MINISTRY OF HEALTH
MANATŪ HAUORA

133 Molesworth Street
PO Box 5013
Wellington 6140
New Zealand
T+64 4 496 2000

18/11/2020

[redacted]

By email: [redacted]
Ref: H202007836

Dear [redacted]

Response to your request for official information

Thank you for your request under the Official Information Act 1982 (the Act) on 16 October 2020 for information relating to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

Under the Act, please find a response to each part of your request below.

> *'Has the SARS-CoV-2 virus been isolated in a laboratory?*
> *If not, what are we testing for?*

Yes, as there are several examples of the virus being isolated and cultured in a laboratory setting. One example provided by the Centers for Disease Control and Prevention (CDC) describes the isolation and culture of SARS-CoV-2. This information and research on SARS-CoV-2 can be found at the following link:
https://wwwnc.cdc.gov/eid/article/26/6/20-0516_article.

> *Has SARS-CoV-2 passed the standards of Koch's Postulates?*

The following steps have been undertaken to provide assurance that SARS-CoV-2 is the virus that causes the severe respiratory illness known as COVID-19.

1. The full genome of the virus was sequenced which has enabled accurate identification of the type of virus as a coronavirus. Its RNA genome provides a way to explore its evolutionary links to other coronaviruses.
2. Culture of the virus (within a laboratory setting) was performed confirming the ability of the virus to infect and replicate in human cells.
3. Cell culture studies all demonstrated that the virus is able to cause damage to human cells (called the cytopathogenic effect or CPE)
4. Virus that is grown in culture is able to infect animals and cause disease.

Further information about studies into SARS-CoV-2 (with reference to Koch's postulates) can be found at the following link: https://www.biorxiv.org/content/10.1101/2020.02.07.939389v3.full.

Is there evidence that SARS-CoV-2 is causing the symptoms of COVID-19?
If so, what standard was used?
Have Koch's Postulates been used to prove that SARS-CoV-2 is the cause of COVID-19?
If not, what standard was used?

This information is provided in the above response. The science behind the association of a specific micro-organism with a specific disease has evolved considerably since Robert Koch's postulates was published.

There have been changes that have replaced the requirement for infectious agents to cause disease in healthy humans in order to prove causation. This includes changes to the concept of infectious diseases, the role that host immunity plays in the development of symptomatology, and the revolution in laboratory testing and genome sequencing. Taken together, there is significant evidence including Koch's postulates that indicate the disease known as COVID-19 is caused by the virus SARS-CoV-2.

Have there been any cases in New Zealand of an asymptomatic carrier passing on SARS-CoV-2 to someone else?

Investigations into clusters with people considered to be close contacts have shown examples of asymptomatic or mildly symptomatic individuals passing on the virus. One of the most visible examples of asymptomatic or mild symptoms being transmitted is in schools or colleges. Both New Zealand and overseas examples show that school-age children are often asymptomatic.

There is often confusion between the differences in definition of asymptomatic carrier and the ways the term is used. One authoritative review on asymptomatic transmission describes that *'we found some evidence that SARS-CoV-2 infection in contacts of people with asymptomatic infection is less likely than in contacts of people with symptomatic infection (relative risk 0.35, 95% CI 0.10–1.27)'.* Further information from this author can be found at the following link: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003346.

Further information relating to SARS-CoV-2 and Koch's postulates is attached to this letter as Appendix One.

I trust this information fulfils your request. Under section 28(3) of the Act you have the right to ask the Ombudsman to review any decisions made under this request.

Please note that this response, with your personal details removed, may be published on the Ministry website.

Yours sincerely

Rebecca Drew
Group Manager, COVID-19 Science and Insights
COVID-19 Health System Response

SARS-CoV-2 is the virus that causes COVID-19

The science behind the association of a specific microorganism with a specific disease has evolved considerably since Koch's postulates were published. Changes to the concept of infectious diseases, the role that host immunity plays in the development of symptomatology, and the revolution in laboratory testing and genome sequencing have replaced the requirement for infectious agents to cause disease in healthy humans in order to prove causation. Taken together, there is an overwhelming body of evidence (including satisfying Koch's postulates) that the disease known as COVID-19 is caused by the SARS-CoV-2 virus.

