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EDITORIAL

MONKEYPOX VIRUS INFECTION IN HUMANS: PAST AND NEW POTENTIAL THREAT AT OUR DOORSTEP

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In 1980, the World Health Assembly announced that smallpox had been successfully eradicated as a disease of humans. The disease clinically and immunologically most similar to smallpox is monkeypox, a zoonosis endemic to moist forested regions in West and Central Africa (1). The name monkeypox originates from the initial discovery of the virus in monkeys in a Danish laboratory in 1958 (2). The first case in humans was diagnosed in 1970 in a 9-month old baby boy in Zaire (now the Democratic Republic of the Congo, DRC). Since that time, monkeypox has become endemic in the DRC, and has spread to other African countries, mainly in Central and West Africa (3). Historical data have indicated that smallpox vaccination with vaccinia virus (another orthopoxvirus) was approximately 85% protective against monkeypox (4). However, following the eradication of smallpox, routine vaccination against smallpox was no longer indicated (5). At the time when smallpox was rampant, no cases of monkeypox were reported. This could have been either because the focus was on smallpox and the presentations of the two diseases are similar or the lack of laboratory confirmation of the etiologic agent led to an assumption of smallpox (6). It is now more than 40 years since the WHO recommended cessation of routine smallpox vaccination. Immunity is waning as a result monkeypox might emerge as a more significant human pathogen, perhaps even 'replacing' smallpox (7).

Monkeypox has both zoonotic and human to human transmission. Zoonotic transmission occurs via direct contact with blood, body fluids or monkeypox lesions of infected animals. Inadequately cooked meat can also be contributing to it. Human to human transmission occurs via respiratory droplets, direct contact with skin lesions of those infected, or getting in contact with objects contaminated from an infected person (8). Sexual transmission of Monkeypox or other members of orthopoxvirus has not been confirmed yet. Reports suggested rather it seemed to have transmitted due to a close contact during sexual encounter with skin lesion (9). Intrauterine transmission is also reported (10).

Clinical manifestation has been divided into invasion and skin manifestation periods. Invasion period is recognized by prodromal symptoms preceding skin eruptions, including fever, chills, headache, body aches, malaise, regional lymphadenopathy and sometimes vomiting. Cutaneous manifestations are observed after 1–3 days of appearance of fever and include successive stages of macules, papules, vesicles, pustules, crusting, and scars for 2–4 weeks. They start to appear first on head and neck region and then moves towards the periphery (11). Clinical presentation of monkeypox resembles that of Smallpox as both have non-pleomorphic skin eruptions. Surprisingly, different reports demonstrated that the clinical presentation of confirmed cases of the current outbreak has been varied. Many

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cases in this outbreak do not present the classic clinical presentation of monkeypox. These atypical clinical findings, different from the classic presentation of monkeypox, are the presence of skin lesions in the genital or perineal/perianal area, without subsequent dissemination, in a small number, and which may precede the general symptoms (fever, malaise, mylagia, etc.), as well as proctitis. Frequently, adenopathies are found. Lesions around the mouth and on the oral mucosa, similar to the classic presentation of monkeypox, have also been described (12).

In 2003, 47 cases of monkeypox were identified in the United States across 6 states in the Midwest and represented the first monkeypox outbreak outside of Africa. Infected people became ill after having contact with pet prairie dogs that were exposed to sick, small mammals from Ghana (13, 14). Other cases outside of Africa have been described in Israel, Singapore, the UK, and the United States (15). Since the 13th of May 2022, cases of monkeypox have been reported to WHO from 12 member States that are not endemic for monkeypox virus. On the 23rd of July, the World Health Organization (WHO) declared monkeybox a global health emergency. At the time more than 16,000 cases had been reported from 75 countries. As of August 4, 2022 there were 26,208 monkeypox cases reported across 87 countries. Up to the 13th of September 2022, 19, 379 confirmed cases of monkeypox have been reported from 29 EU/EEA countries (16). During the week of the 12th to 18th September 2022, the number of monkeypox cases reported in the Regions of Europe and the Americas declined, driving the global downward trend observed since August 2022. Since the last edition published on the 7th of September 2022, 8,757 new cases (16.5% increase in total cases) and five new deaths have been reported (17).

In Africa, monkeypox endemic countries includes Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Ghana (identified in animals only), Ivory Coast, Liberia, Nigeria, the Republic of the Congo, Sierra Leone, and South Sudan (18). From 2000 to 2009, there were 10,027 confirmed or suspected cases of human monkeypox in the Democratic Republic of Congo (DRC); a cumulative tally of more than 18,000 cases was determined in 2019 (19). As of May 31, 2022, there have been 1,400 suspected or confirmed cases of human monkeypox with 66 deaths reported in Sierra Leone, Liberia, Cameroon, Congo, Central African Republic, Nigeria, and Democratic Republic of Congo (20). On the other hand, at joint statement officials of the Ministry of Health and Ethiopian Public Health Institute on the 27th of July 2022, monkeypox is not found in Ethiopia.

Testing capacity for monkeypox is rapidly expanding; the preferred method of diagnosis involves nucleic acid amplification from a direct specimen. Several nucleic acid amplification tests have been developed to detect monkeypox (21). A real-time polymerase chain reaction (PCR) assays targeting different orthopoxvirus genes, including DNA polymerase (E9L) and envelope protein (B6R), demonstrated 100% specificity for monkeypox (22). Despite the approval of a vaccine (MVA-BN) and a treatment (tecovirimat) for monkeypox virus in 2019 and 2022, these counter measures are not yet readily accessible. The vaccine is the only non-replicating smallpox vaccine approved in Europe for use in the general adult population (23).Because earlier smallpox vaccination programs no longer provide immunity for individuals younger than 40 or 50 years old, only the elderly will benefit from cross protective immunity from the smallpox vaccine. However, in the absence of a licensed vaccination for monkeypox virus, the third generation of smallpox vaccine should be administered to prevent pre-and post exposure to smallpox and monkeypox virus (24).

For this epidemic to be managed, the following action must be taken (25). First, the primary preventative method

for monkeypox virus is raising public knowledge of risk factors and informing them of the strategies they may take to decrease their exposure to the virus. Second, scientific research should be conducted to determine the feasibility and suitability of vaccination for preventing and controlling monkeypox virus. Third, these human illnesses have frequently emerged through animal-to-human transmission over time; thus, sick or dead wild animals, the proper handling of potential animal reservoirs, the isolation of diseased animals, and animal flesh must not be handled without protection. Fourth, develop strategies to vaccinate and train medical personnel at risk, including laboratory personnel, frontline practitioners, and nurses. In addition, travel restrictions should be imposed on endemic nations, and adequate screening should be implemented at all national entrance and exit ports to prevent the spread of the virus.

In conclusion, history repeats itself and the little attention the healthcare community pays to what happens in Africa has just resulted in one more international public health alert. The neglected tropical disease of the poor, monkeypox gets attention only after it starts to infect people in wealthy countries. The world is interdependent, what is happening in Africa will definitely impact what is happening in the West and vice versa. Although the international outbreak has again highlighted global health inequities, it has also brought much-needed attention to the smoldering disease in Africa.

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