzten Wahl | Mittel der 1. Wahl

Start | Broschüre | Hilfe | Einstellungen

1. Wahl	Alternative
Penicillin G	Cefuroxim
Azithromycin Clarithromycin Josamycin Roxithromycin	Doxycyclin Levofloxacin Moxifloxacin
Levofloxacin Moxifloxacin	
Piperacillin/Tazobactar Ceftazidim Cefepim Cefpirom	
Ertapenem	
Flucloxacillin	
Linezolid	



CRB-65	Setting	1. Wahl	
0–1	ambulant	Amoxicillin Doxycyclin	3 x 1,0g p.o. 1 x 0,2 – 0.3g p.o.
1	stationär (nicht CAP-bedingt)	Cefuroxim	3 x 1,5g i.v.
2–3	stationär	Amoxicillin/ Clavulansäure Ampicillin/ Sulbactam Cefuroxim Cefotaxim Ceftriaxon	3 x 2,2g i.v. 3 x 3,0g i.v. 3 x 1,5g i.v. 3 x 2,0g i.v. 1 x 2,0 – 4,0g i.v.
4	stationär/ ICU	Cefotaxim **PLUS** (Auswahl) Azithromycin Clarithromycin **ODER** Levofloxacin Moxifloxacin	3 x 2,0g i.v. 1 x 1,5g i.v. 2 x 0,5g i.v. 2 x 0,5g i.v 1 x 0,4g i.v.



www.oeginfekt.eu

AMBULANT ERWORB PNEUMONIE
Dosierungsempfehlungen & Kommentar

Substanz	Tagesdosis i. v.[1]	Tagesdosis p. o.[1]
Aminopenicilline		
Amoxicillin	nicht verfügbar	3 x 750 – 1000 mg
Ampicillin	3 – 4 x 2 g	nicht empfohlen
Penicillin/Betalaktamase-Inhibitor-Kombinationen		
Ampicillin/Sulbactam	3 – 4 x 3 g	initial nicht empfohlen
Amoxicillin/Clavulansäure	3 – 4 x 2,2 g	2 – 3 x 1 g
Piperacillin/Tazobactam	3 – 4 x 4,5 g	nicht verfügbar
Cephalosporine		
Cefuroxim	3 – 4 x 1,5 g	nicht empfohlen
Ceftriaxon	1 x 2 g	nicht verfügbar
Cefotaxim	3 – 4 x 2 g	nicht verfügbar
Carbapeneme		
Ertapenem	1 x 1 g	nicht verfügbar
Meropenem	3 x 1 g	nicht verfügbar
Imipenem	3 x 1 g	nicht verfügbar
Makrolide		
Clarithromycin	2 x 500 mg	2 x 500 mg
Azithromycin	1 x 500 mg	1 x 500 mg
Fluorchinolone		
Moxifloxacin	1 x 400 mg	1 x 400 mg
Levofloxacin	1 – 2 x 500 mg	1 – 2 x 500 mg
Ciprofloxacin	2 – 3 x 400 mg	2 x 500 – 750 mg
Aminoglykoside		
Gentamicin	1 x 4 – 6 mg/kgKG	nicht verfügbar
Tobramycin	1 x 5 – 7 mg/kgKG	nicht verfügbar
Amikacin	1 x 15 – 20 mg/kgKG	nicht verfügbar
Tetracycline		
Doxycyclin	nicht empfohlen	1 x 200 mg
Neuraminidase-Inhibitoren		
Oseltamivir	nicht verfügbar	2 x 75 mg

Hinweis: Die Dosierungen können im Einzelfall von den Zulassungsdosierungen abweichen.
[1] bei normaler Nierenfunktion.
Unabhängig von der Nierenfunktion sollte in den ersten 24 Stunden die volle Tagesdosis gegeben werden.

Substanz	Tagesdosis i. v.	Tagesdosis p. o.
Aminopenicilline		
Amoxicillin	nicht verfügbar	3 x 750 – 1000 mg
Ampicillin	3 – 4 x 2 g	nicht empfohlen
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Cephalosporine		
Cefuroxim	3 – 4 x 1,5 g	nicht empfohlen
Ceftriaxon	1 x 2 g	nicht verfügbar
Cefotaxim	3 – 4 x 2 g	nicht verfügbar
Carbapeneme		
Ertapenem	1 x 1 g	nicht verfügbar
Meropenem	3 x 1 g	nicht verfügbar
Imipenem	3 x 1 g	nicht verfügbar
Makrolide		
Clarithromycin	2 x 500 mg	2 x 500 mg
Azithromycin	1 x 500 mg	1 x 500 mg
Fluorchinolone		
Moxifloxacin	1 x 400 mg	1 x 400 mg
Levofloxacin	1 – 2 x 500 mg	1 – 2 x 500 mg

Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE
Erregerspezifische Therapie

Erreger	AmpC	TEM 1, 2 SHV 1	ESBL: TEM- und SHV-Varianten	ESBL: CTX-M-Varianten u.a.	Metallo-enzyme	Penicillinasen (Gr. 2a)
Staphylokokken						◆◆◆
Pneumokokken	**KEIN BETALAKTAMASEINHIBITOR NOTWENDIG !**					
Enterokokken						
Gonokokken		◆◆				
Haemophilus		◆				
Escherichia coli	◆	◆◆◆	◆◆	◆		
Klebsiella pneumoniae	◆	◆◆	◆◆	◆	◆	
Proteus mirabilis	◆	◆◆	◆◆	◆◆		
Enterobacter sp.	◆◆◆	◆	◆◆	◆◆	◆	
Pseudomonas	◆	◆	◆	◆	◆	
Acinetobacter	◆◆	◆	◆		◆	

Häufigkeit: ◆◆◆ stark ◆◆ mittel ◆ gering

Theuretzbacher, Pharmazie aus unserer Zeit 2006

AMBULANT ERWORB PNEUMONIE
Cefotaxim vs Amoxi/Clav

Are third-generation cephalosporins associated with a better prognosis than amoxicillin–clavulanate in patients hospitalized in the medical ward for community-onset pneumonia?☆

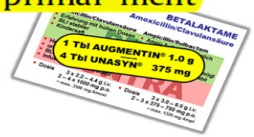
Conclusion: In the largest study aiming to compare amoxicillin–clavulanate and ceftriaxone/cefotaxime in community-onset pneumonia, ceftriaxone/cefotaxime was not associated with lower in-hospital mortality than amoxicillin–clavulanate. Our results suggest that ceftriaxone/cefotaxime should not be preferred over amoxicillin–clavulanate for patients hospitalized in medical wards with community-onset pneumonia.

