

# Therapeutics for Monkeypox

## About the Monkeypox Virus

Monkeypox is a virus from the Orthopoxvirus genus of the Poxviridae family, first discovered during a disease outbreak at a monkey research facility in Copenhagen, Denmark <sup>1</sup>. The first human case of monkeypox was later identified on August 22, 1970, in a 9-month-old boy from the Democratic Republic of the Congo <sup>2</sup>. For a long period, monkeypox was endemic in central and west African countries including South Sudan, Sierra Leone, the Democratic Republic of the Congo, Nigeria, Ivory Coast, Liberia, Republic of the Congo, Gabon, and Ghana <sup>3</sup>. It was not until 2003 that the first monkeypox outbreak occurred outside of Africa, resulting in over 70 cases of monkeypox in the United States <sup>4</sup>. In the 2022 outbreak, over 40,000 cases of monkeypox were detected in 94 countries around the world by August <sup>5</sup>.

According to past studies, there are two general clades of monkeypox: the central African (Congo Basin) clade and the west African clade <sup>6,7</sup>. Historically, the Congo Basin clade has been known to be more transmissible and to cause more severe diseases than the West African clade. Monkeypox infections caused by the Congo Basin clade can have a case fatality rate (CFR) as high as 11%, compared with the West African clade which has a <1% CFR <sup>8-10</sup>. Fortunately, all of the recent outbreak cases, whose samples have been sequenced by PCR, have been attributed to the West African clade <sup>11,12</sup>. However, for unclear reasons, a disproportionate number of cases in the recent monkeypox outbreak have been in populations of men who have sex with men (MSM) <sup>13,14</sup>. In a study which looked at 528 monkeypox infections from 16 countries around the world, researchers found that 98% of cases were among gay or bisexual men <sup>14</sup>.

## Risk to Canadians

On May 19th, 2022, the Public Health Agency of Canada (PHAC) confirmed the first two cases of monkeypox in Montreal, Quebec <sup>15</sup>. Since then, there have been 1,251

confirmed cases of monkeypox in Canada (August 31, 2022) <sup>16</sup>. Similar to other non-endemic countries, most of the monkeypox cases in Canada are also disproportionately within groups of MSM <sup>17</sup>.

## Mode of Transmission

Direct skin-to-skin contact with infectious lesions and scabs <sup>18</sup>

- Direct contact with bodily fluids such as respiratory droplets, saliva, semen, and/or urine containing the virus <sup>19</sup>
- Animal-to-human transmission, including infected domestic pets <sup>20,21</sup>
- Transmission by fomites and contaminated objects <sup>22</sup>
- Vertical transmission (mother-to-foetus) <sup>23</sup>

## Prevention Measures

- Avoid contact with infected animals and/or domestic pets
- Avoid contact with contaminated objects such as bedding and linens
- Avoid direct contact with bodily fluids from people who may be infected with the virus
- Practice safer sex, including the use of condoms and limiting sexual partners
- Clean and disinfect surfaces with potential exposure to the virus
- Provide personal protective equipment (PPE) when caring for people with monkeypox

## Vaccinations

In May 2022, the Modified Vaccinia Ankara - Bavarian Nordic vaccine (MVA-BN; Trade Names: IMVAMUNE in Canada; Jynneos in the U.S) was approved by Health Canada for immunization of adults aged 18 and older against monkeypox. The IMVAMUNE vaccine is a newer formulation of the smallpox vaccine that is based on a modified

attenuated vaccinia virus that is non-replicating called the Ankara strain. Vaccination against smallpox with the vaccinia virus has been shown to yield as much as 85% protection against monkeypox <sup>24</sup>. According to recommendations by the WHO and National Advisory Committee on Immunization (NACI) of Canada, the vaccine is to be administered in two doses at 4 weeks apart <sup>25</sup>. However, due to limited supply, mass vaccination is currently not recommended. Instead, there are several vaccine strategies currently under consideration to better control the monkeypox outbreak:

- Pre-exposure prophylaxis: Immunization of individuals at most risk for acquiring monkeypox, including those working in research, clinical labs, and hospitals.
- Post-exposure prophylaxis: Immunization offered to individuals after infection. The vaccine should ideally be given within 4 days but can be administered up to 14 days following exposure.
- Ring vaccination: Vaccines are administered to transmission clusters including individuals confirmed with monkeypox as well as their close contacts <sup>26</sup>.
- Key populations: Due to the limited supply of vaccines, single-dose immunizations are targeted for populations with higher risk for acquiring monkeypox, including MSM groups, individuals with multiple sex partners, workers and attendees of any social event organized for sexual activity, and those who were recently diagnosed with a sexually transmitted infection <sup>27-30</sup>.

## Vaccination Strategies in Quebec, Canada

Quebec was the first province in Canada to face the monkeypox outbreak. To control the spread of the virus, the province had to deploy an immediate immunization strategy to distribute the IMVAMUNE vaccine <sup>31,32</sup>. Initially, IMVAMUNE was administered as a post-exposure prophylaxis to contact traced individuals, however, >80% of contacts were not retraceable. As a result, the vaccination strategy was revised to target all cis and trans men who had sexual contact or attended an event where sexual activities took place in the last 14 days in Montreal. The vaccine was also provided to those who had worked or attended a social event where sexual activities took place, and those who might be in contact with contaminated materials. Due to the limited supply of vaccines, eligible individuals received only one dose of IMVAMUNE while immunocompromised individuals

received two doses. The Quebec National Institute of Public Health (INSPQ) has not recommended vaccination for healthcare workers, stating that since all healthcare workers wear personal protective equipment, the risk of infection is low (June 3rd, 2022)<sup>33</sup>.

## Treatments

There are two anti-viral treatments used for smallpox that have been repurposed for monkeypox, tecovirimat and brincidofovir, of which only the former has been approved for clinical use in Canada <sup>34</sup>. Tecovirimat works by blocking the interaction of viral p37 protein orthologs and preventing the envelopment and release of orthopoxviruses from infected cells <sup>35,36</sup>. According to one patient study, treatment of monkeypox using tecovirimat was associated with shorter hospitalization and reduced viral shedding <sup>37</sup>.

## Future Therapeutics & Developments

- The Assistance Publique-Hôpitaux de Paris, along with other agencies in Europe, began a clinical trial called the Monkey Vax Study to assess the efficacy of the IMVAMUNE vaccine as a post-exposure prophylaxis. The primary objective of the study will be to assess the failure rate of the vaccine post-exposure in preventing monkeypox infection within 28 days after the first dose <sup>38</sup>.
- The WHO has launched a protocol for an adaptive international randomized, placebo-controlled clinical trial to assess the efficacy and safety of treatment drugs for monkeypox. The primary endpoint will be to assess the rate at which patients with monkeypox lesions are resolved in response to treatment or placebo <sup>39</sup>.
- Moderna has announced on social media that it is currently investigating potential vaccine candidates for monkeypox at the preclinical phase. No information about timelines or development has yet been released <sup>40,41</sup>.
- The US Food and Drug Administration (FDA) recently approved the Jynneos vaccine for administration by intradermal injection. This administration strategy will use one-fifth of the vaccine dose and will allow health providers to vaccinate five times as many people, given limited vaccine supplies <sup>42</sup>. This approval was supported by results from a clinical trial conducted in 2015, which showed both subcutaneous and intradermal administration of the IMVAMUNE vaccine were able to induce similar immune responses in vaccinees <sup>43</sup>.

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