

**Patient outcome on influenza-  
wards during two influenza seasons  
in three hospitals in Vienna after  
PCR point of care diagnosis in the  
emergency room**

Dr. Christoph Wenisch,  
Kaiser Franz Josef Hospital, Vienna

# History: Influenza in Vienna Hospitals

.....1st diagnosis, then therapy.....

- Neglect Phase
  - is a mild, self limiting disease
- Antigen Test Phase
  - Adults (useless) versus Children
- PCR Point of Care Phase
  - Isolate, why?\_ok., but where and who should do this ?

# Management since 2017

- Flu board
- Flu wards
- SOP for influenza testing, treating and prevention



## Hygieneempfehlung Influenza (saisonal)

|           |                           |
|-----------|---------------------------|
| Datum:    | 05 10 2018                |
| Dok. Nr.: | KFJ_HYG_INFLU_SAISO2018_1 |
| Version:  | 04                        |
| Revision: | 05 11 2020                |

| Erreger                  | Übertragung       | Inkubationszeit | Postexpositionsprophylaxe                   | Dauer der Maßnahmen   |
|--------------------------|-------------------|-----------------|---|---|
| Influenza-A- und B-Virus | Tröpfchen Kontakt | 2 – 3 Tage      | Keine generelle Tamifluprophylaxe empfohlen | <ul style="list-style-type: none"> <li>• Erwachsene 7 Tage von Symptombeginn an</li> <li>• Kinder 10 Tage von Symptombeginn an</li> <li>Unter Tamiflu: 1 Tag weniger</li> </ul> |

### Barrieremaßnahmen

|   |  |
|---|--|
| <b>Wartebereiche</b>  | Bereitstellung von Mund-Nasenschutz, Händedesinfektionsmittel, Poster zur Hustenetikette, Abstand halten   |
| <b>Einzelzimmer oder Kohorte</b>  | <ul style="list-style-type: none"> <li>• Keine gemeinsame Unterbringung von Verdachts- und Erkrankungsfällen</li> <li>• Gemeinsame Unterbringung von Influenza-A- und B-Virus Erkrankten prinzipiell möglich</li> </ul>  |
| <b>Mehrbettzimmer</b>   | <ul style="list-style-type: none"> <li>• Aufnahme und/oder Transferierung an die 4. Med. Abteilung, Nachbelegung in diesem Zimmer in Abhängigkeit der epidemischen Influenzaaktivität</li> <li>• Kinder: Aufnahme an der Station 33</li> <li>• Chemoprophylaxe mit Tamiflu überdenken, ev. Rücksprache mit der 4. Med. Abteilung bzw. dem Hygieneteam</li> </ul> |
| <b>Patient, Angehörige, Besucher</b><br>Einweisen in Hustenetikette, Mund-Nasenschutz und Händedesinfektion | <ul style="list-style-type: none"> <li>• Patient trägt einen Mund-Nasenschutz solange nicht isoliert und bei Verlassen des Isolierzimmers</li> <li>• Besucheranzahl minimieren, Begrüßungsküsse vermeiden</li> <li>• Kein Besuch durch Angehörige mit grippalen Infekten</li> </ul>  |
| <b>Anlegen der persönlichen Schutzausrüstung</b>  | <ul style="list-style-type: none"> <li>• Vor Betreten des Patientenzimmers: Händedesinfektion, Mund-Nasenschutz, Einmalschürze, Einmalhandschuhe</li> <li>• Bei Kohortenunterbringung Wechsel der Schutzausrüstung und Händedesinfektion nach jedem Patienten</li> </ul>   |
| Mund-Nasenschutz und Atemschutzmasken zum einmaligen Gebrauch bestimmt                                      | Bei engem Kontakt zu unkooperativen Patienten und/oder Aerosol-generierenden Maßnahmen<br>z.B. offenes tracheales Absaugen, Intubation, Bronchoskopie, Tracheotomie: <ul style="list-style-type: none"> <li>• Atemschutzmaske FFP 3 mit Ausatemventil, Kittel (gelb), Schutzbrille bzw. Schutzschild, Einmalhandschuhe, (Haube)</li> </ul>                       |
| <b>Ablegen der persönlichen Schutzausrüstung</b>  | <ul style="list-style-type: none"> <li>• Vor Verlassen des Patientenzimmers, Händedesinfektion</li> </ul>  |
| <b>Laufende Flächendesinfektion</b>   | <ul style="list-style-type: none"> <li>• Tägliche Wischdesinfektion der patientennahen Flächen und häufig benutzter Handkontaktstellen</li> </ul>  |
| <b>Medizinprodukte, Wäsche, Geschirr</b>  | <ul style="list-style-type: none"> <li>• Standardmaßnahmen</li> </ul>  |
| <b>Schlußdesinfektion</b>   | <ul style="list-style-type: none"> <li>• Nach Aufhebung der Barrieremaßnahmen, Abwarten der Einwirkzeit von 1 Stunde vor Nachbelegung</li> </ul>   |

## 1 Definition

- Die Symptome der Influenza-artigen Erkrankung (ILI) sind unspezifisch. Bei alten Menschen (70+) verläuft die Krankheit oft oligosymptomatisch.
- Während der Grippezeit haben viele PatientInnen gleichzeitig derartige Symptome
- Um die Betten-Kapazitäten für PatientInnen mit Influenza zu steuern und nosokomiale Übertragungen zu vermeiden, muss die Diagnosestellung patientennahe mit Testsystemen (POCT) erfolgen, welche eine möglichst hohe Spezifität und Sensitivität aufweisen.
- PCR-basierte POCT-Testsysteme können mit hohem negativem und positivem prädiktiven Wert sowie patientennahe Influenza-Fälle identifizieren. Sie sind daher anderen Schnelltests überlegen.
- Die Erwartung ist, dass innerhalb von 1-2 Stunden ein Testergebnis vorliegt.