NO

Batard, Clin Microbiol Infect 2018

AMBULANT ERWORB PNEUMONIE
peroral oder intravenös?

Amoxicillin-Clavulansäure kann mit einer relevanten Hepatotoxizität einhergehen (1 – 17/ 100 000 Verordnungen), diesbezüglich scheint Sultamicillin (chemische Verbindung von Ampicillin und Sulbactam) unbedenklicher. Allerdings ist die Datenlage für Sultamicillin bei der Pneumoniebehandlung im Erwachsenenalter unzureichend und die Dosis der Penicillinkomponente innerhalb des Sultamicillins ist sehr niedrig, sodass dieses orale Präparat primär nicht empfohlen werden kann.



Orale Cephalosporine werden nicht empfohlen. Die Gründe dafür sind:

- die Dosierungen aus den Zulassungsstudien stellen regelhaft eine Unterdosierung dar
- orale Cephalosporine sind ein Risikofaktor für die Ausbreitung von ESBL auch im ambulanten Bereich, andererseits aufgrund guter Alternativen entbehrlich
- orale Cephalosporine wurden als signifikant mit einem Therapieversagen und nachfolgender Hospitalisierung assoziiert gefunden (OR 2,86, CI 1,56 – 5,27)
- orale Cephalosporine begünstigen die Selektion von um difficile

Azithromycin 1 x 1.5 g

- langsam infundieren !!!
- Single-Shot Therapie
- ambulant oder stationär
- Entlassung am Tag 3
- kostengünstig

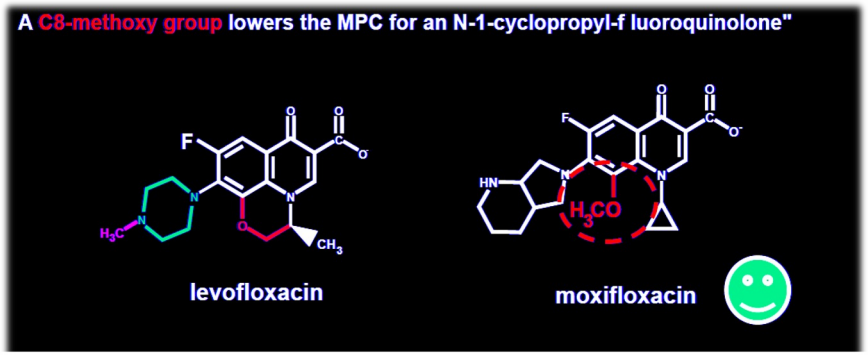
Schonwald, Infection 1999 – Lode, Int J Antimicrob Agents 2001 – Ben-Ami, Clin Infect Dis 2009 – Creutz, J Pulmon Resp Med 2013
Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE

Chinolone

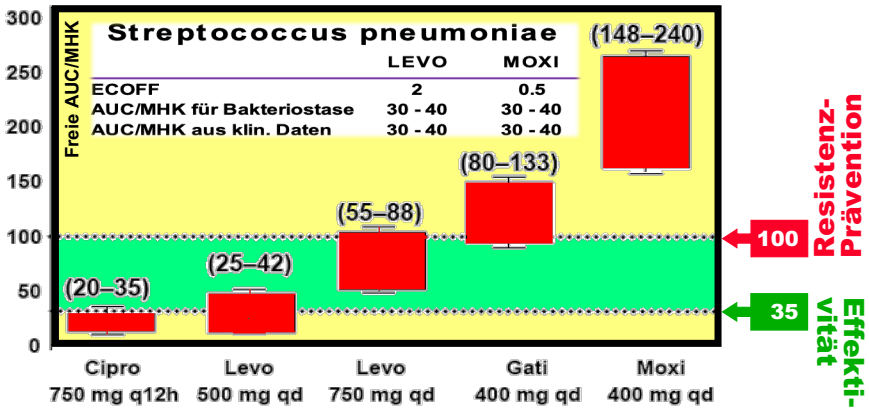
	durchschnittliche MHK_{90} (µg/mL)		
	CIPRO	**LEVO**	**MOXI**
***Staphylococcus aureus* (MSSA)**	0.5	0.25	0.12
***Staphylococcus aureus* (MRSA)**	>32	16	4
Streptococcus pneumoniae	2	1	0.25
Streptococcus pyogenes	2	1	0.25
Streptococcus agalactiae	2	1	0.5

- WT *S. pneumoniae* wird als nicht Ciprofloxacin-sensibel angesehen
- WT *S. pneumoniae* wird als nicht Ofloxacin-sensibel angesehen
- Levo-Breakpoints sprechen für die Hoch-dosistherapie



FULL PRESCRIBING INFORMATION

The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair, and recombination. It appears that the C8-methoxy moiety contributes to enhanced activity and lower selection of resistant mutants of Gram-positive bacteria compared to the C8-H moiety. The presence of the bulky bicycloamine substituent at the C-7 position prevents active efflux, associated with the *NorA* or *pmrA* genes seen in certain Gram-positive bacteria.



Janata, kurz & klar 2006 – Scheld, Chemother J 2003 – Doern, Clin Infect Dis 2001 – Ball, The Quinolones, 3rd Ed 2000 – Blondeau, 1999
Tulkens, Middle East Anti-.Infectives Forum 2017 – www.eucast.or

AMBULANT ERWORB PNEUMONIE
Chinolone

In vitro activity of delafloxacin against highly levofloxacin-resistant invasive isolates of *Streptococcus pneumoniae*

Introduction: We report the activity of delafloxacin, a new fluoroquinolone with high affinity for both topoisomerase IV and DNA gyrase, against highly-levofloxacin-resistant invasive strains of *Streptococcus pneumoniae*.

