

Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Announcement of the Coronavirus Study Group

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IDENTIFICATION OF A NOVEL CORONAVIRUS AS A CAUSE OF SEVERE RESPIRATORY DISEASE

During the summer of 2012, in Jeddah, Saudi Arabia, a hitherto unknown coronavirus (CoV) was isolated from the sputum of a patient with acute pneumonia and renal failure (1, 2). The isolate was provisionally called human coronavirus Erasmus Medical Center (EMC) (3). Shortly thereafter, in September 2012, the same type of virus, named human coronavirus England 1, was recovered from a patient with severe respiratory illness who had been transferred from the Gulf region of the Middle East to London, United Kingdom (4) (GenBank accession no. [KC164505.2](https://www.ncbi.nlm.nih.gov/nuclot/KC164505.2)). The onset of the new disease was traced back to an even earlier time point. Already in April 2012, a cluster of pneumonia cases in health care workers had occurred in an intensive care unit of a hospital in Zarqa, Jordan (5). Two persons died, both of whom were confirmed to have been infected with the novel coronavirus through a retrospective analysis of stored samples (6). These findings met with considerable concern. Although the number of laboratory-confirmed cases is limited (34 as of 12 May 2013), the morbidity and mortality of the infection is alarming, as is its uncanny resemblance—at least in its clinical features—to severe acute respiratory syndrome (SARS). While in a small minority of the known cases the patients developed mild disease, most patients presented with a severe acute respiratory condition requiring hospitalization; the mortality rate is approximately 60% (7).

The infection appears to be geographically linked—at least for now—to the Middle East, with cases originating from Jordan ($n = 2$), Saudi Arabia ($n = 25$), Qatar ($n = 2$), and the United Arab Emirates ($n = 2$). Of the three patients known to have contracted the virus outside the Middle East, two became infected in the United Kingdom through contact exposure to an index patient, shortly after the latter returned from a visit to Pakistan and Saudi Arabia (8). Very recently in France, a tourist returning from the United Arab Emirates fell ill and transmitted the infection to at least one other person, with whom he had shared a hospital room (7). Full-length genome sequences determined for three independent virus isolates from Saudi Arabia (3) (GenBank accession no. [JX869059.2](https://www.ncbi.nlm.nih.gov/nuclot/JX869059.2)), Jordan (GenBank accession no. [KC776174.1](https://www.ncbi.nlm.nih.gov/nuclot/KC776174.1)), and the United Kingdom (9) (GenBank accession no. [KC164505.2](https://www.ncbi.nlm.nih.gov/nuclot/KC164505.2)) revealed more than 99% sequence identity (~100 nucleotide vari-

ations in a 30.1-kb genome), indicating that these viruses diverged from a common ancestor very recently.

PHYLOGENY AND EPIDEMIOLOGY

Within the subfamily *Coronavirinae* (10), the novel virus is a representative of a new, yet-to-be-established species in lineage C of the genus *Betacoronavirus*, which currently includes the species *Tylonycteris bat coronavirus HKU4* and *Pipistrellus bat coronavirus HKU5* (Fig. 1) (3). The novel coronavirus seems most closely related to as-yet-unclassified viruses from insectivorous European and African bats in the *Vespertilionidae* and *Nycteridae* families, respectively (3, 9, 11–13). Of note, for the latter viruses, only partial genome sequences are available. The scarce epidemiological data available suggest that the infection is primarily zoonotic in nature, with limited human-to-human transmission. From what we already know of coronavirus biology (14) and from the accumulating evidence for this particular virus (3, 9, 13), bats appear to be the natural host, and it would be tempting to assume that these animals are also the immediate source. However, this idea is difficult to reconcile with the fact that most patients were unlikely to have been exposed directly to bats, or with the close genetic relationship between the human isolates, indicative of a recent bottleneck. A more likely scenario is that a single variant from a spectrum of related betacoronaviruses in bats successfully crossed over to and rapidly established itself in (an) intermediate animal host species (at least in the Middle East), with subsequent incidental spillover into the human population. Such spillover events would be facilitated through frequent intermediate host-human interactions and perhaps through viral adaptations acquired during the initial species jump. Although at present there is no evidence for sustained community transmission, the obvious concern is that

