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## REVIEW ARTICLE

# What We Know about JN.1 (BA.2.86.1.1) SARS-CoV-2 Variant

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## ABSTRACT

**Background:** JN.1 (BA.2.86.1.1) has become the dominant strain in the U.S. at the end of 2023 according to the U.S. Centers for Disease Control and Prevention. The strain is a descendant of EG.5 family that was identified in China in February 2023 and was first detected in the United States in April 2023. JN.1\* SARSCoV2 lineages: JN.1 (BA.2.86.1.1), JN.1.1, JN.1.1.1, JN.1.2, JN.1.3 and recombinants XDD (EG.5.1.1/JN.1), XDK (XBB\*/JN.1.1.1). There is only a single change between JN.1 and BA.2.86 in the spike protein. JN.1 has inherited more than 30 mutations in its spike protein. It also acquired a new mutation, L455S, which further decreases the ability of antibodies to bind to the virus and prevent infection. A nonspike protein that is heavily mutated in JN.1 is the NSP3 protein. There are six mutations in NSP3 protein, namely T24I, V238L, G489S, K1155R, N1708S, and A1892T. NSP3 is one of the most active proteins in the virus, playing roles in viral RNA binding, polyprotein processing, and other functions. While the exact function of these mutations is unknown, they are likely to increase the efficiency of many of these mechanisms, creating a more functional and pathogenetic virus. The N protein is heavily mutated, R203K and G204R have been mutated in most virus variants throughout the pandemic and likely improve viral replication rate. The other mutations in N may also work to improve viral replication. While the Orf8 protein is truncated in the widespread XBB.1.5 variant, it is fully present in JN.1.

The symptoms of JN.1 appear to be similar to those caused by other strains, which include sore throat, congestion, runny nose, cough, fatigue, headache, muscle aches, fever or chills, loss of sense of taste or smell, shortness of breath or difficulty breathing, nausea or vomiting and diarrhea.

Some doctors have reported that upper respiratory symptoms seem to follow a pattern of starting with a sore throat, followed by congestion and a cough.

**Aim:** The purpose of the manuscript is to present a systematic review on the prevalence, structural, genomic, and pathogenic characteristics of JN.1 from January 1 to February 29, 2024, emphasizing on the variant genetic characteristics, contagiousness, and potential pathogenicity.

**Material and Methods:** Original scientific articles published in Medline, Pubmed, Science Direct, Web of Science, Scopus, EBSCO and BioMed Central databases, official health organizations (World Health Organization, U.S. Centers for Disease Control and Prevention, European Centre for Disease Prevention and Control) electronic publications, and specialized media in the subject, were electronically searched to accomplish the aim of the study. Articles published in any language were included from January 2024 to present using a variety of keywords in combination. The studies relevant to our review were analysed and compared.

**Results and Discussion:** The step-change evolution of BA.2.86, combined with the immune-evading features in JN.1, has given the virus a global growth advantage well beyond the XBB.1-based lineages the world faced in 2023. Evidence suggests the human adaptive immune system could still recognise and respond to BA.286 and JN.1 effectively. Updated monovalent vaccines, tests and treatments remain effective against JN.1. There are two elements to "severity": first if it is more 'intrinsically' severe (worse illness with an infection in the absence of any immunity) and second if the virus has greater transmission, causing greater illness and deaths, simply because it infects more people. The latter is certainly the case with JN.1.

**Conclusions:** The latest data from US-CDC shows JN.1 as the prevalent SARS-CoV-2 variant in the United States. JN.1 in January 2024, quickly increase its prevalence and surpassed other variants, including HV.1 to become the most prevalent strain in The United States of América. JN.1 has a similar transmission rate, exhibits a greater evasive capacity of immune-generated antibodies than HV.1 family of SARS-CoV-2, produce similar symptoms that of other Omicron variants, are expected not to produce an increase in hospitalizations and mortality rate and the SARS-CoV-2 vaccines recently developed by Pfizer and Moderna, must be effective against this Omicron subvariant. For now, the dominant variant JN.1 does not seem harmful in terms of creating a deadly disease but is still contagious enough to not be ignored.

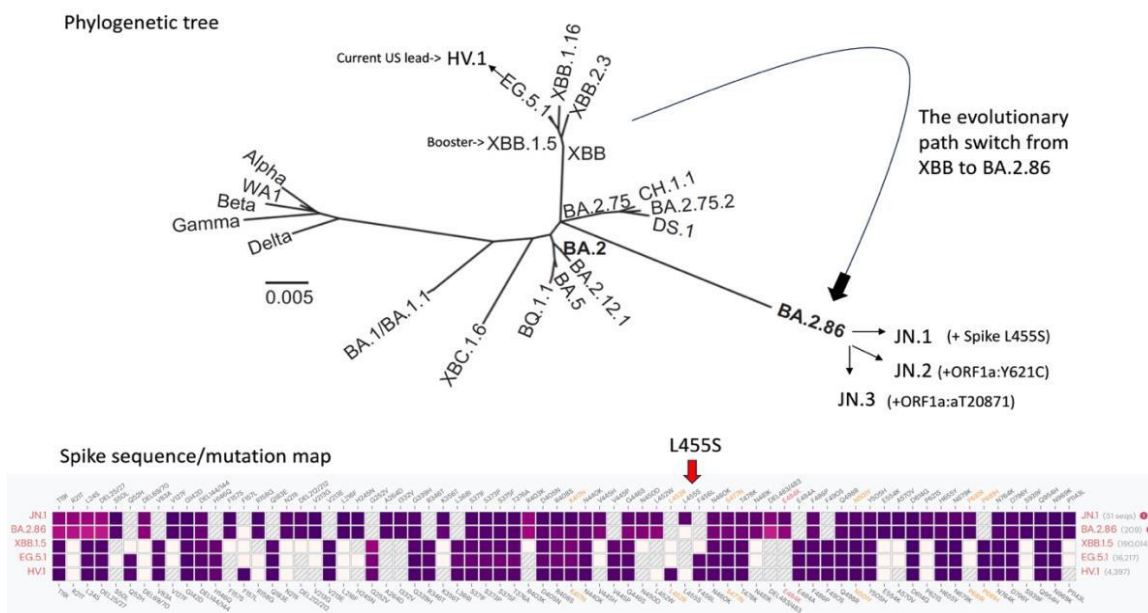
**Keywords:** JN.1, S-protein mutations, NSP3 protein, N-protein mutations, Pathogenic Properties.

## Introduction

JN.1 (BA.2.86.1.1) has become the dominant strain in the U.S. at the end of 2023 according to the U.S. Centers for Disease Control and Prevention (CDC). JN.1\* SARSCoV2 lineages are JN.1 (BA.2.86.1.1), JN.1.1, JN.1.1.1, JN.1.2, JN.1.3 and recombinants XDD (EG.5.1.1/JN.1), XDK (XBB\*/JN.1.1.1). The spike mutation map shows the evolution of BA.2.86 and origin of JN.1.

The Lancet Infectious Diseases Correspondence, published on January 3, 2024, the article by Key Sato and colleagues “Virological characteristics of the SARS-CoV-2 JN.1 Variant” and states<sup>1</sup>: The SARS-CoV-2 BA.2.86 lineage, first identified in August 2023, is phylogenetically distinct from the current circulating SARS-CoV-2 omicron XBB lineages, including EG.5.1 and HK.3.

### Phylogenetic Tree of JN.1\* Variant



Compared with XBB and BA.2, BA.2.86 carries more than 30 mutations in the spike protein, indicating a high potential for immune evasion. BA.2.86 has evolved and its descendant, JN.1 (BA.2.86.1.1), emerged in late 2023. JN.1 harbors Leu455Ser and three mutations in non-spike proteins.

Spike protein mutation Leu455Ser is a hallmark mutation of JN.1. We have recently shown that HK.3 and other flip variants carry Leu455Phe, which contributes to increased transmissibility and immune escape ability compared with the parental EG.5.1 variant.

The authors estimated the relative effective reproductive number of JN.1 using genomic surveillance data from France, the UK, and Spain, where more than 25 sequences of JN.1 have been reported, using a Bayesian multinomial logistic model.

The reproductive number of JN.1 in these three countries was higher than that of BA.2.86.1 and HK.3, one of the XBB lineages with the highest growth advantage at the end of November 2023. These results suggest that JN.1 might soon become the dominant lineage worldwide. Indeed, by the end of November

2023, JN.1 had already overtaken HK.3 in France and Spain.

The *in vitro* ACE2 binding assay showed that the dissociation constant value of the JN.1 receptor-binding domain (RBD) was significantly higher than that of the BA.2.86 RBD, suggesting that Leu455Ser decreases binding affinity to the human ACE2 receptor.

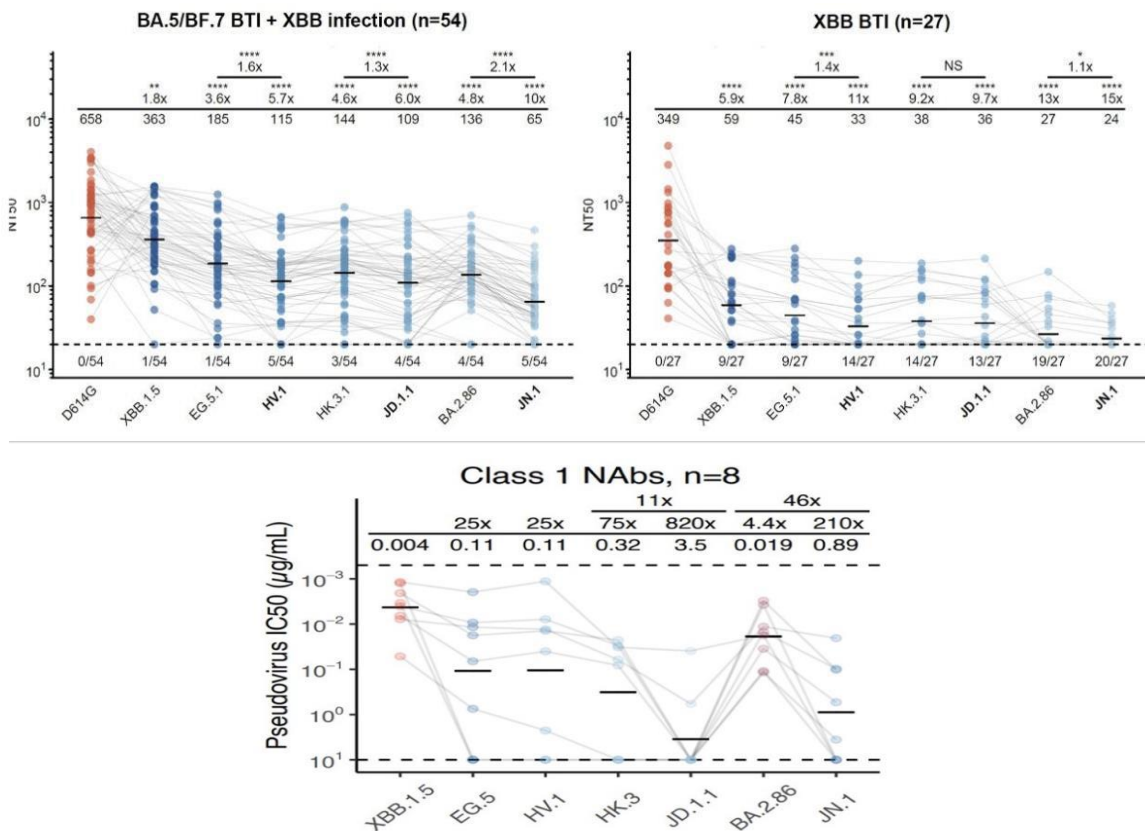
In contrast, the pseudovirus assay showed that the infectivity of JN.1 was significantly higher than that of BA.2.86. This discrepancy could be due to the difference between monomeric RBD and trimerised whole spike protein.

