RESEARCH

A new transmission route for the propagation of the SARS-CoV-2 coronavirus

Antoine Danchin1,2†, Tuen Wai Ng3*† and Gabriel Turinici4†

Abstract

Background: A novel coronavirus spread starting late 2019 from the capital of the Hubei province in China to the rest of the country, then to most of the world. To anticipate future trends in the development of the epidemic, we explore here, based on public records of infected persons how variation in the virus tropism could end up in different patterns, warranting specific way to handle the epidemic.

Methods: We use a compartmental model to describe the evolution of an individual through several possible states: susceptible, infected, alternative infection, detected and removed. We fit the parameters of the model to the existing data taking into account significant quarantine changes where necessary.

Results: The model indicates that Wuhan quarantine measures were effective but that alternative virus forms and a second propagation route are compatible with available data. For Hong Kong, Singapore and Shenzhen region the secondary route does not seem to be active yet and the epidemic size limited.

Conclusions: The alternative infection tropism (the gut tropism) and a secondary propagation route hypotheses are validated using a model fitted by the available data. Corresponding prevention measures that take into account both routes should be implemented to the benefit of epidemic control.

Keywords: SARS; COVID-19; SARS-CoV-2

1 Background

Late in 2019 a novel coronavirus was detected in mainland China originating from Wuhan, the capital of the Hubei province. The importance of the disease took some time to be acknowledged [1, 2] resulting in a fairly significant number of infected persons who subsequently spread the disease throughout China [3] (all provinces had at least one case on January 30th), then world-wide. This makes it essential to explore the way the epidemic may spread in the near future. In the present work we propose several scenarios to this aim. While it is obviously hazardous to advance models of epidemics before their course has been completely unfolded, we think that it is helpful to evaluate methods meant to understand their specificity. In particular by following how the epidemic developed at places other than its original site of onset, we would be able to detect any unexpected development course that might be used by health authorities to react very early on. This would be extremely useful to detect patterns created by socio-political measures meant to contain the disease or mutants of the virus which would result into higher contagion or virulence, thus prompting a rapid response.

It has been established that coronaviruses are versatile in their preferred site of infection. These viruses have the option to pass from a “gut tropism” version to a...
“lung tropism” instance, as was observed for other coronavirus outbreaks [4, 5, 6, 7]. Depending on the infected person or virus spread dynamics, coronavirus effects can be more or less severe: the virus can either preserve its lung tropism correlated with high impact or act as a “gut tropism” version and be relatively harmless (or even asymptomatic). First reports established that SARS-CoV-2 also induces gut symptoms [8]. Its genetic build up and evolution is still subject to intense research [9]. This multifaceted behaviour may result in unexpected local courses of the epidemic as suggested in a scenario of a “double epidemic”, as proposed for the SARS 2003 worldwide epidemic [10], except that in the present situation we would be witnessing the effect of a single epidemic with modulated effects and propagation depending on the affected patients and random virus mutations. The versatility of the virus tropism, in addition to interfering with the immune response, may induce an additional propagation route depending on virus tropism; contagion may involve a variety of causes, such as environments contaminated with virus carrier secretions, dirty water effluents, besides the expected direct contamination via aerosols. This makes that the oro-fecal route should be considered as an important complement of contact with the virus (recent information sustains this hypothesis [11]). This was observed at the Amoy Gardens cluster of cases for SARS [12, 13]. This observation prompted us to include in our model, besides the major respiratory route, an additional propagation route, which is not a direct human-to-human propagation but invokes some indirect, vector, or environment element, to/from human. A second important consequence of assuming the presence of an indirect route is that the selection pressure on virus mutants will differ considerably between lung tropism and gut tropism. Finally, there may be a difference in incubation time, the “gut tropism” version of the virus would possibly cause less fever [14]. This hypothesis is consistent with some propagation patterns, e.g. the first case in Macau, which was not detected at the border, implying that the affected person did not have fever. We should note that this makes the disease considerably more dangerous in terms of propagation because carriers are, at least for some time "invisible" and display a risky behavior [15, 16]. This explains our choice of compartmental model (see below). Nevertheless, it appears that some people were infected and are already discharged from hospitals, which leads to conclude that the disease is, at this time, less dangerous than SARS.

