

## SYNTHESIS

Date 02/03/2021

# COVID-19 P.1 Variant of Concern– What We Know So Far

## Introduction

Public Health Ontario (PHO) is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

See PHO’s rapid review *COVID-19 UK Variant VOC-202012/01 – What We Know So Far* for information on the United Kingdom (UK) (B.1.1.7) variant of concern (VOC),<sup>1</sup> as well as the rapid review *COVID-19 B.1.351 (501Y.V2) Variant of Concern – What We Know So Far*.<sup>2</sup>

## Key Findings

- The P.1 lineage (previously known as B.1.1.28.1) was first reported in Japan and was later identified in Brazil as early as December 4, 2020. As of February 2, 2021, P.1 cases have been confirmed by genetic sequencing in Brazil, Japan, Italy, Faroe Islands, United States (US) and South Korea. As of February 2, 2021, no P.1 cases have been identified in Ontario or Canada.
- While little is known about the transmissibility of the P.1 variant, there is a possibility that the P.1 variant could have higher transmissibility than pre-existing lineages. Contact tracing and outbreak investigation data are needed to better understand relative transmissibility of this lineage.
- Emerging evidence suggests that the E484K mutation present in the P.1 lineage reduces the neutralizing activity of human polyclonal sera among vaccinated individuals and those previously infected with previous strains of SARS-CoV-2, potentially leaving individuals more susceptible to P.1.
- One case of re-infection with the P.1 variant has been documented in Brazil.

## Background

New Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) variants are arising as the virus continues to spread globally. To date, three SARS-CoV-2 variants of public health importance have been identified: lineage B.1.1.7 (501Y.V1, VOC 202012/01; originated in the United Kingdom [UK]); lineage P.1 (previously B.1.1.28; originated in Brazil); and lineage B.1.351 (501Y.V2; originated in South Africa). These variants have been termed variants of concern (VOCs), and have been associated with evidence of increased transmissibility, severity, and/or possible immune evasion with potential implications for reinfection and vaccine effectiveness.

Notably, these VOCs harbour many mutations, including some in the receptor-binding domain (RBD) of the spike (S) protein, encoded by the *S* gene. Mutations in SARS-CoV-2 arise naturally through viral replication. The RBD mutations of interest in the *S* gene include the following amino acid substitutions: N501Y, K417N/T and E484K. The N501Y mutation is found in all three VOCs. The E484K mutation is found in P.1 and B.1.351 and has been associated with potential immune escape.<sup>3</sup>

When transmissibility is higher for a VOC, the VOC can lead to a rapid increase in cases, putting a strain on health care resources. Monitoring for known and emerging mutations and VOCs is critical to the early identification and mitigation against future VOCs. Here we synthesize the current literature examining the P.1 variant.

## Methods

In considering feasibility, scope, and a need for responsiveness, we chose a rapid review as an appropriate method for understanding the P.1 variant. A rapid review is a knowledge synthesis where certain steps of the systematic review process are omitted in order to be timely (e.g., quality assessment).<sup>4</sup>

On February 2, 2021, PHO Library Services conducted a literature search in MEDLINE, National Institutes of Health COVID-19 Portfolio (Preprints), Embase and Scopus. We searched Google on February 2, 2021 for additional articles of interest, including grey literature. English-language peer-reviewed and non-peer-reviewed records that described the P.1 variant were included.

Prior to posting, PHO subject-matter experts review all “What We Know So Far” documents.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in this document is only current as of the date of respective literature searches. It is important to note that the majority of the included papers were preprints.

## Results

### Epidemiology

The first P.1 cases were identified in Japan among four travellers that arrived in Japan from Northern Brazil.<sup>5</sup> It was subsequently traced back to Brazil<sup>5</sup> where the P.1 lineage (previously known as B.1.1.28.1) was first confirmed to be in Brazil as early as December 4, 2020.<sup>3,6</sup> As of February 2, 2021, P.1 has been confirmed in six countries with a total sequence count of 48 (Brazil [n=38], Japan [4], Italy [3], Faroe Islands [1], South Korea [1]), SA [1].<sup>6</sup> The P.1 variant was first identified outside of Brazil in Japan on January 2, 2021, followed by the US (January 9, 2021), South Korea (January 10, 2021), Faroe Islands (January 12, 2021), and Italy (January 18, 2021).<sup>6</sup>

The first US case was identified in a resident of Minnesota with recent travel history to Brazil.<sup>7</sup> In Brazil, the variant has been detected in Rio de Janeiro, São Paulo, and now appears to be the dominant SARS-CoV-2 strain in Manaus.<sup>8</sup> Preliminary investigations conducted in Manaus, Amazonas State, demonstrate an increase in the proportion of cases sequenced as variant P.1, from 52.2% (35/67) in December 2020 to 85.4% (41/48) in January 2021.<sup>9</sup>