They performed a neutralisation assay using rodent sera infected with BA.2.86 or immunised with BA.2.86 spike protein. In both cases, the 50% neutralisation titre (NT50) against JN.1 was similar to that against BA.2.86, suggesting that Leu455Ser does not affect the antigenicity of BA.2.86.

On the other hand, the NT50 of breakthrough infection sera with XBB.1.5 and EG.5.1 against JN.1 was significantly lower than that of HK.3 (2.6-fold to 3.1-fold) and BA.2.86 (3.8-fold). Taken together, these results suggest that JN.1 is one of the most immune-evading variants to date.

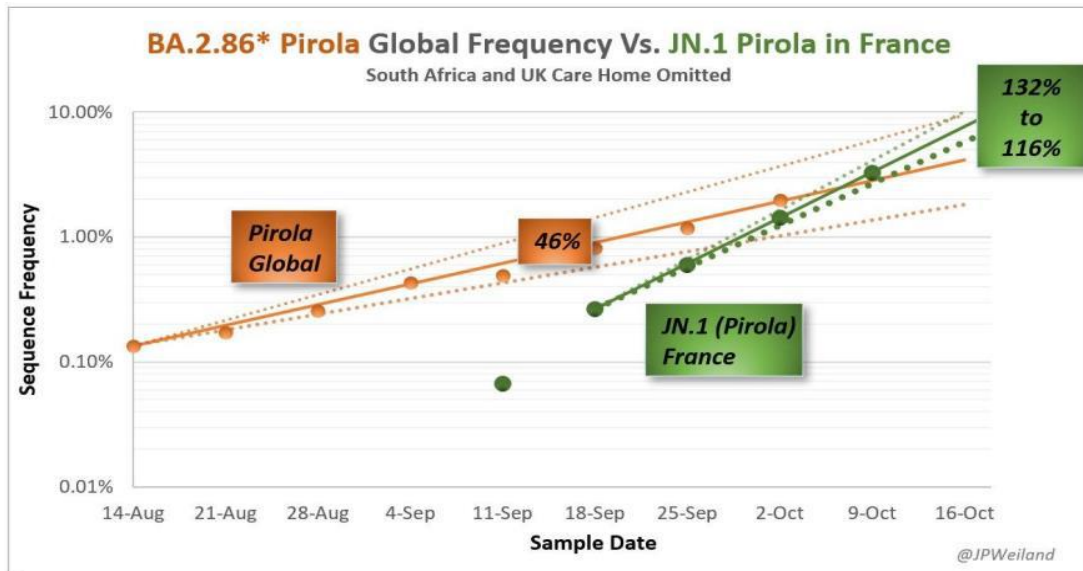
The results suggest that Leu455Ser contributes to increased immune evasion, which partly explains the increased reproductive number of JN.1, and the impact of the L455S mutation on Class 1 monoclonal antibodies differs from BA.2.86. This mutation is key to promoting more evasion to our immune response.

Yunlong Cao's group in Peking was the first to characterize the JN.1 variant, and showed a weak neutralizing antibody response (y-axis, NT50) to breakthrough infections (BTI) of XBB<sup>2</sup> (Figures below).



The FLip variants, which are an ongoing “double whammy mutation” (involving spike sites 455 and 456) are superseded with respect to immune evasion by JN.1. This all seems to be linked with the takeoff of JN.1 in France and other countries. Furthermore, JN.1 shows robust resistance to monovalent XBB.1.5 vaccine sera compared with BA.2.86.

Nick Rose has also done modeling based on the sequences of JN.1 in France and England with a lesser but still high magnitude of growth advantage. JN.1 has shown up in many countries now, besides France and the UK, including the US, Iceland, Portugal, Belgium, Israel, Spain, Netherlands, Canada Germany, and Singapore.



JP Weiland’s model compares BA.2.86 globally with what has been seen for JN.1 in France, suggesting a marked growth advantage of the latter. Other derivatives of BA.2.86 such as JN.2 and JN.3 are also being identified in multiple countries.

The authors won’t know for a few weeks as to whether JN.1 will be linked with a significant rise in Covid or how well our immune response from prior vaccinations, infection(s) and the XBB.1.5 new booster will keep us protected. In the meantime, if you haven’t gotten a booster, it would be a very good idea to go ahead. That’s especially important if you are of older age or are immunocompromised.

In the U.S. they are approved for all age groups 6 months and older, and there would

be some protective benefit, but as with any intervention, a bigger bang for those at highest risk. Even if our current booster does not evoke a strong neutralizing antibody response to JN.1 (or subsequent BA.2.86 descendants), it will rev up our immune system, including cellular immunity, for conferring enhanced protection.

As always, non-pharmacologic means of preventing infections help work against all strains of this and other respiratory viruses that are out there now (including flu and RSV). Even if it turns out that JN.1 is not particularly deleterious, the main message here is that concerning variants keep cropping up and there’s a new path for the virus to find its way, versions that are getting further away from where this all started nearly 4 years ago.

As of February 22, 2024, 12:54 PM (accessed March 3, 2024), 70,123 sequences in the JN.1 lineage have been detected since the lineage was identified<sup>3</sup>.

The strain has been detected in at least 97 countries and 54 U.S. States.

**United States of America** (22,916/4,848,820 -0.472%-), **United Kingdom** (7,330/3,027,728 -0.242%-), **Canada** (5,784/592,247 -0.975%-), **Spain** (4,178/240,375 -1.73%-), **Denmark** (3,749/657,800 -0.569%-), **France** (3,715/604,845 -0.614%-), **Singapore** (2,407/45,627 -5.27%-), **Netherlands** (2,107/173,966 -1.21%-), and **Sweden** (1,606/264,092 -0.608%-), shows the highest JN.1 cases (JN.1 all time prevalence/Omicron-total sequenced samples). **China** (206/62,947 -0.327%-), **Mexico** (62/91,254 -0.067%-), **Costa Rica** (99/12,091 -0.818%-), **Honduras** (20/405 -4.93%-), **Guatemala** (19/5,376 -0.353%-).

**New York** (5,489/343,382 -1.59%-), **California** (4,229/900,684 -0.469%-), **New Jersey** (1,812/118,416 -1.53%-), **Texas** (1,433/307,588 -0.465%-), **Minnesota** (1,004/163,243 -0.615%-), **Virginia** (532/99,947 -0.532%-), **Iowa** (435/29,598 -1.46%-), and **Utah** (97/144,125 -0.067%-), shows the higher JN.1 cases in United States (JN.1 all time prevalence/Omicron -total sequenced samples).

As of January 5 **(1)**, 2024, January 19 **(2)**, February 9 **(3)**, February 16 **(4)**, and March 03 **(5)**, JN.1 Worldwide Prevalence is<sup>4</sup>:

**(1)** France 18%, United States of America 14.0%, Denmark 11.0%, Singapore 1%, and Canada 7.0%.

**(2)** France 18%, United States of America 14.0%, Denmark 11.0%, Singapore 1%, and Canada 7.0%.

**(3)** United States of America 23.0%, United Kingdom 12.0%, Canada 9.0%, France 8.0%, Denmark 7.0%.

**(4)** United States of America 23.0%, United Kingdom 12.0%, Canada 9.0%, France 8.0%, Denmark 7.0%.

**(5)** United States of America 29.0%, United Kingdom 12.0%, Canada 10.0%, Spain 8.0%, France 6.0%.

As of February 9, 2024 **(1)**, February 16 **(2)**, March 03 **(3)**, JN.1.1 and JN.1.4 Worldwide Prevalence is:

#### JN.1.1

**(1)** France 35.0%, United States of America 15.0%, United Kingdom 6.0%, Canada 6.0%, Denmark 5.0%.

**(2)** France 35.0%, United States of America 15.0%, United Kingdom 6.0%, Canada 6.0%, Denmark 5.0%.

**(3)** France 27.0%, United States of America 19.0%, Canada 7.0%, United Kingdom 6.0%, Denmark 4.0%.

#### JN.1.4

**(1)** United States of America 30.0%, Denmark 18.0%, Singapore 11.0%, United Kingdom 7.0%, Canada 6.0%.

**(2)** United States of America 30.0%, Denmark 18.0%, Singapore 11.0%, United Kingdom 7.0%, Canada 6.0%.

**(3)** United States of America 40.0%, Denmark 10.0%, Canada 7.0%, Singapore 7.0%, United Kingdom 7.0%.

## Material and Methods

Original scientific articles published in Medline, Pubmed, Science Direct, Web of Science, Scopus, EBSCO and BioMed Central databases, official health organizations (World Health Organization, U.S. Centers for Disease Control and Prevention, European Centre for Disease Prevention and Control) electronic publications, and specialized media in the subject, were electronically searched to accomplish the aim of the study.

Articles published in any language were included from January 2024 to present using a variety of keywords in combination. The studies relevant to our review were analysed and compared.

## Lirerature and Media Survey

On December 8, 2023, U.S.-CDC publish in the weekly update on SARS-CoV-2 Update on SARS-CoV-2 Variant JN.1 Being Tracked by CDC" and highlights<sup>5</sup>: "JN.1 is closely related to the variant BA.2.86 that CDC has been tracking since August 2023. Even though BA.2.86 and JN.1 sound very different because of the way variants are named, there is only a single change between JN.1 and BA.2.86 in the spike protein".

JN.1 was first detected in the United States in September 2023. By the end of October, it made up less than 0.1% of SARS-CoV-2 viruses. Previously, JN.1 was grouped with BA.2.86 on COVID Data Tracker. CDC projects that the variant JN.1 comprises an estimated 15-29% of in the United States as of December 8, 2023.

CDC projects that JN.1 will continue to increase as a proportion of SARS-CoV-2 genomic

sequences. It is currently the fastest-growing variant in the United States. The continued growth of JN.1 suggests that it is either more transmissible or better at evading our immune systems.

At this time, there is no evidence that JN.1 presents an increased risk to public health relative to other currently circulating variants. There is no indication of increased severity from JN.1 at this time. Updated COVID-19 vaccines are expected to increase protection against JN.1, as they do for other variants.

As noted in previous updates, COVID-19 tests and treatments are expected to be effective against JN.1. The rapid growth of JN.1 compared with other variants raises the question of whether this variant might drive an incremental increase in infections.

COVID-19 activity is currently increasing in the United States. We expected this increase because COVID-19 has had a pattern of increasing and peaking in late summer, and then again peaking around the new year. Right now, we do not know to what extent JN.1 may be contributing to these increases or possible increases through the rest of December like those seen in previous years.

It is not currently known whether JN.1 infection produces different symptoms from other variants. In general, symptoms of COVID-19 tend to be similar across variants. The types of symptoms and how severe they are usually depend more on a person's immunity and overall health rather than which variant causes the infection. COVID-19 activity is likely to increase over the next month.

