PULSE EXPERIENTIAL TEAM ASSIGNMENT

Link to Canva/Digital File: https://canva.link/g3klc9vklwbr6zx

1. Title of your PULSE experiential assignment. *Provide a creative and informative title.*
Title: **COVID Uncovered:** *Pathology, etiology, pathogenesis, transmission, outcomes and lab medicine behind the COVID-19 Pandemic.*
2. Please summarize your PULSE experiential assignment (max 300 words). *Provide a non-technical (lay) summary of your PULSE assignment. Prompts to think about: What is the topic? What is the format? Why did you choose this topic and format? The summary for lay audience is a brief and accessible summary of the assignment that is used to explain complex ideas, technical writing and scientific terms to people who do not have prior knowledge of the subject (e.g., high school science level). This summary should include the importance, impact, and content of your assignment to a broader audience.* *[Team 23 is an example of an informative lay summary.]*
Our PULSE experiential assignment focuses on COVID-19 and explains how this disease develops in the body, from the moment the virus enters a person's cells to the point where it can cause serious complications. We created an educational pathology textbook called COVID-19 Uncovered, organized into chapters on viral entry and mechanisms of infection, spread through the body and immune response, disease outcomes and opportunistic infections, and diagnostics, lab medicine, and therapies. We chose this topic because COVID-19 affected people around the world, yet many people still do not understand why it can be mild in some individuals but severe or life threatening in others. We chose the textbook format because it allowed us to present a complex medical topic in clear sections that build on one another and make the information easier to follow. Our goal was to make scientific ideas understandable for a general audience by explaining them in a logical and accessible way. This assignment is important because it helps readers understand how COVID-19 affects the lungs and immune system, why some people are at greater risk of severe disease, and how diagnosis and treatment connect to what is happening inside the body. By creating this resource, we hope to improve public understanding of COVID-19 and show how pathology can help explain real world health issues in a meaningful and approachable way.
3. Provide up to 6 keywords relevant to your PULSE experiential assignment. *3-6 keywords are ideal.*
COVID-19, SARS-CoV-2, Viral Entry, Immune Response, Disease Outcomes, Diagnostics and Lab Medicine

4. Identify the course topic with which your PULSE assignment most aligns.
Refer to the various topics outlined under 'Course content and Schedule' in the syllabus (e.g. Inflammation).

Section B: Infectious Diseases

5. What are the learning outcomes?
There should be a minimum of 2 learning outcomes for your assignments. For further information on learning outcomes, the Centre for Teaching and Learning offers information: https://teaching.uwo.ca/curriculum/coursedesign/learning-outcomes.html

1) Explain the structure of SARS-CoV-2 and how its components contribute to host cell recognition and infection.

2) Describe how SARS-CoV-2 enters host cells, including the roles of ACE2, the spike protein, furin, TMPRSS2, membrane fusion, and early viral replication.

3) Trace the progression of COVID-19 from infection in the upper airway to spread into the lower respiratory tract and alveoli.

4) Analyze how innate and adaptive immune responses, including interferon signaling, antibodies, and T cells, influence disease severity and recovery.

5) Interpret how severe COVID-19 leads to diffuse alveolar damage, hypoxemia, endothelial dysfunction, thrombosis, and systemic complications.

6) Apply knowledge of COVID-19 pathogenesis to understand how diagnostics, lab medicine, therapies, and vaccination are used at different stages of disease.

6. Why did the team select the chosen topic and the medium? How will the topic and medium of choice help learners?

Our team selected COVID-19 because it remains one of the most significant infectious diseases of the modern era and continues to shape healthcare, scientific understanding, and public life. It was also a valuable topic to explore because it was not previously covered in this course section. As students who lived through the pandemic, we wanted to better understand the pathology behind it and present that knowledge in a way that is accurate, relevant, and accessible. Our textbook, *COVID-19 Uncovered*, follows the progression of disease step by step, from viral entry and spread through the body to immune responses, disease outcomes, diagnostics, lab medicine, and therapies. This makes the topic especially useful for learners because it connects molecular mechanisms to clinical consequences in a logical and meaningful way.

We chose an interactive digital textbook because complex pathology topics can be difficult to follow when they are presented only as dense blocks of text. Our

format helps learners by breaking information into organized chapters and reinforcing it through multiple study tools, including guided flashcards, diagnostic style questions, short answer knowledge checks, games, and clear diagrams and tables that summarize major ideas. The textbook itself includes chapter based learning goals, “Test Your Knowledge” sections, game based review activities, and guided flashcards at the end of chapters, all of which encourage active learning rather than passive reading. This medium is effective because it helps students review high yield content, visualize processes such as viral entry and disease progression, and strengthen understanding through repetition, self testing, and application. Altogether, the topic and medium work well together because they make COVID-19 pathology easier to understand, more engaging to study, and more accessible to a wide range of learners.

7. Did the team use an artificial intelligence (AI) technology tool? If so, which AI technology tool(s) did the team use? What other technology tools did the team use? Is the technology tool novel? Is the team using this technology tool in a novel fashion? If the team did not use technology tool, why did the team decide against using the technology tool(s)?

Please include details (e.g., for what purpose was the tool used for? Why was the tool the best tool to use for your assignment? Are there alternative tools that were considered?)

Our team used several technology tools, including **ChatGPT, Claude, and Replit**. **ChatGPT** was used to help generate and adapt visuals so they matched the style and teaching goals of our COVID-19 textbook. **Claude** was used for some explanatory diagrams, especially for processes that were easier to understand visually than through text alone. **Replit** was used to build the website and organize the project into an interactive digital format. This worked well for our assignment because our goal was not only to present information about COVID-19 pathology, but also to make it easier to understand through clear visuals, structure, and interactive learning features. The textbook itself also includes AI-adapted or AI-assisted visuals, showing how these tools supported the final product.