## Transmissibility

While little is currently known about the transmissibility of the P.1 variant, Sabino et al. suggested that the P.1 variant identified in Manaus, Brazil may have higher transmissibility than pre-existing lineages.<sup>10</sup> They note a high frequency (42%, 13/31) of the P.1 lineage among samples sequenced from a cluster of COVID-19 cases in Manaus in December, 2020, but it was absent in 26 publicly-available genome surveillance samples collected in Manaus between March to November 2020. Additionally, the P.1 variant harbours the N501Y mutation that is found in the B.1.1.7 and B.1.351 variants, that has been associated with increased transmissibility.<sup>10</sup> The authors note that contact tracing and outbreak investigation data are needed to better understand relative transmissibility of this lineage.

## Disease Severity

No research on the impact of the P.1 variant on disease severity was identified.

## Diagnostic Assays

No research on the impact of the P.1 variant on diagnostic assays was identified. Since the P.1 variant does not contain any deletions in the S gene, it is unlikely to cause S gene target failures (e.g. S gene drop-out) that is known to occur with the B.1.1.7 variant.

## Vaccination

While researchers are still investigating the effectiveness of vaccines against the P.1 variant Brazil,<sup>11</sup> two pre-prints (not yet peer-reviewed) have tested plasma from recipients of both authorized mRNA vaccines against SARS-CoV-2 viruses with various spike mutations (i.e., variants of concern).<sup>12,13</sup>

- Wang et al. found that the B.1.351 variant showed resistance to neutralization by convalescent plasma (~11–33 fold) and vaccine sera (~6.5–8.6 fold), and that this was likely due to the E484K mutation, which is also present in P.1.<sup>12</sup> They hypothesized that similar resistance to neutralizing plasma would be found in the P.1 lineage.
- Similarly, Jangra et al. reported that polyclonal sera from vaccinated individuals and those previously infected with previous strains of SARS-CoV-2 had reduced neutralizing activity against the E484K mutation that is present in P.1. Additionally, they suggested that vaccinated individuals may be less protected against P.1, compared to the previous (USA-WA1/2020) strain.<sup>13</sup>
  - Specifically, their *in vitro* study found that serum neutralization efficiency from individuals who received the Pfizer vaccine was lower against a SARS-CoV-2 strain that had the E484K mutation, compared to the USA-WA1/2020 strain. Human sera with high neutralization antibody titers against the USA-WA1/2020 strain were still able to neutralize the E484K SARS-CoV-2 strain.<sup>13</sup> However, neutralization efficiency of donor sera with low or moderate immunoglobulin G (IgG) against the SARS-CoV-2 spike protein had neutralization values similar to negative control samples against the E484K strain. This suggests that to enhance protection against newly emerging SARS-CoV-2 variants the highest vaccine-induced titers possible are needed.

## Immunity and Reinfection

Since SARS-CoV-2 variants with the E484K mutation might be better at evading antibodies from the plasma of recovered COVID-19 patients infected with earlier strains,<sup>13</sup> the P.1 variant, containing this mutation, could increase the risk of re-infection or infection in vaccinated individuals.<sup>14</sup> Some reports support the possibility of reinfection with P.1:

- Naveka et al. describes the first confirmed case of reinfection with the P.1 lineage in a 29 year old female from Amazonas, Brazil, who was previously infected with a B.1 lineage virus.<sup>15</sup> The patient (with no history of immunosuppression) was originally infected on March 16, 2020 with symptoms of myalgia, cough, sore throat, nausea, and back pain. After being exposed to a positive case on December 19, the patient exhibited the second symptomatic COVID-19 episode on December 27, 2020. Genomic sequencing confirmed that the infections were from two different SARS-CoV-2 lineages in each COVID-19 episode: a B.1 lineage in the initial infection and a P.1 lineage at reinfection.
- A report from Brazil described a resurgence of COVID-19 cases in Manaus in January 2021, an area that had reported a high seroprevalence in October 2020 (adjusted seroprevalence of 76% (95% CI 67%-98%)).<sup>10</sup> This suggests a possible increased risk of reinfection with the P.1 variant; however, other contributing factors for the resurgence may include antibody waning and higher transmissibility of the P.1 variant, in addition to immune evasion.<sup>10</sup>

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## Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 P.1 variant of concern— what we know so far. Toronto, ON: Queen’s Printer for Ontario; 2021.

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