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LaDR Der Laborverbund
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Philipps Universität Marburg

Long-/Post-Covid-Symposium

Long-Covid: Klinik und Stand der (Labor-)Diagnostik

Priv.-Doz. Dr. Reinhard Geßner

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Universitätsklinikum Gießen und Marburg
Philipps-Universität Marburg

02.11.2022

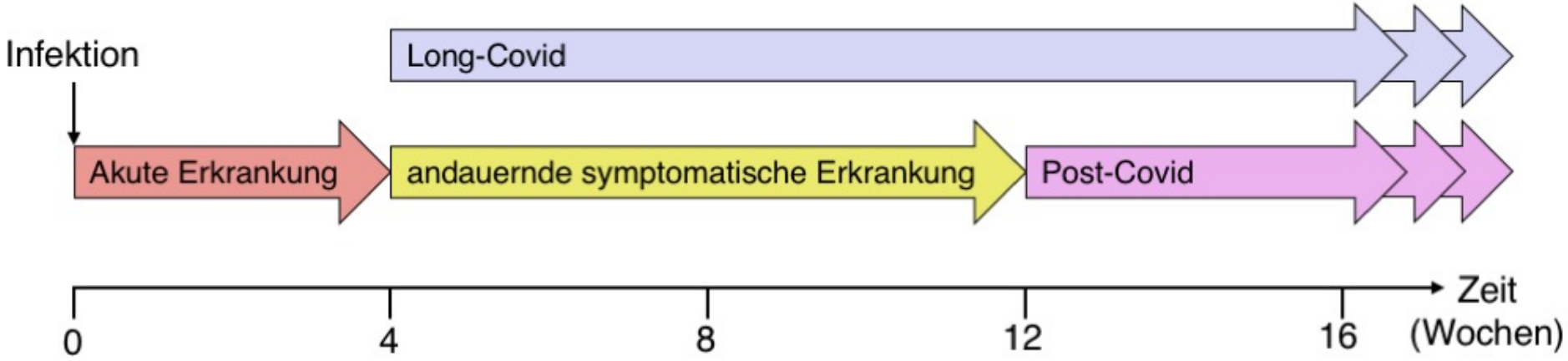
Gliederung

- Definition Long- und Post-Covid
- Klinische und gesellschaftliche Relevanz
- Klinische Diagnostik von Long-Covid
- Mögliche Entstehungsmechanismen
- Biomarker für Long-Covid - Labordiagnostik
- Ausblick
- Zusammenfassung

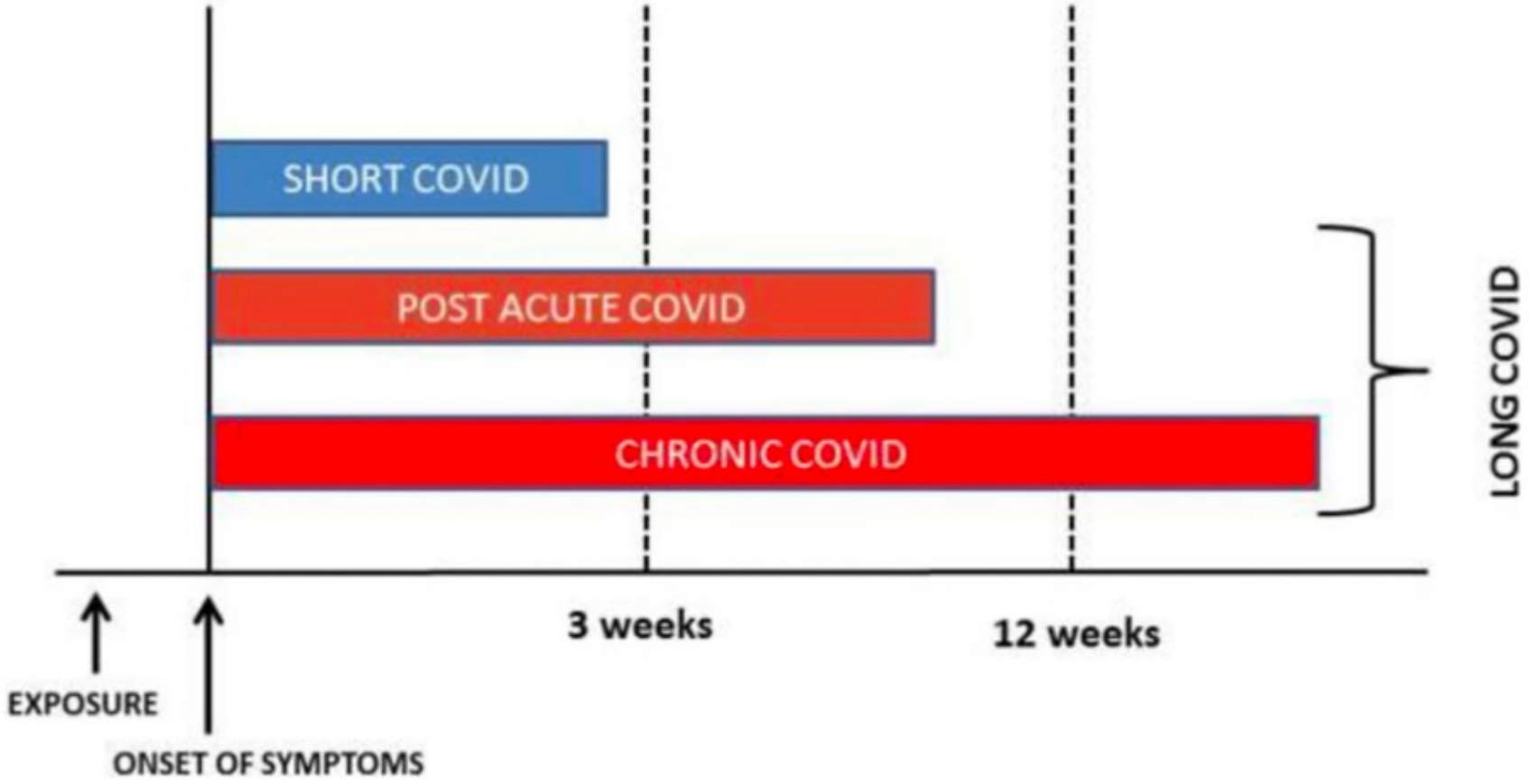
Definition Long- und Post-Covid

Unterschiedliche Bezeichnungen:

- "andauernde symptomatische Erkrankung" (4 – 12 Wochen)
- "Long-Covid":
  Andauernde oder neue Symptome nach > 4 Wochen
- "Post-Covid"
  Andauernde oder neue Symptome nach > 12 Wochen



Definition Long- und Post-Covid



DePace & Colombo, Curr Cardiol Rep Epub (2022) PMID 36178611

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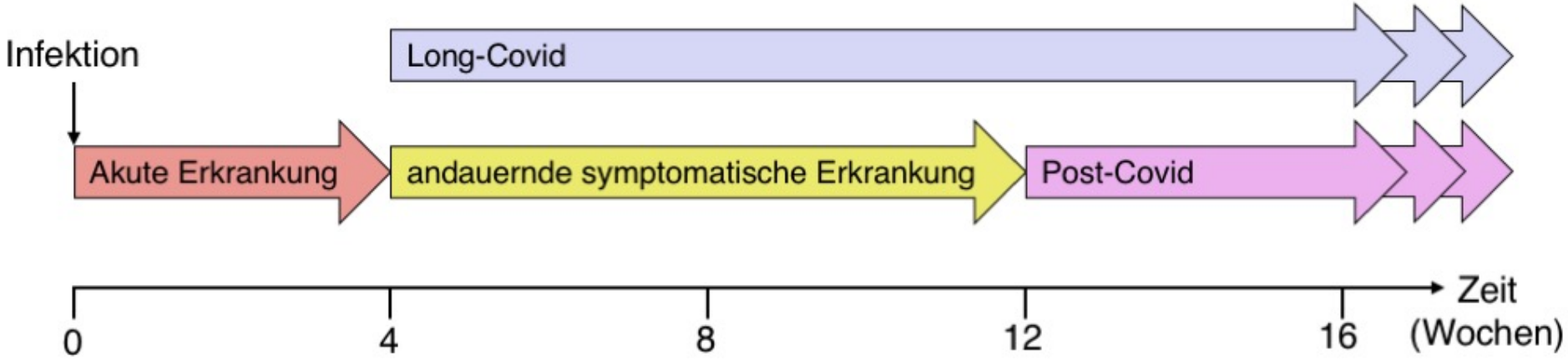


Definition Long- und Post-Covid

nature

NEWS FEATURE | 09 June 2021

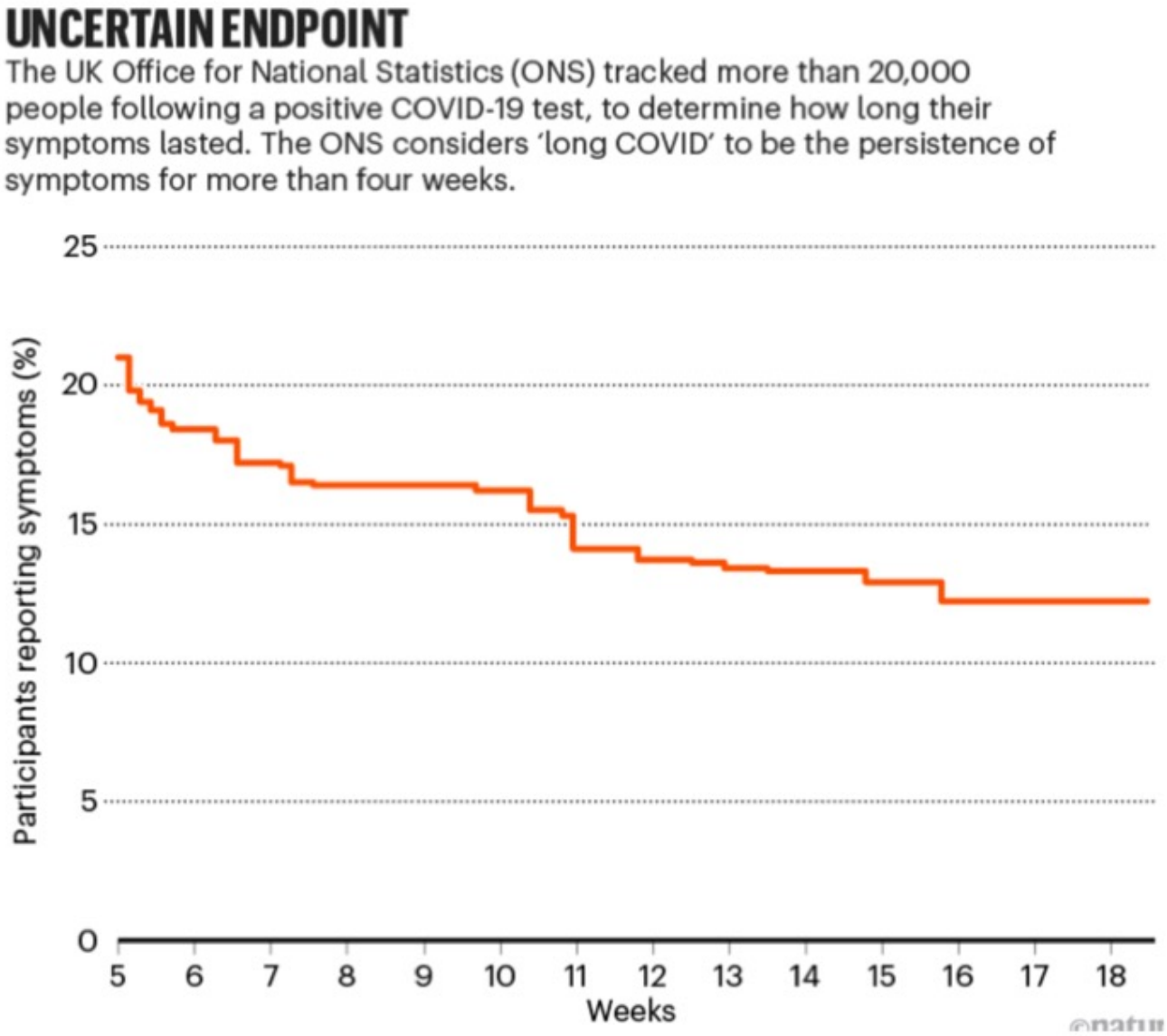
The four most urgent questions about long COVID

Scientists are starting to get insights into the lingering disorder that affects some people infected with SARS-CoV-2 – but many mysteries remain unsolved.

