COVID-19

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Conflict of Interest Disclosure

Member of the provincial (Quebec) PCR laboratory test comity for the detection of SARS-CoV2
PCR testing

• Diagnosis of the SARS-CoV-2 relies on PCR testing which currently is the gold standard.

• Viral ARN is amplified from a patient sample (oral-nasopharyngeal) and the laboratory will release a result as “detected” or “non detected”.

• In Canada, the test was developed by the National Laboratory of Microbiology (NLM) in Winnipeg, and is similar to the one recommended by the CDC in the US.
PCR testing

- The test detects a concentration of virus as low as 300 copies of virus/ml.
- That level of detection (LOD) was well accepted from the beginning of the pandemic in Canada, and we rely on it to contain the infection.
- Currently, there are numerous FDA and Health Canada approved tests that were launched and their level of detection vary between 100-1000 copies.

**COVID-19**
What is the reliability of our test to detect SARS-CoV-2 infected individuals?

• The real epidemiologic sensitivity of the analysis is still unknown.
• We need good specific serologic tests to confirm that a person was really infected by the virus and then corroborate with the PCR analysis.
  • IgM+ and/or IgG+ patient=Truly infected patient
  • IgM+ and/or IgG+ patient with a positive PCR test=True positive PCR
  • IgM+ and/or IgG+ patient with a negative PCR test=False negative PCR

➢ Sensitivity of PCR test=True positive PCR/Truly infected patient
What is the risk that we miss an infection with our PCR test?

What we think we know:

• Most of SARS-CoV-2 infected and symptomatic patients maximally excrete the virus around the time of symptoms appearance.
• Some individuals are asymptomatic yet, they can excrete the virus as much as symptomatic patient.
• Most of those asymptomatic yet infected individuals are in fact pre-symptomatic and will end up with symptoms eventually.

➢ At any time point over the course of the infection, if the individual excretes viruses over the LOD of the test, the PCR should be positive.
What can influence PCR testing?

• Preanalytical variables:
  • Mucosal density of the virus in the sampled patient
  • Type of sample: Nasopharyngeal > nasal > oral (saliva, nasopharyngeal wash, tongue?)
  • Quality of sample collection
  • Storage and transport (media, temperature, delay until processing)

• If collection of a sample (known as acceptable) is done exactly as recommended in a patient whose mucosal density of the virus exceeds the LOD, the PCR should yield a positive result.

• As with any test, clerical mistakes (wrong identification, lost of sample) are possible yet unlikely.
What is the risk that our PCR test misses an infected individual?

• We can calculate the probability that the disease is not present when the test is negative, that is the definition of the Negative Predictive Value (NPV).

• Need to make specific assumptions for:
  • Sensitivity of the test: 70%?, 90%? We don’t actually know (80%)
  • Specificity of the test: 98%
  • Prevalence of infection in asymptomatic patients?
    • Based on PCR testing, we estimate that currently, in Quebec City, the prevalence of the disease in symptomatic patients is 3%. It is therefore reasonable to assume that current infection is not as frequent in asymptomatic individuals so...0,5% 1,0%?
# Prevalence of the infection (CHU de Québec)

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<td><strong>TOTAL</strong></td>
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*Martin Coulombe, M.Sc., MAP*
Negative Predictive Value (NPV): [https://covid-airway-npv.info](https://covid-airway-npv.info)
Results

**Sensitivity** of the test: 80%
**Specificity** of the test: 98%
**Prevalence in asymptomatics:** 1%

**Negative Predictive Value**
99.78 [90% CI: 99.6 - 99.91]

**Post-Test Probability of SARS-CoV-2**
1 in 456 [90% CI: 247 - 1089]
Conclusion

• The tests are evolving consistently, and hopefully they will become more sensitive, with a faster turnaround time and we will be able to demonstrate their true clinical sensitivity.

• But we must keep going, balancing the risks and benefits while answering this crucial question: **What is my (our) risk tolerance??**