## 2 Geltungsbereich

- Alle Krankenanstalten des KAV

## 3 Ziele

- Rasche Diagnose und Therapie der Influenza im Krankenhaus
- Prävention von nosokomialer Influenza bei PatientInnen und dem medizinischen Personal
- Optimale Planung von Kapazitäten und Ressourcen

## 4 Risiken

- Während der Influenzaepidemie gleichzeitiges Eintreffen einer hohen Anzahl von PatientInnen mit grippeartigen Symptomen in der Notfallabteilung
- Belastung der Kapazität der Spitalsbetten
- Unzuverlässige Wirkung des Influenzaimpfstoffes und anderer präventiver Maßnahmen für die Verhinderung der Ansteckung des Krankenhauspersonals durch infektiöse PatientInnen
- Nosokomiale Influenza
- Lieferengpässe für POCT-Testsysteme

## 5 Influenzaverdacht bei Aufnahme

Betroffene Stationen und Zuständigkeit: Aufnahme - Grippestationen

### 5.1 Verdachtsfall

- Schwere Erkrankung (Organsysteminsuffizienzen) bei PatientInnen mit Influenzasymptomen

### 6.1 Falldefinition

- Auftreten einer ILI bei einem auf einer nicht-Grippestation wegen einer nicht ILI aufgenommenen Pat.

### 6.2 Sofortige Durchführung eines PCR-Schnelltests

- Influenza PCR Ergebnis **negativ**: Verbleib auf einer Nicht-Grippestation
- Influenza PCR Ergebnis **positiv**: Therapie mit Neuraminidasehemmer starten
- Weiteres Vorgehen nach Hygieneplan/Influenzaprozessplan der jeweiligen Krankenanstalt (Bei Hochrisiko-

patientInnen post-expositionelle Prophylaxe mit Neuraminidasehemmer überlegen)

## 7 Überprüfung der Effizienz und Effektivität

- 7.1. Messung der Dauer von Eintreffen in der Notfallabteilung bis zur Aufnahme auf Grippestation
- 7.2 Einsatz des PCR-Schnelltests für ambulante und stationäre Fälle (inkl. Erfassung des Aufnahmegrunds)

## 8 Hinweise

- Die Durchführung der Influenza-PCR bei PatientInnen ohne Aufnahmegrund ist meistens nicht indiziert, da die Behandlung der Erkrankung durch die Verfügbarkeit des Testergebnisses nicht verändert wird.
- Die Spitalspflichtigkeit ergibt sich durch das akute klinische Zustandsbild und nicht durch ein Influenza-PCR-Ergebnis. Letzteres entscheidet nur über den Behandlungsort innerhalb des Krankenhauses.
- Die Wiederholung einer positiven PCR ist medizinisch nicht gerechtfertigt.
- Nur im Einzelfall ist eine Testung von ambulanten PatientInnen, die nicht stationär aufgenommen werden müssen (z.B. Schwangerschaft, Immunsuppression, u.ä.), zulässig.
- Ambulante PatientInnen mit Influenza-Verdacht, die keiner Aufnahme bedürfen und auch keiner Risikogruppe angehören, können in Epidemie-Zeiten ohne Testung mit einem Neuraminidasehemmer Rezept versorgt werden.

# These studies

- analyse the effect of the PCR based flu management on
- Flu wards
  - patients and staff
  - Year 1 (2018): one hospital (780 beds)
  - Year 2 (2019): three hospitals (2938 beds)

# Admitted Patients Season 2018

- N=398
- LOS: 7d
- 74 transferred from other wards, 42 where admitted longer than 72h (nosocomial?)
- In-hospital mortality 22 (5,1%)



|   | Total<br>(N=396) | Influenza A<br>(n=96) | Influenza B<br>(n=300) | p-value |
|---|------------------|-----------------------|------------------------|---------|
| <b>Sex</b>  |                  |                       |                        | 0.578   |
| <b>Female</b>                                       | 213 (53.8%)      | 54 (56.3%)            | 151 (53%)              |         |
| <b>Male</b>   | 183 (46.2%)      | 42 (43.8%)            | 141 (47%)              |         |
| <b>Vaccination status</b>                           |                  |                       |                        |         |
| <b>Unknown</b>                                      | 192 (48.5%)      |                       |                        |         |
| <b>Known</b>  | 204 (51.5%)      |                       |                        |         |
| <b>Not vaccinated+</b>                              | 164/204 (80.4%)  | 40 (81.6%)            | 124 (80%)              | 0.802+  |
| <b>Vaccinated+</b>                                  | 40/204 (19.6%)   | 9 (18.4%)             | 31 (20.3%)             |         |
| <b>Age median<br/>(IQR) in years</b>                | 75.5<br>(63-84)  | 67.5<br>(54-79)       | 77<br>(67-85)          | <0.001  |
| <b>History of</b>                                   |                  |                       |                        |         |
| <b>CHF</b>  | 37 (9.3%)        | 7 (7.3%)              | 30 (10%)               | 0.427   |
| <b>Atrial fibrillation</b>                          | 67 (16.9%)       | 10 (10.4%)            | 57 (19%)               | 0.051   |
| <b>Myocardial infarction</b>                        | 47 (11.9%)       | 6 (6.3%)              | 41 (13.7%)             | 0.051   |
| <b>Chronic pulmonary disease<br/>(COPD, Asthma)</b> | 117 (29.5%)      | 38 (39.6%)            | 79 (26.3%)             | 0.013   |
| <b>Currently smoking°</b>                           | 73 (18.4%)       | 26 (27.7%)            | 47 (16.8%)             | 0.021   |
| <b>pAVD</b>   | 26 (6.6%)        | 2 (2.2%)              | 24 (8%)                | 0.055*  |
| <b>Diabetes</b>                                     | 104 (26.3%)      | 24 (25%)              | 80 (26.8%)             | 0.734   |
| <b>CKD</b>  | 122 (30.8%)      | 18 (18.8%)            | 111 (37%)              | <0.001  |
| <b>Stroke</b>                                       | 45 (11.4%)       | 7 (7.3%)              | 38 (12.7%)             | 0.147   |
| <b>Dementia</b>                                     | 49 (12.4%)       | 9 (9.4%)              | 40 (13.3%)             | 0.305   |
| <b>Any tumor</b>                                    | 69 (17.4%)       | 18 (18.8%)            | 51 (17%)               | 0.694   |

