RESPIRATOIRE PATHOGENEN BIJ ATYPISCHE PNEUMONIE : EPIDEMIOLOGIE EN DIAGNOSTIEK

Medische kring AZ Maria Middelares

“Respiratory infections : is there really something else than Covid?”

21 september 2021

Dr Sophia Steyaert

Medisch microbioloog

MARIA MIDDELARES

AZ Sint-Vincentius DEINZE

ATYPISCHE PNEUMONIE - VERWEKKERS

Viral Infections of the Lower Respiratory Tract: Old Viruses, New Viruses, and the Role of Diagnosis

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Department of Pediatrics, Division of Pediatric Infectious Diseases, University of Utah, Salt Lake City

Table 1. Lower Respiratory Tract Infections in Children and Important Etiologic Agents

Syndrome	Etiologic agents
Bronchiolitis	**RSV, hMPV, PIV, adenovirus,** coronaviruses, influenza viruses, *Chlamydophila pneumoniae, Mycoplasma pneumoniae*, rhinovirus, bocavirus,
Exacerbations of Wheezing/Asthma	**RSV, hMPV, rhinovirus,** adenovirus, PIV, coronaviruses, influenza viruses, *Chlamydophila pneumoniae, Mycoplasma pneumoniae*, bocavirus
Croup	**PIV,** Influenza, adenovirus,
Pneumonia	**Influenza, *Streptococcus pneumoniae, Mycoplasma pneumoniae*, PIV, adenovirus, RSV,** hMPV, *Streptococcus pyogenes, Staphylococcus aureus*
Pneumonitis in Transplant Recipients	**RSV, PIV, influenza, hMPV,** adenovirus, rhinovirus

NOTE. Pathogens in bold are thought to be the most common etiologies. hMPV, human metapneumovirus; PIV, parainfluenza virus 1, 2, 3; RSV, respiratory syncytial virus.

Clinical Infectious Diseases 2011;52(S4):S284–S289

Prevalence of Atypical Pathogens in Patients With Cough and Community-Acquired Pneumonia: A Meta-Analysis

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Ariella Perry Dale, MPH
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Duk Soo Han, RN
Mark H. Ebell, MD, MS
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ABSTRACT

PURPOSE Community-acquired pneumonia (CAP), acute cough, bronchitis, and lower respiratory tract infections (LRTI) are often caused by infections with viruses or *Streptococcus pneumoniae*. The prevalence of atypical pathogens *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumophila*, and *Bordetella pertussis* among patients with these illnesses in the ambulatory setting has not been previously summarized. We set out to derive prevalence information from the existing literature.

METHODS We performed a systematic review of MEDLINE for prospective, consecutive-series studies reporting the prevalence of *M pneumoniae, C pneumoniae,*

- Overall prevalences of *M pneumoniae* and *C pneumoniae* were 10.1% (95% CI, 7.1%-13.1%) and 3.5% (95% CI, 2.2%-4.9%), respectively.
- *M pneumoniae* prevalence peaked in roughly 6-year intervals.
- Overall prevalence of *L pneumophila* was 2.7% (95% CI, 2.0%-3.4%), but the organism was rare in children, with only 1 case in 1,765.

ANNALS OF FAMILY MEDICINE • WWW.ANNFAMMED.ORG • VOL. 14, NO. 6 • NOVEMBER/DECEMBER 2016

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ATYPISCHE PNEUMONIE - VERWEKKERS

Shoar and Musher *Pneumonia* (2020) 12:11
https://doi.org/10.1186/s41479-020-00074-3

Pneumonia

REVIEW Open Access

Etiology of community-acquired pneumonia in adults: a systematic review

Saeed Shoar[1] and Daniel M. Musher[1,2*]

Atypische bacterien

- Mycoplasma 4–11%
- Legionella 3–8%
- Chlamydophila 2–7%

Virussen

- Influenza viruses 6.2–13.7%
- Rhinoviruses 4.1–11.5%.
- RSV and human metapneumovirus 0.4–4.7%

Bacterial/viral coinfection 25–35%

Viral Infection in Patients with Severe Pneumonia Requiring Intensive Care Unit Admission

Sang-Ho Choi[1], Sang-Bum Hong[2], Gwang-Beom Ko[1], Yumi Lee[1], Hyun Jung Park[1], So-Youn Park[1], Song Mi Moon[1], Oh-Hyun Cho[1], Ki-Ho Park[1], Yong Pil Chong[1], Sung-Han Kim[1], Jin Won Huh[2], Heungsup Sung[3], Kyung-Hyun Do[4], Sang-Oh Lee[1], Mi-Na Kim[3], Jin-Yong Jeong[1,5], Chae-Man Lim[2], Yang Soo Kim[1], Jun Hee Woo[1], and Younsuck Koh[2]

[1]Department of Infectious Diseases, [2]Department of Pulmonary and Critical Care Medicine, [3]Department of Laboratory Medicine, [4]Department of Radiology, and [5]Asan Institute for Life Sciences, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

- Viral infection is common in adult patients with severe pneumonia (about one-third of patients)
- The mortality from viral and bacterial infection were comparable.
- Rhinovirus as cause of SARI
  - 13/17 samples (76.5%) were isolated from BAL fluid
  - 10/17 patients (58.8%) had rhinovirus as the only identified pathogen, 5/17 (29.4%) had coinfection with other viruses, and 2/17 (11.8%) had coinfection with bacteria.
  - Among the respiratory viruses, rhinovirus infection was associated with the highest mortality (52.9%, 9 of 17).
  - Majority of patients has severe underlying disease or condition (malignancy, chronic obstructive lung disease, interstitial lung disease, bone marrow transplant, solid organ transplant).