Methods: A total of 173 highly-levofloxacin-resistant (MIC >32 mg/L) *S. pneumoniae* invasive isolates were studied. The strains were isolated from blood ($n = 162$) and other sterile fluids ($n = 11$). Serotyping was performed by the Pneumotest-Latex and Quellung reaction.

Delafloxacin, levofloxacin, penicillin, cefotaxime, erythromycin and vancomycin MICs were determined by the gradient diffusion method following EUCAST guidelines and breakpoints.

Results: Among the isolates, 32.9% were penicillin non-susceptible, 19.7% cefotaxime non-susceptible, and 76.9% erythromycin resistant. All were susceptible to vancomycin. Delafloxacin MIC_{50} and MIC_{90} (mg/L) values were 0.064 and 0.12, respectively; 60% (15/25) of serotype 9V isolates showed delafloxacin MICs $\geq$ 0.12 mg/L.

Conclusions: Delafloxacin was very active against highly-levofloxacin-resistant invasive isolates of *S. pneumoniae*. Isolates belonging to serotype 9V showed higher delafloxacin MIC values.

Cercenado, Enferm Infecc Microbiol Clin 2022

AMBULANT ERWORB PNEUMONIE
Chinolone

Background: Only a single meta-analysis has reported the clinical benefit of fluoroquinolones (FQs) for *Legionella* pneumonia; however, there is no robust data available to confirm this result, based on current guidelines.

Methods: We performed a systematic review and meta-analysis comparing FQs with macrolides (MCs) on their efficacy and safety in *Legionella* pneumonia, using studies published until January 2020. The outcomes included mortality (overall; 30-day), clinical cure, time to apyrexia, length of hospital stay, and adverse events.

Results: Five RCTs and twelve retrospective studies were identified. Clinical cure was comparable between the treatment groups (risk rate (RR) 1.07, 95% confidential interval (CI) 0.86—1.31). Mortality was significantly higher for MCs than for FQs (overall, odd rate (OR) 0.59, 95% CI 0.35—0.98; 30-day, OR 0.41, 95% CI 0.20—0.85). FQs significantly reduced the length of hospital stay, compared to MCs (mean difference −3.58, 95% CI -5.48—1.69). Other outcomes were not significantly different between the treatment groups (time to apyrexia; mean difference −1.83, 95% CI -5.15—1.5, adverse events; OR 0.61, 95% CI 0.33—1.15). In subgroup analyses, levofloxacin significantly reduced the length of hospital stay over two specific MCs (azithromycin and clarithromycin) (mean difference −3.03, 95% CI -5.33—0.72), whereas mortality was not significantly different between the treatment groups (overall, OR 0.49, 95% CI 0.19—1.24; 30-day, OR 0.38, 95% CI 0.13—1.13).

Conclusions: FQs exhibited superior effects in terms of mortality and length of hospital stay in *Legionella* pneumonia. These results support current guidelines recommending FQs for the treatment of *Legionella* pneumonia.

Kato, J Infect Chemother 2021

AMBULANT ERWORB PNEUMONIE
Chinolone

Background. The Infectious Diseases Society of America recommends either a fluoroquinolone or a macrolide as a first-line antibiotic treatment for *Legionella* pneumonia, but it is unclear which antibiotic leads to optimal clinical outcomes. We compared the effectiveness of fluoroquinolone versus macrolide monotherapy in *Legionella* pneumonia using a systematic review and meta-analysis.

Methods. We conducted a systematic search of literature in PubMed, Cochrane, Scopus, and Web of Science from inception to 1 June 2019. Randomized controlled trials and observational studies comparing macrolide with fluoroquinolone monotherapy using clinical outcomes in patients with *Legionella* pneumonia were included. Twenty-one publications out of an initial 2073 unique records met the selection criteria. Following PRISMA guidelines, 2 reviewers participated in data extraction. The primary outcome was mortality. Secondary outcomes included clinical cure, time to apyrexia, length of hospital stay (LOS), and the occurrence of complications. The review and meta-analysis was registered with PROSPERO (CRD42019132901).

Results. Twenty-one publications with 3525 patients met inclusion criteria. The mean age of the population was 60.9 years and 67.2% were men. The mortality rate for patients treated with fluoroquinolones was 6.9% (104/1512) compared with 7.4% (133/1790) among those treated with macrolides. The pooled odds ratio assessing risk of mortality for patients treated with fluoroquinolones versus macrolides was 0.94 (95% confidence interval, .71–1.25, $I^2 = 0\%$, $P = .661$). Clinical cure, time to apyrexia, LOS, and the occurrence of complications did not differ for patients treated with fluoroquinolones versus macrolides.

Conclusions. We found no difference in the effectiveness of fluoroquinolones versus macrolides in reducing mortality among patients with *Legionella* pneumonia.

Are Macrolides as Effective as Fluoroquinolones in *Legionella* Pneumonia? Yes, but…

Antoni Torres and Catia Cillóniz

Jasper, Clin Infect Dis 2021 – Torres, Clin Infect Dis 2021

AMBULANT ERWORB PNEUMONIE
Chinolone

Fluoroquinolone treatment as a protective factor for 10-day mortality in *Streptococcus pneumoniae* bacteremia in cancer patients