|   | <b>Total<br/>(N=396)</b> | <b>Influenza A<br/>(n=96)</b> | <b>Influenza B<br/>(n=300)</b> | <b>p-value</b> |
|---|--------------------------|-------------------------------|--------------------------------|----------------|
| <b>Fever (<math>\geq 38^{\circ}\text{C}</math>) #</b> | 271 (69.2%)              | 71 (75.5%)                    | 200 (67.3%)                    | 0.133          |
| <b>Temperature (<math>^{\circ}\text{C}</math>)</b>    |                          | 38.6                          | 38.3                           | 0.004          |
| <b>Md (IQR)</b>                                       |                          | (37.98-39.3)                  | (37.6-39.0)                    |                |
| <b>Cough</b>  | 258 (65.2%)              | 67 (69.8%)                    | 191 (63.7%)                    | 0.273          |
| <b>Malaise/prostration</b>                            | 243 (61.4%)              | 57 (59.4%)                    | 186 (62%)                      | 0.646          |
| <b>Rales</b>  | 147 (37.1%)              | 43 (44.8%)                    | 104 (37.4%)                    | 0.074          |
| <b>Dyspnoea</b>                                       | 124 (31.3%)              | 40 (41.7%)                    | 84 (28%)                       | 0.012          |
| <b>Vomiting</b>                                       | 76 (19.2%)               | 11 (11.5%)                    | 65 (21.7%)                     | 0.027          |
| <b>Abrupt onset (&lt;12 hours)</b>                    | 67 (16.9%)               | 15 (15.2%)                    | 52 (17.3%)                     | 0.698          |
| <b>Muscle ache</b>                                    | 64 (16.2%)               | 17 (17.7%)                    | 47 (15.7%)                     | 0.636          |
| <b>Diarrhoea</b>                                      | 60 (15.2%)               | 16 (16.7%)                    | 44 (14.7%)                     | 0.634          |
| <b>Cognitive impairment</b>                           | 48 (12.1%)               | 8 (8.3%)                      | 40 (13.3%)                     | 0.191          |
| <b>Headache</b>                                       | 43 (10.9%)               | 15 (15.6%)                    | 28 (9.3%)                      | 0.085          |
| <b>Thoracic pain</b>                                  | 38 (9.6%)                | 10 (10.4%)                    | 28 (9.3%)                      | 0.754          |
| <b>Coryza</b>   | 36 (9.1%)                | 5 (5.2%)                      | 31 (10.3%)                     | 0.155*         |
| <b>Incontinence</b>                                   | 34 (8.6%)                | 7 (7.3%)                      | 27 (9%)                        | 0.631          |
| <b>Epigastric pain</b>                                | 31 (7.8%)                | 5 (5.2%)                      | 26 (8.7%)                      | 0.272*         |
| <b>Chills</b>   | 30 (7.6%)                | 4 (4.2%)                      | 26 (8.7%)                      | 0.147          |
| <b>Sore throat</b>                                    | 20 (5.1%)                | 7 (7.3%)                      | 13 (4.3%)                      | 0.247          |

|  | <b>Total<br/>(N=396)</b> | <b>Influenza A<br/>(n=96)</b> | <b>Influenza B<br/>(n=300)</b> | <b>p-value</b> |
|--|--------------------------|-------------------------------|--------------------------------|----------------|
| <b>ICU admission</b>   | 19 (4.8%)                | 6 (6.3%)                      | 14 (4.3%)                      | 0.444          |
| <b>Respiratory failure</b>   | 77 (19.4%)               | 22 (22.9%)                    | 55 (18.3%)                     | 0.323          |
| <b>Pneumonia</b>   | 95 (24%)                 | 23 (24%)                      | 72 (24%)                       | 0.993          |
| <b>Acute heart failure</b>   | 15 (3.8%)                | 4 (4.2%)                      | 11 (3.7)                       | 0.765*         |
| <b>Rhabdomyolysis</b>  | 31 (7.8%)                | 7 (7.5%)                      | 24 (8.1%)                      | 0.870          |
| <b>Acute kidney injury</b>   | 48 (12.1%)               | 7 (7.3%)                      | 41 (13.8%)                     | 0.092          |
| <b>Myocardial infarction</b>   | 4 (1%)                   | 1 (1%)                        | 3 (1%)                         | 1.000*         |
|  |                          |                               |                                |                |
| <b>Duration of hospitalisation<br/>on the ID ward (in days)<br/>Md (IQR)</b> | 7 (5-9)                  | 8 (6-9)                       | 7 (5-8)                        | 0.023#         |