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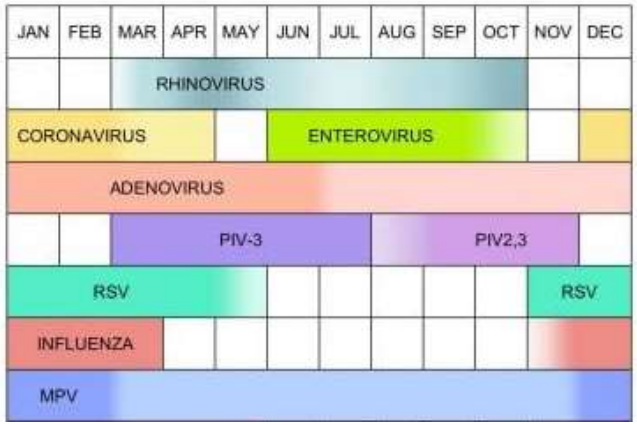
Am J Respir Crit Care Med Vol 186, Iss. 4, pp 325–332, Aug 15, 2012

SEIZOENSGEBONDEN PATRONEN

- Typisch patroon van klassieke virale respiratoire pathogenen
  - leeftijdsgebonden humaan gedrag (bijv. school, meer binnenshuis tijdens wintermaanden, …)
  - meteorologische factoren (bijv. vochtigheid, temperatuur, …)
  - klimatologische factoren (bijv. blootstelling aan zon en vitamine D level, …)



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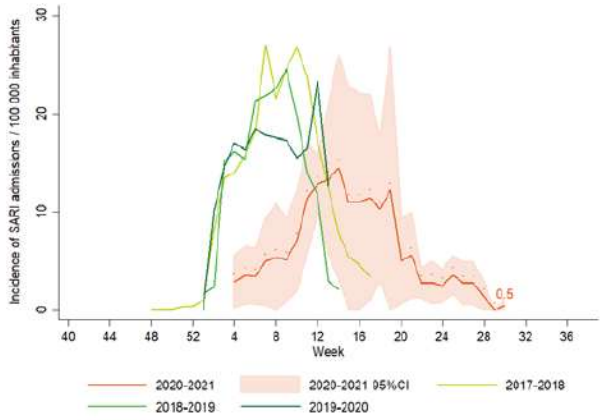
SCIENSANO

Impact of COVID-19 pandemie
Severe acute respiratory infections (SARI)

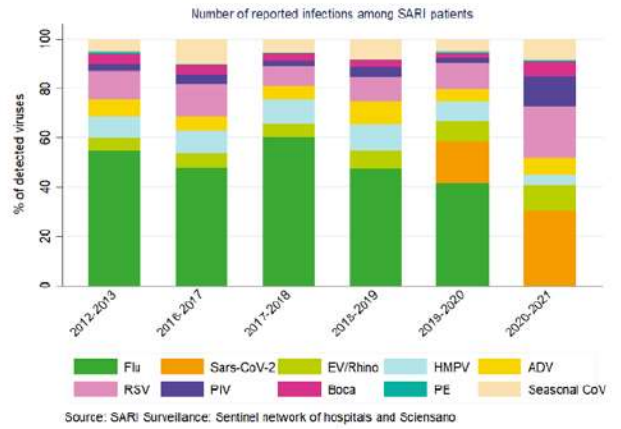
Winter 2020-2021 : Atypisch patroon

Weekrapport 30.08.2021-05.09.2021

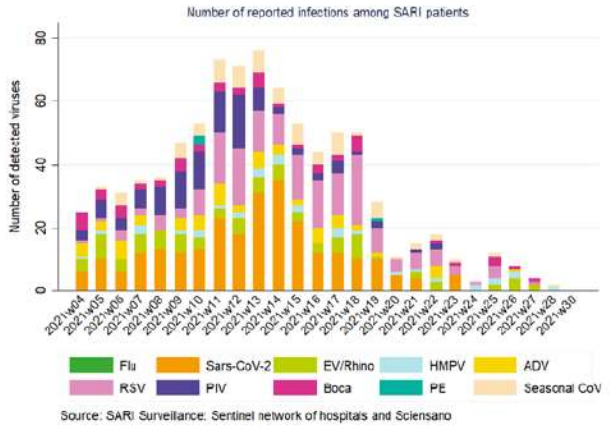
Incidence of hospital admissions for severe acute respiratory infection



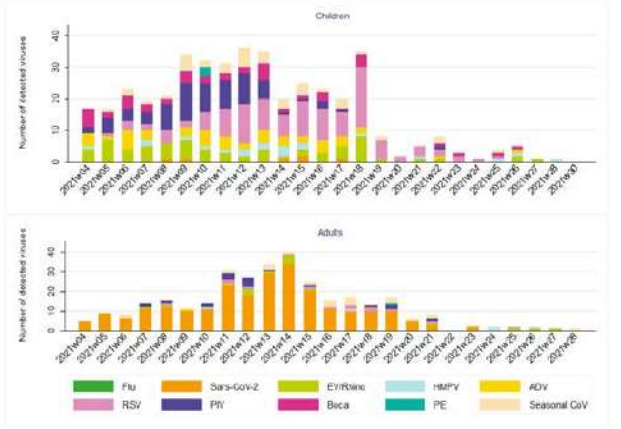
Detected respiratory viruses by season



Number of detected respiratory viruses by week



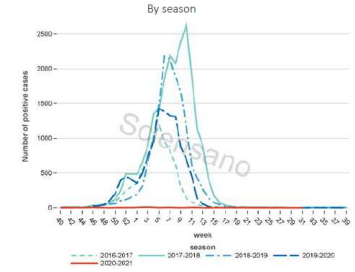
Number of detected respiratory viruses by week and age group

