

# **Issues raised by the Osaka Governor's "Povidone iodine mouthwash" press conference - Science, politics, and populism**

**Shinsuke Shimojo**

California Institute of Technology 139-74,

Division of Biology & Biological Engineering/Computation & Neural Systems,

Pasadena, CA 91125.

"It may be hard to believe, but gargling with povidone-iodine suppresses the coronavirus."

Governor Hirofumi Yoshimura of Osaka Prefecture made such a statement in a press conference (Aug. 4, 2020), and that kind of mouthwash immediately disappeared from shelves at pharmacies all over the country. "The scientific basis is feeble. The governor went too far." - This was the general view, and the governor was forced to explain. The media reported it mainly from a political perspective, but they did not forget to criticize. Some major media neglected it on purpose ("read through" so-called). They demonstrated their scientific literacy and mature judgment, in a way. However, I also feel that from a broader perspective, some important issues have been raised(, not by the governor but as a result of this turmoil). The relationship between science, politics, and populism is questioned, as in the case of Donald Trumps' constant lies on COVID-19 matters.

Let me first preview the main points of this short article. The data in question was not peer reviewed, unpublished and too premature. Scientifically unreliable, even considering the current COVID-19 urgency. Yet, it may be more educational for scientific literacy (than just neglecting) to specifically point out what went wrong in the data. It is because this kind of political

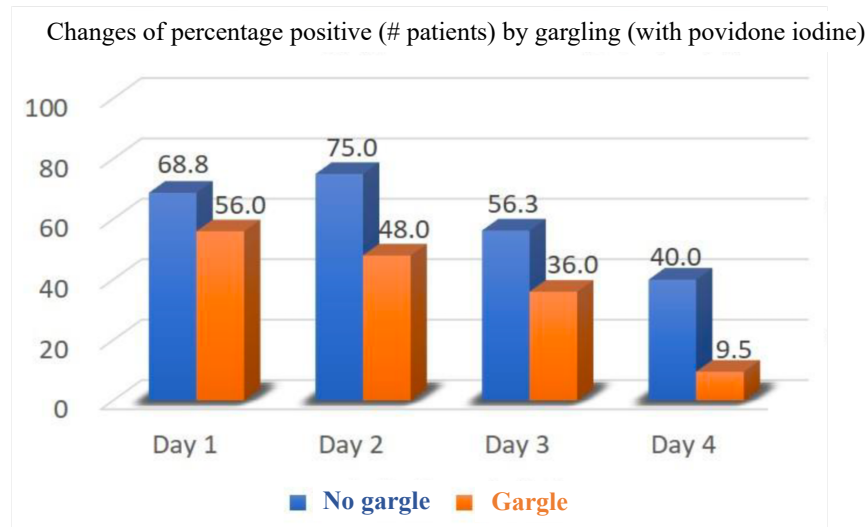
propaganda based on a sparse scientific ground will be repeated in the future (whether on COVID-19 or any other problems). And the scientific problems in the data are often very similar.

From a broader perspective, this affair raises two distinct issues. The first is rather direct, as to whether a politician or an administrative official should be allowed to (mis)guide the citizens with scientifically uncertain dataset. The second is a more fundamental issue as to whether it is allowable to publish a progress of research without waiting for peer review. In an emergency era like this (with the COVID-19), these two issues are often mixed up. There are merits and demerits, but can we draw a line properly?

First, let us quickly review this research and sort out what were scientifically problematic.

### **Habiki Medical Center research report and its problems**

According to the announcement by the Osaka Habiki Medical Center (August 4), which was the basis of the Governor's conference, "Povidone iodine gargling reduced frequency of salivary virus-positive patients who were under medical observation." COVID-19 patients (41 patients) at the medical-treatment accommodation facility in the prefecture were divided into two groups; one group gargled with mouthwash containing povidone-iodine 4 times a day, and the other did not gargle at all. When saliva samples were collected everyday and the PCR test was performed, the positive test rate in the gargling group tended to immediately decrease, and it significantly decreased on the 4th day (Figure below). [Note: Only few-page summary and illustrations on the study have been provided so far. My criticism below is based on those.]



What went wrong with these data? I would summarize as follows.

1) First of all, the sample size was extremely small, thus the data were far from conclusive. There is a reasonable suspicion that the governor has made a big case of success in rush, due to his political motivation (“Osaka model” in his favorite terminology). The graph seemingly indicates that the positive rate in the gargling group reduced greatly especially on the 4th day. Given that the original data were frequency (# patients) in nature (positive/negative), the difference on day 4 is probably significant (in a non-parametric statistical test). However, the results can be easily changed by arbitrarily adding or deleting one or two cases. In addition, the PCR's positive/negative determination itself is actually a continuous figure with a single (somewhat arbitrary) threshold. One can argue that using the original PCR analog values may be more appropriate and sensitive. [Later note by the author: these are frequency data as noted above, but with some oddity in calculation - some experts and journalists pointed out that sample numbers may have changed across the days.]