|                                   | <b>Total</b>   | <b>Influenza A</b> | <b>Influenza B</b> | <b>p-value</b> |
|-----------------------------------|----------------|--------------------|--------------------|----------------|
| <b>In hospital mortality</b>      | 22/396 (5.1%)  | 8 (8.3%)           | 14 (4.7%)          | 0.172          |
| <b>30-day mortality</b>           |                |                    |                    |                |
| <b>From all patients</b>          | 26/396 (6.6%)  |                    |                    |                |
| <b>From all patients followed</b> | 26/252 (10.2%) | 9 (14.3%)          | 17 (9%)            | 0.232          |
| <b>90-day mortality</b>           |                |                    |                    |                |
| <b>From all patients</b>          | 32/396 (8.1%)  |                    |                    |                |
| <b>From all patients followed</b> | 32/222 (14.4%) | 10 (17.5%)         | 22 (13.3%)         | 0.435          |

# Patients

- 300 Influenza B, 96 Influenza A
- Subtypes: 80 „B“, 14 H1N1, 3 H3N2
- Austria B (Yamagata) dominant, H1N1 <sup>[1]</sup>
- A: younger (67,5 vs. 77, total 75,5)  
— [2, 3, 4, 5]
- A: more „chronic pulmonary disease“ 39,6%  
vs. 26,3% <sup>[3, 6]</sup>
- B: more CNI (18,8% vs. 37%)

# Symptoms

- fever 69,2%, cough 65,2%, tired and weak 61,4%
- abrupt onset 16,9%, vomiting 19,2%
- A versus B
  - Temperature: A: 38,6°C vs. B: 38,3°C,
  - Dyspnoe A versus B = 41,7% vs. 28% <sup>[7]</sup>
  - Vomitus A versus B (11,5% vs 21,7%) <sup>[7]</sup>

# Laboratory Values

- Leukos A versus B (8 G/L vs. 6,8 G/L)
- CRP A versus B (41,1 mg/L vs. 22,95 mg/L)

# Complications and outcome

- LOS:
  - A versus B = 8 vs. 7d
  - Tamiflu 1d longer
- A versus B: no difference in complication rates
- Often:
  - Pneumonia (24%) [4, 5, 10]
  - Less in comparison with literature (emergency department 32-38% [5], admitted pat. 43% [8], very old population 67,5% [9])
  - ARF 12,1% (7,3% vs. 13,8%)
- Mortality
  - In-Hospital 22 (5,1%), A: 8 (8,3%) vs. B 14 (4,7%),  $p=0,172$  [6, 8]
  - 90-day: 32/222 (14,4%), A 10 (17,5%) vs. B 22 (13,3%)
- m/w, vaccination status, oseltamivir: no difference



Logistic Regression:

Elevated „in-hospital-mortality“ for:

- age
- atrial fibrillation
- dementia
- Increased leukocytes
- Pneumonia
- Heart failure

Elevated 90-day mortality for :

- Age
- atrial fibrillation
- Increased leukocytes
- Heart failure

Statins: reduced mortality

Oseltamivir and/or vaccination:  
no difference

CAVEAT: small numbers

|                           | dead<br>(n=22) | survived<br>(n=374) | p-value |
|---------------------------|----------------|---------------------|---------|
| Dyspnoea                  | 12 (54.5%)     | 112 (29.9%)         | 0.016   |
| Rales                     | 13 (59.1%)     | 134 (35.8%)         | 0.016   |
| Dementia                  | 9 (49.9%)      | 40 (10.7%)          | <0.001  |
| Atrial fibrillation       | 11 (50%)       | 56 (15%)            | <0.001  |
| Congestive heart failure  | 6 (27.3%)      | 31 (8.3)            | 0.003   |
| Age in years              | 84             | 75                  | <0.001# |
| Md (IQR)                  | (77-92)        | 62-83               |         |
| Leucocyte count in G/L    | 9.4            | 7.1                 | 0.02#   |
| Md (IQR)                  | (6.4-15.3)     | (5.1-9.4)           |         |
| CRP in mg/dl              | 54             | 24.5                | 0.004#  |
| Md (IQR)                  | (30.3-101.3)   | (10.6-58.1)         |         |
| LDH in U/L                | 283            | 232                 | 0.038#  |
|                           | (231-339)      | (200-289)           |         |
| Pneumonia                 | 12 (54.5%)     | 83 (22.2%)          | <0.001  |
| Respiratory insufficiency | 10 (45.5%)     | 67 (17.9%)          | 0.002   |
| Acute heart failure       | 4 (18.2%)      | 11 (2.9%)           | 0.007*  |
| Statin                    | 2 (9.1%)       | 113 (30.2%)         | 0.0497* |

