

What causes COVID deaths?



Average time to death in COVID patients

- Australian and Chinese studies show that the median time to death in COVID is around 18 days. This broadly agrees with UK ONS and global data.
- This is long after the viral phase (up to 7 days) has passed, meaning that almost all the COVID deaths were in the post-viral phase.
- This means something other than the active virus killed many of these people.
- The main causes of death appear to be some form of pneumonia, blood clots, sepsis, multiple organ dysfunction syndrome (MODS), refractory hypoxemia/pulmonary fibrosis or ischaemic events. If correctly diagnosed, most are treatable.
- Sepsis is a potentially life-threatening condition where the body's response to infection triggers excessive inflammation that causes injury to its own tissues and organs, followed by suppression of the immune system. Unless promptly diagnosed and treated, sepsis can rapidly progress to multiple-organ failure.

(Marschner IC. Estimating age-specific COVID-19 fatality risk and time to death by comparing population diagnosis and death patterns: Australian data. BMC Med Res Methodol. 2021 Jun 21;21(1):126; https://www.telegraph.co.uk/news/2020/03/12/coronavirus-kills-average-185-days/; (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/928729/S0803_CO-CIN_-_Time_from_symptom_onset_until_death.pdf; https://ourworldindata.org/covid-deaths) ²



What is causing the severe and fatal outcomes in COVID-19? 1/3

- A review article by Drs Paul Marik and Pierre Kory (of the US Front Line COVID Critical Care Alliance (FLCCC) and others:
- Abstract: 'Based on clinical, proteomic, and genomic studies as well as autopsy data severe COVID-19 disease can be considered to be the connection of three basic pathologic processes, namely a pulmonary macrophage activation syndrome with uncontrolled inflammation, a complement-mediated endothelialitis together with a procoagulant state with a thrombotic microangiopathy.
- 'In addition, platelet activation with the release of serotonin and the activation and degranulation of mast cells contributes to the hyper-inflammatory state. Autoantibodies have been demonstrated in a large number of hospitalized patients which adds to the end-organ damage and pro-thrombotic state.'
- (Marik PE, A scoping review of the pathophysiology of COVID-19. Int J Immunopathol Pharmacol. 2021 Jan-Dec;35:20587384211048026)



And again in English...

Severe and fatal COVID-19 is a combination of:

- Inflammation of the lung
- Inflammation of the blood vessel lining, giving rise to excessive blood clotting and further inflammation
- Auto-antibodies attacking vital organs

i.e. immune system dysregulation



Other views of COVID-19 deaths being due to a hyperactivated immune system

- Dr Stephanie Seneff: "People are dying of the immune response to COVID, they're not dying from the virus. The virus is not killing them. It's the immune response to the virus that's killing them."
- "Our comprehensive analysis...revealed a broad misfiring of immune effectors in COVID-19
 patients...These results suggest that COVID-19 late stage pathology may be driven primarily by
 host immune responses to SARS-CoV-2." (Lucas C, et al. Longitudinal analyses reveal immunological
 misfiring in severe COVID-19. Nature. 2020 Aug;584(7821):463-469)
- "Hyperactivation of the host immune system during infection by SARS-CoV-2 is the leading cause of death in COVID-19 patients" (Ahmad T, et al. COVID-19: The Emerging Immunopathological Determinants for Recovery or Death. Front Microbiol. 2020 Dec 1;11:588409)
- Autopsy studies have noted that COVID-19 tissue damage and organ failure may be caused by an overactivated immune system instead of virus-mediated tissue damage.
- Other have suggested that severe covid appears to be a post-viral autoimmune attack on lung tissue, causing hypercoagulation, thrombosis and respiratory failure. Established autoimmunity and inflammatory conditions also predispose to severe COVID-19. (https://swprs.org/severe-covid-a-post-viral-autoimmune-attack/) 5

The implications of severe COVID being an immune system problem, not a viral problem

- If we caught COVID, UK government advice was to stay home and not go to hospital unless we had breathing difficulties – and even then, some people were still not taken into hospital!
- All the evidence presented here points to the critical importance of an early initial innate immune response, giving minimal inflammation, which in turn will generate early maturation of cytotoxic T cells. This is what will make the difference between mild and severe COVID.
- By the time the patient has developed breathing difficulties, it is far too late to make any immune system interventions, other than possibly corticosteroids.
- Therefore, a better strategy than late-stage treatment, when severe disease is already established, is to support the immune system prior to infection and in its early stages.
- Day 2 will talk about how we can do this.



