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Review

Monkeypox in humans: a new outbreak

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ABSTRACT

Infection caused by Monkeypox Virus (MPVX) has small rodents as its natural reservoir and both monkeys and humans are occasional hosts. The causative agent is an Orthopoxvirus (MPVX) that was isolated in monkeys in 1958 and proved capable of passing to humans in 1970. It remained contained in Africa, causing isolated episodes of infection, until 2003 when an outbreak occurred in the United States following importation of animals from that continent. Since then, anecdotal cases have continued to be reported outside Africa, usually very clearly linked to travelers to those countries, but in May 2022, a broad outbreak of this disease has begun, now affecting several continents, with the emergence of human cases of MPVX (H-MPVX) infection mainly among Men that have Sex with Men (MSM). The disease has an incubation time ranging from 5 to 15 days and is characterized by the presence of pustules, fever, malaise and headache. The presence of significant regional lymphadenopathy is a differential feature with episodes of classical smallpox. Proctitis and pharyngitis, with minimal skin lesions, may be another form of presentation. Diagnosis can be confirmed by PCR testing of lesions or by demonstration of MPVX in other body fluids or tissues, although in the appropriate epidemiologic setting the clinical picture is highly suggestive of the disease. Effective drug treatment has been developed as part of programs to protect against potential bioterrorist agents and smallpox vaccinees are known to have high protection against monkeypox. New vaccines are available, but neither the drugs nor the vaccines are yet freely available on the market. The prognosis of the disease appears, at least in adults in developed countries, to be good, with very low mortality figures and much less aggressive behavior than that described in classical smallpox. Isolation measures, essential for the control of the outbreak, have been published by the health authorities.

Keywords: Monkeypox, MPVX, Poxvirus, outbreaks, vaccines, smallpox, outbreak, sexually transmitted infections

Monkeypox (Viruela del mono) en humanos: un nuevo brote

RESUMEN

La infección causada por el Virus de la Viruela del Mono o Monkeypox (MPVX) tiene como reservorio natural los pequeños roedores y tanto el mono como el hombre son huéspedes ocasionales. El agente causal es un Orthopoxvirus (MPVX) que fue aislado en monos en 1958 y se demostró capaz de pasar a humanos en 1970. Se mantuvo contenido en África, causando episodios aislados de infección, hasta el año 2003 en que se produjo un brote en los Estados Unidos tras la importación de animales desde dicho continente. Desde entonces, han seguido

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comunicándose casos fuera de África, por lo general muy claramente vinculados a viajeros a dichos países, pero en mayo de 2022 se ha iniciado un brote amplio de esta enfermedad que afecta ya a varios continentes, con la aparición de casos humanos de infección por MPVX (H-MPVX) principalmente vinculados a fiestas en las que hay relaciones sexuales de hombres con hombres (HSH). La enfermedad tiene un tiempo de incubación que puede oscilar entre 5 y 15 días y se caracteriza por la presencia de pústulas, fiebre, malestar general y cefalea. La presencia de importantes adenopatías regionales es una característica diferencial con los episodios de viruela clásica. La proctitis y la faringitis, con mínimas lesiones cutáneas, pueden ser otras formas de presentación. El diagnóstico puede confirmarse con una prueba de PCR en las lesiones o con la demostración de MPVX en otros fluidos o tejidos corporales, aunque en el contexto epidemiológico oportuno el cuadro clínico es altamente sugerente de la enfermedad. Hay tratamiento medicamentoso eficaz que ha sido desarrollado como parte de los programas de protección frente a potenciales agentes bioterroristas y se sabe que los vacunados de viruela tienen una protección elevada frente a H-MPVX. Se dispone de nuevas vacunas, pero ni los medicamentos ni las vacunas están todavía libremente disponibles en el mercado. El pronóstico de la enfermedad parece bueno, al menos en países desarrollados y en adultos, con cifras de mortalidad muy bajas y un comportamiento mucho menos agresivo que el descrito en la viruela clásica. Las medidas de aislamiento, imprescindibles para el control del brote, han sido publicadas por las autoridades sanitarias

Palabras clave: Monkeypox, MPVX, Viruela del mono, Poxvirus, brotes, vacunas, viruela

INTRODUCTION

Monkeypox (MP) is a zoonotic viral infection (transmitted to humans from animals) caused by a member of the genus Orthopoxvirus of the family Poxviridae.