We propose several scenarios of coronavirus propagation in parallel with our propagation model. Besides providing an estimation of the impact of the epidemic, this work also suggests some countermeasures to slow down propagation. Compared with SARS, the death burden could become much higher (on a par with what is observed with flu) because of lack of proper containment.

2 Methods

Figure 1

The mathematical model of epidemic propagation is illustrated in Figure 1; it builds on a compartmental model [17, 18] to describe the evolution of an individual through several possible conditions such as susceptible (compartment label "S"),
latent, i.e. infected but not yet infective (label "L"), infective in the lung tropism and highly symptomatic (label "I"), low symptomatic, infective in the gut tropism ("A"); the "I" infected then go to "Detected" ("D") stage while the "A" infected go to "Removed/recovered" stage (label "R"). This is an adaptation of existing models and especially the SLIAR model [19, 20, 21, 22, 23]. We add to the model the possibility for an environmental, local, propagation route (that accounts for soiled water, etc.). This option is represented by the "E" label. With some probability, the contact between infected environmental elements and a susceptible individual gives rise to new infections.

Here \( N \) is the total population; the parameters \( \beta \), \( \beta_{EI} \), \( \beta_{ES} \), \( \delta \), \( \gamma_L \), \( \gamma_I \), \( \gamma_A \), \( \gamma_E \) and \( p \) of the model are fitted so that "D" compartment match the existing cumulative number of cases [24]. The mathematical formulation of the model is:

\[
\begin{align*}
\frac{dS}{dt} &= -\beta S(I + \delta A)/N - \beta_{ES} ES \\
\frac{dL}{dt} &= \beta S(I + \delta A)/N + \beta_{ES} ES - \gamma_L L \\
\frac{dI}{dt} &= p\gamma_L L - \gamma_I I \\
\frac{dA}{dt} &= (1 - p)\gamma_L L - \gamma_A A \\
\frac{dD}{dt} &= \gamma_I I \\
\frac{dR}{dt} &= \gamma_A A \\
\frac{dE}{dt} &= \beta_{EI}(I + \delta A)/N - \gamma_E E
\end{align*}
\]

Simulations start at some date \( t_0 \).

### 3 Results

We start with a simulation of the Wuhan city epidemic. We take into account the quarantine starting January 23rd and impose a reduction of the transmission parameters from nominal values \( \beta \) and \( \beta_{ES} \) to reduced values \( a_1 \beta \) and \( a_2 \beta_{ES} \) post-quarantine start date. The reduction is represented by percentages \( a_1, a_2 \) between 0% and 100% that are fitted numerically.

This attenuation is found, as is the case for all other parameters, in the course of a search procedure that imposes a match of the “Detected” patients predicted by the model and the number of reported cases available from communications of the WHO or Chinese authorities. The results are displayed in figure 2. The epidemic size is around 28,500. The key observation here is the presence and importance of the alternative form "A" and the alternative propagation route E-S (see also below).

**Figure 2**

The effect and importance of quarantine measures: we tested what happens if we discard the attenuation factors found by the fit procedure. We obtained a total epidemic size of 97,400, which is a sharp increase with respect to the baseline scenario.

To demonstrate the importance of the alternative form and the alternative propagation route, we neglected the alternative propagation route by setting the \( \beta_{ES} \)
parameter to zero in the previous run. We obtained the results in figure 3, which shows that absence of the E-S propagation route cannot explain the way the epidemic is unfolding (total epidemic size is down to 112 from previous figure of 28,500, closer to observations).

**Figure 3**

Similar considerations hold when switching down the Alternative form of virus presentation (results not shown here).

A second simulation concerns the Hong Kong propagation (figure 4): here not enough data is available to permit a good fit (the uncertainty in the result is larger) but the epidemic appears to be contained (the final epidemic size is around 190); note that the model cannot foresee what can happen if new infected individuals turn up from outside or if quarantine efforts diminish.