An updated COVID-19 vaccine can help keep you protected against JN.1 and other variants.

It's a great time to get that vaccine if you haven't received one this fall. Regardless of what variants happen, CDC will continue to track them, working closely with partners around the world to understand how they are spreading and how they respond to vaccines and treatments.

On **January 2, 2024**, Shay Fleishon, published in his tweeter account<sup>6</sup>: "On the occasion of the rise of JN.1, I want to return to a cycle I proposed with the rise of BA.2.86. Most importantly, I want to emphasize that this is a possible theory, a thought exercise. It's just to raise a possibility, like others that can be considered".

Added that JN.1 is not like the other variants from the past year plus. It didn't increase gradually. Its not a result of stepwise evolution. It is BA.2.86 with a small addition that apparently released something that the genetic leap of BA.2.86 had brought.

As the mutational pattern accumulated in the genetic leap is huge, and epistatic relations are too complex to check in a simple straightforward experiment on a petri dish, lets think of it as the release of a deleterious variance inter host which might have been advantageous intra host (if it was just simple immune evasion, I would expect star shape phylogeny with many RBD alterations).

After the takeover, of course, new variants will evolve. The molecular clock is ticking and the variant hunter community will fill the PANGO repository. This happened with Alpha (B.1.1.7), without being much defined. It also happened with Delta (B.1.617.2) and its AY lineages, although none of those really showed a clear advantage, and there was not much convergence

of mutations between them (and certainly not in the RBD).

Then came the BAs, the daughter lineages of B.1.1.529 (the first of which, BA.1, was called Omicron, after which they stopped giving Greek letter names) with a record breaking intrinsic infectivity.

Over the past year and a bit, we have witnessed the gradual rise of sub-variants (mainly of XBB, a recombinant of two second-generation BA.2 variants with small leaps), where the successful ones (simultaneously rising in different countries) contained converging mutations in the RBD, without convergence in other genomic regions (as happened in all past VOC).

One option they have is through the intrinsic infectivity, but the ones of the direct descendants of B.1.1.529 (mainly BA.5 and BA.2) might be so high, that over compete it will bring minor advantages (its like every world record in running is held for a longer time than its predecessor and is not broken by much beyond it).

And then there's immune evasion, well that's a better option. Its more easy to disguise differently than to run faster than before, but only if it will bring advantage, and indeed the world's population is increasingly vaccinated (both vaccines and recoveries), changing the fitness landscape the variants are facing, giving benefit to immune evasion evolvment.

Most of the neutralizing antibodies targeting the RBD, pivotal for the infection of our cells. So it might be that over time, to win patients through immune evasion, variants changes the RBD, and sacrificed part of the intrinsic infectivity.

Compared to the variants they were competing, that was a reasonable sacrifice, their combined R was relatively higher but with lesser intrinsic infectivity compared to the basic BA's, and it may be that by the many changes it underwent intra-host, it again reached a similar or even lower intrinsic infectivity than that of the basic BAs, but it did so through a different path in the fitness landscape (and hints for that comes from the convergence it has outside the S1 region).

Because that's how it works, every variant that evolves in a chronic patient is like a scratch card, like a rope sent far in a slightly random azimuth in the fitness landscape of the inter-host. Once out of many tries, this intra host diversity also brings a better fitness inter host.

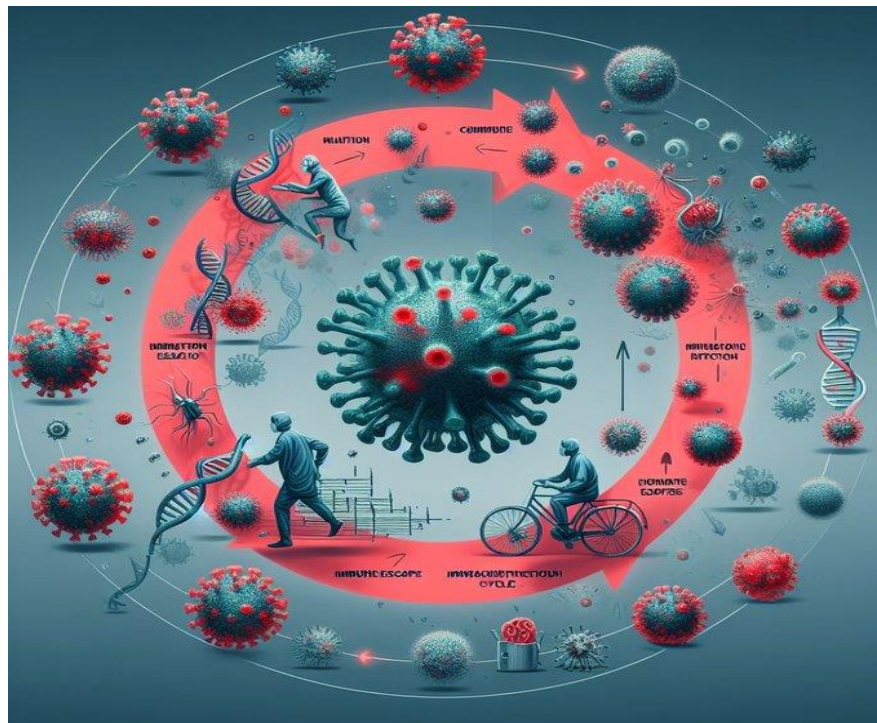
The fact that the evolution path is different means that the RBD (which is before all a key component in infectivity) changes and therefore de facto, even without "knowing" what happened immunologically in the world, it has

the ability to escape the immune response of the population.

So it got a different RBD and still infectious in a closer level to the basic BAs. Which combined leads to a higher R. So, maybe this will be the cycle:

- A genetic leap, which cumulatively leads to a higher R.
- Competitive genetic development that sacrifices infectivity in favor of escaping the immune response.
- The rise of another variant in a leap, with infectivity more similar to the basic Omicrons, and de facto escape, thus a higher R relative to the existing variants.

It may be that in the future this scenario will materialize, and I will be thrilled that I came up with it in advance, and I will share this tweet again, but it's also likely that this virus will surprise us again.





On January 3, The HealthSite.com published the article by Satata Karmakar "4 Years of COVID Marathon: From Lockdowns to Long COVID, JN.1 Sub-Variant Reminds Us, The Pandemic Isn't Over", and about JN.1 variant brief<sup>7</sup>:

The World Health Organisation (WHO) classified the JN.1 on December 19, 2023, as a separate variant of the BA.2.86 Omicron lineage, as a "variant of interest". This was done because this strain of SARS-CoV-2 is spreading rapidly. However, the WHO has said that with the available evidence, the additional public health risk posed by JN.1 is currently evaluated as "low" globally.

Many parts of India have seen a rise in COVID-19 cases as well, with current active cases at over 4,000 with no clusters have been reported yet in the JN.1 sub-variant. In comparison with the parent lineage BA.2.86, the JN.1 COVID sub-variant has the additional L455S mutation in the spike protein. The challenge has always been making effective drugs and vaccines when the virus is constantly mutating.

The pandemic has caused global social disruption by limiting global social relations. The idea of "social distancing" negates regular social interaction. Due to isolation and cessation of some social affairs, this disease causes problems such as:

1. Social anxiety
2. Panic due to insecurity
3. Economic recession, and
4. Severe psychological stress

**On January 3**, The Centers for Disease Control and Prevention (CDC), in an update issued 19 December 2023, said there was no

indication of increased severity from JN.1 at this time<sup>8</sup>. The data highlights "There has been an increase in prevalence of SARS-CoV-2 in England and Scotland during the two weeks leading up to 13 December 2023, the existing vaccines, tests, and treatments still work well against JN.1".

The data showed that as well as the usual symptoms previously reported by people with COVID-19, such as runny noses, coughs, headaches, and weakness, some have said they have experienced trouble sleeping and anxiety as well.

**On January 3**, the Pharmaceutical Executive Editorial Staff of PharmExec.com published "Invivyd Seeks EUA for Monoclonal Antibody Designed to Prevent COVID-19 in Immunocompromised Individuals"<sup>9</sup>.

The company Invivyd, Inc. has filed a request with the FDA for emergency use authorization for VYD222, a broadly neutralizing, half-life extended monoclonal antibody developed specifically to prevent COVID-19 in immunocompromised adults and adolescents. The EUA submission was based on positive initial findings from the pivotal Phase III CANOPY clinical trial for VYD222 and data for ongoing in vitro neutralization activity against relevant COVID-19 variants.

VYD222 was found to demonstrate a potent response against multiple SARS-CoV-2 variants currently circulating, including the fastest growing variant in the United States, JN.1, as well as HV.1, BA.2.86, XBB.1.5.10/EG.5, and HK.3.

That investigators noted that the initial findings from the CANOPY trial support an immunobridging approach with in vitro VYD222

potency data used to calculate and efficiently determine sVNA titer levels against new, emerging SARS-CoV-2 variants. Initial data showed that the safety and tolerability profile of VYD222 was favorable with no reported serious adverse events related to VYD222.

The Lancet Infectious Diseases, Correspondence, published on January 3, 2024, the article by Key Sato and colleagues "Virological characteristics of the SARS-CoV-2 JN.1 Variant" and states<sup>10</sup>: "The SARS-CoV-2 BA.2.86 lineage, first identified in August 2023, is phylogenetically distinct from the current circulating SARS-CoV-2 omicron XBB lineages, including EG.5.1 and HK.3, compared with XBB and BA.2, BA.2.86 carries more than 30 mutations in the spike protein, indicating a high potential for immune evasion. JN.1 harbors Leu455Ser and three mutations in non-spike proteins. Spike protein mutation Leu455Ser is a hallmark mutation of JN.1: we have recently shown that HK.3 and other flip variants carry Leu455Phe, which contributes to increased transmissibility and immune escape ability compared with the parental EG.5.1 variant.

We estimated the relative effective reproductive number of JN.1 using genomic surveillance data from France, the UK, and Spain, where more than 25 sequences of JN.1 have been reported, using a Bayesian multinomial logistic model. The reproductive number of JN.1 in these three countries was higher than that of BA.2.86.1 and HK.3, one of the XBB lineages with the highest growth advantage at the end of November 2023. These results suggest that JN.1 might soon become the dominant lineage worldwide.

The in vitro ACE2 binding assay showed that the dissociation constant value of the JN.1

receptor-binding domain (RBD) was significantly higher than that of the BA.2.86 RBD, suggesting that Leu455Ser decreases binding affinity to the human ACE2 receptor. In contrast, the pseudovirus assay showed that the infectivity of JN.1 was significantly higher than that of BA.2.86.

This discrepancy could be due to the difference between monomeric RBD and trimerised whole spike protein. We then performed a neutralisation assay using rodent sera infected with BA.2.86 or immunised with BA.2.86 spike protein. In both cases, the 50% neutralisation titre (NT50) against JN.1 was similar to that against BA.2.86, suggesting that Leu455Ser does not affect the antigenicity of BA.2.86.

On the other hand, the NT50 of breakthrough infection sera with XBB.1.5 and EG.5.1 against JN.1 was significantly lower than that of HK.3 (2.6-fold to 3.1-fold) and BA.2.86 (3.8-fold). Furthermore, JN.1 shows robust resistance to monovalent XBB.1.5 vaccine sera compared with BA.2.86.