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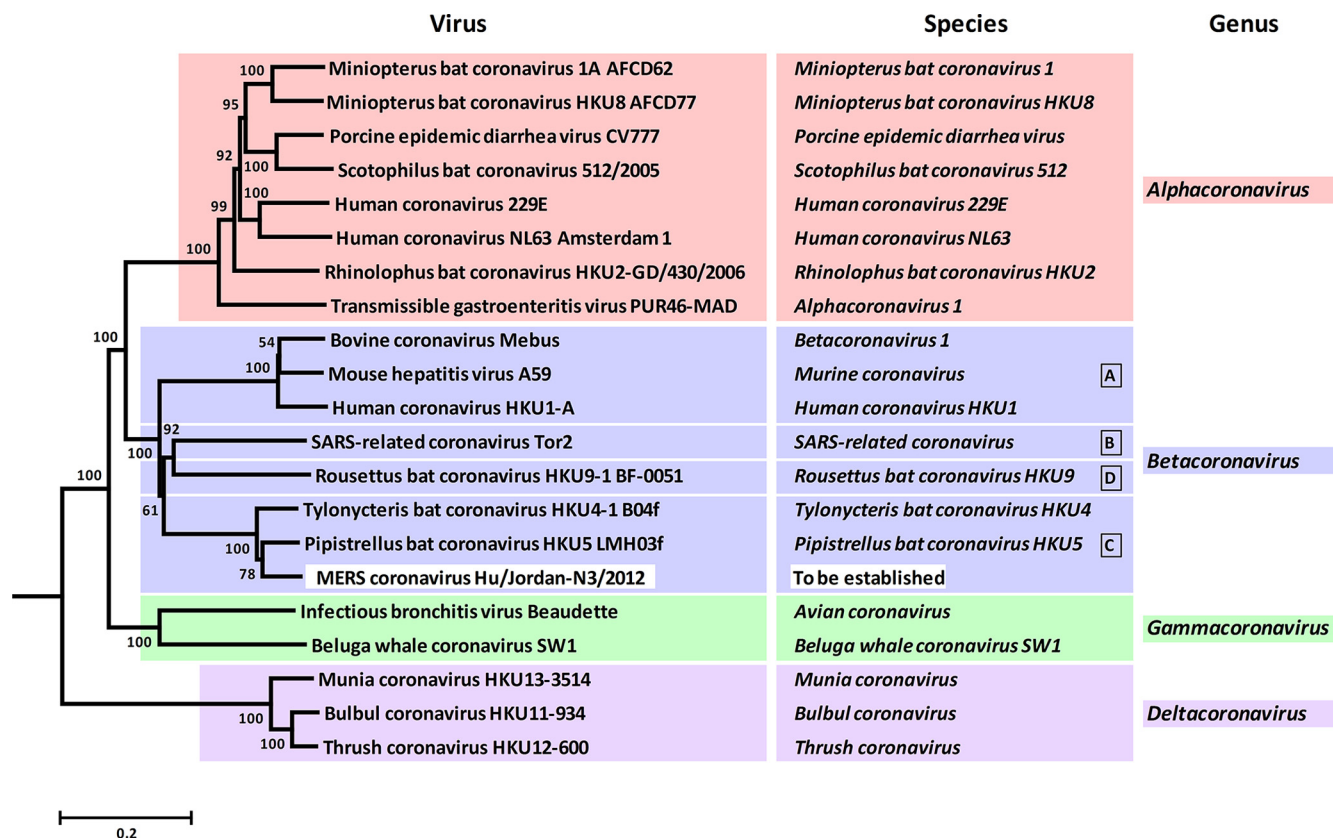


FIG 1 Phylogenetic relationships among members of the subfamily *Coronavirinae* and taxonomic position of MERS-CoV. A rooted neighbor-joining tree was generated from amino acid sequence alignments of *Coronaviridae*-wide conserved domains in replicase polyprotein 1ab (ADRP, nsp3; M^{pro}, nsp5; RdRP, nsp12; Hel, nsp13; ExoN, nsp14; NendoU, nsp15; O-MT, nsp16) for MERS-CoV strain Hu/Jordan-N3/2012 (GenBank accession no. [KC776174.1](http://www.ncbi.nlm.nih.gov/nuccore/KC776174.1)) and for 20 other coronaviruses, each a representative of a currently recognized coronavirus species (10); equine torovirus Berne served as the outgroup. Virus names are given with strain specifications; species and genus names are in italics as per convention. The tree shows the four main monophyletic clusters, corresponding to genera *Alpha*-, *Beta*-, *Gamma*-, and *Deltacoronavirus* (color coded) and the position of MERS-CoV. Also indicated are betacoronavirus lineages A through D (corresponding to former CoV subgroups 2A through D). Bootstrap values (1,000 replicates) are indicated at branch points. The tree is drawn to scale (scale bar, 0.2 amino acid substitutions per site).

the virus may take the next step and adapt to efficient human-to-human transmission.