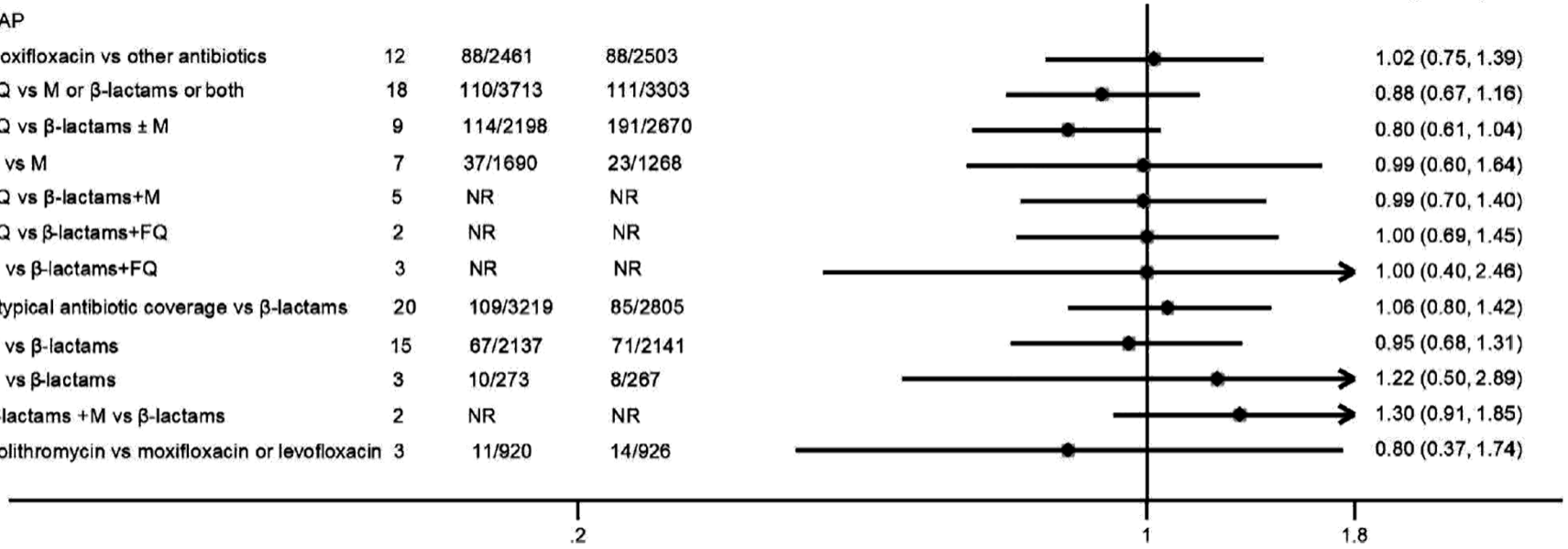
In conclusion, our study corroborated the high mortality associated with pneumococcal bacteremia in cancer patients. Factors associated with a worse prognosis were those intrinsically related to the host and to the episode itself. Despite the observation of high mortality rates in this study, the resistance rate to penicillin was lower than what previously was described in published series. The vast majority of isolated *S. pneumoniae* strains are included in the available vaccines, indicating the need for investment and optimization of vaccine focused prevention in cancer patients. FQ treatment as a protective factor in 10-day mortality shows its potential use for IPDs and severe CAP in cancer patients. Prospective studies should be conducted to confirm this finding in the future.

Fontana, Sci Rep 2021

AMBULANT ERWORB PNEUMONIE

Welche Therapie ist die beste?

ID	Studies	Intervention n/N	Control n/N	RR (95% CI)
CAP				
Moxifloxacin vs other antibiotics	12	88/2461	88/2503	1.02 (0.75, 1.39)
FQ vs M or β-lactams or both	18	110/3713	111/3303	0.88 (0.67, 1.16)
FQ vs β-lactams ± M	9	114/2198	191/2670	0.80 (0.61, 1.04)
Q vs M	7	37/1690	23/1268	0.99 (0.60, 1.64)
FQ vs β-lactams+M	5	NR	NR	0.99 (0.70, 1.40)
FQ vs β-lactams+FQ	2	NR	NR	1.00 (0.69, 1.45)
M vs β-lactams+FQ	3	NR	NR	1.00 (0.40, 2.46)
Atypical antibiotic coverage vs β-lactams	20	109/3219	85/2805	1.06 (0.80, 1.42)
Q vs β-lactams	15	67/2137	71/2141	0.95 (0.68, 1.31)
M vs β-lactams	3	10/273	8/267	1.22 (0.50, 2.89)
β-lactams +M vs β-lactams	2	NR	NR	1.30 (0.91, 1.85)
Solithromycin vs moxifloxacin or levofloxacin	3	11/920	14/926	0.80 (0.37, 1.74)



Effects of different antimicrobial therapy strategies on all-cause mortality.

Conclusions: We cannot evaluate which antibiotic is the best choice for the treatment of pulmonary infection. Carbapenems or adjunctive inhaled antibiotics showed a reasonable choice for HAP or VAP. However, we do not find a statistical difference between most antimicrobial therapy strategies for CAP patients.

Wu, Front Pharmacol 2021

AMBULANT ERWORB PNEUMONIE
Interaktionspotential Clarithromycin

Substrate:

Statine
Simavastatin,
Atorvastatin,
Lovastatin,
nicht Pravastatin

Benzodiazepine

Ethinylestradiol

Ciclosprin

Fentanyl

Gerinnungshemmer
Phenprocoumon,
Apixaban, Edoxaban,
Rivaroxaban

Inhibitoren:

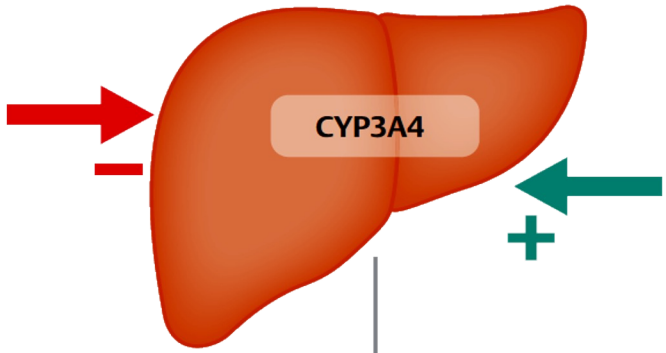
Azol-Antimykotika
Ketoconazol*

Protease-Inhibitoren
Indinavir*

Kalziumantagonisten
Verapamil, Diltiazem

Makrolidantibiotika
Clarithromycin

Grapefruitsaft



Metaboliten

Induktoren:

Antiepileptika
Carbamazepin, Phenytoin

Rifampicin

Hyperforin

Ewig, Pneumologie 2021

AMBULANT ERWORB PNEUMONIE
kombi oder mono?

Ambulant erworbene Pneumonie

Antibiotika-Kombination nicht besser als Betalaktame allein

Leitlinien empfehlen bei unkomplizierter, ambulant erworbener Lungenentzündung entweder ein Betalaktam mit bzw. ohne Makrolid oder ein Fluorchinolon. Die beiden Letzteren tragen aber in hohem Maße zu Resistenzentwicklungen bei. Nun wurde gezeigt, dass die Mortalität bei reiner Betalaktam-Monotherapie nicht ansteigt.