Taken together, these results suggest that JN.1 is one of the most immune-evading variants to date and that Leu455Ser contributes to increased immune evasion, which partly explains the increased reproductive number of JN.1.

**On January 4**, Satata Karmakar from The HealthSite.com, published "New Symptoms of COVID-19 JN.1 Variant: Are you infected by the new variant of COVID-19? Take a look at the signs and symptoms of JN.1 variant"<sup>11</sup>.

In the latest development, UK health authorities have identified new symptoms associated with the latest COVID-19 sub-variant JN.1, which

include anxiety and trouble sleeping. In an interview, Sarah Jones, a leading epidemiologist warned against ignoring the signs and symptoms linked with the new variant, "the JN.1 variant has full potential to trigger anxiety and sleep disturbances in the infected patient, and this is worrisome".

"While more research is needed to understand the reasons behind this, it's crucial to acknowledge and address these symptoms effectively". Individuals experiencing these issues should reach out for help from healthcare professionals or mental health specialists".

Earlier, experts had warned that the JN.1 variant of COVID-19 is most likely to affect the upper respiratory tract, causing severe infections, such as fever, cough, sore throat, body ache, and runny nose. However, in the latest development, UK health authorities have warned that infected patients may also experience trouble sleeping and anxiety.

**On January 5**, the Centers for Disease Control and Prevention (CDC), published "COVID-19 Activity Increases as Prevalence of JN.1 Variant Continues to Rise"<sup>12</sup> and updated the information provided on January 3. As the new year takes off, CDC continues to track the rise of JN.1 across the country. An offspring of BA.2.86, JN.1 is now the most widely circulating variant of SARS-CoV-2 in the United States and globally, and at this time, there is no evidence that JN.1 causes more severe disease.

As of January 5, 2024, JN.1 is estimated to account for approximately 62% (range 55-68%) of all currently circulating SARS-CoV-2 variants, an increase from the estimated prevalence of 44% (range 39-50%) two weeks ago. CDC is also observing an increase in the

prevalence of JN.1 in international travelers and wastewater viral levels, as well as in most regions around the globe and states:

- COVID-19 hospitalizations increased 20.4% the week ending December 30, 2023.
- In that same period, deaths went up by 12.5%, with COVID-19 deaths accounting for 3.6% of total deaths in the United States.
- Wastewater viral activity levels, an important tool used to detect increases of COVID-19 transmission in the community, are currently high and increasing in all regions.
- As of December 25, 2023, 66% of wastewater samples had JN.1 as the dominant variant, up from 58% the previous week.
- JN1.1 is not only rising in the United States, but globally as well.
- JN.1 is the most prevalent variant around the world. It is the dominant variant in Europe and is rising sharply in Asia.
- Not enough Americans are vaccinated. As of December 30, 2023, only 8% of children and 19% of adults report having received the updated COVID-19 vaccine.

Only 38% of adults age 65 years and older report having received this vaccine, which is concerning given that they are at higher risk of hospitalization from COVID-19.

**On January 7**, Prateek Chakraborty from India Today News Desk, published the COVID-19 update in India<sup>13</sup>. India saw a

single-day rise of 756 COVID-19 cases and five deaths in the past 24 hours, the Union Health Ministry said on Sunday.

According to the health ministry data, the active caseload continued to decline to 4,049 from 4,187 the previous day. Five deaths, two each from Maharashtra and Kerala, and one from Kerala, were reported, pushing the death toll to 533,392.

The national recovery rate stood at 98.81 per cent while the fatality rate was pegged at 1.18 per cent, according to the ministry. So far, 4.50 crore (45,018,134) cases have been reported since the COVID-19 outbreak in the country in January 2020, and according to the health ministry, 220.67 crore doses of COVID-19 vaccines have been administered so far in the country.

On Saturday, India reported 774 new COVID-19 cases and two deaths from Tamil Nadu and Gujarat, the ministry said. The number of daily cases was in double digits till December 5, but it began to rise again amid cold weather conditions and after the emergence of a new coronavirus variant JN.1.

After December 5, the highest single-day rise of 841 cases was reported on December 31, 2023, which was 0.2 per cent of the peak cases reported in May 2021, official sources said. The number of cases of COVID-19 sub-variant JN.1 reported from 12 states till January 4 rose to 619, official sources said on Friday.

They said 199 cases have been reported from Kamataka, 148 from Kerala, 110 from Maharashtra, 47 from Goa, 36 from Gujarat, 30 from Andhra Pradesh, 26 from Tamil Nadu, 15 from Delhi, four from Rajasthan, two from Telangana and one each from Odisha and Haryana.

Even though the number of cases is rising and the JN.1 sub-variant has been detected in the country, there is no cause of immediate concern as the majority of those infected are opting for home-based treatment, indicating mild illness, officials said.

**On 9 January**, Aliza Rosen, and Melissa Hartman from Johns Hopkins Bloomberg School, published "What to Know About JN.1, the Latest Omicron Variant. Vaccines, tests, and antivirals are still effective tools in the latest COVID surge", and states<sup>14</sup>: "In early November 2023, the JN.1 variant caused less than 5% of COVID-19 cases in the U.S. Now it is estimated to cause more than 60% of them".

Virologists including Andy Pekosz, a professor in Molecular Microbiology and Immunology, are paying attention. Here, Pekosz explains what virologists are seeing, what this new variant means for case rates and treatments, and why it's so important for more people to get the updated COVID-19 vaccine rolled out this fall.

### What is JN.1?

A SARS-CoV-2 variant called BA.2.86 emerged a few months ago and caught virologists' attention because it contains many more mutations, about 30 of them, to evade immunity than any other variant circulating at that time. However, the BA.2.86 variant never came to dominate among the group of SARS-CoV-2 variants that were circulating in the late summer/early fall of 2023.

### What's happening now with this variant?

The increase in the number of cases caused by JN.1 corresponds to an overall increase in COVID-19 cases. Symptoms of JN.1 infection are very similar to those of previous omicron

variants, and it doesn't seem to cause more severe disease, either. There is some suggestion that JN.1 may be causing more diarrhea than previous variants, but we don't have any firm data supporting that yet.

### **What's most important to understand about this variant?**

This latest variant should be a reminder that we have tools to fight off COVID infection and minimize severe disease: Tests detect JN.1, the new vaccines protect against severe disease, and antivirals are still capable of treating infection from JN.1.

We just have to use these tools more effectively than we have over the last six months. So far, only 8% of children and 19% of adults have received the latest vaccine, so a lot of people are missing out on protection from this virus.

### **What does the transmission timeline look like for JN.1?**

The period of infectiousness for JN.1 is very similar to that of the other omicron variants that have been circulating over the past year: You are contagious one to two days before your symptoms begin, and you are still contagious for at least two to three days after your symptoms begin, though some people can continue to have the detectable live virus for up to a week after symptom onset. After exposure, it may take five days or more before you begin to develop symptoms.

### **Are people who had an older vaccine or who've had COVID from another variant likely to be reinfected by JN.1?**

The older vaccines were based on SARS-CoV-2 variants that are very different from variants circulating now. That, combined with the fact

that your immunity from vaccination or infection tends to drop off over time, means that you won't get a lot of protection from COVID-19 if you are relying on the vaccines you received nearly a year ago.

It's very similar to why we have annual influenza vaccines: The virus is changing, so we have to change the vaccine to make sure it is a good match with the virus variants that are causing infection right now.

### **Do we know yet how well this fall's COVID-19 vaccines work against this variant?**

While the JN.1 variant does have a number of mutations that help it avoid immunity, laboratory studies suggest that the updated COVID-19 vaccine does increase the amount of antibodies that can recognize JN.1, and it is still effective in protecting against severe disease. You really need the newest COVID-19 vaccine formulation to be protected from severe illness from JN.1 and other recent variants.

### **COVID numbers have been rising for a few weeks now. Is it too late to get the vaccine?**

No. Getting vaccinated now can provide protection during this surge. Don't wait, this is particularly important for those in high-risk groups, but it goes for all eligible individuals.

### **Is Paxlovid effective against JN.1?**

Paxlovid is still working very well, particularly in high-risk populations, but it's not being prescribed as frequently as it should be. It's important to remember that Paxlovid needs to be taken as soon as possible after symptoms begin, within five days of symptom onset is the guidance, but the earlier, the better. This means it is particularly important to test when

you start feeling sick and then get a prescription if you test positive.

### What might we expect in terms of case rates over the next few weeks?

Case rates will likely go up. We're coming out of a period when we already expected transmission to go up, due to increased travel and holiday gatherings. For the rest of January and into February, we will continue to have a high amount of respiratory virus activity that includes COVID-19 cases.

Now is the time to get vaccinated if you haven't already, get some COVID-19 tests available for free from the U.S. government, and make sure your local pharmacy can fill a COVID-19 antiviral prescription if you do end up testing positive.

**On January 10,** The American Medical Association published "Symptoms of new COVID variant JN.1, latest studies on Paxlovid rebound and hydroxychloroquine"<sup>15</sup>.

Andrea Garcia, AMA Vice President of Science, Medicine and Public Health, discusses trends in COVID, flu and RSV infections, details of the latest COVID variant and the return of mask mandates, and about JN.1 said:

"The CDC released an update on January 5 about the prevalence of JN.1, explaining that it may be intensifying the spread of COVID-19 this winter. It's currently responsible for about 61% of cases in the U.S., and that's based on data ending the week of January 6, and that's a sharp rise from the 7% of cases in late November".

JN.1 doesn't seem to be causing more severe illness than previous variants. The symptoms you're going to see if you're infected with JN.1

is going to depend in part on your underlying health and the level of immunity you have, but generally speaking, those symptoms are similar to the viruses caused by other variants, so sore throat, congestion, runny nose, cough, fatigue, headache, among others.

So although overall COVID-19 illnesses do seem to be less severe than in previous years, that CDC data does indicate that hospital admissions for COVID-19 right now are up 20% and deaths are up 12.5% from the previous week. We're still losing about 1,500 people per week on average due to COVID-19.

With that new highly infectious JN.1 variant, low uptake of the latest COVID vaccine, we're at about 19% of adults who have received that, and then, of course, few people taking precautions, like masking, we can really expect to see this spread continue.

**On January 11,** The United Kingdom Health Security Agency -UKSHA- published "National Influenza and COVID-19 surveillance report Week 2 report (up to week 1 2024 data)", and in the section Microbiological Surveillance; SARS-CoV-2 variants inform:

This week's report is the first to include data on JN.1 (V-23DEC-01), a sub-lineage of BA.2.86 (V-23AUG-01). This designation has been applied retrospectively to previous weeks data. Once a sub-lineage meets required thresholds, it will be designated as a variant and prevalence of this sub-lineage in positive cases will then be identifiable in the data.

The UKHSA variant definition repository contains the previous genomic definitions for UKHSA declared variants. To account for sequencing delays, we report the proportion of variants

from sequenced cases between 25 December 2023 and 31 December 2023.

Of those sequenced in this period:

- 62.3% were classified as JN.1 (V-23DEC-01),
- 16.2% as BA.2.86 (V-23AUG-01),
- 7.8% as EG.5.1 (V23JUL-01),
- 6% as XBB (V-22OCT-02),
- 3.5% as XBB.1.5 (V-23JAN-01) and,
- 1.5% as BA.2 (V22JAN-01).