|  | <b>dead<br/>(n=22)</b> | <b>survived<br/>(n=374)</b> | <b>p-value°</b> | <b>OR (95% CI)<br/>stepwise regression</b> |
|--|------------------------|-----------------------------|-----------------|--|
| <b>Dyspnoea</b>                                | 12 (54.5%)             | 112 (29.9%)                 | 0.016           |  |
| <b>Rales</b>                                   | 13 (59.1%)             | 134 (35.8%)                 | 0.028           |  |
| <b>Dementia</b>                                | 9 (40.9%)              | 40 (10.7%)                  | <0.001          | 3.98 (1.24-12.78)                          |
| <b>Atrial fibrillation</b>                     | 11 (50%)               | 56 (15%)                    | <0.001          | 5.91 (1.91-18.34)                          |
| <b>Congestive heart failure</b>                | 6 (27.3%)              | 31 (8.3)                    | 0.003           |  |
| <b>Age in years<br/>Md (IQR)</b>               | 84<br>(77-92)          | 75<br>(62-83)               | <0.001#         | 1.1 (1.03-1.17)                            |
| <b>Leucocyte count in<br/>G/L<br/>Md (IQR)</b> | 9.4<br>(6.4-15.3)      | 7.1<br>(5.1-9.4)            | 0.02#           | 1.11 (1.03-1.20)                           |
| <b>CRP in mg/dl<br/>Md (IQR)</b>               | 54<br>(30.3-101.3)     | 24.5<br>(10.6-58.1)         | 0.004#          |  |
| <b>LDH in U/L</b>                              | 283<br>(231-339)       | 232<br>(200-289)            | 0.038#          |  |
| <b>Pneumonia</b>                               | 12 (54.5%)             | 83 (22.2%)                  | <0.001          | 4.39 (1.44-13.39)                          |
| <b>Respiratory insufficiency</b>               | 10 (45.5%)             | 67 (17.9%)                  | 0.002           |  |
| <b>Acute heart failure</b>                     | 4 (18.2%)              | 11 (2.9%)                   | 0.007*          | 23.15 (4.33-123.76)                        |
| <b>Statin</b>                                  | 2 (9.1%)               | 113 (30.2%)                 | 0.0497*         |  |

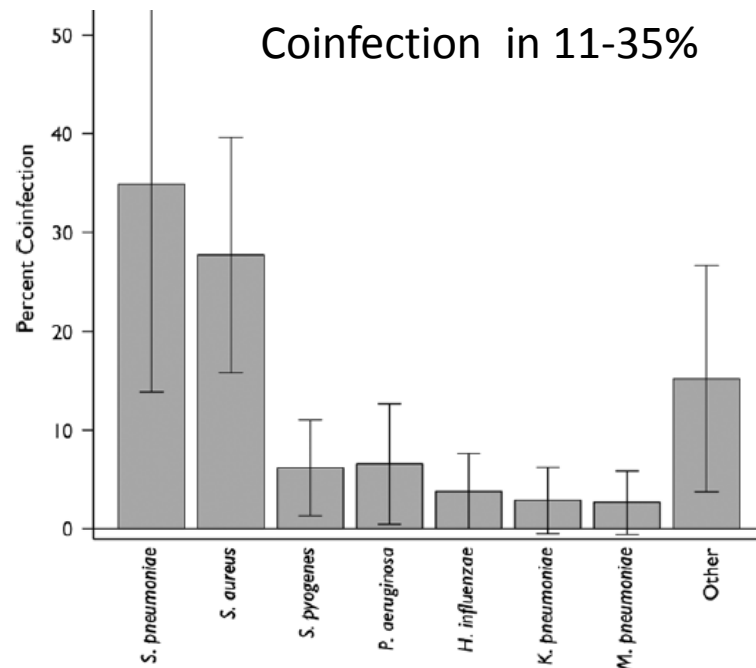
# The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis

Eili Y. Klein,<sup>a,b</sup> Bradley Monteforte,<sup>c</sup> Alisha Gupta,<sup>d</sup> Wendi Jiang,<sup>b</sup> Larissa May,<sup>e</sup> Yu-Hsiang Hsieh,<sup>a</sup> Andrea Dugas<sup>a</sup>

<sup>a</sup>Department of Emergency Medicine, Johns Hopkins University, Baltimore, MD, USA. <sup>b</sup>Center for Disease Dynamics, Economics & Policy, Washington, DC, USA. <sup>c</sup>Eastern Virginia Medical School, Norfolk, VA, USA. <sup>d</sup>Allegheny General Hospital, Pittsburgh, PA, USA. <sup>e</sup>Department of Emergency Medicine, The George Washington University, Washington, DC, USA.

*Correspondence:* Eili Y. Klein, Department of Emergency Medicine, Johns Hopkins University, 5801 Smith Ave, Suite 3220, Office 265, Davis Building, Baltimore, MD 21209, USA. E-mail: eklein@jhu.edu

Accepted 14 May 2016.






nature > nature immunology > articles > article


MENU ▾

nature  
immunology

Article | Published: 29 October 2018

## Inflammation induced by influenza virus impairs human innate immune control of pneumococcus

Simon P. Jochems , Fernando Marcon, Beatriz F. Carniel, Mark Holloway, Elena Mitsi, Emma Smith, Jenna F. Gritzfeld, Carla Solórzano, Jesús Reiné, Sherin Pojar, Elissavet Nikolaou, Esther L. German, Angie Hyder-Wright, Helen Hill, Caz Hales, Wouter A. A. de Steenhuijsen Piters, Debby Bogaert, Hugh Adler, Seher Zaidi, Victoria Connor, Stephen B. Gordon, Jamie Rylance, Helder I. Nakaya  & Daniela M. Ferreira 

Nature Immunology (2018) | Download Citation 

ARTICLES | [VOLUME 6, ISSUE 10, P782-792, OCTOBER 01, 2018](#)