Michael Marshall

Nature News 09.06.2021

Definition Long- und Post-Covid



Marshall, Nature News 09.06.2021

Definition Long- und Post-Covid

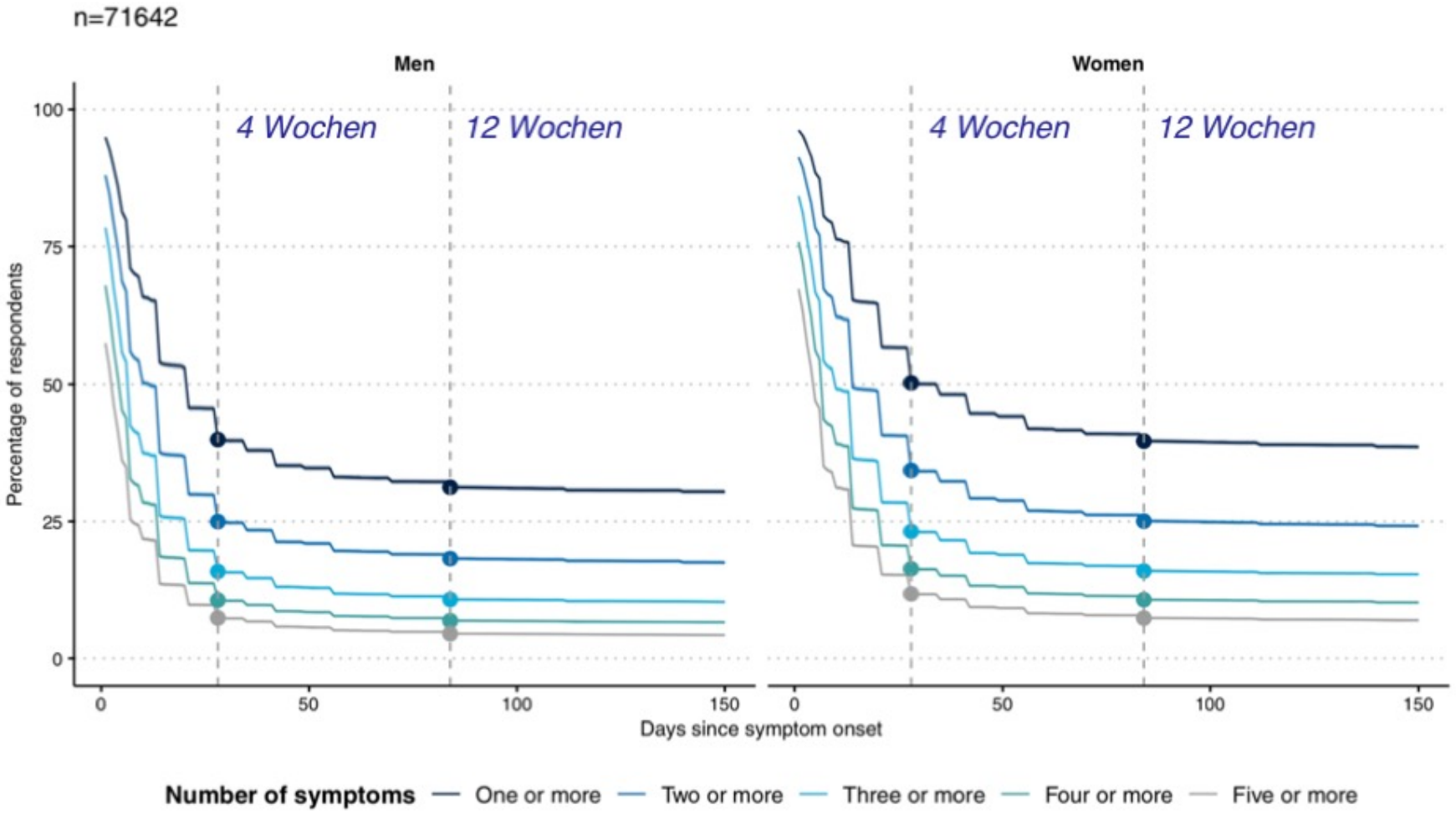
Persistent COVID-19 symptoms in a community study of 606,434 people in England

Matthew Whitaker[1,2,11], Joshua Elliott[3,4,11], Marc Chadeau-Hyam[1,2], Steven Riley[1,5,6], Ara Darzi[3,7], Graham Cooke[3,4,8,12], Helen Ward[3,5,8,12] & Paul Elliott[1,2,3,8,9,10,12]✉

- Cross sectional study
- 508,707 people took part in REACT-2 rounds 3 to 5
- 92,116 respondents reported previous COVID-19 in rounds 3 to 5
- at 12 weeks, 37.7% of those in rounds 3 to 5 reported one or more symptoms

Whitaker at al., Nat Commun 13 (2022) 1957

Definition Long- und Post-Covid



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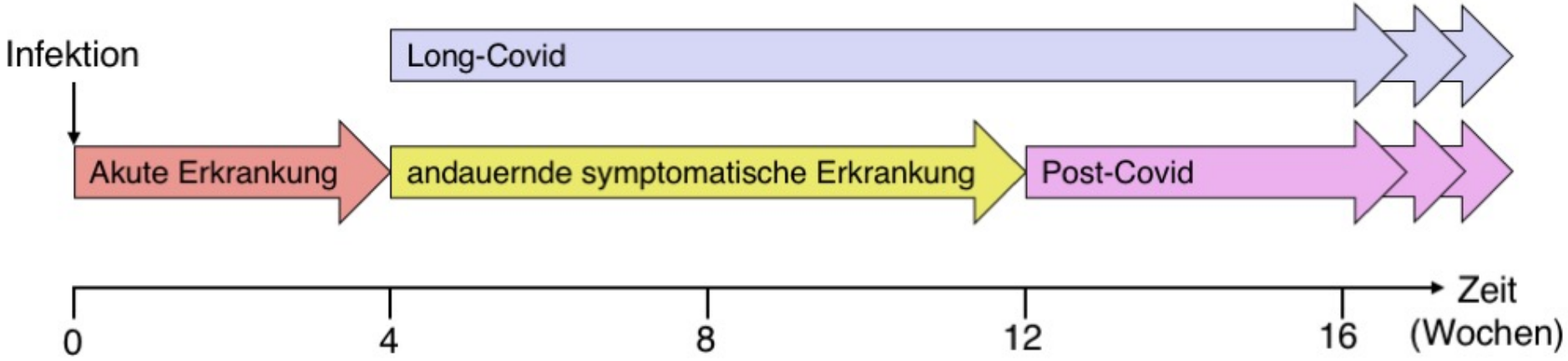
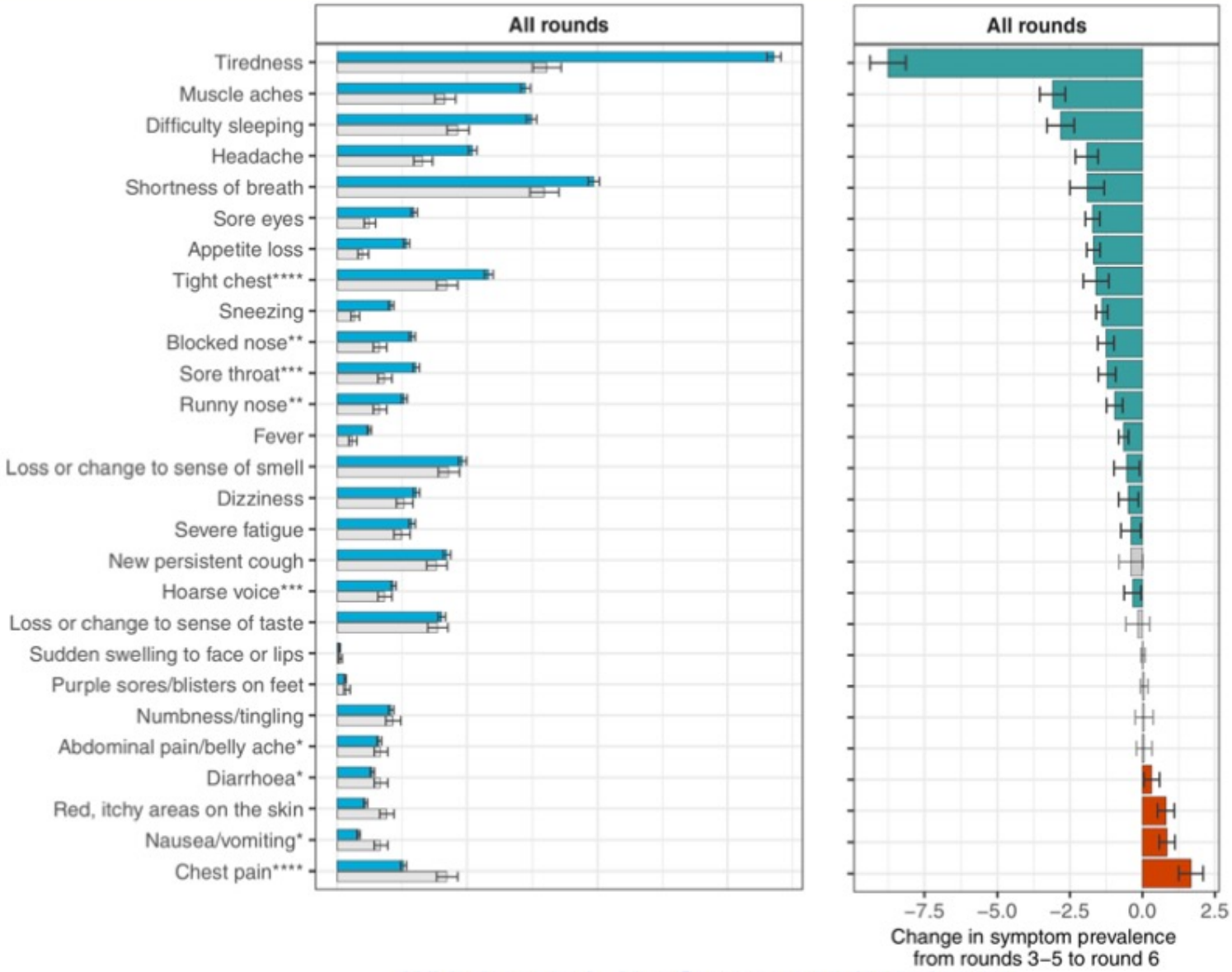


Definition Long- und Post-Covid



Runde 6 fand 3 bis 8 Monate nach den Runden 3 - 5 statt.

Whitaker at al., Nat Commun 13 (2022)1957

Definition Long- und Post-Covid

Klinische Falldefinition einer Post-COVID-19-Erkrankung der WHO

1. Bauchschmerzen
2. Beschwerden mit Menstruation und Periode
3. Veränderter Geruchs-/ Geschmackssinn
4. Angst
5. Verschwommener Blick
6. Brustschmerzen
7. Kognitive Fehlleistung/ vernebeltes Denken
8. Husten
9. Depression
10. Schwindel
11. Erschöpfung
12. Intermittierendes Fieber
13. Gastrointestinale Beschwerden (Durchfall, Verstopfung, Reflux)
14. Kopfschmerzen
15. Gedächtnisstörungen
16. Gelenkschmerzen
17. Muskelschmerzen/Spasmen
18. Neuralgie
19. Neu auftretende Allergien
20. Gefühl von Kribbeln
21. Unwohlsein nach Belastung
22. Kurzatmigkeit
23. Schlafstörungen
24. Tachykardien/Herzrasen
25. Tinnitus und andere Probleme mit dem Gehör

Klinische Falldefinition einer Post-COVID-19-Erkrankung gemäß Delphi-Konsens der WHO vom 6.10.2021

Definition Long- und Post-Covid

Klinische Falldefinition einer Post-COVID-19-Erkrankung der WHO

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Klinische Falldefinition einer Post-COVID-19-Erkrankung gemäß Delphi-Konsens der WHO vom 6.10.2021

Definition Long- und Post-Covid

AWMF S1-Leitlinie unterscheidet 4 Subtypen:

1. "Post-Intensive-Care-Syndrome" (PICS) nach intensivmedizinischer Behandlung der akuten Phase
2. Auftreten von Folgekrankheiten wie kardiovaskulären Komplikationen, kognitiven Leistungsstörungen oder einer post-traumatischen Belastungsstörung mit zeitlicher Latenz nach COVID-19 Erkrankung
3. Deutlichen Erschöpfungssymptomatik und Belastungsinsuffizienz mit/ohne Dyspnoe, welche die Teilhabe am Sozial- und Arbeitsleben deutlich beeinträchtigt
4. Unterschiedlichen Beschwerden, die den Alltag nicht wesentlich beeinträchtigen

AWMF S1-Leitlinie Long/ Post-COVID (Stand17.8.2022)

Definition Long- und Post-Covid

AWMF S1-Leitlinie Long- / Post-COVID vom 17.8.2022

Die Deutsche Gesellschaft für Pneumologie hat 2021 die AWMF S1-Leitlinie Long/Post-COVID initiiert. In einem breiten interdisziplinären Ansatz wurde diese S1-Leitlinie basierend auf dem aktuellen Wissensstand gestaltet.

Die klinische Empfehlung beschreibt die aktuellen Long bzw. Post-COVID-Symptome, diagnostische Ansätze und Therapien.

Neben der allgemeinen und konsentierten Einführung wurde ein fachspezifischer Zugang gewählt, der den aktuellen Wissensstand zusammenfasst.

Die Leitlinie hat einen explizit praktischen Anspruch und wird basierend auf dem aktuellen Wissenszugewinn vom Autorenteam weiterentwickelt und adaptiert.

an der Leitlinie der Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften (AWMF) sind 28 deutsche medizinische Fachgesellschaften beteiligt. Umfang: 122 Seiten, 412 zitierte und aufgeführte Referenzen.

AWMF S1-Leitlinie Long/ Post-COVID (Stand 17.8.2022)

Definition Long- und Post-Covid

Zusammenfassung

- Unterschiedliche Definitionen für Long- und Post-Covid; weitere Einteilungen in Verwendung.
- Long-Covid stützt sich auf alle Symptome, die 4 Wochen nach Erkrankungsbeginn noch vorhanden sind oder in der Folge neu auftreten.
- WHO benennt 25 typische Long-Covid-Symptome, weitere Symptome in der Fachliteratur beschrieben.
- Die meisten Symptome verringern sich nach Monaten, einige wenige verstärken sich.
- AWMF S1-Leitlinie unterscheidet 4 Subtypen.

AWMF S1-Leitlinie Long/ Post-COVID (Stand 17.8.2022)

Klinische und gesellschaftliche Relevanz

Corona-Folgen

Nicht genug Geld für Long-Covid-Versorgung?

Stand: 17.05.2022 10:26 Uhr

Patientenschützer fordern den Staat auf, Long Covid endlich ernst zu nehmen. Für die Versorgung von Patienten gebe es nicht genug Geld. Die Sieben-Tage-Inzidenz sinkt derweil weiter.

https://www.tagesschau.de/inland/corona-long-covid-patientenschuetz/

Klinische und gesellschaftliche Relevanz

WHO-Bericht

Mehr psychische Krankheiten durch Corona

Stand: 17.06.2022 09:14 Uhr

Depressionen, Angststörungen, Süchte - die Corona-Pandemie hat laut der WHO weltweit zu einem starken Anstieg psychischer Krankheiten geführt. Fast eine Milliarde Menschen seien davon betroffen.

https://www.tagesschau.de/ausland/europa/who-corona-anstieg-psychi/

Klinische und gesellschaftliche Relevanz

Folgen des Coronavirus

Ein Fünftel chronisch erschöpft

Stand: 21.09.2022 14:08 Uhr

Eine Vergleichsstudie liefert weitere Erkenntnisse über das Fatigue-Syndrom nach einer Corona-Erkrankung. Ein knappes Fünftel der Infizierten hat demnach nach mehr als sechs Monaten noch Beschwerden.

https://www.tagesschau.de/wissen/gesundheit/coronavirus-erschoepfung-101.html

Klinische und gesellschaftliche Relevanz

Zusammenfassung

- Long-Covid gewinnt immer mehr an Bedeutung.
- ca. 10% bis 20% aller an Covid-19 Erkrankten zeigen mehr oder weniger ausgeprägte Long-Covid-Symptome.
- Long-Covid tritt auch nach milden primären Verläufen auf.
- Long-Covid belastet das Gesundheitssystem aufgrund der hohen Fallzahlen erheblich.
- Long-Covid hat auch eine hohe gesellschafts- und sozial-politische Relevanz, da viele davon Betroffene für lange Zeit arbeitsunfähig sind.