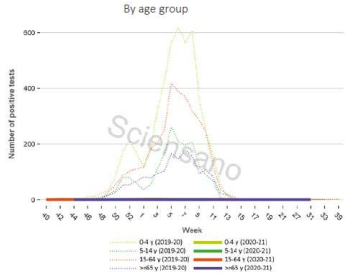


EV/Rhino = entero/rhinovirus; HMPV = Human Metapneumovirus ADV = adenovirus; RSV = Respiratory Syncytial Virus; PIV = Parainfluenzavirus; Boca = Bocavirus; PE = Paraechovirus; Seasonal CoV = Seasonal coronaviruses OC43, NL63, and 229E

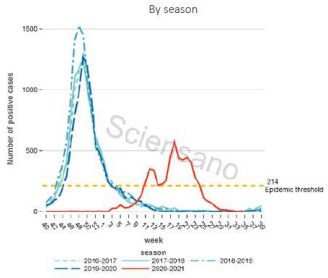
SCIENSANO

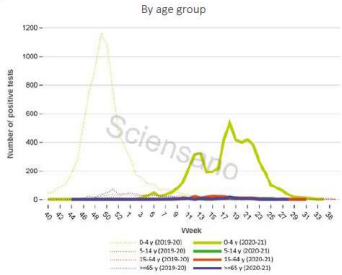
Influenza



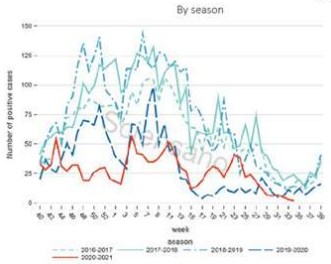


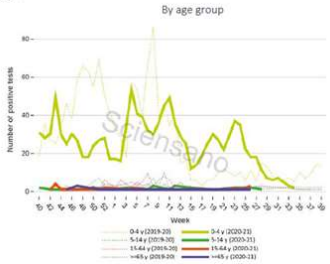
RSV



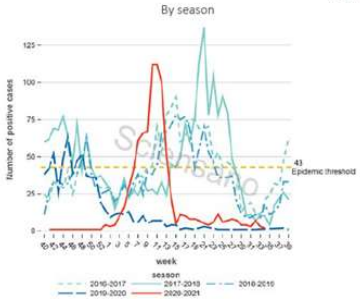


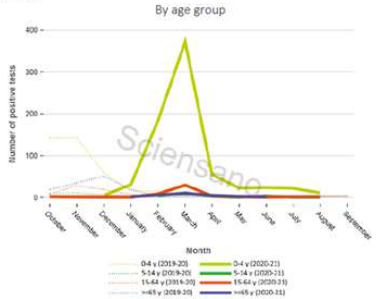
Adenovirus



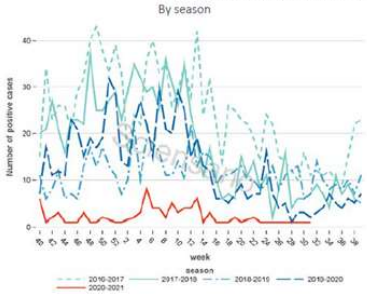


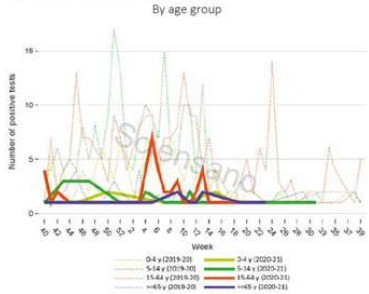
Parainfluenzavirus





Mycoplasma pneumonia (excluding results from serology)





Weekrapport 30.08.2021-05.09.2021

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COVID-19 PANDEMIE

- Atypisch patroon van klassieke respiratoire pathogenen
  - Restrictiemaatregelen
    - » Social distancing – lockdown (voorkomt persoon tot persoon transmissie)
    - » Mond neus maskers (voorkomt inhalatie) rhinovirus aerosol
    - » Handhygiene (voorkomt indirecte transmissie) rhinovirus blijft lang besmettelijk op oppervlakken
  - Andere factoren
    - » Co circulatie van respiratoire pathogenen kan beïnvloed worden door populatie dynamieken waarbij virussen en andere pathogeen in competitie zijn voor gemeenschappelijke niches
    - » Vooraf bestaande immuniteit
  - Effect op lange termijn? Surveillance !