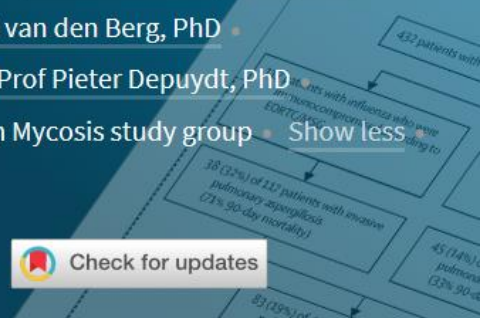
Purchase Su

## Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study

[Alexander F A D Schauwvlieghe, MD](#) <sup>†</sup> • [Bart J A Rijnders, PhD](#) <sup>†</sup> <sup>†</sup> • [Nele Philips, MSc](#) • [Rosanne Verwijs, MSc](#) •  
[Lore Vanderbeke, MD](#) • [Carla Van Tienen, PhD](#) • [Prof Katrien Lagrou](#) • [Prof Paul E Verweij, PhD](#) •  
[Frank L Van de Veerdonk, PhD](#) • [Prof Diederik Gommers, PhD](#) • [Peter Spronk, PhD](#) • [Dennis C J J Bergmans, PhD](#) •  
[Astrid Hoedemaekers, PhD](#) • [Eleni-Rosalina Andrinopoulou, PhD](#) • [Charlotte H S B van den Berg, PhD](#) •  
[Prof Nicole P Juffermans, PhD](#) • [Casper J Hodiamont, PhD](#) • [Alieke G Vonk, PhD](#) • [Prof Pieter Depuydt, PhD](#) •  
[Prof Jerina Boelens, PhD](#) • [Prof Joost Wauters, PhD](#) on behalf of the Dutch-Belgian Mycosis study group • [Show less](#)

[Show footnotes](#)

Published: July 31, 2018 • DOI: [https://doi.org/10.1016/S2213-2600\(18\)30274-1](https://doi.org/10.1016/S2213-2600(18)30274-1) •



## Methods

- We did a retrospective multicentre cohort study. Data were collected from adult patients with severe influenza admitted to **seven ICUs across Belgium and The Netherlands during seven influenza seasons**. Patients were older than 18 years, were admitted to the ICU for more than 24 h with acute respiratory failure, had pulmonary infiltrates on imaging, and a confirmed influenza infection based on a positive airway PCR test (influenza cohort).

## Findings

- Data were collected from patients admitted to the ICU between Jan 1, 2009, and June 30, 2016. **Invasive pulmonary aspergillosis was diagnosed in 83 (19%) of 432 patients admitted with influenza** (influenza cohort), a median of 3 days after admission to the ICU. The incidence was similar for influenza A and B. **For patients with influenza who were immunocompromised, incidence of invasive pulmonary aspergillosis was as high as 32% (38 of 117 patients)**, whereas in the non-immunocompromised influenza case group, incidence was 14% (45 of 315 patients). Conversely, only 16 (5%) of 315 patients in the control group developed invasive pulmonary aspergillosis. **The 90-day mortality was 51% in patients in the influenza cohort with invasive pulmonary aspergillosis and 28% in the influenza cohort without invasive pulmonary aspergillosis (p=0.0001).**

In this study, influenza was found to be independently associated with invasive pulmonary aspergillosis (**AOR 5.19**; 95% CI 2.63–10.26;  $p < 0.0001$ ), along with a higher APACHE II score, male sex, and use of corticosteroids.

## Interpretation

- Influenza was identified as an independent risk factor for invasive pulmonary aspergillosis and is associated with high mortality.** Future studies should assess whether a faster diagnosis or antifungal prophylaxis could improve the outcome of influenza-associated aspergillosis.



## REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

## Acute Infection and Myocardial Infarction

Daniel M. Musher, M.D., Michael S. Abers, M.D.,  
and Vicente F. Corrales-Medina, M.D.

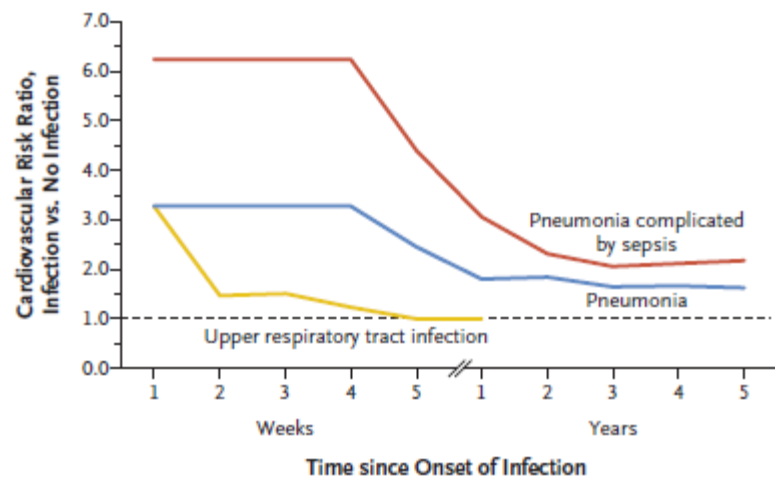
UNTIL THE EARLY 20TH CENTURY, THE HUMAN LIFE EXPECTANCY WAS less than 50 years, and infections were often fatal. Only in the past century have humans, on average, lived long enough for cardiovascular disease to develop regularly and have antimicrobial therapies made survival from infection the norm. Furthermore, sophisticated techniques for assessing myocardial damage have evolved during the past 50 years. It is therefore not surprising that an association between acute infections and myocardial infarction has been appreciated only in the past few decades. We will review the evidence that acute bacterial and viral infections are associated with an increased risk of myocardial infarction in the short, intermediate, and long term, and we will then discuss mechanisms that might explain this association.