CONSENSUS NAME: MERS-CoV

Since the initial discovery, isolates of the virus have been described in the scientific literature, databases, and popular press under various names (e.g., human betacoronavirus 2c EMC, human betacoronavirus 2c England-Qatar, human betacoronavirus 2C Jordan-N3, betacoronavirus England 1) with novel coronavirus (NCoV) as the one used most often. As this lack of uniformity in virus nomenclature complicates communication both in the research field and with health care authorities, governments, and the general public, the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses (<http://ictvonline.org/index.asp?bhcp=1>) took the lead to address this issue. After careful consideration and broad consultation, the CSG has decided to call the new coronavirus Middle East respiratory syndrome coronavirus (MERS-CoV). This name is endorsed by the discoverers of the virus and other researchers that pioneered MERS-CoV studies, by the World Health Organization, and by the Saudi Ministry of Health. We strongly recommend the use of this name in scientific and other communications. New MERS-

CoV isolates or variants detected by reverse transcription (RT)-PCR may be provided with an affix, analogous to convention in influenza virus nomenclature (the host/country of origin plus the strain identification number/year; e.g., MERS-CoV Hu/Jordan-N3/2012). As our knowledge of the epidemiology and host preference of this virus is still incomplete, it seems prudent to refrain from labeling MERS-CoV a human coronavirus, at least for the time being.

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REFERENCES

- Zaki A. 2012. Novel coronavirus—Saudi Arabia: human isolate. *Int. Soc. Infect. Dis. ProMED-mail*. <http://www.promedmail.org/direct.php?id=20120920.1302733>.
- Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. 2012. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N. Engl. J. Med.* 367:1814–1820.
- van Boheemen S, de Graaf M, Lauber C, Bestebroer TM, Raj VS, Zaki AM, Osterhaus AD, Haagmans BL, Gorbalenya AE, Snijder EJ,

- Fouchier RA. 2012. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. *mBio*. 3:e00473. doi:10.1128/mBio.00473-12.
4. Bermingham A, Chand MA, Brown CS, Aarons E, Tong C, Langrish C, Hoschler K, Brown K, Galiano M, Myers R, Pebody RG, Green HK, Boddington NL, Gopal R, Price N, Newsholme W, Drosten C, Fouchier RA, Zambon M. 2012. Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012. *Euro Surveill*. 17:20290. <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20290>.
 5. European Centre for Disease Prevention and Control (ECDC). 2012. Communicable Disease Threats Report, Week 18, 29 April–5 May 2012, p 2. Severe respiratory disease of unknown origin—Jordan—outbreak in ICU. <http://www.ecdc.europa.eu/en/publications/Publications/CDTR%20online%20version%204%20May%202012.pdf>.
 6. World Health Organization. 2012. Global Alert and Response (GAR). Background and summary of novel coronavirus infection—as of 21 December 2012. http://www.who.int/csr/disease/coronavirus_infections/update_20121221/en/index.html.
 7. World Health Organization. Global Alert and Response (GAR). Coronavirus infections. http://www.who.int/csr/disease/coronavirus_infections/en/.
 8. Health Protection Agency (HPA) UK Novel Coronavirus Investigation team. 2013. Evidence of person-to-person transmission within a family cluster of novel coronavirus infections, United Kingdom, February 2013. *Euro Surveill*. 18:20427. <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20427>.
 9. Cotten ML, Lam TT, Watson SJ, Palser AL, Petrova V, Grant P, Pybus OG, Rambaut A, Guan Y, Pillay D, Kellam P, Nastouli E. 2013. Full-genome deep sequencing and phylogenetic analysis of novel human betacoronavirus. *Emerg. Infect. Dis*. 19:736–742.
 10. de Groot RJ, Baker SC, Baric R, Enjuanes L, Gorbalenya AE, Holmes KV, Perlman S, Poon L, Rottier PJM, Talbot PJ, Woo PCY, Ziebuhr J. 2012. Family *Coronaviridae*, p 806–828. In King A, Adams M, Cartens E, Lefkowitz E (ed), *Virus taxonomy: ninth report of the International Committee on Taxonomy of Viruses*. Academic Press, San Diego, CA.
 11. Reusken CB, Lina PH, Pielaat A, de Vries A, Dam-Deisz C, Adema J, Drexler JF, Drosten C, Kooi EA. 2010. Circulation of group 2 coronaviruses in a bat species common to urban areas in Western Europe. *Vector Borne Zoonotic Dis*. 10:785–791.
 12. Falcón A, Vázquez-Morón S, Casas I, Aznar C, Ruiz G, Pozo F, Perez-Breña P, Juste J, Ibáñez C, Garin I, Aihartza J, Echevarría JE. 2011. Detection of alpha and betacoronaviruses in multiple Iberian bat species. *Arch. Virol*. 156:1883–1890.
 13. Annan A, Baldwin HJ, Corman VM, Klose SM, Owusu M, Nkrumah EE, Badu EK, Anti P, Agbenyega O, Meyer B, Oppong S, Sarkodie YA, Kalko EK, Lina PH, Godlevska EV, Reusken C, Seebens A, Gloza-Rausch F, Vallo P, Tschapka M, Drosten C, Drexler JF. 2013. Human betacoronavirus 2c EMC/2012-related viruses in bats, Ghana and Europe. *Emerg. Infect. Dis*. 19:456–459.
 14. Woo PC, Lau SK, Huang Y, Yuen KY. 2009. Coronavirus diversity, phylogeny and interspecies jumping. *Exp. Biol. Med*. 234:1117–1127.