SARS-CoV-2 Infectious Dose and Viral Load

"All things are poison and nothing is without poison; only the dose makes a thing not a poison." (i.e., "The dose makes the poison.")

Paracelsus (1493 -1541), Swiss physician and the "father of toxicology"

As the basic principle behind toxicology and dose-response assessments, the relationship between exposure and potential health effects is very important when evaluating preventative measures and human health risk. In occupational and environmental health, we perform dose-response assessments for materials such as chemicals, minerals and metal solids (e.g., isopropyl alcohol or nickel). Conceptually the same process can be applied to assess risk of disease from viruses, such as influenza.

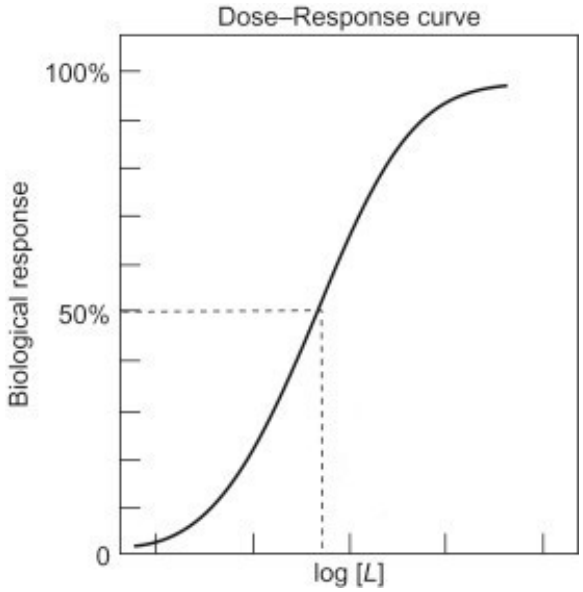

Figure 1: Dose Response Curve. Adapted from J. Feher (2017), Quantitative Human Physiology (2nd Edition) https://doi.org/10.1016/B978-0-12-800883-6.00084-7

Scientists describe the quantity of a particular virus needed to make a person sick as the minimal "infectious dose". The infectious dose, which varies amongst viruses and the characteristics of the population, is expressed as ID_{50} (i.e., the number of pathogens sufficient to infect 50% of a given susceptible population). To experimentally quantify the ID_{50}, researchers often calculate and evaluate a tissue culture infectious dose ($TCID_{50}$). $TCID_{50}$ is defined as the dilution of virus required to infect 50% of the cells within a test tube or culture plate. For influenza, a $TCID_{50}$ of 10^7 has been shown to cause mild to moderate influenza symptoms in greater than 60% of patients and a high infectious dose (i.e., high number of simultaneous contacts between susceptible and infectious individuals) is associated with increased disease severity (Memoli et. al., 2015; Paulo et. al., 2010). The infectious dose for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the link between an initial dose and severity of the disease is still under investigation (Schroder, 2020).

Once a human has received an infectious dose, the amount of virus present in the body is known as the "viral load". More specifically, a viral load is how much of the virus is present within a sample collected from an individual and can increase or decrease within tissue over time. Previous research on severe acute respiratory syndrome coronavirus (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV) specified that the peak viral load for patients with these infections occurs at approximately 7-10 days after symptom onset (Chan et. al., 2015; Peiris et. al., 2003). Furthermore, an association was found between a higher viral load of MERS-CoV or SARS-CoV-1 and worse clinical outcomes (Feikin et. al., 2015; Hung et. al., 2004). Research surrounding the viral load of SARS-CoV-2 and its relationship with the severity of disease is still contradicting with studies showing either a positive or negligible relationship between elevated viral load and disease severity. Recent studies on viral dynamics of SARS-CoV-2 have found that the SARS-CoV-2 viral load peaks around 5-6 days after symptom onset and patients with severe

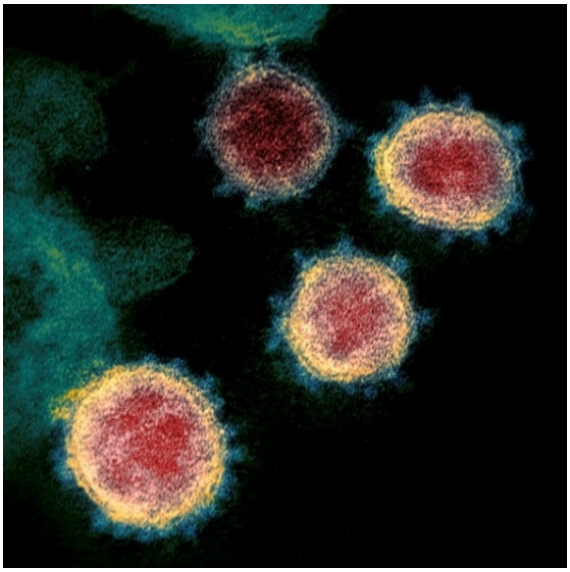

Figure 2: SARS-CoV-2 (2019-nCoV) isolated from a patient in the U.S. Image captured and colorized at NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Montana. Credit: NIAID (www.flickr.com/)