These tools were the best choices because they helped us explain complex pathology in a more engaging and accessible way than a traditional static format. Instead of relying only on dense text or trying to find pre-existing images that did not match our content, we were able to create visuals tailored to our project. The tools themselves are not entirely novel, but our team used them in a meaningful way by combining AI-supported visual design with an interactive pathology textbook and website. As an alternative, we considered using **NotebookLM** for audio-style notes or summaries, and this is something we would explore in the future.

8. How is your PULSE experiential assignment innovative and/or novel?
Describe what about the PULSE assignment is innovative/novel. Is there a particular component or content that is innovative/novel? How is it different from other content that already exists?

Our PULSE experiential assignment is innovative because it does not present COVID-19 as a list of isolated facts. Instead, *COVID-19 Uncovered* teaches the disease as a step by step pathological process, beginning with viral entry and host cell recognition, then following infection through immune response, disease progression, severe outcomes, and finally diagnostics, lab medicine, and therapies. It is also different from many traditional learning resources because it connects molecular mechanisms to clinical consequences in one continuous framework, helping learners see how viral structure, immune dysregulation, vascular injury, and treatment decisions are all related. The project is further strengthened by its inclusion of biological and social determinants of severe disease, which broadens the discussion beyond basic pathophysiology alone.

A particularly novel part of our assignment is the way this content is delivered through an interactive digital textbook and website rather than through a standard static chapter or slide deck. In addition to organized chapters and clear visuals, the resource includes chapter learning goals, guided flashcards, "Test Your Knowledge" questions, game based review, and simplified diagrams that help learners actively apply information instead of only reading it. This makes the project different from existing pathology content, which is often dense, passive, and harder for students to follow as one complete story. By combining written, visual, and interactive study tools in one resource, our assignment makes a complex disease more engaging, accessible, and easier to understand for different types of learners.

9. If you used an AI tool, please copy and paste the prompt(s)/question(s) used along with the output(s)/answer(s) from the AI tool.
The response here is to allow others to replicate the team's work. If the prompts/outputs are lengthy (over 1 page), please attach it as a separate document and note below [Please see attached document].

[Please see attached document]
PULSE Team #39 - AI Prompts

10. If you did not use an AI tool, please attach a copy of the team's notes to the assignment.
The response here is to allow others to observe the 'behind the scenes' team's work.

[Please see attached document]
PULSE Team #39 - Team Notes and Research

11. How did the team ensure the veracity of the information presented in the PULSE assignment?

The response should highlight how the team has ensured that the information presented in the assignment is evidence-based and not spreading misinformation. You should specifically mention which databases (if any) or textbook materials you used, and how you kept track of the sources/references for each claim. If AI provided you with false information, please describe how the team has fact-checked the AI response and the legitimate (scientific) sources you used. A reference document should be provided in the reference section (15. References) below. Please ensure to include in-text citations in your assignment where applicable.

Our team ensured the veracity of the information in our PULSE assignment by basing the project on evidence based pathology sources rather than unsourced online material. Our main anchor text was Robbins & Kumar Basic Pathology (11th ed.), and we supplemented it with peer reviewed journal articles that are listed in the reference section of the textbook. This is the textbook the course follows closely as well. We kept track of evidence by using numbered in text citations throughout the chapters and figures, then matching each citation to the full reference in the final reference list. This allowed us to trace specific claims back to their original source and check accuracy during drafting and revision. The textbook itself reflects this process through its chapter citations and dedicated reference section.

AI was used only as a support tool, not as the final authority for scientific content. When AI helped adapt visuals or organize diagrams, we fact checked the final content against legitimate scientific sources before including it. This is shown directly in the textbook, where one figure is described as adapted using ChatGPT from Robbins & Kumar Basic Pathology, while other figures are labeled as AI assisted image generation verified against specific references. In other words, if AI generated wording, structure, or visuals that were unclear or potentially inaccurate, we compared them against our textbook source and cited journal articles before keeping them in the final product. This helped us reduce misinformation and ensure that the information presented was scientifically accurate, referenced, and evidence based.

12. Write a meaningful team reflection about the PULSE session (max 250 words).
Prompts to help your team write the reflection: Were there any team/individual biases that surfaced when creating content for the assignment? Did the team implement any practices to ensure the content was equitable, diverse, and/or inclusive? How has the PULSE assignment helped with the team's learning? If the team had to estimate, how long did the assignment take? What worked well for your team? What would the team do differently next time? What were the opportunities and challenges with creating the PULSE assignment to help others' learning? Were there any barriers or limitations?

This PULSE assignment was meaningful to our team because we all lived through the COVID-19 pandemic during high school, when it shaped our education, social development, and transition into adulthood. One bias that surfaced during the project was our tendency to focus on the most severe outcomes of COVID-19, such as ARDS, thrombosis, and immune dysregulation, because these were the aspects most emphasized in public discussion. To

address this, we made a conscious effort to present COVID-19 as a spectrum of disease, from mild upper respiratory infection to severe systemic illness, and to base our content on scholarly sources rather than media summaries.

We also tried to make the project equitable, diverse, and inclusive by including a section on the biological and social determinants of severe disease. This helped us recognize that COVID-19 outcomes are shaped not only by pathology, but also by differences in exposure risk, access to care, and broader structural inequities. The assignment strengthened our understanding of COVID-19 pathology and improved our ability to explain complex scientific ideas clearly for different learners.