What is causing the severe and fatal outcomes in COVID-19? 2/3

- 'It is widely, although incorrectly believed, that the pulmonary phase of COVID-19 is typical of ARDS [acute respiratory distress syndrome]. The pulmonary phase of COVID-19 has the features characteristic of an organizing pneumonia rather than that of classic ARDS.
- The radiographic features of COVID-19 are quite distinct and do not resemble the dependent air space consolidation...seen with classic ARDS.
- COVID-19 lung disease is characterized by a massive infiltration of macrophages with few neutrophils. In contrast, ARDS is a neutrophil mediated disease.
- The therapeutic implications of the distinction between COVID organizing pneumonia and ARDS is significant; it is likely that the standard treatment of ARDS....will be injurious to the COVID lung and cause the disease one is trying to prevent.'
- (Marik PE, A scoping review of the pathophysiology of COVID-19. Int J Immunopathol Pharmacol. 2021 Jan-Dec;35:20587384211048026)



And again in English...

- Because severe COVID causes respiratory distress, patients tend to be diagnosed with acute respiratory distress syndrome (ARDS).
- Drs Marik and Kory are saying that they consider that the clinical findings are more indicative of 'organising pneumonia'.
- Organising pneumonia is an inflammatory disorder of the lungs. It may be caused by infection, but also medication, autoimmune disease and other factors.
- It is important to distinguish between ARDS and pneumonia, because the treatment for ARDS will worsen patients who have pneumonia.



Evidence for secondary bacterial pneumonia killing COVID patients

- Many studies show that COVID patients die of secondary bacterial pneumonia.
- A study by Gao et al showed that secondary bacterial lung infection (i.e. pneumonia) was extremely common in patients with severe COVID-19, affecting almost half of those who required support from mechanical ventilation. This was a key driver of death in patients with COVID-19.
- The senior author on the Gao study commented: "Our data suggested that the mortality related to the virus itself is relatively low, but other things happen during the ICU stay, like secondary bacterial pneumonia."
- One study observed a mortality rate of 15.2% due to secondary bacterial infection.
- The most common type of infection observed among COVID-19 patients is ventilatorassociated pneumonia (VAP), followed by bacteraemia with sepsis.
- Furthermore, SARS-CoV-2 may not have been the virus driving the bacterial pneumonia which killed a PCR-positive patient. Suppose they tested positive for other respiratory viruses as well, such as this 'COVID' patient found with Legionnaires' disease (Subedi Y, Haas CJ. Legionella Coinfection in a Patient With COVID-10 Pneumonia. Cureus. 2021 Aug 21;13(8):e17356)? That would have complicated the picture! We shall never know now.



Secondary bacterial pneumonia references

- Gao CA, et al. Machine learning links unresolving secondary pneumonia to mortality in patients with severe pneumonia, including COVID-19. J Clin Invest. 2023 Jun 15;133(12):e170682; https://medicalxpress.com/news/2023-05-covid-patients-wasnt-cytokinestorm.html
- Farrell JM, et al. Causes and Consequences of COVID-19-Associated Bacterial Infections. Front Microbiol. 2021 Jul 20;12:682571
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- Dudoignon E, et al. Bacterial Pneumonia in COVID-19 Critically III Patients: A Case Series. Clin Infect Dis. 2021 Mar 1;72(5):905-906
- Shafran N, et al. Secondary bacterial infection in COVID-19 patients is a stronger predictor for death compared to influenza patients. Sci Rep. 2021 Jun 16;11(1):12703
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- Nag VL, Kaur N. Superinfections in COVID-19 Patients: Role of Antimicrobials. Dubai Medical Journal. 2021 May 4:81–90
- Rawson TM, et al. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis. 2020 Dec 3;71(9):2459-2468.
- Langford BJ, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect. 2020;26:1622–1629 10

Rachel Nicoll PhD. 2024

• Manohar P, et al. Secondary Bacterial Infections in Patients With Viral Pneumonia. Front Med (Lausanne). 2020 Aug 5;7:420



What is causing the severe and fatal outcomes in COVID-19? 3/3

<u>Conclusion</u>:

- '...During the first 6 months of the pandemic, the World Health Organization (WHO) and almost all national guidelines recommended a "supportive care only" strategy for the management of severe COVID-19.
- Based on our increased understanding of this disease, such therapeutic nihilism is no longer acceptable'.

