

National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport

Three sequencing confirmed cases of SARS-CoV-2 reinfection in The Netherlands

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10-09-2020

Timeline case 1

80 year old man with history of COPD, obesity, CHD, prostate carcinoma

16-03 erysipelas lower right leg
20-03 to 03-04 admitted to hospital for erysipelas treatment
12-04 readmitted due worsening of leg wound and low oxygen saturation.
CRP 104. X-thorax: no infiltrates. PCR nose/throat swab: positive (Ct 15). 02 treatment and supportive care. Not intubated.
20-04 discharged from hospital
02-05 complaints of increased drowsiness
04-05 readmitted to hospital due to renal dysfunction, pneumonia and *C. difficile* infection. PCR nose/throat swab: negative.
05-05 admitted to ICU. PCR on lower airways material: positive (Ct 27)
07-05 discharged from ICU
09-05 PCR sputum: negative
15-05 discharged to recovery care centre

Timeline case 2

60 year old man with no relevant medical history

07-04 presented with abdominal pain and progressive dyspnea
14-04 admitted to hospital. X-thorax: bilateral infiltrates.
PCR nose/throat swab: positive (Ct 26). O2 treatment and supportive care. No intubation
17-04 discharge from hospital
19-04 readmitted with progressive dyspnea. PCR nose/throat: negative.
20-04 admitted in ICU, required ventilation
24-04 multiple lung embolisms
26-04 broncho-alveolar lavage PCR positive (CT 26)
12-05 galactomannan positive and treated for pulmonary aspergillosis
09-06 discharge from ICU

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Timeline case 3

82 year old male with history of diabetes, hypertension, CHD, obesity, gout, gonartrosis. Living in long term care facility with a private room.

01-04 presented with fever, less approachable/communicative, general malaise, mild coughing, no respiratory distress. Patient room placed in isolation

02-04 PCR nose/throat swab: positive.

09-04 moved to in-house COVID19 isolation unit

12-04 fever and decubitus treated with amoxicillin/clavulanic acid (augmentin)

14-04 resolution of pulmonary symptoms

16-04 non-productive cough

20-04 discharged from COVID19 unit to personal room

09-06 complaints of increased diarrea and changed defecation. PCR throat/nose swab: positive. No fever, oxygen saturation 92%. Initially interpreted by local municipal health service as remnant RNA. No contact tracing was performed. Did advise 2 week quarantine and care in protective equipment.

12-06 resolution of complaints

18-06 ceased all isolation measures

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SNP analysis selected strains vs ref strain Wuhan-Hu-1

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		С	G	Т	С	С	С	G	т	С	С	т	С	G	т	G	G	с	С	G	с	A	т	т	pair-b(1) 2	20E049528-1	12-04-2020	r36barcode17
		с	G	т	С	С	с	G	т	С	С	т	С	G	С	G	G	с	С	G	С	A	т	т	4	4312000960	03-04-2020	r34barcode17
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		С	G	т	С	С	С	G	т	С	С	т	С	G	т	G	G	с	С	G	т	A	с	G	pair-a(1) 4	4732001872	02-04-2020	r32barcode11
		С	G	С	С	С	с	G	т	С	С	с	Т	G	Т	G	A	С	С	Ţ	С	A	т	G	pair-b(2) 2	20E060375-1	05-05-2020	r34barcode24
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		С	G	Т	С	Т	С	A	Т	С	т	Т	С	G	Т	G	G	т	С	G	С	A	т	G	pair-c(2) 2	20E056819-1	26-04-2020	r34barcode23
		С	G	Т	С	Т	С	A	т	С	т	т	С	G	Т	G	G	Т	С	G	С	A	т	G	4	4312001021	16-04-2020	R23BC21
			A	т	A	С	т	G	т	т	С	т	С	A	т	A	G	С	С	G	с	A	т	G	pair-a(2) 4	4732003627	09-06-2020	r28barcode05

Sequencing regarded as final proof? How much difference? What about reinfection with exactly the same virus?