Betalaktame sind – jetzt erst recht – der Therapiestandard bei der ambulant erworbenen Pneumonie auf Normalstation. Alles andere sind (begründete) Einzelfallentscheidungen.

Für schwerkranke, intensivpflichtige Patienten gibt es hingegen andere Evidenz und es gelten andere Standards.

Postma, N Engl J Med 2015 – Kern, Dtsch Med Wochenschr 2015

AMBULANT ERWORB PNEUMONIE

Tägliche Evaluation der Vitalparameter

72 Stunden

- Atemfrequenz
- Bewusstseinstatus
- Blutdruck
- Herzfrequenz
- Organfunktion
- Sauerstoffsättigung
- Temperatur

Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE
Therapiedauer

- mindestens 2 Tage klinisch stabil
- <5 Tage bei rascher klinischer Stabiliserung möglich
- Sequenztherapie ab Tg4 bei klin. Stabilisierung

Pneumonieschweregrad	Protokoll	Stopp-Empfehlung	Ergebnis
leicht ambulant behandelt	PCT-Bestimmung an Tagen 1, kurzfristige Kontrolle binnen 6 – 24 h sowie 4, 6, 8	Therapieende bei Spiegeln ≤ 0,25 µg/L	mediane Verkürzung der Therapie- dauer von 7 auf 5 Tage kein Unterschied im Therapieergebnis
leicht bis mittelschwer hospitalisiert	PCT-Bestimmung an Tagen 1, kurzfristige Kontrolle binnen 6 – 24 h sowie 4, 6, 8	Therapieende bei Spiegeln ≤ 0,25 µg/L bei hohen Spiegeln Abfall ≥ 90 %	mediane Verkürzung der Therapie- dauer von 12 auf 5 Tage kein Unterschied im Therapieergebnis
schwer	PCT-Bestimmung täglich	Therapieende bei Spiegeln < 0,5 µg/L oder Spiegelabfall > 80 % des höchsten Spiegels	Verkürzung der Therapiedauer von 10,5 auf 5,5 Tage kein Unterschied im Therapieergebnis

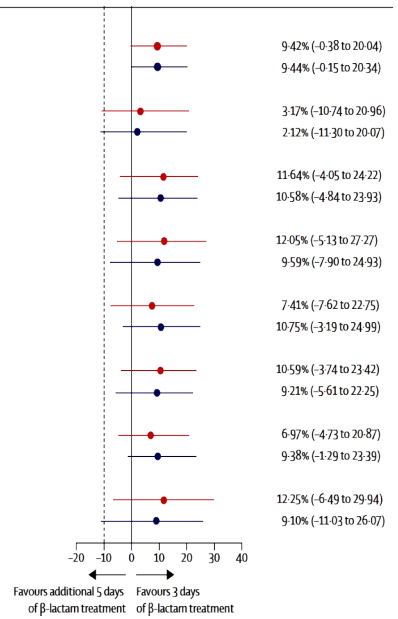
5 – 7 Tage

Christ-Crain, AJRCCM 2006 – Bouadma, Lancet 2010 – Long, Respirology 2011 –Pinzone, Scientific World J 2014 – Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE
Therapiedauer

Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial

	Placebo group	β-lactam group	Risk difference (95% CI)
	n of cure/total n (%)	n of cure/total n (%)	
All patients			
Intention-to-treat analysis	117/152 (77·0%)	102/151 (67·5%)	9·42% (-0·38 to 20·04)
Per-protocol analysis	113/145 (77·9%)	100/146 (68·5%)	9·44% (-0·15 to 20·34)
Age <65 years			
Intention-to-treat analysis	48/58 (82·8%)	39/49 (79·6%)	3·17% (-10·74 to 20·96)
Per-protocol analysis	46/53 (86·8%)	39/48 (81·2%)	2·12% (-11·30 to 20·07)
Age ≥65 years			
Intention-to-treat analysis	69/94 (73·4%)	63/102 (61·8%)	11·64% (-4·05 to 24·22)
Per-protocol analysis	67/92 (72·8%)	61/98 (62·2%)	10·58% (-4·84 to 23·93)
Age ≥75 years			
Intention-to-treat analysis	51/70 (72·9%)	45/74 (60·8%)	12·05% (-5·13 to 27·27)
Per-protocol analysis	49/69 (71·0%)	43/70 (61·4%)	9·59% (-7·90 to 24·93)
PSI score <70			
Intention-to-treat analysis	46/54 (85·2%)	42/54 (77·8%)	7·41% (-7·62 to 22·75)
Per-protocol analysis	45/50 (90·0%)	42/53 (79·2%)	10·75% (-3·19 to 24·99)
PSI score ≥70			
Intention-to-treat analysis	71/98 (72·4%)	60/97 (61·9%)	10·59% (-3·74 to 23·42)
Per-protocol analysis	68/95 (71·6%)	58/93 (62·4%)	9·21% (-5·61 to 22·25)
PSI score <91			
Intention-to-treat analysis	76/95 (80·0%)	65/89 (73·0%)	6·97% (-4·73 to 20·87)
Per-protocol analysis	74/88 (84·1%)	65/87 (74·7%)	9·38% (-1·29 to 23·39)
PSI score ≥91			
Intention-to-treat analysis	41/57 (71·9%)	37/62 (59·7%)	12·25% (-6·49 to 29·94)
Per-protocol analysis	39/57 (68·4%)	35/59 (59·3%)	9·10% (-11·03 to 26·07)



- **CAP im KH**
  - **2013 – 2018 310 Pat*innen**
  - **Alter median 73.0 Jahre**
  - **moderat schwere CAP**
  - **klinisch stabil nach 72 Std ABT**
- **Therapie**
  - **Tg1-3: Betalaktam i.v./p.o.**
  - **Tg4-8: Amoxi/Clav 3x tgl p.o.**
  - **Tg4-8: Placebo**

Dinh, Lancet 2021

AMBULANT ERWORB PNEUMONIE

Therapiedauer

ULTRA SHORT COURSE

1 TAG

CEFTRIAXON

Wunderink, BMJ 2017

AMBULANT ERWORB PNEUMONIE

Kinder & Therapiedauer

IMPORTANCE Childhood community-acquired pneumonia (CAP) is usually treated with 10 days of antibiotics. Shorter courses may be effective with fewer adverse effects and decreased potential for antibiotic resistance.