**Figure 4**

We continue with a simulation of the propagation of the epidemic in Shenzhen (figure 5): the epidemic seems to be relatively under control with a final epidemic size below 600, but data does not seem to be regularly updated at the end of our selected time interval as the "Detected" class remains constant for a long while; this may force the fit procedure to overweight parameters that ensure sudden epidemic stop and thus a smaller total epidemic size. A sensitivity analysis (not shown here) indicate that a pessimistic estimate of the final epidemic size is around 1'000.

**Figure 5**

Finally, we explored also the case of Singapore: the results (not shown here) are similar to those of Hong Kong, there the epidemic does not appear to be self-sustained; the model predicts an epidemic size of 130.

4 Discussion
A word of caution concerning the present analysis: any model is but an imperfect view of reality and this model is no exception. In addition, the quality of the results returned by the model depends directly on the quality of the data input, and it seems likely that some of the reported figures are subject to large error bars (especially the Wuhan city data). Therefore, one should take the exact figures in our simulations with a grain of salt. Yet, the simulation corresponding to the model do show important qualitative features that are now discussed. Specifically, the hypothesis that there exists a secondary route of transmission is validated by existing data while the assumption that two major types of virus tropism coexist is also supported by the simulation outputs. This has the interesting consequence that it appears that, for the city of Wuhan, the quarantine seems to be effective—of course notwithstanding the need for further quarantine efforts to ensure that it remains
under control—. However, since a reservoir is probably present, and the oro-fecal route may be an important propagation factor, the prevention of this transmission element is vital to avoid any resurgence. The first recommendation seems to be the enforcement of strict post-epidemic measures at the possible reservoir sites.

In Hong Kong and Singapore (and partially in Shenzhen as well) even if the current data indicates that the number of cases is likely to increase, it does not indicate that a secondary propagation route is already effective. However, efforts are to be made to ensure that this remains true in the future and the control of the secondary route, which makes the difference between a large scale epidemic and a controlled outbreak, remains an important target for public health measures.

5 Conclusions
Elaborating on the behavior of previous coronavirus outbreaks, we worked out the hypothesis that an alternative infection tropism (the gut tropism) linked to a secondary propagation route (through environment) is affecting the development of the present COVID-19 epidemic. Our epidemic propagation model, when fit to existing data, indicated that, among all regions analyzed (Wuhan city in the Hubei region in mainland China, Hong Kong, Singapore, Shenzhen region), the propagation of the disease in the city of Wuhan underwent an original course. It appeared to be substantially facilitated by a secondary propagation route, thus substantiating the beneficial effect of an effective quarantine. The main message of our exploration is that relevant prevention measures that take into account both propagation routes should be implemented to contain the extension of the epidemic to further sites, especially when novel sites are uncovered. It must be however emphasized that because our work depends on figures provided by official health authorities the scenarios we proposed could be considerably altered if the figures were not reflecting the real situation. In particular the existence of a second, significant, route might in fact provide a way to identify alterations of these figures.

6 Abbreviations

COVID-19: Coronavirus disease 2019
SARS: Severe acute respiratory syndrome
SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2
WHO: The World Health Organization

7 Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.
Availability of data and materials

The datasets generated analysed during the current study are available in
1) Health Commission of Hubei Province repository, http://wjw.hubei.gov.cn/fbjd/dtyw/
2) The Shenzhen Municipal Health Commission repository, http://wjw.sz.gov.cn/yqsz/
3) Department of Health, The Government of Hong Kong SAR repository, https://www.coronavirus.gov.hk/eng/index.html#Updates_on_COVID-19_Situation

Competing interests

AD is employed by Stellate Therapeutics (fka Amabiotics), a company that works on treatment of neurodegenerative diseases.

Funding

Not applicable.

Author’s contributions

AD provided the biological background for setting up the model and proposed, based on the 1983-1985 outbreak of coronavirus infection in European pigs the hypothesis of alternative transmission route for the propagation of the SARS-CoV-2 coronavirus.

TN collected the figures of COVID-19 cases in different cities and carried out some numerical simulations.

GT contributed to the derivation of the differential equations that describe the model, carried out numerical simulations and the parameter fitting procedures.