- 2) There was a big logical leap from the data to conclude that "povidone-iodine mouthwash is (especially) effective" only by comparison with one control group without gargling. Such a conclusion cannot be drawn, unless compared in addition to other mouthwash or just water gargle control groups.
- 3) There is a procedural question in the first place - whether the gargling and the non-gargling groups were distributed fairly so that the two groups were homogenous in terms of medical and other conditions. The problem is greater with fewer samples. Especially in the case of COVID-19, there are large individual differences known in (a)symptoms. In addition, it has been indicated that infectious power is strong only for a few days before and after the onset of the symptom in the individual infection cycle. Thus it should be assumed that there was also big differences in the concentration of viruses in saliva among the 41 patients from the outset. How carefully were they assigned so that there would be no true difference between the two groups in terms of onset, symptoms, etc? Honestly dubious.
- 4) Did their procedures meet the "double-blind" principle, which is the standard in the experimental methodology? The double-blind principle demands is that not only the test participants (in this case the patient)s, but also the experimenters should be blind to the purpose and the hypothesis of the research. The most stringent version of it wouldn't be possible in the current medical emergency situation, but at least saliva collectors and data analysts could have kept uninformed as to which group a particular sample will belong to.

This quick glance may be sufficient to point out several problems, most of which are not limited to this case. It is common in the increasing cases where "political propaganda precedes science". Despite the worst prevailing of COVID-19 in the US, President Trump repeatedly claimed that "malaria-specific drug hydroxychloroquine is effective." It remains in a direct conflict with the

nation's public health officials' view that the scientific basis is closer to zero. Worse than that were the other claims by the same President, such as "injection of antiseptic solution" and "irradiation of ultraviolet rays" would kill the virus.

The above analysis and criteria will be helpful in scientifically evaluating these cases.

Governor Yoshimura successfully attracted attention of media and public by selling such immature data. It became a source of calamity, in that political populism trampled science with the help of populism. Even if the governor himself invited the press purely with a sense of mission and good will, this conclusion should not change. The mouthwash can be obtained at any local pharmacy and costs about 10 yen(=10 cents approximately) per time. Allured by such practical availability, the young and ambitious politician stepped overeagerly.

### **What about publishing without expert review?**

The above is not the only problem brought by this affair, as I mentioned earlier. In addition to the problem of "political propaganda based on scientifically vague data," it does raise yet another issue as to whether it should be allowed to publish new scientific data so that it can be tried/tested in the real world, circumventing the very slow peer-review process. This further can be divided into two aspects.

First aspect is specific to the medical emergency with COVID-19. Since it is globally urgent, everybody tends to publicize premature findings so that they can be immediately tested (and verified later) in various way. This is an implicit agreement under the circumstances. Indeed, the various measures that have been taken to act against COVID-19 have been spread and later verified (or denied) by medical authorities such as the WHO and top medical journals. It is often

months later (from the first report) when the finding is officially published in an authentic academic/clinical journal with peer review. The public health guidelines to avoid infection, how the virus is transmitted to others (contact, droplet, and/or airborne), genetic mutation types - all these pieces of critical knowledge have been accepted in this way.

As for the second aspect, there has been a strong trend towards open-access science in general, started years earlier than the uprising of this pandemic. Information on the latest science discovery and technological development is wealth and power for its own sake, which had been monopolized by advanced nations and their researchers, and commercial-based publishers. Rather, we may want to literally “publicize” such findings made by experts for free, such that tax payers have a free access to it, and researchers without financial or academic advantages can freely test or utilize. This is the ideology behind the “open repository (depository)” movement, which became popular in science in the latest decade. Such an open system prevents profit monopoly and protects benefits for the general public. At a more fundamental level, such a democratic system to manage information may also provide a more flexible and creative incubator for science and technology. Behind this were issues including increasing cost of publishing in scientific journals, monopoly of achievements by leading universities in advanced countries, etc. (for more details, see articles by myself (though still in Japanese language) titled "Revolution by a Russian graduate student" (<https://webronza.asahi.com/science/articles/2016033100002.html>) and "Rapidly increasing accesses to “pirated free cite” of scientific publications" (<https://webronza.asahi.com/science/articles/2018120300005.html>))

**Is this research entirely useless?**

So far I criticized this research report from a scientific standpoint, but there are also several scientific hints in the report.