DESIGN, SETTING, AND PARTICIPANTS Randomized double-blind placebo-controlled clinical trial in outpatient clinic, urgent care, or emergency settings in 8 US cities. A total of 380 healthy children aged 6 to 71 months with nonsevere CAP demonstrating early clinical improvement were enrolled from December 2, 2016, to December 16, 2019. Data were analyzed from January to September 2020.

INTERVENTION On day 6 of their originally prescribed therapy, participants were randomized 1:1 to receive 5 days of matching placebo or 5 additional days of the same antibiotic.

RESULTS A total of 380 children (189 randomized to short course and 191 randomized to standard course) made up the study population. The mean (SD) age was 35.7 (17.2) months, and 194 participants (51%) were male. Of the included children, 8 were Asian, 99 were Black or African American, 234 were White, 32 were multiracial, and 7 were of unknown or unreported race; 33 were Hispanic or Latino, 344 were not Hispanic or Latino, and 3 were of unknown or unreported ethnicity. There were no differences between strategies in the DOOR or its individual components. Fewer than 10% of children in either strategy had an inadequate clinical response. The short-course strategy had a 69% (95% CI, 63-75) probability of a more desirable RADAR outcome compared with the standard-course strategy. A total of 171 children were included in the resistome analysis. The median (range) number of antibiotic resistance genes per prokaryotic cell (RGPC) was significantly lower in the short-course strategy compared with the standard-course strategy for total RGPC (1.17 [0.35-2.43] vs 1.33 [0.46-11.08]; $P = .01$) and β-lactamase RGPC (0.55 [0.18-1.24] vs 0.60 [0.21-2.45]; $P = .03$).

CONCLUSIONS AND RELEVANCE In this study, among children responding to initial treatment for outpatient CAP, a 5-day antibiotic strategy was superior to a 10-day strategy. The shortened approach resulted in similar clinical response and antibiotic-associated adverse effects, while reducing antibiotic exposure and resistance.

FÜNF TAGE ausreichend

Williams, JAMA Pediatrics 2022

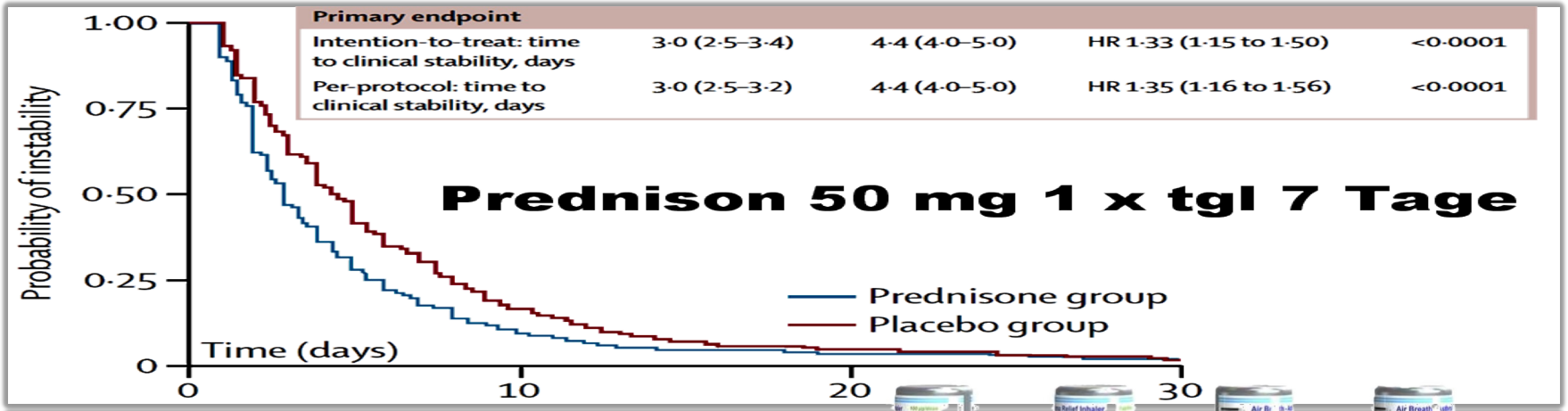
AMBULANT ERWORB PNEUMONIE
Zeichen der klinischen Stabilität

Herzfrequenz	≤ 100/min
Atemfrequenz	≤ 24/min
systolischer Blutdruck	≥ 90 mmHg
Körpertemperatur	≤ 37,8 °C
gesicherte Nahrungsaufnahme	oral oder sichere Zugänge
Bewusstseinszustand	normal bzw. Wiedererreichen des vorbestehenden Zustands bei ZNS-Erkrankungen
keine Hypoxämie	pO_2 ≥ 60 mmHg bzw. SaO_2 ≥ 90 % unter Raumluft bzw. (bei Patienten mit Sauerstoffpflichtigkeit) unter Sauerstoffgabe

Ewig, Pneumologie 2016

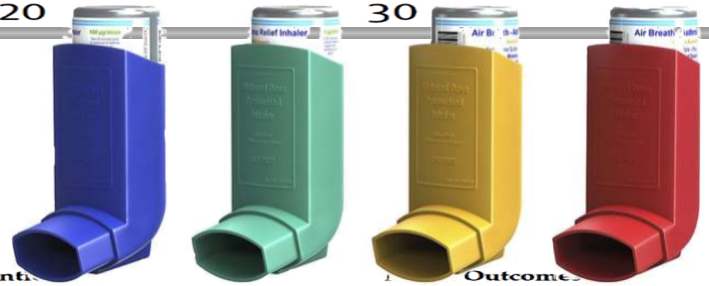
AMBULANT ERWORB PNEUMONIE
Kortison – inhalativ oder systemisch?