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LABODIAGNOSTIEK

Indirecte methoden

- Serologie
  - Opsporen van antilichamen tegen verwekker
  - Gepaarde sera met minstens 10 dagen interval : seroconversie of significante toename van antilichamen in bloed

Directe methoden

- Nasopharyngeale wisser, nasopharyngeal aspiraat, sputum, BAL
  - Gramkleuring : niet bruikbaar
  - Kweek : speciale media/cellijnen (referentielaboratoria)
    - » Trage groei, lage sensitiviteit
  - Antigen testen : opsporen van antigenen (immunofluorescentie, immunochromatografie, enzyme immune assay)
  - Moleculaire methoden : opsporen van RNA/DNA (monoplex, multiplex)
  - Afname tijdens eerste dagen van ziekte (maximale virale lading)

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MYCOPLASMA PNEUMONIAE

- Vrij levende bacterie zonder celwand : niet zichtbaar op gramkleuring
- Kweken : niet geschikt voor routinediagnostiek. Enkel voor referentielaboratoria.
- Serologische test
  - Sensitiviteit : door frequent optreden van herinfecties is de IgM respons lager
  - Commerciële ELISA's : weinig specifiek

JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2002, p. 165–171 Vol. 40, No. 1
0095-1137/02/$04.00+0 DOI: 10.1128/JCM.40.1.165–171.2002
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Evaluation of Four Commercial Immunoglobulin G (IgG)- and IgM-Specific Enzyme Immunoassays for Diagnosis of *Mycoplasma pneumoniae* Infections

J. Petitjean,* A. Vabret, S. Gouarin, and F. Freymuth

Laboratory of Human and Molecular Virology, University Hospital, 14033 Caen, France

TABLE 2. Sensitivities of EIAs for detection of *M. pneumoniae* IgG and IgM antibodies in sera from 39 patients with positive *M. pneumoniae* PCR results (group I)

Patient group	No. of serum samples	Immuno-globulin	No (%) of serum samples positive by[a]:			
			EIA-Platelia	EIA-Sorin	EIA-BMD	EIA-Biotest
Children	27	IgG	15 (55)	14 (52)	18 (66)	21 (78)
		IgM	24 (89)	25 (92)	25 (92)	24 (89)
Adults	12	IgG	10 (83)	9 (75)	9 (75)	9 (75)
		IgM	2 (16)	7 (58)	2 (16)	6 (50)
Total	39	IgG	25 (64)	23 (59)	27 (69)	30 (77)
		IgM	26 (66)	32 (82)	27 (69)	30 (77)

[a] Convalescent- and/or acute-phase serum samples.

JOURNAL OF CLINICAL MICROBIOLOGY, May 2005, p. 2277–2285 Vol. 43, No. 5
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.5.2277–2285.2005
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Evaluation of 12 Commercial Tests and the Complement Fixation Test for *Mycoplasma pneumoniae*-Specific Immunoglobulin G (IgG) and IgM Antibodies, with PCR Used as the "Gold Standard"

Matthias F. C. Beersma,[1]* Kristien Dirven,[2] Alje P. van Dam,[1] Kate E. Templeton,[1] Eric C. J. Claas,[1] and Herman Goossens[1,2]

Department of Medical Microbiology, Center of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands,[1] and Department of Microbiology, University of Antwerp, Antwerp, Belgium[2]

TABLE 3. False-positive results for sera from controls previously diagnosed with infections other than *M. pneumoniae* infection

Virus or bacterium	No. of serum specimens tested	No. of serum specimens with false-positive results by the following serologic assay[a]:												
		Ani	Bio	CFT	Dia	ImC	ImW	Nov	Pla	Rid	SeC	SeM	SII	Vir
None	2		1					2				1	1	
Influenza A virus	4							4						
Influenza B virus	4	2			1	2		2				2	2	
Parainfluenza virus	6		1		1	2		4				4		
Respiratory syncytial virus	3													
Adenovirus	2	1				1	2							
Cytomegalovirus	6					2		5					1	
Ebstein-Barr virus	10	2	3	2	3	1	1	8	2		3	6	6	1
B. henselae	9					2		5				2		1
Bordetella pertussis	5							2				1	1	
Coxiella burnetii	4					3		4				2		
Chlamydia pneumoniae	4					3		2						
Legionella pneumophila	10			1	1	1		4						1
R. conorii	1													
Streptococcus pyogenes	10	3				3		3			1	3	1	
T. pallidum	6						1	4			1	4		
Total	96	8	5	3	6	20	4	49	2	0	5	25	12	3

[a] Ani, AniLabsystems; Bio, Biotest; Dia, Diagnosys; ImC, ImmunoCard; ImW, ImmunoWell; Nov, Novum; Pla, Platelia; Rid, Ridascreen; SeC, Serion classic; SeM, SeroMP; SII, SerodiaMycoII; Vir, Virotech.

MYCOPLASMA PNEUMONIAE

- Moleculaire technieken

Journal of Clinical Microbiology
Volume 58, Issue 6, 26 May 2020
https://doi.org/10.1128/JCM.00242-20

Bacteriology

Evaluation of Commercial Molecular Diagnostic Methods for Detection and Determination of Macrolide Resistance in Mycoplasma pneumoniae

Sixto M. Leal Jr.[a], Arthur H. Totten[b], Li Xiao[c], Donna M. Crabb[b], Amy Ratliff[b], Lynn B. Duffy[a], Karen B. Fowler[b], Emily Mixon[b], Jonas M. Winchell[d], Maureen H. Diaz[d], Alvaro J. Benitez[d], Bernard J. Wolff[d], Xuan Qin[e], Y.-W. Tang[f], Mark Gonzalez[g], Raj Selvarangan[h], Tao Hong[i], Edward Brooks[j], Steve Dallas[k], T. Prescott Atkinson[b], Xiaotian Zheng[l], Jennifer Dien Bard[m], and Ken B. Waites[a]