**As of January 12**, Rita Rubin MA from JAMA Networks, in Medical News & Perspectives “As COVID-19 Cases Surge, Here’s What to Know About JN.1, the Latest SARS-CoV-2 “Variant of Interest”<sup>16</sup>. BA.2.86’s spawn, JN.1, has become the dominant SARS-CoV-2 variant in the US, status its parent variant never achieved.

Fortunately, although COVID-19 cases have surged, hospitalizations and deaths from the disease are still considerably lower than they were the same time a year earlier. When BA.2.86 joined the SARS-CoV-2 Omicron family last summer, it grabbed pandemic trackers’ attention because it was so different from its progenitor, BA.2.

Compared with BA.2, BA.2.86’s spike protein carries more than 30 mutations, suggesting that it might spread more easily than its predecessors, but even armed with those new mutations, BA.2.86 failed to dominate the other subvariants.

Through early January of this year, BA.2.86 never exceeded much more than a 3% share of circulating SARS-CoV-2 subvariants in the US, according to Nowcast estimates from the

US Centers for Disease Control and Prevention (CDC).

Globally, BA.2.86 represented 8.9% of available SARS-CoV-2 sequences by the first week of November 2023, according to the World Health Organization (WHO), which classified BA.2.86, including its sublineages, as a variant of interest on November 20.

Four weeks after labeling the entire burgeoning BA.2.86 family as a variant of interest, the WHO classified JN.1 alone as one, too, due to its rapidly increasing spread. By early January, JN.1’s share of circulating variants in the US had soared to an estimated 61.6%, up from 38.8% just 2 weeks prior, according to the CDC’s Nowcast estimate.

JN.1’s spike protein has just 1 more mutation than BA.2.86’s spike called L455S, that enhances the virus’ ability to bind to the angiotensin-converting enzyme 2 (ACE2) receptor, SARS-CoV-2’s doorway into cells, Nicole Doria-Rose, PhD, chief of the Humoral Immunology Core at the National Institute of Allergy and Infectious Diseases’ Vaccine Research Center, noted in an interview with JAMA.

BA.2.86 “didn’t take off until it picked up this 1 mutation that made it JN.1,” she said. JN.1 appears to be highly contagious, perhaps more than any other member of the Omicron family, Vanderbilt University School of Medicine infectious disease and health policy professor William Schaffner, MD, said in an interview. “That’s maybe why it’s outrunning them now, as JN.1 gained traction, indicators of SARS-CoV-2 infection levels rose”.

In a January 5 report, the CDC estimated that compared with the same time last year, viral

activity levels in wastewater were 27% higher and the percentage of positive COVID-19 tests was 17% higher. Despite apparently higher infection levels, indicators of COVID-19 illness requiring medical attention were lower than a year earlier, the CDC said.

For example, emergency department visits for COVID-19 were down 21%, and the percentage of all US deaths that were attributed to COVID-19 was 3.6% (839 deaths) for the week ending December 30, 2023, compared with 5.2% (3,658 deaths) for the week ending December 31, 2022, according to provisional CDC data.

“I think JN.1 clearly is driving transmission”, epidemiologist Michael Osterholm, PhD, MPH, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, told JAMA, “Fortunately, there’s no evidence it’s producing more severe illness”.

Given the high JN.1 infection rates, people with respiratory symptoms should assume they have COVID-19, even though they might test negative for the first few days, Osterholm said “If you have any symptoms at all of respiratory illness, don’t go to a public or private event, especially indoors”.

Higher rates of COVID-19 and other respiratory infections have spurred hospitals in a handful of states to reinstitute mask mandates, according to news reports, at least for staff who directly interact with patients in their rooms or other clinical care areas. For example, Mass General Brigham implemented the policy on January 2 and will adhere to it until infection levels drop later in the winter or in the spring.

**As of January 14**, Sanchari Sinha Duta from New Medical Life Sciences, publishes “JN.1

variant's spread not due to enhanced immune escape, study suggests”<sup>17</sup>. Summarize the article “Humoral immune escape by current SARS-CoV-2 variants BA.2.86 and JN.1, December 2023”<sup>18</sup>, published in the journal Eurosurveillance on January 11, 2024.

The authors claims that the recent upsurge in cases with the JN.1 variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may not be due to the immune escape ability of the variant. The scientists collected serum samples in September 2023, from a total of 39 vaccinated and SARS-CoV-2-exposed healthy individuals and assessed virus neutralization titers in these samples against seven different viral variants, including B.1, BA.2, BA.5, XBB.1.5, EG.5.1, BA.2.86 and JN.1.

The assessment of neutralization titers revealed the highest neutralizing reactivity against the ancestral B.1 variants, followed by BA.2 and BA.5 variants. This is because of the pre-existing anti-SARS-CoV-2 immunity induced by COVID-19 vaccination or previous SARS-CoV-2 infection.

Compared to the B.1 variant, XBB.1.5 and EG.5.1 variants showed around 15-fold reduction in neutralization. Moreover, no detectable neutralizing reactivity against these variants was observed in 12 out of 39 participants. For the BA.2.86 variant, the reduction in neutralizing titers was 20-fold compared to the ancestral B.1 variant. No neutralizing titers were detected in 11 out of 39 participants. Compared to the BA.2.86 variant, the JN.1 variant showed no further reduction in neutralizing titers.

The study finds that both BA.2.86 and JN.1 variants of SARS-CoV-2 have comparable



immune escape ability, and have a significantly higher ability to escape pre-existing anti-SARS-CoV-2 immunity compared to earlier variants. This could explain the recent predominance of BA.2.86 and JN.1 variants.

The scientists have compared their findings with existing evidence and found that they are not in accord with two previous studies that used a higher proportion of individuals with an infection or vaccination history with XBB variants.

A significant proportion of participants could not exhibit detectable neutralizing titers against the most recently circulating viral variants, including XBB.1.5, EG.5.1, BA.2.86, and JN.1. This indicates waning of vaccine- or infection-induced immunity at the population level, which could increase the incidence of re-infection in upcoming winter months in the northern hemisphere.

**As of January 15**, the UK Health Security Agency published “Should we be worried about the new COVID-19 variant?”<sup>19</sup>. The Blog Editor states: “As of January 2024, approximately 60% of English cases are caused by JN.1. UKHSA is continuing to monitor data relating to variants both in the UK and internationally, including close monitoring of the JN.1 variant, and assessment of severity and vaccine effectiveness. There is no change to the wider public health advice at this time. There are no reports of people becoming more ill with this COVID-19 variant than with previous ones”.

When JN.1 appears on our radar, at the initial stages it is often quite difficult to know whether the mutations provide any advantages to the virus. At these early stages the scientists at the “Vaccine Development and Evaluation Centre”

are busy growing a stock of the JN.1 variant in our high containment facilities, so that we can begin testing.

At the same time, scientists in our COVID-19 Vaccine Unit work hand in glove with vaccine developers to get samples of new, as yet unlicensed, vaccines to assess whether they will give better protection against the virus. Vaccinations for flu and COVID-19 help to keep vulnerable people out of hospital and carrying on with their day-to-day lives, as well as reduce pressure on our NHS which is always critical in the winter.

**On January 16**, The US VCU Health published “Rise in COVID-19 activity as new year begins”<sup>20</sup>. Identified in late 2023, Omicron variant JN.1 now makes up the majority of new COVID-19 cases around the world, and as of early January, the Centers for Disease Control and Prevention estimates Omicron variant JN.1 makes up about 62% of new cases. That’s up nearly 20% from late December.

It’s not clear right now if JN.1 causes symptoms that are different from other variants of COVID-19. Overall, the symptoms of COVID-19 variants tend to be similar, some of these include:

- Fever or chills
- Cough, shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- Sore throat
- Congestion or runny nose
- Nausea, vomiting and diarrhea

It is also important to note that symptoms can vary depending on an individual's overall health, which affects their immune system. Currently, federal health experts say there is no evidence that JN.1 causes more severe disease. There is also no evidence that JN.1 presents an increased risk to public health compared to other variants circulating in communities.

Finally, the article remarks that "the best way to protect from COVID-19 is to stay up to date on voluntary vaccinations and boosters".

**On January 17,** The HealthSite published the article by Satata Karmakar "6 New COVID-19 Variant JN.1 Symptoms: What to Expect After Getting Infected with New COVID-19 Variant"<sup>21</sup>. The article remarks that JN.1 subvariant is considered an Omicron lineage, inheriting its high transmissibility but potentially exhibiting some unique characteristics.

As per experts, JN. falls under the category of highly transmissible variants of COVID-19, with lethal characteristics, scroll down to know what the JN.1 virus variant may do inside your body after infecting your cells.

### **Extreme Tiredness And Exhaustion.**

The signature symptom of the JN.1 strain is a stubborn fever, accompanied by muscle cramps and exhaustion. Those struck by this variant seem to battle soaring body temperatures that won't budge for days. Alongside this, extreme fatigue can ambush you, making simple day-to-day tasks an uphill battle.

### **Digestive Disorders.**

The JN.1 strain seems to take a different turn from the original COVID-19 virus, causing

belly troubles in some people. Signs such as nausea, vomiting, and diarrhea have cropped up, implying the virus has a grip on the digestive tract. Recent studies have highlighted the increased risk of digestive diseases for these patients, lasting up to one year after their recovery.

### **Trouble Sleeping.**

One of the newest signs of this virus variant infection is insomnia. One who is infected with the JN.1 subvariant of COVID-19 may notice a sudden problem in falling asleep at night.

"The JN.1 variant has full potential to trigger anxiety and sleep disturbances in the infected patient, and this is worrisome. While more research is needed to understand the reasons behind this, it's crucial to acknowledge and address these symptoms effectively. Individuals experiencing these issues should reach out for help from healthcare professionals or mental health specialists".

### **Anxiety And Restlessness.**

A person who is infected by the JN.1 COVID-19 virus variant may experience anxiety and restlessness. This is also among the top 5 signs and symptoms listed by the experts under the JN.1 variant name.

### **Neurological Symptoms.**

Alarmingly, there's a connection between the JN.1 strain and neurological symptoms. Sufferers may experience headaches, bouts of dizziness, or even show signs of confusion. These symptoms can be disconcerting and shouting for medical aid when these issues crop up is integral.

### **Breathless And Cough.**

Not straying too far from its cousin strains, JN.1 also interferes with the respiratory system.

If you notice a lingering cough, a shortage of breath, or find it tough to breathe, it could be the JN.1. These symptoms run the mild-severe spectrum, so prompt medical help is non-negotiable if breathing issues escalate.

### How To Stay Safe From JN.1 COVID Variant?

It is important to note that understanding the signs and symptoms of the JN.1 virus infection is important when trying to stay safe. Experts have also urged people to stick to safety protocols; mask up, maintain your distance, and don't sidestep the vaccine, to shield yourself and your dear ones from COVID-19.

**On January 18**, the Bangladesh daily DhakaTribune publish "New Covid-19 variant JN.1 detected in Bangladesh" and cite that<sup>22</sup>:

The government's Institute of Epidemiology, Disease Control and Research (IEDCR) said JN.1 was detected in samples from five people, IEDCR Director Professor Tahmina Shirin confirmed Thursday January 18 afternoon. "This strain has been detected after testing samples of patients infected with coronavirus inside and outside Dhaka".