Primary endpoint				
Intention-to-treat: time to clinical stability, days	3·0 (2·5–3·4)	4·4 (4·0–5·0)	HR 1·33 (1·15 to 1·50)	<0·0001
Per-protocol: time to clinical stability, days	3·0 (2·5–3·2)	4·4 (4·0–5·0)	HR 1·35 (1·16 to 1·56)	<0·0001



Prednison 50 mg 1 x tgl 7 Tage

- **KEINE DATEN**
  - CAP
  - Influenza
  - MERS
  - RSV
  - SARS



Study	Population	Intervention	Outcome
Festic et al. (2017)	Patients admitted through emergency department at risk for ARDS.	Aerosolized budesonide/formoterol for 5 days.	Intervention group: lower rates of mechanical ventilation and ARDS, and shorter hospital and ICU length of stays. Oxygenation improvement was limited to the subgroup of patients with pneumonia.
Ramakrishnan et al. (2021)	Patients with mild COVID-19 within 7 days of symptoms onset.	Inhaled budesonide.	Intervention group: less need for urgent care visit, emergency department assessment or hospitalization related to COVID, and shorter time to clinical recovery by 1 day.

Blum, Lancet 2015 – Torres, JAMA 2015 – Kukhon, Med Sci 2021

AMBULANT ERWORB PNEUMONIE
Systemische Kortikosteroide

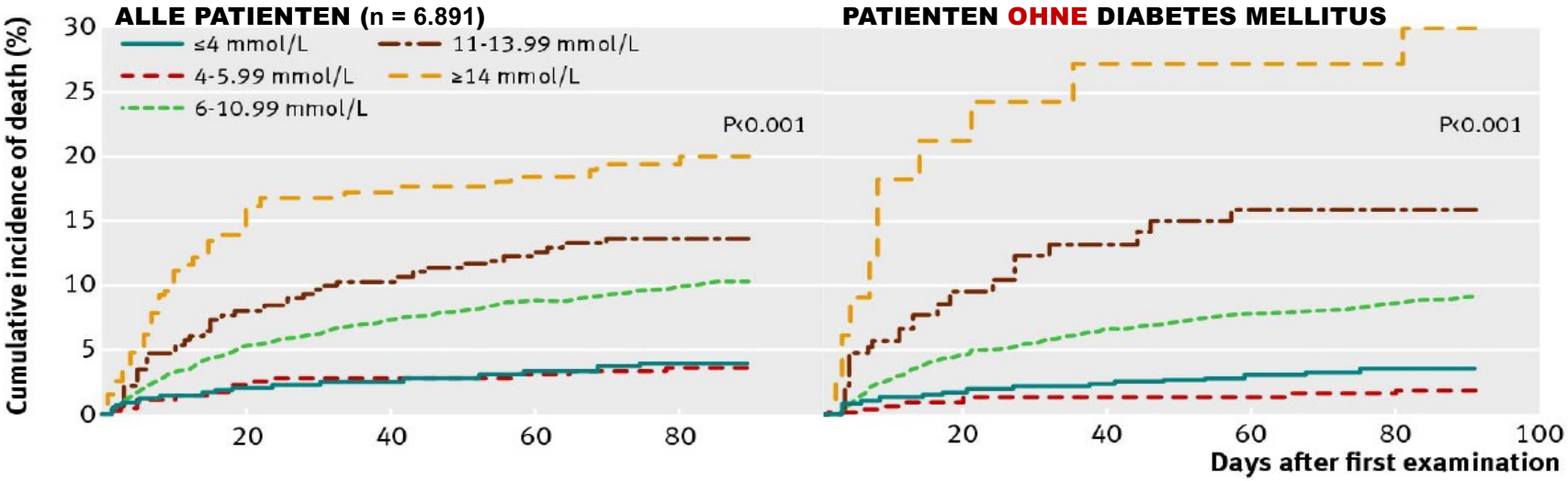
Study	Population	Intervention	Major Outcomes
Nafae et al. (2013)	Patients with CAP admitted to ICU.	Intravenous hydrocortisone for 7 days.	Intervention group: reduction in the inflammatory markers, duration of mechanical ventilation, duration of antibiotic treatment, pneumonia complications, length of hospital stay and improved oxygenation.
Blum et al. (2015)	Patients hospitalized for CAP.	Prednisone daily for 7 days.	Intervention group: shorter median time to clinical stability and higher incidence of in-hospital hyperglycemia. Pneumonia-associated complications were similar in both groups at day 30.
Torres et al. (2015)	Patients with severe CAP and CRP level >150 mg/L.	Intravenous methylprednisolone for 5 days within 36 h of hospital admission.	Intervention group: less treatment failure, which was defined as development of shock, need for invasive mechanical ventilation or death within 72 h of treatment. No difference in in-hospital mortality between both groups.
Confalonieri et al. (2005)	Patients with severe CAP admitted to ICU.	Intravenous hydrocortisone infusion for 7 days.	Intervention group: significant improvement in the oxygenation and chest radiograph score; significant reduction in CRP levels, MODS score, hospital length of stay, mortality; and delayed septic shock (by day 8 of study).
Fernández-Serrano et al. (2003)	Patients hospitalized for CAP.	Intravenous methylprednisolone for 9 days.	Intervention group: improved oxygenation, faster fever improvement and greater radiological improvement by day 7. No statistically significant difference in mortality or need for mechanical ventilation.
Meijvis et al. (2011)	Patients hospitalized for CAP.	Intravenous dexamethasone for 4 days.	Intervention group: shorter length of stay and higher incidence of hyperglycemia. No difference in in-hospital mortality or severe adverse events.
Snijders et al. (2010)	Patients hospitalized for CAP.	Oral prednisolone for 7 days.	Intervention group: faster defervescence and faster decline in CRP levels. No difference in clinical outcomes in patients with severe CAP (subgroup analysis). No difference in adverse events between both groups.
Marik et al. (1993)	Patients with severe CAP.	A single dose of IV hydrocortisone 30 min prior to starting antibiotic therapy.	No significant difference in TNF-α levels between both groups.