If we had to estimate, the project took several weeks of work and many collective hours of researching, writing, designing, and revising. What worked well was dividing sections among team members and then reviewing each other's work for scientific accuracy and clarity. A major challenge was balancing detail with accessibility and deciding how much information to include without overwhelming learners. If we were to do this again, we would leave even more time for revision and user testing. Overall, this assignment connected a shared lived experience with meaningful scientific learning.

13. Write the contributions of individual team members using unique initials.

Example: All team members contributed to the design of the prompts used in the technology tool, ChatGPT (GPT-3.5). T.K and T.K2 fact checked the information presented by ChatGPT using published literature on PubMed (PMID 29211319, 32477271). Y.Z finalized and formatted the final infographic and compiled the prompts and outputs. P.E was involved in…

All team members contributed to researching their assigned sections, preparing annotated bibliographies, fact checking their sources, locating visuals, and using AI supported tools to assist with image and content development. **Y.M.** developed the Replit website, created two games, helped implement the overall aesthetic, led the EDI section, wrote **Chapter 1** and **Chapter 3**, and was responsible for the content within those chapters, including their written material, visuals, flashcards, and diagnostic questions. **L.S.** contributed to aesthetic decisions, wrote **Chapter 4**, and was responsible for the content within that chapter. **M.R.** wrote **Chapter 2** and was responsible for the content within that chapter. **E.A.** wrote **Chapter 5** and was responsible for the content within that chapter. **Y.M.** was also responsible for final submission. All team members reviewed one another's sections to improve scientific accuracy, consistency, and clarity across the final deliverable.

14. Other comments (Optional)

Any comments the team would like to let the coordinator and/or TAs know.

NA

15. References

1. Lamers MM, Haagmans BL. SARS-CoV-2 pathogenesis. Nat Rev Microbiol. 2022 May;20(5):270-84. doi:10.1038/s41579-022-00713-0.
2. Kumar V, Abbas AK, Aster JC, Deyrup AT, editors. Robbins & Kumar basic pathology. 11th ed. Philadelphia (PA): Elsevier; 2023.
3. Mingaleeva RN, Nigmatulina NA, Sharafetdinova LM, Romozanova AM, Gabdoulkhakova AG, Filina YV, et al. Biology of the SARS-COV-2 coronavirus. Biochemistry (Moscow). 2022 Dec;87(12–13):1662–78.
4. Florindo HF, Kleiner R, Vaskovich-Koubi D, Acúrcio RC, Carreira B, Yeini E, et al. Immune-mediated approaches against COVID-19. Nature Nanotechnology. 2020 Jul 13;15(8):630–45.
5. Jackson CB, Farzan M, Chen B, Choe H. Mechanisms of SARS-COV-2 entry into cells. Nature Reviews Molecular Cell Biology. 2021 Oct 5;23(1):3–20.
6. Akıl C, Xu J, Shen J, Zhang P. Unveiling the complete spectrum of SARS-COV-2 fusion stages by in situ cryo-et. Nature Communications. 2025 Feb 25;
7. Pišlar A, Mitrović A, Sabotič J, Pečar Fonović U, Perišić Nanut M, Jakoš T. The role of cysteine peptidases in coronavirus cell entry and replication: The therapeutic potential of cathepsin inhibitors. Hobman TC, editor. PLOS Pathogens. 2020 Nov 2;16(11):e1009013.
8. Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. Methods in Molecular Biology. 2015 Feb 12;1282:11–23.
9. Yang OO. The immunopathogenesis of SARS-CoV-2 infection: overview of lessons learned in the first 5 years. J Immunol. 2025 Jun 1;214(6):1095-104. doi:10.1093/jimmun/vkaf033.
10. Russell CD, Lone NI, Baillie JK. Comorbidities, multimorbidity and COVID-19. Nat Med. 2023 Feb;29(2):334-43. doi:10.1038/s41591-022-02156-9.
11. Puhach O, Meyer B, Eckerle I. SARS-CoV-2 viral load and shedding kinetics. Nat Rev Microbiol. 2023 Mar;21(3):147-61. doi:10.1038/s41579-022-00822-w.
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14. Stölting H, Baillon L, Frise R, Bonner K, Hewitt RJ, Molyneaux PL, et al. Distinct airway epithelial immune responses after infection with SARS-CoV-2 compared to H1N1. Mucosal Immunol. 2022 May;15(5):952-63. doi:10.1038/s41385-022-00545-4.
15. Strunz B, Maucourant C, Mehta A, Wan H, Du L, Sun D, et al. Type I interferon autoantibodies correlate with cellular immune alterations in severe COVID-19. J Infect Dis. 2024 Aug 16;230(2):e318-e326. doi:10.1093/infdis/jiae036.
16. Smith N, Goncalves P, Charbit B, Grzelak L, Beretta M, Planchais C, et al. Distinct systemic and mucosal immune responses during acute SARS-CoV-2 infection. Nat Immunol. 2021 Nov;22(11):1428-39. doi:10.1038/s41590-021-01028-7.
17. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care. 2020;8:36. doi:10.1186/s40560-020-00453-4.

18. Zuo J, Dowell AC, Pearce H, Verma K, Long HM, Begum J, et al. Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection. Nat Immunol. 2021 May;22(5):620-6. doi:10.1038/s41590-021-00902-8.
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20. V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. Nat Rev Microbiol. 2021;19:155-170.
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16. Annotated Bibliography

1) Lamers MM, Haagmans BL. SARS-CoV-2 pathogenesis. Nat Rev Microbiol. 2022 May;20(5):270-84. doi:10.1038/s41579-022-00713-0.