Klinische Diagnostik von Long-Covid

Infect Chemother. 2022 Sep;54(3):566-597
https://doi.org/10.3947/ic.2022.0141
pISSN 2093-2340·eISSN 2092-6448

ic Infection & Chemotherapy

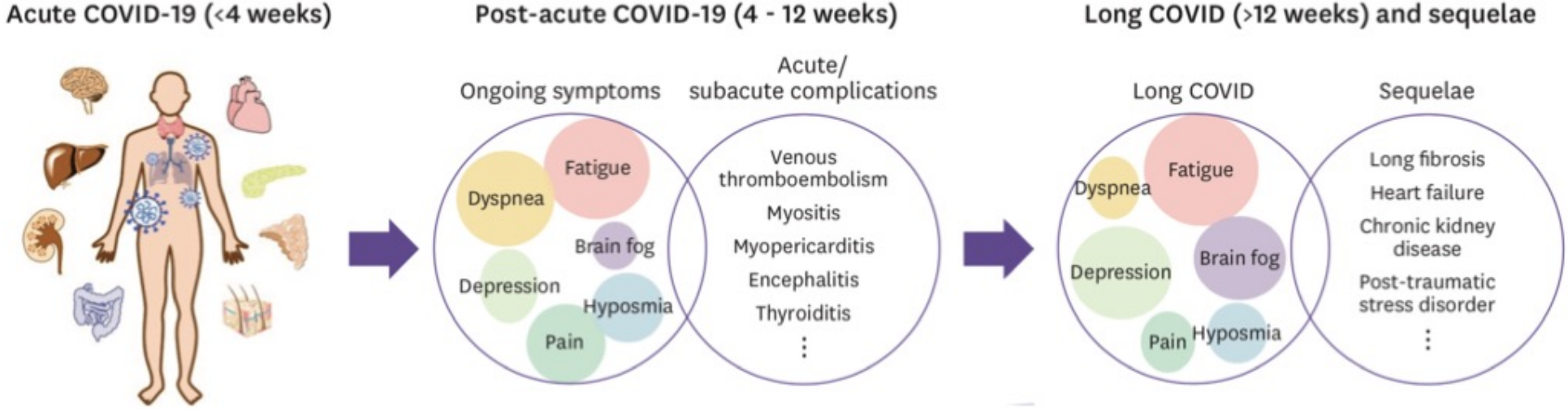
Special Article

Check for updates

Preliminary Guidelines for the Clinical Evaluation and Management of Long COVID

Yoonjung Kim [1], Seong Eun Kim [2], Tark Kim [3], Ki Wook Yun [4], So Hee Lee [5], Eunjung Lee [6], Jun-Won Seo [7], Young Hee Jung [8], and Yong Pil Chong [9]

Continuum of post COVID-19 conditions



Kim et al., Infect Chemother 54 (2022) 566-597

Klinische Diagnostik von Long-Covid

Table 1. Overall and time-specific incidence of long COVID symptoms

Symptom	Meta-analysis[a], % (95% CI)	Domestic (241 subjects)	
		>6 months %	>12 months %
Systemic			
Fever	1.1 (0.2 - 4.7)	1.2	0
Fatigue	31.0 (23.9 - 39.0)	25.3	16.2
Dizziness	4.5 (2.5 - 7.9)	14.9	10.4
Cardiopulmonary			
Cough	8.2 (4.9 - 13.4)	8.7	7.1
Sputum	5.5 (3.2 - 9.2)	8.7	7.1
Sore throat	4.7 (2.4 - 8.9)	12	7.1
Dyspnea	25.1 (17.9 - 34.0)	5.4	2.9
Chest pain/chest discomfort	6.4 (3.2 - 12.4)	8.3	4.6
Palpitation	9.7 (6.0 - 15.3)	2.5	2.5
Gastrointestinal			
Anorexia	17.5 (4.1 - 51.0)	5.4	2.9
Nausea/vomiting	6.7 (1.6 - 23.6)	6.2	0.8
Abdominal discomfort	18.0 (11.5 - 26.1)	8.7	5
Neurological			
Headache	4.9 (2.3 - 10.1)	12.4	4.6
Seizures/cramps	1.3 (0.5 - 2.9)	0.4	0
Taste disturbance	13.5 (9.0 - 19.9)	6.6	3.3
Smell disturbance	15.2 (10.8 - 21.0)	8.7	6.2
Tingling/paresthesia	9.1 (2.2 - 30.9)	11.2	10

Kim et al., Infect Chemother 54 (2022) 566-597

Klinische Diagnostik von Long-Covid

Neurological			
Headache	4.9 (2.3 - 10.1)	12.4	4.6
Seizures/cramps	1.3 (0.5 - 2.9)	0.4	0
Taste disturbance	13.5 (9.0 - 19.9)	6.6	3.3
Smell disturbance	15.2 (10.8 - 21.0)	8.7	6.2
Tingling/paresthesia	9.1 (2.2 - 30.9)	11.2	10
Neurocognitive			
Concentration impairment	26.0 (21.0 - 31.7)	25.3	22.4
Memory impairment	17.9 (5.3 - 46.3)	25.7	19.9
Other cognitive impairment	17.8 (0.1 - 98.2)	25.3	21.2
Psychological			
Depression	8.1 (4.1 - 15.1)	24.9	17.8
Anxiety	18.7 (9.0 - 35.3)	24.1	16.2
Sleep disorder (insomnia)	18.2 (9.6 - 31.6)	21.2	13.3
Post-traumatic stress disorder	9.1 (3.7 - 21.0)	7.9	5
Musculoskeletal			
Muscle pain/myalgia	11.3 (6.2 - 19.8)	6.2	1.7
Joint pain/arthralgia	9.4 (5.7 - 15.0)	11.2	6.6
Other			
Hair loss	14.3 (5.3 - 33.2)	17	14.9
Skin rash	2.8 (1.0 - 8.2)	10.8	6.6

[a]Meta-analysis was conducted on a total of 10,951 patients with confirmed or clinically suspected COVID-19 in 12 countries, 12 weeks or more from the onset of symptoms.
COVID, coronavirus disease; CI, 95% confidence interval.

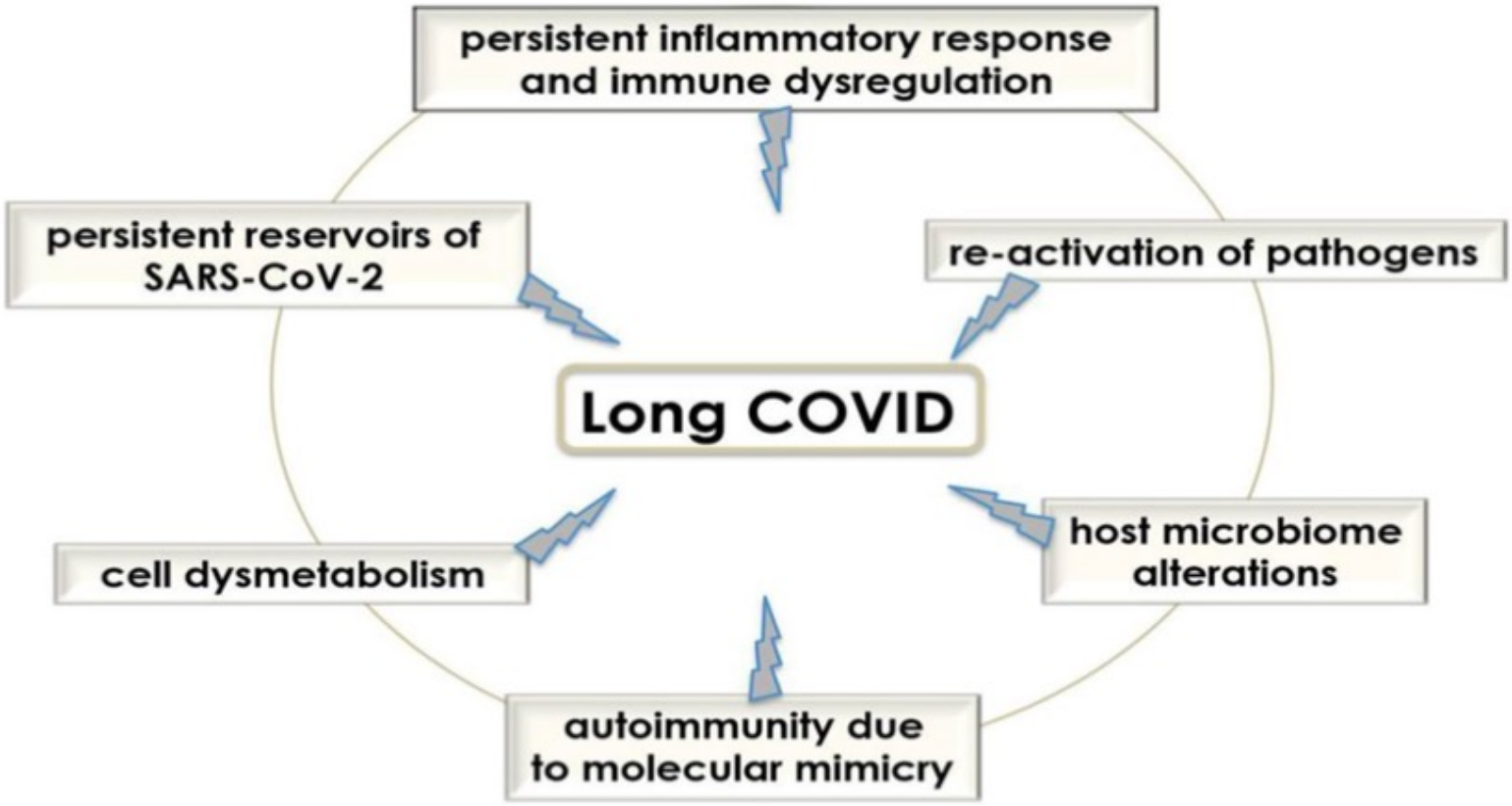
Kim et al., Infect Chemother 54 (2022) 566-597

Klinische Diagnostik von Long-Covid

Zusammenfassung

- Long-Covid ist eine Multiorgan-Erkrankung.
- Es gibt eine Vielzahl von Symptomen, von denen aber keines in allen Fällen vorhanden ist.
- Jeder Patient präsentiert eine individuelle Verteilung der beschriebenen Symptome.
- Die Häufigkeit einiger Symptome nehmen in den ersten Monaten relativ rasch ab, wie z.B. Dyspnoe, Anorexie, Schwindel, Erbrechen, Kopfschmerzen, Geschmacksstörungen, Muskelschmerzen.
- Andere, insbesondere psychoneurologische Symptome, persistieren dagegen für lange Zeit, wie z.B. Parästhesien, Konzentrations- und Erinnerungsverlust, Depressionen sowie auch Haarausfall.

Mögliche Long-Covid Pathomechanismen



Batiha et al., Virol J 19 (2022) 158

Mögliche Long-Covid Pathomechanismen

Batiha *et al. Virology Journal* (2022) 19:158
https://doi.org/10.1186/s12985-022-01891-2

Virology Journal

REVIEW Open Access

Pathophysiology of Post-COVID syndromes: a new perspective

Gaber El-Saber Batiha[1], Hayder M. Al-kuraishy[2], Ali I. Al-Gareeb[2] and Nermeen N. Welson[3*]

Key summary points

- Post-COVID (PCS) syndrome may progress in association with the development of mast cell activation syndrome (MCAS).
- High D-dimer levels and blood urea nitrogen were observed to be risk factors associated with pulmonary dysfunction in COVID-19 survivors 3 months post-hospital discharge with the development of PCS.
- Persistence of inflammatory reactions, autoimmune mimicry, and reactivation of pathogens together with host microbiome alterations may contribute to the development of PCS.
- MCAS is treated by antihistamines, inhibition of synthesis of mediators, inhibition of mediator release, and inhibition of degranulation of mast cells.

Batiha et al., Virol J 19 (2022) 158

Mögliche Long-Covid Pathomechanismen

- Persistenz/Reaktivierung von SARS-CoV-2
- Induktion von Auto-Antikörpern / Autoimmunerkrankungen
- Reaktivierung anderer Viren (z.B. Herpes-Viren) oder anderer Krankheitserreger
- Auftreten von Neuinfektionen (andere Erreger)
- Langanhaltende Gewebeschädigung einschließlich gestörter Mikrovaskularisierung
- Veränderung des Mikrobioms (Dysbiose)
- Nebenwirkungen von Covid-19 Therapien

Mögliche Persistenz von SARS-CoV-2

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Case Report

A case report of SARS-CoV-2 confirmed in saliva specimens up to 37 days after onset: Proposal of saliva specimens for COVID-19 diagnosis and virus monitoring☆

Yasuhisa Tajima [a, *], Yasuo Suda [b], Kunio Yano [a]

[a] Department of Infectious Diseases, Hamamatsu Medical Center, 328 Tomitsukacho, Naka-ku, Hamamatsu-shi, Shizuoka-ken, 432-8580, Japan
[b] Department of Chemistry, Biotechnology and Chemical Engineering, Graduate School of Science and Engineering, Kagoshima University, 1-21-24 Korimoto, Kagoshima-shi, Kagoshima-ken, 890-0065, Japan

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ABSTRACT

We present the case of a 71-year-old man who, despite becoming asymptomatic after having some mild symptoms of COVID-19, had SARS-CoV-2 RNA detected for 37 days after onset, from his concentrated and purified saliva specimens using sugar chain-immobilized gold nanoparticles. It was suggested that the early morning saliva specimens were more likely to show positive results than those obtained later in the day.