From the Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston (D.M.M.); National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD (M.S.A.); and the Ottawa Hospital Research Institute and University of Ottawa, Ottawa (V.F.C.-M.). Address reprint requests to Dr. Musher at Infectious Disease Section, Rm. 4B-370, Veterans Affairs Medical Center, 2002 Holcombe Blvd., Houston, TX 77030, or at [daniel.musher@va.gov](mailto:daniel.musher@va.gov).

N Engl J Med 2019;380:171-6.

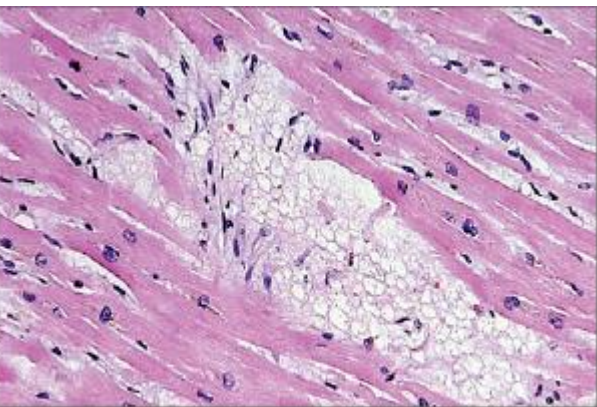
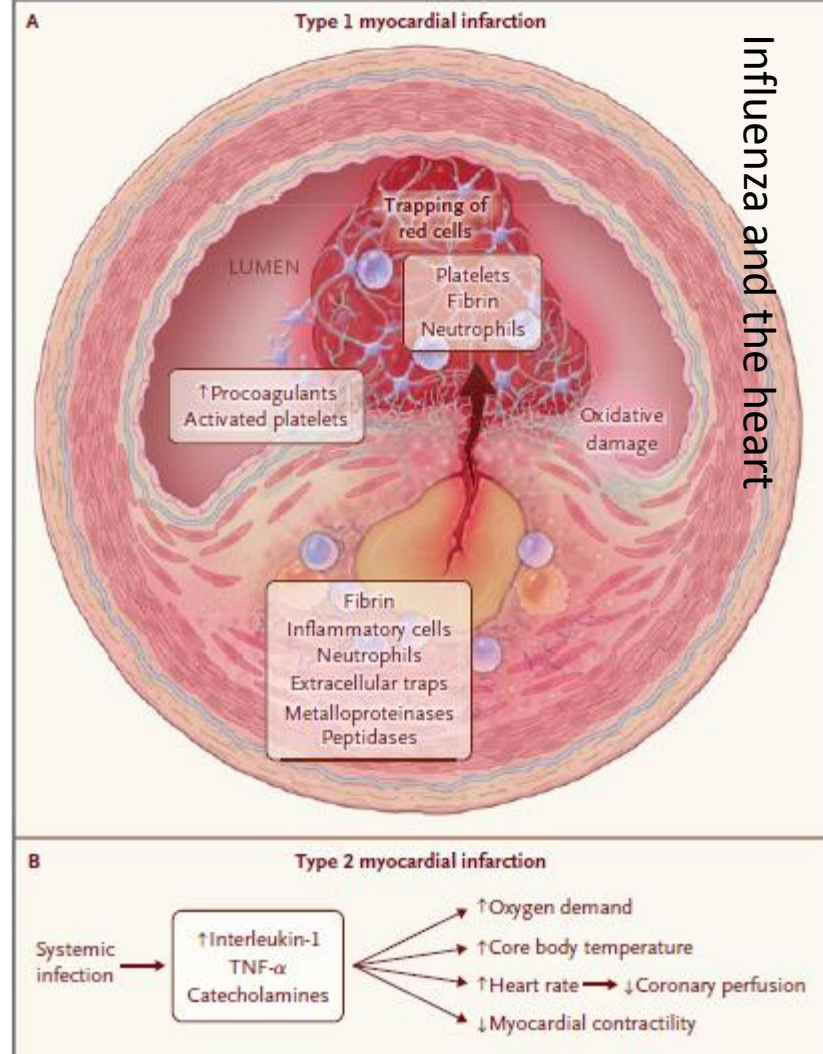
DOI: 10.1056/NEJMr1808137

Copyright © 2019 Massachusetts Medical Society.



**Figure 1. Temporal Pattern of Cardiovascular Risk after the Onset of Acute Infection.**

The risk of a cardiovascular event is several times higher after the onset of respiratory infection than in the absence of infection. The risk of a cardiovascular event is proportional to the severity of the infection. The risk returns to baseline over a period of weeks after an upper respiratory tract infection. However, the time required for the risk to return to baseline is prolonged after a severe infection, such as pneumonia. Data are pooled from Smeeth et al.,<sup>2</sup> Kwong et al.,<sup>5</sup> Corrales-Medina et al.,<sup>12</sup> Warren-Gash et al.,<sup>14</sup> and Warren-Gash et al.<sup>15</sup>