Monkeypox virus (MPVX) was discovered in a Danish laboratory in 1958 [1] when it was identified as the causative agent of a disease in Cynomolgus monkeys similar to human smallpox.

Initially, man was considered to have little susceptibility to this new virus [2], but in 1970 its zoonotic nature was demonstrated by its confirmed transmission to a 9-month-old child (Human Monkeypox) in the Democratic Republic of Congo [3].

The disease in humans has remained endemic in Central African countries [4-9] and, outside Africa, a multistate outbreak of cases occurred in the United States of America [10] in 2003, among people who had contact with imported animals.

The disease has just jumped into the media with an outbreak in humans residing outside Africa starting in May 2022, with more than 3.000 cases reported from more than 50 countries in the first month after the beginning of the outbreak. The outbreak is, at present, linked primarily, but not exclusively, to groups of men who have sex with men (MSM).

The COVID and Transmissible Pathogens Committee of the Illustrious College of Physicians of Madrid (ICOMEM) has tried to bring together existing and rapidly changing information on this topic that could be of interest to members of ICOMEM and anyone else. Trying to stratify the data, we have formulated some questions that the members of the Committee have considered relevant. We have invited physicians from Madrid who are not usually part of the Standing Committee of the College to participate in the writing of this paper because of their experience in the diagnostic and therapeutic management of these cases [11] and from the Center for Molecular Biology Severo Ochoa of the Spanish National Research Council.

We will now discuss some of the questions raised.

WHAT IS A POXVIRUS AND WHAT CHARACTERIZES IT?

The Poxvirus family (Poxviridae) consists of a group of large, complex, double-stranded deoxyribonucleic acid (DNA) viruses that replicate in human cells and are defined by their genomic, structural, and antigenic characteristics.

The 8 vertebrate Poxvirus genera are: Orthopoxvirus, Parapoxvirus, Avipoxvirus, Capripoxvirus, Leporipoxvirus, Suipoxvirus, Molluscipoxvirus and Yatapoxvirus. They all share a similar DNA sequence with very similar antigens that have cross-reactivity [12].

Poxviruses include human smallpox virus (Variola), which was declared eradicated by the World Health Organization (WHO) in 1980. Other poxviruses that can affect humans include cowpox virus (Cowpox), the virus used in the smallpox vaccine (Vaccinia), Akhmeta virus and monkeypox virus (MPVX), as well as other zoonotic species with epidemic potential. Of these, MPVX is the most prevalent in humans.

Bovine smallpox is another zoonotic disease, with a wide reservoir in the animal kingdom, which can produce papulo-vesicular disease in humans, in a clear relationship of contact with cattle, of variable dissemination and severity, generally with very low mortality and weeks of evolution.

Another viral genus of the Poxvirus family are the Parapoxviruses, which include species of wide dissemination in sheep, goats, cattle, camelids and cervids. They are Orf viruses that produce different clinical manifestations in animals, in general with oral or pharyngeal affection (papular stomatitis) or cutaneous (papular dermatosis) that by contact affect humans (milker's nodule) and that induce nodular or macrovesicular lesions with granulomatous reaction, of medium duration. This genus induces less immunity than Orthopoxviruses and therefore reinfections are more frequent.

Molluscum Contagiosum is a frequent disease of humans, children and adults, produced by species of the genus Molluscipoxvirus, with special epidermal tropism and inducing papules that mimic soft tumors, generally small, of variable number depending on the sites of inoculation, preferentially distributed on the trunk and root of the extremities, self-lim-

ited in the immunocompetent. Molluscum Contagiosum is transmitted by direct contact, facilitated by sexual intercourse with genital proximity lesions and also transmitted by fomites.