(Marik PE, A scoping review of the pathophysiology of COVID-19. Int J Immunopathol Pharmacol. 2021 Jan-Dec;35:20587384211048026)



From the Arkmedic blog

- Arkmedic suggests that some of the UK COVID deaths in 2020 were due to patients with bacterial pneumonia <u>not</u> being given antibiotics.
- He extracted the data from openprescribing.net and found that antibiotic prescribing suddenly disappeared in April 2020 when there was a huge spike in COVID deaths.
- In a secondary bacterial infection following a respiratory virus, antibiotics given early are normally quite effective.
- He points out that if it were not for the positive PCR test, antibiotics would likely have been given.
 (https://arkmedic.substack.com/p/there-was-no-virus)



Data extracted from openprescribing.net and modelled based on previous years' average prescribing from 2017-2019. 12



More from the Arkmedic blog

- The protocol for patients with the 2 other serious coronaviruses, SARS-CoV-1 and MERS, specifies antibiotic therapy to be prescribed by GPs, even before a coronavirus diagnosis (https://pubmed.ncbi.nlm.nih.gov/14992536/)
- Sadly for many COVID patients with secondary bacterial pneumonia, no-one learned these lessons from other serious coronaviruses.

(https://arkmedic.substack.com/p/there-was-no-virus)



More from the Arkmedic blog

The COVID test pathway to death.





Dr Anthony Fauci's 2008 paper

- Fauci et al examined cause of death in various viral influenza pandemics.
- Conclusions: 'If severe pandemic influenza is largely a problem of viralbacterial copathogenesis, pandemic planning needs to go beyond addressing the viral cause alone'. This involves:
- 'Prevention, diagnosis, prophylaxis, and treatment of secondary bacterial pneumonia, as well as stockpiling of antibiotics and bacterial vaccines, should also be high priorities for pandemic planning.' (Morens DM, et al. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. J Infect Dis. 2008 Oct 1;198(7):962-70)
- Did we never stockpile the antibiotics?
- Or did we just never think to use them because COVID was not influenza, even though the cause of death (secondary bacterial pneumonia) was the same?



What did NICE Guidelines say?

Professors Martin Neil and Norman Fenton and Dr Jonathan Engler have unearthed a NICE Guideline from 3 April 2020 (since replaced) for managing suspected or confirmed pneumonia, which states:

4.5 As COVID-19 pneumonia is caused by a virus, antibiotics are ineffective.

4.6 **Do not offer an antibiotic for treatment or prevention of pneumonia if:**

- COVID-19 is likely to be the cause and
- symptoms are mild.

Inappropriate antibiotic use may reduce availability if used indiscriminately, and broad-spectrum antibiotics in particular may lead to Clostridioides difficile infection and antimicrobial resistance.'

It's as though they have never heard of secondary bacterial pneumonia!

(https://web.archive.org/web/20200411192035/https://www.nice.org.uk/guidance/ng165/chapter/4-Managing-suspected-or-confirmed-pneumonia) Rachel Nicoll PhD, 2024



And the outcome....

- The PCR test was rarely accompanied by an in-person doctor's assessment, with a stethoscope to listen to the patient's chest, which might has helped determine whether a bacterial infection had set in.
- Fortunately for a few elderly patients, physicians in Toledo, Spain, defied the mainstream guidance and administered antibiotics to patients, mean age 85, already in care homes between March and April 2020. This resulted in zero hospitalisations and zero deaths. (Morán Blanco JI, et al. Antihistamines and azithromycin as a treatment for COVID-19 on primary health care - A retrospective observational study in elderly patients. Pulm Pharmacol Ther. 2021 Apr;67:101989)
- Bacterial infections can cause sepsis, the number one cause of death worldwide. Antibiotics
 are unequivocally needed for sepsis.
- A Canadian paper pointed out that sepsis likely caused the organ failure commonly seen in COVID deaths. 'The pandemic we've all been living through is actually a pandemic of sepsis due to COVID-related pneumonia. Everybody who dies of COVID actually dies of sepsis and pneumonia. Everybody.' (https://helpstpauls.com/promise/2023/septic-shock-research/)
- Sepsis has also been identified as a major contributor in influenza deaths.



What is severe COVID: summary

- The median time to death in COVID is around 18 days. Because this is long after the viral phase (up to 7 days) has passed, this means that most COVID deaths were in the post-viral phase.
- This means something other than the active virus killed many of these people.
- Evidence suggests that likely causes of death may be:
 An immune system over-reaction
 Secondary bacterial pneumonia or sepsis
- This has implications for treatment, as both can be successfully treated if it is initiated sufficiently early. ONS data indicates that COVID antibiotic usage had dropped to zero during peak COVID deaths, in line with NICE guidance.