Kukhon, Med Sci 2021

AMBULANT ERWORB PNEUMONIE
Blutzucker & Diabetes mellitus

- **erhöhtes Mortalitätsrisiko**
  - 1.56-fach bei Bz 6.0 – 10.9 mmol/L
  - 2.37-fach bei Bz ≥ 14 mmol/L
  - 2.47-fach bei DM-Patienten unabhängig vom Aufnahme-Bz

Glukose



Leppert, BMJ 2012

AMBULANT ERWORB PNEUMONIE
Therapieversagen

Typen des Therapieversagens	Ursachen
inadäquate initiale Therapie	falsche Zuordnung innerhalb der Pneumonie-Triade Nichteinhalten von Leitlinien der Therapie bei ambulanten Patienten schlechte Therapiecompliance
erregerassoziiertes Therapieversagen	primär resistente Erreger bisher nicht erfasste Erreger persistierende Erreger erworbene Resistenz Superinfektion
Komplikationen	Empyem, Abszess metastatische Streuung nosokomiale Superinfektion
Sonderformen der Pneumonie	Aspirationspneumonie Retentionspneumonie seltene Erreger
verzögerte Abheilung durch Wirtsfaktoren, Erregerfaktoren und Schweregrad	Alter, Komorbidität, z. B. Legionellen, PSI (pneumonia severity score)
Pseudo-Therapieversagen („mimics“)	interstitielle Lungenerkrankungen Tumore Lungenstauung Embolien/Lungeninfarkte

Ewig, Pneumologie 2016

AMBULANT ERWORB PNEUMONIE
Training inspiratorischer Muskeln

A visual representation of the POWERbreatheKHP2 device that was used by patients as part of the 9-week intervention

This study demonstrates that IMT in adult patients recovering following hospitalisation with CAP is safe and tolerable. We also observed improvement in CAP-symptom scores and lung function tests as would be expected in recovery. The authors acknowledge that the efficacy of IMT methods cannot be determined by this study and the full extent to which IMT may have influenced the rate or extent of improvement in recovery due to the lack of a control group and should be considered with future research. Specifically, the use of IMT methods needs to be evaluated against the low-grade side-effects experienced by patients and the protocol adherence to determine the full extent of the benefits to patients.

Pick, Adv Respir Med 2021

AMBULANT ERWORB PNEUMONIE

Männlein oder Weiblein? ☺☹

Characteristics	Female patients ($n = 404$)	Male patients ($n = 422$)	p Value
Admitted from the ED to the ICU	22 (5)	36 (8)	.1
Admitted from the ED to the ICU by a female physician	5 (2)	15 (7)	.04
Admitted from the ED to the ICU by a male physician	17 (9)	21 (10)	.6
Patients with PSI score II–III admitted from the ED to the ICU	4 (2)	6 (3)	.4
Patients with PSI score IV–V admitted from the ED to the ICU	18 (10)	30 (13)	.4
Patients with PSI score II–III admitted from the ED to the ICU by a female physician	2 (2)	1 (1)	1.0
Patients with PSI score II–III admitted from the ED to the ICU by a male physician	2 (2)	5 (6)	.2
Patients with PSI score IV–V admitted from the ED to the ICU by a female physician	3 (3)	14 (11)	.04
Patients with PSI score IV–V admitted from the ED to the ICU by a male physician	15 (17)	16 (14)	.7

Characteristics	Female physicians' patients n (%) Median min Range min	Male physicians' patients n (%) Median min Range min	p Value
Administered IV or PO in the ED or a hospital ward	411 (100) 290 10–2715	370 (100) 270 1–3165	.07
Administered IV in the ED or a hospital ward	223 (54) 220 10–2145	208 (56) 205 1–1740	.2
Administered PO in the ED or a hospital ward	188 (46) 375 10–2715	162 (44) 400 15–3165	.3
Administered IV or PO in the ED	197 (48) 170 10–625	169 (46) 140 1–755	.02
Administered IV in the ED	153 (37) 165 10–625	126 (34) 130 1–755	.003

Results: Patients mean age was 69 years, 30-day mortality 9%. By use of the pneumonia severity index, male patients were found to be more severely ill at admission ($p = .0008$). Fewer female physicians' patients were admitted from the emergency department (ED) to the ICU when compared to male physicians' patients, 5% versus 10% ($p = .006$), and female physicians' patients received their first intravenous (IV) antibiotic dose later than male physicians' patients in the ED ($p = .003$).

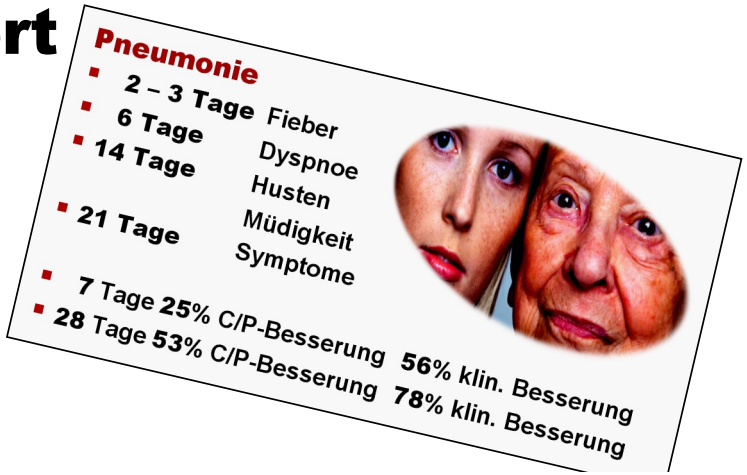
Conclusion: Our study indicates that the sex of the attending physician may affect the chosen level of care and antibiotic treatment, and that admitted male patients with CAP were more seriously ill than admitted female patients with CAP.

Dwyer, Infect Dis 2021

AMBULANT ERWORB PNEUMONIE

Mein persönliches Fazit

- **Pneumokokken** immer empirisch **erfasst** sein
- **Resistenz** bei **M pneumoniae** selten **möglich**
- H influenzae als **Pneumonieerreger** zunehmend
- **Lungenröntgen** ist **obligat**
- **Betalaktamantibiotika** sind **Mittel der Wahl**
- **Ciprofloxacin** ist **kontraindiziert**
- Ersten **72 Stunden** sind kritisch
- Therapiedauer (3) **5 – 7** Tage
- **Pneumokokkenimpfung**



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