J Infect Chemother 26 (2020) 1086-9

Mögliche Persistenz von SARS-CoV-2

nature

NEWS | 11 May 2022

Coronavirus ‘ghosts’ found lingering in the gut

Scientists are studying whether long COVID could be linked to viral fragments found in the body months after initial infection.

Heidi Ledford

Nature News 11.05.2022

Mögliche Persistenz von SARS-CoV-2

INFLAMMATORY BOWEL DISEASE

Postacute COVID-19 is Characterized by Gut Viral Antigen Persistence in Inflammatory Bowel Diseases

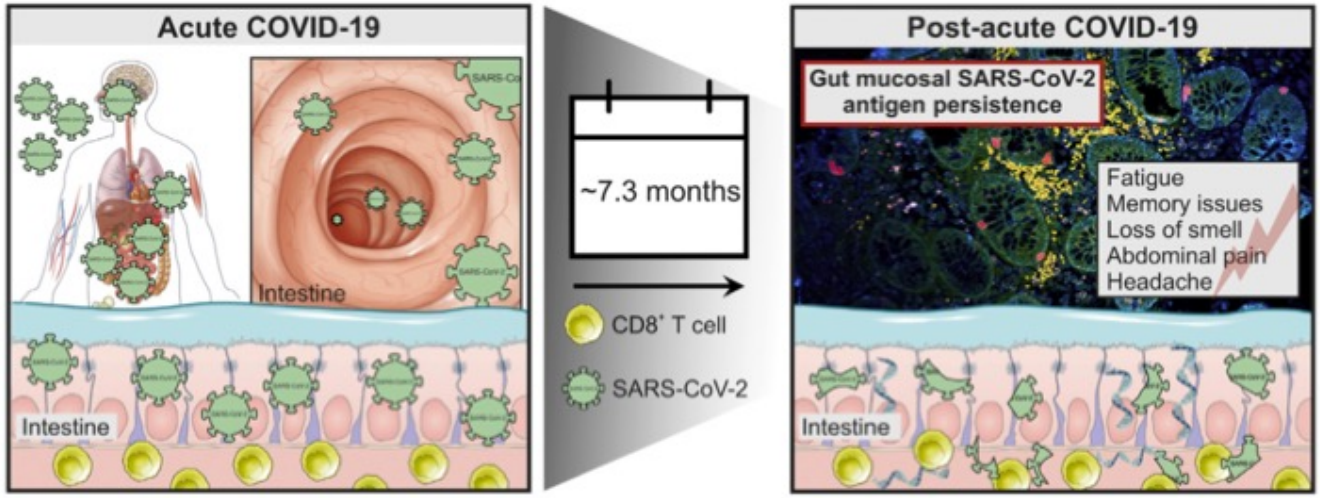
Andreas Zollner,[1,*] **Robert Koch**,[1,*] Almina Jukic,[1] Alexandra Pfister,[1] Moritz Meyer,[1] Annika Rössler,[2] Janine Kimpel,[2] **Timon E. Adolph**,[1,§] and **Herbert Tilg**[1,§]

[1]Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology & Metabolism, Medical University of Innsbruck, Innsbruck, Austria; and [2]Department of Hygiene, Microbiology and Public Health, Institute of Virology, Medical University of Innsbruck, Innsbruck, Austria

Main results:

Biopsies positive for SARS-CoV-2 by RT-PCR and Immunostaining for up to 7 months.

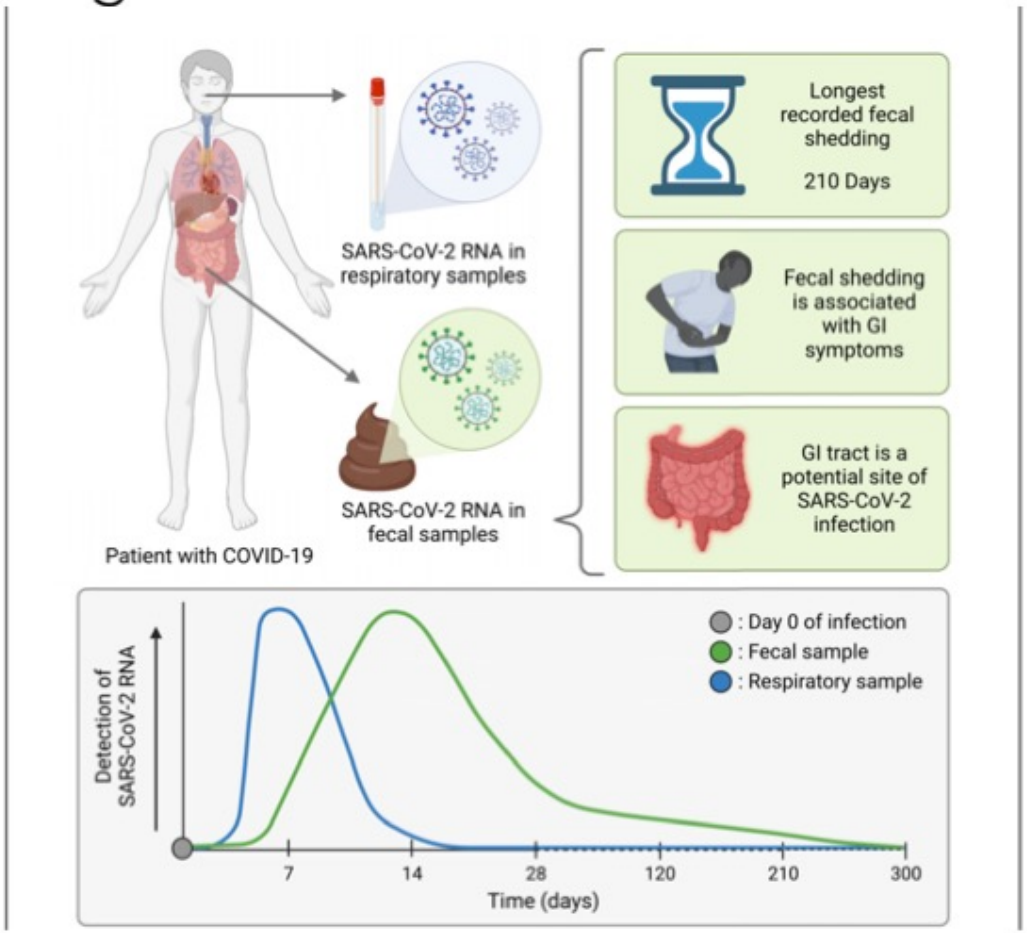
No infectious particles found.



Gastroenterology 163 (2022) 495–506

Mögliche Persistenz von SARS-CoV-2

Gastrointestinal symptoms and fecal shedding of SARS-CoV-2 RNA suggest prolonged gastrointestinal infection



Aravind Natarajan, Soumaya Zlitni, Erin F. Brooks, ..., Jason R. Andrews, Prasanna Jagannathan, Ami S. Bhatt

asbhatt@stanford.edu

Highlights

Approximately one-half of COVID-19 patients shed fecal RNA in the week after diagnosis

Four percent of patients with COVID-19 shed fecal viral RNA 7 months after diagnosis

Presence of fecal SARS-CoV-2 RNA is associated with gastrointestinal symptoms

SARS-CoV-2 likely infects gastrointestinal tissue

Med 3 (2022) 1-17 (Cell Press)

Mögliche Persistenz von SARS-CoV-2

Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues

Liguo Zhang[a], Alexsia Richards[a], M. Inmaculada Barrasa[a], Stephen H. Hughes[b], Richard A. Young[a,c], and Rudolf Jaenisch[a,c,1]

[a]Whitehead Institute for Biomedical Research, Cambridge, MA 02142; [b]HIV Dynamics and Replication Program, Center for Cancer Research, National Cancer Institute, Frederick, MD 21702; and [c]Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02142

Contributed by Rudolf Jaenisch, April 19, 2021 (sent for review March 29, 2021; reviewed by Anton Berns and Anna Marie Skalka)

Prolonged detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA and recurrence of PCR-positive tests have been widely reported in patients after recovery from COVID-19, but some of these patients do not appear to shed infectious virus. We investigated the possibility that SARS-CoV-2 RNAs can be reverse-transcribed and integrated into the DNA of human cells in culture and that transcription of the integrated sequences might account for some of the positive PCR tests seen in patients. In support of this hypothesis, we found that DNA copies of SARS-CoV-2 sequences can be integrated into the genome of infected human cells. We found target site duplications flanking the viral sequences and consensus LINE1 endonuclease recognition sequences at the integration sites, consistent with a LINE1 retrotransposon-mediated, target-primed reverse transcription and retroposition mechanism. We also found, in some patient-derived tissues, evidence suggesting that a large fraction of the viral sequences is transcribed from integrated DNA copies of viral sequences, generating viral–host chimeric transcripts. The integration and transcription of viral sequences may thus contribute to the detection of viral RNA by PCR in patients after infection and clinical recovery. Because we have detected only subgenomic sequences derived mainly from the 3′ end of the viral genome integrated into the DNA of the host cell, infectious virus cannot be produced from the integrated subgenomic SARS-CoV-2 sequences.

Significance

An unresolved issue of SARS-CoV-2 disease is that patients often remain positive for viral RNA as detected by PCR many weeks after the initial infection in the absence of evidence for viral replication. We show here that SARS-CoV-2 RNA can be reverse-transcribed and integrated into the genome of the infected cell and be expressed as chimeric transcripts fusing viral with cellular sequences. Importantly, such chimeric transcripts are detected in patient-derived tissues. Our data suggest that, in some patient tissues, the majority of all viral transcripts are derived from integrated sequences. Our data provide an insight into the consequence of SARS-CoV-2 infections that may help to explain why patients can continue to produce viral RNA after recovery.

Proc. Natl. Acad. Sci. U.S.A. 118 (2021) e2105968118

Induktion von Autoimmunreaktionen

nature COMMUNICATIONS

ARTICLE

Check for updates

https://doi.org/10.1038/s41467-021-25509-3 OPEN

New-onset IgG autoantibodies in hospitalized patients with COVID-19

Sarah Esther Chang[1,2,26], Allan Feng[1,2,26], Wenzhao Meng[3,26], Sokratis A. Apostolidis[4,5,26], Elisabeth Mack[6], Maja Artandi[7,8], Linda Barman[7], Kate Bennett[9], Saborni Chakraborty[10], Iris Chang[2,11], Peggie Cheung[1,2], Sharon Chinthrajah[2,11], Shaurya Dhingra[1,2], Evan Do[2,11], Amanda Finck[12], Andrew Gaano[3], Reinhard Geßner[13], Heather M. Giannini[14], Joyce Gonzalez[3], Sarah Greib[13], Margrit Gündisch[13], Alex Ren Hsu[1,2], Alex Kuo[1,2], Monali Manohar[2,10], Rong Mao[1,2], Indira Neeli[14], Andreas Neubauer[6], Oluwatosin Oniyide[15], Abigail E. Powell[16,17], Rajan Puri[7], Harald Renz[13,18], Jeffrey Schapiro[19], Payton A. Weidenbacher[16,17], Richard Wittman[7], Neera Ahuja[20], Ho-Ryun Chung[21], Prasanna Jagannathan[2,10,22], Judith A. James[23], Peter S. Kim[14,16,24], Nuala J. Meyer[5,15], Kari C. Nadeau[2,11], Marko Radic[14], William H. Robinson[1,2,25], Upinder Singh[2,10,22], Taia T. Wang[10,22,24], E. John Wherry[5,12], Chrysanthi Skevaki[13,18]✉, Eline T. Luning Prak[3,5]✉ & Paul J. Utz[1,2]✉