AD, TN, GT supervised the design of the mathematical model.

Acknowledgements

Not applicable.

Authors’ information (optional)

Not applicable.

Author details

1 Institut Cochin, INSERM U1016 - CNRS UMR8104 - Université de Paris, Paris, France. 2 School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China. 3 Department of Mathematics, The University of Hong Kong, Hong Kong, China. 4 CEREMADE, Université Paris Dauphine - PSL Research University, Place du Marechal de Lattre de Tassigny, 75016 Paris, France.

References

1. Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G.F., Tan, W.: A Novel Coronavirus from Patients with Pneumonia in China. 2019. New England Journal of Medicine (2020). doi:10.1056/NEJMoa2001017. Accessed 2020-02-03
2. Grainisi, L.E., Menachery, V.D.: Return of the Coronavirus: 2019-nCoV. Viruses 12(2), 135 (2020). doi:10.3390/v12020135. Accessed 2020-02-03
3. Wu, J.T., Leung, K., Leung, G.M.: Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. The Lancet 0(0) (2020). doi:10.1016/S0140-6736(20)30260-9. Accessed 2020-02-01
4. Raschka, D., Duarte, M., Laude, H.: Porcine respiratory coronavirus differs from transmissible gastroenteritis virus by a few genomic deletions. Journal of General Virology, 71(11), 2599–2607 (1990). doi:10.1099/0022-1317-71-11-2599. Accessed 2020-01-22
5. Laude, H., Raschka, D., Delmas, B., Eleouët, J.-F.: Le coronavirus respiratoire porcin PRCV : un virus émergent pas comme les autres. Virologie 2(4), 305–16 (1998). Accessed 2020-01-22
6. Garwes, D.J.: Transmissible gastroenteritis. Veterinary Record 122(19), 462–463 (1988). doi:10.1136/vr.122.19.462. Accessed 2020-01-22
7. Song, H.-D., Tu, C.-C., Zhang, G.-W., Wang, S.-Y., Zheng, K., Lei, L.-C., Chen, Q.-X., Gao, Y.-W., Zhou, H.-Q., Xiang, H., Zheng, H.-J., Chen, S.-W.W., Cheng, F., Pan, C.-M., Xuan, H., Chen, S.-J., Luo, H.-M., Zhou, D.-H., Liu, Y.-F., He, J.-F., Qin, P.-Z., Li, L.-H., Ren, Y.-Q., Liang, W.-J., Yu, Y.-D., Anderson, L., Wang, M., Xu, R.-H., Wu, X.-W., Zheng, H.-Y., Chen, J.-D., Liang, G., Gao, Y., Liao, M., Fang, L., Jiang, L.-Y., Li, H., Chen, F., Di, B., He, L.-J., Lin, J.-Y., Tong, S., Kong, X., Du, L., Hao, P., Tang, H., Bernini, A., Yu, X.-J., Spiga, O., Guo, Z.-M., Pan, H.-Y., He, W.-Z., Manuguerra, J.-C., Fontanet, A., Danchin, A., Nicolai, N., Li, Y.-X., Wu, C.-I., Zhao, G.-P.: Cross-host evolution of severe acute respiratory syndrome coronavirus in palm civet and human. Proceedings of the National Academy of Sciences of the United States of America 102(7), 2430 (2005). doi:10.1073/pnas.0409608102
8. Holshue, M.L., DeBolt, C., Lindquist, S., Lofy, K.H., Wiesman, J., Bruce, H., Spitters, C., Ericson, K., Wilkerson, S., Tural, A., Diaz, G., Cohn, A., Fox, L., Patel, A., Gerber, S.I., Kim, L., Tong, S., Lu, X., Lindstrom, S., Pallansch, M.A., Weldon, W.C., Biggs, H.M., Uyeki, T.M., Pillai, S.K.: First Case of 2019 Novel Coronavirus in the United States. New England Journal of Medicine 382(20), 1953–1957 (2020). doi:10.1056/NEJMoa2001191. Accessed 2020-02-01
9. Pradhan, P., Pandey, A.K., Mishra, A., Gupta, P., Tripathi, P.K., Menon, M.B., Gomes, J., Vivekanandan, P., Kundu, B.: Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag. bioRxiv, 2020–0130927871 (2020). doi:10.1101/2020.01.30.927871. Accessed 2020-02-01
10. Ng, T.W., Turinici, G., Danchin, A.: A double epidemic model for the SARS propagation. BMC Infectious Diseases 3(1), 19 (2003). doi:10.1186/1471-2334-3-19. Accessed 2020-01-06