Assay	Total no. of specimens	No. of positives/ no. of true positives	Sensitivity (%)	95% confidence range (%)	No. of negatives/ no. of true negatives	Specificity (%)	95% confidence range	*P* value[b]
FilmArray RP	428	208/212	98.1	96.3–99.9	216/216	100	98.3–100	0.13
ePlex RPP	394[c]	163/195	83.6	77.6–88.5	199/199	100	98.2–100	<0.0001
NxTAG RPP	421[d]	135/209	64.6	57.7–71.1	212/212	100	98.3–100	<0.0001
InGenius MP RUO	426[e]	209/210	99.5	97.4–100	215/216	99.5	97.5–100	1.0
Mycoplasma Direct	427[f]	118/212	55.7	48.7–62.5	215/215[f]	100	98.3–100	<0.0001
Resistance Plus MP	419[g]	195/209	93.3	89.0–96.3	209/210	99.5	97.0–100	0.001

The rate of macrolide-resistant isolates (21/212; 9.9%) and the predominance of A2063G point mutations in the current study is consistent with recently published prevalence rates in the United States

The *Resistance Plus* MP detected 27/33 macrolide-resistant M. pneumoniae isolates, resulting in a sensitivity of 81.8% (95% confidence interval [CI] = 64.5 to 93.0%).

- Vereist bijzondere expertise : apparatuur, personeel
- Hoge kostprijs
- Geen RIZIV nomenclatuur

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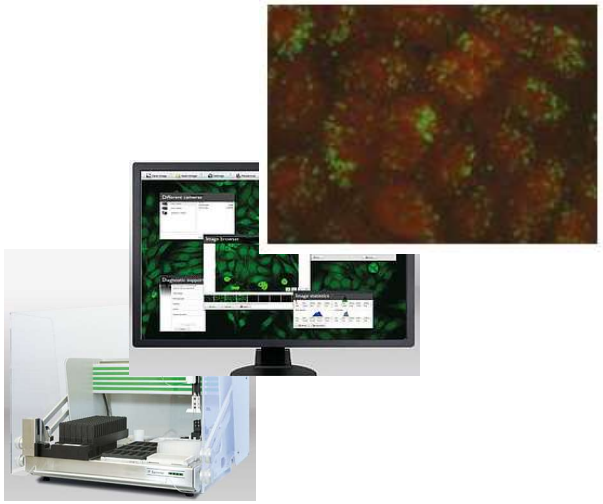
CHLAMYDIA PNEUMONIAE

- Obligaat intracellulaire bacterie : niet zichtbaar op gramkleuring
- Kweek : niet geschikt voor routinediagnostiek. Enkel voor referentielaboratoria.
- Serologie : MIF (micro immunofluorescentie)
  - Species specifieke detectie door LPS inactivatie
  - Subjectiviteit
  - Evaluatie obv titer



Standardizing *Chlamydia pneumoniae* Assays: Recommendations from the Centers for Disease Control and Prevention (USA) and the Laboratory Centre for Disease Control (Canada)

Scott F. Dowell,[1] Rosanna W. Peeling,[5] Jens Boman,[6] George M. Carlone,[1] Barry S. Fields,[1] Jeannette Guarner,[1] Margaret R. Hammerschlag,[4] Lisa A. Jackson,[2] Cho-Chou Kuo,[3] Matthias Maass,[7] Trudy O. Messmer,[1] Deborah F. Talkington,[1] Maria Lucia Tondella,[1] Sherif R. Zaki,[1] and the *C. pneumoniae* Workshop Participants[a]

[1]National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta; Departments of [2]Epidemiology and [3]Pathobiology, School of Public Health and Community Medicine, University of Washington, Seattle; [4]SUNY Health Science Center at Brooklyn, New York; [5]Laboratory Centre for Disease Control, Health Canada, Ottawa, Ontario, Canada; [6]Department of Clinical Virology, University Hospital of Umea, Umea, Sweden; and [7]Institute of Medical Microbiology and Hygiene, Medical University of Lübeck, Lübeck, Germany

Table 4. Recommendations for standardizing *Chlamydia pneumoniae* diagnostic assays.

Assay type	Major recommendations
Serological testing	Microimmunofluorescence remains the only currently acceptable approach
	Acute infection is defined by a 4-fold rise in IgG or an IgM titer of ≥16; use of a single elevated IgG titer is discouraged
	Past exposure is indicated by an IgG titer of ≥16
	Neither elevated IgA titers nor any other serologic marker are validated indicators of persisting infection

Clinical Infectious Diseases 2001;33:492–503

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CHLAMYDIA PNEUMONIAE

- Moleculaire technieken

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Syndromic Panel-Based Testing in Clinical Microbiology

Poornima Ramanan,[a] Alexandra L. Bryson,[a] Matthew J. Binnicker,[a] Bobbi S. Pritt,[a,b] Robin Patel[a,b]

[a]Division of Clinical Microbiology, Mayo Clinic, Rochester, Minnesota, USA
[b]Division of Infectious Diseases, Mayo Clinic, Rochester, Minnesota, USA

January 2018 Volume 31 Issue 1 e00024-17

TABLE 3 FDA-approved/cleared multiplex respiratory panels[a]

Parameter	FilmArray	Verigene	x-TAG RVP	x-TAG RVP Fast	NxTAG-RPP	eSensor RVP	ePlex
Analysis platform	FilmArray system or FilmArray Torch	Verigene system	Luminex 100/200	Luminex 100/200	Luminex Magpix	eSensor	ePlex system
No. of targets	20	16	12	8	20	14	17
Ability to detect pathogen							
Bacteria							
Chlamydophila pneumoniae	✓				✓		✓
Mycoplasma pneumoniae	✓				✓		✓
Bordetella pertussis	✓	✓					
Bordetella parapertussis-Bordetella bronchiseptica		✓					
Bordetella holmesii		✓					
Time to result (h)	~1	~2–3	~8	~6	~4	~6	~1.5

[a]The acceptable specimen type for all panels is a nasopharyngeal swab. RVP, respiratory virus panel; RPP, respiratory pathogen panel.