Lamers and Haagmans provide a clear review of SARS-CoV-2 pathogenesis, focusing on how infection begins in the upper airways, spreads to the lower respiratory tract, and in severe cases leads to alveolar damage, inflammation, coagulation abnormalities, and acute respiratory distress syndrome. As a review article published in Nature Reviews Microbiology, this source is credible and useful for explaining the major mechanisms of COVID-19 in a structured way. It was especially valuable for my assignment because it combined detailed scientific information with clear visual figures. I used its figures to help illustrate viral entry, immune responses, and the progression from early infection to severe lung disease. Overall, this source was helpful for both building background knowledge and supporting the visual explanation of complex disease processes.

2) Kumar V, Abbas AK, Aster JC, Deyrup AT, editors. Robbins & Kumar basic pathology. 11th ed. Philadelphia (PA): Elsevier; 2023.

This textbook provides a clear overview of COVID-19 pathogenesis, explaining how SARS-CoV-2 infects ACE2-expressing cells in the nasopharynx and alveoli and how poor early viral control can lead to severe pulmonary disease, cytokine storm, and multiorgan complications. As a standard pathology textbook, it is a credible and useful source for presenting core disease mechanisms in a structured and accessible way. I used this source specifically for its explanation of the progression from early respiratory infection to severe COVID-19 and for its figure summarizing these steps visually. That figure was especially helpful because it simplified a complex process and made it easier to communicate how viral load, immune dysregulation, and systemic inflammatory responses contribute to disease severity.

3) Mingaleeva RN, Nigmatulina NA, Sharafetdinova LM, Romozanova AM, Gabdoulkhakova AG, Filina YV, et al. Biology of the SARS-COV-2 coronavirus. Biochemistry (Moscow). 2022 Dec;87(12–13):1662–78.

This review summarizes the molecular biology of SARS-CoV-2, including its genome organization, gene expression, and mechanisms of host cell entry. It places the virus in the context of other betacoronaviruses, highlighting its relationship to SARS-CoV and MERS-CoV. The authors critically evaluate existing research, focusing on reliable findings amid rapidly published pandemic data. This source was useful for understanding viral entry mechanisms and how structural features and mutations contribute to infectivity and disease progression.

4) Florindo HF, Kleiner R, Vaskovich-Koubi D, Acúrcio RC, Carreira B, Yeini E, et al. Immune-mediated approaches against COVID-19. Nature Nanotechnology. 2020 Jul 13;15(8): 630–45.

This review provides an overview of SARS-CoV-2 pathogenesis, including mechanisms of infection and interactions with the host immune system. It highlights the rapid spread of COVID-19 due to its long incubation period and emphasizes the importance of developing targeted therapeutics and vaccines. The article also discusses emerging treatment strategies, including immune-based approaches and nanotechnology-driven delivery systems. This source was used for the labeled diagram of the coronavirus virion.

5) Jackson CB, Farzan M, Chen B, Choe H. Mechanisms of SARS-COV-2 entry into cells. Nature Reviews Molecular Cell Biology. 2021 Oct 5;23(1):3–20.

This review focuses on the mechanisms of SARS-CoV-2 entry into host cells, particularly the interaction between the spike (S) protein and the ACE2 receptor. It outlines the multistep entry process, including spike protein structure, conformational changes, proteolytic activation, and membrane fusion. The article also highlights the roles of key host proteases such as furin, TMPRSS2, and cathepsin L in facilitating viral entry. This source was especially useful for

understanding the molecular details of viral entry and how these processes inform therapeutic strategies targeting SARS-CoV-2 infection.

6) Akıl C, Xu J, Shen J, Zhang P. Unveiling the complete spectrum of SARS-COV-2 fusion stages by in situ cryo-et. Nature Communications. 2025 Feb 25;

This study investigates the intermediate steps of SARS-CoV-2 membrane fusion, focusing on structural changes in the spike protein during entry. Using cryo-electron tomography, the authors capture transient fusion intermediates, showing how the spike progresses through multiple conformations before forming a fusion pore. The study also demonstrates how ACE2 binding promotes spike clustering and how protease cleavage triggers the transition to the post fusion state. This source was valuable for understanding the detailed mechanism of membrane fusion and highlights how S2-targeting antibodies can inhibit this process.

7) Pišlar A, Mitrović A, Sabotič J, Pečar Fonović U, Perišić Nanut M, Jakoš T. The role of cysteine peptidases in coronavirus cell entry and replication: The therapeutic potential of cathepsin inhibitors. Hobman TC, editor. PLOS Pathogens. 2020 Nov 2;16(11):e1009013.

This review examines the role of viral and host proteases in coronavirus entry and replication, with a focus on how spike protein activation enables infection. It describes how coronaviruses use multiple entry mechanisms, including activation by cell surface proteases and lysosomal cathepsins. The article also highlights the importance of these proteases in viral replication and their potential as therapeutic targets. This source was used to support and inform the labeled diagram illustrating the two distinct entry pathways of coronavirus infection

8) Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. Methods in Molecular Biology. 2015 Feb 12;1282: 11–23.

This article provides an overview of coronaviruses, including their structure, replication strategies, and pathogenic potential across different species. It highlights key features such as the

spike proteins, large RNA genome, and unique replication mechanisms. The review also discusses major human coronavirus outbreaks, including SARS-CoV and MERS-CoV, and their impact on public health. This source was useful for providing background context on coronavirus biology and situating SARS-CoV-2 within the broader coronavirus family.