According to the World Health Organization (WHO), new types of coronavirus infections are increasing in various countries of the world, including the neighbouring India, meanwhile, on January 14, Health Service Division Secretary Jahangir Alam told reporters: "The government has ensured collection of 25 million doses of vaccine. In 2024 and 2025, these vaccines will be administered as a fourth dose to at-risk populations".

On Tuesday January 16, Directorate General of the Health Services (DGHS) Director General Professor Dr ABM Khurshid Alam told reporters:

"DGHS still has some vaccines for coronavirus. Pfizer's vaccine is also effective against the new coronavirus."

Earlier, DGHS recommended wearing masks as a precautionary measure amid the new outbreak of coronavirus in several countries around the world. The organization gave this suggestion in a press release on January 13. Additionally, it advised against testing for COVID-19 until after surgery or other medical treatments if there are indications or symptoms of the condition.

**On January 19**, The World Health Organization publish "COVID-19 Epidemiological Update" Edition 16323. Globally, during the 28-day period from 11 December 2023 to 7 January 2024, 106 countries reported COVID-19 cases and 51 countries reported COVID-19 deaths. Note that this does not reflect the actual number of countries where cases or deaths are occurring, as many countries have stopped or changed frequency of reporting.

From the available data, the number of reported cases has increased while deaths have decreased during the 28-day period, with over 1.1 million new cases and 8,700 new deaths, an increase of 4% and a decrease of 26%, respectively, compared to the previous 28 days (13 November to 10 December 2023).

Trends in the number of reported new cases and deaths should be interpreted with caution due to decreased testing and sequencing, alongside reporting delays in many countries. According to estimates obtained from wastewater surveillance, clinical detection of cases underestimates the real burden from 2 to 19-fold.

SARS-CoV-2 PCR percent positivity, as detected in integrated sentinel surveillance as part of the Global Influenza Surveillance and Response System (GISRS) and reported to FluNet was around 8% as of 7 January 2024. During the 28-day period from 11 December 2023 to 7 January, 53 and 42 countries provided data at least once on COVID-19 hospitalizations and admissions to an intensive care unit (ICU), respectively.

From the available data, over 173,000 new hospitalizations and over 1,900 new ICU admissions were reported during the 28-day period. Amongst the countries reporting these data consistently over the current and past reporting period, there was an overall increase of 40% and 13% in new hospitalizations and new ICU admissions, respectively.

Globally, JN.1 is the most reported VOI (now reported by 71 countries), accounting for 65.5% of sequences in week 52 compared to 24.8% in week 48. Its parent lineage, BA.2.86, is stable and accounted for 7.8% of sequences in week 52 compared to 7.0% in week 48.

The initial risk evaluation for JN.1 was published on 19 December 2023, with an overall evaluation of low public health risk at the global level based on available evidence. WHO is currently tracking several SARS-CoV-2 variants: five VOIs: XBB.1.5, XBB.1.16, EG.5 BA.2.86 and JN.1; and five VUMs: DV.7, XBB, XBB.1.9.1, XBB.1.9.2 and XBB.2.3.

**On January 20**, Jant Pharmacal Corporation publish "The Current COVID-19 Surge 2024", and states<sup>24</sup>: "The SARS-CoV-2 virus, which spread globally since its outbreak in late 2019, is continuously mutating and posing challenges to public health".

According to the Centers for Disease Control and Prevention -CDC-, COVID-19 has resulted in more than 6.7 million hospitalizations and more than 1.1 million deaths in the US since Jan 2020, COVID-19 hospitalizations increased by 20.4% in the week ending December 30, 2023.

In that same period, deaths went up by 12.5%, with COVID-19 deaths accounting for 3.6% of total deaths in the United States. The CDC data tracker shows a 14.3% increase in deaths during the first week of January 2024.

According to the latest updates from Michael Hoerger, Director of U.S. COVID forecasting dashboard -PMC-, "we are witnessing 2 million new infections per day". Within the next 2 months, nearly one in three Americans will contract the virus resulting in a staggering 105 million infections and over 5 million long-term COVID cases.

The statistics provided by the CDC, along with insights from Time and the Washington Post, bring into focus the gravity of the situation. It was revealed in the WHO media briefing, that the viral levels are 2 to 19 times higher than reported. They also reported over 10,000 deaths in 50 countries in December 2023, and the US accounted for half of those deaths.

These numbers suggest that the 2024 Winter Surge may surpass previous waves, resulting in increased pressure on our healthcare system. The current surge of COVID-19 in the United States is linked to the emergence of the JN.1 variant, a close relative of Omicron variant BA.2.86, a strain that exhibits alarming transmissibility rates.

Recent data from the CDC's update on January 5, 2024, underscores the seriousness

of the situation by revealing high viral activity levels in wastewater across all regions. Wastewater viral activity serves as an effective tool for detecting increases in COVID-19 transmission within communities.

As of December 25, 2023, an unsettling 66% of wastewater samples demonstrated JN.1 as the dominant variant, an increase of 58% from the previous week. This surge in JN.1 prevalence in wastewater corresponds to the 2 million daily infections during the current surge.

New variants with increased transmissibility, along with a decrease in self-testing and waning immunity, due to low vaccination rates, create an environment where the virus can rapidly spread. Global travel patterns and the interconnectedness of our communities further amplify this challenge, as highlighted in the Washington Post. Although the symptoms caused by infection from JN.1 are similar to other variants, they also depend on an individual's immunity and viral load.

According to the CDC, these symptoms include sore throat, congestion, runny nose, cough, fatigue, headache, muscle aches, fever or chills, loss of sense of taste or smell, nausea or vomiting, and diarrhea. To mitigate the impact of this surge, a comprehensive approach is needed. The CDC emphasizes the significance of booster shots to enhance immunity, especially as protection from evolving virus strains.

As of January 12, only 21% of adults aged 18+ and 41% aged 65+ reported having received the updated COVID-19 vaccine. The following actions can help us protect ourselves from the current surge:

- Get updated COVID-19 vaccine shots.

- Self-test regularly with antigen tests especially if you are symptomatic.
- Minimize indoor gatherings.
- Improving the indoor air quality.
- Get help from healthcare professionals if you test positive.
- Use facemasks to help reduce the spread.

As we navigate the current COVID-19 surge, it is important to stay informed and actively participate in the collective effort to decrease transmission. Regular COVID testing is an important tool to reduce this spread, as reported by NY Times. By implementing effective strategies, supporting vaccination efforts, and good preventive measures, we can fight this surge and work towards a healthier future.

The current surge of COVID-19, led by the JN.1 variant, underscores the need for proactive measures. As data from the CDC and from other experts highlight the severity of the situation, it becomes crucial to prioritize vaccination, practice preventive measures, and conduct regular COVID testing. Regular testing, a vital tool in identifying and preventing the spread of COVID-19, plays an important role in ensuring health and safety of self and community.

**On January 21**, The Times of India publish the article "COVID update: 1,513 cases of JN.1 variant detected in India, says INSACOG"<sup>25</sup>. As per the latest reports from the Indian SARS-CoV-2 Genomics Consortium (INSACOG), a total of 1,513 cases of JN.1 variant have been reported in the country. Data compiled by INSACOG shows the number of COVID-19 cases caused due to the JN.1 variant in several Indian states.

The states have been urged to ensure effective compliance of the detailed operational guidelines for the revised surveillance strategy for COVID-19 shared with them by the Union Ministry of Health and Family Welfare. According to the INSACOG data, Maharashtra has recorded the highest number of JN.1 cases at 382 followed by Karnataka at 249.

Andhra Pradesh recorded 189 JN.1 cases while Kerala registered 156, Gujarat recorded 126 such cases, West Bengal 96, Goa 90, Tamil Nadu 89, Rajasthan 38, Telangana recorded 32, Chhattisgarh 25, Delhi 21, Uttar Pradesh 9, Haryana 5, Odisha 3, and Uttarakhand, Manipur and Nagaland 1 each.

The Centre has asked the states and Union territories to maintain a constant vigil amid an uptick in the number of Covid cases and the detection of the JN.1 sub-variant in the country. The states have been asked to regularly monitor and report district-wise cases of influenza-like illness (ILI) and severe acute respiratory illness (SARI) from all health facilities for an early detection of a rising trend of COVID-19 cases.

JN.1 that produce Influenza-like illness (ILI) symptoms include fever, chills, cough, sore throat, body aches, fatigue, and sometimes diarrhea and vomiting. These symptoms resemble those of influenza but can also be caused by other respiratory viruses. To stay safe from COVID-19, practice frequent handwashing with soap, maintain social distancing, and wear masks in crowded or enclosed spaces.

Stay updated on vaccination schedules and get vaccinated for added protection, avoid large gatherings, especially indoors, and prioritize outdoor activities, monitor your health

for symptoms and seek testing if needed, follow guidelines from health authorities, adhere to quarantine or isolation protocols if necessary, and stay informed about the virus's latest developments.

Combining personal precautions with community efforts helps reduce the risk of transmission and safeguards both individual and public health.

**On January 22**, CDC Respiratory Illnesses publish "Influenza Viruses Spreading This Season and Update on JN.1 Variant"<sup>26</sup>, and about JN.1 states: "CDC continues to track the rise in prevalence of the JN.1 that remains the most widely circulating variant of SARS-CoV-2 in the United States and globally".

As of January 19, 2024, JN.1 is estimated to account for approximately 83% to 88% of all currently circulating SARS-CoV-2 variants, an increase from the estimated prevalence of 55% to 68% two weeks ago. JN.1 remains at high prevalence among variants in international travelers and wastewater viral levels, as well as in most regions around the globe.

COVID-19 activity is currently high, most prominently in the eastern half of the country, COVID-19 infections, hospitalizations, and deaths have remained elevated in recent weeks, with JN.1 contributing to the spread of COVID-19 this winter.

CDC continues to learn more about JN.1, but currently there is no evidence that it causes more severe disease, current COVID-19 vaccines are expected to increase protection against JN.1, as they do against other variants, by helping prevent severe illness.

**On January 23**, The National Herald, publish in the Health section, the article "JN.1 represents 'very serious evolution' of Covid virus, say global experts" and cites experts that quotes<sup>27</sup>: Dr Michael Osterholm, director of the University of Minnesota's Center for Infectious Disease Research and Policy (CIDRAP); "JN.1 represents a very serious evolution of the virus. And it isn't over".

Dr Eric Topol, founder and director of the Scripps Research Translational Institute in California; "The WHO has "called JN.1 a VOI (variant of interest), and that just doesn't cut it, with the growth advantage this variant has demonstrated. JN.1 is a descendent lineage of BA.2.86, with the earliest sample collected on 25 August 2023. In comparison with BA.2.86, JN.1 has the additional L455S mutation in the spike protein, making it more transmissible".

Dr Rajeev Jayadevan, co-chairman of the National Indian Medical Association Covid Task Force; "JN.1 is an all new variant with numerous changes never seen in any commonly circulating lineage before. This is unlike other recent variants, which were merely a few mutations from their predecessor, therefore, the disease patterns from an immune evasiveness and spread capability of this variant needs careful attention". He explained immune invasiveness of a variant as the ability of a virus to overcome the existing immune response within an individual.

Ryan Gregory, a biology professor at the University of Guelph in Canada; "After the major variants of Covid like Alpha, Delta and Omicron, JN.1 very likely represents a new chapter in pandemic evolution, claimed the expert. According to, JN.1 has ushered in "a new era", the highly transmissible variant is on

track to become the lineage from which most variants are descended for the foreseeable future".