Finally, the genus Yatapoxvirus, which includes the Tana River pox virus (Kenya), induces in humans a vesicular-papular disease in areas of exposed skin, with adenopathic reaction and systemic symptoms of up to 6 weeks of evolution.

Equivalent in African and Asian apes is the disease produced by the Yaba virus, which produces lesions that mimic histiocytomas and can be transmitted to humans by bites or direct inoculation.

Unlike other viruses, the ability of Poxviruses to mutate is much lower than that exhibited by RNA viruses, such as influenza virus or SARS-CoV-2. Nevertheless, these viruses have a large genetic endowment responsible for their virulence and ability to invade and evade the immune system [13,14].

Interest in these viruses has been sustained, among other reasons, because of the potential use of some of these agents, particularly Variola virus, as a biological weapon since Orthopoxviruses and Poxviruses can be created and modified in laboratories using molecular biology tools [15,16].

Two distinct genetic clades of MPVX have been identified, Congo Basin and West African. The former is more virulent and transmissible than the latter. The geographical division between the two clades is believed to be in Cameroon, as it is the only country where both clades of the virus have been detected simultaneously. The cases currently affecting Spain are caused by the less virulent West African clade [17].

WHAT DID SMALLPOX MEAN IN THE HISTORY OF MANKIND?

Smallpox was a disease with very high mortality, which fortunately was eradicated in 1980 thanks to vaccination and the fact that its reservoir was only human [18,19]. Smallpox lesions have already been identified in Egyptian mummies from 300 BC, and it has subsequently affected humanity periodically through large epidemic outbreaks [20-22]. Recent studies have sequenced complete smallpox virus genomes in human remains from the Viking era (9th-12th centuries), a Lithuanian mummy (18th century) and specimens from a 19th century Czech museum [23]. Human smallpox, after infection, is followed by an incubation period ranging from 7 to 14 days, after which skin lesions appear abruptly and intensely. A rash usually appears, either diffuse (scarlatiniform) or macular (macular or measles) and with variable involvement of the skin surface, mainly on the face, extremities, hands and feet and later on the trunk, evolving into papules.

Between the fifth and sixth day after their appearance, the papules become round vesicles, with a central umblication and on the eighth day they become clear pustules with a grayish and turgid content. It is very characteristic, from the semiological point of view, that all the cutaneous elements are in the same morphological stage, a fact that differentiates it from other vesicular-eruptive diseases, mainly with chickenpox.

In the crust formation phase, these may remain adhered to the skin for a long time and their fall will leave a scar.

Smallpox was, for centuries, one of the first causes of blindness in mankind and its mortality has ranged from 10-75%, It is estimated that in the 20th century approximately 300 million people worldwide still died from smallpox before its eradication [20-22,24-28].

Smallpox was the first disease against which a vaccine was available, and Spain played a key role in spreading smallpox vaccination throughout its extensive empire, by means of the famous Royal Philanthropic Vaccine Expedition, led by Francisco Javier Balmis [29-32].

WHAT ANIMALS ARE INFECTED BY MPVX?

There are multiple animals that are susceptible to infection by MPVX including non-human primates, rodents, squirrels and dormice. Some of these animals have been used as models on poxvirus acquisition and transmission and for testing vaccines and protective drugs after it was learned that the former Soviet Union had turned these viruses into potential biological weapons [33].

In non-human primates, MPVX usually produces a short-lived rash. Initial clinical signs are fever and cutaneous papules of 1-4 mm, which develop into pustules and then crust over. A typical lesion has a red, necrotic, depressed center surrounded by epidermal hyperplasia. These "smallpox pustules" can be located all over the body, but preferentially on the face and extremities. Most infected animals recover quickly; however, fatal cases can occur, especially in neonatal monkeys.