9) Yang OO. The immunopathogenesis of SARS-CoV-2 infection: overview of lessons learned in the first 5 years. J Immunol. 2025 Jun 1;214(6):1095-104. doi:10.1093/jimmun/vkaf033.

This review explains how SARS-CoV-2 infection begins as a virus-driven process and can later progress into severe immune-mediated inflammation that is no longer fully dependent on active viral replication. It was useful for my assignment because it helped clarify the immunopathogenesis of COVID-19, especially the shift from early infection to later dysregulated immune responses. As a review article in The Journal of Immunology, it is a credible source that synthesizes major findings from the first five years of research. I used this source mainly for its explanation of immune mechanisms and disease progression, which helped support my discussion of how severe COVID-19 develops beyond the initial stage of viral entry and replication.

10) Russell CD, Lone NI, Baillie JK. Comorbidities, multimorbidity and COVID-19. Nat Med. 2023 Feb;29(2):334-43. doi:10.1038/s41591-022-02156-9.

This review examines how specific comorbidities and overall multimorbidity shape COVID-19 outcomes across three mechanistically distinct phases of disease, from early viral replication to inflammatory lung injury and later sequelae. It was useful for my assignment because it helped explain why pre existing conditions can worsen disease severity and how patient risk is shaped by more than one illness at a time. As a review article published in Nature Medicine, it is a strong and credible source that synthesizes clinical and mechanistic evidence. I used this source to support my discussion of risk factors for severe COVID-19 and to strengthen the explanation of how underlying health conditions influence disease progression.

11) Puhach O, Meyer B, Eckerle I. SARS-CoV-2 viral load and shedding kinetics. Nat Rev Microbiol. 2023 Mar;21(3):147-61. doi:10.1038/s41579-022-00822-w.

This review explains how SARS-CoV-2 viral load changes over the course of infection and how viral shedding relates to transmission and disease progression. It was useful for my assignment because it helped clarify when the virus is most active, how long shedding can continue, and why timing matters when discussing infection dynamics. As a review article published in Nature Reviews Microbiology, it is a credible source that brings together current evidence in a clear and organized way. I used this source to support my explanation of early infection, viral replication, and the relationship between viral burden and the course of disease. It was especially helpful for strengthening the scientific background of my discussion.

12) Xu SW, Ilyas I, Weng JP. Endothelial dysfunction in COVID-19: an overview of evidence, biomarkers, mechanisms and potential therapies. Acta Pharmacol Sin. 2023 Apr;44(4):695-709. doi:10.1038/s41401-022-00998-0.

This review examines how endothelial dysfunction contributes to COVID-19 severity, including its role in inflammation, vascular injury, coagulation abnormalities, and potential treatment approaches. It was useful for my assignment because it helped explain how COVID-19 is not only a respiratory disease but also one that affects blood vessels and circulation. As a review article published in Acta Pharmacologica Sinica, it is a credible source that brings together evidence on biomarkers, mechanisms, and possible therapies. I used this source to support my discussion of vascular damage and the broader systemic effects of severe COVID-19. It was especially helpful for explaining how endothelial injury connects inflammation and clotting in disease progression.

13) Conway EM, Mackman N, Warren RQ, Wolberg AS, Mosnier LO, Campbell RA, et al. Understanding COVID-19-associated coagulopathy. Nat Rev Immunol. 2022 Oct;22(10):639-49. doi:10.1038/s41577-022-00762-9.

This review explains how COVID-19-associated coagulopathy develops through interactions between inflammation, endothelial injury, platelets, and the coagulation system. It was useful for my assignment because it helped clarify why severe COVID-19 is often linked to thrombosis and abnormal clotting, not just lung infection alone. As a review article published in Nature Reviews Immunology, it is a strong and credible source that synthesizes current understanding of these mechanisms. I used this source to support my discussion of immunothrombosis and the way clotting abnormalities contribute to severe disease. It was especially helpful for connecting immune dysregulation with vascular and hematologic complications in COVID-19 progression.

14) Stölting H, Baillon L, Frise R, Bonner K, Hewitt RJ, Molyneaux PL, et al. Distinct airway epithelial immune responses after infection with SARS-CoV-2 compared to H1N1. Mucosal Immunol. 2022 May;15(5):952-63. doi:10.1038/s41385-022-00545-4.

This study compares airway epithelial responses to SARS-CoV-2 and H1N1 infection. It was useful for my assignment because it showed that SARS-CoV-2 triggered lower interferon and inflammatory protein release, caused less epithelial disruption, and had less impact on cell morphology than H1N1. As a peer reviewed article in Mucosal Immunology, it is a credible source for understanding early airway level immune responses. I used this source to support my discussion of how SARS-CoV-2 can produce a more limited epithelial immune response than influenza, which helps explain differences in early pathogenesis and disease progression.

15) Strunz B, Maucourant C, Mehta A, Wan H, Du L, Sun D, et al. Type I interferon autoantibodies correlate with cellular immune alterations in severe COVID-19. J Infect Dis. 2024 Aug 16;230(2):e318-e326. doi:10.1093/infdis/jiae036.

This study examines how type I interferon autoantibodies are linked to severe COVID-19 and shows that these autoantibodies are associated more with altered immune cell composition than with major changes in adaptive antibody or T cell responses. It was useful for my assignment because it helped explain one mechanism behind severe disease, especially the role of disrupted

interferon signaling in shaping immune dysfunction. As a peer reviewed article in The Journal of Infectious Diseases, it is a credible source for understanding immune alterations in severe COVID-19. I used this source to support my discussion of interferon-related immune dysregulation and why some patients develop more serious disease.