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VIROLOGY

Multicenter Evaluation of BioFire FilmArray Respiratory Panel 2 for Detection of Viruses and Bacteria in Nasopharyngeal Swab Samples

Amy L. Leber,[a] Kathy Everhart,[a] Judy A. Daly,[b] Aubrey Hopper,[b] Amanda Harrington,[c] Paul Schreckenberger,[c] Kathleen McKinley,[d] Matthew Jones,[d] Kristen Holmberg,[d] Bart Kensinger[d]

June 2018 Volume 56 Issue 6 e01945-17

TABLE 4 Performance summary and characteristics of FilmArray RP2 versus those of the comparator assays[a]

Analyte	PPA[b] TP/(TP + FN)	%	95% CI	NPA TN/(TN + FP)	%	95% CI
Chlamydia pneumoniae	5/5	100	56.6–100	1,606/1,607	99.9	99.6–100
Mycoplasma pneumoniae	23/24	95.8	79.8–99.3	1,583/1,588	99.7	99.3–99.9

- Vereist bijzondere expertise : apparatuur, personeel
- Hoge kostprijs
- Geen RIZIV nomenclatuur

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LEGIONELLA

- Antigen test : urine
  - Legionella pneumophila serogroep 1
  - Systematisch bij CAP IV
  - Kan nog gebruikt worden na start antibiotica
  - Immunochromatografische test
  - Sensitiviteit/specificiteit

- Sputum :
  - Kweek : niet geschikt voor routinediagnostiek. Enkel voor referentielaboratoria.
  - PCR : typering (op vraag van VAZG)

microorganisms MDPI

Communication

Evaluation of Four Lateral Flow Assays for the Detection of *Legionella* Urinary Antigen

Alicia Y. W. Wong [1,*], Alexander T. A. Johnsson [2], Aina Iversen [1,3], Simon Athlin [4] and Volkan Özenci [1,2,*]

Table 1. Sensitivity of four *Legionella* urine antigen assays on samples *.

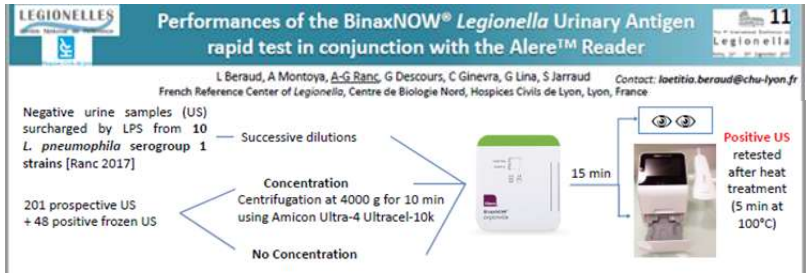
Assay	Positive Result	Negative Result	Sensitivity (95% CI)
BinaxNOW	7	0	100.0 (64.6–100.0)
ImmuView	7	0	100.0 (64.6–100.0)
STANDARD F	7	0	100.0 (64.6–100.0)
Sofia	7	0	100.0 (64.6–100.0)

* Urine samples from patients with PCR-confirmed *L. pneumophila* infection.

Table 3. Specificities of four *Legionella* urine antigen assays.

Assay	Positive Result	Negative Result	Invalid/Error	Specificity (95% CI)
BinaxNOW	3	37	0	92.5 (80.1–97.4)
ImmuView	4	36	0	90.0 (77.0–96.0)
STANDARD F	2	37	1	94.9 (83.1–99.1)
Sofia	3	37	0	92.5 (80.1–97.4)

Microorganisms **2021**, *9*, 493. https://doi.org/10.3390/microorganisms9030493



RESPIRATOIRE VIRUSSEN

- Kweken
  - Niet beschikbaar voor alle virussen. Adenovirus, influenza A/B, RSV en hPIV : meest geschikt.
  - Niet geschikt voor routinediagnostiek. Enkel voor referentielaboratoria.
  - Voorbehouden voor speciale situaties : onbekende infectieuze agentia opsporen (bijv. SARS-CoV-2)
- Antigen test
  - RSV, Influenza
  - Goedkoop, eenvoudig, resultaat binnen 15-30 min
  - Lage PPV bij lage prevalentie
  - Overall lage sensitiviteit 44-95%

Diagnostic Accuracy of Rapid Antigen Detection Tests for Respiratory Syncytial Virus Infection: Systematic Review and Meta-analysis

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TABLE 3 RSV RADT accuracy estimates from subgroup analyses[a]

Study characteristic(s) (no. of studies)	Pooled sensitivity (95% CI)	Pooled specificity (95% CI)	*P* value for the joint model[c]
Population[b]			
Children (63)	0.81 (0.78–0.84)	0.96 (0.95–0.98)	**<0.001**
Adults (4)	0.29 (0.11–0.48)	0.99(0.98–1.00)	Ref. Cat.