The disease caused by MPVX has also been observed naturally in some rodents, such as prairie dogs, and after inoculation in dormice and squirrels. In all of these cases, clinical manifestations are varied, but fever, weight loss, nasal discharge, sneezing and/or coughing, respiratory involvement, and nodular skin rash or mouth ulcers may occur [33-37].

WHAT CASES OF MPVX INFECTION HAVE BEEN DESCRIBED IN HUMANS?

Until recently, MPVX was an occasional, endemic disease in humans in contact with animals that spread mainly in rainforest areas of Central and West Africa, causing isolated cases or small outbreaks in 11 African countries: Benin, Cameroon, Central African Republic, Democratic Republic of Congo, Gabon, Ivory Coast, Liberia, Nigeria, Republic of Congo, Sierra Leone and South Sudan.

In 1996-1997, a large outbreak of MPVX in humans was described in the Democratic Republic of Congo with a low case fatality rate, but with a higher than usual attack rate [38-42]. In 2017 Nigeria experienced the largest documented outbreak, 40 years after the last confirmed case [43].

As of 2018, occasional cases have been reported in Israel [44] in September 2018, in the United Kingdom in December

2019 [45,46] and in Singapore in May 2019 [47] in travelers from Nigeria who became ill with monkeypox after arrival. One health care worker was infected and became ill.

WHEN AND HOW DOES THE CURRENT OUTBREAK BEGIN?

On May 7, 2022, a case of H-MPVX is confirmed in the United Kingdom in a patient with recent travel to Nigeria [48). On May 14, 2022, two additional cases of H-MPVX were identified in London in two unrelated cohabitants of the previous case and new cases have been confirmed in the United Kingdom, in and outside of London. The current outbreak is multinational and includes more than 50 countries as far afield as Australia, North America and Europe [49-51].

The majority of cases have occurred in young men, many of whom were identified as MSM, with genital lesions suggesting that transmission likely occurred through close physical contact [52-58].

In Spain, the number of confirmed cases as of June 10 exceeds 200, mostly related to MSM parties.

WHAT ARE THE CLINICAL MANIFESTATIONS OF MONKEYPOX IN HUMANS?

A publication presents the clinical features and evolution of 282 patients with H-MPVX in the Congo during 1980-1985. The ages of the patients ranged from one month to 69 years; 90% were younger than 15 years. The clinical picture was similar to that of the ordinary and modified forms of smallpox. Lymphadenopathy, appearing early in the disease, was the most important sign differentiating monkeypox from smallpox and chickenpox in humans. Symptoms, signs, and disease course in patients who had been vaccinated against smallpox differed significantly from those of unvaccinated subjects. Varicella-like pleomorphism and cropping occurred in 31% of vaccinated and 18% of unvaccinated patients. Prognosis was largely dependent on the presence of severe complications, and no deaths occurred among vaccinated patients. In unvaccinated patients, the crude mortality rate was 11%, but was higher among younger children (15%) [59].

Clinical manifestations of human infection usually appear after incubation periods of 5 to 21 days. It usually presents clinically with fever, rash and swollen lymph nodes. It is usually a self-limiting disease with symptoms lasting 2 to 4 weeks. Severe cases are more frequent in children and are related to the degree of exposure to the virus, the patient's state of health and the nature of the complications.

Skin lesions are more frequent on the face and extremities than on the trunk. The lesions do not affect the palms of the hands and soles of the feet (in 75% of cases) or the oral, genital or rectal mucous membranes. The conjunctiva and cornea may be affected.

Complications of monkeypox may include deep abscesses and secondary infections.

Some patients, in this outbreak, manifest preferentially with proctitis or pharyngitis with minimal or absent skin lesions.

WHAT IS THE EPIDEMIOLOGY OF HUMAN MPVX DISEASE?

In 1980 the WHO [60] reported that since 1970 there have been 47 human cases of monkeypox in 5 countries in Central and West Africa; 38 of which have been reported in the Congo. Human MPVX disease had at that time a mortality rate of approximately 17% and children under 10 years of age accounted for 83% of the cases. All cases had occurred in tropical rainforest areas and clustering of cases had been observed in certain areas within countries and within families. Although the low rate of transmission and the low frequency of disease indicated that monkeypox was not then a public health problem, authorities cautioned that more data on this disease were needed.