16) Smith N, Goncalves P, Charbit B, Grzelak L, Beretta M, Planchais C, et al. Distinct systemic and mucosal immune responses during acute SARS-CoV-2 infection. Nat Immunol. 2021 Nov;22(11):1428-39. doi:10.1038/s41590-021-01028-7.

This study examines how immune responses differ between the bloodstream and the nasopharynx during acute SARS-CoV-2 infection. It was useful for my assignment because it showed that systemic and mucosal immunity are compartmentalized, with plasma viral load linked to systemic inflammatory cytokines and nasopharyngeal viral load linked to local antibody responses and reduced interferon activity. The paper also highlights a possible role for the nasopharyngeal microbiome in shaping these responses and influencing clinical severity. As a peer reviewed article in Nature Immunology, it is a strong and credible source. I used it to support my discussion of local versus systemic immune responses and how these differences help explain COVID-19 disease progression.

17) Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care. 2020;8:36. doi:10.1186/s40560-020-00453-4.

This source examines lymphopenia as a marker of severe COVID-19 through a systematic review and meta-analysis. It was useful for my assignment because it showed that lower lymphocyte counts on admission were associated with worse outcomes, including severe disease. As a systematic review and meta-analysis, it is a strong source because it combines findings from multiple studies. I used this article to support my discussion of immune abnormalities in severe COVID-19 and to show that lymphopenia can be used as a clinical indicator of disease severity.

18) Zuo J, Dowell AC, Pearce H, Verma K, Long HM, Begum J, et al. Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection. Nat Immunol. 2021 May;22(5):620-6. doi:10.1038/s41590-021-00902-8.

This study examines T cell immunity six months after primary SARS-CoV-2 infection and found that functional virus-specific T cell responses were retained in all donors studied, with predominant CD4+ responses and strong IL-2 expression. It was useful for my assignment because it supported the idea that adaptive immune responses, especially T cell immunity, can persist after acute infection. As a peer reviewed article in Nature Immunology, it is a strong and credible source. I used this source to support my discussion of longer-term immune responses to SARS-CoV-2 and the role of T cells in ongoing protection after infection.

19) Yin K, Peluso MJ, Luo X, Thomas R, Shin MG, Neidleman J, et al. Long COVID manifests with T cell dysregulation, inflammation and an uncoordinated adaptive immune response to SARS-CoV-2. Nat Immunol. 2024 Feb;25(2):218-25. doi:10.1038/s41590-023-01724-6.

This study examines immune changes in people with long COVID about eight months after infection. It was useful for my assignment because it showed that long COVID is associated with persistent inflammation, T cell dysregulation, and poor coordination between T cell and antibody responses to SARS-CoV-2. As a peer reviewed article in Nature Immunology, it is a strong and credible source. I used this paper to support my discussion of longer-term immune consequences of SARS-CoV-2 infection and to show that COVID-19 can continue to affect immune function well after the acute phase has ended.

20) V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. Nat Rev Microbiol. 2021;19:155-170.

This review discusses coronavirus structure, genome organization, and replication of mechanisms, specifically focusing on SARS-CoV-2. It provides details about major processes

including viral RNA production, processing, and virion assembly. The review article is credible and was published in Nature Reviews Microbiology. The article synthesizes a lot of original research into a coherent piece of information. One of its strong points is the emphasis on the mechanisms that makes this resource relevant when studying virus-related diseases. One of the drawbacks is that it is a review article and therefore lacks any primary data and might not incorporate more recent variants. In Section 1, this source helped me provide necessary explanations regarding virus structure and replication.

21) Blanco-Melo D, Nilsson-Payant BE, Liu WC, Uhl S, Hoagland D, Møller R, Jordan TX, Oishi K, Panis M, Sachs D, Wang TT, Schwartz RE, Lim JK, Albrecht RA, tenOever BR. Imbalanced host response to SARS-CoV-2 drives development of COVID-19. Cell. 2020;181:1036-1045.e9.

This paper describes how SARS-CoV-2 triggers a dysregulated immune response with impaired interferon signaling and increased inflammatory cytokine levels. The study uses real-world and laboratory evidence to show how this imbalance results in the pathogenesis of the disease. One major strength is that it utilizes various models, thereby enhancing validity and relevance. It is a reliable publication appearing in the journal Cell. One limitation is that the paper only contains early pandemic data so it may overlook newer virus strains and vaccine impacts. This paper was applied in Section 2 to understand the complexity of the immune response.

22) Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A, Li WW, Li VW, Mentzer SJ, Jonigk D. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in COVID-19. N Engl J Med. 2020;383:120-128.

The study outlines the damage done by coronavirus to the lung endothelium, formation of microthrombi, and angiogenesis defects. By making comparisons with influenza virus, the study emphasizes the unique vascular component of COVID-19 pathology. One of the key strengths lies in the author’s focus on histological evidence and its comparison with other diseases, thus adding value to its findings. It is reliable due to its publication in the NEJM. However, this article

is limited to fatal outcomes only, thus reducing its generalizability. This sourcee provided details about hypercoagulability, endothelial dysfunction, and increased D-dimer levels in patients suffering from COVID-19 relevant to section 3.

23) Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, Mehra MR, Schuepbach RA, Ruschitzka F, Moch H. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020;395:1417-1418.