**Figure 4. Features Present after Cardiac Involvement in Acute Infection.**

- Influenza = 6x increased risk for myocardial infarction

ORIGINAL ARTICLE

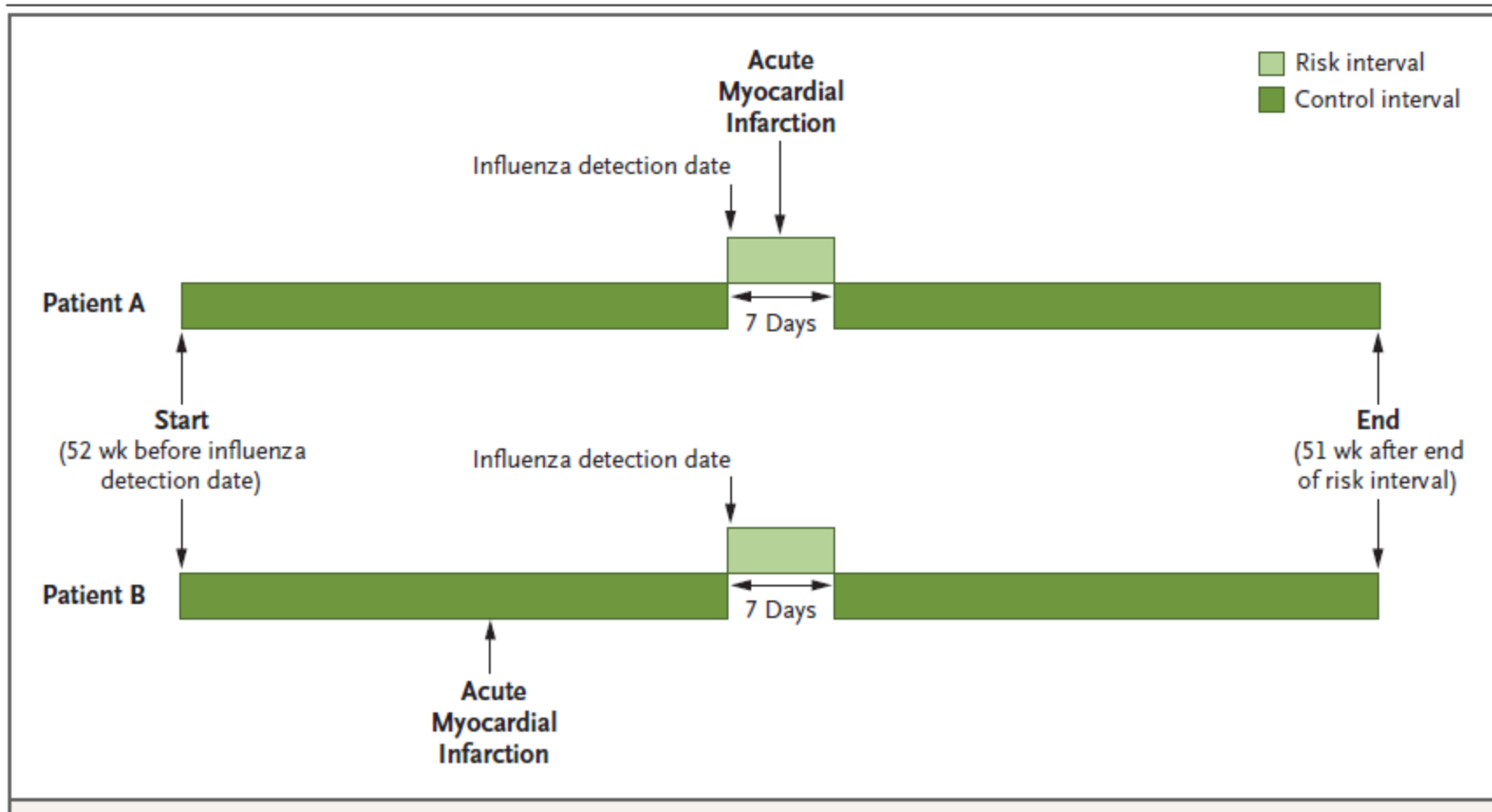
# Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection

Jeffrey C. Kwong, M.D., Kevin L. Schwartz, M.D., Michael A. Campitelli, M.P.H.,

N Engl J Med 2018

Retrospektive Analyse von 364 Patienten mit MCI innerhalb eines  
Jahres vor oder nach einer bestätigten Influenzainfektion





**Table 2.** Incidence Ratios for Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection.\*

| Variable                                  | Incidence Ratio<br>(95% CI) |
|---|-----------------------------|
| Primary analysis: risk interval, days 1–7 | 6.05 (3.86–9.50)            |
| Days 1–3                                  | 6.30 (3.25–12.22)           |
| Days 4–7                                  | 5.78 (3.17–10.53)           |
| Days 8–14                                 | 0.60 (0.15–2.41)            |
| Days 15–28                                | 0.75 (0.31–1.81)            |

# Season 2018/2019

- Ongoing trial with 2 additional flu wards in 2 other hospitals in Vienna
  - Provide information on 2 seasons (B and A)
  - Specific hospital effects
  - Increase database (target 2000 hospitalized flu-patients)
  - Confirm or reject results of 2017/2018
  - Provide rationale for management and medical decisions
    - available summer 2019

# Conclusion

## Influenza in Hospital

- Hospital patient:
  - Risk factors, symptoms, laboratory values, complications depend of subtype and underlying diseases
  - No specific pattern for A or B
  - Often atypical presentation (GI, acute heart or renal failure)
  - POCT PCR necessary for differentiation
  - Pneumonia = no1 complication
  - Mortality high 5% - very high 14% (90 days)
  - Influenza B is not a mild diseases
- Hospital staff:
  - Profound negative effects on staff health and costs