Many animals near human cases of MPVX were shown to have antibodies to Orthopoxvirus, but the natural reservoirs and vectors of MPVX were unknown [61]. Even so, the disease was beginning to be accepted as a probable zoonosis [60,62-64].

Human-to-human transmission was progressively well demonstrated [65] by small family outbreaks after acquisition of the index case from a monkey [65].

A study of 2,510 contacts of 214 patients with H-MPVX was conducted in Zaire between 1980 and 1984 [66]. Among the contacts of 130 primary cases, an additional 22 co-primary and 62 secondary cases were detected, and fourteen other persons who had no evidence of clinical disease had positive serological results. Most of those clinical and subclinical cases of monkeypox occurred in children under 10 years of age. The overall attack rate of contacts without smallpox vaccination scar (7.2%) was significantly different from those with vaccination scar (0.9%) [66].

Secondary or person-to-person transmission would occur by close contact with infected respiratory tract secretions or skin lesions of an infected person, or with objects recently contaminated with the patient's fluids or lesion materials. Transmission occurred mainly by respiratory droplets, usually after prolonged face-to-face contact with the patient, exposing family members of active cases to an increased risk of infection [67).

Infection of index cases results from direct contact with blood, body fluids, or skin or mucosal lesions of infected animals.

In recently reported cases outside the African continent, the virus is transmitted from person to person by contact with skin lesions, body fluids, respiratory droplets, and contaminated materials such as bedding. This form of transmission is what is occurring in the present outbreak. Transmission via respiratory droplet particles usually requires prolonged face-to-face contact, which poses a greater risk to unprotected health care

workers and specially to close household members of active cases. Transmission can also occur through the placenta from mother to fetus (congenital monkeypox).

WHAT SHOULD BE DONE AT THIS TIME IN SPAIN IN THE EVENT OF A SUSPECTED CASE? HOW IS THE DIAGNOSIS CONFIRMED?

If H-MPVX is suspected, healthcare personnel should:

1) Attend patients with appropriate PPE: waterproof gown, gloves, FP2 mask and closed goggles.

2) Inform the Microbiology laboratory of the existence of a suspected case.

3) Prior to sampling, make sure to have a swab for sample collection, which should be sent in a dry sterile tube or in virus transport medium and kept cold. The sample should be accompanied by sufficient clinical information so that the microbiologist can fill in all the sections requested by the reference laboratory. At a minimum: age, sex, risk factors, date of onset of symptoms, date of onset of rash.

4) So far, a blood sample for serology and another in an EDTA tube can also be obtained, as well as a urine sample to be sent in the urine culture bottle.

5) It should be noted that the optimal samples for MPVX diagnosis come from skin lesions: the roof or fluid of vesicles and pustules, and dry crusts.

6) Once ready, the on-call microbiologist will be notified of their shipment, correctly identified.

7) The Microbiology laboratory staff will arrange for the samples to be sent to the corresponding reference laboratory where the polymerase chain reaction (PCR) will be performed, this being the laboratory test of choice due to its accuracy and sensitivity.

8) Clinical samples are considered category B samples. Similar precautions to those used for COVID with three successive containers are sufficient for specimen transport.

Mucosal specimens showing lesions, including respiratory, vaginal or rectal mucosa, may also be used. In cases of proctitis, it is recommended to send rectal specimens as well, since in current cases there is a strong association with sexual transmission.

In biopsy specimens, the histopathological lesions of MPVX are indistinguishable from those of human smallpox [68] and consist of necrosis affecting the stratum basale of the skin and adjacent areas of the dermal papillae. The necrosis also affects the stratum spinosum above the destroyed stratum basale. There are occasional multinuclear giant cells and some bodies resembling Guarnieri bodies.