Journal of Clinical Microbiology December 2015 Volume 53 Number 12

MARIA MIDDELARES

RESPIRATOIRE VIRUSSEN

- Moleculaire methoden
  - LAMP, real-time PCR, …

Comparison of the ID Now Influenza A & B 2, Cobas Influenza A/B, and Xpert Xpress Flu Point-of-Care Nucleic Acid Amplification Tests for Influenza A/B Virus Detection in Children

Neena Kanwar,[a] Jeffrey Michael,[a] Kathryn Doran,[a] Emily Montgomery,[a] Rangaraj Selvarangan[a]

[a]Children's Mercy Hospital and Clinics, Kansas City, Missouri, USA

TABLE 2 Performances of the ID Now, LIAT, Xpert, and BD assays versus that of the CDC Flu A/B PCR assay

Assay	Virus target	No. with results[a]				% (95% CI) for:	
		TP	FP	TN	FN	Sensitivity	Specificity
ID Now	Flu A	68	1	127	5	93.2 (84.1–97.5)	99.2 (95.1–100.0)
	Flu B	35	2	163	1	97.2 (83.8–99.9)	98.8 (95.2–99.8)
LIAT	Flu A	73	1	127	0	100 (93.8–100)	99.2 (95.1–100.0)
	Flu B	34	4	161	2	94.4 (80.0–99.0)	97.6 (93.5–99.2)
Xpert	Flu A	73	3	125	0	100 (93.8–100)	97.7 (92.8–99.4)
	Flu B	33	3	162	3	91.7 (76.4–97.8)	98.2 (94.4–99.5)
BD[b]	Flu A	58	1	126	15	79.5 (68.1–87.7)	99.2 (95.0–99.9)
	Flu B	24	1	163	12	66.7 (48.9–80.9)	99.4 (96.1–99.9)

[a]TP, true positive; FP, false positive; TN, true negative; FN, false negative. The number of dual Flu A/B-positive results were 2 for the CDC Flu A/B PCR, 4 for the ID Now assay, 0 for the LIAT, 0 for the Xpert assay, and 0 for the BD assay.
[b]BD results were available for 200 subjects. Standard-of-care testing for one subject was PCR based.

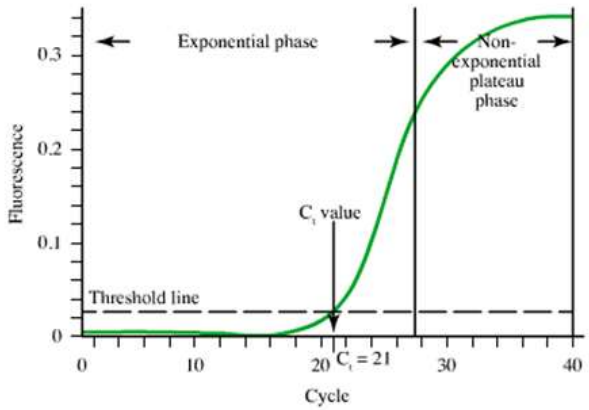
March 2020 Volume 58 Issue 3 e01611-19 Journal of Clinical Microbiology

- Snel. Sample to result. Lage capaciteit.
- Hoge kostprijs
- Geen RIZIV nomenclatuur

MARIA MIDDELARES

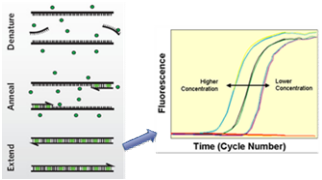
LABO DIAGNOSTIEK

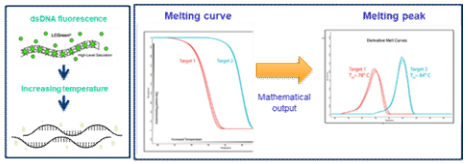
- PCR multiplex mini panel
  - Real time RT-PCR
  - Verschillende combinaties
    - » RSV, Influenza A, Influenza B, SARS-CoV-2
    - » M pneumoniae, C pneumoniae, L pneumophila
    - » …
  - Hoge(re) capaciteit



LABO DIAGNOSTIEK

- PCR multiplex maxi panel
  - Nested PCR





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Syndromic Panel-Based Testing in Clinical Microbiology

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January 2018 Volume 31 Issue 1 e00024-17

TABLE 3 FDA-approved/cleared multiplex respiratory panels[a]

Parameter	FilmArray	Verigene	x-TAG RVP	x-TAG RVP Fast	NxTAG-RPP	eSensor RVP	ePlex
Analysis platform	FilmArray system or FilmArray Torch	Verigene system	Luminex 100/200	Luminex 100/200	Luminex Magpix	eSensor	ePlex system
No. of targets	20	16	12	8	20	14	17
Ability to detect pathogen							
Viruses							
Adenovirus	✓	✓	✓	✓	✓	✓ (differentiates subgroup B/E from C)	✓
Coronavirus							✓
Coronavirus HKU1	✓				✓		
Coronavirus NL63	✓				✓		
Coronavirus 229E	✓				✓		
Coronavirus OC43	✓				✓		
Human bocavirus					✓		
Human metapneumovirus	✓	✓	✓	✓	✓	✓	✓
Influenza A virus	✓	✓	✓	✓	✓	✓	✓
Subtype H1	✓	✓	✓	✓	✓	✓	✓
Subtype H3	✓	✓	✓	✓	✓	✓	✓
Subtype 2009 H1N1	✓					✓	✓
Influenza B virus	✓	✓	✓	✓	✓	✓	✓
Parainfluenza virus 1	✓	✓	✓		✓	✓	✓
Parainfluenza virus 2	✓	✓	✓		✓	✓	✓
Parainfluenza virus 3	✓	✓	✓		✓	✓	✓
Parainfluenza virus 4	✓	✓			✓		✓
Respiratory syncytial virus	✓			✓			
Respiratory syncytial virus A		✓	✓		✓	✓	✓
Respiratory syncytial virus B		✓	✓		✓	✓	✓
Rhinovirus/enterovirus	✓	✓	✓	✓	✓	✓	✓
Bacteria							
Chlamydophila pneumoniae	✓				✓		✓
Mycoplasma pneumoniae	✓				✓		✓
Bordetella pertussis	✓	✓					
Bordetella parapertussis-Bordetella bronchiseptica		✓					
Bordetella holmesii		✓					
Time to result (h)	~1	~2–3	~8	~6	~4	~6	~1.5