The relationship between SARS-CoV-2 and COVID-19

In late 2019 a cluster of cases of severe pneumonia in Wuhan, China, was identified through a local severe illness reporting system which was set up after the SARS outbreak. On 31 December the WHO China country office was informed of the cases and on 3 January 2020, 44 cases of pneumonia of unknown cause were reported of whom 11 were very ill. At that time the infectious agent had not been identified. Respiratory samples from the symptomatic individuals were tested and a corona virus, similar to SARS-CoV was identified in all the patients. The virus was named SARS-CoV-2. The following steps have been undertaken to provide assurance that SARS-CoV-2 is the virus that causes the severe respiratory illness known as COVID-19.

- The full genome of the virus was sequenced which has enabled accurate identification of the type of virus as a coronavirus. Its RNA genome provides a way to explore its evolutionary links to other coronaviruses.
- Culture of the virus (within a laboratory setting) was performed confirming the ability of the virus to infect and replicate in human cells.
- Cell culture studies all demonstrated that the virus is able to cause damage to human cells (called the cytopathogenic effect or CPE).

- Virus that is grown in culture is able to infect animals and cause disease.

Koch's Postulates

Approximately 200 years ago, a German physician named Robert Koch proposed that four conditions were required to demonstrate the causal relationship between a particular microorganism and disease.

These became known as Koch's postulates, which are as follows:

1. The microorganism must be found in diseased but not healthy individuals;
2. The microorganism must be cultured from the diseased individual;
3. Inoculation of a healthy individual with the cultured microorganism must recapitulated the disease; and finally
4. The microorganism must be re-isolated from the inoculated, diseased individual and matched to the original microorganism.

These criteria were further updated in 1937 by Rivers for viral diseases to allow for the fact that viruses are unable to survive without a host [1].

1. Regarding the first postulate, the concept of an infectious agent has markedly changed over the last 100+ years. In particular it is increasingly recognised that different individuals will have different responses to a particular micro-organism. While some people develop a life threating illness, others will remain without symptoms from a given illness. Koch himself recognised that there were asymptomatic cases of cholera. The risk of becoming ill from a particular microorganism then becomes a matter of probabilities, not an "all or none" phenomenon, as originally implied in Koch's postulates. Although not all individuals will develop symptoms of COVID-19, any individual infected with SARS-CoV-2 (asymptomatic or not) is able to pass the virus on to other individuals.

2. Most viruses can be cultured in specifically designed laboratory 'medium' that promotes their growth. Because viruses require a host cells to grow and reproduce, the type of cell required for culture will vary. However, viruses are not always easy to grow in culture and therefore to identify the presence of virus other means may be used which are more rapid, reliable and cost-effective. In particular, genetic tests are often used to identify sections of RNA which are unique to a specific virus.
3. The inoculation of a potentially deadly virus into healthy individuals is unnecessary to identify a particular virus as the cause of a disease. This step in Koch's postulates is usually determined by the observation of natural infection in groups of individuals, in cell culture or in animals. However, human challenge studies are being undertaken in young health individuals in order to accelerate the development of vaccines [2] and fulfils the third postulate.
4. The identification of the same virus in groups of infected individuals (clusters), as identified by genomic testing validates this point.

Supporting information/evidence

[1] Rivers TM. Viruses and Koch's Postulates. J Bacteriol. 1937;33(1):1-12. PubMed PMID: 16559982.
[2] Eyal N, Lipsitch M, Smith PG. Human Challenge Studies to Accelerate Coronavirus Vaccine Licensure. The Journal of Infectious Diseases. 2020;221(11):1752-6.