Electron microscopy shows abundant orthopoxvirus particles in the cytoplasm of infected epidermal cells. In general, the features are indistinguishable from the papulonecrotic phase of smallpox [68].

Viral strains of MPVX isolated initially were readily differentiated from Variola and Vaccinia viruses. The isolated strains produced small necrotic hemorrhagic spots, grew well at 39.0 degrees, formed large plaques in Vero cell cultures and showed markedly greater virulence to chick embryos and mice than the Variola strains [6,7,69,70].

ARE THERE DRUGS EFFECTIVE AGAINST MPVX IN HUMANS?

Tecovirimat (ST-246) is a drug first reported in 2005. It is a low molecular weight compound with potent activity against multiple Orthopoxviruses, including smallpox, vaccinia, MPVX, camelpox, cowpox and mousepox viruses. It acts against the Orthopoxvirus V061 gene that encodes an important envelope protein (p37) required for extracellular virus production. In cell culture. ST-246 inhibited plaque formation and virus-induced cytopathic effects [71-76). Oral administration of ST-246 protected BALB/c mice from lethal infection following intranasal inoculation of the vaccinia virus strain. ST-246-treated mice that survived infection acquired protective immunity and were resistant to subsequent challenge with a new lethal dose (10x LD(50)) of vaccinia virus [71,76].

Tecovirimat is an antiviral drug tested in several animal species in which it has demonstrated efficacy against Orthopoxvirus infections. The drug has undergone clinical trials in non-human primates and human volunteers demonstrating good tolerance for up to 14 days of oral administration [77-80]. Also in the treatment of cases of bovine smallpox in accidentally infected or vaccinated immunodeficient patients [81, 82]. A British patient who received the drug in 2021 experienced very short duration of symptoms and viral excretion from the respiratory tract [83]

The approval of tecovirimat to treat smallpox represents a major milestone in biosafety preparedness. Incorporation of the drug into the CDC smallpox response plan, development of pediatric liquid and intravenous formulations, and approval for post-exposure prophylaxis would be an additional health security benefit. Although currently stockpiled by the U.S. Strategic National Stockpile, use of ST-246 may be administered under special circumstances (IND) [84-90].

Tecovirimat's efficacy is maintained even when administration is delayed a few days after inoculation in animal models of Poxvirus infection [73,75]. Its activity is synergistic with other drugs such as cidofovir or CMX001 [74].

No data are available on the efficacy of cidofovir and brincidofovir in the treatment of human cases of MPVX. However, both have demonstrated activity against poxviruses in in vitro and animal studies [91,92].

WHAT VACCINES ARE AVAILABLE AGAINST THIS DISEASE?

The first vaccines, without even knowing the viral nature of smallpox, were made from the material of bovine smallpox pustules. Subsequently, the vaccine virus replaced attenuated strains of smallpox for mass immunization of

populations prior to the eradication of smallpox. It was administered by scarification with a bifurcated needle, inducing a suffusion in the skin on which a papule appeared between the following two and five days, evolving into a vesicle and pustule from the eighth to the tenth day. The vaccinal pustule reached up to 1 cm in diameter, which finally dried and left a scab, which after falling off, between the 14th and 21st day, left a scar. The development of regional adenopathy was frequent.

The efficacy of these vaccines against smallpox is estimated to be complete in the first years, very important in the following twenty years and with protection against severe disease, of longer duration, probably for life.

These vaccines, however, had their complications. One of them was the local extension of the vaccine inoculation lesion to a necrotizing or gangrenous lesion, sometimes with little inflammatory component, with high mortality, and which has been described even in immunocompetent patients. Another more frequent complication (4.6 cases per million vaccinees) was the so-called Eczema Vaccinatum, or extension by inoculation on atopic skin or skin with other skin diseases, of the vaccinee himself or of accidental contacts. As in the previous complication, it was treated with hyperimmune serum.