Maria Van Kerkhove, WHO's COVID-19 technical lead, said the next sub-lineages of the Covid virus can come from JN.1, "but we could also see something quite different, we could see something like an Omicron again".

**On January 25**, NPR-Health publishes the article for Vanessa Romo "JN.1 takes over as the most prevalent COVID-19 variant. Here's what you need to know"<sup>28</sup> and remarks: "In mid-October, CDC data shows JN.1 made up about 0.1% of all COVID-19 cases around the country. As of Jan. 20, the CDC estimates that's now up to approximately 86%".

"Most likely, if you're getting COVID right now, you're getting this particular variant mutation", Eyal Oren, a director and professor of epidemiology at the School of Public Health at San Diego State University, told NPR, added that one of the reasons for the latest surge is that the virus continues to evolve so rapidly that "our immune systems have not been able to keep up". Another reason is that "not enough Americans are vaccinated," according to the CDC.

Earlier this month, only 11% of children and 21% of adults were reported to have received the updated COVID-19 vaccine, meanwhile, only 40% of adults age 65 and older, which are the highest risk group, have gotten the updated vaccine in the last year. The CDC says COVID-19 vaccines can reduce severe illness and hospitalizations.

The low rates for COVID-19 vaccinations, along with those against influenza and respiratory

syncytial virus (RSV), are of such great concern that the CDC issued to health care workers last month. The combination of rising flu, RSV and COVID cases "could lead to more severe disease and increased healthcare capacity strain in the coming weeks," the agency predicted.

"People may be wrongly assuming that the current COVID booster won't protect them from JN.1 or other new strains, but the most recent vaccines from Pfizer-BioNTech, Moderna and Novavax are all expected to help lower chances of serious illness or hospitalization from JN.1" Oren said.

**On February 6,** The University of Nebraska, Medicine; The Global Center of Health Security publishes "COVID variant JN.1 now more than 90% of cases in U.S., CDC estimates"<sup>29</sup>. The CDC published new data on February 1st from its pharmacy testing program that suggests this season's updated COVID-19 vaccines had 49% effectiveness against symptomatic JN.1 infection, among people between two to four months since they got their shot.

"New data from CDC show that the updated COVID-19 vaccines were effective against COVID-19 during September 2023-January 2024, including against variants from the XBB lineage, which is included in the updated vaccine, and JN.1, a new variant that has become dominant in recent weeks," the CDC said in the post.

CDC officials have said that other data from ongoing studies using medical records also offered "early signals" that JN.1's severity was indeed not worse than previous strains. That is a step beyond the agency's previous

statements simply that there was "no evidence" the strain was causing more severe disease. The CDC's new variant estimates mark the culmination of a swift rise for JN.1, which had still made up less than half of infections in the agency's estimates through late December.

**On February 9,** The World Health Organization publishes "Updated Risk Evaluation of JN.1, 09 February 2024"<sup>30</sup> and states that JN.1 is a descendent lineage of BA.2.86, with the earliest sample collected on 25 August 2023. As of 5 February 2024, there were 79107 JN.1 sequences submitted to GISAID (1) from 94 countries, representing 89.0% of the globally available sequences in epidemiological week 4, (22 to 28 January 2024) added that this is a significant rise in prevalence from 64.5% four weeks prior in epidemiological week 52 (25 to 31 December 2023).

The JN.1 variant is also the most prevalent SARS-CoV-2 variant in all the four WHO regions with consistent sharing of SARS-CoV-2 sequences at epidemiological week 4, i.e. 83.3% for the South East Asian region (SEAR), 71.1% for the Western Pacific region (WPR), 91.7% for the European region (EUR), and 86.0% for the region of the Americas (AMR). There was only a single sequence from the East Mediterranean Region (EMR) and none from the African Region (AFR) in epidemiological week 4.

**On February 12,** The Thailand Medical News publishes "COVID-19 News. Ireland Witnesses New SARS-CoV-2 Surge as JN.1 Becomes Dominant Strain"<sup>31</sup>. Into the global context, the prevalence of SARS-CoV-2 variants has been a consistent theme since February 2023. Variants like XBB and other recombinant forms dominated the circulating virus worldwide.



Mid-June 2023 witnessed the emergence of XBB.1.5 and related lineages with distinctive spike protein mutations -F456L and subsequently L455F-, however the landscape shifted once again in November 2023 when the BA.2.86 sub-lineage, represented by JN.1, started rapidly replacing XBB.1.5-like lineages.

First detected in Israel on August 13, 2023, the BA.2.86 variant has become a global presence, extending its reach to Denmark, the UK, USA and South Africa. Despite its unusually high mutation count, there is currently no evidence to suggest increased transmissibility or heightened clinical severity associated with this variant. The sub-lineage JN.1 however, has gained predominance in recent weeks, prompting the WHO to designate it as a Variant of Interest on December 19, 2023.

**On February 16**, Pengfei Wang and colleagues of Shanghai Pudong Hospital, Shanghai, China, publishes New Results of “Robust Neutralization of SARS-CoV-2 Variants Including JN.1 and BA.2.87.1 by Trivalent XBB Vaccine-Induced Antibodies” and states<sup>32</sup> that Newly emerged SARS-CoV-2 variants like JN.1, and more recently, the hypermutated BA.2.87.1, have raised global concern.

They recruited two groups of participants who had BA.5/BF.7 breakthrough infection post three doses of inactivated vaccines: one group experienced subsequent XBB reinfection, while the other received the XBB-containing trivalent WSK-V102C vaccine.

The comparative analysis of their serum neutralization activities revealed that the WSK-V102C vaccine induced stronger antibody responses against a wide range of variants,

notably including JN.1 and the highly escaped BA.2.87.1.

Furthermore, the investigation into specific mutations revealed that fragment deletions in NTD significantly contribute to the immune evasion of the BA.2.87.1 variant. The findings emphasize the necessity for ongoing vaccine development and adaptation to address the dynamic nature of SARS-CoV-2 variants.

**On February 17**, Nikhil Prasad from Thailand Medical News team, published “The Impact of the SARS-CoV-2 ORF7a: H47Y Mutation Found in BF.5 and B.F7 Sub-lineages in Viral Functions”, and briefs<sup>33</sup>:

#### **Emergence of the ORF7a: H47Y Mutation**

The ORF7a: H47Y mutation emerged within the Omicron variant, specifically in the BF.5 and BF.7 sub-lineages. Initially identified in cases originating from China and Japan, this mutation garnered interest due to its potential impact on viral protein function and virus-host interactions. The mutation results in the substitution of histidine (H) with tyrosine (Y) at position 47 of the ORF7a protein sequence.

#### **Impact on Anti-SERINC5 Function**

One of the critical functions of ORF7a is its ability to counteract the antiviral effects of SERINC5, a host factor that inhibits virus-cell membrane fusion. Previous studies have shown that ORF7a plays a pivotal role in antagonizing SERINC5 activity, thereby promoting viral entry and replication.

Surprisingly, the H47Y mutation did not significantly affect ORF7a's ability to counteract SERINC5, suggesting that this particular viral function remains largely intact despite the amino acid substitution.

## Impaired Antagonism of Type I Interferon (IFN-I) Response

Another crucial aspect of ORF7a's function is its ability to inhibit the type I interferon (IFN-I) response, which is essential for orchestrating the host's antiviral defenses, however, the H47Y mutation significantly impaired ORF7a's capacity to suppress the IFN-I response, potentially altering the dynamics of viral immune evasion.

This finding highlights the importance of specific amino acid residues in maintaining the protein's ability to modulate host immune pathways.

## Disruption of Major Histocompatibility Complex Class I (MHC-I) Downregulation

ORF7a also plays a role in downregulating major histocompatibility complex class I (MHC-I) molecules on the surface of infected cells, thereby impairing antigen presentation to cytotoxic T cells. This immune evasion strategy allows the virus to evade detection by the adaptive immune system.

However, the H47Y mutation disrupts this function, leading to sustained MHC-I levels on the cell surface. Consequently, infected cells may become more susceptible to recognition and elimination by cytotoxic T lymphocytes, potentially impacting viral replication and spread.

## Mechanistic Insights

To gain further insights into the structural and functional changes associated with the ORF7a: H47Y mutation, researchers conducted molecular dynamics simulations and co-immunoprecipitation assays. These experiments

revealed alterations in protein-protein interactions and decreased ubiquitination of the mutated ORF7a protein compared to its wild-type counterpart.

These findings suggest that the H47Y mutation may alter the conformation and stability of ORF7a, leading to functional changes that impact its interactions with host cellular factors.

## Implications for Virus Pathogenesis

The observed alterations in viral protein function due to the ORF7a: H47Y mutation have significant implications for virus pathogenesis and host immune responses. Impaired immune evasion mechanisms and disrupted antigen presentation dynamics may influence viral replication, spread, and disease outcomes.

Moreover, the emergence of variants carrying mutations in non-spike proteins underscores the importance of comprehensive surveillance and characterization of viral variants to guide public health interventions and therapeutic strategies.

In conclusion, the ORF7a: H47Y mutation identified in the BF.5 and BF.7 sub-lineages of SARS-CoV-2 represents a novel genetic variant with potential implications for virus-host interactions and disease pathogenesis. While the mutation does not seem to significantly affect ORF7a's ability to counteract SERINC5, it disrupts critical functions related to IFN-I antagonism and MHC-I downregulation.

Further studies are warranted to elucidate the broader impacts of this mutation on viral fitness, immune evasion, and disease severity. Insights gained from these investigations will be crucial for informing the development of

targeted interventions and vaccine strategies tailored to combat emerging SARS-CoV-2 variants.

The study findings were published in the peer reviewed International Journal of Molecular Sciences<sup>34</sup>.

**On February 17**, Anne J. Huiberts from Centre for Infectious Disease Control, National Institute for Public Health and Environment (RIVM), Bilthoven, the Netherlands and colleagues, publishes in medRxiv<sup>35</sup> “Effectiveness of Omicron XBB.1.5 vaccine against SARS-CoV-2 Omicron XBB and JN.1 infection in a prospective cohort study in the Netherlands, October 2023 to January 2024”.

They estimated vaccine effectiveness (VE) of SARS-CoV-2 Omicron XBB.1.5 vaccination against self-reported infection between 9 October 2023 and 9 January 2024 in 23,895 XBB.1.5 vaccine-eligible adults who had previously received at least one booster. A monovalent mRNA vaccine targeting the SARS-CoV-2 Omicron XBB.1.5 subvariant (Comirnaty) was used in the 2023 Dutch COVID-19 vaccination campaign that started on October 2, 2023.

The results showed that XBB.1.5 vaccination also provided considerable protection against SARS-CoV-2 infection in the first three months post-vaccination. Recent prior infection also protects against new infection, but it should be kept in mind that experiencing a SARS-CoV-2 infection carries risk of severe disease in vulnerable groups, and of post-COVID condition.

Interestingly, they found indications of immune escape of the emerging BA.2.86 (JN.1) variant from XBB.1.5 vaccination and prior infection,

possibly explaining the rapid increase of this variant worldwide.