Labinf@ct sent on 15-07-2020

Nationwide notification system by e-mail to all laboratories, municipal health services and relevant clinicians, requesting notification of suspected cases of COVID19 re-infection.

Reporting criteria:

 Patients with a first COVID19 episode with a positive PCR or first clinical episode from a household contact with a previous PCRpositive case

AND

- A second clinical episode with symptoms matching COVID19 and a positive PCR and symptom-free interval of at least 8 weeks

Limitation: often low viral load during 2nd episode; no testing for other causes eg rhinovirus

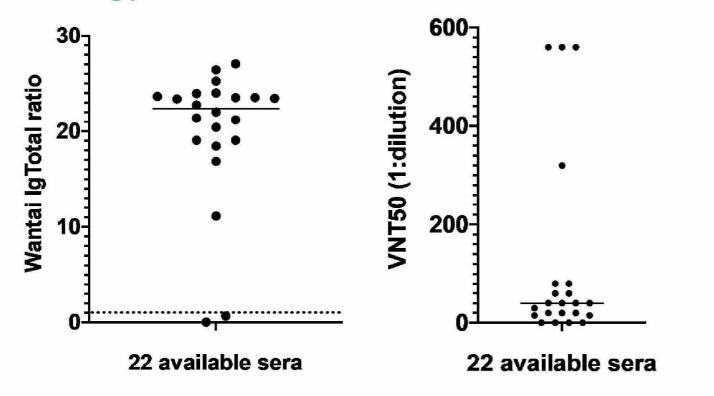
Reported reinfection

As of 31^{st} of August 2020

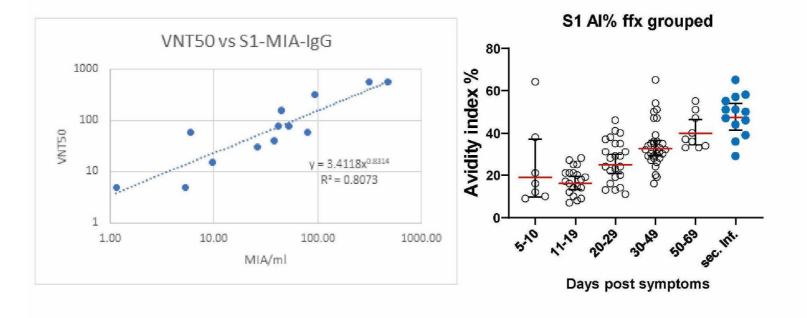
- 38 reported cases of possible reinfection
- 22 possible cases had available materials
- 15 of 22 cases had >8 weeks of symptom-free period
- 5 of 22 cases did not report symptoms or <8 weeks symptom-free period
- 2 of 22 cases dates of symptom onset unknown

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Serology and virus neutralization



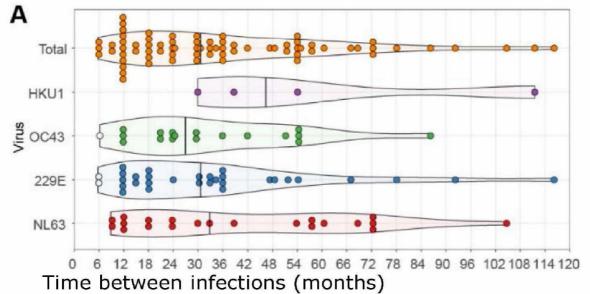
Serological response after reinfection Multiplex Immunoassay (MIA, Luminex)



Conclusions

- In total three sequencing confirmed reinfection cases in The Netherlands
- 2 of the 3 described cases had short intervals between reinfections, but no adequate virus neutralization capabilities were observed suggesting lack of protective antibodies after the initial infection
- For the third case no serology could be performed as no samples were available
- In 22 clinically reported suspected reinfection cases lack or very low level neutralizing antibodies were observed in 82% (18/22) of cases.

Endemic coronaviruses



Reinfections can occur as early as 6 months after initial infection for endemic coronaviruses.

Edridge et al. MedRxiv May 2020



Acknowledgements