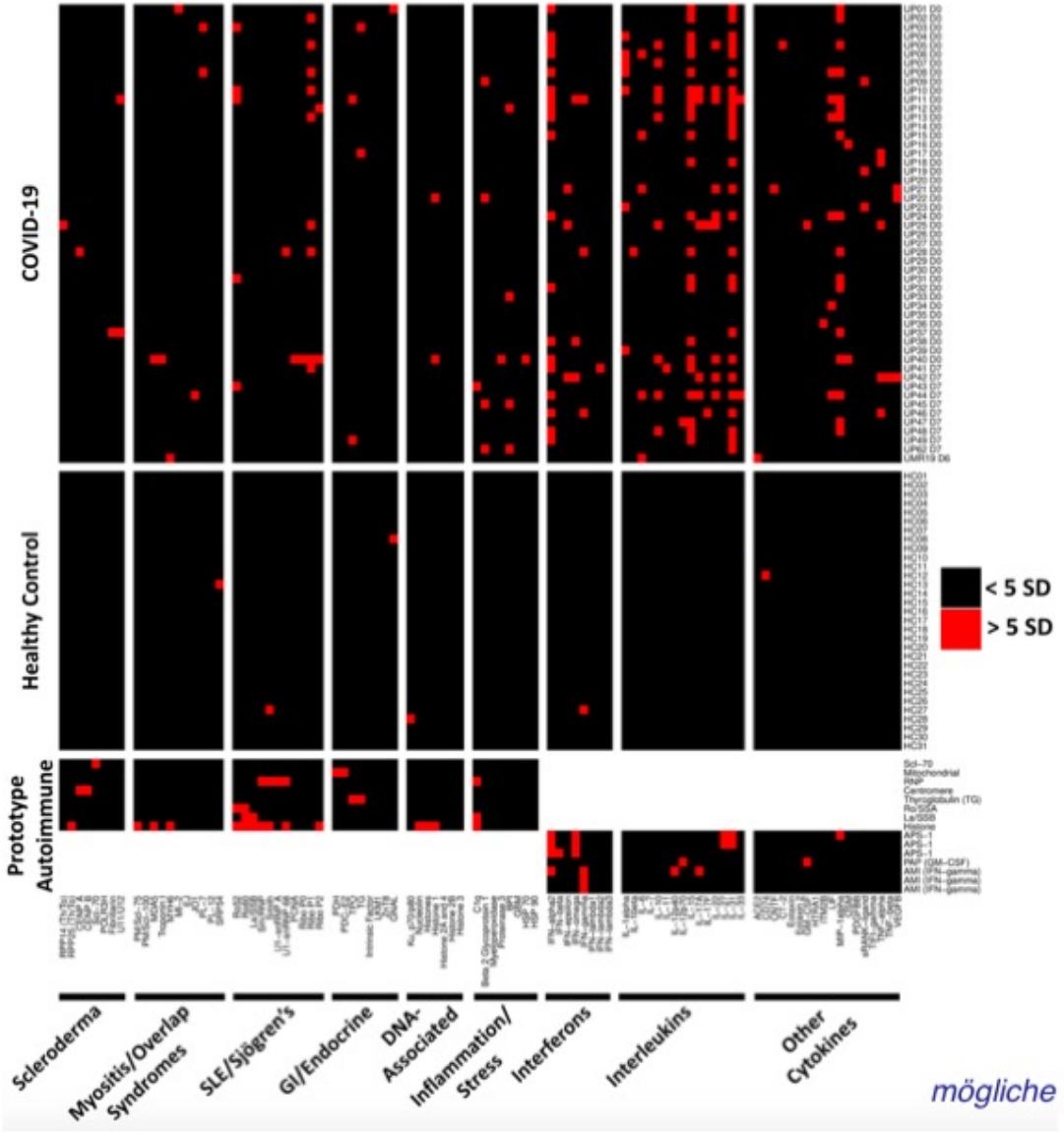
Nature Communications 12 (2021) 5417

Induktion von Autoimmunreaktionen

COVID-19 is associated with a wide range of clinical manifestations, including autoimmune features and autoantibody production. Here we develop three protein arrays to measure IgG autoantibodies associated with connective tissue diseases, anti-cytokine antibodies, and anti-viral antibody responses in serum from 147 hospitalized COVID-19 patients. Autoantibodies are identified in approximately 50% of patients but in less than 15% of healthy controls. When present, autoantibodies largely target autoantigens associated with rare disorders such as myositis, systemic sclerosis and overlap syndromes. A subset of autoantibodies targeting traditional autoantigens or cytokines develop de novo following SARS-CoV-2 infection. Autoantibodies track with longitudinal development of IgG antibodies recognizing SARS-CoV-2 structural proteins and a subset of non-structural proteins, but not proteins from influenza, seasonal coronaviruses or other pathogenic viruses. We conclude that SARS-CoV-2 causes development of new-onset IgG autoantibodies in a significant proportion of hospitalized COVID-19 patients and are positively correlated with immune responses to SARS-CoV-2 proteins.

Nature Communications 12 (2021) 5417

Induktion von Autoimmunreaktionen



mögliche Kombinationen 13.818

Nature Communications 12 (2021) 5417

Induktion von Autoimmunreaktionen

Diverse functional autoantibodies in patients with COVID-19

https://doi.org/10.1038/s41586-021-03631-y
Eric Y. Wang[1,16], Tianyang Mao[1,16], Jon Klein[1,16], Yile Dai[1,16], John D. Huck[1], Jillian R. Jaycox[1],

COVID-19 manifests with a wide spectrum of clinical phenotypes that are characterized by exaggerated and misdirected host immune responses[1–6]. Although pathological innate immune activation is well-documented in severe disease[1], the effect of autoantibodies on disease progression is less well-defined. Here we use a high-throughput autoantibody discovery technique known as rapid extracellular antigen profiling[7] to screen a cohort of 194 individuals infected with SARS-CoV-2, comprising 172 patients with COVID-19 and 22 healthcare workers with mild disease or asymptomatic infection, for autoantibodies against 2,770 extracellular and secreted proteins (members of the exoproteome). We found that patients with COVID-19 exhibit marked increases in autoantibody reactivities as compared to uninfected individuals, and show a high prevalence of autoantibodies against immunomodulatory proteins (including cytokines, chemokines, complement components and cell-surface proteins). We established that these autoantibodies perturb immune function and

mögliche Kombinationen 537.380 (x39)

Wang et al., Nature 595 (2021) 283

Induktion von Autoimmunreaktionen

Autoimmunity is a hallmark of post-COVID syndrome

Manuel Rojas[1], Yhojan Rodríguez[1,2], Yeny Acosta-Ampudia[1], Diana M. Monsalve[1], Chengsong Zhu[3], Quan-Zhen Li[3], Carolina Ramírez-Santana[1] and Juan-Manuel Anaya[1,2*]

Abstract

Autoimmunity has emerged as a characteristic of the post-COVID syndrome (PCS), which may be related to sex. In order to further investigate the relationship between SARS-CoV-2 and autoimmunity in PCS, a clinical and serological assessment on 100 patients was done. Serum antibody profiles against self-antigens and infectious agents were evaluated by an antigen array chip for 116 IgG and 104 IgM antibodies. Thirty pre-pandemic healthy individuals were included as a control group. The median age of patients was 49 years (IQR: 37.8 to 55.3). There were 47 males. The median post-COVID time was 219 (IQR: 143 to 258) days. Latent autoimmunity and polyautoimmunity were found in 83% and 62% of patients, respectively. Three patients developed an overt autoimmune disease. IgG antibodies against IL-2, CD8B, and thyroglobulin were found in more than 10% of the patients. Other IgG autoantibodies, such as anti-interferons, were positive in 5–10% of patients. Anti-SARS-CoV-2 IgG antibodies were found in > 85% of patients and were positively correlated with autoantibodies, age, and body mass index (BMI). Few autoantibodies were influenced by age and BMI. There was no effect of gender on the over- or under-expression of autoantibodies. IgG anti-IFN-λ antibodies were associated with the persistence of respiratory symptoms. In summary, autoimmunity is characteristic of PCS, and latent autoimmunity correlates with humoral response to SARS-CoV-2.

Keywords: Post-COVID syndrome, Post-COVID, Long COVID, Post-acute COVID-19, COVID-19, Autoimmunity, Autoantibodies, Latent autoimmunity, Antigen array

mögliche Kombinationen 22.000 (x1,6)

Rojas et al., Journal of Translational Medicine 20 (2022) 129

Induktion von Autoimmunreaktionen

Table 1 Main IgG autoantibodies found in patients with post-COVID syndrome

Anti-Tg	14 (14.0%)	Anti-Ku (p70/p80)	6 (6.0%)
Anti-CENP-B, CENP-A	9 (9.0%)	Anti-MDA5	6 (6.0%)
Anti-IFN-αF	9 (9.0%)	Anti-PL-7	6 (6.0%)
Anti-IFN-α4B	8 (8.0%)	Anti-U1-snRNP (68, A, C, B)	6 (6.0%)
Anti-IFN-αD	8 (8.0%)	Anti-Histone	5 (5.0%)
Anti-IFN-αI	8 (8.0%)	Anti-IFN-αG	5 (5.0%)
Anti-IFN-αJ1	8 (8.0%)	Anti-IFN-β, IFN-β1	5 (5.0%)
Anti-GAD65	7 (7.0%)	Anti-PM/Scl75	5 (5.0%)
Anti-IFN-αC	7 (7.0%)	Anti-CD8B	18 (18.0%)
Anti-IFN-αH2	7 (7.0%)	Anti-IL-2	10 (10.0%)
Anti-IFN-αWa	7 (7.0%)	Anti-Collagen V	8 (8.0%)
Anti-IFN- ω	7 (7.0%)	Anti-IFN-αA	8 (8.0%)
Anti-La/SS-B	7 (7.0%)	Anti-Aldolase C	6 (6.0%)
Anti-IFN-αB2	6 (6.0%)	Anti-IL-17F	6 (6.0%)
Anti-IFN-αK	6 (6.0%)	Anti-SRP54	6 (6.0%)
Anti- IFN-λ1	6 (6.0%)	Anti-PTH	5 (5.0%)

Rojas et al., Journal of Translational Medicine 20 (2022) 129

Induktion von Autoimmunreaktionen

Clin Chem Lab Med 2022; 60(7): 1116–1123 DE GRUYTER

Antigona Ulndreaj, Mingyue Wang, Salvia Misaghian, Louis Paone, George B. Sigal, Martin Stengelin, Christopher Campbell, Logan R. Van Nynatten, Antoninus Soosaipillai, Atefeh Ghorbani, Anu Mathew, Douglas D. Fraser, Eleftherios P. Diamandis* and Ioannis Prassas*

Patients with severe COVID-19 do not have elevated autoantibodies against common diagnostic autoantigens

Methods: Acute and post-acute serum (from 1 to 26 ICU days) was collected from 18 ICU COVID-19-positive patients at three to six time points; 18 ICU COVID-19-negative patients (sampled on ICU day 1 and 3); 21 ward COVID-19-positive patients (sampled on hospital day 1 and 3); and from 59 healthy uninfected controls deriving from two cohorts. Levels of IgG autoantibodies against 23 autoantigens, commonly used for autoimmune disease diagnosis, were measured in serum samples using MSD® U-PLEX electrochemiluminescence technology (MSD division Meso Scale Discovery®), and results were compared between groups.

Results: There were no significant elevations of autoantibodies for any of the markers tested in patients with severe COVID-19.

Conclusions: Sample collections at longer time points should be considered in future studies, for assessing the possible development of autoantibody responses following infection with SARS-CoV-2.

mögliche Kombinationen: 414 (x0,03)

Ulndreaj et al., Clin Chem Lab Med 60 (2022) 1116-23

Post-akutes Infektionssyndrom

nature medicine

REVIEW ARTICLE

https://doi.org/10.1038/s41591-022-01810-6

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Unexplained post-acute infection syndromes

Jan Choutka[1]✉, Viraj Jansari[2], Mady Hornig[3] and Akiko Iwasaki[2,4,5,6]✉

SARS-CoV-2 is not unique in its ability to cause post-acute sequelae; certain acute infections have long been associated with an unexplained chronic disability in a minority of patients. These post-acute infection syndromes (PAISs) represent a substantial healthcare burden, but there is a lack of understanding of the underlying mechanisms, representing a significant blind spot in the field of medicine. The relatively similar symptom profiles of individual PAISs, irrespective of the infectious agent, as well as the overlap of clinical features with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), suggest the potential involvement of a common etiopathogenesis. In this Review, we summarize what is known about unexplained PAISs, provide context for post-acute sequelae of SARS-CoV-2 infection (PASC), and delineate the need for basic biomedical research into the underlying mechanisms behind this group of enigmatic chronic illnesses.

Table 1 | Overview of unexplained PAISs associated with documented infections

Pathogen	Name of PAIS
Viral pathogens	
SARS-CoV-2	Post-acute sequelae of SARS-CoV-2 infection (PASC) Post-acute COVID-19 syndrome (PACS) Long COVID
Ebola	Post-Ebola syndrome (PES) Post-Ebola virus disease syndrome (PEVDS)
Dengue	Post-dengue fatigue syndrome (PDFS)
Polio	Post-polio syndrome (PPS)
SARS	Post-SARS syndrome (PSS)
Chikungunya	Post-chikungunya chronic inflammatory rheumatism (pCHIK-CIR) Post-chikungunya disease
EBV	No name
West Nile virus	No name
Ross River virus[a]	No name
Coxsackie B[a]	No name
H1N1/09 influenza[a,b]	No name
VZV[a,b]	No name
Non-viral pathogens	
Coxiella burnetii	Q fever fatigue syndrome (QFS)
Borrelia[c]	Post-treatment Lyme disease syndrome (PTLDS)
Giardia lamblia[a,d]	No name