[a]The acceptable specimen type for all panels is a nasopharyngeal swab. RVP, respiratory virus panel; RPP, respiratory pathogen panel.

LABO DIAGNOSTIEK

- PCR multiplex maxi panel

TABLE 4 Performance summary and characteristics of FilmArray RP2 versus those of the comparator assays[a]

	PPA[b]			NPA		
Analyte	TP/(TP + FN)	%	95% CI	TN/(TN + FP)	%	95% CI
Viruses						
Adenovirus	70/74	94.6	86.9–97.9	1,490/1,538	96.9	95.9–97.6
Coronavirus 229E	11/12	91.7	64.6–98.5	1,595/1,600	99.7	99.3–99.9
Coronavirus HKU1	43/43	100	91.8–100	1,557/1,569	99.2	98.7–99.6
Coronavirus NL63	40/40	100	91.2–100	1,562/1,572	99.4	98.8–99.7
Coronavirus OC43	33/41	80.5	66.0–89.8	1,566/1,571	99.7	99.3–99.9
Human metapneumovirus	73/75	97.3	90.8–99.3	1,529/1,537	99.5	99.0–99.7
Human rhinovirus/enterovirus	425/436	97.5	95.5–98.6	1,099/1,176	93.5	91.9–94.7
Influenza virus A	78/78	100	95.3–100	1,531/1,531	100	99.7–100
H1	0/0			1,609/1,609	100	99.8–100
H1-2009	74/74	100	95.1–100	1,535/1,535	100	99.8–100
H3	4/4	100	51.0–100	1,605/1,605	100	99.8–100
Influenza virus B	14/14	100	78.5–100	1,596/1,598	99.9	99.5–100
Middle East respiratory syndrome coronavirus (MERS-CoV)	0/0			1,612/1,612	100	99.8–100
Parainfluenza virus 1	9/9	100	70.1–100	1,602/1,603	99.9	99.6–100
Parainfluenza virus 2	46/47	97.9	88.9–99.6	1,557/1,565	99.5	99.0–99.7
Parainfluenza virus 3	43/45	95.6	85.2–98.8	1,557/1,567	99.4	98.8–99.7
Parainfluenza virus 4	9/9	100	70.1–100	1,596/1,603	99.6	99.1–99.8
Respiratory syncytial virus	175/176	99.4	96.9–99.9	1,412/1,436	98.3	97.5–98.9
Bacteria						
Bordetella parapertussis (IS*1001*)	6/7	85.7	48.7–97.4	1,605/1,605	100	99.8–100
Bordetella pertussis (*ptxP*)	2/3	66.7	20.8–93.9	1,608/1,609	99.9	99.6–100
Chlamydia pneumoniae	5/5	100	56.6–100	1,606/1,607	99.9	99.6–100
Mycoplasma pneumoniae	23/24	95.8	79.8–99.3	1,583/1,588	99.7	99.3–99.9

[a]These data are presented based on a comparator assay only and do not reflect any discordant analysis.
[b]The terms PPA (positive percent agreement) and NPA (negative percent agreement) are used instead of sensitivity and specificity to indicate that a non-gold standard comparator (e.g., PCR) was used for the analysis.

RP2.1 plus : SARS-CoV-2

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VIROLOGY

Multicenter Evaluation of BioFire FilmArray Respiratory Panel 2 for Detection of Viruses and Bacteria in Nasopharyngeal Swab Samples

Amy L. Leber,[a] Kathy Everhart,[a] Judy A. Daly,[b] Aubrey Hopper,[b] Amanda Harrington,[c] Paul Schreckenberger,[c] Kathleen McKinley,[c] Matthew Jones,[d] Kristen Holmberg,[d] Bart Kensinger[d]

June 2018 Volume 56 Issue 6 e01945-17

- Snel. Sample to result. Lage capaciteit.
- Zeer hoge kostprijs
- Geen RIZIV nomenclatuur muv SARS-CoV-2 en/of BAL bij orgaantransplanten
- Kritische indicatiestelling

MARIA MIDDELARES

CONCLUSIE

- Verwekkers atypische pneumonie
  - Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, respiratoire virussen
- Seizoensgebonden patronen verstoord door COVID-19 pandemie
  - Wat zal het nieuwe respiratoire seizoen brengen?
- Laboratoriumdiagnostiek
  - Serologie Mycoplasma pneumoniae en Chlamydia pneumoniae
    - » Niet steeds eenvoudig te interpreteren
  - Antigen testen RSV, influenza
    - » Overall lage gevoeligheid muv RSV bij kinderen
  - Moleculaire technieken monoplex of multiplex mini of maxi panel
    - » Hoge gevoeligheid en specificiteit
    - » Niet terugbetaald muv orgaantransplantpatiënten en SARS-CoV-2
    - » Kritische indicatiestelling