cases of COVID-19 tended to have a higher mean viral load and longer virus-shedding period than mild cases. (Liu et. al., 2020, Pan et. al., 2020, and Yu et. al., 2020). On the other hand, research by Cereda et. al., 2020 (pre-print) surrounding the early phases of the COVID-19 outbreak in Lombardy, Italy and by He et. al., 2020 in Guangzhou Eighth People's Hospital in Guangzhou, China did not observe significantly different viral loads across disease severity or symptoms. Discrepancies between research surrounding viral load and severity could be due to a number of factors including the influence of underlying health conditions, diversity in the populations studied, and overall lack of research and experiments. Experts, in general, do believe that the higher the viral load an individual has within their body, the more they can release and transmit to others (Gaglia and Lakdawala, 2020) and a person in the vicinity of multiple infected people breathing and/or coughing out virus particles will likely receive a higher infectious dose than someone in the vicinity of only one infected person.

As restrictions begin to relax and business and recreational activities slowly resume, with little known on the minimal infectious dose of SARS-CoV-2 needed to cause COVID-19 and the knowledge that an individual with a high viral load can spread the disease, the recommendations from the medical community are to continue to follow safe and effective control solutions to mitigate exposure to a potentially infectious dose until more definitive information is available or a vaccine seems prudent. To determine control solutions for occupational exposures, an industrial hygienist follows the hierarchy of controls (Elimination, Substitution, Engineering Controls, Administrative Controls, and Personal Protective Equipment (PPE)). This hierarchy may further be used as a guide or template to determine controls for exposure to infectious diseases. As stated in "Managing Risks Require Understanding Hazards and Changing Behavior", Fred Boelter stated:

> *"In the industrial hygiene profession, we have the hierarchy of controls that from top to bottom are the most-effective to least-effective, in terms of risk reduction. With COVID-19, Elimination and Substitution are not options. Mother Nature makes those choices. But Engineering Controls such as vaccinations, fast analyzers, and the cleaning of surfaces are helpful. Administrative Controls include social distancing and self-quarantine, demanding behavioral change. Personal Protective Equipment (PPE) is always the least effective control and for COVID-19 this includes masks and other protective gear as well as ventilators which are the last line of defense for patients suffering respiratory failure. An ultimate reliance on PPE means more effective controls failed for any number of reasons."*

As the research and data builds and we continue to see new cases of COVID-19, we must remember to remain informed and follow safe and effective hygiene and work practices to reduce risk of exposure to an infectious dose. Behaviors such as wash hands with soap and water; use of hand sanitizer; minimize touching your eyes, nose and mouth; cover coughs and sneezes; and clean and disinfect frequently

touched surfaces have been shown to lessen a person's risk of a dose that could cause infection (CDC, 2020).

Further social distancing (a.k.a "physical distancing") continues to be recommended by the CDC and medical professionals as a barrier to infection. This means keeping space between yourself and anyone outside of residential housemates by staying at least six feet from other people, not gathering in groups, and staying out of crowded spaces (CDC, 2020). Visiting parks and recreational facilities are typically open enough to allow for increased social distancing while providing an outlet for stress to keep your mind and body healthy. When visiting parks, it is recommended by the CDC to visit those parks close to your home, check with the park or recreation area in advance to prepare safely, continue to practice social distancing when outdoors, and carefully consider the use of any equipment, pools, hot tubs and water playgrounds (CDC, 2020). Remember, if social distancing measures are difficult to maintain, such as in public settings, the CDC recommends wearing a cloth face covering. Cloth face coverings are not designed to comprehensively protect the wearer, they are designed to provide a layer of protection to keep the wearer from spreading the virus to others (CDC, 2020). Coupled with handwashing and physical distancing, one's risk of infection is notably reduced.

Following safe and effective hygiene and work practices should not be limited to a single task as each barrier such as social distancing, cloth masks, and personal hygiene work together to reduce the risk of reaching an infectious dose.

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