Choutka et al., Nature Medicine 28 (2022) 911-23

Post-akutes Infektionssyndrom

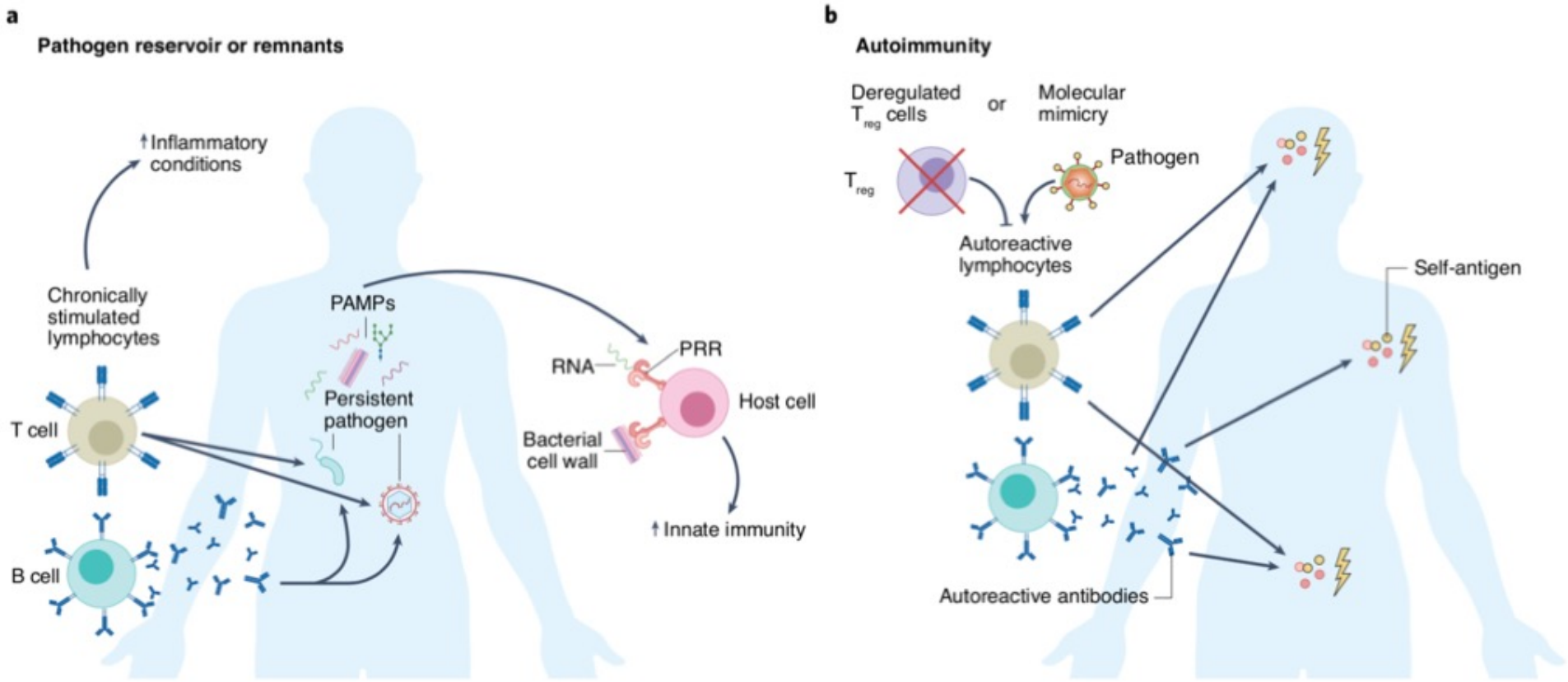
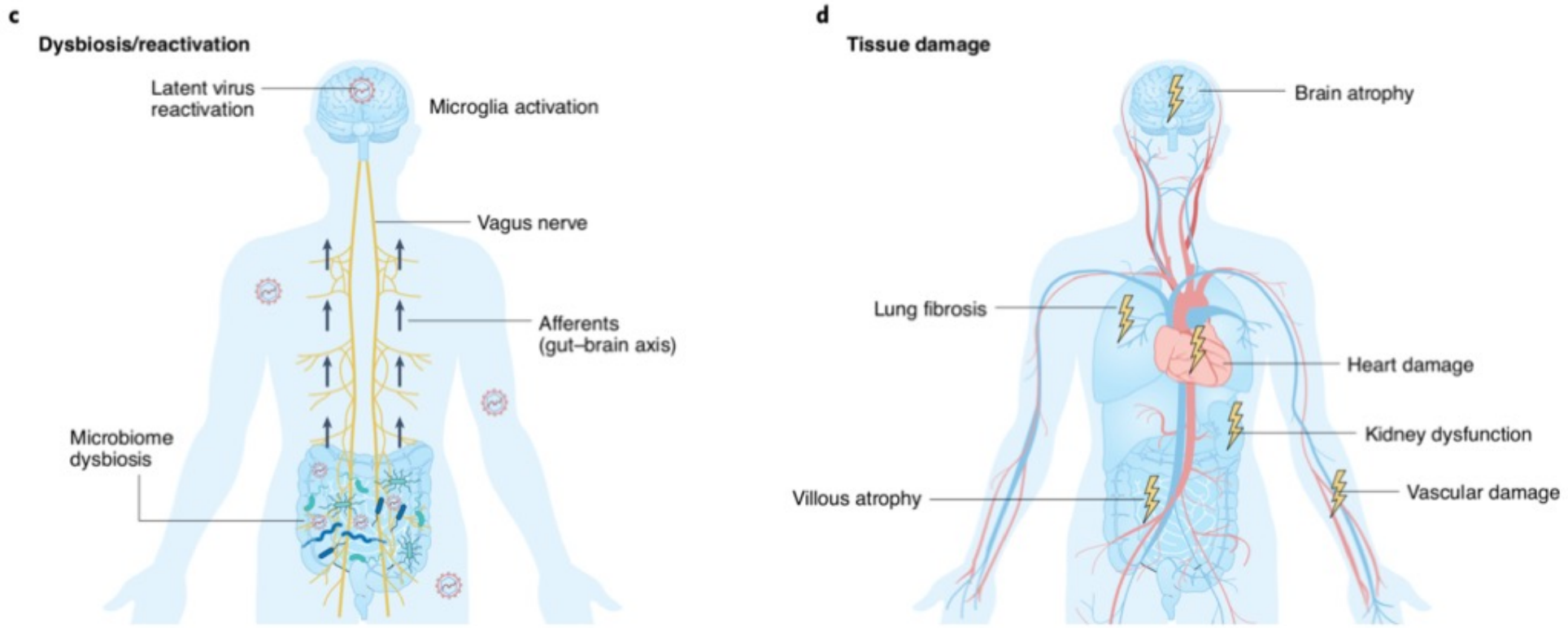


Fig. 2 | Commonly suggested biomedical hypotheses explaining PAISs. a, Possible pathogenic mechanisms might include chronic stimulation of the immune system as a result of persistent infection or persistent unviable pathogen structures. **b**, Alternative modes of immune activation might involve targeting self-antigens either due to infection-triggered impairment of regulatory T (T_{reg}) cell function, molecular mimicry, or other mechanisms. **c**, Chronic pathology might also result from dysregulation of the microbiota–gut–brain axis. **d**, Some features of PAISs could be explained by permanent organ damage. These processes are not mutually exclusive and could exist in combination or be pronounced with varied intensity in different PAIS subsets. Created with BioRender.com.

Choutka et al., Nature Medicine 28 (2022) 911-23

Post-akutes Infektionssyndrom



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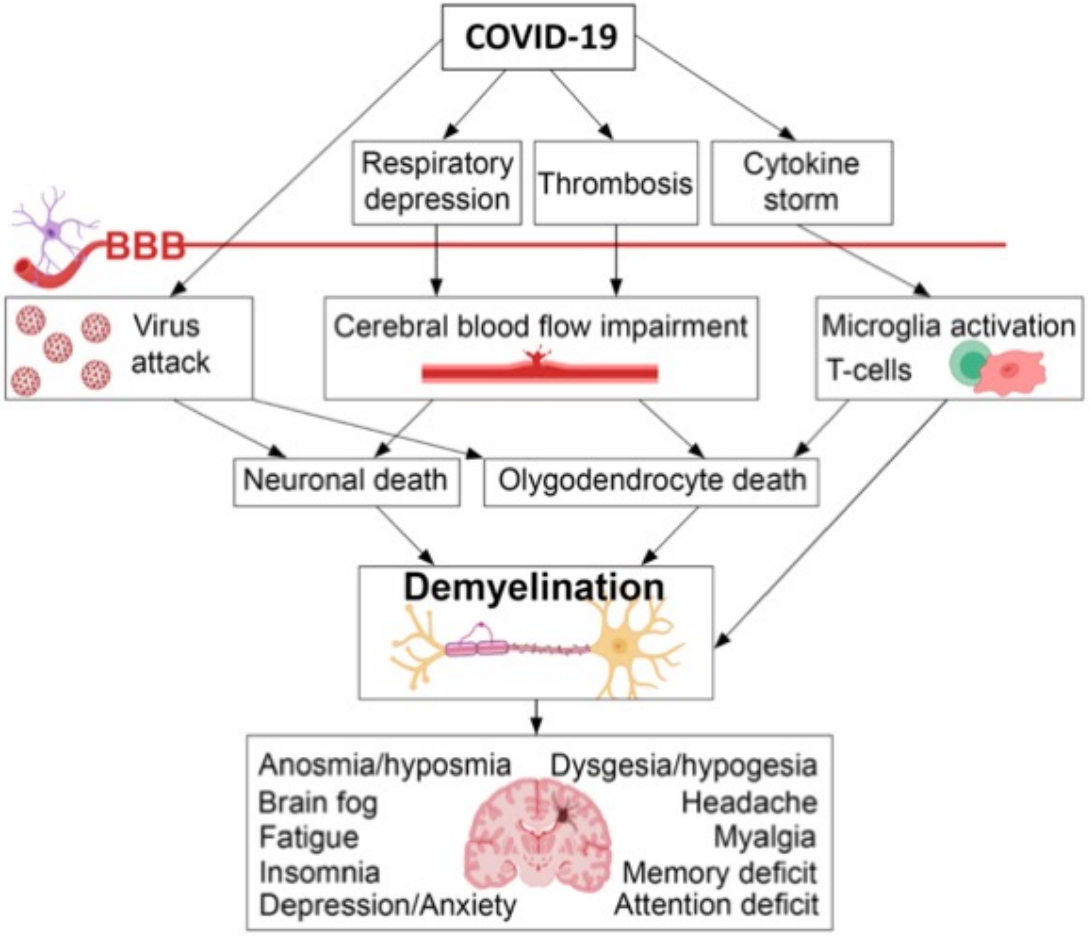
Choutka et al., Nature Medicine 28 (2022) 911-23

Long-Covid – neuronale & mentale Defekte

Review

Role of Demyelination in the Persistence of Neurological and Mental Impairments after COVID-19

Marina Y. Khodanovich [1,*], Daria A. Kamaeva [1,2] and Anna V. Naumova [1,3]



Khodanovich et al., Int J Mol Sci 23 (2022) 11291

Long-Covid – neuronale & mentale Defekte

Neuron

CellPress
OPEN ACCESS

Perspective

The neurobiology of long COVID

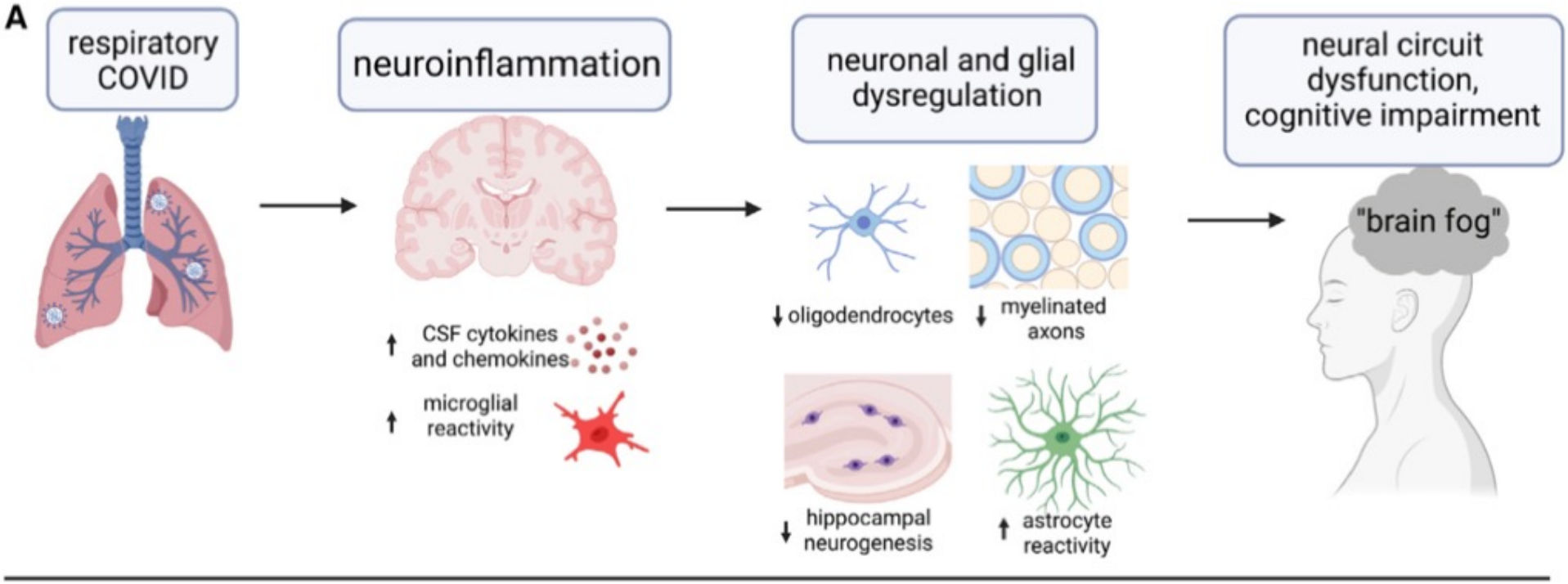
Michelle Monje[1,2,*] and Akiko Iwasaki[3,4,*]
[1]Department of Neurology, Stanford University, Stanford, CA 94305, USA
[2]Howard Hughes Medical Institute, Stanford University, USA
[3]Department of Immunobiology, Yale University, New Haven, CT 06520, USA
[4]Howard Hughes Medical Institute, Yale University, USA
*Correspondence: mmonje@stanford.edu (M.M.), akiko.iwasaki@yale.edu (A.I.)
https://doi.org/10.1016/j.neuron.2022.10.006

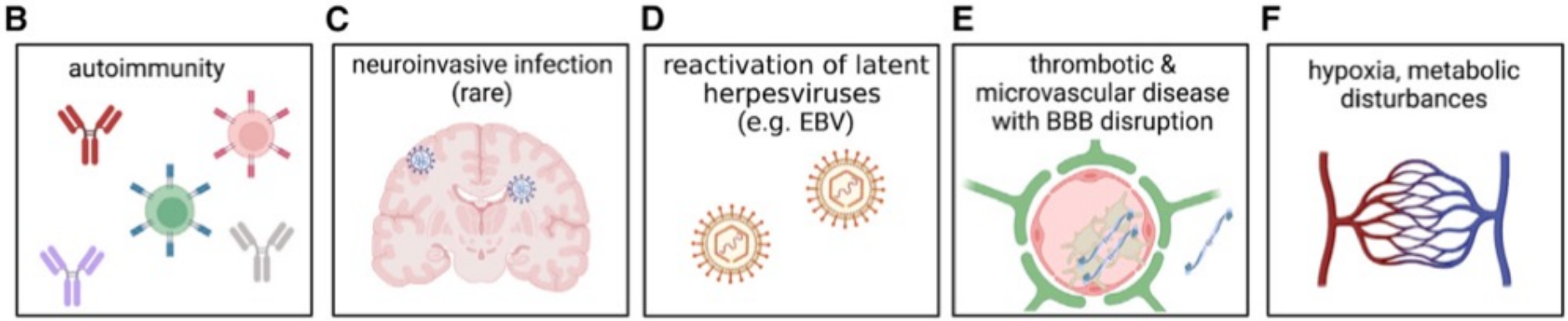
SUMMARY

Persistent neurological and neuropsychiatric symptoms affect a substantial fraction of people after COVID-19 and represent a major component of the post-acute COVID-19 syndrome, also known as long COVID. Here, we review what is understood about the pathobiology of post-acute COVID-19 impact on the CNS and discuss possible neurobiological underpinnings of the cognitive symptoms affecting COVID-19 survivors. We propose the chief mechanisms that may contribute to this emerging neurological health crisis.