**On February 19**, Quian Wang and colleagues from Aaron Diamond AIDS Research Center, Columbia University Vagelos College of Physicians and Surgeons, New York, USA, published in the Cell Host & Microbe, the short article “XBB.1.5 monovalent mRNA vaccine booster elicits robust neutralizing antibodies against XBB subvariants and JN.1” and states<sup>36</sup>:

The administration of an updated monovalent mRNA vaccine booster (XBB.1.5 MV) to previously uninfected individuals boosted serum virus-neutralizing antibodies significantly against not only XBB.1.5 (27.0-fold increase) and EG.5.1 (27.6-fold increase) but also key emerging viruses such as HV.1, HK.3, JD.1.1, and JN.1 (13.3- to 27.4-fold increase).

Individuals previously infected by an Omicron subvariant had the highest overall serum neutralizing titers (ID<sub>50</sub> 1,504-22,978) against all viral variants tested, while immunological imprinting was still evident with the updated vaccines, it was not nearly as severe as observed with the previously authorized bivalent BA.5 vaccine.

**On February 23**, Laith J. Abu-Raddad and colleagues from Weill Cornell Medicine-Qatar, Cornell University, Doha, Qatar, publishes “Protection of natural infection against reinfection with SARS-CoV-2 JN.1 variant”<sup>37</sup>. This study investigated the effectiveness of natural infection in preventing reinfection with the JN.1 variant during a large JN.1 wave in Qatar, using a test-negative case-control study design.

The overall effectiveness of previous infection in preventing reinfection with JN.1 was

estimated at only 1.8% (95% CI: -9.3-12.6%). This effectiveness demonstrated a rapid decline over time since the previous infection, decreasing from 82.4% (95% CI: 40.9-94.7%) within 3 to less than 6 months after the previous infection to 50.9% (95% CI: -11.8-78.7%) in the subsequent 3 months, and further dropping to 18.3% (95% CI: -34.6-56.3%) in the subsequent 3 months.

The findings show that the protection of natural infection against reinfection with JN.1 is strong only among those who were infected within the last 6 months, with variants such as XBB\*, however, this protection wanes rapidly and is entirely lost one year after the previous infection.

The findings support considerable immune evasion by JN.1. BA.2.86 has evolved and its descendant, JN.1 (BA.2.86.1.1), emerged in late 2023. JN.1 harbor's Leu455Ser and three mutations in non-spike proteins, the authors affirm. HK.3 and other flip variants carry Leu455Phe, which contributes to increased transmissibility and immune escape ability compared with the parental EG.5.1 variant.

The authors conclude that the results of the study, suggest that JN.1 might soon become the dominant lineage worldwide. Indeed, by the end of November 2023, JN.1 had already overtaken HK.3 in France and Spain. Taken together, these results suggest that JN.1 is one of the most immune-evading variants to date.

**On February 24**, The Lancet Infectious Diseases publishes "Virological characteristics of the SARS-CoV-2 JN.1 variant"<sup>38</sup>. The authors briefs that the in vitro ACE2 binding assay showed that the dissociation constant

value of the JN.1 receptor-binding domain (RBD) was significantly higher than that of the BA.2.86 RBD, suggesting that Leu455Ser decreases binding affinity to the human ACE2 receptor.

In contrast, the pseudovirus assay showed that the infectivity of JN.1 was significantly higher than that of BA.2.86. This discrepancy could be due to the difference between monomeric RBD and trimerised whole spike protein.

The researches performed a neutralisation assay using rodent sera infected with BA.2.86 or immunised with BA.2.86 spike protein. In both cases, the 50% neutralisation titre (NT50) against JN.1 was similar to that against BA.2.86, suggesting that Leu455Ser does not affect the antigenicity of BA.2.86.

On the other hand, the NT50 of breakthrough infection sera with XBB.1.5 and EG.5.1 against JN.1 was significantly lower than that of HK.3 (2.6-fold to 3.1-fold) and BA.2.86 (3.8-fold). Furthermore, JN.1 shows robust resistance to monovalent XBB.1.5 vaccine sera compared with BA.2.86.

Taken together, these results suggest that JN.1 is one of the most immune-evading variants to date. Our results suggest that Leu455Ser contributes to increased immune evasion, which partly explains the increased reproductive number of JN.1.

**On February 26**, The Public Health Ontario; Weekly Epidemiological Summary<sup>39</sup>, publishes "SARS-CoV-2 Genomic Surveillance in Ontario, February 26, 2024". Summarizes the results of SARS-CoV-2 whole genome sequencing completed by the Ontario

COVID-19 Genomics Network as of February 21, 2024, and Highlights:

- In the most recent week (February 4 to February 10), a total of 896 cases were sequenced. JN.1 was the most prevalent lineage (56.4%), followed by JN.1.4 (20.2%), and JN.1.1 (6.2%).
- The proportion of JN.1 decreased from 58.5% (January 28 to February 3) to 56.4% (February 4 to February 10).
- Based on the Nowcast model, JN.1 is projected to increase to 63.4% (95% CI: 58.9%-67.6%) by February 28, 2024.
- The proportion of JN.1.4 increased from 17.7% (January 28 to February 3) to 20.2% (February 4 to February 10).
- Based on the Nowcast model, JN.1.4 is projected to increase to 25.6% (95% CI: 21.6%-30.1%) by February 28, 2024.
- The weekly growth rate of JN.1.4 is 1.06 (95% CI: 1.02-1.10) times that of JN.1.

**On February 28**, the National Institute of Public Health and the Environment of Netherlands, publishes in his current information about COVID-19, "Variants of the coronavirus SARS-CoV-2" and states<sup>40</sup>: Since week 46, the most common variant seen in pathogen surveillance is BA.2.86, a BA.2 sub-variant which has also been designated as a VOI by the WHO. Since week 48, BA.2.86 sub-variants have been dominant in the Netherlands. The most prevalent in the Netherlands at this time is JN.1, which has been designated as a VOI by the WHO.

BA.2.86 variants show many genetic differences compared to the other variants currently circulating internationally, and is

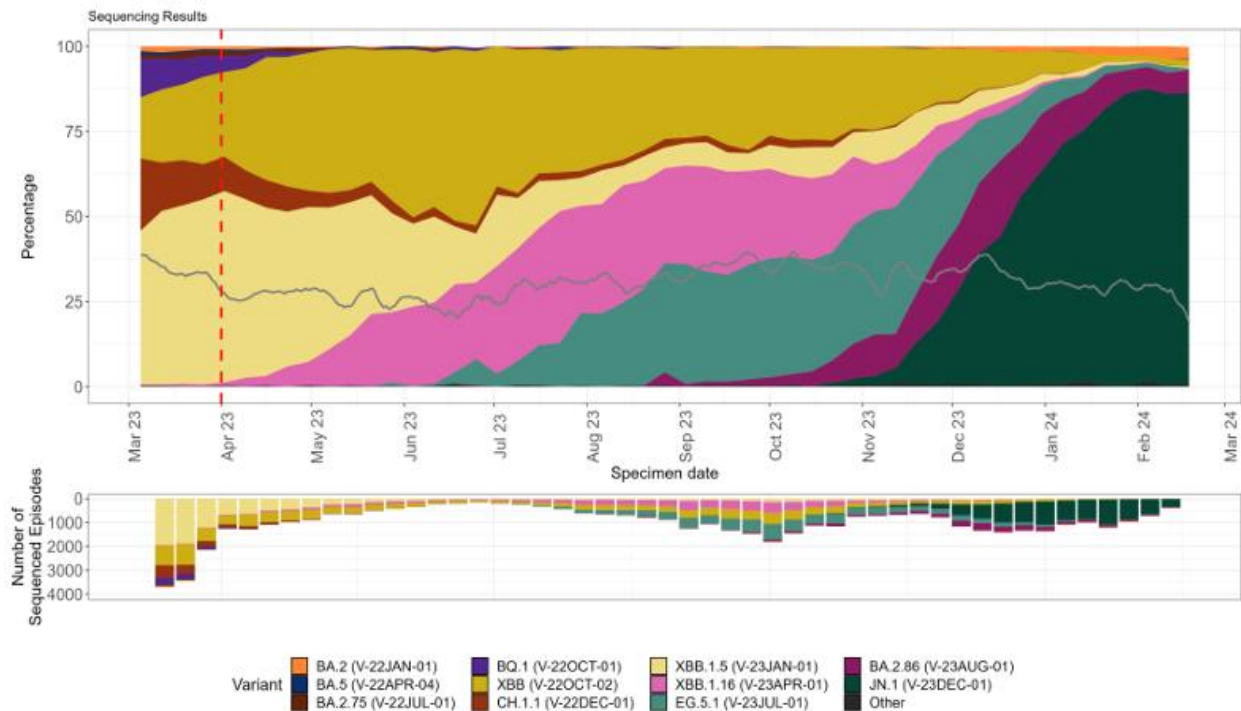
therefore being closely monitored worldwide. At this time, there are no indications that these sub-variants would be more likely to cause severe illness compared to previous Omicron sub-variants. The trends seen in sewage generally correspond to the trends observed in pathogen surveillance. At this time, sewage research shows the presence of BA.2.86 and mainly the sub-variant JN.1.

**On February 29**, The UK Health Security Agency, National Influenza and COVID-19 surveillance report Week 9 report (up to week 8 2024 data) 29 February 2024 "Microbiological surveillance SARS-CoV-2 variants"<sup>41</sup>. UKHSA defines variants based on a set of mutations common to a lineage to allow consistent detection, monitoring and reporting. The prevalence of different UKHSA-designated variants amongst sequenced cases is presented in Figure.

The UKHSA variant definition repository contains the previous genomic definitions for UKHSA declared variants. Poorer quality sequence data may be classified as a more ancestral variant due to missing data. Furthermore, variants may include sub-lineages that have not been individually designated for example HK.3 within EG.5.1 (V-23JUL-01).

Once a sub-lineage meets required thresholds, it will be designated as a variant and prevalence of this sub-lineage in positive cases will then be identifiable in the data. To account for sequencing delays, we report the proportion of variants from sequenced cases between 5 February 2024 and 11 February 2024.

Prevalence of SARS-CoV-2 variants amongst available sequenced cases for England from 27 February 2023 to 18 February 2024.



The grey line indicates proportion of cases sequenced. The vertical dashed line (red) in April 2023 denotes changes in PCR testing in social care and hospital settings. Recombinants such as XD, are not specified but are largely within the 'Other' group currently as numbers are too small.

Of those sequenced in this period, 85.5% were classified as JN.1 (V-23DEC-01), 6.2% as BA.2.86 (V-23AUG-01), 3.7% as BA.2 (V22JAN-01), 1.9% as EG.5.1 (V-23JUL-01) and 1.8% as XBB (V-22OCT-02).

## Conclusions

The latest data from US-CDC shows JN.1 as the prevalent SARS-CoV-2 variant in the United States.

JN.1 in January 2024, quickly increase its prevalence and surpassed other variants, including HV.1 to become the most prevalent strain in The United States of America.

JN.1 has a similar transmission rate, exhibits a greater evasive capacity of immune-generated antibodies than HV.1 family of SARS-CoV-2, produce similar symptoms that of other Omicron variants.

JN.1 is expected not to produce an increase in hospitalizations and mortality rate and the SARS-CoV-2 vaccines recently developed by Pfizer and Moderna, must be effective against this Omicron subvariant.

For now, the dominant variant JN.1 does not seem harmful in terms of creating a deadly disease but is still contagious enough to not be ignored.

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None

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