This study described inflammation of endothelial cells and vascular dysfunction contribution in multi-organ involvement in COVID-19. This study offers early evidence showing that COVID-19 is not only a respiratory disorder but equally one that is vascular. One strong point about this study is that it is clinically applicable. Nonetheless, a drawback is the limited sample size which limits reliability and generalizability. Published in The Lancet, this paper is reputable and highly cited. Section 3 used this article to explain systemic effects, including organ damage beyond the lungs.

24) Jackson CB, Farzan M, Chen B, Choe H. Mechanisms of SARS-CoV-2 entry into cells. Nat Rev Mol Cell Biol. 2022;23:3-20.

This article outlines the mechanisms behind SARS-CoV-2 entry into cells, which include ACE2 binding, spike protein structural change, and protease activation using TMPRSS2 and cathepsins. The article also highlights the difference between membrane fusion and endocytosis. One of the strengths is the well explained mechanistic detail, making this complex topic more accessible. This source is highly reputable as an article from Nature Reviews. One of the limitations is that it contains only the findings of other studies and does not contain any novel data. This source was important to section 1 because it helped explain viral entry and host-cell interactions.

25) Carsana L, Sonzogni A, Nasr A, Rossi RS, Pellegrinelli A, Zerbi P, Rech R, Colombo R, Antinori S, Corbellino M, Galli M, Catena E, Tosoni A, Gianatti A, Nebuloni M. Pulmonary post-mortem findings in COVID-19 cases. Lancet Infect Dis. 2020;20:1135-1140.

This study provides the pathology of diffuse alveolar damage, inflammation, and thrombosis in the lungs of patients with COVID-19. It explains the pathophysiology of respiratory failure through pathological evidence. One strength of this study is the use of autopsy, which offers a clear understanding of structural changes in the lungs. This peer-reviewed study was published in The Lancet Infectious Diseases, making it very credible. However, a limitation is that it represents only the severe cases of the illness. Section 3 used this source to explain pneumonia progression and ARDS, linking microscopic findings to decreased gas exchange and clinical symptoms.

26) Sinha P, Matthay MA, Calfee CS. Is a "cytokine storm" relevant to COVID-19? JAMA Intern Med. 2020;180:1152-1154.

This article questions the use of the term "cytokine storm" in the context of COVID-19 by explaining how inflammatory responses might be milder in comparison to other diseases such as sepsis. One of its strengths is that it provides a critical perspective that prompts careful interpretation of immunological dysfunction. The article was published in JAMA Internal Medicine, which makes it an reliable commentary. Nevertheless, it is not a primary source since it is not based on any experimental studies and presents interpretations of existing data. This source was employed to clarify misconceptions in Section 2, ensuring the discussion of inflammation associated with COVID-19 would be informed and accurate.

27) Koehler P, Cornely OA, Bassetti M, Chakrabarti A, Colombo AL, Hoenigl M, Klimko N, Lass-Flörl C, Oladele RO, Vinh DC, Verweij PE. COVID-19-associated pulmonary aspergillosis. Lancet Microbe. 2020;1:e241-e242.

This paper emphasizes the danger of secondary fungal infections such as aspergillosis, especially among severe COVID-19 patients. It reflects how immune dysregulation and lung damage lead to an increased likelihood of contracting opportunistic infections. A key strength is the clinical relevance in discussing an important complication. Although, it is not comprehensive in terms of epidemiological data. This article was published in the Lancet Microbe, which makes it a credible source. Section 3 utilized this article for explaining opportunistic infections in severe cases of COVID-19 to highlight that disease outcomes are more than direct viral effects.

28) Alyafei K, Ahmed R, Abir FF, Chowdhury MEH, Naji KK. A comprehensive review of COVID-19 detection techniques: From laboratory systems to wearable devices. Comput Biol Med. 2022;149:106070.

This comprehensive review evaluates a wide range of COVID-19 diagnostic approaches, highlighting their respective strengths and limitations. It covers gold-standard RT-PCR assays, rapid antigen tests, serological methods, and emerging wearable biosensors designed for continuous monitoring. The authors critically analyze the sensitivity, specificity, turnaround time, and scalability of each method, addressing challenges such as false negatives, sample collection variability, and accessibility in low-resource settings. By integrating conventional and novel diagnostic technologies, the article provides a valuable framework for optimizing COVID-19 detection strategies in diverse clinical and public health contexts. It also contains several pertinent figures and diagrams describing the workflow of various diagnostic techniques.

29) Alves MCS, Da Silva RCC, De Leitão-Júnior SSP, De Balbino VQ. Therapeutic Approaches for COVID-19: A Review of Antiviral Treatments, Immunotherapies, and Emerging Interventions. Adv Ther. 2025;42:3045–3058.

This extensive review covers the therapeutic landscape of COVID-19, encompassing antiviral agents (molnupiravir, remdesivir, etc), immunomodulatory drugs, and innovative treatments under development. The authors detail mechanisms of action, summarize clinical trial results, and

highlight challenges such as antiviral resistance and timing of interventions. Special attention is given to immune-targeting therapies like corticosteroids and cytokine inhibitors, aligned with disease phase-specific pathology. The review serves as a comprehensive guide for clinicians and researchers aiming to optimize treatment strategies and accelerate development of effective COVID-19 therapies. It was of particular use in integrating the various described treatments and therapies with the appropriate phase of disease for which they are indicated.

30) Beladiya J, et al. Safety and efficacy of COVID-19 vaccines: A systematic review and meta-analysis of controlled and randomized clinical trials. Rev Med Virol. 2024;34:e2507.