Monje & Iwasaki, Neuron 110 (2022) PMID 36288726

Long-Covid – neuronale & mentale Defekte





Monje & Iwasaki, Neuron 110 (2022) PMID 36288726

Long-Covid – kardiovaskuläre Schäden

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-022-01689-3

Check for updates

OPEN

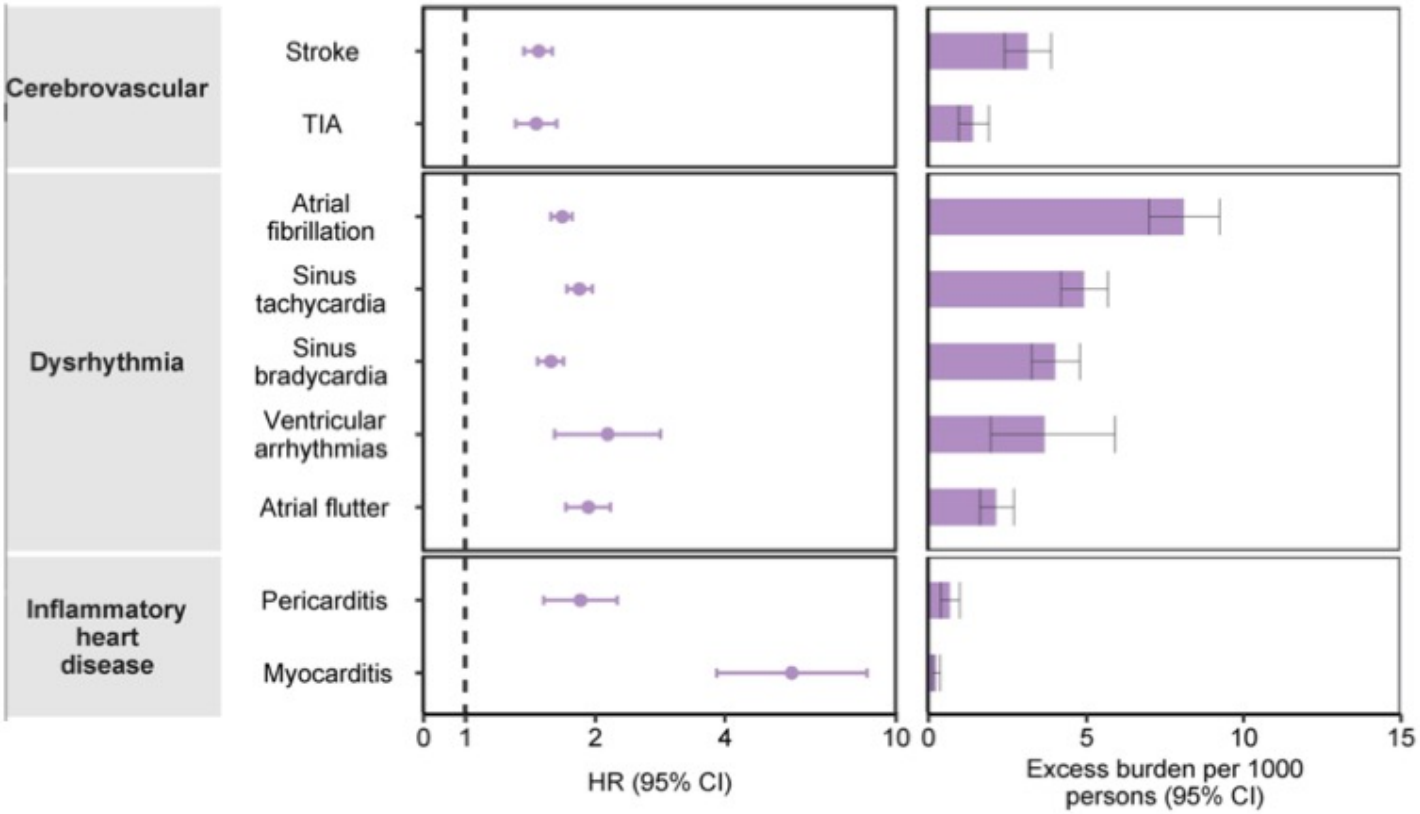
Long-term cardiovascular outcomes of COVID-19

Yan Xie[1,2,3], Evan Xu[1,4], Benjamin Bowe[1,2] and Ziyad Al-Aly[1,2,5,6,7] ✉

The cardiovascular complications of acute coronavirus disease 2019 (COVID-19) are well described, but the post-acute cardiovascular manifestations of COVID-19 have not yet been comprehensively characterized. Here we used national healthcare databases from the US Department of Veterans Affairs to build a cohort of 153,760 individuals with COVID-19, as well as two sets of control cohorts with 5,637,647 (contemporary controls) and 5,859,411 (historical controls) individuals, to estimate risks and 1-year burdens of a set of pre-specified incident cardiovascular outcomes. We show that, beyond the first 30 d after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease spanning several categories, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease. These risks and burdens were evident even among individuals who were not hospitalized during the acute phase of the infection and increased in a graded fashion according to the care setting during the acute phase (non-hospitalized, hospitalized and admitted to intensive care). Our results provide evidence that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are substantial. Care pathways of those surviving the acute episode of COVID-19 should include attention to cardiovascular health and disease.

Xie et al., Nature Medicine 28 (2022) 583-90

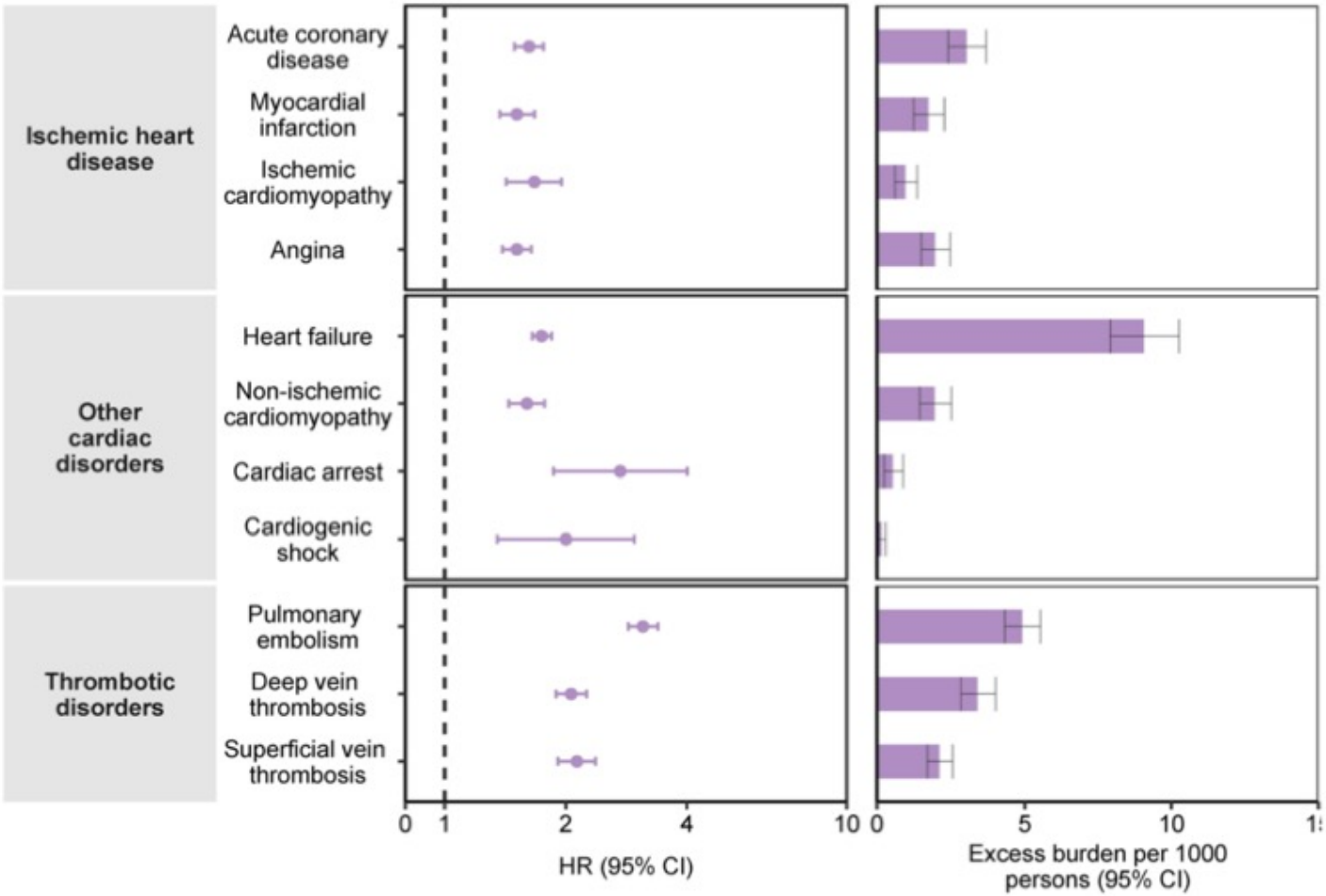
Long-Covid – kardiovaskuläre Schäden



Extended Data Fig. 2 | Risks and 12-month burdens of incident post-acute COVID-19 cardiovascular outcomes in participants without any history of cardiovascular outcomes prior to COVID-19 exposure compared to the contemporary control cohort. Outcomes were ascertained 30 days after the COVID-19 positive test until the end of follow-up. COVID-19 cohort without any history of cardiovascular outcomes (N = 126,575) and contemporary control cohort without any history of cardiovascular outcomes (N = 5,010,542). Adjusted hazard ratios and 95% confidence intervals are presented. Length of the bar represents the excess burden per 1000 persons at 12 months and associated 95% confidence intervals are also shown. TIA, transient ischemic attack.

Xie et al.,, Nature Medicine 28 (2022) 583-90

Long-Covid – kardiovaskuläre Schäden



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Xie et al., Nature Medicine 28 (2022) 583-90

Long-Covid – Diabetes mellitus

Risks and burdens of incident diabetes in long COVID: a cohort study

Lancet Diabetes Endocrinol 2022; 10: 311–21

Published Online March 21, 2022

Yan Xie, Ziyad Al-Aly

Research in context

Evidence before this study

We searched PubMed for human studies published between Dec 1, 2019, and Sept 6, 2021, using terms "COVID-19", "SARS CoV-2" or "long COVID", and "diabetes", with no language restrictions. Small studies (<1000 people) limited to short follow-up periods (up to 3 months) showed that people with COVID-19 might be at increased risk of incident diabetes. A large-scale in-depth assessment of the risks and burdens of incident diabetes over a longer time horizon has not been done. In this study, we aimed to examine the post-acute risk and burden of diabetes in people who survived the first 30 days of SARS-CoV-2 infection.

Added value of this study

In this study involving 181 280 people with COVID-19, 4 118 441 contemporary controls, and 4 286 911 historical controls, we provide estimates of risks and 12-month burdens of incident diabetes outcomes. Our results suggest that beyond the first 30 days of infection, COVID-19 survivors exhibited increased risks and burdens of incident diabetes and antihyperglycaemic use. The risks and burdens were significant among those who were non-hospitalised and increased in a graded fashion according to the care setting of the acute phase of the disease (that is whether people were non-hospitalised, hospitalised, or admitted to intensive care during the acute phase of COVID-19). The risks and associated burdens were evident in comparisons versus both the contemporary control group and the historical control group.

Implications of all the available evidence

Altogether, there is evidence to suggest that beyond the acute phase of COVID-19, survivors might be at an increased risk of developing incident diabetes, and increased risk of incident antihyperglycemic use in the post-acute phase of the disease. Diabetes should be considered as a facet of the multifaceted long COVID syndrome. Post-acute care strategies of people with COVID-19 should integrate screening and management of diabetes.

Xie & Al-Aly, Lancet Diabetes Endocrinol 10 (2022) 311-21

Mögliche Long-Covid Pathomechanismen

Zusammenfassung

- Viele Hinweise auf mögliche Mechanismen gefunden.
- Persistenz von SARS-CoV-2 im Darm unwahrscheinlich, aber nicht ausgeschlossen.
- Genomische Integration von revers transkribierter SARS-CoV-2 DNA und dessen Expression nachgewiesen.
- Induktion von Auto-Antikörpern nachgewiesen; sehr vielfältig insbesondere auch gegen Cytokine und deren Rezeptoren.
- Post-akutes Infektionssyndrom analog zu andere Infektionskrankheiten offensichtlich bei SARS-CoV-2 sehr ausgeprägt.
- Mehrere Mechansimen offensichtlich an ZNS-Schädigung geteiligt.
- Zahlreiche Biomarker entdeckt.