Measures against COVID-19 can be divided into three phases in general: 1) protection, 2) treatment (once infected), and 3) prevention to infect other people. The study drew attention to the last of these, which is of course the key to suppress the pandemic in a global scale. (The Governor's first press conference unfortunately mixed up all the three phases, leading to a confusion and a turmoil.) How to avoid transmission of virus via saliva droplets (and possibly airborne) is the focus here.

In this context, the study pointed to a possibility (though only a possibility) that the effect of gargling to suppress virus in the mouth can be sustained and cumulative to some extent. At the first glance, people may complain (indeed they did) that it is trivial to argue that density of the virus in the mouth is reduced by gargling. Note, however, that the PCR testing in the study was done in the morning *before* the first gargling of the day(, as explained in the Governor's second press conference).

It should be noted that preventive/curative effects is very limited because the viruses would constantly live and rise from the patient's trachea and lung. Even when talking only about prevention to infect other people, the effect of gargling would be limited because it is transmitted not via droplets but also airborne. (On the other hand, it is hard to believe at this moment that it is airborne only, not at all via droplets.) Having all these said, however, the study evokes lots of interesting questions.

Can the sustained and cumulative effect of gargling be tested with a larger sample size and better procedures (as described above)? How about other types of mouthwash than povidone iodine?

Would it be possible to develop something like a "disinfectant candy" that contains effective ingredient and can be kept in mouth for minutes to hours? If any of these have some effect, then would the effect be limited to reduce virus in saliva, thus infection via droplets only? Or rather it could have any effect, albeit weaker, on respiratory virus(, thus airborne infection)? Also, the effect would be doubled if we have the same in the recipient (uninfected) as well as the transmitter (infected) - for instance, two of them engaged in a conversation with the candy in both their mouths? It might then be effective against infection, both airborne and from touches (on surfaces).

Clinical trials may be hard to conduct, but we may start with computer simulations. Needless to say, a collaboration of various experts and a large-scale, well-controlled research is necessary, perhaps with a special attention to potential side effects.

As mentioned earlier, "open, free publication before peer review" is already the mainstream of science in general, and it has advanced further due to the COVID-19 crisis. This should not mean, however, that the peer review system is meaningless. Without it, hardly anything else can stop mere superstitions and political propaganda disguised in science, as well as marketing by false information. Where should we draw a border and how it be adjusted depending on the context? I predict that this will become a more acute problem in the near future.

Some reform may be needed in the peer review and information flow control in science and technology, on one hand. On the other hand, citizens should be informed and educated appropriately for better scientific literacy.



### **[Authors' notes (090520)]**

I have been publishing journalistic articles as a semi-regular writer for a Japanese newspaper site - Asahi digital RONZA (Science/Environment section; <https://webronza.asahi.com/authors/2010110800008.html>) for almost one decade or so. My latest articles are mostly related to COVID-19. I decided that this article (the latest one; published on-line on Aug. 15) in particular is worth having translated and accessible here in English. It is partly because it shows my view on the "open access journal" trend. But it is also because I have been fascinated by the scientific possibilities inspired by the concerned study, which is described in the last section. **Just to quickly reiterate:**

- 1. Distinction among three phases; (1)prevention, (2)cure, and (3)avoidance of further transmission.**
- 2. Focusing on the last, virus density in the saliva is the key.**
- 3. There, reduction of virus in the mouth/throat may be a good news.**
- 4. The sustained and cumulative effect of the mouthwash - need to test further?**
- 5. Explore preventives other than povidone iodine (effect and side effect).**
- 6. New idea of "preventive candies"? (It does not seem to exist yet.) It could stay much longer in the mouth (minutes-hours).**
- 7. Can we double the effect by applying it not just in the sender (infected) but also in the receiver (uninfected)?**
- 8. Potential advantages;**
  - a) 80% of the infected individuals are known to reveal no or very light symptoms. Thus, we need something applicable to everybody.**
  - b) widely applicable to most of daily life situations (including outdoor), but especially high-risk situations such as a party, a close conversation or eating together.**
  - c) also indirectly prevent viral transmission (1) airborne, or (2) from objects' surfaces (by reducing the chance of infection in mouth/throat in the receiver).**
  - d) also prevents flu, and other infections.**
  - e) cheap and reachable.**

While many nations, companies and medical experts are rushing into vaccination as soon as this fall, it will take a while till the majority of us will be vaccinated safely, with a robust sustained effect, but no negative side effects such as Antibody-Dependent infection Enhancement(ADE). Meanwhile, we do need something. Since none of us in our laboratory are experts on the topics (with some having biology and public health background, to help me), I put these ideas here with a hope that some experts would be inspired. We all work for better together.