This meta-analysis synthesizes evidence from controlled and randomized trials evaluating COVID-19 vaccine safety and efficacy. It confirms robust protection against symptomatic infection, hospitalization, and severe outcomes with very low incidence of serious adverse events. The analysis spans multiple vaccine platforms and diverse populations, enhancing its applicability. The authors discuss vaccine performance against variants of concern and identify research gaps, such as long-term efficacy and rare side effects. This evaluation supports global vaccination strategies and informs ongoing vaccine development and deployment. It was of use in the section pertaining to COVID vaccinations, allowing for preventative measures to be evaluated alongside antiviral treatments.

31) Filchakova O, et al. Review of COVID-19 testing and diagnostic methods. Talanta. 2022;244:123409.

This review article systematically examines the array of COVID-19 diagnostic techniques, including molecular assays, antigen tests, serological methods, and imaging tools. The authors critically compare test performance, discussing sensitivity, specificity, operational considerations, and appropriate clinical contexts. They emphasize the complementary roles of rapid antigen testing for community screening and RT-PCR for definitive diagnosis. The review also addresses the challenges of false negatives, timing of testing, and combining diagnostic data with clinical

findings to optimize patient management. Its thorough analysis makes it a practical resource for clinicians and laboratory professionals navigating COVID-19 diagnostics. It was of use in the sections regarding various diagnostic methods, their uses, benefits, limitations, and future directions.

32) Marangoni D, et al. Combination regimen of nirmatrelvir/ritonavir and molnupiravir for the treatment of persistent SARS-CoV-2 infection: A case report and a scoping review of the literature. Int J Infect Dis. 2023;133:53–56.

This article presents an in-depth case report on the use of combined antiviral therapy involving nirmatrelvir/ritonavir and molnupiravir in a patient with persistent SARS-CoV-2 infection. The case highlights the potential benefits of combination therapy in cases where viral clearance is delayed or incomplete with monotherapy, suggesting a synergistic effect. The accompanying scoping review places this approach within the broader literature, which remains limited but promising. The authors discuss mechanisms of action, resistance concerns, and pharmacokinetic interactions, providing a nuanced perspective on antiviral strategy evolution. While the clinical improvement observed is promising, the report acknowledges the need for larger, controlled studies to confirm efficacy and safety, especially given the risk of adverse effects and drug interactions inherent in combination regimens. The report also contained diagrams and images that were of use for contextualizing various therapies and summarizing critical information in an effective visual platform.

33) PubChem. Molnupiravir [Internet]. 2023 [cited 2026 Apr 4]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/145996610

This database entry provides essential chemical and pharmacological information on molnupiravir, an oral antiviral drug authorized for COVID-19 treatment. It includes molecular structure, mechanism of action, and safety data, serving as a useful reference for researchers and

clinicians seeking detailed compound profiles. Used in the textbook section as a source for the 3 dimensional chemical structure of the drug.

34) PubChem. Nirmatrelvir [Internet]. 2023 [cited 2026 Apr 2]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/155903259

This database record contains essential chemical and biological information on nirmatrelvir, a protease inhibitor used in combination with ritonavir for COVID-19 therapy. It details the compound's molecular characteristics, mechanism of viral protease inhibition, pharmacology, and safety considerations, aiding research and clinical decision-making. Used in the textbook section as a source for the 3 dimensional chemical structure of the drug.

35) PubChem. Remdesivir [Internet]. 2023 [cited 2026 Apr 3]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/121304016

This entry provides detailed chemical and pharmacological information on remdesivir, an antiviral drug authorized for COVID-19 treatment. It includes data on molecular structure, mechanism of action as an RNA polymerase inhibitor, pharmacokinetics, and safety profile. The resource supports researchers and clinicians seeking comprehensive compound data for drug development and clinical use. Used in the textbook section as a source for the 3 dimensional chemical structure of the drug.

36) Rong G, et al. COVID-19 Diagnostic Methods and Detection Techniques. Encycl Sens Biosens. 2023;17–32. https://doi.org/10.1016/B978-0-12-822548-6.00080-7

This encyclopedic chapter provides a detailed overview of sensor-based technologies for COVID-19 diagnosis, focusing on biosensors that promise rapid, sensitive, and portable testing. The authors describe molecular diagnostic techniques such as RT-PCR and antigen detection before delving into innovative biosensor platforms that employ nanomaterials, electrochemical, optical, and piezoelectric detection methods. Emphasis is placed on improving detection limits, reducing

assay times, and enabling point-of-care applications. The chapter also explores challenges including sample preparation, environmental interference, and device calibration. While primarily technical, the work highlights the potential impact of biosensor integration in expanding testing capacity and accessibility, particularly in decentralized or resource-limited settings. Although biosensors are not heavily discussed in the textbook section, the paper provided valuable supplementary information regarding other diagnostic methods such as RT-PCR and antigen detection.

37) Trinh N T, et al. Effectiveness of COVID-19 vaccines to prevent long COVID: data from Norway. Lancet Respir Med. 2024;12:e33–e34.

This concise report leverages comprehensive national data from Norway to assess the protective effect of COVID-19 vaccination against long COVID, a syndrome of prolonged symptoms following acute infection. The authors find vaccination significantly reduces the incidence and severity of long COVID, supporting the vaccine's role beyond preventing initial infection and severe disease. By adjusting for confounding variables such as demographics and pre-existing conditions, the study strengthens the inference, though the observational nature and follow-up duration limit definitive conclusions. This contribution provides important context given concerns about long-term post-COVID morbidity, reinforcing vaccination as a critical public health tool for mitigating both acute and chronic disease burdens.