11. Scientists say deadly virus may live and spread in human faeces (2020). https://www.scmp.com/news/china/politics/article/3048611/coronavirus-scientists-identify-possible-new-mode-transmission Accessed 2020-02-03

12. Abdullah, A.S.M., Tomlinson, B., Cockram, C.S., Thomas, G.N.: Lessons from the Severe Acute Respiratory Syndrome Outbreak in Hong Kong - Volume 9, Number 9—September 2003 - Emerging Infectious Diseases journal - CDC. doi:10.3201/eid0909.030366. Accessed 2020-01-22

13. Amoy Gardens. Page Version ID: 932854963, https://en.wikipedia.org/w/index.php?title=Amoy_Gardens (2019)

14. ncov – CSSE. https://systems.jhu.edu/research/public-health/ncov/ Accessed 2020-02-03

15. Maghool, S., Maleki-Jirsaraei, N., Cremonini, M.: The coevolution of contagion and behavior with increasing and decreasing awareness. PLOS ONE 14(12), e0225447 (2019). doi:10.1371/journal.pone.0225447. Accessed 2020-02-03

16. Rothe, C., Schunk, M., Sothmann, P., Bretzel, G., Froschl, G., Wallrauch, C., Zimmer, T., Thiel, V., Janke, C., Guggemos, W., Seilmaier, M., Drosten, C., Vollmar, P., Zwigirmaier, K., Zange, S., Wölfel, R., Hoelscher, M.: Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. New England Journal of Medicine 0(0) (2020). doi:10.1056/NEJMc2001468. Accessed 2020-02-03

17. Anderson, R.M., May, R.M.: Infectious Diseases of Humans Dynamics and Control. Oxford University Press, ??? (1992). http://www.oup.com/uk/catalogue/?ci=9780198540403

18. Murray, J.D.: Mathematical Biology: I. An Introduction. Springer, ??? (2007)

19. Brauer, F.: Some simple epidemic models. Mathematical Biosciences and Engineering 3(1), 1 (2006). doi:10.3934/mbe.2006.3.1. Accessed 2020-01-22

20. Arino, J., Brauer, F., van den Driessche, P., Watmough, J., Wu, J.: A final size relation for epidemic models. Mathematical Biosciences & Engineering 4(2), 159 (2007). doi:10.3934/mbe.2007.4.159. Accessed 2020-02-01

21. Arino, J., Brauer, F., van den Driessche, P., Watmough, J., Wu, J.: Simple models for containment of a pandemic. Journal of The Royal Society Interface 3(8), 453–457 (2006). doi:10.1098/rsif.2006.0112. Accessed 2020-01-22

22. Gumel, A.B., Ruan, S., Day, T., Watmough, J., Brauer, F., van den Driessche, P., Gabrielson, D., Bowman, C., Alexander, M.E., Ardal, S., Wu, J., Sahai, B.M.: Modelling strategies for controlling SARS outbreaks. Proceedings of the Royal Society of London. Series B: Biological Sciences 271(154), 2223–2232 (2004). doi:10.1098/rspb.2004.2800. Accessed 2020-01-22

23. Longini, I.M., Halloran, M.E., Nizam, A., Yang, Y.: Containing Pandemic Influenza with Antiviral Agents. American Journal of Epidemiology 159(7), 623–633 (2004). doi:10.1093/aje/kwh092. Accessed 2020-01-24

24. News / Wuhan Coronavirus. http://www.imperial.ac.uk/medicine/departments/school-public-health/infectious-disease-epidemiology/src-global-infectious-disease-analysis/news---wuhan-coronavirus/ Accessed 2020-01-22