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## A *Rashomon* Moment? Ocular Involvement and COVID-19

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In the 1950 Japanese movie *Rashomon*, 4 characters present 4 completely different accounts of a sordid crime. Over time, the film's title has become part of the lexicon to describe the relativity of truth and the unreliability, indeed subjectivity, of memory. Science should be able to provide accurate and reliable explanations. Therefore, emerging reports on coronavirus disease 2019 (COVID-19) and tear or conjunctival involvement may give readers reason to pause.

In this issue, 2 articles present seemingly disparate results of testing tears (see page 977) or conjunctival swabs of patients (see page 982) with COVID-19 for the presence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).<sup>1,2</sup> Combined with 3 articles reporting the presence of SARS-CoV-2 in such specimens,<sup>3–5</sup> what is the proper conclusion one can draw? Is SARS-CoV-2 present in tears or conjunctiva of such patients? And—on the mind of many ophthalmologists—is the virus transmissible through tears or conjunctival secretions?

A few possibilities exist for these varying results of reverse-transcriptase polymerase chain reaction (RT-PCR) of “tears,”<sup>2</sup> “tears and conjunctival secretions,”<sup>3</sup> or “conjunctival swabs.”<sup>1,4,5</sup> First, the diagnostic criteria used by authors vary from article to article. Some authors refer to the report “Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (5th–7th editions),” updated by the National Health Commission of China on March 4, 2020. An online translation of the seventh edition by a physician society carries the caveat that “healthcare providers . . . make clinical decisions based on [their] own nation's medical guidelines and regulations.” “Suspected” cases meet 1 of the travel or contact history criteria and 2 of the clinical ones, which include fever, radiographic findings of viral pneumonia, and change in lymphocyte or leukocyte count. “Confirmed” cases are “suspected” cases with 1 piece of “etiology or serological evidence: real-time RT-PCR is positive for COVID-19 nucleic acid; the viral gene identified by gene sequencing is . . . homologous with . . . COVID-19,” or immunoglobulin M and immunoglobulin G presence with immunoglobulin G titer increase in recovery. Reverse-transcriptase polymerase chain reaction analysis is performed most commonly on respiratory tract specimens, with testing of lower respiratory samples being more sensitive than of upper respiratory samples; testing also can be carried out on blood and feces.

Some authors adhere to the above definitions.<sup>1</sup> Others define COVID-19 cases as only patients having both positive RT-PCR results in “respiratory or blood specimens” and

computerized tomographic findings.<sup>3</sup> Still others seem to combine “suspected” and “confirmed” cases.<sup>4</sup> Therefore, authors may be describing different patient populations, which may affect results of RT-PCR analysis of tears or conjunctival swabs.

The second possibility is the experimental setup. The College of American Pathologists requires that each specimen source be validated before implementation as a clinical assay; no guidelines exist for a test performed in a research laboratory. Few publications on COVID-19 and the eye provide details on the type of laboratory performing testing, standard operating procedures, or positive and negative controls regarding polymerase chain reaction or viral culture.

Third, assuming proper validation and controls were performed, RT-PCR is highly specific and may lack sensitivity. Negative results may be true negatives (virus not in tears or conjunctiva) or false negatives. Transient presence of virus, inadequate sampling, or timing of sample collection such that the virus is not yet in the tissue may require that sampling be performed more than once and separated over time. The last has been true for RT-PCR analysis of respiratory samples.

Another potential source of confusion is publication descriptors ranging from “ocular manifestations”<sup>5</sup> to “findings”<sup>4</sup> to “symptoms” disclosed in medical records and findings from penlight examination.<sup>1</sup> Only 1 article explicitly describes biomicroscopic slit-lamp examination of a COVID-19 patient who progressed to hospital admission and development of symptomatic bilateral “follicular conjunctivitis.”<sup>5</sup> Another article describes SARS-CoV-2 in “tears and conjunctival secretions” of the 1 patient with conjunctivitis.<sup>3</sup> In yet another study, it is unclear by what means “ocular abnormalities” were found in “one third of patients [or 12/38] with COVID-19.”<sup>4</sup> The preponderance (8/12) of patients were classified as having “severe” and “critical” disease, defined as respiratory failure, shock, or multiorgan failure.<sup>4</sup> Abnormalities like “conjunctival hyperemia, chemosis, epiphora, or increased secretions”<sup>4</sup> are not uncommon in ventilated patients.

The discovery of SARS-CoV-2 tears or conjunctiva is not surprising. Severe acute respiratory syndrome coronavirus,<sup>6</sup> human coronavirus NL63, and other viruses (e.g., adenovirus) provide examples of ocular tropism of respiratory viruses. Possible reasons include anatomic linkage, structure and distribution of cellular receptors, and immunologic interdependence.<sup>7</sup> Experiments strongly suggest that the eye is a potential entry portal for these viruses and emphasize the importance of masking and eye protection for ophthalmologists,<sup>8</sup> who sit far closer to

patients than the 6 feet recommended by the Centers for Disease Control and Prevention for social distancing. Severe acute respiratory syndrome coronavirus-2 may end up in tears and conjunctiva because of such direct inoculation, migration of an upper respiratory tract infection, or hematogenous involvement of the lacrimal gland. However, further study is needed to determine whether the viral load in tears or conjunctiva is enough to transmit infection.

*Rashomon* is set during a time of social crisis; autonomous provincial political and military powers were undermining the central government in 12th-century Japan. The film's director used this backdrop to reveal extremities of human behavior. The coronavirus pandemic has exposed geopolitical differences in preparation and approach to COVID-19: screening, contact tracing, self-quarantine, masking, and providing personal protective equipment for healthcare workers. *New Yorker* film critic Pauline Kael described *Rashomon* as the "classic film statement of the relativism, the unknowability of truth." Other viewers have insisted there must be 1 true account of the crime, discoverable if one diligently sifts through the clues. Two truths may emerge here: the presence of SARS-CoV-2 in ocular tissue or secretions would not be surprising, and ophthalmologists are at increased risk for infection without adequate protection.

## Footnotes and Financial Disclosures

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