Biomarker für Long-Covid - Labordiagnostik

SOLM-Biomarker nach Organmanifestation (1)

Herzbeteiligung

- hs kardiales Troponin
- NT-proBNP
- Myoglobin
- Herzmuskel Ak-Screening

Neurologisch Beteiligung

- anti-Acetylcholin-Rez. Ak
- anti-GABA Ak
- anti-NMDAR Ak
- anti-CASPR2 Ak
- anti-MOG AK
- anti-Myelin Ak
- anti-GAD Ak
- oligoklonale Banden
- Reiber Schema

Lungenbeteiligung

- pO2
- LDH

Leber-/Pankreas-Beteiligung

- AST
- ALT
- γGT
- AP
- Bilirubin
- Lipase und Pankreas-Amylase

Nierenbeteiligung

- Kreatinin / eGFR
- Harnstoff
- Urinstatus/Sediment
- ANCA-Screening

Biomarker für Long-Covid - Labordiagnostik

SOLM-Biomarker nach Organmanifestation (2)

Diabetes

- Glucose / HbA1c
- anti-Insulin Ak
- anti-GAD Ak und anti-IA2 Ak
- anti-Tyrosinphosphatase Ak

Chronisch Inflammation

- hsCRP
- TNFα, IL-1β
- löslicher IL2-Rezeptor
- ANA-Screening
- ds-DNS-Ak
- CCP-Ak
- Zirkulierende Immunkomplexe
- Lupus-Antikoagulans
- CK
- Rheumafaktor

EBV-Reaktivierung

- EBV-IgG/IgM
- EBV nuclear antigen 1 IgG
- EBV early antigen IgG
- EBV heterophile Ak
- T-Cellspot© EBV
- EBV-PCR

Hämatologie/Gerinnung

- Ferritin
- D-Dimere
- Thrombozyten
- Prothrombinzeit (Quick)
- aPTT
- anti-Annexin Ak
- anti-Cardiolipin Ak
- anti-β2 Glykoprotein AK

Ausblick

- Long-Covid erst seit 2 Jahren bekannt – daher ist die maximale Dauer und der langfristige Verlauf noch nicht bekannt.
- Da ständig neue Covid-19 Infektionen auftreten, wird es auch ständig neue Long-Covid Fälle geben.
- Ständig werden neue Erkenntnise publiziert, neue Pathomechanismen entdeckt.
- Daraus werden ständig neue Biomarker abgeleitet.
- Neue Biomarker werden auch ständig durch den Vergleich von Long-Covid-Fällen mit Vergleichskollektiven gefunden.
- Daher muß die Labordiagnostik ständig an die neuen Erkenntnisse angepaßt werden.
- Diagnostische Labore sollten selbst Studien koordinieren.

Ausblick

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-022-01840-0

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OPEN

Long COVID after breakthrough SARS-CoV-2 infection

Ziyad Al-Aly[1,2,3,4,5] ✉, Benjamin Bowe[1,2] and Yan Xie[1,2,6]

The post-acute sequelae of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection—also referred to as Long COVID—have been described, but whether breakthrough SARS-CoV-2 infection (BTI) in vaccinated people results in post-acute sequelae is not clear. In this study, we used the US Department of Veterans Affairs national healthcare databases to build a cohort of 33,940 individuals with BTI and several controls of people without evidence of SARS-CoV-2 infection, including contemporary ($n = 4,983,491$), historical ($n = 5,785,273$) and vaccinated ($n = 2,566,369$) controls. At 6 months after infection, we show that, beyond the first 30 days of illness, compared to contemporary controls, people with BTI exhibited a higher risk of death (hazard ratio (HR) = 1.75, 95% confidence interval (CI): 1.59, 1.93) and incident post-acute sequelae (HR = 1.50, 95% CI: 1.46, 1.54), including cardiovascular, coagulation and hematologic, gastrointestinal, kidney, mental health, metabolic, musculoskeletal and neurologic disorders. The results were consistent in comparisons versus the historical and vaccinated controls. Compared to people with SARS-CoV-2 infection who were not previously vaccinated ($n = 113,474$), people with BTI exhibited lower risks of death (HR = 0.66, 95% CI: 0.58, 0.74) and incident post-acute sequelae (HR = 0.85, 95% CI: 0.82, 0.89). Altogether, the findings suggest that vaccination before infection confers only partial protection in the post-acute phase of the disease; hence, reliance on it as a sole mitigation strategy may not optimally reduce long-term health consequences of SARS-CoV-2 infection. The findings emphasize the need for continued optimization of strategies for primary prevention of BTI and will guide development of post-acute care pathways for people with BTI.

Al-Aly et al., Nature Medicine 28 (2022) 1461-7

Ausblick

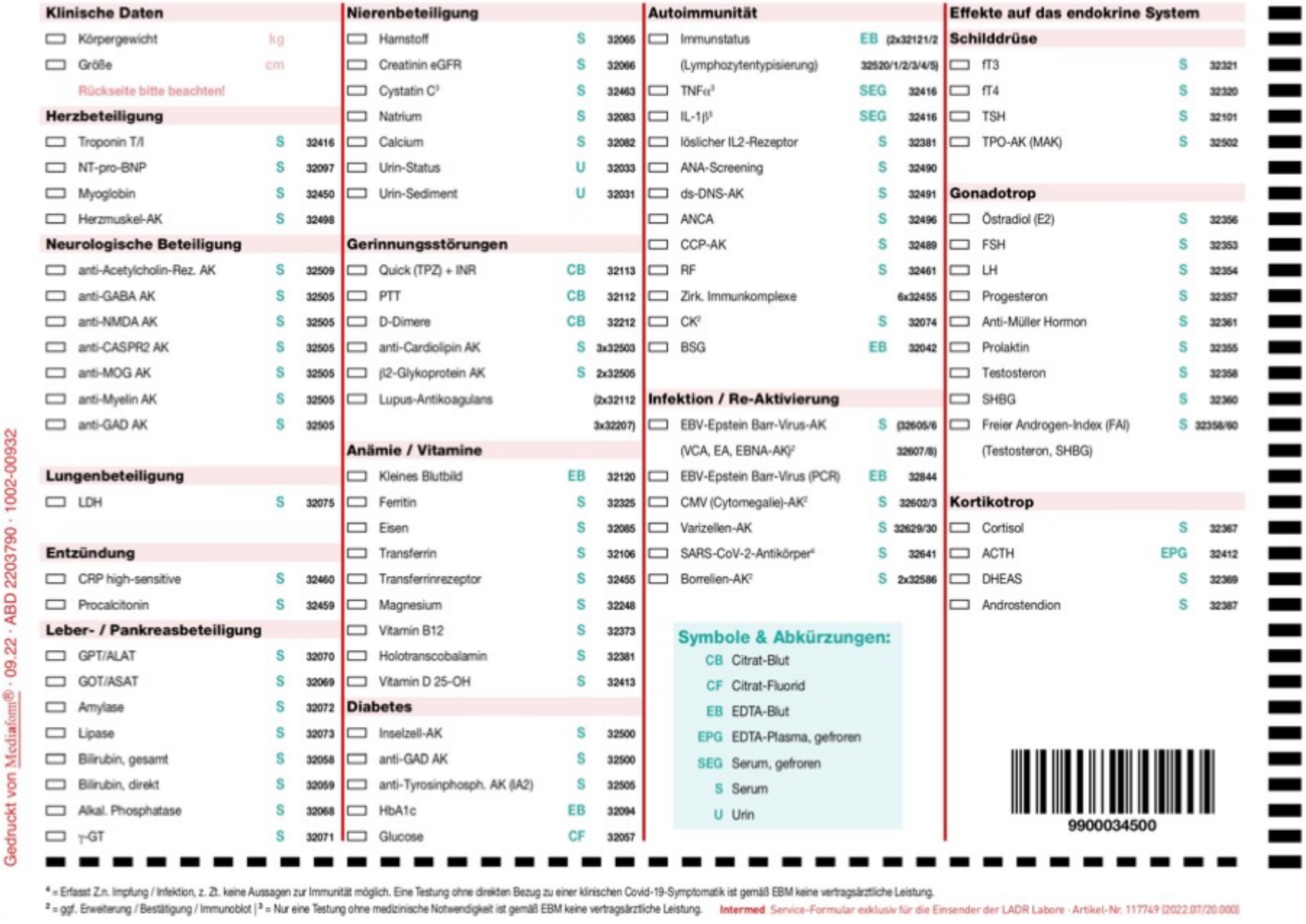
Interpretation der Ergebnisse der Studie von Al-Aly et al.:

- Die derzeit verfügbaren Impfungen schützen vor schweren Verläufen, aber leider nicht vor Covid-19 Infektionen.
- Covid-19 wird inzwischen von vielen Experten nicht mehr als Pandemie, sondern Endemie bezeichnet; SARS-CoV-2 kann nicht eliminiert werden.
- Es ist daher wahrscheinlich, daß sich letztlich ein sehr hoher Anteil der Bevölkerung, einschließlich der vollständig Geimpften, infizieren wird.
- Ohne Impfung führen ca. 10% bis 20% der Infektionen zu Long-Covid.
- Long-Covid betrifft alle Altersgruppen.
- Bei Break-through-Infektionen (BTI) von vollständig Geimpften beträgt die OR für Long-Covid im Vergleich zu Ungeimpften laut Al-Aly et al. 66%.
- Folglich muß auch bei vollständiger Impfung der gesamten Bevölkerung langfristig mit einer Inzidenz von Long-Covid von ca. 6% bis 13% gerechnet werden (die Prävalenz kann derzeit nicht abgeschätzt werden).

Gesamt-Zusammenfassung

- Long-Covid ist eine große Herausforderung für unser Gesundheitssystem und letztlich auch die gesamte Gesellschaft, einschließlich Arbeitsmarkt.
- Es ist mittelfristig mit einer weiteren Zunahme der Prävalenz von Long-Covid zu rechnen, da ständig neue Fälle hinzukommen und die Heilungserfolge noch nicht genau abgeschätzt werden können.
- Die klinische Diagnostik ist schwierig, weil nur der zeitliche Zusammenhang mit einer akuten Covid-19 Erkrankung eindeutig ist und sehr unterschiedliche Manifestationen beobachtet werden.
- Eine gute Labordiagnostik kann die klinische Diagnosestellung verbessern und auch zur Kontrolle des Therapieerfolgs beeitragen. Leider wurde bisher noch kein hochspezifischen Biomarker für Long-Covid entdeckt, so daß mehrere Marker kombiniert werden müssen.
- Es werden ständig neuer Marker entdeckt und damit die Labordiagnostik kontinuierlich verbessert.
- Weitere Studien werden dringend benötigt, um die Diagnostik und Therapie von Long-Covid zu verbessern.

Labordiagnostik von Long-Covid bei LADR



Klinische Daten

Körpergewicht	kg	
Größe	cm	
Rückseite bitte beachten!		

Herzbeteiligung

Troponin T/I	S	32416
NT-pro-BNP	S	32097
Myoglobin	S	32450
Herzmuskel-AK	S	32498

Neurologische Beteiligung

anti-Acetylcholin-Rez. AK	S	32509
anti-GABA AK	S	32505
anti-NMDA AK	S	32505
anti-CASPR2 AK	S	32505
anti-MOG AK	S	32505
anti-Myelin AK	S	32505
anti-GAD AK	S	32505

Lungenbeteiligung

LDH	S	32075

Entzündung

CRP high-sensitive	S	32460
Procalcitonin	S	32459

Leber- / Pankreasbeteiligung

GPT/ALAT	S	32070
GOT/ASAT	S	32069
Amylase	S	32072
Lipase	S	32073
Bilirubin, gesamt	S	32058
Bilirubin, direkt	S	32059
Alkal. Phosphatase	S	32068
γ-GT	S	32071

Nierenbeteiligung

Harnstoff	S	32065
Creatinin eGFR	S	32066
Cystatin C[3]	S	32463
Natrium	S	32083
Calcium	S	32082
Urin-Status	U	32033
Urin-Sediment	U	32031

Gerinnungsstörungen

Quick (TPZ) + INR	CB	32113
PTT	CB	32112
D-Dimere	CB	32212
anti-Cardiolipin AK	S	3x32503
β2-Glykoprotein AK	S	2x32505
Lupus-Antikoagulans		(2x32112 3x32207)

Anämie / Vitamine

Kleines Blutbild	EB	32120
Ferritin	S	32325
Eisen	S	32085
Transferrin	S	32106
Transferrinrezeptor	S	32455
Magnesium	S	32248
Vitamin B12	S	32373
Holotranscobalamin	S	32381
Vitamin D 25-OH	S	32413

Diabetes

Inselzell-AK	S	32500
anti-GAD AK	S	32500
anti-Tyrosinphosph. AK (IA2)	S	32505
HbA1c	EB	32094
Glucose	CF	32057

Autoimmunität

Immunstatus	EB	(2x32121/2
(Lymphozytentypisierung)		32520/1/2/3/4/5)
TNFα[3]	SEG	32416
IL-1β[3]	SEG	32416
löslicher IL2-Rezeptor	S	32381
ANA-Screening	S	32490
ds-DNS-AK	S	32491
ANCA	S	32496
CCP-AK	S	32489
RF	S	32461
Zirk. Immunkomplexe		6x32455
CK[2]	S	32074
BSG	EB	32042

Infektion / Re-Aktivierung

EBV-Epstein Barr-Virus-AK	S	(32605/6
(VCA, EA, EBNA-AK)[2]		32607/8)
EBV-Epstein Barr-Virus (PCR)	EB	32844
CMV (Cytomegalie)-AK[2]	S	32602/3
Varizellen-AK	S	32629/30
SARS-CoV-2-Antikörper[4]	S	32641
Borrelien-AK[2]	S	2x32586

Symbole & Abkürzungen:

CB Citrat-Blut
CF Citrat-Fluorid
EB EDTA-Blut
EPG EDTA-Plasma, gefroren
SEG Serum, gefroren
S Serum
U Urin

Effekte auf das endokrine System

Schilddrüse

fT3	S	32321
fT4	S	32320
TSH	S	32101
TPO-AK (MAK)	S	32502

Gonadotrop

Östradiol (E2)	S	32356
FSH	S	32353
LH	S	32354
Progesteron	S	32357
Anti-Müller Hormon	S	32361
Prolaktin	S	32355
Testosteron	S	32358
SHBG	S	32360
Freier Androgen-Index (FAI)	S	32358/60
(Testosteron, SHBG)		

Kortikotrop

Cortisol	S	32367
ACTH	EPG	32412
DHEAS	S	32369
Androstendion	S	32387

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[4] = Erfasst Z.n. Impfung / Infektion, z. Zt. keine Aussagen zur Immunität möglich. Eine Testung ohne direkten Bezug zu einer klinischen Covid-19-Symptomatik ist gemäß EBM keine vertragsärztliche Leistung.
[2] = ggf. Erweiterung / Bestätigung / Immunoblot | [3] = Nur eine Testung ohne medizinische Notwendigkeit ist gemäß EBM keine vertragsärztliche Leistung. Intermed Service-Formular exklusiv für die Einsender der LADR Labore · Artikel-Nr. 117749 (2022.07/20.000)

Vielen Dank

für Ihre Aufmerksamkeit