The generalized extension of the vaccine lesion was another complication, difficult to justify. It was usually self-limited and generally did not require treatment and its incidence was estimated in large vaccination series at 242 cases per million vaccinated. Finally, encephalomyelitis could appear between day 11 to 15 of the first vaccination and was not described in the revaccinations. Its incidence was between 2.9 to 12.3 cases per million vaccinated. Focal lesions with aphasia or hemiplegia presenting closer to vaccination could occur in children under two years of age.

A vaccine produced with an attenuated, non-replicating strain approved for Smallpox and Monkeypox (AVA/ANKARA) could be considered in the immunocompromised and is licensed for use in emergency situations. It has different names in different regions (Invanex; Jynneos; Imvamune). It was approved by the EMA in 2013 for the prevention of human smallpox in adults aged 18 years and older (data sheet updated in April 2022 in Spanish). In the U.S., it received approval for the prevention of human and monkeypox in 2019.

The vast majority of H-MPVX, both in Africa and worldwide, have occurred in people who were not vaccinated against human smallpox [4,34,93-102]. Furthermore, in a study of confirmed and suspected cases of monkeypox in Central Africa, the disease attack rate was much lower in subjects with variola vaccination than among unvaccinated subjects (0.95/1000 versus 3.6/1000) [103].

The smallpox vaccine has so far not been available to the general public and was part of a strategic stockpile.

WHAT SHOULD BE THE PREVENTION MEASURES IN CONTACTS OF PATIENTS WITH H-MPVX?

In any case of H-MPVX under investigation or confirmed, the search for and identification of close contacts will be initiated both among healthcare personnel and among work or social cohabitants. The search for contacts will be interrupted if the case is ruled out after laboratory results.

Contacts of cases will be classified as close, direct or low-risk contacts.

Close contact (less than 1 meter in the same room is defined as contact with an investigational or confirmed case of monkeypox virus in its infectious period, without PPE (or with incidences in its use). Cohabitants, contacts at work, social activities and health personnel who have cared for the patient should be assessed.

Direct contact is defined as contact with clothing, bedding or fomites used by an investigational or confirmed case of monkeypox virus during the infectious period, without the appropriate PPE (or with incidences in its use).

Low-risk contacts are those that do not meet the above criteria.

All contacts will be informed of the symptoms of monkeypox and will be instructed to self-monitor their temperature twice daily for 21 days after exposure. Close contacts will not be quarantined, but should exercise extreme caution and reduce social interactions as much as possible by wearing a facemask at all times.

The responsible person/institution will contact high-risk contacts at least once daily to record temperature and inquire about the presence of any symptoms related to the disease. Contacts should be reachable throughout the follow-up period.

In any of the cases, if any of the contacts presents fever or any other symptom compatible with the clinical signs of the disease, they should immediately self-isolate at home, and urgently contact the person in charge of the follow-up. In this case, the contact will be considered as a case under investigation until laboratory results are available.

The recommended environmental control measures are as follows:

Bed linens, towels, etc., should be washed in a standard washing machine with hot water (60 degrees) and detergent. Bleach may be added, but is not necessary. Care should be taken when handling soiled linen to avoid direct contact with contaminated material. Soiled linen should not be shaken or handled in a manner that could disperse infectious particles.

Dishes and other eating utensils should not be shared with those of cases. Dirty dishes and eating utensils should be washed in a dishwasher or by hand with soap and hot water.

Contaminated surfaces and objects should be cleaned and disinfected with a hospital-grade disinfectant or a 1:100 dilution of household sodium hypochlorite (bleach) [104,105].

WHAT IS THE PROGNOSIS OF MONKEYPOX IN HUMANS?

The case fatality rate of monkeypox has ranged from 0 to 11% in the general population of African countries, and is highest among young children. In addition, persons younger than 40 or 50 years of age (depending on the country may be more susceptible to monkeypox as a result of the end of routine smallpox vaccination worldwide following the eradication of smallpox.

The clade currently circulating in Spain, in adult patients, is associated with very low mortality [93].

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest

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